Circulation

AHA SCIENTIFIC STATEMENT

Cardiopulmonary Resuscitation in Infants and Children With Cardiac Disease

A Scientific Statement From the American Heart Association

ABSTRACT: Cardiac arrest occurs at a higher rate in children with heart disease than in healthy children. Pediatric basic life support and advanced life support guidelines focus on delivering high-quality resuscitation in children with normal hearts. The complexity and variability in pediatric heart disease pose unique challenges during resuscitation. A writing group appointed by the American Heart Association reviewed the literature addressing resuscitation in children with heart disease. MEDLINE and Google Scholar databases were searched from 1966 to 2015, cross-referencing pediatric heart disease with pertinent resuscitation search terms. The American College of Cardiology/American Heart Association classification of recommendations and levels of evidence for practice guidelines were used. The recommendations in this statement concur with the critical components of the 2015 American Heart Association pediatric basic life support and pediatric advanced life support guidelines and are meant to serve as a resuscitation supplement. This statement is meant for caregivers of children with heart disease in the prehospital and in-hospital settings. Understanding the anatomy and physiology of the high-risk pediatric cardiac population will promote early recognition and treatment of decompensation to prevent cardiac arrest, increase survival from cardiac arrest by providing high-quality resuscitations, and improve outcomes with postresuscitation care.

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Key Words: AHA Scientific Statements ■ arrhythmias ■ cardiopulmonary arrest ■ cardiopulmonary resuscitation ■ cardiopulmonary resuscitation/methods ■ extracorporeal membrane oxygenation ■ heart defects, congenital ■ heart defects, congenital/surgery

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The American Heart Association (AHA) has published guidelines for pediatric basic life support since 1980[1] and for pediatric advanced life support (PALS) since 1986.[2] These guidelines have been based on research involving both animals and infants, children, and adult human subjects and provide recommendations for resuscitation of infants and children with structurally normal hearts. The most recent guidelines update, published in 2015,[3,4] focused on the quality of cardiopulmonary resuscitation (CPR), with an emphasis on minimizing interruptions in chest compressions, providing adequate rate and depth of compressions, and avoiding excessive ventilation.[3–5] Although this emphasis is also recommended in infants and children with heart disease, there are additional important considerations. This scientific statement is important for 3 reasons specific to this unique population: (1) The frequency of cardiac arrest is higher in infants and children with congenital heart disease (CHD), and the pathogenesis of these events can differ from infants and children without heart disease; (2) congenital heart defects have a wide variety of hemodynamic and physiological influences on cardiac output, and the specific cardiorespiratory interactions and response to resuscitation can be quite variable; and (3) the response of the neonate and the postoperative patient with complex CHD to pharmacological intervention can differ from the response of infants and children without heart disease.

There is a wide spectrum of cardiac disease in infants and children. Cardiac disease in infants and children is primarily congenital but can be acquired. In many circumstances, the heart defects are surgically corrected or palliated, but blood flow pathways are not normal. Patients can carry the burden of residual lesions or develop new problems over time, with an increased risk of cardiac arrest. This population commonly develops myocardial dysfunction, arrhythmia, and unbalanced pulmonary and systemic circulation. Specific drugs and the indications for administration and dosing can differ for infants and children with heart disease. In addition, there are many variations of CHD, and the underlying physiological substrates can have a significant impact on systemic perfusion and pulmonary blood flow (PBF). An example unique to the spectrum of CHD is the patient with a single ventricle. These patients typically undergo a series of surgical procedures culminating in a unique functional palliation, the modified Fontan operation, in which the systemic venous return is connected directly to the pulmonary circulation and there is no pulmonary ventricle.

The anatomic and physiological substrates of congenital heart defects can limit the effectiveness of conventional CPR. At best, CPR is inefficient, with compressions providing only ≈10% to 30% of normal blood flow to the heart and 30% to 40% of normal blood flow to the brain.[6] The inherent inefficiency associated with CPR can be further exacerbated in the patient with CHD, in which the underlying anatomy limits effective PBF, systemic blood flow (SBF), and cerebral perfusion. Given these issues, survival after cardiac arrest can be low in infants and children with cardiac disease. To improve resuscitation outcomes, a strong emphasis must be placed on the prearrest phase to prevent cardiac arrest and on the arrest phase to provide high-quality CPR. Use of extracorporeal life support (ECLS) to support failed conventional CPR (ie, extracorporeal cardiopulmonary resuscitation [ECPR]) in highly specialized environments has allowed the resuscitation of some patients who would otherwise have died and could be particularly useful for patients in whom the conditions causing arrest are thought to be potentially reversible (eg, after cardiac surgery) or could be used as a bridge to other therapy, such as heart transplantation.[7,8]

The purpose of this consensus statement is to highlight the unique aspects of cardiac resuscitation in children with congenital and acquired heart disease and to provide evidence-based recommendations for modifying resuscitation for this high-risk patient population to improve survival. The management of specific phases of cardiac arrest (prearrest, arrest, and postarrest stabilization) is examined, along with gaps in knowledge that highlight future directions for research relevant to the pediatric cardiac population.

The contributors to this scientific statement were selected on the basis of their expertise in disciplines related to the management of children with congenital and acquired heart disease. The writing group for this statement was selected and organized according to the conflict-of-interest management policy of the AHA.

The writing group performed MEDLINE database searches of English-language articles from 1966 to 2015, cross-referencing congenital and acquired heart disease with pertinent MESH search terms, as follows: *acute cardiac tamponade; acute kidney injury; adolescent; adult; amiodarone; aortic valve insufficiency/surgery; aortic valve stenosis/congenital; aortic valve stenosis/surgery; aortic valve stenosis/therapy; arrhythmias, cardiac; atropine; bicarbonates; biomarkers; calcium; cardiac arrest; cardiac catheterization; cardiac output, low; cardiac surgical procedures; cardiac tamponade; cardiac tamponade/surgery; cardiopulmonary arrest; cardiopulmonary resuscitation; cardiopulmonary resuscitation/statistics and numerical data; cardiopulmonary resuscitation/methods; catheterization, central venous; catheterization, peripheral; child; clinical alarms; death, sudden, cardiac; diagnosis; echocardiography; echocardiography/methods; echocardiography/mortality; echocardiography/utilization; electrocardiogram; epinephrine; extracorporeal membrane oxygenation; ethics; Fontan procedure; heart arrest; heart arrest/etiology; heart arrest/prevention and control; heart arrest/surgery; heart arrest/therapy; heart defects, con-*

genital; heart defects, congenital/classification; heart defects, congenital/complications; heart defects, congenital/diagnosis; heart defects, congenital/etiology; heart defects, congenital/genetics; heart defects, congenital/mortality; heart defects, congenital/pathology; heart defects, congenital/physiology; heart defects, congenital/physiopathology; heart defects, congenital/prevention and control; heart defects, congenital/surgery; heart defects, congenital/therapy; heart diseases; heart failure; hospital rapid response team; hospitals, pediatric; hypertension, pulmonary; hyperthermia; hypothermia; hypoplastic left heart syndrome; infant, newborn; infusions, intraosseous; intensive care units, neonatal; intensive care units, pediatrics; ischemia; isoproterenol; kidney injury; kidney; lidocaine; medical response team; mitral valve insufficiency/surgery; natriuretic peptide, brain; neonatology; nitric oxide; Norwood procedures; out-of-hospital cardiac arrest; patient transfer; pediatric early warning system; pediatrics; pericardial effusion; pericardial tamponade; pericardiocentesis; pericardiectomy; pharmaceutical preparations; phenylephrine; pneumothorax; postpericardiotomy syndrome; pulsus paradoxus; quality; quality improvement; quality of life; radiography, thoracic; resuscitation; resuscitation orders; scimitar syndrome/surgery; signs and symptoms; sodium bicarbonate; spectroscopy, near-infrared; sudden death; therapy; transportation of patients; treatment; treatment outcome; vasopressin; ventricular dysfunction, left; ventricular dysfunction, right.

The reference lists of identified articles were also searched. Published abstracts from major pediatric scientific meetings in 2014 and 2015 were also reviewed. Classification of recommendations and levels of evidence were assigned to each recommendation using the 2009 American College of Cardiology/AHA guidelines grading schema (Table 1).[9] This classification system combines an objective description of the types of published studies supporting each recommendation and the strength of expert consensus. Statements generated from literature review were drafted by each section's writing group and presented to the entire writing group for editing and ultimate incorporation into this document.

CURRENT EPIDEMIOLOGY AND SURVIVAL

It is estimated that 16 000 children in the United States experience an out-of-hospital cardiac arrest each year.[10] An estimated 5800 experience an in-hospital cardiac arrest each year.[11,12] Hospitalized children with cardiovascular disease are at increased risk for cardiac arrest.[13] Cardiac arrest requiring resuscitation occurs in ≈7 per 1000 hospitalizations of children with cardiovascular disease, a rate >10-fold higher than that observed in children hospitalized without cardiovascular disease.[13] The frequency of cardiac arrest is also reported to be higher in dedicated cardiac intensive care units (ICUs) (4% to 6% of admissions) than in medical-surgical pediatric ICUs (2% to 4% of admissions).[3,4,14–16]

Since 2005, there have been substantial efforts to improve the quality of all CPR, including that provided to children.[6,15,16] On the basis of data from the AHA's Get With The Guidelines–Resuscitation Registry (GWTG-R), formerly the AHA National Registry of Cardiopulmonary Resuscitation, the risk-adjusted rates of survival in children with an in-hospital cardiac arrest have improved nearly 3-fold over a decade (from 14.3% to 43.4% over the period 2000 to 2009).[17] In that same registry, survival to hospital discharge of pediatric surgical cardiac patients was higher (37%) than that reported for pediatric medical cardiac (28%) or noncardiac (23%) patients.[5] In the Kids' In-hospital Database (KIDS), survival after cardiac arrest was also higher among pediatric surgical cardiac patients (52%) than among pediatric medical cardiac patients (43%)[13]; however, children with single-ventricle disease had a lower survival rate (35%) than did children with other forms of cardiovascular disease (45%).[13] Possible explanations for the differences in survival relate to the specific causes of arrest, the availability of specialized invasive monitoring, and access to interventions and management subsequent to the arrest.

MANAGEMENT OF THE CRITICAL PATIENT WITH CONGENITAL OR ACQUIRED HEART DISEASE

The purpose of this section of the statement is to highlight anatomic and physiological aspects of specific high-risk cardiac lesions or cardiac diseases that impact prearrest stabilization and resuscitation. Each section on a specific cardiac lesion is concluded with a section on unique challenges in CPR and gaps in knowledge.

Single-Ventricle Lesions

Surgical and Resuscitation Overview

Children with single-ventricle CHD typically undergo a series of staged operations. The aim of the first palliative procedure, typically performed during the neonatal period, is to create unobstructed systemic blood flow, create an effective atrial communication to allow for atrial level mixing, and to regulate PBF to prevent overcirculation and decrease the volume load on the systemic ventricle prior to future staged procedures. For patients with hypoplastic left heart syndrome (HLHS), the stage 1 Norwood palliation typically involves 3 key steps: (1) reconstruction of the aorta and systemic outflow; (2)

Table 1. Applying Classification of Recommendations and Level of Evidence

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	SIZE OF TREATMENT EFFECT: CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *No Benefit* or CLASS III *Harm* Procedure/Test / Treatment COR III: No benefit — Not Helpful / No Proven Benefit COR III: Harm — Excess Cost w/o Benefit or Harmful / Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit: is not recommended; is not indicated; should not be performed/ administered/ other; is not useful/ beneficial/ effective COR III: Harm: potentially harmful; causes harm; associated with excess morbidity/mortality; should not be performed/ administered/ other
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations such as sex, age, history of diabetes mellitus, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

atrial septectomy to ensure removal of any restriction to pulmonary venous return; and (3) creation of a source of PBF via either a systemic-to-pulmonary shunt (modified Blalock-Taussig shunt [MBTS]) or a right ventricle (RV)–to–pulmonary artery shunt (RVPAS). Depending on patient and anatomic characteristics, other options to regulate PBF might include placement of a pulmonary artery band across the main pulmonary artery or bilateral pulmonary bands to limit PBF, placement of a systemic-to–pulmonary artery shunt, and placement of a stent across the ductus arteriosus.

During the second stage of palliation, a bidirectional Glenn procedure or hemi-Fontan operation is performed to create a superior cavopulmonary anastomosis (CPA). The superior CPA is typically performed at 3 to 6 months of age and involves the anastomosis of the superior vena cava (SVC) to the pulmonary artery. After creation of the superior CPA, PBF is dependent on the SVC flow, the transpulmonary pressure gradient, and vascular resistance within arterial vascular beds (both cerebral and pulmonary). The third palliative operation, known as the modified Fontan procedure, is typically performed at 2 to 4 years of age. After Fontan completion, all systemic venous return is baffled directly to the pulmonary circulation, and the single (systemic) ventricle preload is dependent on passive flow across

the pulmonary vascular bed without the benefit of a pulmonary ventricle.

Specific anatomy and cardiopulmonary interactions have a significant impact on resuscitation of the child with single-ventricle anatomy. Table 2 delineates various resuscitation profiles for the structurally normal heart and the unique single-ventricle palliated states. The circulation is described, and the impact of chest compressions, chest recoil, and positive-pressure ventilation is discussed.

Single-Ventricle Palliation: Perioperative Management

Risk Factors for Cardiac Arrest and Death

The following factors have been identified as contributing to early death in the neonate or infant with single ventricle: (1) anatomic diagnosis of HLHS, total anomalous pulmonary venous connection (TAPVC), and pulmonary atresia with intact ventricular septum with RV-dependent coronary circulation; (2) decreased ventricular function; (3) hemodynamically significant semilunar or atrioventricular valve insufficiency; and (4) comorbidities including prematurity and genetic syndrome.[18–21]

Neonates with single-ventricle physiology have an increased risk of cardiac arrest as the result of (1) increased myocardial work as a consequence of volume overload, (2) imbalances in relative systemic and PBF, and (3) potential shunt occlusion.[3,4,22–24] The risk of cardiac arrest remains high until the superior CPA is created.[25–27] For patients with HLHS, the frequency of in-hospital cardiac arrest after stage 1 Norwood palliation is lower after placement of an RVPAS than after creation of an MBTS,[26–29] although interestingly, there is no difference in hospital mortality relative to shunt type.[20,29,30]

The risk of death between hospital discharge from the stage 1 Norwood palliation and the second-stage superior CPA (ie, interstage mortality) is also lower if an RVPAS is placed rather than an MBTS.[20,26,31] The Single Ventricle Reconstruction Trial reported a 12-month 31% incidence of death or transplantation after stage 1 Norwood for HLHS,[26] with most serious adverse events occurring between 30 days after the stage 1 palliation and the time of the superior CPA procedure. As a result, the interstage period before the superior CPA can be characterized as a prearrest state that requires active monitoring and intervention to improve survival.[23]

Assessment of Systemic Oxygen Balance

Organ dysfunction, reversible and irreversible injury, and mortality can occur secondary to reduced systemic oxygen delivery (Do_2). Abnormalities in systemic oxygen balance can be detected through monitoring of the systemic venous oxygen saturation (Svo_2) and the arteriovenous oxygen content or saturation difference (AVo_2D).[32] Monitoring devices to detect low systemic Do_2 and guide intervention can be invasive, such as indwelling SVC oximetric catheters,[19,33–35] or noninvasive multisite near-infrared spectroscopy (NIRS).[36–43] With arterial pulse oximetry and quasi-mixed venous NIRS, continuous, noninvasive measurement of the dynamic ratio of PBF to SBF (Qp:Qs) can be estimated, cardiac output can be estimated, and interventions can be targeted. These measurements can be confirmed periodically with measured systemic arterial O_2 saturation and an Svo_2 sample from the SVC[18,33,34] or (less preferably) the inferior vena cava (IVC).[44] Although O_2 saturation in the IVC has been correlated with adverse events in the postoperative pe-

Table 2. Resuscitation Profiles for the Structurally Normal Heart and Those That Have Undergone Single-Ventricle Palliation

Physiology	Circulation Description	Circulation of Blood	Chest Compressions	Chest Recoil	Positive-Pressure Ventilation
Structurally normal heart	Two-ventricle series circulation without heart disease	Systemic veins – lungs – pulmonary veins – body	1. RV compression results in PBF 2. LV compression results in SBF	Increases the transthoracic gradient from the systemic veins to the RA, increasing RV filling	Decreases the transthoracic gradient from the systemic veins to the RA, decreasing RV filling
Stage 1 Norwood or shunted physiology	Single-ventricle parallel circulation with shunt-dependent PBF	Systemic veins – single ventricle – lungs (via shunt) or body	Single-ventricle compression results in PBF (shunt ± PVR) and SBF (SVR)	Increases filling to the preload-dependent single ventricle	Decreases filling to the preload-dependent single ventricle
Bidirectional Glenn and hemi-Fontan	Single-ventricle parallel circulation with PBF dependent on multiple arteriolar vascular beds	IVC – single ventricle – body/brain – SVC – lungs – pulmonary veins – body	Single-ventricle compression results in SBF	1. Predominantly fills the RA from the IVC 2. SVC flow dependent on cerebral vascular resistance and PVR	Decreases filling to the single ventricle by impeding SVC flow and IVC filling
Fontan	Single-ventricle series circulation	Systemic veins – lungs – pulmonary veins – body	Single-ventricle compression results in SBF	1. Predominantly fills the PAs with IVC blood flow (PVR) 2. SVC flow dependent on cerebral vascular resistance and PVR	Decreases filling to the single ventricle by impeding both SVC and IVC flow

IVC indicates inferior vena cava; LV, left ventricle; PA, pulmonary artery; PBF, pulmonary blood flow; PVR, pulmonary vascular resistance; RA, right atrium; RV, right ventricle; SBF, systemic blood flow; SVC, superior vena cava; and SVR, systemic vascular resistance.

riod after stage 1 Norwood,[44] O_2 saturation in the SVC is thought to be a better surrogate for the true mixed Svo_2.

In patients with obligate left-to-right atrial shunting, blood sampled from the systemic atrium can have a saturation that is very close to the systemic arterial saturation, so the SVC saturation is most representative of systemic Svo_2. Given that pulmonary venous saturation is not typically measured, the calculation of Qp:Qs based on the arterial and Svo_2 saturation from the SVC requires an assumption of the pulmonary venous O_2 saturation. If there is concurrent pulmonary venous desaturation from intrapulmonary shunt or low supplementary O_2, there will be an overestimation of the pulmonary venous O_2 saturation and underestimation of the Qp:Qs.[45] Notwithstanding the issues related to an assumed pulmonary venous O_2 saturation, the use of systemic arterial O_2 saturation and Svo_2 to guide acute pharmacological interventions during high-risk periods is associated with improved outcomes.[19,35,46–48]

NIRS provides a noninvasive measurement of regional oxygen economy (ie, balance between Do_2 and consumption). NIRS monitoring is suitable for longer-term use or during periods of possible hemodynamic instability (eg, agitation, fever, intercurrent illness, infection, dehydration, new or worsening ventricular dysfunction, new or worsening moderate or greater neoaortic insufficiency or atrioventricular valve regurgitation) to help quantify and trend early acute hemodynamic instability and to monitor response to therapy, ideally avoiding deterioration and cardiac arrest.[33,35,49]

Although both Svo_2 and NIRS monitoring fulfill criteria for potential goal-directed measures in high-risk patient populations, there is variation in their application.[23,43,50–52] Because disorders that start with low cardiac output, high Qp:Qs, or low Qp:Qs will ultimately result in inadequate Do_2, the antecedent cause of arrest might not be obvious once arrest has ensued. Physiological information from the prearrest state is useful for diagnosing pathogenesis and reversible causes of arrest and can guide resuscitation in the arrest and postarrest states.

Pathogenesis, Recognition, and Treatment of Hemodynamic Compromise

Assessment of Cardiac Output. Inadequate acute and chronic systemic Do_2 results in organ dysfunction, ischemic injury, or both. To achieve normal Do_2 in the presence of parallel pulmonary and systemic circulations, the single ventricle needs to produce at least twice normal cardiac output, and as a result, it has limited ability to further increase cardiac output and Do_2 in response to increased oxygen demand.

A reduction in cardiac output increases the AVo_2D. The presence of intracardiac mixing and reduced PBF also contributes to a reduction in arterial oxygen content and reduced Do_2 and therefore a higher risk of anaerobic metabolism.[18] The risk of inadequate cardiac output is increased in the early postoperative period and during periods of increased oxygen demand, such as from agitation, fever, inflammation, and pain. Postoperative ischemia-reperfusion injury and mural edema can reduce diastolic and systolic function and stroke volume, resulting in heart rate and preload dependence and risk of rapid deterioration.

Inadequate cardiac output can be detected by close observation of trends and changes in continuously measured hemodynamic variables (eg, invasive systemic arterial and central venous pressures [CVPs], heart rate), physical examination, and specific laboratory tests. Laboratory data that can reveal inadequate cardiac output include direct or estimated measurements of Svo_2, arterial blood gas analysis, and serum lactate assessment. The ECG can document the presence of ischemia or arrhythmias that can cause or result from low cardiac output. Echocardiography can elucidate systolic and diastolic function, residual anatomic lesions, and pericardial fluid.

Both physical findings and detection of residual lesions can enable early intervention to prevent or treat low cardiac output. The strength of palpable peripheral pulses, however, can be a misleading physical finding in patients who have aortic runoff through the MBTS, because pulses can remain palpable even when cardiac output is compromised. In addition, high sympathetic tone will usually preserve systolic blood pressure despite a fall in cardiac output, systemic perfusion, and Do_2 to the tissues. An inadequate coronary perfusion pressure caused by a high atrial filling pressure and low aortic diastolic blood pressure can result in myocardial ischemia that can rapidly progress to cardiac arrest unless it is recognized promptly and treated effectively.[3,4,22,24] It is critical to identify residual surgical lesions, most importantly arch obstruction or a restrictive atrial septum, or new hemodynamically significant systemic atrioventricular or neoaortic valve insufficiency. ECLS should be considered for patients in a low cardiac output state that is unresponsive to medical management. Hemodynamic compromise in a shunt-dependent physiology can typically be reversed with inotropic support, preload modification, mechanical ventilation and sedation/analgesia, manipulation of systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR), and anticoagulation if shunt obstruction is suspected.

Balancing SBF and PBF. When the balance of the patient's PBF and SBF is maintained through a patent ductus arteriosus, aortopulmonary shunt, or direct communication between the aorta and pulmonary artery (eg, aortopulmonary window, truncus arteriosus), variations in SVR and PVR directly impact Qp:Qs. The circulatory balance is highly dynamic and can vary widely when the infant is awake and active, during illness, and with acute anatomic or hemodynamic changes.[53]

Pulmonary overcirculation, defined as a high Qp:Qs, can result from either high SVR or low PVR. Typically, there is an initial widening of the systemic pulse pressure and high arterial saturation, with a later reduction in arterial saturation resulting from worsening systemic venous desaturation.[33,46] The initial symptoms of a high Qp:Qs include tachypnea and tachycardia. The tachypnea results from increased pulmonary interstitial edema and poor lung compliance associated with elevated pulmonary venous pressure. The tachycardia represents an attempt to increase cardiac output to meet systemic oxygen requirements. Signs and symptoms of shock develop once a critical reduction of SBF is present.[54] The development of a prearrest state can be heralded by lactic acidosis, renal insufficiency, gut ischemia and feeding intolerance, or ECG changes consistent with coronary ischemia.[23,24] The risk of high Qp:Qs is increased in patients with a large shunt size relative to body weight. In the vulnerable patient, any increase in SVR can cause rapid deterioration from a state of adequate circulatory balance to one of extreme pulmonary overcirculation and shock. In these patients, high SVR will in turn cause increased Qp:Qs, and the resulting fall in SBF causes further sympathetic activation in a harmful feedback loop.[46,54,55]

Manipulation of PVR. If the shunt is inadequately restrictive, maneuvers to increase PVR by manipulating ventilation and gas exchange might not be well tolerated and could contribute to further deterioration and even cardiac arrest. In the period before single-ventricle palliation, cautious use of a hypoxic inspired gas mixture or inspired carbon dioxide with controlled hypoventilation can reduce Qp:Qs[56–59]; however, a hypoxic inspired gas mixture does not improve Do_2.[59] Although the addition of inspired carbon dioxide with controlled hypoventilation can increase PVR, narrow the AVo_2D, and increase cerebral oxygen saturation and Do_2,[60] this intervention is not commonly recommended and should only be used as a temporizing measure until surgical intervention can create regulated PBF. Simple hypoventilation can also increase the PVR but can be associated with unwanted atelectasis or respiratory acidosis.[56,58]

The effects of manipulation of PVR are less important when an appropriately restrictive shunt is in place. In patients with a restrictive shunt, supplementary oxygen administration generally increases Do_2 and maintains AVo_2D, and the absence of supplementary oxygen may be associated with pulmonary venous desaturation.[45]

Manipulation of SVR. Reducing SVR can favorably modify a high Qp:Qs state, improving cardiac output and Do_2.[61] A reduction in SVR will also have the benefit of reducing myocardial wall stress and oxygen demand.[61,62] Although SVR is not routinely measured, it can be calculated using the Fick principal and measurement of oxygen consumption. The ideal SVR indexed to body surface area has not been determined for infants with single ventricle and will be influenced by other patient-specific variables, including ventricular function, atrioventricular valve function, PVR, and the geometry of the shunt.

After the stage 1 Norwood palliation, systemic vasodilators such as phosphodiesterase inhibitors (milrinone, enoximone) and α-adrenergic blockers (phenoxybenzamine, phentolamine) are associated with both reduced Qp:Qs and increased Svo_2. The risk of cardiac arrest or prearrest instability appears to be reduced by perioperative strategies that include α-adrenergic blockade or phosphodiesterase inhibition. Although α-blockade is used in some centers for initial single-ventricle palliation, controlled trials are lacking.[63,64] For interstage afterload reduction, there appears to be no benefit from routine use of the angiotensin-converting enzyme inhibitor enalapril.[64]

The risk of high Qp:Qs is present with both the RVPAS and the MBTS.[65] If the patient with deteriorating SBF caused by a large or inadequately restrictive shunt is not responsive to medical management, consider emergent shunt revision or stabilization with ECLS. Distal arch obstruction will mimic elevated SVR by increasing Qp:Qs, especially in those patients with an MBTS; even mild arch obstruction can be clinically important and warrants consideration for intervention.

Recognition and Management of Shunt Obstruction. There are 3 principal reasons for a lower than expected systemic arterial oxygen saturation after the stage 1 Norwood palliation: (1) inadequate PBF; (2) intrapulmonary shunting and pulmonary venous desaturation; and (3) low mixed Svo_2 from a low cardiac output state, decreased oxygen-carrying capacity from anemia, or increased oxygen consumption. Inadequate PBF can result from pulmonary artery hypertension (PAH); however, it occurs more often as a result of inadequate shunt perfusion pressure or mechanical obstruction of the shunt or from pulmonary venous hypertension secondary to pulmonary vein stenosis or restrictive atrial communication.[29,52]

The constellation of low systemic oxygen saturation that is not responsive to an increase in inspired oxygen with preserved SBF and unchanged AVo_2D (initially) should raise concern for shunt obstruction. Additionally, patients receiving mechanical ventilation may demonstrate a fall in end-tidal CO_2 ($ETco_2$) with an increase in the arterial partial pressure of carbon dioxide ($Paco_2$).[66–70] The estimation of Qp:Qs using systemic arterial oxygen saturation and Svo_2 (or Svo_2 estimation with NIRS) can add to the physiological evaluation. During the interstage period, the risk of shunt thrombosis can be higher with an MBTS than with an RVPAS.[29,71,72] However, in patients with HLHS after stage 1 Norwood

palliation, the need for an unplanned shunt intervention is higher with the RVPAS.[28]

Prophylactic anticoagulation strategies include heparin therapy early after shunt placement, with a transition to aspirin when enteral medications are tolerated.[23] In a multicenter observational study, aspirin reduced the risk of shunt thrombosis and death during the first year after placement.[71] In a multicenter randomized clinical trial in patients with shunted single-ventricle physiology, a majority of whom were receiving aspirin therapy, the addition of clopidogrel did not reduce the incidence of shunt thrombosis.[73]

Treatment of acute shunt obstruction can include the following: (1) administration of increased inspired oxygen to maximize alveolar oxygenation; (2) administration of vasoactive agents to maximize shunt perfusion pressure (eg, phenylephrine, norepinephrine, epinephrine); (3) anticoagulation with heparin (50–100 U/kg bolus) to prevent clot propagation[22,24]; (4) shunt intervention by catheterization or surgery; and (5) stabilization with ECLS. In patients with shunt obstruction, maneuvers to decrease PVR (eg, oxygen, inhaled nitric oxide [iNO]) will provide little benefit and could delay the diagnosis of the actual problem. Reduction in oxygen consumption can be accomplished through sedation and neuromuscular blockade, avoidance of hyperthermia, the insertion of an advanced airway, and mechanical ventilation at low mean airway pressure.[70] In the early postoperative period, it may be useful to emergently open the sternum to rule out tamponade and to inspect the aortopulmonary or RVPAS. If the shunt obstruction produces persistent and profound arterial hypoxemia, myocardial performance will deteriorate rapidly. The outcome of ECPR in the circumstance of acute shunt obstruction is favorable, provided it is undertaken promptly.[7,29,74–77]

Systemic Illness and the Interstage Period. Other noncardiac causes of arrest or prearrest in patients with shunted physiology include dehydration, infection, and anemia. Each of these contributes to inadequate Do_2 by a different mechanism, but the end result will be shock, with regional or systemic ischemia and end-organ injury.[33,35,52,78–80] Because many physiological threats can initiate the low systemic perfusion and high SVR feedback loop, early recognition, evaluation, and intervention are important.[24] Careful routine medical assessment is needed, with special attention to hydration, nutrition, and identification of signs of infection. Specific laboratory evaluation of hemoglobin concentration, electrolyte balance, and concentration of brain natriuretic peptide, as well as echocardiography, is also important and should be performed judiciously.[81] The hemoglobin is typically maintained in the 13 to 15 g/dL range, although no trials of transfusion strategy exist in this patient population.[47,80,82] For newborns with HLHS, the reported incidence of interstage (ie, between discharge after stage 1 Norwood and admission for superior CPA) mortality is often as high as the hospital mortality after stage 1 Norwood palliation, particularly if the infant was palliated with an MBTS. (See Home Monitoring in the section on Location-Specific Arrest Prevention and Response Measures.)

Unique Challenges in CPR

Data from the Society of Thoracic Surgeons Congenital Heart Surgery Database (STS-CHSD) from 2007 through 2012 document a 12.7% incidence (350 of 2757) of cardiac arrest among patients undergoing stage 1 Norwood palliation.[83] Once the patient with shunted single-ventricle physiology develops cardiac arrest, it will be challenging to restore spontaneous circulation. In fact, in the STS-CHSD registry, 62.3% of patients who developed postoperative cardiac arrest after stage 1 Norwood palliation died compared with a mortality rate of 12.5% among those patients who did not develop postoperative cardiac arrest.[83]

It is difficult to obtain effective PBF during resuscitation because PBF is shunt dependent and will likely be affected by the relationship between PVR and either the aortic relaxation (diastolic) pressure (for MBTS) or the SVR (for MBTS and the RVPAS). During CPR in patients with normal cardiac anatomy, compressions generate only ≈10% to 30% of normal blood flow to the heart and 30% to 40% of normal blood flow to the brain.[6] In patients with single-ventricle shunted physiology, systemic output (Qs) is even lower, because there is loss of potential SBF to the lungs given the parallel circulation (Table 2). As a result, SBF often has low oxygen content and in the presence of reduced coronary perfusion will result in persistent and likely severe coronary ischemia. Prolonged CPR in the shunt-dependent single-ventricle patient will be associated with hypoxemia, systemic ischemia, and significant end-organ injury, particularly neurological injury.

When cardiac arrest develops, providers should begin conventional high-quality CPR. The AHA recommends that compressions be performed on the sternum just below the intermammary line in infants and on the lower half of the sternum in children.[84] However, data regarding the need to modify this position in infants and children with single ventricle (or any congenital heart defect) are limited. A recent Korean single-center case series of 185 patients (median age 0.5–12.5 years) with single ventricle (73 before creation of the superior CPA, 61 after superior CPA, and 51 after Fontan procedure) found that in all patients, the largest cross-sectional area of the systemic ventricle (assessed by computed tomography [CT] scan) was under the lower quarter (ie, bottom 25%) of the sternum.[85] More data such as these are needed. If the patient with single-ventricle arrests in the ICU and has indwelling monitor-

ing catheters, it is reasonable for providers to monitor arterial and central venous pressures and pressure tracings and modify compression technique as needed to optimize blood pressure and coronary perfusion pressure generated during compressions.[86]

Because of the limitations to conventional CPR described above, it is important to consider additional management within the first minutes of the resuscitation. These include urgent opening of the sternum (in the immediate postoperative period), treatment of arrhythmias or use of external pacing if indicated, treatment of possible shunt thrombosis, and early activation of the ECLS team, if available in the institution. Longer-duration in-hospital CPR efforts that include ECPR can be successful, but prolonged out-of-hospital resuscitation efforts are generally unsuccessful.[74,87]

Gaps in Knowledge

Management of newborns with single-ventricle physiology after stage 1 Norwood palliation or shunt placement is based on reported institutional practices. Data from the Single Ventricle Reconstruction Trial,[63] national database extractions,[88,89] and clinical program surveys about single-ventricle care[90] demonstrate considerable variation in practice among centers. Of concern, few modifiable risk factors related to the perioperative critical care management of patients with single-ventricle physiology that could contribute to cardiac arrest have been identified. To improve outcomes, it is essential to reduce practice variability through benchmarking and sharing of physiological, management, and outcome data. Additional studies are needed to determine whether modifications in chest compression technique are needed in patients with single ventricles.

Recommendations: Single-Ventricle Palliation Perioperative Management

1. **In the mechanically ventilated preoperative neonate with pulmonary overcirculation and symptomatic low systemic cardiac output and Do_2, inspired carbon dioxide can be beneficial to provide a short-term increase in cardiac output *(Class IIa; Level of Evidence C)*. Hyperventilation and hyperoxygenation may be potentially harmful in this circumstance *(Class III: Harm; Level of Evidence C)*.**
2. **Direct (SVC catheter) or indirect (NIRS) monitoring can be beneficial to follow AVo_2D and to direct management in the critically ill neonate after stage 1 Norwood palliation or shunt placement *(Class IIa; Level of Evidence B)*.**
3. **In the patient with an appropriately restrictive shunt, manipulation of PVR may have little effect, whereas lowering SVR and use of oxygen as needed can be useful to increase systemic Do_2 *(Class IIa; Level of Evidence C)*.**
4. **In the situation of known or suspected shunt obstruction, it is reasonable to administer oxygen, vasoactive agents to increase shunt perfusion pressure, and heparin (50–100 U/kg bolus) while preparing for catheter-based or surgical intervention *(Class IIa; Level of Evidence C)*.**

Superior CPA and Fontan

In the prearrest phase with low cardiac output or respiratory failure, strategies to improve venous return to the superior CPA will increase PBF. In particular, strategies to increase relative cerebral blood flow and minimize intrathoracic pressure have been successful. Although spontaneous ventilation is preferable to augment PBF and stroke volume in the superior CPA or Fontan physiology, judicious mechanical ventilation is usually well tolerated in circumstances of respiratory failure or low cardiac output. Positive-pressure ventilation has the benefit of reducing afterload and wall stress to the systemic ventricle for the patient with significant myocardial dysfunction or atrioventricular valve insufficiency; however, it does so at the expense of compromising PBF and ventricular preload. Optimum titration of inotropic support, afterload reduction, and positive-pressure ventilation are challenging and must be tailored to each individual patient.

After the superior CPA and Fontan operations, the relationship between mean CVP or superior CPA/Fontan pressure and left atrial (LA) pressure often identifies potential causes of low cardiac output syndrome (LCOS). Low CVP and LA pressures are consistent with hypovolemia. High CVP and low LA pressure (increased transpulmonary gradient) can result from reactive pulmonary vasoconstriction or fixed pulmonary vascular disease, pulmonary artery hypoplasia or stenosis, or pulmonary venous obstruction. High CVP and LA pressure are associated with ventricular dysfunction, hemodynamically significant atrioventricular valve regurgitation, systemic atrioventricular valve stenosis, ventricular outflow tract obstruction, or arrhythmia or loss of atrioventricular synchrony. The transpulmonary pressure gradient (the difference between the mean PA pressure [CPA or Fontan pressure] and the mean LA pressure) is an important determinant of PBF and systemic ventricular preload. Appropriate strategies of mechanical ventilation are critical, because PBF occurs predominantly during exhalation, when the intrathoracic pressure is at its lowest. It is important to rule out anatomic factors that limit effective PBF (deoxygenated blood through into the pulmonary capillary bed), including stenosis of the pulmonary arteries, large veno-venous collateral vessels from the SVC to the pulmonary veins or to the systemic venous return via the IVC

Table 3. Effect of Respiratory Manipulations on Circulatory Parameters at Different Stages of Palliation of Children With Univentricular Physiology[56,58–60,91–96]

Stage and Respiratory Strategy (Alveolar Gas)	Sa_{O_2}	Sv_{O_2}	Qp/Qs	TPG	AVo_2D	Vo_2	Lactate	CBF	rSo_2C	rSo_2S
0										
Hypocapnic										
Hyperoxic										
Hypercapnic[56,59]	↑	↑	↓		↓				↑	
Hypoxic[56,59]	↓	↓	↓		↔				↔	
1										
Hypocapnic[97]	↔	↔			↔					
Hyperoxic[97]	↑	↑			↔					
Hypercapnic[60,94]	↔	↔↑	↔		↓	↓	↓	↑	↑	↓
Hypoxic										
2										
Hypocapnic[58]	↓				↔				↓	
Hyperoxic[93]	↑									
Hypercapnic[58,91–94]	↑↑		↔	↑	↓	↓	↓	↑	↑	
Hypoxic										

Measured parameters in multiple studies are shown. Stage 0: Uncorrected/unpalliated ductal-dependent parallel pulmonary and systemic circulations. Maintenance of ductal patency is necessary for systemic perfusion, and prostaglandin E_1 is indicated. No human experimental data exist for measures such as hyperoxic or hypocapnic alveolar gas strategies that tend to reduce pulmonary vascular resistance, and such strategies should generally be avoided without significant monitoring of systemic oxygen delivery. The greatest improvement in systemic oxygenation occurs with induction of hypercapnic ventilation. Stage 1: After surgical palliation of parallel circulation with relief of arch obstruction and limitation of pulmonary blood flow with a systemic-to–pulmonary artery shunt. Hypercapnia can improve cerebral more than systemic oxygen delivery. Stage 2: After superior cavopulmonary anastomosis. The cerebral and pulmonary circulations are in series, and hypercapnia can improve systemic arterial oxygen saturation and systemic oxygen delivery by increasing cerebral blood flow, superior vena cava flow, and therefore pulmonary blood flow. Stage 3: After superior and inferior cavopulmonary anastomoses (post-Fontan). No systematic data exist for alveolar gas manipulation. See references for details.

AVo_2D indicates arteriovenous oxygen saturation difference; CBF, cerebral blood flow; lactate, lactate or metabolic acid change; Qp/Qs, pulmonary/systemic blood flow ratio; rSo_2C, cerebral oxygen saturation by near-infrared spectroscopy; rSo_2S, somatic oxygen saturation by near-infrared spectroscopy; Sa_{O2}, arterial oxygen saturation; Sv_{O_2}, systemic venous saturation; TPG, transpulmonary pressure gradient; Vo_2, oxygen consumption.

or azygous systems (only in the superior CPA), pulmonary arteriovenous malformations, and in the case of the fenestrated Fontan operation, a large right-to-left shunt across the fenestration.

Management of Ventilation

Physiological studies argue against use of hyperventilation in single-ventricle patients with superior CPA, and complementary studies support the use of maintaining high $Paco_2$ using hypoventilation (Table 3).[91–94] A low $Paco_2$ or alkalosis can be detrimental, and after the superior CPA, hypoxemia can be reversed by using a higher $Paco_2$.[91] Similar to the 2-ventricle heart, hypoventilation and acidosis after the modified Fontan operation in the single-ventricle patient can lead to a low cardiac output state.

Hypoventilation and mild hypercapnia improve systemic oxygenation and Do_2 and reduce oxygen consumption and arterial lactate in patients after creation of a superior CPA.[92,95] The cerebral CO_2 feedback loop dominates over the pulmonary feedback loop when they are in direct competition with one another.[93] Carbon dioxide plays a significant role in flow distribution in this cerebral-pulmonary arteriolar hierarchy, whereas O_2 has little impact. An increase in $Paco_2$ improves cerebral Do_2. By decreasing cerebral vascular resistance, hypoventilation-induced hypercarbia increases cerebral blood flow, SVC blood flow, and pulmonary blood flow. This can be a useful clinical strategy in patients with superior CPA who have hypoxemia resulting from limited PBF early in the postoperative period.

Alternatively, hyperventilation lowers arterial partial pressure of carbon dioxide, thereby increasing cerebral vascular resistance and lowering cerebral blood flow, SVC blood flow, and pulmonary blood flow in patients with superior CPA.[58,96] Hyperventilation significantly impairs systemic oxygenation after the superior CPA, despite a decrease in transpulmonary gradient.[98] Hyperventilation causes a decrease in cerebral blood flow velocity and in cerebral oxygenation.[58] Therefore, normoventilation or mild hypoventilation preserves cerebral oxygenation in patients with superior CPA. Although not studied in patients with superior CPA, it might be beneficial to use a mechanical ventilation strategy of higher tidal volume and lower ventilation

rate while aiming for the lowest possible mean airway pressure.

In patients with Fontan physiology, negative-pressure ventilation has been shown to improve stroke volume and cardiac output by augmenting PBF without an increase in heart rate[99,100]; however, the use of negative-pressure ventilation might not be practical for many centers. Current research involving the combination of intermittent positive-pressure ventilation in conjunction with a device that generates a negative intrathoracic pressure during the expiratory phase could allow for augmentation of PBF, stroke volume, and cardiac output in these populations.[101] In a small case series after superior CPA or tetralogy of Fallot (TOF) repair, airway pressure release ventilation was shown to increase PBF at a comparable mean airway pressure but did not improve Do_2.[102]

Unique Challenges in CPR

Survival from cardiac arrest in a patient with superior CPA or Fontan physiology is low. In the STS-CHSD registry, 0.9% of patients (17 of 1923) undergoing a Fontan correction developed postoperative cardiac arrest, and 41.2% of these patients died.[83] To optimize survival, it is important to recognize the physiological differences between patients with superior CPA and those with a Fontan, as well as the special considerations each requires during CPR (Table 2). As noted above, during CPR in patients with normal cardiac anatomy, cardiac output is thought to be approximately one-third that of normal.[6] In patients with either a superior CPA or a Fontan, chest compressions create SBF but minimal PBF. This reduction in PBF limits oxygenation and preload to the systemic ventricle, thereby further reducing cardiac output.

Cardiac output in patients with superior CPA can be further limited in the presence of atrioventricular or semilunar valve regurgitation. An additional important consideration is the elevation in SVC and cerebral venous pressure that occurs during chest compressions in patients with a superior CPA, which will limit cerebral blood flow and increase the risk for neurological injury.[103]

In the patient with a bidirectional Glenn/hemi-Fontan, chest recoil produces flow through the superior CPA and lungs, as well as from the IVC into the systemic venous atrium, providing important preload to the single ventricle for the next compression. In contrast, chest recoil in Fontan physiology results in filling of the total cavopulmonary connection from the SVC and IVC.

Gaps in Knowledge

Publications describing inotropic and ventilatory management of the patient with superior CPA or Fontan physiology with respiratory or cardiac failure are limited to case reports and case series. Patient heterogeneity relative to hemodynamic and cardiorespiratory interactions challenges the practicality of prospective trials.

Recommendations: Superior CPA and Fontan

1. **For patients with a superior CPA or Fontan physiology, ventilatory strategies such as spontaneous or negative-pressure ventilation can be useful to increase cardiac output *(Class IIa; Level of Evidence C)*.**
2. **For patients with a superior CPA and severe hypoxemia in a prearrest state, ventilatory strategies that target a mild respiratory acidosis and a minimum mean airway pressure without atelectasis can be useful to increase cerebral and systemic arterial oxygenation *(Class IIa; Level of Evidence B)*.**
3. **If the patient with a superior CPA develops cardiac arrest, the survival is poor, and risk for end-organ injury is increased. As a result, it is important for providers to recognize and intervene when prearrest low cardiac output and impaired Do_2 develop *(Class IIa; Level of Evidence C)*.**

Right-Sided Heart Disease

Patients undergoing reconstruction of the RV outflow tract (eg, TOF, double-outlet RV TOF type, truncus arteriosus) are at risk for both systolic and diastolic RV dysfunction. The risk is determined by the age of the patient, the degree of volume or pressure overload imposed on the RV, the duration the RV has been exposed to abnormal loading conditions, and residual or additional postoperative lesions. The following physiological and anatomic factors are associated with an increased risk of postoperative RV systolic or diastolic dysfunction: (1) preoperative RV hypertrophy with an RV that functions at systemic (or suprasystemic) pressures and decompresses through a ventricular septal defect (VSD); (2) an operative procedure that includes VSD closure and RV outflow tract reconstruction; (3) postoperative pulmonary valve insufficiency with acute RV volume loading (particularly if the RV is hypertrophied); and (4) RV dysfunction from resection of muscular obstruction (especially if the moderator band is damaged or excised) or ventriculotomy with or without insertion of an RV-to–pulmonary artery conduit. These acute changes in anatomy and physiology result in a heart that is predisposed to various degrees of RV systolic and diastolic dysfunction.

The RV with systolic and diastolic dysfunction is exquisitely dependent on sinus rhythm for the atrial contribution to ventricular filling to maintain cardiac output. Such an RV is intolerant of positive-pressure ventilation with high mean airway pressures.[99,104–110] Residual

VSDs, proximal or distal RV outflow tract or pulmonary artery obstruction, increased PVR, moderate or greater pulmonary insufficiency or tricuspid valve regurgitation, and left ventricular (LV) dysfunction are poorly tolerated and compound postoperative LCOS. An understanding of these issues will be helpful in the mitigation of postoperative LCOS and during postoperative resuscitation.

Intraoperative Assessment

The intraoperative acquisition of key hemodynamic data is helpful to rule out residual VSD or outflow tract obstruction before conclusion of the surgical procedure. Helpful intraoperative evaluations include the presence or absence of a step-up in oxygen saturation from SVC to pulmonary artery, RV and pulmonary artery pressure (PAP) measurements, and the results of a postoperative transesophageal echocardiogram.[111–116] Intraoperative estimation of Qp:Qs can be derived by dividing the oxygen saturation difference across the systemic capillary bed (systemic arterial oxygen saturation–mixed Svo_2 [SVC or right atrial saturation]) by the oxygen saturation difference across the pulmonary capillary bed (pulmonary venous or LA saturation–pulmonary artery saturation). A Qp:Qs >2:1 suggests the presence of a residual shunt that is likely to be hemodynamically significant. The usual source of the residual left-to-right shunt is incomplete closure of the VSD or additional undiagnosed muscular VSDs.[112,117,118]

Increased RV pressure can be caused by the following: (1) distal pulmonary artery obstruction (congenital or related to residual ductal tissue encircling the left pulmonary artery); (2) suboptimal surgical reconstruction of the proximal pulmonary artery anastomoses with the conduit; (3) residual subvalvar, valvar, or supravalvar stenosis; and (4) elevated PVR. Postoperative transesophageal echocardiography might not demonstrate discrete stenosis of the left pulmonary artery and underestimates valve regurgitation, especially if the systemic pressure is low. However, the Doppler peak instantaneous gradient will overestimate the peak-to-peak pressure gradient in long-segment stenosis. Tricuspid valve regurgitation in the presence of RV dysfunction with pulmonary insufficiency is tolerated poorly and can be caused by inclusion of the septal leaflet in the VSD patch.

Postoperative Course

Restrictive RV Physiology

Postoperative restrictive RV physiology is characterized by Doppler demonstration of persistent antegrade diastolic blood flow into the pulmonary artery in late diastole at the time of atrial contraction.[119] After TOF repair, ventricular diastolic dysfunction is thought to be associated with intraoperative myocardial injury and postoperative oxidant stress.[119] In the most severe cases, the RV acts as a passive conduit between the right atrium and pulmonary artery. There is often an elevated RV end-diastolic pressure and RV hypertrophy. Diastolic RV dysfunction is characterized by impaired relaxation and filling.[120]

A stiff, poorly compliant, and hypertrophied RV is associated with an elevated ventricular end-diastolic pressure and systemic venous hypertension. Reduced RV preload reduces RV stroke volume and therefore LV preload and cardiac output. RV and LV interdependence and the effect on septal position affects LV compliance and function, further contributing to impaired stroke volume.[121] Such a clinical scenario might be particularly evident after neonatal and infant RV outflow reconstruction and ventriculotomy, such as after truncus arteriosus or TOF repair. Hemodynamically significant residual defects, including residual VSD, outflow tract obstruction, or dysrhythmias will exacerbate RV failure and the low cardiac output state.

Atrial Shunt

In the presence of right-sided heart diastolic dysfunction or RV systolic failure, an atrial septal defect that allows right-to-left shunting can be helpful to preserve LV preload and decrease RV wall stress and systemic venous hypertension. This has been studied primarily in patients with idiopathic PAH.[122,123] Simple calculations demonstrate that preservation of LV preload with shunted systemic venous blood will improve systemic Do_2 even if there is systemic arterial desaturation. However, it is difficult to judge the size of the atrial communication, and on occasion, severe hypoxemia requires reoperation to close or reduce the size of the atrial defect.

Tissue Edema and Tamponade

During the postoperative period after reconstruction of the RV outflow tract, fluid is progressively given to maintain RV preload, and thereby LV preload, to prevent systemic hypotension.[124] Over time, the increase in blood pressure and mixed Svo_2 in response to fluid administration diminishes, the patient becomes edematous, and further fluid administration is counterproductive. The capillary leak and third-space accumulation of fluid can reflect direct endothelial injury as a result of the inflammatory response to bypass, but after RV outflow reconstruction, it can also be caused by elevated RV end-diastolic pressure and CVP.[125–128] Both capillary leak and an elevated CVP result in fluid collection in the peritoneal and pleural cavities and tissue edema despite relative intravascular volume depletion and inadequate RV preload. This phase of capillary leak typically will resolve over the subsequent 1 to 2 postoperative days; however, it is extremely important to rule out residual anatomic defects.

The RV is also susceptible to compression from tissue edema in the mediastinum, resulting in so-called tissue tamponade, which further restricts filling. If there is risk of tamponade physiology, it can be useful to leave the

sternum open or reopen the sternum if signs or symptoms of tamponade develop during the early postoperative period.[129–133]

Fluid accumulation in the lungs or pleural spaces will result in higher ventilator pressures further impairing RV filling and cardiac output. Pleural fluid evacuation is usually helpful. Abdominal compression from ascites impairs IVC flow. Prophylactic placement prior to surgery or early consideration of placement after surgery of a peritoneal drain can be helpful.[134–136]

Mechanical Ventilation and Cardiopulmonary Interactions

Mechanical ventilation can have a significant impact on RV afterload and the amount of pulmonary regurgitation.[137] Both hypoinflation and hyperinflation of the lung will increase afterload of the RV and can reduce preload to the LV, with a resultant fall in cardiac output. There is also the potential for worsening pulmonary regurgitation if PVR increases. In addition, RV ischemia can develop from increased wall stress and increased RV myocardial oxygen demand.

There is evidence that positive-pressure ventilation is harmful and negative-pressure ventilation is beneficial in right-sided heart diastolic dysfunction. Spontaneous ventilation and negative-pressure ventilation improve cardiac output and renal function.[99,138,139] There is reported benefit to airway pressure release ventilation.[102] Positive-pressure ventilation with the lowest mean airway pressure and early postoperative extubation can be advantageous, although in a patient with an LCOS, this must be balanced against the potential detrimental effects of increased work of breathing and loss of airway control.

Cardiac Rhythm and Pacing

Right atrial contraction associated with sinus rhythm can make an important contribution to RV filling and cardiac output in patients with right-sided heart dysfunction.[109,110] Atrial arrhythmias, especially if associated with atrioventricular dissociation (eg, junctional ectopic tachycardia [JET]) can be poorly tolerated. These arrhythmias must be diagnosed promptly, and if hemodynamically significant, treated with measures including mild hypothermia, minimization of catecholamine use, minimization of O_2 demand, administration of amiodarone or procainamide, and cardiac pacing.[140,141] After reconstruction of the RV outflow tract, right bundle-branch block and ventricular dyssynchrony are common and can be exacerbated by RV pacing. Biventricular pacing can improve cardiac output in children with postoperative right- or left-sided heart dysfunction.[142–144]

Pharmacological Management of Right-Sided Heart Dysfunction

When a patient develops postoperative right-sided heart dysfunction, inotropic and vasoactive agents must be carefully selected and titrated.[120] Coronary blood flow to the RV occurs during both systole and diastole in the normal heart but can be reduced when the RV is hypertrophied and end-diastolic pressure is elevated. As a result, when oxygen demand is increased, such as with tachycardia and elevated wall stress, the RV is at risk for ischemia.[145] Low-dose epinephrine infusion is an adjunctive therapy for systolic dysfunction of the RV; however, catecholamines can cause tachycardia and increase oxygen demand and wall stress, thereby worsening RV diastolic dysfunction.[120] Systemic vasoconstrictors, especially vasopressin[146,147] and norepinephrine,[146,147] can be useful to support mean arterial pressure, reducing the need for fluid administration; they will also maintain coronary perfusion pressure and potentially improve ventricular interactions. If there is pulmonary vasoconstriction, iNO can be a useful therapy in RV failure.[148,149]

Unique Challenges in CPR

Cardiac output during CPR can be very limited in patients who have undergone reconstruction of the RV outflow tract. The recommendations for high-quality CPR should be followed; however, filling of the RV during chest recoil can be limited if the RV has restrictive physiology with diastolic dysfunction. Additional fluid should be administered to augment intravascular volume. Pulmonary regurgitation can be worsened by chest compressions, resulting in decreased PBF, LV preload, and cardiac output. Coronary perfusion and blood flow to a hypertrophied RV can be limited during chest compressions, and it is important to minimize the time to first administration of epinephrine. The risk for hemodynamically significant supraventricular arrhythmia (ie, supraventricular tachycardia [SVT]) or JET) is high, and these arrhythmias should be viewed as prearrest states and must be identified and treated promptly. Chest compressions can compress and obstruct the reconstructed RV outflow tract. Thus, if CPR is needed in the immediate postoperative period, it may be necessary to open the chest as quickly as possible to enable open-chest cardiac massage.

Gaps in Knowledge

Evidence to support management of the patient with right-sided hemodynamic compromise after congenital heart surgery is limited to case reports and a few case series; more research is needed.

Recommendations: Right-Sided Heart Disease

1. **In patients with postoperative RV systolic and/or diastolic dysfunction, an atrial shunt can be helpful to increase systemic cardiac output and systemic Do_2, despite systemic**

oxygen desaturation *(Class IIa; Level of Evidence C)*.

2. **In postoperative patients with restrictive RV physiology or tamponade physiology, an open sternum can be useful to improve hemodynamics *(Class IIa; Level of Evidence C)*.**

Pulmonary Arterial Hypertension

PAH is a major cause of morbidity and mortality in children with congenital and acquired heart disease. Much of the data regarding the incidence of PAH after pediatric cardiothoracic surgery and the risk of, therapies for, and outcomes after pulmonary hypertensive crises are from single-center case series. The disease is difficult to study because of the heterogeneity of the pediatric population and the small number of patients seen at each center. The Pediatric Pulmonary Hypertension Network Informatics Registry (ClinicalTrials.gov identifier No. NCT02249923) has been established to better understand disease processes and facilitate treatment. In the interim, efforts to standardize definitions and treatment led to the 2015 publication of the first Pediatric Pulmonary Hypertension Guidelines from the AHA and the American Thoracic Society.[150] Recommendations contained herein are consistent with those guidelines.

Pulmonary hypertension occurs in 2% to 5%[151] of pediatric patients after cardiac surgery, and 0.7%[152] to 5%[151] of all cardiovascular surgical patients experience postoperative pulmonary hypertensive crises, with the highest reported risk among patients with atrioventricular septal defects, truncus arteriosus, TAPVC, transposition of the great arteries (TGA), and VSD.[151,153] In a case series from Sweden, the incidence of pulmonary hypertensive crises was higher after atrioventricular septal defect repair (14%) and in patients with trisomy 21 (10%).[152] In other case series,[154,155] up to 20% of high-risk pediatric cardiac surgical patients had postoperative pulmonary hypertension. Postoperative pulmonary hypertension prolongs ICU stay and time to extubation,[154,155] and the in-hospital mortality rate among patients who have pulmonary hypertensive crises might be as high as 20%.[151,152,156] Even when patients with pulmonary hypertension do not experience a postoperative pulmonary hypertensive crisis, they still have a higher mortality risk during the first 12 months after surgery, accounting for up to 8% of late deaths after cardiac surgery.[152,157,158]

Pulmonary Hypertensive Crises

Pulmonary hypertensive crises are acute and potentially lethal increases in PAP and PVR that cause acute right-sided heart failure accompanied by tricuspid regurgitation, systemic hypotension, myocardial ischemia, and even cardiac arrest. They can be triggered by a variety of stimuli, including pain, anxiety, tracheal suctioning, hypoxia, and acidosis.[159–165] Pulmonary hypertensive crises have been described and studied most frequently when they occur after cardiac surgery,[159–166] but they can also accompany modulation or withdrawal of pulmonary hypertension–specific therapy.[164,167–171] Pulmonary hypertensive crises can be precipitated outside of the perioperative period by intercurrent illness, lung injury, or infection[166,172–174] or by noncardiac interventions.[166,175–177] If pulmonary hypertensive crises are incompletely treated initially, they recur, and subsequent crises can be more severe and prolonged.[153,159,160]

Histological examination of the lung vasculature in patients who experience fatal pulmonary hypertensive crises usually reveals reversible changes. There is medial hypertrophy with abnormal peripheral extension of muscle into normally nonmuscularized arteries.[159] The histological examination of lung tissue obtained from patients who have had pulmonary hypertensive crises after repair of TAPVC can show not only the vascular changes described above but also lymphangiectasia.[178–180]

Clinical and hemodynamic findings associated with postoperative pulmonary hypertensive crises include an abrupt increase in PAP (ratio of PAP to systemic artery pressure >0.75), followed by increased right atrial and RV end-diastolic pressures and CVP, decreased systemic and mixed Svo_2, decreased systemic arterial pressure (by >20%), and decreased cardiac output. Bronchoconstriction or increased airway resistance can also be noted.[150] Intraoperatively placed pulmonary artery catheters can be useful to confirm diagnosis and evaluate management after cardiac surgery. There is great variability in the use of these catheters. It is difficult to predict which patients at risk for pulmonary hypertension and pulmonary hypertension crises will benefit from a pulmonary artery catheter, which alters the risk-benefit ratio associated with the use of these catheters.

Management Plan for Patients at Risk for Pulmonary Hypertensive Crisis

Patients with PAH require a comprehensive plan of care that includes meticulous care to prevent episodes of pulmonary hypertensive crises.[181] This plan must also include a plan for postoperative hemodynamic monitoring and the recommended sequence of interventions to be initiated in response to development of pulmonary hypertensive crises.

Palliative right-sided heart and pulmonary artery decompression procedures (such as an atrial septostomy and placement of Potts shunt) can significantly reduce the risk of pulmonary hypertensive crises and prolong survival in idiopathic PAH.[122,123,182–185] It is important to optimize the size of the atrial shunt to avoid a large right-to-left shunt and profound hypoxemia and cyanosis. Atrial septostomy, performed at a center with experience in treatment of pulmonary hypertension, is recommended for patients with RV failure, recurrent

syncope, or pulmonary hypertensive crises that persist despite optimized medical management.

Treatment of pulmonary hypertension and prevention of pulmonary hypertensive crises include provision of adequate analgesia, sedation, and the use of muscle relaxants; avoidance of hypoxia and acidosis; administration of inhaled pulmonary vasodilators; and use of oral and systemic vasodilators. Pulmonary vasodilators must be weaned carefully; if the child develops a pulmonary hypertensive crisis during weaning, administration of the previously successful dose of the drug should be resumed. During a crisis, administration of systemic vasoconstrictors can also be considered to maintain coronary perfusion of the RV.

Adequate Analgesia, Sedation, and Use of Muscle Relaxants

The association of pulmonary hypertensive crises with sympathetic stimulation has been documented.[159,160] Neonates undergoing cardiac surgery demonstrate high levels of sympathetic stress hormones that are attenuated with administration of high-dose fentanyl analgesia.[186,187] For pediatric cardiovascular surgical patients who are at risk for pulmonary hypertensive crises, provision of adequate opiates, sedatives, and muscle relaxants is recommended.[150] In general, continuous infusion of the synthetic opioid fentanyl with the use of muscle relaxants is beneficial for early postoperative care of high-risk patients. It can be beneficial to supplement baseline analgesic drugs with additional doses before high-risk procedures such as suctioning of the endotracheal tube.[150]

Avoidance of Hypoxia and Acidosis

There is considerable evidence that hypoxia and acidosis are each powerful pulmonary vasoconstrictors.[188–191] As a result, the care of the child with pulmonary hypertension who is at risk for pulmonary hypertensive crisis requires meticulous respiratory management and monitoring to avoid and promptly treat hypoxia and acidosis.

Alkalosis is as potent a vasodilator as iNO. During pulmonary hypertensive crises, oxygen administration and induction of alkalosis through hyperventilation or alkali administration are recommended while pulmonary-specific vasodilators are administered.[150] However, alkalosis can have detrimental sequelae, whether it is induced by hyperventilation or by alkali administration.[188] Hyperventilation can induce lung injury, and the response to sodium bicarbonate administration can be only transient. In addition, sodium bicarbonate can decrease cardiac output and cerebral blood flow and increase CVP and SVR.[150]

Inhaled Pulmonary Vasodilators

iNO[163,190,192–202] and prostacyclin (PGI_2)[194,196,203] are currently available inhaled pulmonary vasodilators that can be used to prevent and treat pulmonary hypertensive crises in patients with pulmonary hypertension. In one prospective, randomized controlled trial of 124 children after cardiac surgery for large VSDs or atrioventricular septal defects, iNO treatment reduced the frequency of pulmonary hypertensive crises and shortened the time to extubation.[164] In a retrospective review from 1984 to 1994 of 294 patients with atrioventricular septal defect repair and severe postoperative pulmonary hypertension, iNO administration was associated with reduced mortality.[204] Inhaled PGI_2 has been shown to transiently produce pulmonary vasodilation and improve oxygenation, but the alkalinity of the drug can irritate airways, and precise dosing can be complicated by drug loss in the nebulization circuit.[150,205] Inhaled iNO or PGI_2 should be used in the initial therapy for pulmonary hypertensive crises and right-sided heart failure.

To minimize the side effects from intravenous vasodilator drugs, there has been great interest in delivering drugs such as milrinone, nitroglycerin, and PGI_2 through inhalation.[153,196,206] In one randomized controlled trial of 35 children with acyanotic heart disease and pulmonary hypertension, both inhaled milrinone and iNO produced a fall in systolic pressure, diastolic pressure, and mean PAPs and PVR.[206] These inhaled drugs could offer an alternative to intravenous routes of administration, but experience with them is limited.

Systemic Vasodilators

The intravenous vasodilators PGI_2 and nifedipine have been used to decrease PVR, predominantly during acute vasoreactivity testing with continuous systemic and PAP monitoring.[207–209] However, there is no intravenous vasodilator that has a discrete and specific effect on the pulmonary circulation, so the use of these agents must be balanced against the potential risk of complications, many of which result from the systemic arterial effects. In adults, a fall in SVR and hypotension, particularly in patients with idiopathic pulmonary hypertension and Eisenmenger syndrome,[162,181,210] can contribute to an increased right-to-left shunt, progressive hypoxemia, and even cardiac arrest. Such a fall in SVR might occur in children with dehydration or those receiving procedural sedation. In children and adults, worsening hypoxemia can also result from the inhibition of hypoxic pulmonary vasoconstriction with an increase in intrapulmonary shunting.[211,212]

The intravenous vasodilators recommended for use in children for the treatment of PAH include drugs that have a predominant effect on the β-adrenergic receptors (eg, isoproterenol), phosphodiesterase inhibitors (eg, milrinone [type 3 inhibition] and sildenafil [type 5 inhibition]), eicosanoids (eg, prostaglandin E_1 [PGE_1] and PGI_2 and the PGI_2 analogue treprostinil [remodulin]), and other drugs that increase intracellular cyclic guanosine monophosphate (eg, nitroglycerin).[150] Intravenous sildenafil infusions can decrease time to extuba-

tion and length of ICU stay[156] and can be effective in children with decreased gut perfusion or ischemia with poor enteral drug absorption.[213] However, the effect of intravenous sildenafil during cardiac arrest related to pulmonary hypertension is unknown. For further information on the use of systemic vasodilators, the reader is referred to the 2015 guidelines on pediatric pulmonary hypertension published by the AHA and the American Thoracic Society.[150]

Oral Vasodilators

Oral vasodilator drugs administered to pediatric patients with pulmonary hypertension include the phosphodiesterase type 5 inhibitor (eg, sildenafil)[150,214,215] and an endothelin receptor antagonist[150] (eg, bosentan). In pediatric studies including children with CHD, sildenafil has been shown to improve peak oxygen consumption and functional class and reduce mean PAP and PVR. Sildenafil has been used effectively during withdrawal of iNO and in children with postoperative PAH,[216] but its pulmonary vasodilator effects must be balanced against the consequences of increased intrapulmonary shunt. Sildenafil can be administered either as a 1-time dose to prevent rebound or repeatedly every 6 to 8 hours to treat ongoing PAH. In a multicenter, double-blind, randomized, placebo-controlled trial of bosentan versus placebo in 54 patients with class III Eisenmenger syndrome, bosentan was associated with a significant fall in PVR index and mean PAP without a fall in SVR.[217]

Calcium channel blockers (amlodipine, diltiazem, and nifedipine) can be used to treat the relatively stable patient with pediatric arterial hypertension; however, these drugs can cause a decrease in cardiac output and a significant drop in systolic blood pressure.[150] As a result, calcium channel blockers are recommended only for those patients who are noted to have a reactive pulmonary vascular bed (as assessed by acute vasoreactivity testing) and who are older than 1 year of age.[180]

Rebound Pulmonary Hypertension

Rebound pulmonary hypertension occurs in approximately one-third of patients whose iNO is being weaned. Rebound pulmonary hypertension can be managed effectively with the use of intravenous sildenafil or (when the patient is stable) oral sildenafil.[170,171] Intravenous sildenafil can cause systemic hypotension.[150]

Systemic Vasoconstrictors

During pulmonary hypertensive crises, the RV fails, and the increased RV afterload produces increased myocardial oxygen demand at the same time that the coronary perfusion pressure and coronary blood flow are decreased. As a result, the RV can become ischemic, worsening right-sided heart failure. The elevated PVR and RV failure lead to a fall in PBF and left-sided heart filling, with a resultant fall in cardiac output. Volume replacement is needed. In addition, inotropic agents can be administered to improve RV function, and vasopressors can be administered to treat systemic hypotension and improve coronary artery perfusion pressure. There are animal data that suggest that vasopressin can increase SVR without causing a similar increase in PVR[218]; however, in vivo studies of the pulmonary vascular response to vasopressin in adults have yielded inconsistent results.[219] A prospective pilot study of phenylephrine, arginine vasopressin, and epinephrine in pediatric patients with pulmonary hypertension showed an increase in aortic pressure with all drugs, although only vasopressin resulted in a consistent decrease in the ratio of PVR to SVR.[220] Mechanical cardiopulmonary support should be considered in cases of right-sided heart failure refractory to inotropes and vasoconstrictors (see Mechanical Support section).

Unique Challenges in CPR

When adult patients with PAH develop cardiac arrest, conventional resuscitation with CPR and medications is rarely effective, with a 6% reported survival rate.[221] Similar to adults, children with PAH can develop sudden cardiac arrest.[157,221–224] The cardiac arrest can be triggered by arrhythmia, pulmonary hemorrhage, left main coronary compression by the pulmonary artery, pulmonary artery dissection or embolus, spontaneous PAH crisis, or dose reduction or withdrawal of a pulmonary artery vasodilator. The ultimate cause of the cardiac arrest is usually acute RV decompensation in a patient with little reserve.

Once cardiac arrest develops in a child with PAH, chest compressions and resuscitation drugs might be ineffective in generating PBF, LV filling, and cardiac output. It is extremely important to search for and treat possible reversible causes of increased PVR, including inadvertent interruption in targeted pulmonary hypertension drugs, hypercarbia, hypoxia, arrhythmia, cardiac tamponade, or drug toxicity. There is no evidence that alkali administration improves outcome, and there is evidence that excessive ventilation during resuscitation is harmful[222]; positive-pressure ventilation will decrease systemic venous return, RV filling, and cardiac output generated during chest compressions.

If high-quality CPR remains ineffective despite provision of pulmonary hypertension–specific therapy, including pulmonary vasodilators, rapid consideration of ECLS might offer the best chance of survival, either as a bridge to heart/lung transplantation or to permit recovery from the inciting factor.[223,225–227] Survival has been reported using conventional ECLS or ECLS with a pumpless lung assist device.[228–231]

Reports of cardiac arrest during cardiac catheterization of children with PAH suggest that use of specific pulmonary vasodilators can be beneficial when delivered with careful hemodynamic monitoring.[175,176] Once cardiac arrest has occurred, outcomes can be improved

in the presence of an anatomic right-to-left shunt that permits LV preload to be maintained without PBF. We identified no studies reporting the outcome of CPR after cardiac arrest in children with Eisenmenger syndrome or after postoperative cardiac arrest in children with PAH.

Intravenously administered PGI_2 could have a role in resuscitation of children with PAH, but there is no evidence to support this. Abrupt cessation of pulmonary hypertension–targeted therapies can result in rebound pulmonary hypertension and cardiac arrest (see Rebound Pulmonary Hypertension section). Therefore, it is always prudent to determine whether impediment to drug delivery is the cause of hemodynamic deterioration, especially in patients receiving chronic infusions of PGI_2 or analogues. This requires rapid assessment and correction of problems with the central venous catheter, the subcutaneous site, or the drug-infusion system (including tubing and pump).

The poor outcome after cardiac arrest in patients with PAH reinforces the need for a preventative approach for high-risk patients (ie, those with established Eisenmenger syndrome, RV dysfunction, suprasystemic PAPs, and tricuspid and pulmonary valve regurgitation). Given the risk for cardiac arrest in these patients, admission to the ICU should be considered during any intercurrent illness or when the child is undergoing noncardiac or other procedures.

Gaps in Knowledge

Much of our understanding of the management of pulmonary hypertension has emerged from the adult population, with very limited pediatric data available. A data registry for pediatric patients with PAH will allow for critically needed clinical and translational research and quality improvement science that will better inform our clinical care for this high-risk population.

Recommendations: Pulmonary Arterial Hypertension

1. **Atrial septostomy is recommended for patients with RV failure, recurrent syncope, or pulmonary hypertensive crises that persist despite optimized medical management but should ideally be performed in an experienced pulmonary hypertension center *(Class I; Level of Evidence B)*.**
2. **For pediatric patients who are at high risk for pulmonary hypertensive crises, provision of adequate opiates, sedatives, and muscle relaxants is recommended to minimize risk of pulmonary hypertensive crises *(Class I; Level of Evidence B)*.**
3. **The postoperative care of the child with pulmonary hypertension at high risk for pulmonary hypertensive crises requires careful respiratory management and monitoring to avoid hypoxia and acidosis *(Class I; Level of Evidence B)*.**
4. **For the initial treatment of pulmonary hypertensive crises, oxygen administration and induction of alkalosis through hyperventilation or alkali administration can be useful while pulmonary-specific vasodilators are administered *(Class IIa; Level of Evidence C)*.**
5. **iNO or PGI_2 should be used as the initial therapy to treat pulmonary hypertensive crises or acute right-sided heart failure secondary to increased PVR *(Class I; Level of Evidence B)*.**
6. **Sildenafil should be prescribed to prevent rebound pulmonary hypertension in patients who are at risk for or demonstrate hemodynamic instability or symptomatic PAH during weaning or discontinuation of the iNO dose *(Class I; Level of Evidence B)*.**
7. **In patients with pulmonary hypertensive crises, inotropic/vasopressor therapy should be used to avoid RV ischemia caused by systemic hypotension *(Class I; Level of Evidence B)*.**
8. **ECLS can be useful in cases of refractory pulmonary hypertensive crises *(Class IIa; Level of Evidence B)*.**
9. **It is reasonable to undertake early postoperative investigation to assess the operative result and identify additional or undetected lesions in patients with hemodynamically significant postoperative pulmonary hypertension *(Class IIa; Level of Evidence C)*.**

Left-Sided Heart Disease

Severe Mitral Valve Stenosis and Mitral Regurgitation

Severe Mitral Valve Stenosis

Severe mitral stenosis results in elevated LA pressure, pulmonary venous hypertension, and PAH. Although the PAH can be reversible after relief of the stenosis, the pulmonary vascular bed can be quite labile in the immediate postoperative period after mitral valve surgery. This reactivity is exacerbated by preoperative pulmonary edema and the inflammation caused by cardiopulmonary bypass, both of which affect pulmonary function and can further increase PVR. After relief of mitral stenosis, prophylactic administration of a pulmonary vasodilator such as iNO or a nonspecific vasodilator such as intravenous milrinone can be useful during the immediate postoperative period to minimize pulmonary vascular reactivity and pulmonary hypertensive crises.

The LV can also be less compliant postoperatively than preoperatively, and higher filling pressure might be required in the immediate postoperative period to maintain adequate cardiac output. Volume resuscitation should be given cautiously, with attempts to avoid a rapid elevation of LA pressure, acute development of pulmonary edema, and the precipitation of a pulmonary hypertensive crisis.

Mitral stenosis in isolation is uncommon. Children with mitral stenosis typically have multiple levels of left-sided outflow tract obstruction, with possible LV hypoplasia and endocardial fibroelastosis.[232] As a result, in many instances after mitral valve repair, the LV end-diastolic pressure remains elevated, even in the absence of a mitral valve gradient. Mechanical ventilation strategies to improve pulmonary compliance and oxygenation, such as use of higher positive end-expiratory pressure, can reduce PVR and improve cardiac output, but excessive positive end-expiratory pressure can impede systemic and pulmonary venous return, resulting in a fall in cardiac output.

Severe Mitral Valve Regurgitation

Severe mitral regurgitation produces LA and LV volume overload, causing progressive LV dilation, dilation of the mitral valve annulus, and progressive LV dysfunction.[233] Long-standing mitral regurgitation can result in LA hypertension and elevated PVR.

Postoperative LCOS can occur after mitral valvuloplasty or replacement, particularly in patients with preoperative ventricular dysfunction and higher LV end-systolic dimension.[234,235] Other factors that can contribute to LCOS after mitral valvuloplasty or replacement include myocardial reperfusion injury after prolonged cross-clamp time, postoperative complications such as arrhythmias and complete heart block, coronary artery obstruction or injury during valve replacement, and increased pulmonary vascular reactivity. In a study of >100 children undergoing mitral valve repair or replacement predominantly for mitral regurgitation, the mortality rate was nearly 10%, and 10% required mechanical circulatory support in the immediate postoperative period.[236]

In the immediate postoperative period after mitral valve repair or replacement, patients require close monitoring of cardiac output. If LA pressure is measured directly with an LA catheter, the catheter and tubing must be carefully maintained and scrutinized to avoid any air emboli. Afterload reduction with intravenous milrinone[237] and inotropic support is typical for at least 24 hours after surgery, and the duration of intravenous afterload reduction should be extended in the setting of preoperative or persistent postoperative ventricular dysfunction. For patients with severe postoperative LV dysfunction after mitral valve repair or replacement, extubation can be deferred until the LV function improves and the LV is deemed able to tolerate the increase in afterload that will result from loss of positive-pressure ventilation.

If LCOS persists despite escalation of inotropic support, early initiation of ECLS should be considered. ECLS is currently used primarily as a bridge to recovery, but in rare cases it can be considered as a bridge to placement of a long-term LV assist device (LVAD). Mitral valve replacement with a prosthetic valve is a relative contraindication for LVAD placement and entails technical modifications.[238]

Unique Challenges in CPR

In the presence of severe mitral stenosis or regurgitation, elevated LA pressure and PVR limit effective PBF and ultimately the systemic cardiac output generated by chest compressions. In severe mitral stenosis, cardiac output generated by chest compressions is further limited by restriction of flow of pulmonary venous return across the mitral valve and decreased filling of the LV. In severe mitral regurgitation, cardiac output generated by chest compressions is further limited by the regurgitant blood flow from the LV across the mitral valve. If high-quality CPR remains ineffective, early consideration of ECLS might offer the best chance of survival.

Critical Aortic Valve Stenosis and Severe Aortic Valve Regurgitation

Critical Aortic Valve Stenosis

Newborns with critical aortic stenosis have a fixed elevation in LV afterload and will present with either a hypertrophied or dilated LV with decreased contractility. If LV hypertrophy is inadequate, wall stress increases and LV ejection fraction falls. LV endocardial fibroelastosis can be present and suggests subendocardial ischemia. Additional anatomic features that can affect cardiac output include abnormalities in the mitral valve, subaortic stenosis, and in some cases aortic arch obstruction (eg, coarctation of the aorta). An elevated LV end-diastolic pressure can result in high LA pressure and pulmonary edema. In newborn infants with critical aortic stenosis, PGE_1 infusion is required to keep the ductus arteriosus open, enabling a pulmonary-to-aortic shunt that will support systemic perfusion. In addition, these infants often benefit from inotropic support to maintain adequate cardiac output before intervention.

Percutaneous aortic balloon valvuloplasty is associated with low mortality and is the preferred approach in most centers.[239] Surgical aortic valvotomy can be performed with similar results.[240,241] Relief of aortic stenosis without significant aortic regurgitation can result in a dramatic improvement in contractility and cardiac output if LV function is preserved. However, both percutaneous and surgical interventions are associated with higher mortality in the presence of preexisting LV dysfunction.[239,241,242] In newborns with critical aortic ste-

Circulation. 2018;137:00–00. DOI: 10.1161/CIR.0000000000000524

nosis, the presence of endocardial fibroelastosis is another risk factor for early mortality and poor long-term outcome.[243]

After percutaneous balloon valvuloplasty in the neonate, the PGE_1 infusion is discontinued. Inotropic support or afterload reduction might be needed in the immediate postintervention period to support cardiac output. Serial echocardiography with Doppler color flow is used to assess the magnitude and direction of shunting through the ductus arteriosus, LV function, and the degree of aortic stenosis and regurgitation to determine the need for and duration of inotropic support (eg, epinephrine) or afterload reduction (eg, milrinone).[237] If LV function is poor, LA hypertension can persist, which leads to pulmonary venous and arterial hypertension and further compromise of pulmonary function and cardiac output.

It can be difficult to assess the adequacy of left-sided heart structures in patients with critical aortic stenosis. If LCOS persists despite adequate relief of aortic stenosis, the LV or mitral valve could be structurally and functionally inadequate to support a biventricular circulation. In such patients, it is important to consider early conversion to a univentricular strategy; such a conversion can be beneficial if performed before the onset of irreversible end-organ dysfunction.[243,244] When the neonate with critical aortic stenosis has LV failure, severe mitral regurgitation, and a restrictive atrial septum, a balloon aortic valvuloplasty or a surgical aortic valvotomy and hybrid procedure[245] can be beneficial to reduce LA hypertension and increase PBF. This hybrid procedure could include a balloon atrial septostomy or septectomy, bilateral pulmonary artery banding, and maintenance of ductal patency with stenting or PGE_1 infusion. These procedures convert the patient to a palliated single-ventricle physiology in the short term without precluding later conversion to a biventricular circulation.[242,246]

Severe Aortic Valve Regurgitation

Aortic regurgitation creates a volume load for the LV that is similar to that resulting from mitral regurgitation. The volume load causes progressive LV dilation, concentric and eccentric hypertrophy, remodeling, and eventually LV dysfunction. Development of acute severe aortic regurgitation (eg, after balloon valvuloplasty for congenital aortic stenosis or with bacterial endocarditis) is not well tolerated and can cause coronary insufficiency, myocardial ischemia, and rapid progression of LV dilation and dysfunction.

Chronic aortic regurgitation represents a condition of increased volume load and afterload. As the disease progresses, the preload reserve and LV function decline. The risk of postoperative dysfunction increases in the presence of preoperative symptoms, LV dysfunction, and increased LV volume, particularly LV end-systolic volume.[247–250] Postoperative management principles are similar to those outlined in the section on Severe Mitral Valve Regurgitation and include the use of vasodilator agents such as milrinone[237] to reduce afterload and improve cardiac output.

Unique Challenges in CPR

Resuscitation from cardiac arrest in the presence of significant aortic valve disease presents several challenges. In aortic stenosis, the stroke volume and cardiac output generated during chest compressions are reduced because flow across the aortic valve is obstructed. In addition, if the LV is hypertrophied and poorly compliant, limited LV filling will further compromise stroke volume and cardiac output. Chest compressions must generate sufficient aortic root pressure to support adequate coronary perfusion to the hypertrophied myocardium.

In aortic regurgitation, the stroke volume and cardiac output generated during chest compressions are limited by the regurgitant flow across the aortic valve back into the LV. As a result, coronary perfusion pressure and cardiac output can be compromised.

Total Anomalous Pulmonary Venous Connection

In TAPVC, both systemic and pulmonary venous blood return to the right atrium; this results in right atrial dilation and RV dilation and hypertrophy. The LA and the LV are usually adequate but small relative to the RV.

Obstruction to pulmonary venous return results in pulmonary venous congestion and interstitial edema, which impairs gas exchange and increases PVR and PAP. This in turn increases RV afterload, causing RV systolic dysfunction and worsening of RV compliance. Neonates with obstructed TAPVC can present in extremis immediately after birth with a combination of respiratory failure, pulmonary hypertension, and circulatory collapse; preoperative ECLS is occasionally indicated to support Do_2.[251–253]

Surgical repair for neonates with TAPVC and biventricular physiology can be accomplished with low mortality.[254] In the postoperative period, the chronically underfilled LV can have poor compliance,[255] requiring higher filling pressures to maintain adequate stroke volume. Milrinone is often helpful to reduce systemic afterload and improve LV lusitropy and LV function.[237,253] Inadequate LV filling can be exacerbated by the presence of pulmonary hypertension. iNO can be useful and has improved the postoperative care and outcome of neonates with TAPVC.[198] If respiratory failure was present preoperatively (eg, in obstructed TAPVC), it can be further exacerbated after cardiopulmonary bypass. Postoperative respiratory insufficiency and pulmonary hypertension require use of positive end-expiratory pressure to improve alveolar oxygenation. In addition, the standard therapies for treatment of PAH are recommended, including maintenance of adequate oxygen-

ation, avoidance of acidosis and hypoxia, and provision of sedation, analgesia and neuromuscular blockade.[253]

If pulmonary hypertension persists, it is imperative to rule out residual pulmonary venous obstruction by echocardiography and cardiac catheterization, if necessary. ECLS may occasionally be needed for short-term support.[254]

Unique Challenges in CPR

High-quality CPR and resuscitation drugs may be ineffective in generating PBF, LV filling, and cardiac output in infants who have poor LV diastolic function and pulmonary hypertension after correction of TAPVC. It is extremely important to search for and treat possible reversible causes of increased PVR, including inadvertent interruption in targeted pulmonary hypertension drugs, hypercarbia, hypoxia, acidosis, arrhythmia, or cardiac tamponade. If high-quality CPR remains ineffective despite provision of pulmonary hypertension–specific therapy including iNO, 100% oxygen, and establishment of adequate ventilation, ECLS can be beneficial.

Gaps in Knowledge

The evidence supporting recommendations for the care of infants and children with mitral and aortic valve disease is largely extrapolated from adult data, with very limited evidence derived from infants and children.

Recommendations: Left-Sided Heart Disease and TAPVC

1. **Given the increased risk of LCOS after repair or replacement of a significantly regurgitant mitral valve, positive-pressure ventilation and vasodilator agents such as milrinone can be useful to provide afterload reduction and improve cardiac output *(Class IIa; Level of Evidence C)*.**
2. **Persistence of LCOS despite adequate relief of critical aortic stenosis should prompt assessment of adequacy of left-sided structures to support a biventricular circulation *(Class I; Level of Evidence B)*. Conversion to a univentricular strategy can be beneficial before the onset of irreversible end-organ dysfunction *(Class IIa; Level of Evidence C)*.**
3. **Given the increased risk of LCOS after repair or replacement of a significantly insufficient aortic valve, vasodilator agents such as milrinone can be useful to provide afterload reduction and improve cardiac output *(Class IIa; Level of Evidence C)*.**
4. **iNO can be useful for newborns with obstructed TAPVC who demonstrate postoperative pulmonary hypertension after surgical repair *(Class IIa; Level of Evidence B)*.**

Cardiomyopathy and Myocarditis

Cardiomyopathy

The therapies used to treat LCOS and prevent cardiopulmonary arrest in patients with cardiomyopathy are determined by the cardiomyopathy phenotype. The distinct cardiomyopathy phenotypes include (1) dilated cardiomyopathy, (2) hypertrophic cardiomyopathy, (3) restrictive cardiomyopathy, (4) LV noncompaction, and (5) arrhythmogenic RV cardiomyopathy.[256]

Dilated Cardiomyopathy

Dilated cardiomyopathy is the most common phenotype encountered clinically in both children and adults. Careful electrocardiographic monitoring is indicated to assess for atrial or ventricular tachyarrhythmias that could be causing the cardiomyopathy and to assess for frequent ectopy or nonsustained arrhythmias, because these can be harbingers of myocardial irritability or ischemia/infarction and can indicate worsening clinical status. Invasive and noninvasive hemodynamic monitoring can also offer important information to assist in detection and management of prearrest deterioration.

Afterload reduction is an important clinical goal in the setting of dilated cardiomyopathy but must not occur at the expense of end-organ perfusion or coronary/myocardial perfusion. Invasive arterial monitoring provides continuous data to enable better titration of therapy to optimize blood pressure and arterial blood gases. Correction of electrolyte disturbances and avoidance of acidosis are important to maintain cardiac function and avoid worsening ischemia or arrhythmias. Invasive measurement of CVP or PAP provides additional information regarding ventricular preload, diastolic pressures, and cardiac output to aid the titration of therapies and to optimize cardiac function. Ongoing, frequent assessment is required to identify trends in clinical status and need for escalation of care. The potential positive effects of inotropic support must be weighed carefully against the potential negative effects of tachyarrhythmias and increased myocardial oxygen demand and afterload. There are no data to support the use of β-blocking drugs or angiotensin-converting enzyme inhibitors in the management of acute heart failure in the prearrest phase; however, recommendations for their use in stable and chronic heart failure have been described.[257] Consideration of inotropic therapy should prompt a discussion of possible use of ECLS. If ECLS or LVAD support is not available on site, any worsening in the child's clinical status should trigger consideration of referral to a pediatric cardiovascular tertiary care center with mechanical support capability.

Hypertrophic Cardiomyopathy

The management of hypertrophic cardiomyopathy is directed at controlling heart rate and optimizing preload. An elevated heart rate will increase myocardial oxygen

demand, which can create or worsen myocardial ischemia and increase the risk of life-threatening arrhythmias. Any reduction in preload could lead to worsening outflow gradients and could also exacerbate ischemia. In addition, a reduction in preload can decrease cardiac output and compromise end-organ perfusion and function.

Inotropes should be used with caution in patients with hypertrophic cardiomyopathy. Ongoing ischemia or recalcitrant arrhythmias should prompt consideration of ECLS, but the approach might require modification given anatomic constraints of the hypertrophied ventricle. In the later stages of hypertrophic cardiomyopathy, fibrotic burden from persistent ischemia can result in a dilated cardiomyopathy phenotype, for which management principles are outlined in the Dilated Cardiomyopathy section.

Restrictive Cardiomyopathy

Restrictive cardiomyopathy, although a rare phenotype, requires treatment with careful attention to electrocardiographic changes and monitoring for evidence of myocardial ischemia such as symptoms of chest pain and syncope.[258] These patients present with biventricular diastolic dysfunction resulting in pulmonary edema, elevated PVR, myocardial ischemia, and worsening systolic function. As such, the role of inotropes is limited. Blood pressure is optimized through maintenance of adequate diastolic pressures to ensure adequate coronary perfusion in the setting of elevated LV end-diastolic pressures. Patients with restrictive cardiomyopathy, and some subsets of hypertrophic cardiomyopathy, can be prone to bradyarrhythmias and asystole, requiring pacing to avoid cardiovascular collapse.[259]

ECLS should be considered early in the patient's clinical course, because patients with restrictive cardiomyopathy can deteriorate quickly or arrest suddenly with little opportunity for preventative measures.[258,260] In a Pediatric Cardiomyopathy Registry study, the median time from diagnosis to death for those patients who died without transplantation was 0.3 months.[260] ECLS for restrictive cardiomyopathy requires an individualized approach that can be limited by anatomic constraints and the presence of pulmonary hypertension.

LV Noncompaction

LV noncompaction can be associated with other concomitant cardiomyopathy phenotypes, including dilated, hypertrophic, and restrictive cardiomyopathy.[261] Management is typically focused on the associated cardiomyopathy phenotype, which can change over the course of the disease.[262,263] Particular attention should be given to assessment of LV systolic function and monitoring for ectopy and ventricular arrhythmias, because these appear to be strong predictors of outcome.[264]

ECLS strategies are largely dependent on the associated phenotype. As with other cardiomyopathy phenotypes, LV noncompaction is often associated with metabolic diseases and syndromes that may affect other organ systems and device management.[260,261,265]

Arrhythmogenic RV Cardiomyopathy

The development of the arrhythmogenic RV cardiomyopathy phenotype is exceedingly rare in pediatric populations, and management strategies can be found elsewhere.[266]

Myocarditis

Outcomes of infants and children with suspected or confirmed myocarditis can be optimized by early clinical diagnosis and prompt intervention, including early consideration of ICU monitoring and therapy. Fulminant myocarditis can result in decreased cardiac output with end-organ compromise, conduction system disease including complete heart block, and persistent supraventricular or ventricular arrhythmias, all of which can ultimately result in cardiac arrest.[267] Sudden onset of heart block and multifocal ventricular ectopy should be considered as a prearrest state in a patient with fulminant myocarditis. Treatment with external or intracardiac pacing or antiarrhythmic drugs might not be successful, and early transfer to a center for ECLS is recommended.[268,269]

Appropriate treatment of myocarditis can include mechanical ventilation, diuretic drugs for volume overload, afterload reduction, antiarrhythmic drugs or cardioversion for significant arrhythmias, defibrillation for ventricular fibrillation (VF)/pulseless ventricular tachycardia (VT), pacing for advanced heart block, and inotropes for poor perfusion. Inotropes must be titrated with caution, using the lowest possible effective doses, because these drugs can promote arrhythmias and increase myocardial oxygen consumption.[267]

ECLS offers unique opportunities in the clinical management of myocarditis but must be considered in a timely fashion. For patients who have worsening clinical status or incessant ventricular arrhythmias, ECLS can be lifesaving and can help avoid cardiac arrest. ECLS also offers an opportunity to wean inotropic support and assist myocardial recovery or serve as a bridge to cardiac transplantation. The use of ECLS and the use of temporary or more durable ventricular assist devices (VADs) have improved outcomes of myocarditis, with a high possibility of partial or complete recovery of systolic function in the setting of acute fulminant myocarditis.[268]

Unique Challenges in CPR

Once the child with cardiomyopathy or myocarditis develops cardiac arrest, the outcome is poor.[268,270] Patients with dilated cardiomyopathy have extremely poor ventricular function at baseline, and the dramatic reduction in coronary blood flow and myocardial perfusion that occurs with cardiac arrest further worsens an already

fragile myocardial oxygen supply and demand balance, which makes the likelihood of return of spontaneous circulation (ROSC) low. Patients with hypertrophic cardiomyopathy require high ventricular filling pressures to generate adequate stroke volume and cardiac output. In addition, delivery of blood flow from the epicardium through the hypertrophied myocardium to the endocardium is very dependent on an adequate coronary perfusion pressure and perfusion time. During CPR in the patient with hypertrophic cardiomyopathy, it is difficult to maintain a sufficiently high ventricular filling pressure and coronary perfusion pressure to support effective cardiac output and myocardial perfusion. Causes of cardiac arrest in patients with myocarditis include tachyarrhythmias, conduction abnormalities, and severe ventricular dysfunction, often refractory to CPR, defibrillation, and vasopressors. Therefore, for patients with cardiomyopathy and myocarditis, care providers must focus on arrest prevention.

Early ECLS can prevent arrest and enable survival after cardiac arrest, so early consideration is essential.[268,270] Mechanical ventilation might be necessary in the patient with cardiomyopathy or myocarditis who presents with severe LCOS and pulmonary edema. It is important to recognize that this is a prearrest state. The negative inotropic effects of drugs used to induce loss of consciousness, as well as the fall in preload after the loss of spontaneous ventilation and the start of positive-pressure ventilation, can culminate in cardiac arrest. Careful preparation and anticipation are essential so that if intubation is necessary, it is performed under controlled conditions, with immediate availability of ECLS, if possible. Such planning might include early transfer to a center that can provide ECLS.

Gaps in Knowledge

Much of the literature addressing arrest prevention and resuscitation of children with cardiomyopathy is extracted from adult experience and single-center experience. Acute fulminate myocarditis is inadequately studied because it is an uncommon disease, and there is no national myocarditis registry to enable creation of adequate data sets for analysis.

Recommendations: Cardiomyopathy and Myocarditis

1. **Given the high risk of cardiac arrest in children with acute myocarditis who demonstrate high-risk ECG changes (arrhythmias, heart block, ST-segment changes) and/or low cardiac output, early consideration of transfer for ICU monitoring and therapy is recommended *(Class I; Level of Evidence C)*.**
2. **For children with cardiomyopathy or myocarditis and refractory low cardiac output, prearrest use of ECLS can be beneficial to provide end-organ support and prevent cardiac arrest *(Class IIa; Level of Evidence B)*.**
3. **Given the challenges to successful resuscitation of children with cardiomyopathy and myocarditis, once cardiac arrest occurs, early consideration of ECLS can be beneficial *(Class IIa; Level of Evidence B)*.**

Arrhythmias

Cardiac arrhythmias are generally less likely to cause hemodynamic compromise in children than in adults; however, in the setting of CHD with abnormalities in anatomy, physiology, or hemodynamics, cardiac arrhythmias can be the primary cause of cardiac arrest, can contribute to the development of cardiac arrest, or can result from cardiac arrest in children. Given that specific effective therapies are available to treat arrhythmias, prompt recognition and treatment of life-threatening arrhythmias are essential components of pediatric cardiac arrest prevention and cardiac resuscitation.

Supraventricular Tachycardia

Definitions and Mechanisms

SVT is the most common tachyarrhythmia in children,[271] constituting ≈95% of all tachyarrhythmias of childhood.[272] The most common types of SVT are atrioventricular reciprocating tachycardia (bypass tract mediated) and atrioventricular nodal reentrant tachycardia.[273] These tachyarrhythmias are called *atrioventricular node dependent* because the atrioventricular node forms part of the reentrant circuit. One mechanism of atrioventricular reciprocating tachycardia is orthodromic, in which the conduction proceeds antegrade down the atrioventricular node to the ventricle and retrograde conduction occurs from the ventricle through the accessory atrioventricular connection (bypass tract) to the atrium in a circular movement; this results in a narrow QRS tachycardia. Another mechanism of atrioventricular reciprocating tachycardia is antidromic, in which conduction proceeds antegrade down the accessory pathway to the ventricle and retrograde conduction occurs through the atrioventricular node to the atrium; this results in a wide QRS tachycardia.[273] Atrioventricular nodal reentrant tachycardia involves the presence of dual atrioventricular nodal pathways (often referred to as fast and slow pathways), with a reentrant circuit developing between the two.

SVT is characteristically a narrow QRS tachycardia (ie, the QRS configuration is similar to the patient's intrinsic QRS) with little beat-to-beat variability. Heart rates in infants are generally >220 beats per minute and >180 beats per minute in children.[3,4,274] P waves are often difficult to identify because they are obscured by the T

wave and, if present, will be negative (ie, retrograde) in leads II, III, and aVF.

Atrioventricular node–independent atrial tachycardias including atrial flutter, intra-atrial reentrant tachycardia, ectopic atrial tachycardia, and atrial fibrillation can be termed *atrioventricular node–independent tachyarrhythmias* because the atrioventricular node does not form part of the arrhythmia circuit. Atrial flutter involves a reentrant circuit confined to the atria. In typical atrial flutter, the reentry circuit originates near the tricuspid valve annulus. The atrial rate often exceeds 250 beats per minute, which results in a classic sawtooth pattern of the P waves. Intra-atrial reentrant tachycardia, commonly seen after modified Fontan completion, originates from atrial tissue and might not have a classic sawtooth pattern. After surgery for CHD, cardiac surgical incisions can create zones of slow conduction within the atria, which can then become the basis for a reentrant circuit, often referred to as intra-atrial reentrant tachycardia.[275]

In ectopic atrial tachycardia, disordered automaticity causes an atrial focus (or foci) to depolarize at a faster rate than the sinoatrial (sinoatrial node). The P-wave morphology differs from that of the sinus P wave, indicating an origin distinct from the sinoatrial node. Multifocal atrial tachycardia is characterized by at least 3 different P-wave morphologies. Atrial rates range from near normal for ectopic atrial tachycardia to >300 beats per minute for multifocal atrial tachycardia. Atrioventricular conduction is usually 1:1 but can be variable at higher atrial rates.

Atrioventricular node–independent SVT can have a regular or irregular ventricular rate depending on the variability of atrioventricular conduction. P waves can be obvious or indistinct but will differ from those present with a sinus rhythm; the morphology of the P wave is determined by the origin of the atrial arrhythmia.

Clinical Implications of SVT in Children With Cardiac Disease

With the exception of the early postoperative period or in the presence of myocardial dysfunction, most infants are able to tolerate SVT without hemodynamic compromise; however, prolonged episodes of SVT can cause deterioration of cardiac function, and infants can present with or develop congestive heart failure or cardiovascular collapse.[276] Older children might complain of palpitations, chest discomfort, lightheadedness, or dizziness. Children with underlying CHD or myocardial dysfunction can have a variable presentation depending on the rate of ventricular response and degree of ventricular dysfunction. They often demonstrate signs and symptoms of poor perfusion. The combination of an atrioventricular node–independent tachycardia with antegrade accessory pathway conduction can result in rapid atrioventricular conduction and hemodynamic collapse. In children with CHD and myocardial dysfunction or severe atrioventricular valve or semilunar valve insufficiency, SVT can cause poor ventricular diastolic filling, reduced cardiac output, and even cardiac arrest.

Junctional Ectopic Tachycardia

JET is an automatic rhythm that originates from the atrioventricular node or high in the His-Purkinje system and gives rise to a narrow QRS complex similar to that of sinus rhythm. It is most commonly observed in the early postoperative period, when patients are most vulnerable to hemodynamic instability. Postoperative JET occurs in ≈14% of infants[277] and 6% to 8% of children after CHD surgery.[278,279] The highest incidence (20%–26%) of JET after surgery occurs for TOF, aortic arch/VSD repair, d-TGA with VSD, and atrioventricular septal defect repair, as well as after procedures with longer aortic cross-clamp times.[277,279,280]

Although JET is usually self-limited, it can cause significant hemodynamic instability. JET is effectively treated with atrial overdrive pacing (or dual-chamber pacing if heart block is present). Adjunctive therapies to treat JET include limiting the use of inotropic agents, ensuring adequate sedation and analgesia, and temperature reduction (hypothermia). These therapies can eliminate JET or slow it sufficiently to facilitate atrial overdrive pacing.[280,281] Procainamide has been effective in treating JET in single-center case series.[280,282] Amiodarone was successful in treating JET in a multicenter, randomized, prospective dose-response study, but adverse events (including dose-related hypotension, bradycardia, and atrioventricular block) were common.[283]

VT and VF

VT produces rapid, wide QRS complexes that differ from the patient's intrinsic QRS complexes. VT can be monomorphic (uniform QRS complexes) or polymorphic (differing QRS complexes). A specific type of polymorphic VT is torsade de pointes ("turning of points"), in which the QRS complexes gradually change phase from positive to negative polarity. Monomorphic VT can produce a pulse if the rate of the VT is not too rapid. Although polymorphic VT can initially produce a pulse, it typically deteriorates very rapidly to pulseless VT or VF. VF is marked by coarse or fine disorganized, chaotic electrical activity with no discernible QRS complexes and no pulses.

VF and pulseless VT are shockable cardiac arrest rhythms. Pulseless VT is uncommon in children and is grouped with VF because it soon degenerates into VF.[284,285] VF/pulseless VT are less common terminal rhythms during cardiac arrest in children than in adults, occurring in 5% to 18% of pediatric out-of-hospital cardiac arrests and up to 27% of pediatric in-hospital cardiac arrests.[286–294] The incidence of VF/pulseless VT as a terminal arrest rhythm increases with age and has a cardiac origin in 21% to 74% of reported cases.[291–299]

Survival from VF/pulseless VT ranges from 0% to 30% and is typically associated with good neurological outcome when it is the initial arrest rhythm.[288,292,293] In a study from the GWTG-R Registry of CPR involving 1005 children who experienced in-hospital cardiac arrest, 27% had documented VF/pulseless VT during the arrest; initial VF/pulseless VT was present in 10%; and subsequent VF/pulseless VT occurred in 15% (in 2% of the patients, the timing of the VF/pulseless VT was not noted). Among children who experienced initial VF/pulseless VT, 35% survived to hospital discharge compared with 11% of those who experienced subsequent VF/pulseless VT. Survival in those who had subsequent VF/pulseless VT was also substantially worse than in those who had no VF/pulseless VT at all during their arrest. Subsequent VF or pulseless VT likely occurs as a reperfusion arrhythmia in the course of resuscitative efforts. Possible explanations for the lower survival include delayed diagnosis of VF/pulseless VT during resuscitation or severity of the underlying myocardial condition. Although the CPR interventions were similar, administration of sodium bicarbonate, epinephrine, atropine, vasopressin, calcium, and antiarrhythmic agents and use of extracorporeal membrane oxygenation (ECMO) were higher in the subsequent VF/pulseless VT group.[293]

Long-QT Syndrome

Long-QT syndrome (LQTS) is a disorder of prolonged cardiac repolarization associated with ventricular arrhythmia and an increased risk of syncope and sudden death throughout childhood and young adulthood. The syndrome results from genetic defects in cardiac ion channel function, causing QT-interval prolongation and increased risk of the torsade de pointes–type of polymorphic VT.[295,296] Classification is based on genetic analyses of distinct ion channel mutations, which account for ≈70% of LQTS case.[295]

Specific triggers of torsade de pointes include exercise, swimming, startle response, loud noises, emotional lability, and bradycardia during sleep.[296,297] Molecular analysis of victims of sudden infant death syndrome has implicated LQTS as a potential cause of some deaths.[298]

Drug-induced prolongation of the QT interval led to the description of acquired LQTS.[299] The pathophysiology of acquired LQTS is believed to be similar to congenital LQTS.

Treatment of Arrhythmias

Vagal Maneuvers and Pharmacological Interventions

Vagal maneuvers are noninvasive, nonpharmacological techniques to convert SVT to sinus rhythm through slowing of atrioventricular nodal conduction. Valsalva maneuver, ice to the face, and carotid sinus massage have varying degrees of success and minimal adverse effects.[300,301]

Adenosine is the drug of choice for atrioventricular node–dependent SVT that occurs from a reentrant mechanism.[302,303] Adenosine slows conduction through the atrioventricular node, terminating the SVT. Because adenosine has a short duration of action, the tachyarrhythmia can recur, and repeat doses may be needed. Administration of adenosine should not delay direct current cardioversion for tachyarrhythmia resulting in hemodynamic instability. Adenosine will not effectively terminate atrioventricular node–independent tachycardias, such as atrial flutter, ectopic atrial tachycardia, or atrial fibrillation; however, its use in these arrhythmias can have diagnostic value in slowing atrioventricular conduction so that in the presence of atrioventricular block, the type of atrial activity is identifiable on ECG.[302]

Esmolol is an ultrashort-acting agent with specific β_1-adrenergic antagonism that has also been shown to be an effective treatment for SVT in children.[304,305] Propranolol is a longer-acting nonspecific β-blocker that in addition to termination of the SVT can also prevent recurrence. However, bradycardia, hypotension, and hypoglycemia are side effects.[306,307]

Procainamide and amiodarone are effective for treating various types of SVTs in children.[280,283,308–322] These agents both prolong the QT interval and should not be used concurrently without expert consultation from a cardiologist because they could precipitate the torsade de pointes–type VT. Verapamil should not be used in infants because it has caused shock and cardiac arrest in this population.[323,324] A small, prospective, nonrandomized trial showed that dexmedetomidine reduced the incidence of tachyarrhythmia after congenital heart surgery in infants and children[282]; additional supportive data are needed.

Wide QRS complex tachycardia warrants special mention. In the absence of an underlying bundle-branch block, wide QRS complex tachycardia represents 1 of 4 arrhythmias: VT, orthodromic SVT with aberrant QRS conduction, antidromic SVT, or atrial arrhythmia with antegrade accessory pathway conduction. In one series describing children with wide QRS tachycardia, 20% were found to have VT, whereas 80% had variable mechanisms of SVT as the cause.[325] In another study, orthodromic SVT with aberrant QRS conduction was reported to occur in up to 10% of cases of wide QRS complex tachycardia in children.[326] Adenosine should not be administered for wide QRS complex tachycardia unless it is clear that the underlying rhythm is not atrial fibrillation or atrial flutter with associated antegrade accessory pathway conduction. Blocking of the atrioventricular node in this setting can result in rapid atrioventricular conduction and likely hemodynamic collapse. Expert consultation should be obtained before administration of adenosine as a diagnostic and potentially therapeutic intervention for stable patients who have wide QRS complex tachycardia.

Unstable wide QRS complex tachycardia should be assumed to be ventricular in origin, and prompt cardioversion (if pulses are present) or defibrillation (if pulses are absent) is indicated (see Cardioversion and Defibrillation During Resuscitation). For incessant or unstable ventricular arrhythmias (VF or pulseless VT), amiodarone can be considered, although careful monitoring for hypotension and other adverse effects is required.[3,283,327] On the basis of the 2015 AHA PALS guidelines update, lidocaine may also be considered for the treatment of VF or pulseless VT.[3]

β-Blockers and implantable cardioverter-defibrillators are the mainstays of therapy for LQTS. Advances in the past 2 decades have facilitated gene-directed therapy.[328]

Breakthrough or refractory episodes of torsade de pointes have been described and should be treated according to AHA/PALS guidelines,[3,329,330] with infusion of magnesium sulfate and avoidance of antiarrhythmic drugs such as amiodarone and procainamide that prolong the QT interval. Increasing the heart rate, thus shortening the QT interval, is standard therapy for critically ill patients with breakthrough or refractory torsade de pointes and VF in the setting of LQTS. This can be accomplished with temporary pacing or isoproterenol infusion.[299]

Pacing

After surgical repair or palliation of CHD, temporary epicardial pacing wires are typically inserted. Recommendations regarding pacing in the postoperative setting are empirical rather than evidence based. Pacing is routinely used in critical but nonemergent situations to improve cardiac output. Overdrive burst pacing can terminate reentrant atrial and VTs. Other indications for atrial pacing include sinus node dysfunction and overdrive pacing for JET.

The major indication for dual-chamber or ventricular pacing is complete heart block. Biventricular pacing has been examined as a means of improving ventricular dysfunction via cardiac resynchronization.[144,331] If pacing is effective, there will be an improvement in cardiac output, as assessed by improved perfusion and blood pressure, fall in serum lactate, and rise in mixed Svo_2 or NIRS.

The 2015 AHA Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care[3,4] recommendations regarding pacing during resuscitation in children are also empirical. Pacing wires, if present, should be used for pacing patients with sinus bradycardia or complete heart block. For symptomatic bradycardia unresponsive to oxygen and adequate airway and ventilation, transcutaneous cardiac pacing is of potential benefit for patients with intrinsic sinus node dysfunction or complete heart block, especially if associated with congenital or acquired heart disease.

Transcutaneous pacing may have a potential role in the management of the following[332]: (1) sinus node dysfunction with bradycardia after cardioversion for atrial tachyarrhythmia; (2) complete heart block with development of significant bradycardia during general anesthesia for a surgical procedure; (3) patients with permanent pacemakers who are at risk for developing significant bradycardia during pacemaker reprogramming or replacement; and (4) patients who develop a drug-induced bradycardia.

Cardioversion and Defibrillation

Please refer to the Cardioversion and Defibrillation During Resuscitation section.

Gaps in Knowledge

Little information is available regarding the optimal drugs and doses for treatment of pediatric arrhythmias. In addition, although there are data on the use of multisite pacing for cardiac resynchronization in the postoperative setting, the longer-term benefit is unknown.

Recommendations: Arrhythmias

1. **Adenosine is an effective therapy for orthodromic (narrow QRS complex) reentrant SVT *(Class I; Level of Evidence B)*.**
2. **Adenosine administration can be useful as a diagnostic tool but may not be effective to convert wide-complex SVT, ectopic atrial tachycardia, atrial fibrillation, and atrial flutter *(Class IIa; Level of Evidence B)*.**
3. **Amiodarone and procainamide can be effective therapies for JET, although side effects are common *(Class IIa; Level of Evidence B)*.**
4. **Postoperative JET is effectively treated with atrial overdrive pacing *(Class I; Level of Evidence B)*. Adjunctive therapies that can be useful to treat JET include careful titration to limit the use of inotropic agents, ensuring adequate sedation and analgesia, treatment of fever, and, as tolerated, temperature reduction (hypothermia). These therapies may eliminate JET or slow it sufficiently to facilitate atrial overdrive pacing *(Class IIa; Level of Evidence B)*.**
5. **Amiodarone or lidocaine can be considered for postoperative VF and pulseless VT *(Class IIb; Level of Evidence C)*.**
6. **Neither amiodarone nor procainamide should be administered in patients with known or suspected LQTS without expert consultation *(Class III: Harm; Level of Evidence C)*.**
7. **Temporary epicardial pacing can be effective for postoperative patients in low cardiac output with sinus node dysfunction,**

JET, or complete heart block *(Class IIa; Level of Evidence C)*.

8. **For postoperative patients who develop symptomatic complete heart block, epicardial pacing is recommended *(Class I; Level of Evidence C)*. When pacing wires are not present, transvenous or short-term transcutaneous pacing can be beneficial *(Class IIa; Level of Evidence C)*.**

Age-Dependent Factors Influencing CPR in the Neonate and Infant

An understanding of late fetal and early neonatal myocardial, pulmonary, and brain developmental physiology is helpful to tailor resuscitation therapies in the neonatal and infant population. During the late fetal and early neonatal period, cell division is the major cause of the increase in myocardial mass. This cell division largely ceases by the second month of life; any further increase in ventricular mass is related to hypertrophy.[333,334] During the neonatal and infant period, myocyte and myocardial organization and development of the contractile apparatus and extracellular matrix result in increased ventricular compliance and contractility.[335,336] The heart of the premature infant has smaller myocardial mass and a thinner LV free wall relative to that of the older infant or child, which results in limited ability to increase stroke volume.[333] After birth, LV work increases significantly as separation from the placenta increases SVR. As a result, LV muscle mass increases and LV filling pressure rises, which increases LV stroke volume. At the same time, RV work decreases as PVR falls, and RV stroke volume, PBF, and LV preload increase.[337] These changes produce a gradual increase in systemic cardiac output and Do_2 during infancy and childhood. Although neonates can modestly increase stroke volume in response to volume administration, the Frank-Starling relationship between filling pressure and stroke volume seemingly exerts a greater effect on ventricular function with increasing postnatal age. For these reasons, neonates and young infants are very dependent on adequate heart rate to maintain and increase cardiac output, an important consideration during all phases of resuscitation.

The neonatal cardiovascular system functions with high levels of endogenous catecholamines and is more dependent on sympathetic stimulation than the adult heart. Inotropic agents can further increase cardiac output in the sick neonate, although response to catecholamines will be modified by conditions that produce upregulation or downregulation of adrenergic receptors.[338,339] The junctional sarcoplasmic reticulum is the region of the sarcoplasmic reticulum closest to the sarcolemma and is the most important structure in controlling cytosolic calcium concentration in the myocardium during contraction. The number of junctional sarcoplasmic reticula increases during late gestation and neonatal life, which, over time, increases the inotropy that can be modulated by cytosolic calcium.[340] This maturation process influences any measures targeting increasing intracellular calcium as a means to improve contractility.[340] As a result, calcium administration to the neonate or infant with low cardiac output can be beneficial to increase both heart rate and contractility.[341,342] Similarly, administration of calcium channel blockers to the neonate can compromise myocardial performance.

The fetal and neonatal myocardium appears to be more resistant to hypoxemia than adult myocardium.[343] The neonatal heart can work almost as effectively after the reversal of a significant hypoxic-ischemic event as before the ischemic event, whereas the function of the adult heart usually becomes significantly depressed after a hypoxic-ischemic insult.[343,344] This increased resilience of the neonatal myocardium to hypoxemia is beneficial during the surgical repair, recovery, and resuscitation of newborns with CHD.

Congenital heart lesions are often classified as critical if they are dependent on blood flow through the ductus arteriosus to support either PBF or SBF. PVR in the fetus is greater than SVR. PVR normally decreases to one-half systemic arterial pressure in the first 24 hours of life and further falls to normal levels by ≈2 weeks after birth.[345] The postnatal decline in PVR can be slower in neonates with CHD because of the presence of elevated PAP, LA or pulmonary venous pressure, or left-to-right shunting. Once PVR falls, signs and symptoms of congestive heart failure can develop secondary to increasing left-to-right shunting. In very premature newborns with CHD, the PVR can be low at birth, leading to a very large Qp:Qs and poor systemic cardiac output, which can be difficult to manage. Any conditions that cause a fall in PVR (eg, administration of supplementary oxygen, creation of respiratory alkalosis) can result in significant pulmonary overcirculation and inadequate systemic cardiac output and Do_2.[346] To improve systemic cardiac output and Do_2 and reduce the risk of cardiac arrest, it can be necessary to increase PVR to modify the unfavorable Qp:Qs ratio. (See Balancing SBF and PBF in the section on Single-Ventricle Lesions.)

The capacity of organs to sustain perfusion in low cardiac output states is determined by their capacity for autoregulation; the neonatal heart, brain, and kidneys are efficient at autoregulation and can maintain blood flow over a wide range of perfusion pressures. Skin and muscles have poor autoregulatory capabilities, and decreased skin perfusion is characteristically an early visible marker for decreased systemic cardiac output in infants. Anaerobic metabolism is used when organ blood flow and Do_2 decrease below a critical level (the anaerobic threshold), causing accumulation of lactic acid and impairment of organ function. Through adrenergic stimulation, which increases heart rate, SVR, and the

redistribution of blood flow, neonates and pediatric patients can initially maintain SVR, systolic blood pressure, and organ perfusion despite a fall in cardiac output. Blunting of this neurohumoral response in critically ill children (eg, with administration of sedation) can produce circulatory collapse; therefore, sedatives and analgesic drugs should be given with caution, especially in the unstable neonate with CHD.

Data suggest that brain maturation and development are impaired in neonates with complex CHD.[347–349] The delays in development arise from failures in brain oxygen and nutrient delivery unique to certain forms of CHD, with examples of deficient content (dextro-TGA)[350] or abnormalities in blood flow (HLHS).[351,352]

Brain and heart development occur simultaneously in the fetus with CHD. Early morphogenetic programs in each organ share common genetic pathways.[353–355] Brain development occurs across a more protracted time course, with striking brain growth and activity-dependent formation and refinement of connections in the third trimester.[356]

Delayed fetal brain maturation and development in utero appears to begin in the third trimester of gestation and is consistent with postnatal data demonstrating smaller head circumferences and structurally immature brains in term gestation neonates with CHD, particularly in those with HLHS, compared with normal term neonates.[357] Delays in cellular maturation contribute to the gross structural immaturity of the brain. The maturation of oligodendrocytes has been closely associated with an increased risk for hypoxic and oxidative injury to the white matter that is often seen in neonates with complex CHD both before and after cardiac surgery.[358,359] Brain immaturity is also a risk factor for periventricular leukomalacia in these neonates.[347] Understanding cerebral blood flow regulation during fetal development, the transitional circulation, intraoperative perfusion strategies, and postoperative recovery will be central to neuroprotective studies in the future.[360]

To minimize the risk of brain injury in the neonate or infant with CHD, every effort must be made to optimize systemic Do_2 during the perioperative period. Use of therapeutic induced hypothermia has been reported to improve functional survival in neonates after birth-related hypoxic-ischemic insult,[361] but there are no data to support this treatment after delivery, after cardiac arrest, or after cardiac surgery. The neonatal brain has significant potential for regeneration, and the extent of neurological injury related to cardiac arrest can be difficult to determine in the post–cardiac arrest phase.[362] Intraventricular hemorrhage can occur in sick neonates secondary to rupture of immature vessels in and around the germinal matrix. Intraventricular hemorrhage has very little predictive value for neurodevelopmental outcomes and should not be used as a deterrent to continue resuscitative efforts and optimization of care.[363]

The neonatal periventricular white matter is sensitive to inflammation that can be triggered by cardiopulmonary bypass or ECMO. This effect seems less pronounced in more mature (>36 weeks' gestational age) neonates.[347,364]

Gaps in Knowledge

Little is known about the optimal timing of and the potential limits to interventions in premature infants, small for gestational age neonates, or full-term neonates with CHD. Even less is known about the effects of resuscitative strategies on premature or underdeveloped lungs and relatively immature brains. Cardioprotective and neuroprotective therapies in the perioperative period continue to be investigated.

Recommendations: Age-Dependent Factors Influencing CPR

1. **Newborns with ductal-dependent systemic circulation are at risk for pulmonary overcirculation and inadequate systemic perfusion and Do_2. In the neonate with pulmonary overcirculation, minimizing exposure to supplementary oxygen and minimizing hyperventilation can be beneficial to maintain adequate systemic perfusion and Do_2 *(Class IIa; Level of Evidence C)*.**
2. **Calcium administration to the neonate or infant with low cardiac output can be considered to increase both heart rate and contractility *(Class IIb; Level of Evidence C)*.**
3. **Calcium channel blockers should be used with caution in newborns *(Class IIa; Level of Evidence C)*.**

PHARMACOLOGICAL INTERVENTIONS

Dosing and Delivery

Drug doses should be based on ideal body weight, which can be estimated from length (using a length-based tape) if needed.[3,4] Subsequent doses can be titrated to effect but should not exceed adult doses. Effective medication delivery requires circulation, which can be delayed in the prearrest phase or require chest compressions if there is inadequate native cardiac output.

Central venous access, if already present, is the preferred route of medication delivery for the unstable patient and during resuscitation.[3,4] During cardiac arrest, if central venous access is not present or readily established, peripheral venous access is acceptable if it can be placed rapidly. If peripheral intravenous access is not already present and cannot be achieved immediately, intraosseous access should be established. The current

ease and sophistication of intraosseous devices makes intraosseous access a reliable route for drug delivery and minimizes the need for the (less reliable) endotracheal route of drug administration. Peripheral intravenous administration of vasoactive medication and electrolytes can result in significant damage at the site and to distal extremities if the medications infiltrate the tissue.

Anesthetic and Analgesic Agents

The provision of sedation and analgesia in the child with congenital or acquired heart disease often requires a modified approach based on the impact of various medications on ventricular preload, ventricular function, and arteriolar resistance in the pulmonary and systemic vascular beds.[365] During the prearrest phase, patients often require sedation and analgesia during escalating care for low cardiac output or for associated procedures. In the setting of effective CPR and semiconsciousness, the patient may require sedation and analgesia. The choice and dosing of medications should minimize hypotension.

Dexmedetomidine

Dexmedetomidine is an α_2-receptor agonist. It provides effective sedation and mild analgesia without respiratory depression.[366] Retrospective reviews noted a significant decrease in heart rate early during dexmedetomidine infusion in infants and children after cardiac surgery, including heart transplantation.[367–369] In 2 small case series of children during electrophysiological testing, dexmedetomidine caused a mild but significant decrease in sinus[370,371] and atrioventricular node function,[371] with neonates and infants demonstrating a more significant decrease in heart rate. Although clinically significant bradycardia was not reported, the effect of dexmedetomidine on heart rate can be more pronounced in children at high risk for postoperative heart block or those receiving other drugs (eg, β-blockers or antiarrhythmic drugs) that can produce bradycardia. Rebound tachycardia and an increase in mean arterial pressure have been reported.[367,370,371] Inotropic scores are reportedly lower with dexmedetomidine after heart surgery.[367–369]

Dexmedetomidine has additional benefits as an antiarrhythmic drug (see Arrhythmias). The terminal elimination half-life of dexmedetomidine in adults is ≈2 hours, whereas it is 3.2 hours in term neonates and 7.6 hours in preterm neonates.[372] Elimination is prolonged by hepatic dysfunction.

The combined benefit of sedation without respiratory depression, reduction in inotropic requirements, and antiarrhythmic effects makes dexmedetomidine an appealing therapy for sedation after congenital heart surgery. Caution is needed for patients with heart rate–dependent cardiac output and those at risk for symptomatic bradycardia or heart block, unless pacing wires are present.

Etomidate

Etomidate is a nonbarbiturate hypnotic drug with a rapid onset and short half-life. It has minimal hemodynamic effects. It reversibly inhibits 11-β-hydroxylase, causing adrenal suppression, which has been reported after even a single dose.[373] Etomidate can be used for the stable patient who requires a short procedure or rapid sequence intubation, but in 2010, the AHA PALS guidelines noted that etomidate should not be used routinely in pediatric patients with evidence of septic shock,[4] citing reports of adrenal suppression and higher mortality rates after use of the drug in this population.[374]

Fentanyl

Fentanyl is a synthetic opioid that provides effective analgesia with minimal hemodynamic effects. Bolus dosing to the naive infant can cause chest wall rigidity.[375]

Ketamine

Ketamine causes dissociation between the cortex and the limbic system, providing sedation, analgesia, and amnesia while maintaining respiratory drive and hemodynamics. Ketamine is thought to be an ideal drug for use in children with heart disease because it provides central cardiovascular stimulation and inhibits the reuptake of catecholamines, typically resulting in mild to moderate increases in blood pressure, heart rate, and cardiac output. It can have direct negative inotropic properties and should be titrated cautiously in patients with very poor ventricular function.[376] Because it can increase myocardial oxygen demand, it should be used cautiously in patients with severe heart failure and risk of myocardial ischemia.[377] The incidence of agitation during recovery in children is reported at 8%, with increasing incidence with older age and higher dose.[378,379] Prospective trials failed to show significant relief of the agitation with adjunctive low-dose midazolam.[379,380] Although there is little downside to use of supplementary low-dose midazolam in the hemodynamically stable patient, it should be used cautiously in the child with cardiovascular instability.

Propofol

Propofol is a rapid-onset, short-acting hypnotic agent that allows rapid recovery of level of consciousness after administration is stopped. It can cause hypotension and a decrease in cardiac output, cardiac index, and stroke volume index through direct myocardial depression and vasodilation; it should be used with extreme caution in the setting of hypotension and compromised cardiac function. In addition, propofol can inhibit mitochondrial function because it acts as an uncoupling agent in oxidative phosphorylation, so it should not be used in children with mitochondrial disease.[381] Propofol is not approved in children for prolonged sedation after cardiac surgery or in the critical care unit because of the hemodynamic complications and risk for propofol-infusion syndrome.[382]

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To minimize the risk of brain injury in the neonate or infant with CHD, every effort must be made to optimize systemic Do_2 during the perioperative period. Use of therapeutic induced hypothermia has been reported to improve functional survival in neonates after birth-related hypoxic-ischemic insult,[361] but there are no data to support this treatment after delivery, after cardiac arrest, or after cardiac surgery. The neonatal brain has significant potential for regeneration, and the extent of neurological injury related to cardiac arrest can be difficult to determine in the post–cardiac arrest phase.[362] Intraventricular hemorrhage can occur in sick neonates secondary to rupture of immature vessels in and around the germinal matrix. Intraventricular hemorrhage has very little predictive value for neurodevelopmental outcomes and should not be used as a deterrent to continue resuscitative efforts and optimization of care.[363]

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PHARMACOLOGICAL INTERVENTIONS

Dosing and Delivery

Drug doses should be based on ideal body weight, which can be estimated from length (using a length-based tape) if needed.[3,4] Subsequent doses can be titrated to effect but should not exceed adult doses. Effective medication delivery requires circulation, which can be delayed in the prearrest phase or require chest compressions if there is inadequate native cardiac output.

Central venous access, if already present, is the preferred route of medication delivery for the unstable patient and during resuscitation.[3,4] During cardiac arrest, if central venous access is not present or readily established, peripheral venous access is acceptable if it can be placed rapidly. If peripheral intravenous access is not already present and cannot be achieved immediately, intraosseous access should be established. The current

with amiodarone and lidocaine in the treatment of pediatric patients with VF/pulseless VT in-hospital cardiac arrest, lidocaine (versus no lidocaine) was associated with an increase in likelihood of ROSC.[386] These same registry data did not show an association between lidocaine or amiodarone use and survival to hospital discharge.[3] For patients with LQTS or other channelopathies, lidocaine can be safely delivered, whereas amiodarone can precipitate torsade de pointes.[387]

Dexmedetomidine

Dexmedetomidine is an α_2-receptor agonist, initially introduced as a sedative. In pediatric patients with SVT, dexmedetomidine has been shown to decrease sinus and atrioventricular node function while maintaining blood pressure.[371] In a prospective, nonrandomized study of pediatric postoperative patients after surgery for CHD, dexmedetomidine was associated with a significant reduction in arrhythmias, including VT, JET, and SVT, without a significant increase in heart block.[282]

Esmolol

Esmolol is a cardioselective β_1-antagonist with a short half-life[304] and minimal side effects.[388] Esmolol can decrease the rate and occasionally suppress ectopic atrial tachycardia. Refractory or recurrent reentrant SVT can be slowed and converted (often in conjunction with rapid atrial pacing, adenosine, or electric cardioversion).

Procainamide

Procainamide is a class Ia antiarrhythmic that blocks sodium channels and prolongs QRS duration. It is most commonly used for atrial tachyarrhythmias and JET.[280] Serum levels should be monitored to avoid toxicity, and it depresses myocardial function.[280] In a single-center case series of 37 pediatric patients, procainamide was more effective than amiodarone for treatment of recurring SVT, with a lower incidence of adverse effects.[389] Procainamide should not be used in children with LQTS without expert consultation.

Verapamil

Verapamil is a class IV antiarrhythmic drug that functions as a calcium channel blocker. It can be used for SVT in older children but should not be used in infants <1 year of age and should be particularly avoided in neonates, because they have limited intracellular calcium stores.[3,4] In patients with Wolff-Parkinson-White syndrome, verapamil can facilitate conduction through the accessory pathway, resulting in hemodynamic collapse or VF in the setting of associated atrial fibrillation or flutter.[390]

Electrolytes and Minerals

Electrolyte and mineral imbalances can cause arrhythmias and attenuate the effectiveness of cardioversion, defibrillation, and pacing.

Calcium

Calcium is a potent inotrope in neonates and infants because they have limited intracellular calcium stores. Administration of calcium can be associated with improved myocardial function, as demonstrated by improved blood pressure and echocardiographic evidence of improved systolic function.[341,342] Calcium can also be effective in other patients with limited intracellular calcium stores, such as those receiving blood products containing citrate-phosphate dextran preservative (see Age-Dependent Factors Influencing CPR in the Neonate and Infant).

Calcium can be administered as calcium chloride or calcium gluconate, with little evidence that either is superior. The 2010 AHA PALS guidelines[3,4] note that calcium chloride may be preferred because it results in a greater increase in ionized calcium during therapy than calcium gluconate. However, calcium gluconate has lower osmolality and is recommended if the drug must be administered through a peripheral intravenous catheter or to a neonate.

Once an arrest has occurred, however, the role of calcium is less clear. Two recent articles reported an association between calcium use during in-hospital pediatric CPR and risk of mortality.[391,392] Both were retrospective reviews, 1 single-center (n=19)[392] and 1 multicenter (n=1477)[391] study that found that patients receiving calcium were significantly less stable and were more likely to be in an ICU, receiving mechanical ventilation support and vasoactive infusions. Factors not included in either analysis were prearrest serum ionized calcium concentration, the hemodynamic response to calcium administration, the dose of calcium, and the point during the arrest when calcium was administered. During cardiac arrest, calcium administration is not recommended in the absence of documented ionized hypocalcemia, hypermagnesemia, or hyperkalemia, and it can be harmful by increasing intracellular calcium after myocardial reperfusion.

Magnesium

Magnesium is helpful for treatment of torsade de point or when hypomagnesemia is present. Other than hypotension, there is little downside to administration of magnesium.

Potassium

Administration of potassium is rarely indicated during resuscitation, because metabolic acidosis is associated with intravascular shift of potassium and a rise in serum potassium concentration. However, potassium administration may be required to treat hypokalemia associated with arrhythmias.

Sodium Bicarbonate

Early animal studies showed improved myocardial performance in the absence of acidosis. Significant meta-

bolic acidosis can result in myocardial dysfunction and pacemaker noncapture. In addition, sodium bicarbonate is a reasonable therapy for hyperkalemia in the presence of acidosis. Alkalosis is a potent pulmonary vasodilator, and sodium bicarbonate is a useful therapy during pulmonary hypertensive crises while specific pulmonary vasodilators are being prepared.[188]

In a retrospective, multicenter cohort study of pediatric patients who had out-of-hospital cardiac arrest, the use of sodium bicarbonate was associated with worse survival.[393] The routine use of sodium bicarbonate during cardiac arrest is not recommended in the 2010 PALS guidelines.[3,4]

Other Drugs

Furosemide

Furosemide has limited use in the prearrest phase and likely no use during CPR. For patients with a perfusing rhythm but a dilated heart with poor function and volume overload, furosemide can help reduce myocardial stretch and avoid cardiac arrest.

Heparin

Heparin should be part of the first line of therapy for a patient with decompensation secondary to known or presumed aortopulmonary shunt occlusion. A heparin dose of 50 to 100 U/kg is appropriate,[394] depending on the clinical situation.

Heparin (100 U/kg) is usually administered to patients immediately before ECLS cannulation.[395] The dose can be modified in patients at high risk for bleeding, with known or anticipated coagulation abnormalities, or with heparin-bonded circuits, as well as for venovenous ECLS.[394]

Inhaled Medications

Nitric Oxide

iNO is a selective pulmonary vasodilator that results in smooth muscle relaxation and vasodilation.[201] iNO has been well demonstrated to attenuate pulmonary hypertension of the neonate.[396] iNO is a first-line therapy for postoperative pulmonary hypertension.[397] In the acute setting, there is little downside to a therapeutic trial of iNO unless the patient has pulmonary venous obstruction, mitral stenosis, or dilated cardiomyopathy. In patients with elevated pulmonary venous pressure, iNO will increase PBF and venous return, which, in the face of fixed obstruction or a dilated heart with elevated filling pressure, can worsen pulmonary edema and result in clinical deterioration.

Oxygen

Supplementary oxygen administration is generally helpful for treatment of the patient in prearrest and arrest, although caution should be used when administering high concentrations of oxygen to premature infants or to anyone with an unrestrictive aorta-to-pulmonary connection (eg, patent ductus arteriosus, aortopulmonary window, truncus arteriosus), because it can cause pulmonary vasodilation with increased Qp:Qs, compromising SBF. It is unknown whether hyperoxia is detrimental in the post–cardiac arrest phase, and the 2015 PALS guideline update recommendation is that once the patient is stable in the post–cardiac arrest period, it can be reasonable for providers to target normoxemia[3,398] (see Pulmonary Management in the section on Post–Cardiac Arrest Stabilization).

Administration of oxygen, with close monitoring, can be beneficial in the setting of apnea or lung disease, while preparing for endotracheal intubation, and before and after suctioning of the endotracheal tube. A past concern that oxygen was harmful to neonates after the stage 1 Norwood palliation more likely reflected the negative effects of oxygen in the setting of an inappropriately large systemic-to-pulmonary shunt. In patients with an appropriately sized shunt after the stage 1 Norwood palliation, oxygen administration has been shown to improve systemic Do_2 without compromising SBF (as determined by unchanged AVo_2D).[94]

Muscle Relaxants and Neuromuscular Blockade

In the prearrest phase, patients requiring endotracheal intubation will likely require administration of a muscle relaxant. When the child is in shock or has severe heart failure, administration of muscle relaxants and loss of spontaneous ventilation can precipitate decompensation, so providers must be prepared to support airway, oxygenation, and ventilation, as well as cardiac output and systemic perfusion. Administration of neuromuscular blockers will prevent motor responses to pain and will mask signs of seizures. The patient's level of consciousness will then have to be assessed by vital sign responses to stimulation, voice, or painful stimuli.

Steroids

The relationship between serum cortisol levels and postoperative hemodynamics after congenital heart surgery is not well understood.[399,400] Although administration of stress doses of hydrocortisone are reported to improve systolic blood pressure and reduce inotropic score,[400–402] a survival benefit has not been demonstrated. Hydrocortisone is typically used for neonates and infants with volume-resistant hypotension requiring escalating inotropic support. Short-term stress dosing of hydrocortisone is preferred because of the risk for healthcare-acquired infection and delayed wound healing.[403,404] Single-center studies of preoperative and intraoperative methylprednisolone for neonatal and infant congenital

heart surgery showed reduction in inflammatory mediators and postoperative morbidity[405,406]; however, these findings were not supported in a multicenter database analysis.[407]

Atropine

Atropine is a parasympathetic agent. Functioning as an acetylcholine antagonist, atropine augments atrioventricular node conduction and sinus node automaticity. Atropine is effective for vagally mediated bradycardia and can sometimes be helpful in the setting of complete heart block. Atropine can be considered for premedication of patients who are unlikely to tolerate bradycardia, (eg, such as can occur with the administration of succinylcholine and during laryngoscopy). There is little evidence that atropine is beneficial in the treatment of cardiac arrest, but it has been demonstrated to be effective in adults in the prearrest phase for symptomatic bradycardia or atrioventricular block.[408] Atropine is less arrhythmogenic than epinephrine. It will cause pupil dilation, which can complicate neurological assessment.

Although a minimum dose of 0.1 mg for patients weighing <5 kg was recommended in pre-2015 AHA PALS guidelines,[3,4] the 2015 ILCOR (International Liaison Committee on Resuscitation) evidence evaluation process[398] and 2015 AHA PALS guideline update[3] reported no evidence to support a minimum prophylactic atropine dose during emergency intubation[409]; lower doses may be appropriate.[410]

Vasoactive Agents

Dobutamine

Dobutamine is primarily a β_1-adrenergic agonist with weak β_2 and α_1 activity. It can be used for patients with LCOS with dilated cardiomyopathy or after cardiac transplantation. A recent European survey reported <20% of pediatric cardiac surgical centers routinely used dobutamine for LCOS after pediatric heart surgery.[411]

Dopamine

Dopamine is a sympathomimetic amine that directly stimulates β_1 and α_1 and dopaminergic receptors. In addition, dopamine is a norepinephrine precursor, so dopamine administration increases norepinephrine release. It functions as an inotrope and chronotrope at lower doses and as a vasoconstrictor at higher doses. It has widespread use for LCOS after pediatric heart surgery,[411] including after stage 1 Norwood palliation.[90] In a small case series of 13 neonates after stage 1 Norwood palliation, dopamine administration was associated with an increase in oxygen consumption[412] presumed to be secondary to the increase in heart rate.

Epinephrine

Epinephrine is a β-agonist at lower doses and an α-agonist at higher doses. It is an effective inotrope and chronotrope and at higher doses is a vasoconstrictor. However, epinephrine also increases myocardial oxygen consumption and in bolus doses causes vasoconstriction that can limit blood flow to end organs. Epinephrine administration can trigger arrhythmias and even VF in an irritable myocardium.

A prearrest small dose of epinephrine can be used in treatment of hypotension or persistent bradycardia with a pulse in the patient with an at-risk myocardium to prevent cardiac arrest and allow time to treat an acute reversible problem (eg, draining of pericardial effusion, sternal opening, revascularization of a shunt) or to initiate ECLS without requiring ECPR. Doses in this scenario should be administered via central venous catheter or intraosseous catheter and titrated to effect based on the patient's response, with a reasonable starting dose of 1 μg/kg (ie, one-tenth the standard resuscitation dose for pulseless cardiac arrest or symptomatic bradycardia).

A pediatric prospective, randomized, double-blind, controlled trial comparing high-dose (0.1 mg/kg) versus standard dose (0.01 mg/kg) epinephrine for in-hospital cardiac arrest demonstrated that high-dose epinephrine was associated with worse 24-hour survival.[413] Epinephrine produces undesirable dose-related effects, such as increased myocardial oxygen consumption, so the goal of therapy is use of the lowest effective dose. If epinephrine does not produce improved hemodynamic function and the patient is thought to be an ECLS candidate, then the focus of the resuscitation should be the delivery of high-quality CPR and rapid activation of ECLS, rather than the administration of repetitive doses of epinephrine.

In some patients, epinephrine administration can contribute to ventricular ectopy or fibrillation.[14] Such patients may include those who required a prolonged aortic cross-clamp time, preoperative patients with truncus arteriosus, patients with pulmonary atresia with intact ventricular septum and RV-dependent coronary circulation, patients with LQTS, patients with catecholaminergic polymorphic VT, and those with acute fulminant myocarditis. In these situations, if heart function is poor, consider using a lower dose of epinephrine or administering phenylephrine if heart function is reasonable but hypotension is present.

Isoproterenol

Isoproterenol is a β-adrenergic agonist with no α-adrenergic activity. It functions as an inotrope, chronotrope, and vasodilator. Isoproterenol can increase the ventricular escape rate in patients with complete heart block.[414] In addition, it is helpful to maintain heart rate and decrease afterload after cardiac trans-

plantation. Isoproterenol is also helpful for patients with β-blocker overdose. It can maintain heart rate and suppress torsade in patients with LQTS. At a low dose, isoproterenol will increase the heart rate, as well as LV preload, without compromising systemic diastolic pressure.

Levosimendan

Levosimendan increases the sensitivity of myocardial troponin c to calcium, functioning as an inotrope. In addition, it acts on adenosine triphosphate–sensitive potassium channels, resulting in vasodilation. Levosimendan is an effective therapy for decompensated heart failure,[415] and it has been shown to improve LCOS after pediatric heart surgery.[416] In a randomized pilot study, levosimendan and milrinone were found to have similar effects on cardiac index after pediatric heart surgery, although the effects of the 2 drugs followed different time courses[417] (see Low Cardiac Output Syndrome).

Milrinone

Milrinone is a type III phosphodiesterase inhibitor that increases myocardial and vascular smooth muscle cyclic adenosine monophosphate, causing increased intracellular calcium and smooth muscle relaxation, which results in increased contractility and afterload reduction. In a placebo-controlled, multicenter trial of children with CHD undergoing 2-ventricle repair, a high-dose regimen of prophylactic milrinone administration reduced the incidence of LCOS after heart surgery.[237]

Norepinephrine

Norepinephrine is a potent β_1- and α-agonist with only minor β_2 effects. It can augment coronary blood flow by increasing systemic diastolic pressure at the expense of increased systemic afterload. Norepinephrine is helpful for treatment of LCOS with low SVR.[418]

Phenylephrine

Phenylephrine is an α_1-agonist with very little β effect. It causes arterial vasoconstriction, increasing blood pressure with the potential for reflex bradycardia. Phenylephrine is an important therapy for hypercyanotic spells in patients with unrepaired TOF.[419] It is useful for treatment of low SVR caused by vasodilator medications, labile vascular tone (eg, vasculopathy), or sepsis. Phenylephrine maintains arterial diastolic pressure and coronary perfusion pressure; both are important for patients at risk for myocardial ischemia.

Terlipressin and Vasopressin

Vasopressin causes peripheral vasoconstriction without a direct cardiac effect because it acts on vasopressin receptors in blood vessels. The theoretical advantage of using vasopressin (relative to epinephrine) is that it can increase SVR and blood pressure and improve coronary perfusion pressure without increasing the contractile state or the heart rate, which independently increase myocardial workload or oxygen consumption. Increasing doses of vasopressin will result in increasing blood pressure and afterload, which at higher doses will increase myocardial work. In adult studies of prehospital cardiac arrest, vasopressin did not improve survival over epinephrine. Although in the past, vasopressin was included in the advanced cardiac life support algorithm for treatment of shock-refractory VF or pulseless VT,[420] it is no longer included in the advanced cardiac life support recommendation, because the combination of epinephrine plus vasopressin offers no advantage over the use of epinephrine alone.[421,422] The pediatric experience with the use of vasopressin in cardiac arrest is limited to small case series.[422]

There are data supporting the use of a vasoconstrictor in the setting of persistent hypotension after pediatric heart surgery. A prospective observational study noted significant variability in plasma arginine vasopressin levels after surgery for CHD, but low levels were not found to be associated with poor hemodynamics or inotropic score.[423] However, several case series have shown improved hemodynamics and decreased inotropic score with administration of terlipressin[424] or vasopressin in the setting of extreme LCOS or vasodilatory shock after surgery for CHD.[425]

Guiding Therapy

Recommended initial doses of drugs commonly used in the treatment of LCOS and cardiac arrest are listed in Table 4. Monitoring of heart rate and rhythm, blood pressure, pulse pressure, oxygen saturation, CVP, $ETco_2$ pressure, and Svo_2 (or NIRS), as well as blood gas and electrolyte analysis, is needed when the child is unstable. Therapy and subsequent drug doses must be individualized and adjusted for each patient. If no improvement is noted in the clinical status of the patient, further administration of the same medication must be viewed with caution, and additional contributing factors that cause decompensation must be considered and investigated.

Gaps in Knowledge

The US Food and Drug Administration Modernization Act (1997) established economic incentives to pharmaceutical companies by providing an additional 6 months of marketing exclusivity in return for approved sponsor-performed pediatric trials. Nonetheless, in the pediatric cardiac care unit, nearly 40% of the medications used in a pediatric critical care are used for purposes not approved by the US Food and Drug Administration for inclusion in the drug labeling (ie, they are off-label uses).[426] Thus, safety and efficacy of pediatric medication administration is generally based on clini-

Table 4. Pharmacology: Typical Doses and Indications

Medication	Dose	Indications	Cautions/Precautions
Adenosine	Initial dose: 100 µg/kg (0.1 mg/kg; maximum single dose: 6 mg) rapid IV push; second dose can be double the first dose (ie, give 200 µg/kg [0.2 mg/kg] for second dose, maximum 12 mg)	Atrioventricular node–dependent SVT	Adenosine will not effectively terminate atrioventricular node–independent tachycardias, such as atrial flutter, ectopic atrial tachycardia, or atrial fibrillation Should not be administered for wide QRS complex tachycardia unless it is clear that the underlying rhythm is not atrial fibrillation or atrial flutter with associated antegrade accessory pathway conduction Expert consultation should be obtained before administration of adenosine as a diagnostic and potentially therapeutic intervention for stable patients who have wide QRS complex tachycardia
Amiodarone	For VF/pulseless VT, in absence of known or suspected long-QT syndrome: Initial dose: 5.0 mg/kg IV/IO bolus Maximum single dose: 300 mg; can repeat to a total of 3 doses Total: 15 mg/kg per 24 h; in adolescents, maximum 2.2 g per 24 h For perfusing atrial or ventricular arrhythmias: Give loading dose of 5 mg/kg over 30–60 min* Maximum single dose: 300 mg; can repeat to a maximum of 3 doses Total: 15 mg/kg per 24 h; in adolescents, maximum 2.2 g/24 h If patient hemodynamically unstable or receiving other medications that lower heart rate, consider lower dose and slower infusion	Shock-refractory cardiac arrest (VF/pulseless VT); atrial and ventricular arrhythmias; JET	Use lower dose and/or slower infusion if patient is hemodynamically unstable or receiving other medications that lower heart rate; can cause hypotension; can prolong QT interval: 1. Obtain expert consultation before administering, if known or suspected long-QT syndrome. 2. Routine administration in combination with procainamide or digoxin is not recommended without expert consultation
Atropine	For symptomatic bradycardia: 20 µg/kg (0.02 mg/kg); minimum single dose: 0.5 mg; maximum single dose: 500 µg (0.5 mg) For emergent preintubation bradycardia prophylaxis: 20 µg/kg (0.02 mg/kg) Intubation: No minimum dose; maximum single dose 500 µg (0.5 mg)	Vagal-mediated bradycardia; primary atrioventricular block; emergent intubation bradycardia prophylaxis	Loss of constrictive pupillary reflex to light
Calcium chloride (10%=100 mg/mL=27.2 mg/mL elemental calcium)	10–20 mg/kg; maximum single dose: 2g	Hypocalcemia	Precipitates with sodium bicarbonate; rapid IV administration can cause hypotension, bradycardia, or asystole (particularly if patient is receiving digoxin)
Calcium gluconate (10%=100 mg/mL= 9 mg/mL elemental calcium)	50–100 mg/kg; maximum single dose: 3g	Hypocalcemia	Precipitates with sodium bicarbonate; rapid IV administration can cause hypotension, bradycardia, or asystole (particularly if patient is receiving digoxin)
Dexmedetomidine	0.5–1 µg/kg bolus; infusion 0.25–1 $\mu g \cdot kg^{-1} \cdot h^{-1}$; titrate to effect	For sedation and mild analgesia	If at risk for heart block or symptomatic bradycardia, pacing capability should be available; can cause hypotension or bradycardia
Dobutamine	2–20 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Myocardial systolic dysfunction (ie, as inotrope and/or vasodilator)	Titrate to effect; can produce hypotension or tachyarrhythmias
Dopamine	2–20 $\mu g \cdot kg^{-1} \cdot min^{-1}$; if ≥20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ is required, consider using an alternative adrenergic agent	Systolic dysfunction; postoperative LCOS	Titrate to effect; can produce vasoconstriction and hypertension or tachyarrhythmias; increases myocardial oxygen consumption

(*Continued*)

Table 4. Continued

Medication	Dose	Indications	Cautions/Precautions
Epinephrine	For pulseless cardiac arrest: Bolus: 10 µg/kg (0.01 mg/kg, or 0.1 mL/kg of 0.1 mg/mL) concentration during cardiac arrest; maximum dose: 1 mg For symptomatic bradycardia: Bolus: 10 µg/kg (0.01 mg/kg, or 0.1 mL/kg of 0.1 mg/mL) concentration; maximum dose: 1 mg For treatment of hypotension or persistent bradycardia with a pulse in the patient with an at-risk myocardium†: Give low dose via central administration 1 µg/kg (0.001 mg/kg); continuous infusion: 0.01–0.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Cardiac arrest; symptomatic bradycardia; systolic dysfunction; postoperative LCOS	Significant vasoconstriction at higher doses; increases myocardial oxygen consumption
Esmolol	Bolus: 100–500 µg/kg (0.1–0.5 mg/kg) over 1–2 min Infusion: 50–500 $\mu g \cdot kg^{-1} \cdot min^{-1}$	SVT; hypertension	Can cause bradycardia, hypotension, and/or hypoglycemia
Etomidate	Bolus: 0.2–0.4 mg/kg, over 30–60 s; maximum dose: 20 mg	Procedural sedation	Can cause apnea and adrenal suppression
Fentanyl	Bolus: 1–5 µg/kg Continuous infusion for neonates and young infants: 0.5–5 $\mu g \cdot kg^{-1} \cdot h^{-1}$ Continuous infusion for older infants and children: 1–3 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Analgesia	Can cause apnea and chest wall rigidity in the naive patient
Furosemide	1 mg/kg; starting dose of up to 10 mg to naïve patient	Diuresis	Can cause hypokalemia, hypochloremic metabolic acidosis, or hypotension if preload dependent
Heparin	Presumed shunt occlusion: 50–100 U/kg; anticoagulation before ECLS cannulation: 100 U/kg	Presumed shunt occlusion; ECLS cannulation	Can cause bleeding
Hydrocortisone	1–2 mg/kg; maximum dose: 100 mg	LCOS not responsive to inotropic agents	Can cause hyperglycemia and/or hypokalemia
Isoproterenol	0.05–2 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Post–cardiac transplantation; long QT with torsade des pointes; primary atrioventricular block	Can cause hypotension, tachycardia, and increased myocardial oxygen consumption
Ketamine	0.5–2 mg/kg	Procedural sedation	Can cause apnea and increased respiratory secretions; myocardial depressant at high doses
Levosimendan	Bolus: 12 µg/kg; infusion: 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$	LCOS	
Lidocaine	Bolus: 1 mg/kg, may repeat Infusion: 20–50 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (repeat bolus dose if infusion initiated >15 min after initial bolus dose)	VF/pulseless VT cardiac arrest; ventricular arrhythmias	Monitor QTc and lidocaine levels; can cause seizures at high levels
Magnesium sulfate	Pulseless VT with torsade des pointes; bolus: 25–50 mg/kg; maximum dose: 2 g VT with pulses: 25–50 mg/kg over 10–20 min; maximum dose: 2 g	VF/pulseless VT arrest with torsade des pointes; hypomagnesemia	Can cause hypotension with rapid administration
Midazolam	0.05–0.2 mg/kg	Sedation	Can cause apnea or hypotension
Milrinone	Bolus: 50 µg/kg, administered over 10–60 min Maintenance infusion: 0.25–1.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$	LCOS	Hypotension
Nitric oxide	Up to 40 ppm	Increased pulmonary vascular reactivity; pulmonary hypertension ± crisis	Methemoglobinemia
Norepinephrine	Infusion: 0.025–0.3 $\mu g \cdot kg^{-1} \cdot min^{-1}$	LCOS with low SVR; clinically significant vasodilation	Vasoconstriction; increases myocardial oxygen consumption
Oxygen	Fio_2 = 21%– 100%	Alveolar desaturation	Pulmonary overcirculation with unrestrictive aortopulmonary shunt

(*Continued*)

Table 4. Continued

Medication	Dose	Indications	Cautions/Precautions
Phenylephrine	Bolus: 5–20 μg/kg; (0.005–0.020 mg/kg) Infusion: 0.1–0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Cyanotic spell in unrepaired tetralogy of Fallot; symptomatic hypotension because of low SVR; shunt obstruction; coronary hypoperfusion	Can cause vasoconstriction or hypertension
Propofol	Bolus: 1–3 mg/kg Infusion: 50–100 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Sedation, amnesia	Hypotension; contraindicated in children with mitochondrial disease and not approved in children for prolonged sedation
Procainamide	Bolus: 15 mg/kg over 30–60 min; maximum dose: 100 mg Infusion: 20–60 $\mu g \cdot kg^{-1} \cdot min^{-1}$	JET; SVT; atrial fibrillation	Monitor ECG and procainamide and NAPA levels; can prolong QT interval: 1. Obtain expert consultation before administering, if known or suspected long QT; 2. Routine administration in combination with amiodarone is not recommended without expert consultation
Prostaglandin E_1	To establish ductal patency: 0.05–0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$, IV/IO infusion To maintain ductal patency: 0.01–0.05 to 0.01 to 0.02 $\mu g \cdot kg^{-1} \cdot min^{-1}$ IV/IO infusion	Maintain patency of ductus arteriosus	Apnea; fever and hypotension
Sodium bicarbonate	Bolus: 1–2 mEq/kg slow IV push; dose adjusted to severity of base deficit; use 4.2% (0.5 mEq/L) concentration for neonates	Metabolic acidosis	Precipitates with calcium
Vasopressin	Infusion: 0.0005–0.01 $U \cdot kg^{-1} \cdot min^{-1}$	LCOS with low SVR; vasodilatory shock; diabetes insipidus	Hypertension and increased afterload; fluid retention
Verapamil	Bolus: 0.1–0.2 mg/kg Do not administer to infants <12 mo of age without expert consultation	SVT	Hypotension; have calcium available; not to be administered to infants (can cause apnea, bradycardia and hypotension); avoid in patients with WPW

ECLS indicates extracorporeal life support; Fio_2, fractional inspired oxygen; IO, intraosseus; IV, intravenous; JET, junctional ectopic tachycardia; LCOS, low cardiac output syndrome; NAPA, *N*-acetylprocainamide; SVR, systemic vascular resistance; SVT, supraventricular tachycardia; VF, ventricular fibrillation; VT, ventricular tachycardia; and WPW, Wolff-Parkinson-White syndrome.

*The time range for administration of the loading dose of amiodarone for the child with a perfusing rhythm is slightly longer (ie, 30–60 minutes) than the pediatric advanced life support (PALS) 2015 recommended time for administration (ie, 20–60 minutes). The reason for this slight difference is that the child with cardiac disease is likely to be or is at risk for hemodynamic compromise.

†For treatment of hypotension or persistent bradycardia with a pulse in the patient with an at-risk myocardium, give low dose via central administration 1 μg/kg (0.001 mg/kg), which is one-tenth the standard recommended resuscitation dose for symptomatic bradycardia in PALS 2015.

cal experience, and many more data about pediatric drugs are needed.

Recommendations: Pharmacological Interventions

1. **For prearrest intubation of the airway: (a) Ketamine can be used to induce acute sedation and loss of consciousness and support hemodynamics *(Class IIa; Level of Evidence C)*. (b) Etomidate may also be used to induce acute sedation and loss of consciousness with minimal hemodynamic impact; however, etomidate is potentially harmful in the setting of septic shock because of the increased risk of adrenal insufficiency *(Class III: Harm; Level of Evidence B)*. (c) Dexmedetomidine can be useful for procedures with the intention to avoid respiratory depression or for patients with arrhythmia requiring sedation *(Class IIa; Level of Evidence B)*. (d) Sedative drugs are potentially harmful for patients with severe ventricular dysfunction or LCOS and should be used with appropriate monitoring and the personnel available to initiate resuscitation, if needed *(Class III: Harm; Level of Evidence C)*.**
2. **Adenosine is not useful to treat ectopic atrial tachycardia, atrial fibrillation, or atrial flutter *(Class III: No Benefit; Level of Evidence B)*. Adenosine can be life-threatening for atrial fibrillation with an antegrade accessory pathway *(Class III: Harm; Level of Evidence B)*. In postoperative patients with temporary atrial epicardial pacing wires, rapid atrial pacing has fewer side effects than adenosine**

and can be effective as the preferred initial therapy for reentrant SVT *(Class IIa; Level of Evidence C)*. A reduced dose (one-fifth to one-third) of adenosine should be administered to post–cardiac transplantation patients *(Class I; Level of Evidence B)*.

3. **Verapamil is not recommended for the treatment of SVT in neonates and infants <1 year of age without expert consultation because it may cause harm *(Class III: Harm; Level of Evidence C)*.**
4. **During cardiac arrest, calcium administration is not recommended in the absence of documented ionized hypocalcemia, hypermagnesemia, or hyperkalemia and can be harmful *(Class III: Harm; Level of Evidence B)*.**
5. **Given that severe metabolic acidosis can lead to pacemaker noncapture, sodium bicarbonate can be useful to facilitate pacemaker function *(Class IIa; Level of Evidence C)*.**
6. **During cardiac arrest, the routine use of sodium bicarbonate administration is not recommended *(Class III: Harm; Level of Evidence B)*. Sodium bicarbonate administration is reasonable during special situations such as severe metabolic acidosis with myocardial dysfunction or pacemaker noncapture and hyperkalemic cardiac arrest *(Class IIa; Level of Evidence C)*.**
7. **Hydrocortisone may be considered to treat the patient with hypotension unresponsive to vasoactive therapy or volume resuscitation *(Class IIb; Level of Evidence C)*.**
8. **Atropine administration may be reasonable as a premedication in specific emergency situations where there is a high risk of bradycardia (ie, such as may occur during emergency intubation) *(Class IIb; Level of Evidence C)*. A typical dose is 20 μg/kg, with a maximum dose of 500 μg (per the 2015 PALS guidelines update, there is no longer a minimum dose of 100 μg when atropine is given for emergency intubation) *(Class IIb; Level of Evidence C)*.**
9. **During CPR, it is reasonable to give 10 μg/kg (0.01 mg/kg, or 0.1 mL/kg of the 0.1 mg/mL concentration) of intravenous epinephrine *(Class IIa; Level of Evidence C)*.**
10. **For treatment of hypotension or persistent bradycardia with a pulse in the patient with an at-risk myocardium, it is reasonable to titrate a smaller prearrest dose of epinephrine (eg, 1 μg/kg [0.001 mg/kg]) to achieve a desired hemodynamic effect and reduce the risk for ventricular arrhythmias *(Class IIa; Level of Evidence C)*.**
11. **Phenylephrine can be an effective therapy for hypercyanotic spells in patients with unrepaired TOF *(Class IIa; Level of Evidence C)*.**

PHASES OF CARDIAC ARREST

Prearrest Phase

Principles of Intubation, Airway Management, and Respiratory Support

Children with congenital or acquired cardiac disease often require respiratory support. Indications for advanced airway management include respiratory failure, cardiac failure, and the need for procedural sedation and analgesia (depending on the sedation and analgesia agents used and doses given). Importantly for the child with systemic ventricular dysfunction or systemic valvar insufficiency, positive-pressure ventilation can provide a form of ventricular support by reducing systemic ventricular afterload and work of breathing.

Children with cardiac disease have an increased incidence of extracardiac anomalies or concomitant syndromes that can include airway anomalies.[427] Preparation for intubation should include consideration of conditions that could lead to a difficult airway (eg, macroglossia [trisomy 21], tracheal stenosis or tracheomalacia [VACTERL Association], and cleft palate [velocardiofacial syndrome]).[428–431]

The goals of airway management include maintenance or improvement of Do_2, reduction in oxygen consumption, and control of minute ventilation and carbon dioxide elimination. Adverse events during airway management occur more frequently in patients with cardiac disease or comorbidity, especially single-ventricle patients.[432,433] Therefore, a complete understanding of the patient's cardiac and airway anatomy, current cardiac function and valvar insufficiency, presence of tamponade physiology, and predisposition for arrhythmia, as well as knowledge of the child's sedation/analgesia and airway history, is imperative when planning for an airway intervention. For some patients, a resuscitation plan may be required before placement or removal of an airway. Noninvasive ventilation techniques, with a lower associated risk profile, can at times be an effective alternative to tracheal intubation and ventilation.[434]

Both the desired and undesired consequences of intubation can be ascribed to 3 unavoidable effects of initiation of assisted ventilation and airway instrumentation. First, the transition from spontaneous ventilation, with net negative (relative to the atmosphere) high-amplitude swings in pleural and intrathoracic pressure, to positive-pressure ventilation is associated with both increased CVP and decreased venous return. Second, the effects of the pharmacological agents used

during intubation on myocardial performance and vascular tone can only be partially anticipated, and there can be significant individual and condition-dependent variability. Third, the combination of pharmacology, stimulation during instrumentation, and subsequent altered lung expansion and gas exchange impacts autonomic tone and circulating catecholamines and can cause (unintended) deterioration of myocardial performance or development of myocardial ischemia. Because the rapid superimposition of reduced venous return, impaired contractility, and reduction in vascular tone has the potential to significantly reduce cardiac output, the clinician should consider the need for preventative or prophylactic administration of vasoactive agents in addition to ECLS standby. Low cardiac output leads to a delay in onset of administered drugs. Impatience and readministration can lead to unwanted side effects of the accumulated dose. Hemodynamic collapse usually develops several minutes after airway manipulation has occurred, because the combined effects of sedation, analgesia, and the drop in intrinsic catecholamines can markedly compromise coronary perfusion.

Administration of pharmacological agents (see Pharmacological Interventions) should be undertaken with anticipation of both the intended and undesired effects and the likely response of the individual patient. Bradycardia associated with succinylcholine administration or vagal stimulation can result in decreased arterial diastolic pressure, decreased coronary perfusion pressure, myocardial ischemia, and cardiac arrest. Prevention of bradycardia can be achieved with anticipatory administration of atropine or glycopyrrolate,[3,409,435,436] but the onset of these drugs is delayed once bradycardia ensues.[437] Furthermore, cardiac output might not be increased by anticholinergic drugs if hypoxia is present or bradycardia persists.[438] Low-dose epinephrine (1 μg/kg) should be available for treatment of hypotension or persistent bradycardia with a pulse in the patient with an at-risk myocardium.[338] Combinations of sedative-hypnotic and analgesic medications can be used to control arousal responses, pain, and agitation (see Pharmacological Interventions).

When the use of neuromuscular blockade is considered, indications for and effects of the drugs should be clarified before use. In addition, neuromuscular blockade must be undertaken with appropriate monitoring and a backup plan for support of the airway and ventilation. Although the use of neuromuscular blockers with sedation/analgesia generally creates better conditions for intubation, their administration is occasionally followed by a "can't intubate, can't ventilate" crisis, so the healthcare team must have a plan in place.

Succinylcholine can transiently increase oxygen consumption, carries risks of hyperkalemia and malignant hyperthermia in susceptible children, and has a long enough duration of action that in the event of failure to ventilate, return of spontaneous ventilation will not reliably occur before hypoxic injury. Nondepolarizing muscle relaxants might be a safer alternative, because they have fewer adverse effects, produce excellent intubating conditions,[439] and can be reversed within 3 minutes if necessary.[440]

Neuromuscular blockade alone does not prevent nonshivering thermogenesis in neonates, whereas opioids and inhaled anesthetic agents do.[441,442] Reduction in muscle work is ensured by neuromuscular blockade (with appropriate sedative and analgesic drugs), but effects on whole-body oxygen consumption depend on the patient's condition.[443]

Endotracheal intubation can be performed with either cuffed or uncuffed tracheal tubes.[444] An appropriately sized uncuffed or a cuffed endotracheal tube is necessary to minimize air leak and resultant inadequate positive-pressure ventilation during resuscitation. Position of the endotracheal tube should be confirmed by direct $ETco_2$ waveform capnography combined with clinical assessment, including auscultation and assessment of chest expansion. If continuous waveform capnography is not available, a litmus exhaled carbon dioxide indicator can be used, with clinical assessment to confirm tracheal tube placement. Success of tracheal intubation via direct laryngoscopy is increased with proper positioning of the child to align the oral, pharyngeal, and laryngeal axes to create a direct line of sight from the child's mouth to the vocal chords/glottic opening, and with the use of appropriately sized laryngoscope blades and tubes. The use of video laryngoscopy has a theoretical advantage, but its use has not been shown to increase success.[445] For patients with known or suspected difficult airways, expert consultation and reference to algorithms should be sought,[446] although pediatric-specific algorithms have not been validated.[447]

Because of the rapid changes in arterial oxygenation, systemic and pulmonary resistances, cardiac output, and metabolism that accompany airway management, continuous monitoring should include, when possible, continuous waveform display of $ETco_2$,[448] pulse oximetry, Svo_2 (using the oxygen saturation in the SVC as a surrogate for a true mixed venous sample),[449,450] and multisite NIRS.[43] These variables will complement the clinical assessment of airway, ventilation, and perfusion.

The continuous presence of exhaled carbon dioxide during ventilation requires alveolar ventilation, PBF and SBF, and metabolism. As a result, monitoring of the $ETco_2$ provides information about gas exchange from airway to mitochondria. The end-expiratory and arterial carbon dioxide gradient is increased with both dead space and shunt[451] and is increased proportionally to the degree of desaturation in children with

CHD.[69,452,453] In children with no intracardiac or great vessel shunt, changes in $ETco_2$ can be a direct indication of changes in PBF and herald hemodynamic compromise.[66,68–70]

When positive-pressure ventilation is provided, the airway pressures used and the blood gas values to be targeted must be individualized for each patient on the basis of the child's cardiac lesion and hemodynamic status. Airway pressures in infants and children with cardiac disease should be titrated judiciously in the setting of parenchymal lung disease. In children with complete mixing or single-ventricle physiology, higher airway pressures can be beneficial to restrict PBF. Alternatively, lower airway pressures can be desirable for patients with RV systolic and diastolic dysfunction. No matter what the underlying cardiovascular physiology is, it is important to remember that high airway pressures will reduce systemic venous return and PBF in a 2-ventricle heart or will reduce total cardiac output in the child with complete mixing or single-ventricle physiology. Inadvertent hyperventilation or hyperoxygenation in the child with complete mixing or single-ventricle physiology can result in an unbalanced parallel circulation with pulmonary overcirculation, reduced SBF, and inadequate Do_2 to the tissues.

Although positive-pressure ventilation can provide afterload reduction to the systemic ventricle and increase cardiac output, it can also impede systemic and pulmonary venous return. Increases in intrathoracic pressure will initially recruit lung volume, minimizing PVR, thereby reducing the afterload on the pulmonary ventricle. However, if the lungs are overinflated, PVR will increase, leading to an increase in afterload on the pulmonary ventricle and a reduction in PBF. In the setting of pulmonary hypertension, positive-pressure ventilation has the potential to reduce preload to the pulmonary ventricle, increase intrathoracic pressures and PVR to critical levels, and severely compromise PBF and overall cardiac output. When systolic function is diminished in the child who has no pulmonary ventricle (eg, after a superior cavopulmonary connection or modified Fontan operation), positive-pressure ventilation can improve cardiac output but can compromise PBF by increasing intrathoracic pressure.

Recommendations: Principles of Intubation, Airway Management, and Respiratory Support

1. **Patients with CHD have an increased incidence of associated airway anomalies. In-depth understanding of the underlying heart disease and potential associated airway anomalies can be useful before airway manipulation *(Class IIa; Level of Evidence C)*.**
2. **Risks of anesthetic and sedative agents, airway manipulation, and positive-pressure ventilation associated with intubation in hemodynamically marginal cardiac patients can result in cardiac arrest. Before attempted intubation, providers should discuss strategies to maintain hemodynamics and a resuscitation plan *(Class I; Level of Evidence C)*.**

Transport of the Critical Cardiac Patient

The regionalization of pediatric cardiac care has necessitated the transport of critically ill infants and children with heart disease over significant distances. Transport of these high-risk infants and children is associated with potential morbidity and mortality. The goal of prenatal screening is to identify neonates with significant CHD and facilitate antenatal maternal transport rather than postnatal transport of the critically ill newborn. However, high-risk neonates are not always identified prenatally or even at the time of birth. In addition, older infants and children will continue to present with symptomatic heart disease. As a result, interfacility transport of critically ill infants and children will continue to be necessary.[454]

Transported critically ill neonates with CHD are at risk for development of hypothermia, hypoglycemia, hypoxia, and acidosis during transport.[448,455] Although prospective studies are lacking, large single-center[456] and multicenter[457] registry studies have shown that the transport of infants and children with complex disease (including those with critical cardiac disease) is accomplished with lower patient morbidity and mortality when performed by specialized neonatal and pediatric critical care transport teams, staffed by personnel accustomed to the prevention of complications in the transport setting.

Pretransport Stabilization

The newborn with critical CHD can present in a variety of settings, from the delivery room to a community hospital emergency department. The most common initial symptoms are cyanosis caused by reduction in ductal-dependent PBF, transposition physiology, complete mixing/single-ventricle physiology, or shock caused by reduction of ductal-dependent SBF. Pretransport stabilization includes supportive care for respiratory or cardiac failure, in addition to specific therapies to maintain ductal patency (ie, PGE_1 infusion), treat arrhythmias, and correct metabolic derangements.

Parallel Circulations

Newborns with a patent ductus arteriosus or systemic-to–pulmonary artery shunt have parallel (as opposed to in-series) circulations. Changes in PVR or SVR in these patients can cause the pulmonary and systemic circulations to become unbalanced and in the extreme can

cause either severe hypoxemia from insufficient PBF or pulmonary overcirculation with inadequate SBF and Do_2 to the tissues (see sections on Age-Dependent Factors Influencing CPR in the Neonate and Infant and Single-Ventricle Palliation: Perioperative Management). Newborns with unrepaired TGA also have an anatomic parallel circulation. If mixing of systemic and pulmonary venous blood is inadequate (ie, with a restrictive foramen ovale), the infant will be profoundly cyanotic and hypoxemic, requiring a balloon atrial septostomy. Newborns with obstructed TAPVC require urgent surgical intervention, and respiratory and cardiac support is typically provided preoperatively.

Airway Management

Some infants and children with cardiac disease will benefit from assisted ventilation during transport (see Intubation and Airway Management). The major indication for the placement of an advanced airway before transport is cardiorespiratory failure that is present or likely to develop before arrival at the receiving facility. In this setting, it is essential to adequately secure the advanced airway before patient transport, because reintubation during transport will be difficult. A single-center retrospective case series describing the pretransport and transport management of infants receiving PGE_1 infusion for CHD noted that elective intubation for transport significantly increased the odds of a major transport complication.[458] The risks of prophylactic intubation before the transport of otherwise stable infants on PGE_1 must be weighed carefully against possible benefits.

Respiratory Management of the Critically Ill Infant or Child With Cardiac Disease During Transport

To provide optimal transport of the child with cardiac disease, close monitoring of the child's $Paco_2$ and $ETco_2$ and the titration of fractional inspired oxygen (Fio_2) to target optimal patient systemic oxygen saturation and SBF and PBF are recommended. This will require specialized equipment, including oxygen blenders, capnometry, and point-of-care blood gas analysis. Discrepancies can develop between the $ETco_2$ and the arterial $Paco_2$ in the setting of limited PBF with intracardiac shunt and low cardiac output.

Prostaglandin E_1

Neonates presenting with ductal-dependent SBF or PBF are treated with intravenous PGE_1 to maintain patency of the ductus arteriosus. Complications associated with PGE_1 use include apnea, fever, and hypotension.[459] The risk of apnea might indicate the need for insertion of an advanced airway before transport, but the potential benefits of intubation must be weighed against the risk of sedation, positive-pressure ventilation, and potential airway complications. Patient complications are documented in ≈42% of neonatal transports.[458] In one recent series, apnea or hypoventilation developed in 5% of newborns receiving PGE_1 during transport, and elective intubation was independently associated with adverse events.[458] In addition, preoperative intubation (including elective intubation for transport) in newborns with HLHS has been shown to be a risk factor for postoperative morbidity.[29] Because side effects of PGE_1 are typically dose dependent, lower doses of prostaglandin have been recommended if the ductus appears to be open based on echocardiographic evaluation and clinical assessment.[460,461] The use of lower doses of PGE_1 ($<0.015\ \mu g \cdot kg^{-1} \cdot min^{-1}$) was associated with a lower incidence of apnea during transport.[462] In that report, 2 (2.6%) of the 78 infants transported with PGE_1 infusion and without endotracheal intubation developed apnea in transit, and both were receiving $PGE_1 > 0.015\ \mu g \cdot kg^{-1} \cdot min^{-1}$.[462] In addition to using lower doses of PGE_1, minimizing the concurrent use of respiratory depressants (eg, narcotic drugs and midazolam) during transport reduces the likelihood of apnea with PGE_1.

Inotropic and Metabolic Support

In addition to restoring and maintaining ductal patency, supportive care of the newborn with critical CHD includes support of myocardial function. Correction of hypoxemia and acidosis will typically improve cardiac output. For significant myocardial dysfunction, inotropic infusions are typically used. The use of sodium bicarbonate for severe metabolic acidosis can be appropriate while the underlying issue with SBF and Do_2 is also addressed. Correction of hypocalcemia and hypoglycemia can also improve myocardial function, because the neonatal myocardium is sensitive to insufficient calcium and glucose stores. Such supportive care is consistent with the AHA 2010 PALS guidelines.[3,4] (See Low Cardiac Output Syndrome.)

ECLS and Interfacility Transport

ECLS is used for management of cardiac or respiratory failure. The need for ECLS is one indication for interfacility transfer. Transport of the ECLS candidate carries significant risk of deterioration and adverse events, because most patients will already be dependent on high levels of mechanical ventilation and pharmacological support. Given the high risk associated with transport, selected institutions have developed mobile ECLS services with the capability of performing cannulation at the referring hospital and transporting the cannulated patient. Several single-institution case series have described this practice and reported outcomes.[463–465]

Considerations for Transport to Catheterization Laboratory or Operating Room

Patients with shock or hypoxemia refractory to maximal medical support may be candidates for emergency procedures such as catheter-based balloon/blade septostomy, surgical creation of a shunt, repair of TAPVC, or initiation of ECLS. The optimal location for life-saving

interventions will vary with the institution, personnel, and patient condition, but individual patients might benefit from direct transport from the referring hospital to the optimal site for definitive intervention, such as the catheterization laboratory or operating room. A well-orchestrated team approach for support, diagnosis, and intervention is required regardless of location.

Gaps in Knowledge

The benefits of centralized care for high-risk infants and children with heart disease have been demonstrated. Incorporation of the risks and costs of transport to tertiary centers has not been well evaluated.

Recommendations: Transport of the Critical Cardiac Patient

1. **PGE_1 should be initiated for newborns with suspected ductal-dependent CHD *(Class I; Level of Evidence B)*.**
2. **For neonates with prenatal diagnosis of CHD with ductal-dependent circulations and those postnatally diagnosed with echocardiographic documentation of adequate ductal patency, low-dose PGE_1 infusion (0.01–0.02 $\mu g \cdot kg^{-1} \cdot min^{-1}$) can be effective to maintain ductal patency while minimizing risk of apnea and avoiding the need for intubation *(Class IIa; Level of Evidence C)*.**

Low Cardiac Output Syndrome

Children with congenital or acquired heart disease are at increased risk for cardiac arrest and early mortality. Ideally, prevention of cardiac arrest requires patient stratification to match the level of risk with the intensity of monitoring and therapy. There are no universally accepted risk models for patients with congenital or acquired heart disease, but it is generally acknowledged that high-risk patients include those with uncorrected CHD requiring mechanical ventilation, continuous infusion of PGE_1, or vasoactive infusions; postoperative cardiac surgery patients; and those patients with severe myocardial dysfunction (myocarditis or cardiomyopathy), pulmonary hypertension, and pulmonary vascular disease or life-threatening arrhythmias.

ICU monitoring often includes continuous monitoring of ECG, blood pressure, CVP, and pulse oximetry.[466–470] In addition, capnography is used either continuously or intermittently with either nasal cannula or mechanical ventilation. ECG and hemodynamic monitoring, combined with careful clinical assessment, should allow immediate identification of life-threatening arrhythmias, LCOS, bleeding, and tamponade. Cardiac output, perfusion, and Do_2 can be indirectly assessed by physical examination, evaluation of central versus peripheral temperature gradient, NIRS, AVo_2D, and lactate.[471] (See Precautions in the ICU section under the Location-Specific Arrest Prevention and Response Measures heading.)

LCOS can occur after complex cardiac surgery and can be caused by endothelial dysfunction, activation of the inflammatory cascades, myocardial stunning from intraoperative ischemia and reperfusion injury, changes in loading conditions, and residual lesions or palliated physiology with continued parallel circulation or cyanosis.[237,278,472,473] LCOS and subsequent cardiac arrest can be prevented by strategies that lower oxygen consumption and minimize anaerobic metabolism. These include strategies such as sedation and analgesia with neuromuscular blockade and hypothermia to diminish oxygen consumption,[61] as well as an open sternum in neonates and infants during the postoperative period to limit development of tamponade physiology.[474]

Mechanical ventilation strategies have been tailored to ameliorate the physiological impairment of specific cardiac pathology. For example, providers can facilitate spontaneous breathing or early extubation after repair of "right-sided" lesions such as TOF (see Right-Sided Heart Disease) or for patients with single ventricle who are undergoing superior CPA or Fontan procedures (see Superior CPA and Fontan) to increase pulmonary blood flow.[475–478] Medical gas therapy includes the use of inspired carbon dioxide to promote pulmonary vasoconstriction or cerebral vasodilatation among patients with parallel circulation or use of iNO to induce pulmonary vasodilation.[95,479,480]

Drug therapy is marked by a high degree of interinstitutional variability, with no universally accepted strategy.[411,481,482] Therapy includes the use of prophylactic inotropic support and augmentation of support for worsening cardiac output. Commonly used classes of drugs include phosphodiesterase inhibitors, catecholamines, and nitric oxide donors/generators (nitroprusside and nitroglycerin), as well as pure vasoconstrictors such as norepinephrine, vasopressin, or phenylephrine.

The Prophylactic use of Milrinone After Cardiac Operations in Pediatrics (PRIMACORP) study demonstrated a 64% relative risk reduction in LCOS in children with CHD undergoing 2-ventricle repair who were prophylactically treated with a high-dose regimen of milrinone (75 $\mu g/kg$ bolus followed by 0.75 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 24–36 hours).[237,278] A low-dose regimen (25 $\mu g/kg$ bolus followed by 0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 24–36 hours) was not beneficial in reducing LCOS. A limitation of this study was that the diagnosis of LCOS was based on clinical judgment rather than objective evidence of diminished systemic Do_2.

Levosimendan sensitizes myocardial troponin C to calcium and increases inotropy. Intracellular calcium is not increased, so diastolic properties are maintained. Levosimendan also results in systemic, pulmonary, and coronary vasodilation through adenosine triphosphate–

dependent potassium channels, and favorable impact on myocardial oxygen consumption has been reported.[416,483] In 2 randomized controlled trials, levosimendan administration lowered myocardial oxygen consumption, improved cardiac output, or both.[417,484,485] Levosimendan is not available in the United States.

In the absence of residual anatomic lesions or coronary insufficiency, postoperative LCOS often resolves. In adult studies, preemptive goal-directed hemodynamic management, including administration of catecholamines, improved outcome.[486,487] There is no consensus regarding the threshold of catecholamine and vasoactive infusions that should trigger the initiation of mechanical circulatory support for postoperative LCOS. However, stabilizing a patient with ECLS allows reduction of inotropic support and can prevent cardiac arrest. For patients with heart failure awaiting transplantation, portable VADs are often used if heart failure worsens (as demonstrated by the need for escalating inotropic or vasodilator support, mechanical ventilation, or worsening renal function). Both ECLS and VAD therapy are best used for LCOS before cardiac arrest in appropriate patients.

Hypotension in the postoperative cardiac patient might not be from LCOS but from vasodilatory shock. These hypotensive patients have low SVR with normal or increased cardiac output. They are typically warm, with strong pulses, brisk capillary refill, and no evidence of acidosis. Therapy for these patients includes vasoconstrictors and hydrocortisone (see Endocrine Management section under the Pharmacological Interventions heading). Their hypotension is typically catecholamine resistant, and fluid resuscitation is minimally effective.

Gaps in Knowledge

Although LCOS is well described after heart surgery in infants, therapy is variable and is based on the child's condition and the congenital heart lesion present. This heterogeneity creates challenges for prospective trials to evaluate the efficacy of specific management or pharmaceutical therapies.

Recommendations: Low Cardiac Output Syndrome

1. **Milrinone is effective to decrease LCOS in infants after surgery for CHD *(Class I; Level of Evidence B)*.**
2. **Levosimendan can be useful to decrease LCOS after surgery for CHD *(Class IIa; Level of Evidence B)*.**

Location-Specific Arrest Prevention and Response Measures

Precautions in the ICU

It can be very challenging to reestablish spontaneous circulation after cardiac arrest in children with heart disease. Data from the STS-CHSD from 2000 through 2009 revealed an overall mortality rate after postoperative cardiac arrest of 49.4%, ranging from 15.1% to 62.3%, varying by age and complexity of the heart disease, compared with a 2.8% mortality rate in children who did not experience cardiac arrest after surgery.[83] In the AHA GWTG-R Registry, children who experienced cardiac arrest after cardiac surgery had an in-hospital mortality rate of 63% (ie, only 37% survival to hospital discharge), and those with medical cardiac disease had an in-hospital mortality rate of 72% (ie, only 28% survival to hospital discharge).[5] Thus, measures to avoid cardiac arrest are of utmost importance.

Prevention of cardiac arrest in an intensive care setting requires optimal staffing with experienced personnel, appropriate monitoring, and an index of suspicion for underlying complications.[14] Improving outcomes for patients at risk for arrest requires not only preventive strategies but also the capabilities to intervene with appropriate goals across the continuum of conditions from prearrest to postresuscitation intensive care.[488] In the STS-CHSD, the incidence of cardiac arrest was no lower among high-volume surgical centers (ie, >350 cases per year) than among low-volume surgical centers (ie, <150 cases per year), but survival was higher among the high-volume centers. This information supports the growing recognition that high-volume centers might be more successful at "rescuing" patients once complications occur.[83]

Staffing. Staffing considerations include provider level of experience, nurse to patient ratios, presence of unit-designated specialists, and level of physician coverage. In a recent survey, 50% of reported centers performing congenital heart surgery had a dedicated cardiac ICU,[489] although such units have not yet documented improved outcomes.[490] Descriptive studies have documented associations between lower patient to nurse ratios and increased nursing level of experience with improved outcomes in pediatric cardiac ICUs[491] and improved resuscitation outcomes with more experienced bedside nurses.[492]

In-hospital versus out-of-hospital attending physician coverage varies across cardiovascular surgical centers. Any differences between in-hospital versus out-of-hospital attending physician coverage can be blunted if the physician is able to monitor many hemodynamic variables and review digital images of x-rays and scans off-site. In a retrospective case series, the presence of an attending physician at the bedside at a tertiary training program was not associated with increased resuscitation success; however, arrests on weekend days were associated with worse outcome.[492] Multi-institutional nursing survey data demonstrated significant improvement in hospital survival after pediatric heart surgery when an experienced critical care nurse provided the patient care.[493] Similarly, nursing survey data linked to

STS data revealed that higher levels of nursing education and experience were significantly associated with fewer complications.[494]

Monitoring.

Brain Natriuretic Peptide. The concentration of brain natriuretic peptide is monitored clinically in adults to trend heart failure severity and predict death.[495] Serum brain natriuretic peptide can also be used to determine the impact on the myocardium of acute events such as endotracheal extubation,[496] weaning of inotropic support, and recovery during mechanical circulatory support.[497] In some patient populations, such as neonates after the stage 1 Norwood palliation, trends in postoperative brain natriuretic peptide levels are predictive of outcome.[498] Although brain natriuretic peptide concentration alone does not predict an impending cardiac arrest, an acute increase or upward trend can suggest the need to alter management, such as increasing inotropic support or initiating mechanical ventilation or mechanical circulatory support, as appropriate.

Lactate. Lactate accumulates from anaerobic metabolism when there is inadequate SBF and Do_2 to the tissues. An elevated serum lactate has prognostic significance when the serum lactate rises in the presence of a larger base deficit and metabolic acidosis.[499] In 2 case series, survival among children with elevated serum lactate after cardiovascular surgery was lower than survival among children in whom the serum lactate was not elevated.[500,501] However, the reported absolute levels and the rate of rise of lactate[502] that predicted poor outcome, including cardiac arrest or need for ECLS, varied among the reported studies. In single-institution case series, a pattern of rising lactate, worsening metabolic acidosis, and longer time that the lactate remained elevated have been associated with a higher risk of adverse outcomes, including the need for ECLS and cardiac arrest.[503,504]

Mixed Svo_2. Despite the use of critical postoperative monitoring, identification of subtle decreases in systemic Do_2 or early LCOS is difficult. The mixed Svo_2 can be used to assess for changes in systemic Do_2, oxygen consumption, or both. A true mixed venous oxygen sample can only be obtained in the pulmonary artery in patients with a structurally normal heart with no left-to-right intracardiac shunts. Saturation of systemic venous blood, sampled preferably from the SVC[33,505,506] or, alternatively, the IVC, can be used as a surrogate for the mixed Svo_2.[44] Monitoring of the Svo_2 can be accomplished with periodic sampling or use of a continuous monitor.[18,19,21,35,47,507]

The Svo_2 reflects the balance between Do_2 and oxygen utilization (ie, oxygen supply-demand ratio).[33] An increase in the Svo_2 can reflect improvement in systemic Do_2, a reduction in oxygen consumption, or both. Continuous Svo_2 monitoring, as part of a bundle of goal-directed therapy, has been shown in a randomized clinical trial of pediatric patients with sepsis to improve survival.[508,509] The Svo_2 can be used as a target biomarker for intervention to optimize systemic Do_2 and improve outcome.[34,94]

AVo_2D, the difference between the systemic arterial oxygen saturation and Svo_2, is a function of cardiac output, oxygen carrying capacity, and oxygen consumption. In patients with arterial oxygen desaturation, the AVo_2D can help distinguish intracardiac mixing, compromised alveolar oxygenation, and low cardiac output. When oxygen carrying capacity and cardiac output are adequate, the Svo_2 will be ≈25% to 30% lower than the Sao_2, indicating that systemic Do_2 is adequate. A larger AVo_2D (ie, >30% difference between the Svo_2 and the Sao_2) indicates a fall in cardiac output and Do_2 to the tissues, with resulting increase in tissue oxygen extraction.

A low Svo_2 after the stage 1 Norwood palliation is predictive of worsening outcome, including worse neurodevelopmental performance[49] and need for ECLS.[35] Increasing AVo_2D reflects worsening Do_2 or increased oxygen consumption (or both), and the Svo_2 and AVo_2D provide gauges of the need for and efficacy of therapies such as inotropic and vasoactive agents, sedation/analgesia and neuromuscular blockade, mechanical ventilation, and temperature control. An increasing AVo_2D in the face of maximum medical management can be an indication for ECLS to avoid cardiac arrest. For additional information, please see Assessment of Systemic Oxygen Balance.

Near-Infrared Spectroscopy. NIRS provides a noninvasive continuous estimation of venous-weighted oxygen saturation in different regions of the body. Typically, 2 probes are used to provide cerebral and somatic (splanchnic, renal) estimates of oxygenation, reflecting circulations with intense flow-metabolism coupling and sympathetic controls, respectively.[36] The value recorded from the somatic site is typically higher than that recorded from the head. With development of shock, there is a shift of blood flow from the splanchnic and somatic circulations to preserve cerebral blood flow. This physiological response to shock is reflected in the NIRS data by a drop in somatic oxygen saturation compared with the cerebral values.

NIRS technology is less invasive than direct Svo_2 measurement, and it can be used in non-ICU settings and during dynamic conditions, allowing assessment of venous oxygen status during physiological or hemodynamic stress.[510–513] In combination with pulse oximetry, a noninvasive estimate of AVo_2D is possible. With noninvasive estimates of arterial and venous saturation, changes in complex cardiovascular physiology can be decoded, including changes in shunt magnitude and direction and the distribution

of cardiac output.[36,78] Although controversy remains as to the predictive value of NIRS to direct clinical care,[43,51,514] it has been shown to correlate with serum lactate[40] and Svo_2.[38,515,516] Prolonged cerebral NIRS desaturation after cardiopulmonary bypass is associated with worse neurological outcome in single-ventricle patients.[48,517,518] Low renal/somatic NIRS is associated with renal dysfunction,[519,520] metabolic acidosis,[38,44] and a range of poor outcomes, including need for CPR and ECLS.[47,51,78] Although more evidence exists for the clinical utility of NIRS than is available for most other monitoring devices, its use is not universal.[23] However, consensus assessment supports its use as safe and effective.[43]

Arterial Blood Gas, Point-of-Care Testing. Rapid arterial blood gas analysis is important for patients with marginal hemodynamic status and those with acute changes in clinical status. Current bedside point-of-care testing systems can provide immediate, reliable arterial blood gas analysis and electrolyte, lactate, and hemoglobin concentrations.[521,522] Although intuitive, there are no data showing that more rapid availability of laboratory results is associated with improved outcomes.

On-Unit Chest Radiograph. On-unit chest radiography has become a current standard of care. It includes rapid technician response, immediate viewing of the radiograph, and wireless radiologist interpretation. This immediate access to interpreted radiographs is important for the care of the patient with acute or rapidly worsening cardiorespiratory function and can be very valuable to confirm appropriate device placement and to assess for abnormal fluid or air collections.

On-Unit Echocardiography. Echocardiography is invaluable in the pediatric and neonatal intensive care settings.[523] In addition to evaluation of CHD, echocardiography enables evaluation of systolic and diastolic function, estimation of PAP, evaluation of volume status and valvar insufficiency, and assessment for pericardial fluid or clot. Targeted echocardiography performed by noncardiologists in the ICU and emergency department can be useful to evaluate hemodynamic status, but in the presence of underlying cardiac pathology, input from a pediatric cardiologist is strongly recommended.[524,525]

Echocardiography for emergent or urgent use requires on-unit equipment and acquisition and interpretation of images. Anticipation of patient deterioration and close patient monitoring can transition an emergent echocardiogram to an urgent echocardiogram. Important reasons to perform an urgent echocardiogram include the need to evaluate ductal patency, residual postoperative lesions, ventricular function, valvar insufficiency, PAP estimate, effusions (pericardial or pleural), and atrial septal position after ECLS cannulation. Accurate identification of the pathogenesis of hemodynamic compromise can guide management to avoid clinical deterioration.[526]

Rapid-Deployment ECLS. Rapid-deployment ECLS can be used to prevent cardiac arrest when a patient's clinical condition continues to worsen despite maximal medical therapy. Rapid deployment is also used to provide ECPR if cardiac arrest does develop. Small-volume circuits require only saline prime, whereas larger-volume circuits require blood prime. With the exception of isolated hypoxemia, venoarterial ECLS is usually required. (See ECLS and ECPR section under the Mechanical Support heading.)

ECLS has been shown to be useful in supporting patients with complex CHD and respiratory failure caused by viral respiratory infections and cardiac dysfunction related to arrhythmias.[527–530] Such support can prevent deterioration to cardiac arrest.

Detection and Management of Complications After Cardiac Surgery.

Pericardial Tamponade. Pericardial effusions occur commonly after cardiac surgery, either early because of residual bleeding or as a complication of transthoracic intracardiac line displacement, or later because of postpericardiotomy syndrome. Pericardial effusions can be benign or hemodynamically significant, and their hemodynamic significance is not always related to the size of the effusion or presence of atrial or RV diastolic collapse. Classic signs of cardiac tamponade include tachycardia, hypotension, and pulsus paradoxus; however, such classic signs can be absent or difficult to detect in the presence of LCOS. The sensitivity of the echocardiographic right atrial and RV diastolic collapse is variable[531]; however, even moderate effusions can add to the instability of a patient with already compromised hemodynamics (eg, myocardial dysfunction, arrhythmia, single-ventricle physiology). Access to emergent interpreted imaging for pericardial effusion is important. This can be in the form of on-unit echocardiogram or ultrasound. In the postoperative patient, pericardial tamponade can also occur with the accumulation of clot, which is more difficult to interpret by echocardiogram than fluid but should be suspected in the presence of tamponade physiology. Tamponade physiology, even in the absence of pericardial fluid by echocardiogram, warrants sternal reopening or exploration.

Provision of positive-pressure ventilation and procedural sedation and analgesia for pericardiocentesis can precipitate cardiac arrest, particularly in neonates and infants. Positive-pressure ventilation reduces preload to the RV, further contributing to the tamponade physiology; as a result, it should be administered with knowledge of its potential downside. Ketamine is often preferred because it has a minimal effect on blood pressure[532] and allows patients to continue to breathe spontaneously. Neurohumoral mechanisms that main-

tain contractility and SVR can be reduced by all sedative-hypnotic medications,[533] and anticipatory administration of fluid to increase preload and epinephrine to increase circulating catecholamine can be helpful to prevent or treat deterioration in circulatory function during sedation and respiratory support.[3,4,534]

Arrhythmias. Arrhythmia can be an undetected cause of refractory low cardiac output. If not identified and treated, chronic arrhythmia can result in myocardial dysfunction. Arrhythmias that can continue undetected include ectopic atrial tachycardia and atrial flutter (fixed heart rate of 150 to 160 beats per minute if 2:1 block). For further detail, see section on Arrhythmias.

Low Cardiac Output Syndrome. LCOS is predictable after surgery for CHD,[472] particularly in neonates, but it can also occur in the setting of progressive heart failure. Goal-directed treatment including assessment of mixed Svo_2 can guide intervention and improve end-organ function and clinical outcome.[35] It is important to rule out residual anatomic lesions or coronary insufficiency as the cause of postoperative LCOS. (See section on Low Cardiac Output Syndrome).

Pulmonary and Airway Complications. Inadequate ventilation and oxygenation can be caused by parenchymal lung disease, mainstem intubation, pneumothorax, hemothorax, chylothorax, or significant pleural effusion. If untreated, particularly in neonates with compromised myocardial function, inadequate oxygenation and ventilation can lead to bradycardia and cardiac arrest. On-unit chest radiograph with immediate viewing is optimal, and arterial blood gas analysis will complement bedside assessment of airway and ventilation.

In neonates and infants, paralysis of the diaphragm from inadvertent phrenic nerve injury during cardiac surgery can prevent weaning from positive-pressure ventilation. Although eventual recovery of function should be anticipated, intervention with surgical plication of the diaphragm might be needed to facilitate successful extubation. Injury to the recurrent laryngeal nerve and paresis of a vocal cord can compromise the ability to protect the airway and clear pulmonary secretions.

Pulmonary Hypertension. Pulmonary hypertensive crises arise from an acute increase in PVR and PAPs resulting in RV distension and dysfunction, which compromises LV filling and contractility and systemic cardiac output. Pulmonary hypertensive crises are difficult to reverse; thus, it is critical to prevent such crises in at-risk patients.

For patients with known PAH, it is important to understand the underlying RV function; presence or absence of an atrial, ventricular, or aortic level shunt; and known reactivity to oxygen or iNO. In addition to common triggers of hypoxia and acidosis, postoperative pulmonary hypertensive crises can be associated with inflammation (eg, lung injury, surgical trauma, post cardiopulmonary bypass), and they can also be triggered by fever, infection, pain, anxiety, tracheal suctioning, dehydration, or rebound when reducing or discontinuing pulmonary vasodilators. Preemptive treatment with iNO, sedation/analgesia, and neuromuscular blockade may be indicated for some high-risk PAH patients.

The goals of therapy to reduce the risk of pulmonary hypertensive crises include reducing triggering stimuli (ie, avoid and correct hypoxia and acidosis); administering sedation, analgesia, and neuromuscular blockade and minimizing stimulation and pain; and reducing RV afterload through the administration of inhaled pulmonary vasodilators (eg, nitric oxide). Although acute hyperventilation is effective in lowering PVR,[535] use of iNO is as effective as hyperventilation without its potentially undesirable systemic effects, including detrimental effects on cerebral blood flow.[188] During a crisis, administration of systemic vasoconstrictors can also be considered. For further information, see Pulmonary Arterial Hypertension.

Precautions in the Step-Down Unit/Ward

Cardiac patients are typically transferred from the ICU when it is determined that they have reached a point of stability where they are less likely to have acute hemodynamic or respiratory compromise or cardiac arrest. No universally accepted criteria are available to determine when a patient is ready to move from the ICU to a step-down unit or ward. Routine postoperative patient criteria might include recovery from postoperative myocardial dysfunction (as evidenced by adequate perfusion after discontinuation of inotropic support), effective airway and ventilation without an oral or nasotracheal tube, and a stable cardiac rhythm. The interinstitutional strategies for management of cardiac patients in the nonintensive care environment are highly variable and determined by local expertise, healthcare provider experience, and other factors such as the hospital physical structure and bed space availability.

Monitoring on the step-down unit/ward is generally noninvasive and might include routine vital signs (measurement of temperature, heart rate, respiratory rate, and noninvasive blood pressure), as well as pulse oximetry and continuous ECG monitoring. Patients transferred to the step-down unit/ward should be considered sufficiently low-risk so that these strategies can reliably identify perturbations in cardiopulmonary status. An early warning score designed specifically for and validated in hospitalized children with heart disease is now available.[536]

Home Monitoring

Although discharge from the hospital typically occurs when patients are at low risk for cardiac and respiratory events and have an established nutrition regimen,

some patients with CHD, especially infants with single-ventricle anatomy and shunt-dependent PBF, remain at risk for acute deterioration as a result of the intrinsic inefficiencies of the parallel circulation. For newborns after the stage 1 Norwood palliation, the reported incidence of interstage mortality (ie, death between discharge after the stage 1 Norwood and admission for superior CPA) is often as high as the hospital mortality after the stage 1 Norwood palliation itself, particularly if the infant was palliated with an MBTS.[20,26]

Relatively minor illnesses can result in elevation of SVR or hypovolemia with an increase in Qp:Qs and decreased systemic perfusion and Do_2 to the tissues. In addition, there is the potential for a decrease in PBF attributable to neointimal proliferation in the systemic-to–pulmonary artery shunt or increased somatic growth rendering the shunt relatively smaller and physiologically insufficient.

In single-center studies, close monitoring of patients, particularly those with HLHS, in the home setting has been associated with reduced mortality before creation of the superior CPA.[537–541] These programs provided families with the following supplies and guidance: (1) pulse oximeter to monitor Sao_2 and identify worsening cyanosis (this might identify a shunt problem) or increased saturations (which might identify an early state of increased SVR); (2) a scale to determine daily weights to identify problems with growth, as well as evidence of acute dehydration; (3) a mechanism to record dietary intake; and (4) guidelines regarding contacting the referral center when vital signs are outside strict parameters. In these programs, patients not meeting guidelines were generally evaluated within 24 hours. In addition, parents were typically contacted weekly to review data. To further assess the impact of home monitoring on single-ventricle HLHS interstage mortality, the multicenter National Pediatric Cardiology Quality Improvement Collaborative (NPC-QIC) adopted a home monitoring quality improvement project involving 52 pediatric cardiac surgical centers and 1163 interstage infants between 2008 and 2014. Assessment of baseline interstage monitoring of HLHS infants performed at the participating NPC-QIC sites revealed significant variation nationally.[542] The key drivers that were deemed necessary to achieve a reduction in interstage mortality included engaging the parents, improving care transitions at stage 1 Norwood discharge, optimizing growth, and improving coordination among the care team and families.[11] Multiple change strategies or activities in these areas were recommended for centers participating in the collaborative, including caregiver preparation during the Norwood hospitalization; providing caregivers with a red flag action plan; establishing collaboration between the family, primary physician, cardiologist, and other team members; activities related to assessment and optimization of feeding and weight gain; standardization of assessments and action plans at clinic visits; and home monitoring during the interstage period of oxygen saturation and weight gain. Cumulative aggregate mortality between 2008 and May 2013 in NPC-QIC centers was 9.5%, lower than published previously in single-center studies.[11] From June 2013 to August 2014, cumulative aggregate mortality was 5.3%, a relative reduction of 44%.[11]

Although a recent study[543] analyzing NPC-QIC data from 2008 to 2012 did not find any association between home oxygen saturation or weight monitoring with either mortality or readmission, these data should be assessed with the following notable caveats. The analysis did not examine trends over time. Using statistical process control methodology, examination of interstage mortality rates over time within the NPC-QIC revealed no change in mortality rates initially (during the time period of the study by Oster et al[544]) but trends toward decreasing mortality within the collaborative more recently, beginning in 2013.[11] Additionally, home monitoring was just 1 component of the overall efforts supported by the NPC-QIC (and individual institutions that have adopted these methods) and was intertwined with numerous other activities related to engaging families and the care team, as well as coordination and standardization of care. In addition, the group with no home monitoring (36 patients in the group with no oxygen saturation monitoring) was very small, which limited the study's power and raised issues regarding generalizability, because this group reflected outcomes at no more than a handful of centers.

Gaps in Knowledge:

The existing published data regarding standard monitoring and staffing in the pediatric ICU are limited to surveys. Criteria to enable comparisons among units are difficult to establish because there is significant interinstitutional practice pattern variation. Similarly, limited quantitative data exists pertaining to pediatric cardiac ICU complications.

Children with complex CHD, particularly neonates, have a high risk of early and late postoperative morbidity and mortality. Evidence-based best practices to avoid and successfully manage these events have not yet been identified.

Recommendations: Location-Specific Arrest Prevention and Response Measures

1. **Increased nursing experience can be effective to improve outcomes for pediatric patients after congenital heart surgery *(Class IIa; Level of Evidence B)*.**
2. **Rapid access to or in-unit blood gas, radiograph, echocardiogram, and ECLS can be beneficial to optimize patient outcome *(Class IIa; Level of Evidence C)*.**

3. **Use of a home monitoring program (daily oxygen saturations, daily weights, diet record, and close communication with discharging facility) to manage neonates and infants after the stage 1 Norwood palliation for HLHS during the interstage period may be considered to reduce interstage morbidity and mortality *(Class IIb; Level of Evidence B)*.**

Cardiac Arrest Phase

Onset

Pediatric cardiac arrest in general is most often asphyxial/ischemic rather than arrhythmic, and it is typically associated with progression of shock or respiratory failure.[3,4,292] In a review of in-hospital cardiac arrest from the GWTG-R Registry, ≈60% of the children with cardiac arrest were already receiving mechanical ventilation and nearly 40% were receiving vasopressors at the time of arrest.[292] Data from the same registry revealed that nearly all cardiac surgical patients who had cardiac arrest had continuous ECG monitoring and vascular access in place at the time of arrest, 74% were receiving mechanical ventilation, and 60% were receiving vasoactive infusions.[5]

Cardiac arrest is 10 times more likely among children with CHD compared to critically ill children with noncardiac medical or surgical problems.[5,14,145] In the most recent data from the AHA GWTG-R Registry from 2000 to 2008, precipitating factors of cardiac arrest included hypotension or hypoperfusion (eg, LCOS or vasodilatory shock),[5] arrhythmias, and acute respiratory insufficiency. If low cardiac output is refractory to maximal medical management, institution of ECLS should be considered before cardiac arrest occurs. Unless cardiac arrest is precipitated by a sudden arrhythmia, inadequate Do_2 is likely to be present even before the arrest, adding to the ischemic insult of the arrest itself. Management of these children focuses on support of airway, ventilation, and perfusion to prevent the arrest.

When cardiac arrest develops, immediate provision of high-quality CPR is required. Simultaneously, providers must search for reversible or treatable causes of arrest, such as LCOS, cardiac tamponade, closure of a ductus arteriosus, acute pulmonary hypertensive crisis, or acute occlusion of a systemic-to–pulmonary artery shunt or a conduit. If modification of medications (eg, vasoactive drugs, prostaglandins), inspired oxygen concentration, iNO, or mechanical ventilation support preceded the arrest, providers must evaluate the effect of the modification on cardiac output.[4]

Bradycardia often precedes pediatric cardiac arrest and is typically caused by hypoxia or hypotension. The heart rate threshold for initiation of chest compression varies with the clinical scenario and the child's baseline heart rate. For the monitored child with bradycardia and pulses, the decision to initiate chest compressions requires consideration of blood pressure, heart rate, and timely access to medications, as well as consideration of the risk (in the early postoperative period) of compressions. For the seriously ill child, a heart rate of <60 beats per minute with signs of poor perfusion despite adequate ventilation with oxygen is a reasonable threshold indication for initiation of chest compressions (with ventilation). Initiation of chest compressions with ventilation before development of cardiac arrest might explain the better survival (40.7%) reported from the National Registry of CPR among 1353 children who received CPR for in-hospital bradycardia with pulses and poor perfusion compared with the 24.5% survival rate among 1489 children who received CPR only after development of asystole/pulseless electrical activity cardiac arrest.[292,545] The combination of chest compressions with the patient's intrinsic cardiac output can maintain critical blood flow and assist delivery of life-saving medications.

The most common terminal rhythm in pediatric cardiac arrest is brady-asystole,[292] and asystole and pulseless electrical activity were the most common terminal rhythms in children with both surgical and medical cardiac disease.[5] Prompt initiation of high-quality CPR with administration of oxygen is essential to restore effective Do_2 and limit the ischemic insult.

In the GWTG-R Registry, children with surgical or medical cardiac disease were much more likely than children with no cardiac disease to demonstrate VF or pulseless VT as a terminal rhythm of cardiac arrest.[5] VF or pulseless VT (see Arrhythmias section) should raise suspicion of myocardial ischemia, or in the specific example of torsade de pointes, should raise suspicion of LQTS, either congenital or acquired. In such patients, prompt recognition of the degenerating rhythm and provision of high-quality CPR with rapid defibrillation are of utmost importance.[292,293] (See Cardioversion and Defibrillation During Resuscitation.)

Gaps in Knowledge

Cardiac arrest in children with cardiac disease can be somewhat categorized by situation, although the primary cause of the arrest may be unknown. More data are needed regarding specific alterations (if any) that may be necessary in basic or advanced life support to improve survival of pediatric patients with CHD, open sternum, long QT, fulminant myocarditis, pulmonary hypertension, arrhythmia, and postoperative complications, particularly LCOS and respiratory insufficiency.

Recommendations: Cardiac Arrest Phase – Onset

1. **For children with asystole or pulseless electrical activity, prompt initiation of high-quality CPR is essential, and providers must search**

for and treat any reversible causes *(Class I; Level of Evidence C)*.

2. **For children with VF or pulseless VT, high-quality CPR and prompt defibrillation are indicated *(Class I; Level of Evidence B)*.**

Cardiopulmonary Resuscitation

Cardiac Arrest and CPR

CPR provided to a patient with a structurally normal heart delivers ≈10% to 30% of normal blood flow to the heart and 30% to 40% of normal blood flow to the brain.[6,546,547] As a result, high-quality CPR is vital to the success of any resuscitation attempt,[6] to maintain blood flow and Do_2. There are no data to support modification of the AHA-recommended pediatric CPR skills for children with CHD, although unique aspects of the child's anatomy and condition in the early postoperative period (eg, open sternum, fresh sutures lines, anterior conduit) could compromise the effectiveness of chest compressions. Appropriate rescuer hand position is critical to create blood flow during compressions. In addition, the components of high-quality CPR recommended by the AHA are also required to optimize blood flow: adequate compression rate, adequate compression depth, allowing full chest recoil after each compression, minimizing interruptions in compressions, and avoiding excessive ventilation.[84]

The 2-finger compression technique is used for the single rescuer of the newborn or infant; the 2 fingers compress the lower third of the sternum in the newborn and just below the intermammary line in the infant.[546,548] The preferred compression technique for 2-rescuer CPR for newborns and infants is the 2-thumb, encircling hands technique, with thumbs together compressing the lower third of the sternum and the fingers encircling the infant's thorax. This compression technique provides better coronary artery perfusion pressure and results in improved depth of compression, and it can generate higher aortic systolic and diastolic pressures than the 2-finger technique.[549,550] For children, rescuers should use the heel of 1 or 2 hands to compress over the lower half of the sternum, avoiding the xyphoid.[546]

A compression rate of at least 100 per minute was recommended in the 2010 AHA pediatric basic life support guidelines.[546] A recent study of adult out-of-hospital resuscitation suggested that the optimum compression rate might be 100 to 120 per minute,[551] and this range of compression rate has been endorsed in the 2013 AHA "Cardiopulmonary Resuscitation Quality" article[6] and recommended in the 2015 pediatric basic life support guidelines update.[84] There is no evidence to identify an optimum compression rate for infants and children, but in the absence of direct information, a compression rate of 100 to 120 per minute is reasonable for infants and children.

Compressions are thought to generate blood flow during resuscitation by compressing the heart between the sternum and vertebral column (so-called cardiac pump mechanism) and by creating intrathoracic-to-extrathoracic pressure gradients (the so-called thoracic pump mechanism); both mechanisms have been demonstrated during CPR using echocardiography in adult patients,[552–554] although comparable pediatric clinical data have not been published.

Recommendations for chest compression depth and technique vary with the size of the infant and child. All compressions in infants and children (beyond the newborn period) should be to a depth of at least one-third the depth of the chest. This depth of compression will correspond to a depth of ≈1.5 inches (4 cm) in infants beyond the newborn period and ≈2 inches (5 cm) in children.[546,555] Once the child has signs of puberty, the adult compression depth of at least 2 inches (5 cm) but no more than 2.4 inches (6 cm) can be used. It is important to allow for full chest recoil after each compression, so the heart can refill with blood.[556,557] Incomplete recoil occurs when the rescuer leans on the chest and fails to allow the chest to reexpand after each compression. Leaning is more likely if the rescuer is fatigued and can be minimized by lifting the fingers or hand(s) between compressions. Inadequate recoil maintains high intrathoracic and right atrial pressure, so it will reduce coronary perfusion pressure (aortic end-diastolic pressure minus right atrial pressure), blood flow through the heart, venous return to the heart, and blood flow generated by the next compression. Although there are no human data linking inadequate recoil with reduced survival, in data from a piglet model,[558] a pediatric model,[559] and hemodynamic studies,[556] inadequate recoil reduced coronary and cerebral perfusion pressure, cardiac output/index, and LV myocardial blood flow.

Minimizing interruptions to compressions is vital to a successful resuscitation.[557,560] Strategies to minimize interruptions include using the recommended compression to ventilation ratio (15 to 2 for infants and children with ≥2 rescuers when no advanced airway is in place, and once an advanced airway is in place, continuous chest compressions with asynchronous breaths at a rate of 10 breaths per minute) and minimizing interruptions for airway placement, rhythm checks, shocks, and ECLS cannulation.[6] The 2013 AHA CPR quality statement recommends compressions be performed at a minimum of 60% with a target of 80% of the total resuscitation time for patients of all ages.[6]

Excessive ventilation during resuscitation can be harmful and should be avoided. Positive-pressure ventilation increases intrathoracic pressure and impedes venous return. During CPR with an advanced airway in place, as noted above, compressions are delivered continuously at a rate of 100 to 120 per minute, and

ventilation is delivered asynchronously (with an attempt to deliver breaths between compressions) at a rate of 10 breaths per minute (or 1 breath every 6 seconds).

Special Considerations for the Delivery Room

There are important differences between priorities for resuscitation of premature newborns with lung disease and priorities for resuscitation of newborns with CHD. For the newborn with the structurally normal heart, the most common reason for resuscitation is respiratory failure, so establishment of an adequate airway and ventilation with oxygen are priorities. In the unlikely event that compressions are required, a total of 90 compressions and 30 breaths (120 events) are delivered each minute, ensuring adequate balance of cardiac output and ventilation.[548]

For the newborn with a prenatal diagnosis of CHD, resuscitation in the delivery room is planned to target immediate problems created by the heart lesion. Lesions likely to cause inadequate oxygenation and ventilation include severe forms of TOF with absent pulmonary valve, and Ebstein anomaly of the tricuspid valve. Patients with mitral atresia and an intact atrial septum will present with immediate hemodynamic instability. Patients with TGA and an intact atrial septum will be profoundly cyanotic and hypoxemic. The latter 2 lesions will require transcatheter or surgical intervention for stabilization; in the absence of a prenatal diagnosis and preplanned intervention, survival is poor. Newborns with obstructed TAPVC or TGA with restrictive atrial septum will likely require mechanical ventilation and hemodynamic support, rapid diagnosis (if not already known), and prompt intervention but are unlikely to require CPR. In general, newborns with a prenatal diagnosis of ductal-dependent heart disease will be stable in the delivery room with initiation of low-dose PGE_1 infusion (0.01 $\mu g \cdot kg^{-1} \cdot min^{-1}$).

Special Considerations for the Immediate Postoperative Patient

The vast majority of patients after cardiac surgery will have an arterial and a CVP catheter with continuous waveform display that will enable immediate assessment of the effectiveness of compressions and any need for modifications in resuscitation techniques or therapies. Use of hemodynamic monitoring to optimize resuscitation technique enables estimation of coronary perfusion pressure (aortic relaxation/diastolic pressure–right atrial pressure/CVP)[86] and tailoring of type of compression, location, and depth to optimize coronary perfusion pressure.

Both the cardiac pump and thoracic pump mechanisms can be compromised in the patient with CHD. The cardiac pump mechanism can be compromised by the presence of an anterior conduit through decreased direct compression of the RV body. In the setting of severe valvar insufficiency, there can be decreased PBF or SBF with each chest compression. PBF can be limited in the presence of an MBTS or during a pulmonary hypertensive crisis.

It is important to develop a resuscitation strategy for each postoperative patient before an arrest occurs. This strategy includes optimal hand position for chest compressions and planned cannulation site for ECLS. Although major thoracic and myocardial injuries are rare in CPR-treated pediatric and adult patients, occurring in 3% and 7% of those undergoing CPR, respectively, the immediate postoperative period after sternotomy and cardiotomy in the pediatric patient may carry greater risk. Although there are no data assessing the absolute risk from direct chest compressions after pediatric cardiac surgery, teams resuscitating children with cardiac disease should note the potential risk of myocardial or thoracic injury, bleeding, or dehiscence of intracardiac repairs.[561,562] In patients with an open sternum, external chest compressions are generally less effective than open-chest cardiac massage.

Although open-chest (direct) cardiac massage is frequently performed in infants and children with open sternums, there are no data on which to base recommendations regarding technique. Direct cardiac massage should ideally be undertaken with oversight of the surgical team. A sterile field must be maintained. Compressions of the ventricle or ventricles should avoid suture lines and be gentle to avoid unnecessary direct damage to the myocardium. An arterial pressure monitor will document the effectiveness of compressions during open-chest massage.[86]

Monitoring During CPR

The child's arterial pressure waveform provides useful feedback about the adequacy of compressions and chest recoil. The waveform not only provides the systolic (compression) and diastolic (relaxation) pressures, but the width of the waveform enables assessment of the stroke volume. In a study of adult patients during CPR, a coronary perfusion pressure of at least 15 mm Hg was required for ROSC, and survival increased if the coronary perfusion pressure was >20 mm Hg.[563] In adults, the 2013 CPR quality statement[6] recommends maintaining the aortic diastolic pressure (between compressions) above 25 mm Hg and targeting a coronary perfusion pressure >20 mm Hg. There is insufficient evidence to recommend coronary perfusion pressure goals for infants and children, although expert consensus is that it is reasonable to attempt to maintain the coronary perfusion pressure above 20 mm Hg.[6] Early data in adults have shown that higher saturations by NIRS monitoring during CPR are associated with increased likelihood of ROSC.[564,565]

In patients with a structurally normal heart, continuous waveform capnography monitoring of $ETCO_2$ can provide useful information about PBF and hence

the effectiveness of chest compressions. In these patients, if the $ETco_2$ remains low (eg, ≤10–15 mm Hg), it is reasonable for providers to attempt to optimize CPR technique to improve the $ETco_2$. In patients with shunt-dependent PBF or significant pulmonary insufficiency, $ETco_2$ might underestimate systemic cardiac output, so establishment of target threshold $ETco_2$ is challenging. There are insufficient data to use the $ETco_2$ as a prognostic indicator in infants and children.[4]

Cardioversion and Defibrillation During Resuscitation

Children with CHD frequently require cardioversion for acute treatment of arrhythmias, most commonly atrial flutter or atrial fibrillation. They might also require defibrillation for treatment of VF or pulseless VT. Cardioversion or defibrillation can be performed on patients with internal pacemakers and patients on ECLS.

Sedation for Cardioversion. In the prearrest setting, adequate sedation and analgesia can be achieved with short-acting intravenous agents. Because the child with CHD may be more sensitive to the vasodilatory effects of these drugs, dose adjustment may be required. Performing cardioversion with the assistance of anesthesiologist or intensivist results in the safest experience for the child; however, when cardiovascular collapse is present or imminent, cardioversion can be performed without sedation or analgesia.

Pad Position and Size. The general techniques for cardioversion and defibrillation in children with CHD do not differ from general recommendations for these procedures in infants and children without CHD.[4] Handheld paddles or self-adhesive pads can be used. Anterior-posterior or anterior-lateral pad position may be appropriate; providers should follow the defibrillator manufacturer's recommendations. If the child has dextrocardia, defibrillator pads should be placed over the right side of the chest to keep the heart between the defibrillation pads. If the child's chest is small, placing the pads in the anterior posterior position will prevent overlap. No difference in cardioversion success has been reported with various pad positions.[415] For patients with an open sternum, paddle and pad positions may need to be modified, or internal paddles can be used under sterile conditions.

Energy Doses for Cardioversion and Defibrillation. Rapid direct-current cardioversion or defibrillation is indicated for tachyarrhythmia (eg, cardioversion for atrial flutter or atrial fibrillation; defibrillation for VF or pulseless VT) that results in hemodynamic instability (eg, hypotension, acutely altered mental status, signs of shock). The energy must be delivered to the myocardium, and placement of the pads may need to be modified in special circumstances, such as for patients with an implanted pacemaker or dextrocardia. For cardioversion of SVT or VT/wide-complex tachycardia with a pulse, an initial energy dose of 0.5 to 1 J/kg can be effective. This low-dose shock is delivered in a synchronized mode to avoid precipitating VF. If the initial cardioversion dose is not effective, the dose is increased to 2 J/kg and again delivered in a synchronized mode.

For VF/pulseless VT, an initial dose of 2 to 4 J/kg is acceptable, although for ease of teaching, a dose of 2 J/kg can be considered. For subsequent doses, it is reasonable to use 4 J/kg, and higher doses can be considered, although the dose should not exceed 10 J/kg.[3,4] In the setting of an open sternum and internal paddles, the adult dose for defibrillation is 10 to 20 J,[415,566] and 0.6 to 0.7 J/kg in children.

Integration of Attempted Defibrillation With CPR. Analysis of CPR process recordings from 815 adult out-of-hospital resuscitations in the Resuscitation Outcomes Consortium cardiac arrest registry documented a strong relationship between short preshock and perishock pauses and shock success, including survival to hospital discharge. The preshock pause is the interval between the last chest compression and shock delivery. The perishock pause is the sum of the preshock pause and the interval between shock delivery and the next (postshock) chest compression. Adult patients with preshock pauses of 20 seconds or longer and those with perishock pauses of 40 seconds or longer were approximately half as likely to survive to hospital discharge as patients who had shorter pauses. Survival fell by ≈18% for every 5-second increase in preshock pause and by ≈14% for every 5-second increase in perishock pause.[567] Shortening these pauses by even 5 seconds was associated with substantial improvement in survival. Although this study has not been replicated in pediatric patients, it is likely that the effect of prolonged pauses in compressions is detrimental to survival in children. In animal models, VF increases myocardial oxygen consumption by 70%.[568] Animals allowed to fibrillate for 10 minutes were more likely to have ROSC if they received CPR (with or without epinephrine) before defibrillation compared with those who received an immediate shock.[569] CPR increased the amplitude of fibrillation and was associated with more successful defibrillation. In the fibrillating heart, CPR improves myocardial creatine phosphate levels, reflecting an improved cardiac energy state.[568] The improved amplitude of fibrillation during CPR is likely related to an improved cardiac energy state, in part attributable to improved myocardial Do_2; the improved energy state just before shock delivery is likely to improve shock success. To minimize preshock and perishock pauses, the resuscitation team must carefully integrate high-quality CPR and shock delivery. This requires practice, and analysis of these pauses should be part of the monitoring of resuscitation quality and postresuscitation debriefing.

Pacing

Several clinical trials have examined the role of transcutaneous cardiac pacing for out-of-hospital resuscitation for children and adults with bradycardia/asystole. Sherbino et al[570] reviewed the experience of 34 of these trials in a meta-analysis of the literature. To date, no study has shown improved outcomes of cardiac arrest in response to pacing[332,571–580]; however, no study specifically examined pacing in the resuscitation of patients with CHD. For patients with a perfusing rhythm and symptomatic heart block or sinus node dysfunction, pacing is indicated (see Arrhythmias section).

Intubation and Airway Management

During the early postoperative period, an advanced airway is often in place. If the child in cardiac arrest has no invasive airway in place, the decision to intubate and the timing of intubation must be considered carefully. Initially, effective ventilation can be accomplished with bag and mask. For a patient with difficult mask ventilation, placement of an oral airway, placement of the endotracheal tube in the nasopharyngeal space with a closed mouth, or placement of a laryngeal mask airway can permit assisted ventilation and oxygenation without tracheal intubation. Placement of a gastric tube to decompress the stomach should be considered both to facilitate ventilation and to reduce the risk of regurgitation, and the tube can be left in place during laryngoscopy.[581] If effective oxygenation and ventilation cannot be achieved, insertion of an advanced airway is indicated. Endotracheal intubation in infants and children requires special training and ongoing experience, and special expertise is required for intubation during CPR to minimize interruptions in chest compressions (see Principles of Intubation, Airway Management, and Respiratory Support). In children with no intracardiac or great vessel shunt, changes in $ETco_2$ during CPR can be a direct indication of changes in PBF and cardiac output.[66–70]

Vascular Access

There are no published data to suggest that the AHA PALS vascular access guidelines should be modified for children with heart disease who require resuscitation. Administration of resuscitation drugs through an indwelling central venous catheter is preferred if one is in place. If vascular access is not in place at the time of arrest, the AHA PALS 2010 guidelines recommend the use of intraosseous or peripheral venous access (if it can be placed rapidly) for the initial route of vascular access during resuscitation.[3,4] The intraosseous route of administration has been shown to be safe, rapidly achievable, and comparable to administration of medications using an intravenous route.

Placement of central venous access is not generally recommended as the initial vascular access for administration of medications during resuscitation, unless experienced providers are readily available to place the catheter quickly and with minimal complications. Central venous access can be helpful for hemodynamic monitoring and administration of vasoactive medications. A long central venous catheter can contribute to increased resistance to rapid fluid or drug administration. Children with heart disease, especially those with CHD, can have occlusion of central veins and arteries from prior procedures, or they may have anomalies of the central venous system, including bilateral SVC. Information about occluded vessels must be documented so it is readily available to the resuscitation team to prevent delay in obtaining vascular access. Current ease and sophistication of intraosseous access provides excellent vascular access and minimizes the need for endotracheal drug delivery.[3,4]

Pharmacological Therapy

For patients receiving CPR in the hospital, age and size, anatomy, and physiology are known even if the immediate cause of the arrest is uncertain. Effective medication delivery requires cardiac output (blood flow) and delivery near the central arteries or veins. During cardiac arrest, circulation is created by high-quality CPR, and high-quality chest compressions are necessary to circulate any drugs administered. Medication administration can be distant from the site of effect (eg, with peripheral intravenous or intraosseous catheters) or at the site of effect (eg, central venous or intracardiac catheters). To date, there have been no published studies to establish the optimal timing and doses of resuscitation drugs in any pediatric population. As a result, providers should follow the AHA PALS CPR and Emergency Cardiac Care algorithms relative to drug administration and dosing.

For shock-refractory VF/pulseless VT, intravenous epinephrine can be administered (0.01 mg/kg, or 0.1 mL of the 0.1 mg/mL concentration; maximum 1 mg) every 3 to 5 minutes.[3,4] For recurrent VF/pulseless VT in the absence of LQTS, either amiodarone (5 mg/kg IV/IO bolus up to a maximum dose of 15 mg/kg) or lidocaine (1 mg/kg) can be administered. The recommendations for the use of amiodarone are extrapolated from adult studies of prehospital VF/pulseless VT cardiac arrest that showed increased survival to hospital admission but not to hospital discharge[384,385,568] and a report of the use of amiodarone in the treatment of life-threatening (but nonarrest) ventricular arrhythmias in children.[312] In a multivariate analysis of data from the GWTG-R Registry, among pediatric patients with in-hospital cardiac arrest associated with VF/pulseless VT, use of lidocaine was associated with increased ROSC and 24-hour survival, whereas amiodarone was not. Neither drug was associated with improved survival to hospital discharge.[385,386,582] On the basis of these reports, lidocaine can be considered in the setting of VF/pulseless VT in children with congenital or acquired heart disease.[3,398] (See Arrhythmias section.)

Gaps in Knowledge

There are few published data regarding effective CPR techniques in the patient with CHD, and even less information about CPR in the immediate postoperative period. Should CPR be unsuccessful, strategies for ECLS are currently institutionally developed and take into account the availability of the surgical and ECMO teams. In addition, the impact of hemodynamic monitoring on outcomes from CPR in infants and children with CHD is not well documented.

Variability in patient habitus and pad/paddle positions and contact, as well as variability in underlying cardiac anatomy and function among pediatric patients who develop cardiac arrest, creates challenges in determining optimal energy doses for cardioversion and defibrillation. The data regarding management and outcome of VF/pulseless VT arrests in adults with coronary artery disease cannot be applied directly to infants and children with CHD. Research regarding the management of pediatric postoperative VF/pulseless VT is needed.

There are few data regarding indications for pacing during CPR in children with cardiac disease. In addition, there is no published evidence to modify the PALS recommendations regarding priorities for inserting an advanced airway or establishing vascular access in patients with congenital and acquired heart disease who do not have these devices in place when cardiac arrest develops.

Recommendations: Cardiac Arrest Phase – CPR

1. **In general, AHA recommendations for pediatric CPR skills can be effective for children with CHD *(Class IIa; Level of Evidence C)*.**
2. **If hemodynamic monitoring (particularly arterial and CVP monitoring) is in place during CPR, it is reasonable to use these values to modify and optimize CPR technique *(Class IIa; Level of Evidence C)*.**
3. **Conventional high-quality CPR (closed chest compressions and positive-pressure ventilation) must be provided when the child with CHD develops cardiopulmonary arrest, but CPR may be less effective in the presence of single-ventricle physiology (shunt, superior CPA, or Fontan), severe valvar insufficiency, or pulmonary hypertensive crisis. Until there is sufficient evidence to support specific alternative recommendations for CPR technique to improve survival in these populations, it is reasonable to use the conventional CPR technique *(Class IIb; Level of Evidence C)*.**
4. **It is reasonable to consider deployment of ECLS before cardiac arrest and in the early minutes of resuscitation *(Class IIa; Level of Evidence B)*.**
5. **Arterial blood pressure and $ETco_2$ should be monitored when possible to provide feedback regarding quality of chest compression technique and other aspects of resuscitation *(Class I; Level of Evidence C)*.**
6. **For cardioversion of SVT or VT with pulses, an initial dose of 0.5 to 1 J/kg is recommended. Subsequent doses of 2 J/kg may be used *(Class I; Level of Evidence C)*.**
7. **For defibrillation for VF/pulseless VT, an initial dose of 2 to 4 J/kg is reasonable *(Class IIa; Level of Evidence C)*. For subsequent shocks, a dose of 4 J/kg is reasonable, and higher doses may be considered, although they should not exceed 10 J/kg *(Class IIa; Level of Evidence C)*.**
8. **For defibrillation for VF/pulseless VT in the setting of an open sternum and internal paddles, the dose is 0.6 to 0.7 J/kg in children (*Class IIa; Level of Evidence B*).**
9. **The resuscitation team should integrate high-quality CPR and shock delivery to minimize pauses in CPR associated with defibrillation *(Class I; Level of Evidence B)*.**
10. **For patients who develop bradycardia during CPR, there is no evidence that pacing will improve ROSC. Pacing may be considered but should not interrupt chest compressions. Appropriate sensing is important to avoid inducing VF *(Class IIb; Level of Evidence C)*.**
11. **Central venous access, if available, is the recommended route of vascular access for medication administration and potential hemodynamic monitoring *(Class 1; Level of Evidence C)*.**
12. **In the absence of central venous access, vascular access via peripheral intravenous catheter can be useful for administration of medications if it can be established rapidly *(Class IIa; Level of Evidence C)*.**
13. **Intraosseous access is rapid, safe, effective, and useful as the initial route of vascular access in pediatric cardiac arrest *(Class I; Level of Evidence C)*.**

Mechanical Support

ECLS and ECPR

ECLS (also known as ECMO) is increasingly used in adults and children for treatment of in-hospital cardiac arrest refractory to initial high-quality CPR.[75,76,583–586] When ECLS is deployed during cardiac arrest, it is referred to as ECPR. In observational studies with propensity analyses of adult patients in refractory cardiac arrest, the use of ECPR has been shown to improve

both survival and favorable neurological outcomes[587] compared with conventional CPR. Similarly, in a pediatric analysis from the AHA GWTG-R Registry, the use of ECPR was associated with higher acute resuscitation survival but lower postresuscitation survival than conventional CPR. In addition, the use of ECPR was not associated with overall survival to discharge.[17]

Until recently, data regarding the association between ECPR and survival of children with heart disease after cardiac arrest was limited to case series.[588] However, in a multivariate analysis of factors associated with survival from cardiac arrest among children with both medical and surgical heart disease, the AHA GWTG-R Registry data demonstrated improved survival with the use of ECPR.[5] A recent study from the GWTG-R showed that for children with in-hospital CPR of ≥10 minutes' duration, ECPR was associated with improved survival to hospital discharge and survival with favorable neurological outcome compared with conventional CPR.[589]

For children with heart disease, ECPR is most commonly used to support those who have cardiac arrest in the postoperative period after congenital heart surgery[8,75,590–593] and less commonly in the setting of acquired heart disease (eg, acute fulminant myocarditis, cardiomyopathy, or refractory arrhythmias). No differences in survival between unoperated versus postoperative patients or between single versus 2-ventricle congenital heart defects have been observed.[8,591] In some observational studies, infants and children with acute fulminant myocarditis resuscitated with ECLS after cardiac arrest have been shown to have good outcomes.[269,270,594]

Prearrest Factors. Prearrest factors that predict mortality in children supported with ECLS have been evaluated in many observational studies.[8,586,591,593] The severity of prearrest metabolic acidosis based on arterial blood pH and lactic acidosis has been shown to be associated with both mortality and neurological injury; however, the timing of laboratory measurements (prearrest versus immediate postarrest) varies considerably in these studies.

Duration of CPR Before ECLS. Prolonged duration of CPR before ECLS can increase the risk of mortality and neurological injury in ECPR patients[8,75,586,588,595,596]; however, the duration of CPR has not consistently been shown to be a risk factor for mortality and cannot be used exclusively to guide patient selection for ECPR. Survival with good neurological outcome has been documented in some patients receiving >60 minutes of CPR before ECLS deployment.[75]

ECPR Deployment Location. ECPR is currently deployed in many areas of the hospital, with locations varying widely based on institutional policies. Common areas for provision of ECLS include ICUs, emergency departments, inpatient wards, and operating rooms.[8,597,598] One study showed improved survival for patients placed on ECPR in the catheterization laboratory and ICU compared with other areas.[8] ECPR outcomes can be improved by restricting ECLS cannulation to areas where equipment required for ECLS deployment during cardiac arrest can be accessed easily and personnel skilled at providing high-quality CPR and managing ECLS are readily available.

There is some evidence that centers with higher ECPR volumes achieve better survival than low-volume centers. Several studies have demonstrated that mortality is lower in pediatric cardiac ECLS patients treated in higher-volume centers (>15–22 patients per year).[599–601] As a result, it is reasonable to refer complex patients at high risk of cardiac arrest to centers with established, high-volume ECPR programs.

The use of ECPR for out-of-hospital cardiac arrest in adults was associated with better survival with favorable neurological outcomes at 6 months in one study (11.2% versus 2.6%, P=0.001)[602]; however, the proportion of witnessed arrests was high (>90%), and bystander CPR was performed in >70% of cases. Survival rates were higher in those with VT/VF than in those with nonshockable rhythms.[602] Many more data are required before the indications for and utility of ECMO can be determined in patients who have an out-of-hospital arrest and arrive at the hospital still receiving CPR. Extreme caution must be exercised before extrapolating these data and deploying ECPR for out-of-hospital cardiac arrest to children, because the causes are usually different.

Vessels Used for ECLS Cannulation. ECLS cannulation strategies for use during CPR based on cardiac anatomy are shown in Table 5. Venous sites commonly used for ECLS cannulation include the internal jugular vein, femoral vein, and right atrium. Common arterial cannulation sites include the carotid artery, femoral artery, and ascending aorta. In children cannulated for ECLS after recent cardiac surgery, the right atrium and aorta are commonly used, because these sites can be accessed rapidly through the sternotomy incision. One study showed that use of neck vessels for ECLS cannulation was associated with better survival,[591] a result that can be explained by fewer interruptions in CPR when the neck veins are used. However, another analysis of the Extracorporeal Life Support Organization (ELSO) Registry did find an association between increased neurological complications and carotid artery cannulation.[603] Although there is no published information regarding femoral vessel cannulation and ECPR outcomes, it is possible that femoral vessel cannulation for ECPR in older children might also require fewer interruptions of CPR, resulting in better outcomes.

ECLS Circuitry and Management. ECLS circuit components such as the pump, tubing, and oxygenator vary widely among ECLS centers, but there is no information

Table 5. Cannulation Strategies for ECPR*

Physiology	Peripheral Cannulation		Central Cannulation		Comments
	Venous	Arterial	Venous	Arterial	
Biventricular circulation	Internal jugular or femoral	Common carotid or femoral	Systemic venous atrium	Aorta	Left atrial decompression may be required
Single ventricle or shunted physiology	Internal jugular	Common carotid	Systemic venous or common atrium	Aorta	Shunt restriction may be required; for carotid cannulation with an MBTS, cannula position can result in shunt overcirculation or occlusion
Superior cavopulmonary anastomosis	Internal jugular and/or femoral	Common carotid	SVC and/or systemic venous or common atrium	Aorta	Additional venous cannula may be required
Fontan	Internal jugular and/or femoral	Common carotid or femoral	Fontan baffle	Aorta	Additional venous cannula may be required; pulmonary venous atrial drainage may be required

ECPR indicates extracorporeal life support to support failed cardiopulmonary resuscitation; MBTS, modified Blalock-Taussig shunt; and SVC, superior vena cava.

*General principles for efficient use of extracorporeal life support (ECLS) to support cardiopulmonary resuscitation include the following: (1) Venoarterial ECLS should be used in all cases. (2) Knowledge of venous anatomy and previously occluded vessels is critical for successful and timely deployment of ECLS. (3) Central (transthoracic) cannulation may be considered in patients who have undergone a recent sternotomy. (4) Peripheral (percutaneous) cannulation may be preferred for patients without recent sternotomy. (5) ECLS cannulas should be large enough to provide complete cardiac output (cardiac index >2.5 $L \cdot min^{-1} \cdot per\ m^{-2}$). If extracorporeal membrane oxygenation flow is limited by inadequate venous drainage, secondary drainage sites should be considered.

as to whether these components influence outcomes for ECPR patients. Most centers use crystalloid primed circuits for ECPR deployment. One study has shown that the use of blood prime increased mortality in ECPR patients.[8] Generally, heparin 100 U/kg is administered at the time of ECLS cannulation. ECLS circuit management strategies are affected by the patients' underlying disease and vary among ECLS centers.[394]

ECLS Team and Training issues. ECPR teams should be readily available for deployment at the discretion of the institution. The composition of the ECPR team varies by institution, and there is no evidence to suggest that the type of ECPR team available influences survival. Pediatric ECPR teams should include specialists to manage resuscitation, to cannulate, and to prime and deploy ECLS. Seamless teamwork and communication is essential for successful and safe ECLS deployment. ECLS team training using medical simulation can help maintain teamwork and the procedural expertise required for safe ECPR deployment. In one preintervention and postintervention study at a single institution, ECLS simulation training resulted in subjective reports of smoother team coordination and significant reduction in median time to deployment (from 51 to 40 minutes) during actual pediatric ECPR.[604]

ECLS Complications and Outcomes. Complications related to ECLS often limit survival in children.[8,584] Neurological complications are common after ECPR and occur in at least 20% of ECPR patients.[605] Neurological complications can result from prearrest illness, the quality of CPR provided before and during ECLS deployment, or as a complication of ECLS itself. As noted above, an analysis of multicenter data from the ELSO database documented an association of decreased mortality with cannulation of the right carotid artery compared with aortic cannulation[591]; however, another analysis of the ELSO Registry did find an association between increased neurological complications and carotid artery cannulation.[603] There is no published evidence to support or refute the effectiveness of therapeutic hypothermia after ECPR.

Survival after ECPR is higher in children with cardiac disease than in those with noncardiac disease.[188,584] Hospital survival from ECLS in the cardiac ICU is reported at 34% to 45%,[7,188,606,607] with in-hospital survival from ECPR being 33% to 79%, although transplantation may be required for survival.[7,8,75,76,588,606,608] Although duration of CPR before ECLS has not consistently been shown to be associated with greater hospital mortality,[8,76] the rapidity with which ECLS can be deployed could impact neurological outcomes.

Mechanical Support of Single-Ventricle CHD After Cardiac Arrest

After Stage 1 Norwood Palliation. Although ECLS is rarely necessary for preoperative stabilization in infants with single-ventricle heart disease,[609] it is increasingly being used to support children with single-ventricle CHD after palliative surgery.[607] The use of ECLS after stage 1 Norwood palliation is reported at 10% to 15%.[30,74] The Single Ventricle Reconstruction Trial reported the incidence of cardiac arrest during the postoperative stage 1 Norwood palliation hospitalization at 13%, and it was more likely to occur in those with an MBTS.[26,29] Because of the difficulty attaining ROSC after cardiac arrest, half of these stage 1 Norwood patients required ECPR.[29]

In the Single Ventricle Reconstruction Trial, the need for ECLS was independent of the type of shunt.[26,29] From 2000 to 2009, 738 neonates in the ELSO Registry were supported with ECLS after stage 1 Norwood pallia-

tion,[610] with a survival rate of 31%. Other single-center and multicenter studies have reported survival rates of 30% to 50%.[74,607,611] The presence of acute shunt occlusion or hypoxemia in patients requiring ECLS has been associated with better survival to discharge, whereas failure to separate from cardiopulmonary bypass at the end of a surgical procedure or the use of ECLS within 24 hours of stage 1 Norwood palliation has been associated with worse outcome.[74,77,610] Not unexpectedly, longer duration of support has been associated with poor survival; the ELSO Registry reported no survivors after 10 days of ECLS (2000–2009).[29,610] Survival from ECLS after stage 1 Norwood palliation at a median of 33 months is 25% to 30%, with no difference found between patients requiring ECPR versus conventional CPR.[29] Longer-term survival of 13% to 20% has been reported at 3 to 5 years.[74,612] Fourteen-month neurodevelopmental evaluation of patients undergoing the stage 1 Norwood palliation in the Single Ventricle Reconstruction Trial found the use of ECLS to be a risk factor for lower mental developmental index scores on univariate analysis but not by multivariate analysis.[613] Similar follow-up in the Infant Single Ventricle Trial found the use of ECLS after neonatal palliative surgery predicted lower mental developmental index scores.[64,614]

Worse outcomes have been reported after ECLS for the hybrid procedure for HLHS. In a retrospective analysis of data from the ELSO Registry, 44 patients were supported with ECLS after the hybrid procedure, and only 16% survived to hospital discharge.[615]

Superior CPA and Fontan. When the patient with superior CPA develops cardiac arrest, elevated SVC pressure combined with low systemic blood pressure puts these patients at high risk for neurological injury.[527] Given the high risk of neurological injury, it may be reasonable to consider deployment of ECLS early in the attempted resuscitation in patients with a superior CPA.

The use of ECLS after superior CPA and the Fontan completion poses unique anatomic, technical, and physiological challenges, but published experience is limited. In a single-center case series of patients receiving ECPR, 7 of 14 patients with Fontan physiology survived to discharge, with 36% alive at 36-month follow-up compared with survival of only 1 of 7 patients with superior CPA; the lone survivor was noted to have significant neurological disability.[527] ECPR in patients with superior CPA is associated with poor survival and neurological outcome as the result of a combination of high CVP and high intrathoracic pressure, which impedes venous return, oxygenation, and cardiac output during resuscitation.[103] Prompt and effective decompression of the SVC can minimize neurological injury.

In a retrospective analysis of data from the ELSO Registry, 230 patients were supported with ECLS after the Fontan operation; one-third of these patients received ECPR. Eighty-one of the 230 patients (35%) survived to hospital discharge.[616] A higher percentage of nonsurvivors (34% versus 21%) had pre-ECLS cardiac arrest. Factors independently associated with higher mortality included surgical bleeding, neurological complications, and renal failure.

In another retrospective analysis of data from the ELSO Registry,[103] 103 patients were supported with ECLS after the superior CPA, with 42 (41%) surviving to hospital discharge. Twenty-three percent of the patients had documented neurological complications, including seizure, cerebral hemorrhage, or embolic stroke. Survival was similar whether or not CPR was required during the hospital admission. Factors independently associated with higher mortality included longer duration of support, combined cardiopulmonary indication for ECLS, and renal failure.[103]

Gaps in Knowledge

Long-term, functional, and neurodevelopmental outcomes for ECPR survivors are not known. The influence of prearrest severity of illness and comorbid conditions on outcomes for ECPR is poorly characterized. There are no data regarding quality of CPR in ECPR recipients and its association with ECPR outcomes. The effects of ECPR location, equipment, personnel, and center characteristics on outcome have not been reported. The benefits of neuroprotective strategies during ECPR have not been well characterized.

Evidence for the use of mechanical support in patients with single-ventricle physiology is based on single institutional reports, the ELSO Registry, and the Single Ventricle Reconstruction Trial. Little information exists on the conduct of ECLS in single-ventricle patients, including shunt management during ECLS after stage 1 Norwood palliation and choice of ECLS cannulation site for support in patients with superior CPA and Fontan There are limited data on long-term neurodevelopmental outcome and quality of life in survivors of ECLS after stage 1 Norwood palliation. Data are needed regarding indications for use, devices most appropriate for patient subgroups, and outcomes of therapies.

Recommendations: Mechanical Support

1. **ECLS may be considered in patients with severe metabolic acidosis before cardiac arrest *(Class IIb; Level of Evidence C)*.**
2. **If cardiac arrest develops in the child with heart disease and there is no prompt ROSC, it is reasonable to initiate ECPR *(Class IIa; Level of Evidence C)*.**
3. **In institutions with the requisite resources, equipment, and infrastructure, ECPR can be effective to improve survival in children with heart disease *(Class IIa; Level of Evidence B)*.**

4. **ECPR can be most effectively deployed in locations with rapid access to ECLS equipment, skilled ECLS personnel, and adequate space to accommodate a large team *(Class IIa; Level of Evidence C)*.**
5. **ECLS after stage 1 Norwood palliation can be useful to treat low systemic Do_2 *(Class IIa; Level of Evidence C)*.**
6. **ECPR may be considered to treat cardiac arrest after stage 1 Norwood palliation, including in those who have shunt thrombosis *(Class IIb; Level of Evidence B)*.**
7. **ECLS in patients with superior CPA or Fontan circulation can be considered to treat low Do_2 from reversible causes or as a bridge to a VAD or surgical revision *(Class IIb; Level of Evidence B)*.**
8. **ECPR may be considered in patients with superior CPA or Fontan circulation *(Class IIb; Level of Evidence C)*; however, prearrest use of ECLS in patients with superior CPA or Fontan physiology may be reasonable, because neurological outcomes from ECPR are poor *(Class IIb; Level of Evidence C)*.**

Special Considerations

Impact of Resuscitation Location

In-hospital pediatric cardiac arrests occur most frequently in ICUs. Patients with cardiac arrest requiring CPR in monitored environments have higher survival than those who experience arrest outside ICUs.[617] No studies have directly assessed the impact of location on resuscitation outcomes in patients with CHD. From the GWTG-R Registry, 24-hour survival rates from 677 pediatric in-hospital cardiac arrests occurring in various hospital locations were as follows: ICU, 54%; inpatient ward, 52%; emergency department, 26%; operating room or recovery room, 26%; interventional or diagnostic suites, 35%; and other (eg, ambulatory), 43%. Although this study did not separate survival by arrest location for patients with cardiac disease, patients having a medical cardiac diagnosis had lower 24-hour survival rates than those having a surgical cardiac diagnosis (47% versus 59%; $P<0.05$).[618] In a more recent GWTG-R Registry multivariate analysis comparing outcomes of cardiac arrest in children with medical and surgical cardiac disease to those of children without cardiac disease, cardiac arrest in the emergency department rather than the ICU was associated with decreased survival among children in the medical cardiac group.[5] There are insufficient data to support transporting patients during active CPR into a monitored environment such as an ICU to improve survival.

Cardiac arrest associated with VF or pulseless VT was examined in another study from the GWTG-R Registry.[619] In the vast majority of patients (76%), VF or pulseless VT occurred in ICUs (including operating rooms and postanesthesia care units). Other locations where VF/pulseless VT occurred less frequently included inpatient wards (10%), emergency department (10%), and inpatient-monitored units (3%). Patients with cardiac diagnoses constituted 57% of those experiencing VF/pulseless VT (medical cardiac patients 22% and surgical cardiac patients 35%). Of patients with non-VF/VT cardiac arrest, there were relatively fewer patients having cardiac diagnoses (32%) compared with patients with noncardiac diagnoses (68%). Cardiac arrests associated with VT/pulseless VT are more likely to occur in patients with cardiac diagnoses.

Personnel and ICU factors have been shown to influence survival from cardiac arrest, with an increased risk of unsuccessful resuscitation after cardiac arrest on a weekend and when the primary nurse had <1 year of experience in pediatric cardiac intensive care.[492]

Cardiac Catheterization Laboratory. Cardiac arrest in the cardiac catheterization laboratory is relatively uncommon. In one report from the United Kingdom, the incidence of cardiac arrest was 0.5% (22 of 4454 patients) with 4 ensuing deaths (0.01% mortality rate among all catheterized patients; 19% mortality rate among those with cardiac arrest) over a 9-year period.[619] Another study from Canada reported 14 cardiac arrests in 11 073 pediatric catheterizations (0.1%) that resulted in 8 deaths (0.07% mortality rate among all catheterized patients, but 57% rate mortality among those with cardiac arrest) over a 13-year period. A single US center report estimated the incidence of cardiac arrest in children undergoing cardiac catheterization to be 0.96 per 100 procedures.[620]

More recently, multicenter surveys and registries have reported more widespread experience. In Japan, a survey of 82 institutions found a 0.6% incidence of major complications, including death.[621] A US registry involving 6 large pediatric cardiology centers reported a mortality rate of 0.3% (11 of 3385 children) during cardiac catheterization.[622] Risk factors for major complications during cardiac catheterization, including cardiac arrest and death, in all studies included specific patient characteristics, younger age (ie, neonates), anesthesia provider, and recent postoperative status.[619,623]

Cardiac Operating Room. In a single-center study, the reported incidence of cardiac arrest in the cardiac operating room was 0.79%.[432] This incidence is low compared with the occurrence of cardiac arrest in other locations. Cardiac arrest in children undergoing cardiac surgery can be related to anesthesia or to the procedure itself and is most common in neonates and infants.[432]

Gaps in Knowledge

There are limited reported data on outcomes based on location of cannulation for mechanical support in patients with CHD.

Recommendations: Impact of Resuscitation Location

1. **The vast majority of cardiac arrests should occur in ICUs. A cardiac arrest occurring on a ward service or in a nonacute area of the hospital should prompt investigation to determine whether the child's deterioration was unrecognized and to identify and initiate the appropriate education to reduce the risk of future events *(Class I; Level of Evidence C)*.**

Training and Continuous Quality Improvement

Multiple studies have documented poor performance of CPR in the hospital setting and decay of provider skills soon after CPR training.[624] Recent studies have shown that brief (as short as 4 minutes) refresher or booster training can improve CPR manikin skill performance.[625–627] "Just-in-time" simulation at the bedside in the ICU serves to heighten awareness of providers for patients at risk of cardiac arrest.[628] It is important to determine whether such improvement in skill performance leads to improved survival after cardiac arrest.

After any attempted resuscitation, providers should debrief team performance to identify areas for improvement. Devices such as defibrillators or accelerometers that record important aspects of CPR quality, including chest compression frequency and depth, compression fraction, and ventilation rate and volume, can be helpful during resuscitation training, during the resuscitation attempt itself, and later in the debriefing and quality improvement process.[629–631] In data from the GWTG-R Registry, self-reported errors during resuscitation of adults, such as delay in recognition of arrest, delay in shock delivery, delay in airway insertion, intubation failure, and failure to promptly start and continue compressions of adequate rate, were associated with lower survival.[632] The use of medical simulation, video recordings, and other visual feedback devices have been shown in randomized trials to improve the quality of CPR in children.[633,634] ECLS programs incorporating simulation training have been associated with faster cannulation times,[635] improved trainee satisfaction,[636] enhanced provider knowledge,[637] and better team performance. In one preintervention and postintervention study at a single institution, ECLS simulation training resulted in subjective reports of smoother team coordination and significant reduction in median time to deployment (from 51 to 40 minutes) during actual pediatric ECPR.[604]

Gaps in Knowledge

CPR quality is essential to maximize patient survival from cardiac arrest, yet there are few data to guide quality improvement efforts. The optimal retraining interval and the types of retraining needed to maintain CPR skills have not been established, but it is clear that providers must practice skills much more frequently than once per year to optimize CPR quality and team performance and to increase survival from cardiac arrest. Although CPR prompt devices can improve skill performance during training, their usefulness during actual resuscitation attempts and their effect on resuscitation outcomes (particularly survival to hospital discharge) have not yet been established.

Recommendations: Training and Continuous Quality Improvement

1. **Adequate training, an ongoing system to maintain skill competence, monitoring of skills during resuscitation, postresuscitation debriefing, and careful identification and targeting of areas where improvement is needed can be useful to maximize the likelihood of successful resuscitation *(Class IIa; Level of Evidence C)*.**
2. **Monitoring performance and documenting improvement can be useful to resuscitation systems attempting to improve their resuscitation quality *(Class IIa; Level of Evidence C)*.**
3. **Using medical simulation to train clinicians in both conventional CPR and ECPR can be beneficial *(Class IIa; Level of Evidence C)*.**

POST–CARDIAC ARREST STABILIZATION

Most research in resuscitation science has concentrated on improving the rate of successful ROSC; however, the original 1966 consensus statement on CPR by the National Academy of Sciences–National Research Council's Ad Hoc Committee on Cardiopulmonary Resuscitation outlined the ABCDs of resuscitation as follows: *A* for airway; *B*, breathing; *C*, circulation; and *D*, definitive therapy.[638] Definitive therapy includes the management of pathologies that result from cardiac arrest, which has become known as postarrest syndrome.[639–641] The 4 components of post–cardiac arrest syndrome are myocardial dysfunction, brain injury, systemic ischemia/reperfusion response, and persistent precipitating pathology.

The high mortality of patients who initially achieve ROSC after cardiac arrest can often be attributed to failure of organ systems that have endured a period of ischemia, as well as the damage caused by the postisch-

emic inflammatory response. The response to the arrest ischemia can be exacerbated by the very therapies instituted for resuscitation. For example, post–cardiac arrest myocardial dysfunction can be worsened by epinephrine use during resuscitation or by inotropic therapies aimed at maintaining renal perfusion. In addition, potential reperfusion brain injury can be made worse by therapies aimed at myocardial support.[413,642,643]

Myocardial Management

Myocardial Dysfunction

Myocardial dysfunction develops after cardiac arrest and contributes to mortality.[644] This dysfunction is responsive to therapies and is potentially exacerbated by therapies; it is, in some cases, reversible.[645–649] Myocardial dysfunction can be more detrimental to the child with CHD, because the child has limited prearrest reserve. Systolic and diastolic myocardial dysfunction is progressive in the first hour that follows ROSC.[644] In young children, this dysfunction can be correlated to myocyte injury and typically reverses over 24 hours.[645,650]

Major contributors to post–cardiac arrest myocardial dysfunction include myocardial ischemia-reperfusion injury and the therapies, particularly vasopressors, used during CPR. Vasopressor agents are administered during CPR to improve coronary perfusion pressure and therefore myocardial blood flow. Restoration of coronary perfusion is the single overriding determinant of the success of cardiac resuscitation efforts.[651] However, epinephrine leads to high afterload and increased myocardial oxygen consumption in the initial post–cardiac arrest phase at the time when the myocardium is most vulnerable to increased oxygen demands and imbalance of oxygen supply versus delivery.[413,652] This concern for increasing myocardial work at a time of myocardial vulnerability has led to the evaluation of alternative vasoactive agents such as vasopressin and other agents in resuscitation.[653,654]

Myocardial Support

Hemodynamic instability is common after cardiac arrest, and pharmacological support is often needed. No individual drug or combination of drugs has been demonstrated to be superior in the postarrest phase. Inotropes and vasopressors should be considered if cardiovascular function remains inadequate after establishment of adequate preload. Vasoactive drugs must be titrated to achieve adequate cardiac output and systemic and coronary perfusion. This can require a balance of inotropic agents that will increase cardiac output as well as oxygen demand and vasodilators that reduce afterload and decrease myocyte oxygen consumption, while avoiding hypotension that will compromise coronary perfusion. The choice of inotrope or vasopressor can be guided by blood pressure, heart rate, echocardiographic indices, and surrogate measures of Do_2 such as AVo_2D, lactate clearance, and urine output. Mechanical circulatory support and heart transplantation can be considered for patients who do not achieve myocardial recovery.[8,608]

Hemodynamic Monitoring

Recommended hemodynamic monitoring in the post–cardiac arrest patient is similar to that used for the care of any child with critical cardiac disease and includes continuous monitoring of heart rate and blood pressure (systolic, diastolic, and mean arterial pressure) and evaluation of arterial and central Svo_2 and serum lactate. However, the precise hemodynamic goals are unclear. The optimal mean arterial pressure for post–cardiac arrest patients has not been defined.[640] Although particular attention may need to be paid to afterload during management of post–cardiac arrest myocardial dysfunction, the optimal mean arterial pressure is likely to be influenced by the duration of cardiac arrest, with higher mean arterial pressures benefitting cerebral perfusion.[655]

Monitoring of Svo_2 is a useful tool to evaluate the adequacy of oxygen transport balance.[449] Svo_2 monitoring can serve as an early indicator of a persistent postarrest LCOS. A single lactate measurement after resuscitation from cardiac arrest will most likely be elevated and is of limited monitoring or prognostic value. However, trending of the serum lactate will provide an important indication of the child's response to therapy; lactate clearance has been associated with outcome in patients after cardiac arrest.[656] Finally, monitoring troponin peak and clearance has also been associated with outcome after adult cardiac arrest.[650]

Ventricular Assist Devices

The use of an LVAD, a right VAD, or a biventricular VAD in the management of infants and children has increased recently secondary to wider device availability and a broader understanding of the potential role of these devices in the setting of myocardial dysfunction and heart failure. Many centers have historically used ECLS as a bridge to cardiac transplantation; however, ECLS has limitations regarding the duration of support and potentially unfavorable effects on transplant outcomes. The use of VADs offers different strategies, which can be of significant benefit to postarrest survivors. These include bridge to transplantation, bridge to recovery, and rarely in pediatrics, destination therapy.[657] Bridge to transplantation remains the most common use of VAD therapy and should be considered in patients who are clinically deteriorating despite maximal medical and surgical management.

The use of VAD support in children can be further complicated by anatomic constraints in the setting of CHD, which may necessitate individualized implantation strategies and postoperative management.[658] No

universally accepted pediatric indications exist for VAD implantation, although the International Society for Heart and Lung Transplantation has recently published clinical guidelines.[257] Pediatric VAD placement can be considered in patients requiring high-dose inotropes after cardiac arrest, those with persistent arrhythmias, or those with persistent myocardial dysfunction on ECLS. The Figure delineates mechanical circulatory support strategies in rapidly deteriorating children with heart disease.

Bridge to transplantation is the most common VAD implant strategy in pediatric centers. There are a variety of flow profiles available for current devices, including pulsatile flow and continuous flow devices. The most widely used device in children is the Berlin EXCOR device, which is a pulsatile paracorporeal VAD that can provide left, right, or biventricular support.[238] The recent Berlin EXCOR study comparing survival in 2 cohorts, patients <0.7 m^2 and patients >0.7 m^2 to <1.5 m^2, to historical ECLS results found that survival rates to transplantation were much higher in those supported with VAD.[660] Both cohorts experienced significant morbidity, however, with the majority of patients experiencing significant bleeding, infection, stroke, or hypertension. On the basis of the improved survival to transplantation, the Berlin EXCOR device was granted US Food and Drug Administration approval in 2011.

For patients with adequate lung function not requiring a membrane oxygenator, a VAD can be used as a bridge to transplantation regardless of patient size. Adult devices can be used in adolescent patients. The HeartMate II LVAD (Thoratec, Inc., Pleasanton, CA) is an axial continuous flow device currently approved for bridge to transplantation. This device is increasingly used in children, with a reported rate of 6-month survival to transplantation, ongoing support, or recovery of 95%.[661] The HeartMate II has also been successfully used as a bridge to transplantation in the failing Fontan circulation.[662] The HeartWare LVAD (HeartWare Inc., Framingham, MA) is a newer-generation centrifugal device also approved for bridge to transplantation in the United States. Successful use of the HeartWare device has been reported in pediatric patients with dilated cardiomyopathy and in palliated CHD with successful bridge to cardiac transplantation.[663,664]

Consideration of temporary VAD support should be given to patients who have a potentially reversible condition such as myocarditis or transplant rejection. In addition, temporary VAD support can be used in clinical situations such as patients with infection or cerebrovascular injury that may preclude permanent VAD placement or consideration of heart transplantation, until the patient's candidacy can be established or ruled out. Temporary support can be provided centrally or percutaneously based on anatomy, size, and type of support needed. Potential recovery of myocardial function should be assessed periodically during VAD support, and decannulation should be considered at the earliest period when functional viability is thought to be established.

For those patients with biventricular heart failure, support might be possible with either biventricular VAD

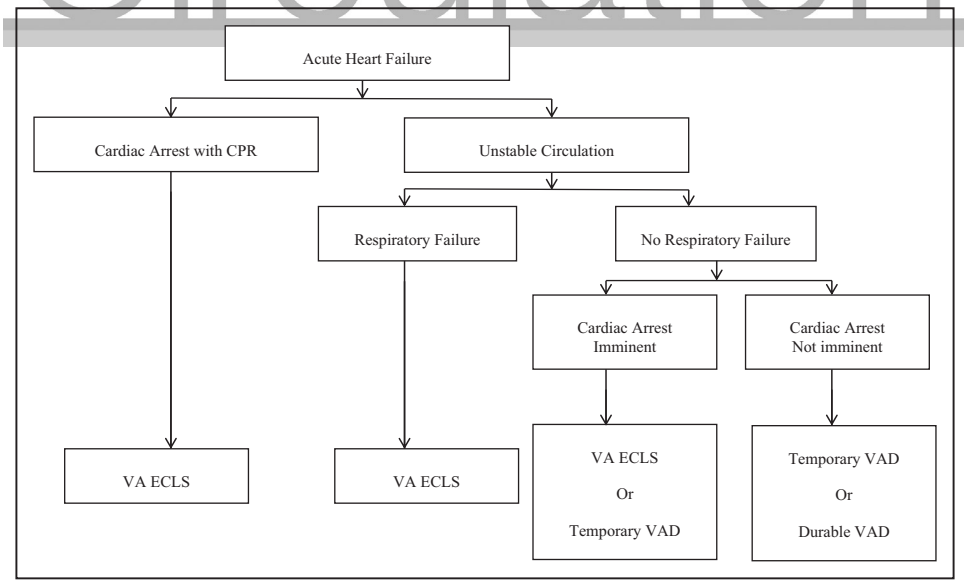

Figure. Mechanical circulatory support device strategy in rapidly deteriorating children with heart disease.[4,8,35,81,144,271–276,283,298,302,303,312,325–327,331,386,650,659]

Choice of ventricular assist device (VAD) depends on patient size and need for left ventricular or biventricular support. Examples of temporary VADs include centrifugal pump extracorporeal life support (ECLS) without oxygenator, Impella, and Tandem Heart. Examples of durable VADs include Berlin Heart EXCOR, Thoratec paracorporeal VAD, HeartMate, HeartWare, and total artificial heart/SynCardia. CPR indicates cardiopulmonary resuscitation; and VA ECLS, venoarterial ECLS.

support or a total artificial heart. However, although reports of successful use exist, size constraints greatly limit the use of these devices in children.[660,665]

Gaps in Knowledge

There are few data available that specifically relate to the support of the pediatric myocardium after resuscitation. There are no universally accepted indications for pediatric VAD implantation. There are no universally accepted strategies for anticoagulation to minimize the risk of stroke during VAD therapy. Individual centers typically follow local protocols or the recommendations of the VAD manufacturer.

Recommendations: Post–Cardiac Arrest Stabilization – Myocardial Management

1. **Vasoactive drugs can be beneficial to augment coronary perfusion pressure during myocardial recovery but may also contribute to myocardial oxygen consumption and post–cardiac arrest myocardial dysfunction. Therefore, careful titration of vasoactive drugs can be beneficial to minimize post–cardiac arrest myocardial dysfunction *(Class IIa, Level of Evidence C)*.**
2. **Post–cardiac arrest hemodynamic monitoring should include continuous monitoring of heart rate and rhythm; systolic, diastolic and mean arterial pressure; arterial and venous oxygen saturations; and serum lactate clearance *(Class I; Level of Evidence B)*.**
3. **Mechanical circulatory support may be considered for some patients who do not achieve ROSC and adequate perfusion *(Class IIb, Level of Evidence C)*.**
4. **In survivors of cardiac arrest who require mechanical circulatory support while awaiting cardiac transplantation, the use of VAD can be more effective than ECLS *(Class IIa; Level of Evidence B)*.**

Pulmonary Management

Provision of effective oxygenation and ventilation via a bag-mask or through an advanced airway is imperative during resuscitation. Many patients undergo establishment of an advanced airway with placement of an endotracheal tube; however, positive-pressure ventilation can have both helpful and harmful effects on postarrest cardiopulmonary and cerebral physiology.

Pulmonary Dysfunction

Pulmonary dysfunction is common after cardiac arrest. This dysfunction can result from pulmonary edema secondary to postischemic diastolic dysfunction, aspiration, neurological impairment of respiratory dynamics, or ischemia-reperfusion injury to the lung parenchyma.[666] Each of these potential pulmonary morbidities must be treated effectively to achieve long-term survival after resuscitation.

Respiratory Support

The optimal ventilatory management strategy, including the optimal supplementary oxygen to provide during post–cardiac arrest care, has not been established. Existing guidelines recommend the use of 100% oxygen during CPR in infants (not including newborns in the delivery room) and children; however, it is not clear how long this high oxygen concentration should be administered after ROSC. Harmful effects of hyperoxia have been documented; animal data suggest that hyperoxia increases direct neurological injury during the post–cardiac arrest time period.[667,668] An adult randomized prospective clinical trial comparing the use of 30% to 100% oxygen found no difference in serial markers of acute brain injury and survival to hospital discharge.[669] Three small pediatric case series[670–672] failed to show either benefit or harm from post-ROSC normoxemia or hyperoxemia, whereas a larger pediatric case series[673] did show higher survival among children with post-ROSC normoxemia (Pao_2 60–300 mm Hg) than those with post-ROSC hyperoxemia. However, the timing of the evaluation of oxygen saturation and arterial oxygen tension during the post–cardiac arrest care varied between and even within the studies.[670–673] These data led to the 2015 PALS guideline update recommendation that once the patient is stable in the post–cardiac arrest period, it may be reasonable for providers to target normoxemia.[3,398] Ideally, inspired oxygen is titrated to a value appropriate to the specific patient condition.

Ventilation strategies during post–cardiac arrest care can potentially have a greater impact on outcome than strategies to support oxygenation, because the arterial carbon dioxide tension affects cerebrovascular reactivity.[674–677] Hyperventilation is undesirable because it reduces cerebral blood flow and can have other detrimental effects during resuscitation. Excessive ventilation (rate or volume) during and immediately after CPR can lead to increased intrathoracic pressure and gas trapping, as well as reduced venous return and cardiac output. One small observational study from the Pediatric Emergency Care Medicine Applied Research Network of both pediatric in-hospital and out-of-hospital cardiac arrest patients demonstrated no association between hypercapnia ($Paco_2$ >50 mm Hg) or hypocapnia ($Paco_2$ <30 mm Hg) and survival to hospital discharge.[670] However, in an observational study from the Pediatric Cardiac Arrest Study Network of pediatric in-hospital cardiac arrest, hypercapnia ($Paco_2$ ≥50 mm Hg) was associated with worse survival to hospital discharge.[672] Because many infants who experience cardiac arrest have co-

morbidities that may include chronic lung disease, the AHA 2015 PALS guideline update suggested titration of post–cardiac arrest ventilation support to target a $Paco_2$ that is appropriate to the individual child's condition while limiting exposure to severe hypercapnia or hypocapnia.[3]

Respiratory Monitoring

Respiratory monitoring during post–cardiac arrest care should follow standard ICU practice for any critically ill patient. Chest radiographs should be reviewed at an appropriate frequency to assess lung fields and detect hyperexpansion that could lead to decreased venous return, as outlined above. Similarly, monitoring of arterial blood gases and systemic oxygen saturations should be aimed at maintaining normocarbia (or a $Paco_2$ appropriate for the patient) and avoiding hypoxemia and hyperoxia.

Gaps in Knowledge

There are no prospective data in children regarding optimal oxygenation or ventilation support during post–cardiac arrest care. Developmental differences in lung physiology after cardiac arrest in children have not been studied.

Recommendations: Post–Cardiac Arrest Stabilization – Pulmonary Management

1. **It is reasonable to target normal oxygen saturation without hyperoxia after resuscitation from pediatric cardiac arrest; oxygen administration may need to be modified in newborns or based on the underlying heart defect *(Class IIa; Level of Evidence B)*.**
2. **It is reasonable to target normocapnia or a $Paco_2$ appropriate for each patient after resuscitation from pediatric cardiac arrest *(Class IIa; Level of Evidence C)*.**

Neurological Assessment and Management

Brain ischemia and injury develop when the cellular demand for oxygen is not met by Do_2. Do_2 is proportional to cerebral blood flow and systemic oxygen saturations. Do_2 falls when respiratory insufficiency results in poor arterial oxygen saturation, when low cardiac output leads to inadequate cerebral blood flow, or when cardiac arrest leads to global ischemia. There is no clinical, laboratory, or neurological test administered in the first few days after cardiac arrest that accurately predicts neurological outcome in children who have survived cardiac arrest. Brain magnetic resonance imaging (MRI) with other clinical, laboratory, and neurological tests can be considered to assist in neuroprognostication.

Brain Imaging

For those patients who undergo post–cardiac arrest brain imaging, head CT is often the first neuroimaging test performed early after ROSC. It may show cerebral swelling with effacement of the sulci, widespread loss of grey-white differentiation, or low density in the basal ganglia or in the watershed regions. The "reversal sign," with low density in the cerebral hemispheres and relatively higher densities in the basal ganglia, is not uncommon on head CT.[678] All these patterns are associated with poor prognosis, but a normal CT scan does not guarantee a good outcome.[679] A recent retrospective analysis of 78 pediatric patients (<18 years of age) with out-of-hospital cardiac arrest for any reason and a head CT performed 1 to 6 hours after ROSC found that loss of grey-white differentiation, sulcal effacement, basilar cistern effacement, and reversal sign on head CT performed early after resuscitation were associated with mortality and unfavorable neurological outcome.[680]

For neonates and infants with open anterior fontanels, the first imaging modality can be a head ultrasound, which is portable and requires no ionizing radiation. Head ultrasound offers a limited view of brain anatomy but can quickly aid in the diagnosis of problems that require emergent attention, such as intracranial hemorrhage and hydrocephalus. Transcranial Doppler ultrasonography, used to measure cerebral blood flow velocities and pulsatility index, can be performed in conjunction with head ultrasound. Like head ultrasound, transcranial Doppler is a noninvasive bedside procedure; however, continuous transcranial Doppler measurements in small infants can be limited by heat deposition.[681] Transcranial Doppler studies have been used to monitor metabolic coupling and vascular reactivity in comatose adults after cardiac arrest.[682] Furthermore, transcranial Doppler is capable of measuring the macroscopic cerebral hyperemic reperfusion caused by the increase of the cerebral perfusion pressure and deterioration of cerebral autoregulation after ROSC.[683] After ROSC, the presence of a closing pressure, or pressure at which brain vessels collapse and cerebral blood flow ceases, is a grim prognostic finding in adults after cardiac arrest.[684]

Brain MRI can be used in survivors of cardiac arrest to assess the extent of brain injury and in combination with clinical examination and other factors to assist in determining prognosis for neurological recovery. Patterns of injury have been detailed and used in studies to help understand cognitive and motor prognosis. Patterns of injury are not specific for the mechanism of arrest (respiratory versus cardiac), because the injury results from metabolic failure in the most metabolically active areas of the brain. With hypoxic-ischemic arrest, the areas of the brain most commonly affected are the deep grey nuclei (putamen and globus pallidus), the occipital lobe (visual cortex), and the central sulcus (sensory motor

strip). In one retrospective case series[685] of pediatric subjects undergoing brain MRI after surviving cardiac arrest, patients with diffusion-weighted imaging abnormalities in the basal ganglia and brain lobes had increased risk for poor outcome (Glasgow outcome score <4). During sudden cardiac arrest, the precipitous fall in cerebral perfusion pressure is often associated with watershed ischemia between the major vascular territories of the brain. Watershed injury can be seen in isolation or in combination with the hypoxic-ischemic injuries described above. Infants with CHD, particularly those requiring surgery during the neonatal period, have an increased incidence of native (20%–40%) and postoperative (60%–73%) brain injury including white matter injury, stroke, and intraparenchymal hemorrhage.[348,358,517]

Neurological Monitoring

Major goals of post–cardiac arrest care are mitigating the extension of the primary ischemic brain injury and prevention of secondary brain injury. Intensive care monitoring is focused on calculation of Do_2 and consumption, which may or may not be reflective of cerebral hemodynamics and metabolism. Clinical neurological examination is often hindered by the use of medications (sedatives, analgesics, and paralytics) or limited by the patient's age (eg, in the infant). Medical devices to monitor brain function and cerebral blood flow are needed both for goal-directed therapy and to enable prediction of outcome.

Electroencephalography

Electroencephalography has been used to identify seizures that may not be clinically apparent. Identifying and treating seizures in post–cardiac arrest patients can reduce cerebral metabolic demand and mitigate secondary injury. However, seizures can be a symptom (as opposed to the cause) of the degree of injury that is already present.[686–688]

A prospective consecutive series of 19 pediatric, postarrest, intensive care patients monitored with continuous electroencephalography[689] demonstrated that electrographic seizures occurred in 47% (9 of 19), and 32% (6 of 19) developed status epilepticus. More importantly, the majority of the seizures were subclinical and undetected by the bedside caregivers. Other retrospective studies have documented a similar high incidence of nonconvulsive seizures.[690–696] Clinical studies are consistent with the hypothesis that continuous electrographic discharges, even without clinical seizures, can be harmful. The presence of nonconvulsive status epilepticus has been associated with mortality of 51% to 57% in adults.[697,698]

A recent practice parameter addressing outcome prediction in adults after cardiac arrest described several electroencephalography features that were useful for prognosis.[699] Myoclonic status epilepticus on the first day best predicted unfavorable outcome, whereas diffuse voltage suppression <20 μV, burst suppression, and generalized periodic complexes were strongly but not invariably associated with poor outcome. Several classification systems that group electroencephalography features into predictive categories have been developed in adults[700–702] and children.[703,704] Caution must be taken when interpreting these data, because it could be that the more critically ill children had the worst electroencephalography and hence the worst outcome.

Near-Infrared Spectroscopy

Unlike pulse oximetry, NIRS measurements made in cerebral tissues reflect a weighted average of venule (≈75%) and arteriole (≈25%) blood saturations[705] in very metabolically active tissue. Meticulously performed animal studies have demonstrated that an ischemic threshold can be measured in piglets,[706] although for obvious ethical reasons, such studies not been replicated in humans. In a porcine model of infant cardiac arrest, NIRS monitoring was used to detect the lower limit of cerebral hemodynamic autoregulation.[707]

NIRS offers bedside availability and the promise of a noninvasive view of cerebral oxygenation. Commercially available instruments are not capable of quantitative measurements of hemoglobin concentrations, are sensitive to ambient light, and suffer from poor reproducibility. Although NIRS technology does monitor in vivo tissue oxygen saturations and is increasingly used in pediatric ICUs, there is a paucity of data linking it to positive neurological outcomes.

Several studies have used NIRS to investigate risk for perioperative brain injury in infants with complex CHD[48,347,517]; however, the results have been contradictory. Two studies in infants after stage 1 Norwood palliation found that cerebral oxygen saturations below 45% were predictive of structural brain injury and worse neurodevelopmental outcome,[48,517] whereas a third study of neonates with single-ventricle and 2-ventricle complex CHD showed no association between NIRS saturations <45% and any measure of any postoperative MRI brain injury.[347] After stage 1 Norwood palliation, sustained NIRS <45% has been shown to be related to low visual-motor integration, and sustained NIRS <55% has been shown to be associated with lower neurodevelopmental index scores at 4 to 5 years of age.[48] Despite these conflicting results, some advocate the use of neuroprotective protocols, driven by NIRS measures, for managing intraoperative and postoperative patients with severe forms of CHD.[347]

Neurological Resuscitation

Resuscitation from cardiac arrest does not end after ROSC. Post–cardiac arrest care has significant potential to prevent the early mortality caused by hemodynamic instability and prevent secondary injury at the cellular level. The objectives of resuscitation include optimiza-

tion of cardiopulmonary function and systemic perfusion, identification of the precipitating causes of the arrest, institution of measures to prevent recurrence of cardiac arrest, administration of therapies that might facilitate long-term survival, and above all, protection of cognitive and neurological function.

Hyperoxia

The pediatric basic and advanced life support section of the 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations suggested that rescuers measure Pa_{O_2} after ROSC and target a value appropriate to the specific patient condition. In the absence of specific patient data, this consensus statement suggests that rescuers target normoxemia after ROSC.[398] The Iberoamerican Pediatric Cardiac Arrest Study Network, in a prospective multicenter study, concluded that there was no impact of hyperoxia on mortality but did not address neurological outcomes.[671,672] Two meta-analyses (the first in 2004, with an update in 2010) noted an association between hyperoxia in the resuscitation of neonates and an increased risk of death (relative risk, 0.69; 95% confidence interval, 0.54–0.88), with a trend toward increased risk for hypoxic-ischemic encephalopathy.[708,709] No studies exist for infants outside of the newborn period.

Hypercapnia

Carbon dioxide is a potent cerebral vasodilator and thus a potential therapeutic tool to increase D_{O_2} to the brain after ROSC. Although the Iberoamerican study showed that both hypercapnia and hypocapnia were associated with increased mortality,[672] there are not sufficient data to determine whether manipulation of cerebral blood flow can affect outcome after circulatory arrest. As noted previously, the AHA 2015 PALS guideline update suggested titration of post–cardiac arrest ventilation support to target a Pa_{CO_2} that is appropriate to the individual child's condition while limiting exposure to severe hypercapnia or hypocapnia.[3]

Targeted Temperature Management

Importance of Controlling Fever

Fever (>38°C) on the first day after reperfusion from cardiac arrest in children is a common consequence of the postresuscitation syndrome and can be detrimental to outcomes.[641,710,711] Of the 547 children who experienced in-hospital cardiac arrest in the GWTG-R Registry, children with persistent fever in the first 24 hours postarrest had more unfavorable neurological outcomes than children without persistent fever.[712,713] Additionally, in a subset of newborns with birth asphyxia (with or without associated cardiac arrest) from the National Institute of Child Health and Human Development Neonatal Research Network, the odds of death or disability increased by 3.6-fold for each 1°C increase in mean temperature.[713] This association persisted at the 6- to 7-year follow-up of noncooled infants with birth asphyxia: the likelihood of death, IQ <70, or cerebral palsy was much higher among newborns who demonstrated elevated temperature in the first postnatal days.[714]

Consideration of Therapeutic Hypothermia After Pediatric Cardiac Arrest

Initial randomized clinical trials showed that therapeutic hypothermia (32°C to 34°C) can improve neurological outcome in some adults after witnessed out-of-hospital cardiac arrest attributable to ventricular arrhythmia[715,716] and in encephalopathic asphyxiated newborns.[362,717] However, a recent adult randomized controlled trial of targeted temperature management showed no difference in neurological outcomes and survival in adults with out-of-hospital cardiac arrest when temperature was controlled at 33°C versus 36°C.

In 2015, the results of the THAPCA trial (Therapeutic Hypothermia After Out-of-Hospital Pediatric Cardiac Arrest) were published. This trial enrolled infants and children <18 years of age (median age 2 years) who remained comatose at 6 hours after ROSC. Patients were randomized to therapy with hypothermia (32°C–34°C for 72 hours with 16-hour rewarming and 32 hours of normothermia) versus therapeutic normothermia (temperature actively maintained at 36°C–37.5°C for 5 days). Significant differences between the 2 treatment groups included a higher incidence of hypokalemia and thrombocytopenia in the hypothermia group and more frequent renal replacement therapy in the normothermia group. There was no significant difference in 1-year developmental testing or survival.[718] Results from the cohort with in-hospital cardiac arrest are pending. In their review of the THAPCA trial results, the pediatric task force of the International Liaison Committee on Resuscitation (the group responsible for the scientific consensus that supports the AHA PALS guidelines) noted that the study was underpowered to demonstrate improvement in survival with good neurological outcome and also noted that the Kaplan-Meier survival curves in the appendix of the published study showed a trend toward better outcomes at the lower (hypothermia) temperature range,[398] which suggests that therapeutic hypothermia might improve outcome in some patients. The protocols chosen for the THAPCA trial represent 2 potential protocols for targeted temperature management.

Two observational studies found that therapeutic hypothermia tended to be applied in the sickest children after resuscitation with a wide range of target temperatures and durations used in the absence of a protocol.[719,720] In one case series, >75% of study subjects had recent cardiac surgery, and 70% of those children

had a cardiac pathogenesis that led to their arrest; hypothermia did not lead to improved outcomes in these patients.

Recommendations for Targeted Temperature Management

On the basis of available evidence, the AHA 2015 PALS guidelines update recommended continuous measurement of temperature in the first 5 days after ROSC after any cardiac arrest, with aggressive treatment of fever (temperature 38°C or higher). In addition, the guidelines update noted that it is reasonable for infants and children who remain comatose after out-of-hospital cardiac arrest to either maintain 5 days of continuous normothermia (36°C to 37.5°C) or 2 days of initial continuous hypothermia (32°C to 34°C) followed by 3 days of continuous normothermia (36°C to 37.5°C). For infants and children who remain comatose after in-hospital cardiac arrest, there was insufficient evidence (pending publication of results from the multi-institutional study) to recommend cooling versus maintenance of normothermia.[3]

There are no data to guide the mechanism of hypothermia induction or rewarming details or the best mechanism to treat fever. In the 2010 PALS guidelines, the AHA recommended avoidance of rewarming from 32°C to 34°C faster than 0.5°C every 2 hours unless the patient requires rapid rewarming for clinical reasons.[4]

Methods to control fever include the use of a cooling blanket, ice packs, cold saline infusion, tepid baths, and ECLS circuit.[721,722] Pharmacological interventions are unproven in the pediatric population, but acetaminophen can be helpful to prevent fever after ischemia.[723,724]

When determining the best route for targeted temperature management, providers should carefully consider the known and potential risks of hypothermia in children with CHD, particularly its effects on hemodynamics.[725,726] Hypothermia characteristically decreases the heart rate, increases contractility, and increases SVR. Tachycardia, hypotension, and decreased SVR typically develop during rewarming. Overall cardiac output is unevenly affected by hypothermia in infants.[727,728] Therapeutic hypothermia appears to have variable effects on PVR, with some researchers reporting no effects and some case reports suggesting an exacerbation of pulmonary hypertension during rewarming.[729,730] Sarkar et al[731] reported no difference in pulmonary hypertension between hypothermic and normothermic groups whether using whole body or focal head cooling, and Shankaran et al[726] reported no differences in nitric oxide use or ECLS in asphyxiated babies with proven pulmonary hypertension who underwent hypothermia.

Hypothermia can prolong the PR and corrected QT intervals[732]; however, hypothermia has been applied successfully in patients with congenital QT syndrome and cardiac arrest.[733] Significant hypothermia is associated with increased risk of atrial and ventricular arrhythmias, but there is no evidence in the neonatal or adult randomized controlled trials that hypothermia (32°C–34°C) subjects had more clinically significant arrhythmias than normothermia subjects (aside from sinus bradycardia).[726,734,735] Additionally, in pediatric cardiac arrest, children who were treated with hypothermia had fewer rearrests.[719] To reduce the incidence of arrhythmia during therapeutic hypothermia, it can be helpful to provide adequate sedation and analgesia to lessen endogenous catecholamine release, to promptly treat acidosis and electrolyte disturbances, and to avoid medications that could exacerbate or prolong the QT interval.

Gaps in Knowledge

Prospective studies of the validity of specific MRI findings on predicting future neuromotor or cognitive deficits are lacking in pediatrics. Because a large proportion of seizures after cardiac arrest are electrographic only (not clinically apparent), there is a demonstrated need to perform continuous electroencephalography to detect seizures. Although the presence of seizures after cardiac arrest has been associated with increased risk of death, it is unclear whether detecting and treating the seizures with anticonvulsant agents actually improves neurocognitive outcomes. Possible unintended consequences of anticonvulsant therapy include sedation and lowering of blood pressure.

Commercially available NIRS instruments calculate relative cerebral oxygen saturations without identifying whether oxygen metabolism or Do_2 are limiting factors. As such, NIRS thresholds may have limited value. Prospective studies of cerebral oxygen saturation trends after cardiac arrest are needed.

Vital questions to be answered regarding the use of targeted temperature management in infants and children after in-hospital cardiac arrest include optimal target temperature and duration of control (hypothermia versus normothermia). In addition, more information will be needed to determine the optimal method of targeted temperature management for children with heart disease who experience in-hospital cardiac arrest.

Recommendations: Post–Cardiac Arrest Stabilization – Neurological Assessment and Management

1. **There is no clinical, laboratory, or neurological test that accurately predicts neurological outcome in children who have survived**

cardiac arrest. Brain MRI with other clinical, laboratory, and neurological tests may be considered to assist in neuroprognostication *(Class IIb; Level of Evidence C)*.

2. The use of head CT or ultrasound may be considered in the child or infant after cardiac arrest to assess for cerebral edema, impending herniation syndromes, or intracranial hemorrhage *(Class IIb; Level of Evidence C)*.
3. Brain MRI can be useful to diagnose acute brain injury that results from cardiac arrest; however, children with CHD may have preexisting white matter changes and other neuroanatomic abnormalities *(Class IIa; Level of Evidence B)*.
4. After cardiac arrest, continuous electroencephalography monitoring may be helpful to identify clinically occult seizures and status epilepticus in children who have an unreliable neurological examination or who remain comatose *(Class IIa; Level of Evidence B)*.
5. Seizure detection and management can be considered to prevent secondary brain insult after cardiac arrest *(Class IIb; Level of Evidence C)*.
6. After resuscitation from pediatric cardiac arrest, the use of NIRS to assess and manage cerebral Do_2 may be considered *(Class IIb; Level of Evidence B)*.
7. After resuscitation from pediatric cardiac arrest, oxygen administration tailored to target the "appropriate" oxygen saturation for the individual patient can be beneficial *(Class IIa; Level of Evidence B)*.
8. It is important to avoid hyperoxia in newborns or excessive arterial oxygen saturation in patients at risk for pulmonary overcirculation *(Class III: Harm; Level of Evidence B)*. (For further information, see Single-Ventricle Lesions.)
9. After resuscitation from pediatric cardiac arrest, it is reasonable to target normocapnia *(Class IIa; Level of Evidence B)*.
10. After resuscitation from pediatric cardiac arrest, continuous core temperature monitoring is recommended *(Class I; Level of Evidence C)*.
11. After resuscitation from pediatric cardiac arrest, management strategies to prevent and treat hyperthermia are recommended for all patients to minimize secondary neurological injury *(Class I; Level of Evidence B)*.
12. For neuroprotection for children who remain comatose after resuscitation from out-of-hospital pediatric cardiac arrest, targeted temperature management with either strict maintenance of normothermia (36°C–37.5°C) for 5 days or 2 days of hypothermia (32°C–34°C) followed by 3 days of normothermia (36°C–37.5°C) is reasonable *(Class IIa; Level of Evidence B)*.

Acute Kidney Injury Management

Organ dysfunction is common after resuscitation from cardiac arrest, and the kidney is very susceptible to ischemic injury. Although the impact and prognosis of acute kidney injury (AKI) have been well described in other forms of ischemia, such as cardiopulmonary bypass, and in other critical illnesses, such as sepsis, the incidence and outcome of AKI after cardiac arrest have not been well described. In a recent series of 311 adults who survived out-of-hospital cardiac arrest, more than one-third had some degree of postresuscitation renal dysfunction.[736] In other critical illnesses, AKI has been independently associated with worse short- and long-term outcomes, including higher mortality. As a result, measures to prevent or attenuate AKI will likely be beneficial.

The diagnosis of AKI has been made difficult by a lack of a "gold standard" diagnostic test. The serum creatinine concentration is influenced by a number of factors, including fluid status and nutritional state, and is unreliable in the acute setting. Additionally, the reported incidence of AKI has varied greatly in the absence of a standard consensus definition. These challenges led to the proposed RIFLE criteria.[737] The RIFLE consensus definition is a mnemonic for 3 levels of severity (risk, injury, and failure) and 2 outcomes (loss and end-stage kidney disease). These criteria have been validated in critically ill adults and children. In 2012, to further refine AKI definition and achieve consistent terminology, KDIGO (Kidney Disease: Improving Global Outcomes) created guidelines for the evaluation and management of AKI, including a definition and classification of AKI. AKI diagnosis with the KDIGO guidelines can be made by oliguria or creatinine elevation criteria. Importantly, the KDIGO definition of AKI was not modified for pediatric patients. More recently, novel serum and urine biomarkers have been discovered and validated for the early diagnosis of AKI.[738] The theoretical advantage of using these biomarkers is the opportunity for very early diagnosis of AKI, before irreversible damage has occurred. This could enable attenuation of the injury or improved recovery via therapeutic intervention.

Despite multiple studies of and guidelines for management of AKI, there are no evidence-based

recommendations for prevention and treatment of ischemic AKI. Current management involves supportive care, including optimizing hemodynamics to maintain renal perfusion, with careful balancing of fluid status to optimize intravascular volume without fluid overload, and avoiding nephrotoxins (including medications).[739] In studies of AKI in other critical illnesses, the use of sodium bicarbonate and *N*-acetylcysteine for emergency procedures using contrast media and the judicious use of hemofiltration[740] have been beneficial, but these have not been specifically evaluated after cardiac arrest. Similarly, although the use of renal replacement therapy for the prevention or early treatment of fluid overload has reduced mortality in other forms of AKI,[741] the frequency of use and ideal timing for renal replacement therapy in the post–cardiac arrest care of children with heart disease has not been studied.

The response of the kidney to therapeutic hypothermia after cardiac arrest is unclear. A retrospective review of asphyxiated newborns treated with therapeutic hypothermia suggested a lower incidence of AKI than in historical reports.[742] In a systematic review of adult trials, however, therapeutic hypothermia was not associated with a reduced incidence of AKI or reduced need for dialysis after cardiac arrest. However, different definitions and rates of AKI, differences in mortality rates, and uncertainty about the optimal target cooling temperature confound conclusions.[743]

Our understanding of AKI after cardiac arrest is incomplete. Predictive factors and diagnosis and treatment of AKI have been limited by a suboptimal diagnostic definition. Although progress has been made in standardization of nomenclature, the availability of biomarkers for more rapid and definitive diagnosis should facilitate studies addressing the epidemiology and potential therapies of AKI after cardiac arrest. In addition, the inclusion of AKI as an outcome in therapeutic studies after cardiac arrest should provide additional information.

Gaps in Knowledge

The diagnosis of AKI is limited by a suboptimal diagnostic standard. In addition, no proven therapies for treatment of ischemic AKI have been established.

Recommendations: Post–Cardiac Arrest Stabilization – AKI Management

1. **Supportive care can be useful after ischemic AKI, including optimizing cardiac output, maintaining adequate renal perfusion pressure, optimizing fluid balance while avoiding fluid overload, and limiting use of nephrotoxins *(Class IIa; Level of Evidence B)*.**

Endocrine Management

Glycemic Control

Both hypoglycemia[744] and hyperglycemia[745] are associated with poor outcome in critically ill children. Van den Berghe and colleagues[746,747] reported that controlling blood glucose in stress hyperglycemia to within normal limits in critically ill adult patients improved survival and reduced complications compared with patients allocated to standard care at higher glucose levels; however, other trials in critically ill adults, including a large international multicenter study,[748] failed to clearly demonstrate improved outcomes with tight glucose control, so the role of glycemic control in adult critical care remains hotly debated.[749]

There are few data available on which to base guidelines for the management of glucose after cardiac arrest in children. In a single-center retrospective cohort study of 378 consecutive pediatric cardiovascular surgical patients,[750] longer duration of hyperglycemia (defined as hours with serum glucose >126 mg/dL) was associated with longer postoperative hospitalization. In the 72 hours after surgery, average glucose <110 mg/dL or >143 mg/dL and minimum glucose ≤75 mg/dL or peak glucose level ≥250 mg/dL were all associated with a greater adjusted odds of reaching the composite morbidity-mortality endpoint (eg, mortality, nosocomial infection, cardiovascular failure requiring ECMO, acute renal failure requiring dialysis, hepatic dysfunction, or new central nervous system injury). The authors concluded that in children undergoing complex congenital heart surgery, the optimal postoperative glucose range may be 110 to 126 mg/dL. Although there was a high incidence of hypoglycemia, a subsequent follow-up study of neurocognitive outcomes found no important differences between children who were hypoglycemic and those who were not.[751] Tight glucose control in children after cardiac surgery was not associated with reduced mortality but with reduced postoperative troponin levels and heart-type fatty acid protein and reduced blood lactate concentrations.[751] Two large randomized controlled trials have addressed glucose control after pediatric cardiac surgery. Agus et al[752] demonstrated that tight glucose control did not significantly change mortality, length of stay, infection rate, or other measures of organ failure in nearly 1000 children. In a series of nearly 1400 children in the United Kingdom (60% were postoperative), Macrae et al[753] found no difference in the number of days alive and free from mechanical ventilation at 30 days after randomization between those with and without tight glycemic control. Episodes of severe hypoglycemia (≤36 mg/dL) occurred in a higher proportion of those in the tight glucose control group that of those receiving conventional management.[753] However, hos-

Circulation. 2018;137:00–00. DOI: 10.1161/CIR.0000000000000524

pital discharge occurred significantly earlier in those patients with tight glucose control in the noncardiac surgical cohort.[753]

All of these studies differed in design, with markedly different patterns in the use of insulin. Further studies of glucose control and insulin administration regimens in children will be required before definitive recommendations can be made concerning the utility of glucose control algorithms in children, including those after cardiac arrest.

Several animal studies, but no clinical studies in children, have shown poorer outcomes when glucose is given after or during cardiac arrest. There is also evidence in studies of neonatal hypoxia-ischemia of an association between hypoglycemia and subsequent brain injury.[754–757] Tight glucose control has been shown to increase global glucose uptake and to increase cerebral metabolic crisis after traumatic brain injury,[758] although the associated mechanisms are unclear. A further recent report concluded that hypoglycemia aggravates critical illness–induced neurocognitive dysfunction to a significant extent.[753,759]

Detection and Management of Adrenal Insufficiency

There are insufficient data regarding the incidence of adrenal insufficiency after cardiac arrest in children with heart disease to accurately assess the scope of the problem or to make firm treatment recommendations. Several studies have shown that relative adrenal insufficiency is common after out-of-hospital cardiac arrest in adults and is associated with worse outcomes, including higher mortality.[760–765] It is uncertain whether the administration of hydrocortisone or other forms of corticosteroid is beneficial in this group. A recent randomized controlled adult trial compared survival after conventional cardiac arrest management to the administration of vasopressin and a single dose of methylprednisolone during the arrest, followed by a course of hydrocortisone.[766] Higher rates of both ROSC and survival-to-hospital-discharge with favorable neurological outcome were seen in the treatment arm.[766]

There are several reasons for caution in extrapolating adult data to children, one of which concerns the definition of hypoadrenalism. The use of corticotrophin stimulation tests and the use of arbitrary levels of total or free cortisol to define hypoadrenalism have not been validated in children with low cardiac output in the pediatric cardiac ICU.[400,767] No consistent relationship between total or free cortisol levels and hemodynamic status has been observed in children with heart disease after cardiopulmonary bypass,[399,768,769] and an accurate and reliable definition of hypoadrenalism in children with cardiac disease has not yet been established.

Steroid administration has been associated with short-term hemodynamic benefits for children in various shock states, including LCOS after cardiac surgery. Observed benefits included an increase in mean arterial pressure and a decrease in both heart rate and inotrope requirements.[401,402,767] The adverse effects from corticosteroid administration are well established. Cumulative corticosteroid dosing in children with heart disease undergoing surgery has been associated with increased risk of postoperative infection and prolonged hospitalization.[403,404]

The uncertain long-term benefits and potential harm associated with corticosteroid use prohibits their routine administration after cardiac arrest in children with heart disease. However, in patients with established risk factors for hypoadrenalism or in patients with catecholamine-resistant shock, it is reasonable to use low-dose hydrocortisone (2–4 $mg \cdot kg^{-1} \cdot d^{-1}$) or an equivalent and assess the impact on short-term hemodynamic status.

Gaps in Knowledge

To date, trials of tight glycemic control in children have focused mainly on levels of glycemia. Although they differ to some extent in target glucose control limits, these studies differed significantly in insulin administration regimens. It is not known whether different insulin administration regimens might have led to different results. Future studies should therefore focus on the roles of both glucose and insulin on the outcome and investigate whether there are identifiable subgroups of cardiac patients, including those requiring CPR, who might predictably benefit from glucose control or insulin treatment. The potential mechanisms by which hyperglycemia may adversely influence clinical outcomes in critically ill children are incompletely understood.

No consistent definition of hypoadrenalism has been validated in children with heart disease. The incidence of hypoadrenalism after cardiac arrest in these patients is unknown. It is unclear what, if any, are the indications for corticosteroid administration in children with heart disease, either during or after cardiac arrest.

Recommendations: Post–Cardiac Arrest Stabilization – Endocrine Management

1. **After CPR in children with heart disease, hypoglycemia is harmful and should be avoided *(Class III: Harm; Level of Evidence B)*.**
2. **The administration of low-dose hydrocortisone to children with heart disease may be considered in postarrest, catecholamine-resistant shock *(Class IIb; Level of Evidence C)*.**

MEDICAL-LEGAL AND ETHICAL CONSIDERATIONS

Ethical decision making during the resuscitation of neonates, infant, children, and adults with CHD must be based on clear communication and a sound physician-nurse-patient-family relationship, as well as knowledge of ethical principles (including beneficence, nonmaleficence, and autonomy), justice, and an understanding of current standards of care for patients with CHD. Guidelines for healthcare providers who are faced with ethical and legal considerations during acute resuscitation have been provided in the 2010 AHA Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care[770] and in the 2015 AHA Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care.[771]

On the basis of the Born Alive Infant Protection Act, any newborn infant believed to be alive, no matter how severe the underlying disease or pathology, has the right to be assessed by a healthcare provider for viability.[772] The decision to not initiate resuscitative measures and cardiac interventions is based on life-limiting comorbidities rather than the CHD alone. Patients with most forms of CHD, including HLHS, have a reasonable likelihood of survival. Therefore, an independent decision by a clinician to not resuscitate and not initiate cardiac intervention based on CHD alone is not considered to be standard of care.[773,774] Furthermore, based on the Baby Doe rulings, decisions on whether to initiate care, continue intensive care management, or resuscitate cannot be based solely on the perceived future quality of life or judgment made by clinicians.[775,776] Initiation or termination of intensive care management or a resuscitation event should be based on futility of care. If the medical condition is considered futile (in that no medical or surgical management will prevent the infant from having an inevitable death, or the chance of survival is extremely low and the burden of care and potential for suffering is high), redirection of care should be sought. Note that "futility of care" in any given case may not be easy to define. Clinicians and parents might assess the parameters that determine futility differently, and they may disagree whether futility has been reached. Parents/guardians and families may see burden of care quite differently, which may modify the overall assessment of futility parameters. If after resuscitation, discussions between parents/guardians for the child and the care team relative to futility and possible termination of care are at an impasse, an ethics consultation can be helpful.

Patients with CHD are often critically ill, and invasive life-sustaining therapies, including CPR and ECLS, might be necessary to achieve good outcomes. Timely multidisciplinary evaluation of the individual patient that considers all interventional and medical options is expected before a decision about futility of care is made.

Once futility of care is present, the "do no harm" principle (nonmaleficence) becomes relevant, because the clinician is then providing treatment that would merely prolong dying and/or not be effective in ameliorating or correcting all the infant's life-threatening conditions.

As noted at the beginning of this consensus statement, there are considerable pathophysiological considerations in patients with CHD that alter the effectiveness of resuscitation in the event of a cardiac arrest. The AHA PALS recommendations were developed for infants and children with normal cardiac anatomy. It is important to emphasize that any such recommendations are guidelines, based on the best available evidence at the time, and they will continue to be revised. They are not to be viewed as hard rules. There are specific circumstances in which such recommendations will need to be modified, such as patients with single-ventricle physiology. More important, the effectiveness of resuscitation must always be monitored, and the technique (including the rate of chest compressions, the specific drugs used, and the use of ECLS) must be modified according to the known underlying pathophysiology and patient response. Therefore, clinicians are not vulnerable to legal penalty if they deviate from the PALS guidelines as written. Nevertheless, it is very important that managers or leaders of resuscitation events explain to the team the rationale for modification of techniques and priorities during resuscitation and that this information be clearly documented in the subsequent debriefing and notes describing the event.

Gaps in Knowledge

There appears to be considerable variation in counseling practices among professionals regarding infants with CHD. Future work is needed to establish the expectation of regular multidisciplinary ethical discussions as part of standard of care for patients with CHD. The more data available to establish best practices, the better the cardiovascular team can evaluate their outcomes and make recommendations to families.

Recommendations: Medical-Legal and Ethical Considerations

1. **Discussions with families and patients with CHD about treatment options, outcomes, and "futility of care" should be multidisciplinary and occur when possible before acute resuscitation events *(Class IIa; Level of Evidence C)*.**
2. **Team debriefing and documentation of resuscitation efforts should be recorded accurately *(Class I; Level of Evidence C)*.**

Circulation. 2018;137:00–00. DOI: 10.1161/CIR.0000000000000524

SUMMARY

Pediatric patients with congenital and acquired heart disease pose unique challenges in the periarrest period. The risk of cardiac arrest is increased as a result of potential imbalance between SBF and PBF, altered ventricular volume and pressure loads, systolic and diastolic ventricular dysfunction, pulmonary hypertension, valvar stenosis and insufficiency, and other alterations in hemodynamics. These perturbations can evolve rapidly, producing an inadequate balance between oxygen supply and demand, resulting in cardiac arrest. An understanding of the evolving physiology is critical to prevent cardiac arrest in this high-risk population. Thus, close invasive and noninvasive monitoring and anticipatory care, including a low threshold for transfer to intensive care, cardiology/intensive care consultation, or hospital readmission, are important to avoid hemodynamic instability and to prevent cardiac arrest.

Once cardiac arrest occurs, it is appropriate to initiate standard resuscitation measures, but these could be unsuccessful because the child's underlying physiology can limit effective cardiac output and Do_2 during chest compressions. As a result, clinicians must individualize resuscitation strategies in light of each patient's cardiovascular anatomy and physiology. Early consideration of other interventions, including ECPR, can be lifesaving.

ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on March 15, 2017, and the American Heart Association Executive Committee on April 17, 2017. A copy of the document is available at http://professional.heart.org/statements by using either "Search for Guidelines & Statements" or the "Browse by Topic" area. To purchase additional reprints, call 843-216-2533 or e-mail kelle.ramsay@wolterskluwer.com.

The American Heart Association requests that this document be cited as follows: Marino BS, Tabbutt S, MacLaren G, Hazinski MF, Adatia I, Atkins DL, Checchia PA, DeCaen A, Fink EL, Hoffman GM, Jefferies JL, Kleinman M, Krawczeski CD, Licht DJ, Macrae D, Ravishankar C, Samson RA, Thiagarajan RR, Toms R, Tweddell J, Laussen PC; on behalf of the American Heart Association Congenital Heart Defects Committee of the Council on Cardiovascular Disease in the Young; Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Cardiovascular Surgery and Anesthesia; and Emergency Cardiovascular Care Committee. Cardiopulmonary resuscitation in infants and children with cardiac disease: a scientific statement from the American Heart Association. *Circulation.* 2018;137:e•••–e•••. DOI: 10.1161/CIR.0000000000000524.

Expert peer review of AHA Scientific Statements is conducted by the AHA Office of Science Operations. For more on AHA statements and guidelines development, visit http://professional.heart.org/statements. Select the "Guidelines & Statements" drop-down menu, then click "Publication Development."

Disclosures

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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

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This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

REFERENCES

1. Standards and guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiac care (ECC) [published correction appears in *JAMA*. 1981;246:920]. *JAMA*. 1980;244:453–509.
2. Standards and guidelines for Cardiopulmonary Resuscitation (CPR) and Emergency Cardiac Care (ECC) [published correction appears in *JAMA*. 1986;256:1727]. *JAMA*. 1986;255:2905–89.
3. de Caen AR, Berg MD, Chameides L, Gooden CK, Hickey RW, Scott HF, Sutton RM, Tijssen JA, Topjian A, van der Jagt ÉW, Schexnayder SM, Samson RA. Part 12: pediatric advanced life support: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132(suppl 2):S526–S542. doi: 10.1161/CIR.0000000000000266.
4. Kleinman ME, Chameides L, Schexnayder SM, Samson RA, Hazinski MF, Atkins DL, Berg MD, de Caen AR, Fink EL, Freid EB, Hickey RW, Marino BS, Nadkarni VM, Proctor LT, Qureshi FA, Sartorelli K, Topjian A, van der Jagt EW, Zaritsky AL. Part 14: pediatric advanced life support: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2010;122(suppl 3):S876–S908. doi: 10.1161/CIRCULATIONAHA.110.971101.
5. Ortmann L, Prodhan P, Gossett J, Schexnayder S, Berg R, Nadkarni V, Bhutta A; for the American Heart Association's Get With the Guidelines–Resuscitation Investigators. Outcomes after in-hospital cardiac arrest in children with cardiac disease: a report from Get With the Guidelines–Resuscitation. *Circulation*. 2011;124:2329–2337. doi: 10.1161/CIRCULATIONAHA.110.013466.
6. Meaney PA, Bobrow BJ, Mancini ME, Christenson J, de Caen AR, Bhanji F, Abella BS, Kleinman ME, Edelson DP, Berg RA, Aufderheide TP, Menon V, Leary M; on behalf of the CPR Quality Summit Investigators, the American Heart Association Emergency Cardiovascular Care Committee, and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. Cardiopulmonary resuscitation quality: improving cardiac resuscitation outcomes both inside and outside the hospital: a consensus statement from the American Heart Association [published corrections appear in *Circulation*. 2013;128:e120 and *Circulation*. 2013;128:e408]. *Circulation*. 2013;128:417–435. doi: 10.1161/CIR.0b013e31829d8654.
7. Joffe AR, Lequier L, Robertson CM. Pediatric outcomes after extracorporeal membrane oxygenation for cardiac disease and for cardiac arrest: a review. *ASAIO J*. 2012;58:297–310. doi: 10.1097/MAT.0b013e31825a21ff.
8. Kane DA, Thiagarajan RR, Wypij D, Scheurer MA, Fynn-Thompson F, Emani S, del Nido PJ, Betit P, Laussen PC. Rapid-response extracorporeal membrane oxygenation to support cardiopulmonary resuscitation in children with cardiac disease. *Circulation*. 2010;122(suppl):S241–S248. doi: 10.1161/CIRCULATIONAHA.109.928390.
9. Kushner FG, Hand M, Smith SC Jr, King SB 3rd, Anderson JL, Antman EM, Bailey SR, Bates ER, Blankenship JC, Casey DE Jr, Green LA, Hochman JS, Jacobs AK, Krumholz HM, Morrison DA, Ornato JP, Pearle DL, Peterson ED, Sloan MA, Whitlow PL, Williams DO. 2009 Focused updates: ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction (updating the 2004 guideline and 2007 focused update) and ACC/AHA/SCAI guidelines on percutaneous coronary intervention (updating the 2005 guideline and 2007 focused update): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines [published correction appears in *Circulation*. 2010;121:e257]. *Circulation*. 2009;120:2271–306.
10. Topjian AA, Nadkarni VM, Berg RA. Cardiopulmonary resuscitation in children. *Curr Opin Crit Care*. 2009;15:203–208.
11. Anderson JB, Beekman RH 3rd, Kugler JD, Rosenthal GL, Jenkins KJ, Klitzner TS, Martin GR, Neish SR, Brown DW, Mangeot C, King E, Peterson LE, Provost L, Lannon C; for the National Pediatric Cardiology Quality Improvement Collaborative. Improvement in Interstage survival in a national pediatric cardiology learning network. *Circ Cardiovasc Qual Outcomes*. 2015;8:428–436. doi: 10.1161/CIRCOUTCOMES.115.001956.
12. Knudson JD, Neish SR, Cabrera AG, Lowry AW, Shamszad P, Morales DL, Graves DE, Williams EA, Rossano JW. Prevalence and outcomes of pediatric in-hospital cardiopulmonary resuscitation in the United States: an analysis of the Kids' Inpatient Database. *Crit Care Med*. 2012;40:2940–2944. doi: 10.1097/CCM.0b013e31825feb3f.
13. Lowry AW, Knudson JD, Cabrera AG, Graves DE, Morales DL, Rossano JW. Cardiopulmonary resuscitation in hospitalized children with cardiovascular disease: estimated prevalence and outcomes from the Kids' Inpatient Database. *Pediatr Crit Care Med*. 2013;14:248–255. doi: 10.1097/PCC.0b013e3182713329.
14. Peddy SB, Hazinski MF, Laussen PC, Thiagarajan RR, Hoffman GM, Nadkarni V, Tabbutt S. Cardiopulmonary resuscitation: special considerations for infants and children with cardiac disease. *Cardiol Young*. 2007;17(suppl 2):116–126. doi: 10.1017/S1047951107001229.
15. Kleinman ME, de Caen AR, Chameides L, Atkins DL, Berg RA, Berg MD, Bhanji F, Biarent D, Bingham R, Coovadia AH, Hazinski MF, Hickey RW, Nadkarni VM, Reis AG, Rodriguez-Nunez A, Tibballs J, Zaritsky AL, Zideman D; Pediatric Basic and Advanced Life Support Chapter Collaborators. Pediatric basic and advanced life support: 2010 International consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. *Pediatrics*. 2010;126:e1261–e1318. doi: 10.1542/peds.2010-2972A.
16. Topjian AA, Berg RA, Nadkarni VM. Pediatric cardiopulmonary resuscitation: advances in science, techniques, and outcomes. *Pediatrics*. 2008;122:1086–1098. doi: 10.1542/peds.2007-3313.
17. Girotra S, Spertus JA, Li Y, Berg RA, Nadkarni VM, Chan PS; for the American Heart Association Get With the Guidelines–Resuscitation Investigators. Survival trends in pediatric in-hospital cardiac arrests: an analysis from Get With the Guidelines-Resuscitation. *Circ Cardiovasc Qual Outcomes*. 2013;6:42–49. doi: 10.1161/CIRCOUTCOMES.112.967968.
18. Tweddell JS, Hoffman GM, Fedderly RT, Ghanayem NS, Kampine JM, Berger S, Mussatto KA, Litwin SB. Patients at risk for low systemic oxygen delivery after the Norwood procedure. *Ann Thorac Surg*. 2000;69:1893–1899.
19. Tweddell JS, Hoffman GM, Mussatto KA, Fedderly RT, Berger S, Jaquiss RD, Ghanayem NS, Frisbee SJ, Litwin SB. Improved survival of patients undergoing palliation of hypoplastic left heart syndrome: lessons learned from 115 consecutive patients. *Circulation*. 2002;106(suppl 1):I82–I89.
20. Tabbutt S, Dominguez TE, Ravishankar C, Marino BS, Gruber PJ, Wernovsky G, Gaynor JW, Nicolson SC, Spray TL. Outcomes after the stage I reconstruction comparing the right ventricular to pulmonary artery conduit with the modified Blalock Taussig shunt. *Ann Thorac Surg*. 2005;80:1582–90. doi: 10.1016/j.athoracsur.2005.04.046.
21. Tweddell JS, Hoffman GM. Postoperative management in patients with complex congenital heart disease. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2002;5:187–205. doi: 10.1053/pcsu.2002.31499.
22. Tibby S, Hoffman G. Worksheet for Evidence-Based Review of Science for Emergency Cardiac Care: Resuscitation of the Patient With Single Ventricle. Worksheet No. Peds-059b. International Liaison Committee on Re-

suscitation. 2010. http://circ.ahajournals.org/sites/default/files/additional-assets/pdfs/Peds-059.pdf. Accessed March 23, 2013.
23. Feinstein JA, Benson DW, Dubin AM, Cohen MS, Maxey DM, Mahle WT, Pahl E, Villafañe J, Bhatt AB, Peng LF, Johnson BA, Marsden AL, Daniels CJ, Rudd NA, Caldarone CA, Mussatto KA, Morales DL, Ivy DD, Gaynor JW, Tweddell JS, Deal BJ, Furck AK, Rosenthal GL, Ohye RG, Ghanayem NS, Cheatham JP, Tworetzky W, Martin GR. Hypoplastic left heart syndrome: current considerations and expectations [published correction appears in *J Am Coll Cardiol*. 2012;59:544]. *J Am Coll Cardiol*. 2012;59(suppl):S1–42. doi: 10.1016/j.jacc.2011.09.022.
24. Marino BS, Tibby SM, Hoffman GM. Resuscitation of the patient with the functionally univentricular heart. *Curr Pediatr Rev*. 2013;9:148–157.
25. Ghanayem NS, Tweddell JS, Hoffman GM, Mussatto K, Jaquiss RD. Optimal timing of the second stage of palliation for hypoplastic left heart syndrome facilitated through home monitoring, and the results of early cavopulmonary anastomosis. *Cardiol Young*. 2006;16(suppl 1):61–66. doi: 10.1017/S1047951105002349.
26. Ohye RG, Sleeper LA, Mahony L, Newburger JW, Pearson GD, Lu M, Goldberg CS, Tabbutt S, Frommelt PC, Ghanayem NS, Laussen PC, Rhodes JF, Lewis AB, Mital S, Ravishankar C, Williams IA, Dunbar-Masterson C, Atz AM, Colan S, Minich LL, Pizarro C, Kanter KR, Jaggers J, Jacobs JP, Krawczeski CD, Pike N, McCrindle BW, Virzi L, Gaynor JW; Pediatric Heart Network Investigators. Comparison of shunt types in the Norwood procedure for single-ventricle lesions. *N Engl J Med*. 2010;362:1980–1992. doi: 10.1056/NEJMoa0912461.
27. Graham EM, Forbus GA, Bradley SM, Shirali GS, Atz AM. Incidence and outcome of cardiopulmonary resuscitation in patients with shunted single ventricle: advantage of right ventricle to pulmonary artery shunt. *J Thorac Cardiovasc Surg*. 2006;131:e7–e8. doi: 10.1016/j.jtcvs.2005.12.028.
28. Ohye RG, Schonbeck JV, Eghtesady P, Laussen PC, Pizarro C, Shrader P, Frank DU, Graham EM, Hill KD, Jacobs JP, Kanter KR, Kirsh JA, Lambert LM, Lewis AB, Ravishankar C, Tweddell JS, Williams IA, Pearson GD; Pediatric Heart Network Investigators. Cause, timing, and location of death in the Single Ventricle Reconstruction trial. *J Thorac Cardiovasc Surg*. 2012;144:907–914. doi: 10.1016/j.jtcvs.2012.04.028.
29. Tabbutt S, Ghanayem N, Ravishankar C, Sleeper LA, Cooper DS, Frank DU, Lu M, Pizarro C, Frommelt P, Goldberg CS, Graham EM, Krawczeski CD, Lai WW, Lewis A, Kirsh JA, Mahony L, Ohye RG, Simsic J, Lodge AJ, Spurrier E, Stylianou M, Laussen P; Pediatric Heart Network Investigators. Risk factors for hospital morbidity and mortality after the Norwood procedure: a report from the Pediatric Heart Network Single Ventricle Reconstruction trial. *J Thorac Cardiovasc Surg*. 2012;144:882–895. doi: 10.1016/j.jtcvs.2012.05.019.
30. Cua CL, Thiagarajan RR, Gauvreau K, Lai L, Costello JM, Wessel DL, Del Nido PJ, Mayer JE Jr, Newburger JW, Laussen PC. Early postoperative outcomes in a series of infants with hypoplastic left heart syndrome undergoing stage I palliation operation with either modified Blalock-Taussig shunt or right ventricle to pulmonary artery conduit. *Pediatr Crit Care Med*. 2006;7:238–244. doi: 10.1097/01.PCC.0000201003.38320.63.
31. Ghanayem NS, Allen KR, Tabbutt S, Atz AM, Clabby ML, Cooper DS, Eghtesady P, Frommelt PC, Gruber PJ, Hill KD, Kaltman JR, Laussen PC, Lewis AB, Lurito KJ, Minich LL, Ohye RG, Schonbeck JV, Schwartz SM, Singh RK, Goldberg CS; Pediatric Heart Network Investigators. Interstage mortality after the Norwood procedure: results of the multicenter Single Ventricle Reconstruction trial. *J Thorac Cardiovasc Surg*. 2012;144:896–906. doi: 10.1016/j.jtcvs.2012.05.020.
32. Rixen D, Siegel JH. Bench-to-bedside review: oxygen debt and its metabolic correlates as quantifiers of the severity of hemorrhagic and post-traumatic shock. *Crit Care*. 2005;9:441–453. doi: 10.1186/cc3526.
33. Hoffman GM, Ghanayem NS, Kampine JM, Berger S, Mussatto KA, Litwin SB, Tweddell JS. Venous saturation and the anaerobic threshold in neonates after the Norwood procedure for hypoplastic left heart syndrome. *Ann Thorac Surg*. 2000;70:1515–1520.
34. Bradley SM, Atz AM. Postoperative management: the role of mixed venous oxygen saturation monitoring. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2005;8:22–27.
35. Tweddell JS, Ghanayem NS, Mussatto KA, Mitchell ME, Lamers LJ, Musa NL, Berger S, Litwin SB, Hoffman GM. Mixed venous oxygen saturation monitoring after stage 1 palliation for hypoplastic left heart syndrome. *Ann Thorac Surg*. 2007;84:1301–1310. doi: 10.1016/j.athoracsur.2007.05.047.
36. Hoffman GM, Ghanayem NS, Tweddell JS. Noninvasive assessment of cardiac output. *Semin Thorac Cardiovasc SurgPediatr Card Surg Annu*. 2005;8:12–21.
37. Tortoriello TA, Stayer SA, Mott AR, McKenzie ED, Fraser CD, Andropoulos DB, Chang AC. A noninvasive estimation of mixed venous oxygen saturation using near-infrared spectroscopy by cerebral oximetry in pediatric cardiac surgery patients. *Paediatr Anaesth*. 2005;15:495–503. doi: 10.1111/j.1460-9592.2005.01488.x.
38. Kaufman J, Almodovar MC, Zuk J, Friesen RH. Correlation of abdominal site near-infrared spectroscopy with gastric tonometry in infants following surgery for congenital heart disease. *Pediatr Crit Care Med*. 2008;9:62–68. doi: 10.1097/01.PCC.0000298640.47574.DA.
39. Ranucci M, Isgrò G, De la Torre T, Romitti F, Conti D, Carlucci C. Near-infrared spectroscopy correlates with continuous superior vena cava oxygen saturation in pediatric cardiac surgery patients. *Paediatr Anaesth*. 2008;18:1163–1169. doi: 10.1111/j.1460-9592.2008.02783.x.
40. Chakravarti SB, Mittnacht AJ, Katz JC, Nguyen K, Joashi U, Srivastava S. Multisite near-infrared spectroscopy predicts elevated blood lactate level in children after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2009;23:663–667. doi: 10.1053/j.jvca.2009.03.014.
41. Johnson BA, Hoffman GM, Tweddell JS, Cava JR, Basir M, Mitchell ME, Scanlon MC, Mussatto KA, Ghanayem NS. Near-infrared spectroscopy in neonates before palliation of hypoplastic left heart syndrome. *Ann Thorac Surg*. 2009;87:571–577. doi: 10.1016/j.athoracsur.2008.10.043.
42. Bernal NP, Hoffman GM, Ghanayem NS, Arca MJ. Cerebral and somatic near-infrared spectroscopy in normal newborns. *J Pediatr Surg*. 2010;45:1306–1310. doi: 10.1016/j.jpedsurg.2010.02.110.
43. Ghanayem NS, Wernovsky G, Hoffman GM. Near-infrared spectroscopy as a hemodynamic monitor in critical illness. *Pediatr Crit Care Med*. 2011;12(suppl):S27–S32. doi: 10.1097/PCC.0b013e318221173a.
44. Dabal RJ, Rhodes LA, Borasino S, Law MA, Robert SM, Alten JA. Inferior vena cava oxygen saturation monitoring after the Norwood procedure. *Ann Thorac Surg*. 2013;95:2114–2120. doi: 10.1016/j.athoracsur.2013.01.076.
45. Taeed R, Schwartz SM, Pearl JM, Raake JL, Beekman RH 3rd, Manning PB, Nelson DP. Unrecognized pulmonary venous desaturation early after Norwood palliation confounds Gp:Gs assessment and compromises oxygen delivery. *Circulation*. 2001;103:2699–2704.
46. Tweddell JS, Hoffman GM, Fedderly RT, Berger S, Thomas JP Jr, Ghanayem NS, Kessel MW, Litwin SB. Phenoxybenzamine improves systemic oxygen delivery after the Norwood procedure. *Ann Thorac Surg*. 1999;67:161–167.
47. Ghanayem NS, Hoffman GM, Mussatto KA, Frommelt MA, Cava JR, Mitchell ME, Tweddell JS. Perioperative monitoring in high-risk infants after stage 1 palliation of univentricular congenital heart disease. *J Thorac Cardiovasc Surg*. 2010;140:857–863. doi: 10.1016/j.jtcvs.2010.05.002.
48. Hoffman GM, Brosig CL, Mussatto KA, Tweddell JS, Ghanayem NS. Perioperative cerebral oxygen saturation in neonates with hypoplastic left heart syndrome and childhood neurodevelopmental outcome. *J Thorac Cardiovasc Surg*. 2013;146:1153–1164. doi: 10.1016/j.jtcvs.2012.12.060.
49. Hoffman GM, Mussatto KA, Brosig CL, Ghanayem NS, Musa N, Fedderly RT, Jaquiss RD, Tweddell JS. Systemic venous oxygen saturation after the Norwood procedure and childhood neurodevelopmental outcome. *J Thorac Cardiovasc Surg*. 2005;130:1094–1100. doi: 10.1016/j.jtcvs.2005.06.029.
50. Hirsch JC, Charpie JR, Ohye RG, Gurney JG. Near infrared spectroscopy (NIRS) should not be standard of care for postoperative management. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2010;13:51–54. doi: 10.1053/j.pcsu.2010.01.005.
51. Tweddell JS, Ghanayem NS, Hoffman GM. Pro: NIRS is "standard of care" for postoperative management. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2010;13:44–50. doi: 10.1053/j.pcsu.2010.02.008.
52. Lowry AW. Resuscitation and perioperative management of the high-risk single ventricle patient: first-stage palliation. *Congenit Heart Dis*. 2012;7:466–478. doi: 10.1111/j.1747-0803.2012.00710.x.
53. Migliavacca F, Pennati G, Dubini G, Fumero R, Pietrabissa R, Urcelay G, Bove EL, Hsia TY, de Leval MR. Modeling of the Norwood circulation: effects of shunt size, vascular resistances, and heart rate. *Am J Physiol Heart Circ Physiol*. 2001;280:H2076–H2086.
54. Hoffman GM, Tweddell JS, Ghanayem NS, Mussatto KA, Stuth EA, Jaquis RD, Berger S. Alteration of the critical arteriovenous oxygen saturation relationship by sustained afterload reduction after the Norwood procedure. *J Thorac Cardiovasc Surg*. 2004;127:738–745. doi: 10.1016/S0022.
55. Wright GE, Crowley DC, Charpie JR, Ohye RG, Bove EL, Kulik TJ. High systemic vascular resistance and sudden cardiovascular collapse in recovering Norwood patients. *Ann Thorac Surg*. 2004;77:48–52.

56. Ramamoorthy C, Tabbutt S, Kurth CD, Steven JM, Montenegro LM, Durning S, Wernovsky G, Gaynor JW, Spray TL, Nicolson SC. Effects of inspired hypoxic and hypercapnic gas mixtures on cerebral oxygen saturation in neonates with univentricular heart defects. *Anesthesiology*. 2002;96:283–288.
57. Jobes DR, Nicolson SC, Steven JM, Miller M, Jacobs ML, Norwood WI Jr. Carbon dioxide prevents pulmonary overcirculation in hypoplastic left heart syndrome. *Ann Thorac Surg*. 1992;54:150–151.
58. Mott AR, Alomrani A, Tortoriello TA, Perles Z, East DL, Stayer SA. Changes in cerebral saturation profile in response to mechanical ventilation alterations in infants with bidirectional superior cavopulmonary connection. *Pediatr Crit Care Med*. 2006;7:346–350. doi: 10.1097/01.PCC.0000224949.25692.87.
59. Tabbutt S, Ramamoorthy C, Montenegro LM, Durning SM, Kurth CD, Steven JM, Godinez RI, Spray TL, Wernovsky G, Nicolson SC. Impact of inspired gas mixtures on preoperative infants with hypoplastic left heart syndrome during controlled ventilation. *Circulation*. 2001;104(suppl 1):I159–I164.
60. Li J, Zhang G, Holtby H, Bissonnette B, Wang G, Redington AN, Van Arsdell GS. Carbon dioxide–a complex gas in a complex circulation: its effects on systemic hemodynamics and oxygen transport, cerebral, and splanchnic circulation in neonates after the Norwood procedure. *J Thorac Cardiovasc Surg*. 2008;136:1207–1214. doi: 10.1016/j.jtcvs.2008.02.096.
61. Li J, Zhang G, McCrindle BW, Holtby H, Humpl T, Cai S, Caldarone CA, Redington AN, Van Arsdell GS. Profiles of hemodynamics and oxygen transport derived by using continuous measured oxygen consumption after the Norwood procedure. *J Thorac Cardiovasc Surg*. 2007;133:441–448. doi: 10.1016/j.jtcvs.2006.09.033.
62. Bove EL, Migliavacca F, de Leval MR, Balossino R, Pennati G, Lloyd TR, Khambadkone S, Hsia TY, Dubini G. Use of mathematic modeling to compare and predict hemodynamic effects of the modified Blalock-Taussig and right ventricle-pulmonary artery shunts for hypoplastic left heart syndrome. *J Thorac Cardiovasc Surg*. 2008;136:312–320.e2. doi: 10.1016/j.jtcvs.2007.04.078.
63. Pasquali SK, Ohye RG, Lu M, Kaltman J, Caldarone CA, Pizarro C, Dunbar-Masterson C, Gaynor JW, Jacobs JP, Kaza AK, Newburger J, Rhodes JF, Scheurer M, Silver E, Sleeper LA, Tabbutt S, Tweddell J, Uzark K, Wells W, Mahle WT, Pearson GD; Pediatric Heart Network Investigators. Variation in perioperative care across centers for infants undergoing the Norwood procedure. *J Thorac Cardiovasc Surg*. 2012;144:915–921. doi: 10.1016/j.jtcvs.2012.05.021.
64. Hsu DT, Zak V, Mahony L, Sleeper LA, Atz AM, Levine JC, Barker PC, Ravishankar C, McCrindle BW, Williams RV, Altmann K, Ghanayem NS, Margossian R, Chung WK, Border WL, Pearson GD, Stylianou MP, Mital S; for the Pediatric Heart Network Investigators. Enalapril in infants with single ventricle: results of a multicenter randomized trial. *Circulation*. 2010;122:333–340. doi: 10.1161/CIRCULATIONAHA.109.927988.
65. Ghanayem NS, Jaquiss RD, Cava JR, Frommelt PC, Mussatto KA, Hoffman GM, Tweddell JS. Right ventricle-to-pulmonary artery conduit versus Blalock-Taussig shunt: a hemodynamic comparison. *Ann Thorac Surg*. 2006;82:1603–9; discussion 1609. doi: 10.1016/j.athoracsur.2006.05.103.
66. Fletcher R, Niklason L, Drefeldt B. Gas exchange during controlled ventilation in children with normal and abnormal pulmonary circulation: a study using the single breath test for carbon dioxide. *Anesth Analg*. 1986;65:645–652.
67. Fletcher R. End-tidal carbon dioxide as a noninvasive monitor of circulatory status during cardiopulmonary resuscitation. *Crit Care Med*. 1989;17:970–971.
68. Fletcher R, Malmkvist G, Lührs C, Mori N, Drefeldt B, Brauer K, Jonsson B. Isocapnic high frequency jet ventilation: dead space depends on frequency, inspiratory time and entrainment. *Acta Anaesthesiol Scand*. 1991;35:153–158.
69. Short JA, Paris ST, Booker PD, Fletcher R. Arterial to end-tidal carbon dioxide tension difference in children with congenital heart disease. *Br J Anaesth*. 2001;86:349–353.
70. Tugrul M, Camci E, Sungur Z, Pembeci K. The value of end-tidal carbon dioxide monitoring during systemic-to-pulmonary artery shunt insertion in cyanotic children. *J Cardiothorac Vasc Anesth*. 2004;18:152–155.
71. Li JS, Yow E, Berezny KY, Rhodes JF, Bokesch PM, Charpie JR, Forbus GA, Mahony L, Boshkov L, Lambert V, Bonnet D, Michel-Behnke I, Graham TP, Takahashi M, Jaggers J, Califf RM, Rakhit A, Fontecave S, Sanders SP. Clinical outcomes of palliative surgery including a systemic-to-pulmonary artery shunt in infants with cyanotic congenital heart disease: does aspirin make a difference? *Circulation*. 2007;116:293–297. doi: 10.1161/CIRCULATIONAHA.106.652172.
72. Dirks V, Prêtre R, Knirsch W, Valsangiacomo Buechel ER, Seifert B, Schweiger M, Hübler M, Dave H. Modified Blalock Taussig shunt: a not-so-simple palliative procedure. *Eur J Cardiothorac Surg*. 2013;44:1096–1102. doi: 10.1093/ejcts/ezt172.
73. Wessel DL, Berger F, Li JS, Dähnert I, Rakhit A, Fontecave S, Newburger JW; CLARINET Investigators. Clopidogrel in infants with systemic-to-pulmonary-artery shunts. *N Engl J Med*. 2013;368:2377–2384. doi: 10.1056/NEJMoa1114588.
74. Ravishankar C, Dominguez TE, Kreutzer J, Wernovsky G, Marino BS, Godinez R, Priestley MA, Gruber PJ, Gaynor WJ, Nicolson SC, Spray TL, Tabbutt S. Extracorporeal membrane oxygenation after stage I reconstruction for hypoplastic left heart syndrome. *Pediatr Crit Care Med*. 2006;7:319–323. doi: 10.1097/01.PCC.0000227109.82323.CE.
75. Raymond TT, Cunnyngham CB, Thompson MT, Thomas JA, Dalton HJ, Nadkarni VM; American Heart Association National Registry of CPR Investigators. Outcomes among neonates, infants, and children after extracorporeal cardiopulmonary resuscitation for refractory inhospital pediatric cardiac arrest: a report from the National Registry of Cardiopulmonary Resuscitation. *Pediatr Crit Care Med*. 2010;11:362–371. doi: 10.1097/PCC.0b013e3181c0141b.
76. Wolf MJ, Kanter KR, Kirshbom PM, Kogon BE, Wagoner SF. Extracorporeal cardiopulmonary resuscitation for pediatric cardiac patients. *Ann Thorac Surg*. 2012;94:874–879. doi: 10.1016/j.athoracsur.2012.04.040.
77. Allan CK, Thiagarajan RR, del Nido PJ, Roth SJ, Almodovar MC, Laussen PC. Indication for initiation of mechanical circulatory support impacts survival of infants with shunted single-ventricle circulation supported with extracorporeal membrane oxygenation. *J Thorac Cardiovasc Surg*. 2007;133:660–667. doi: 10.1016/j.jtcvs.2006.11.013.
78. Hoffman GM, Tweddell JS. Regional blood flow monitoring in the perioperative period. In: Kleinman CS, Seri I. *Hemodynamincs and Cardiology: Neonatology Questions and Controversies*. Philadelphia, PA: Saunders; 2012:473–487.
79. Mahle WT, Spray TL, Wernovsky G, Gaynor JW, Clark BJ 3rd. Survival after reconstructive surgery for hypoplastic left heart syndrome: a 15-year experience from a single institution. *Circulation*. 2000;102(suppl 3):III136–III141.
80. Li J, Zhang G, Holtby HM, McCrindle BW, Cai S, Humpl T, Caldarone CA, Williams WG, Redington AN, Van Arsdell GS. Inclusion of oxygen consumption improves the accuracy of arterial and venous oxygen saturation interpretation after the Norwood procedure. *J Thorac Cardiovasc Surg*. 2006;131:1099–1107. doi: 10.1016/j.jtcvs.2005.10.057.
81. Hehir DA, Dominguez TE, Ballweg JA, Ravishankar C, Marino BS, Bird GL, Nicolson SC, Spray TL, Gaynor JW, Tabbutt S. Risk factors for interstage death after stage 1 reconstruction of hypoplastic left heart syndrome and variants. *J Thorac Cardiovasc Surg*. 2008;136:94–99, 99.e1. doi: 10.1016/j.jtcvs.2007.12.012.
82. Lacroix J, Demaret P, Tucci M. Red blood cell transfusion: decision making in pediatric intensive care units. *Semin Perinatol*. 2012;36:225–231. doi: 10.1053/j.semperi.2012.04.002.
83. Gupta P, Jacobs JP, Pasquali SK, Hill KD, Gaynor JW, O'Brien SM, He M, Sheng S, Schexnayder SM, Berg RA, Nadkarni VM, Imamura M, Jacobs ML. Epidemiology and outcomes after in-hospital cardiac arrest after pediatric cardiac surgery. *Ann Thorac Surg*. 2014;98:2138–2143. doi: 10.1016/j.athoracsur.2014.06.103.
84. Atkins DL, Berger S, Duff JP, Gonzales JC, Hunt EA, Joyner BL, Meaney PA, Niles DE, Samson RA, Schexnayder SM. Part 11: pediatric basic life support and cardiopulmonary resuscitation quality: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132(suppl 2):S519–S525. doi: 10.1161/CIR.0000000000000265.
85. Park JB, Song IK, Lee JH, Kim EH, Kim HS, Kim JT. Optimal chest compression position for patients with a single ventricle during cardiopulmonary resuscitation. *Pediatr Crit Care Med*. 2016;17:303–306. doi: 10.1097/PCC.0000000000000658.
86. Sutton RM, Friess SH, Maltese MR, Naim MY, Bratinov G, Weiland TR, Garuccio M, Bhalala U, Nadkarni VM, Becker LB, Berg RA. Hemodynamic-directed cardiopulmonary resuscitation during in-hospital cardiac arrest. *Resuscitation*. 2014;85:983–986. doi: 10.1016/j.resuscitation.2014.04.015.
87. Berens RJ, Cassidy LD, Matchey J, Campbell D, Colpaert KD, Welch T, Lawson M, Peterson C, O'Flynn J, Dearth M, Tieves KS. Probability of survival based on etiology of cardiopulmonary arrest in pediatric patients. *Paediatr Anaesth*. 2011;21:834–840. doi: 10.1111/j.1460-9592.2010.03479.x.

88. Welke KF, Diggs BS, Karamlou T. Chance, bias, and confounding: threats to valid measurement of quality in the context of pediatric cardiac surgery. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2010;13:79–83. doi: 10.1053/j.pcsu.2010.01.003.
89. Welke KF, Karamlou T, Ungerleider RM, Diggs BS. Mortality rate is not a valid indicator of quality differences between pediatric cardiac surgical programs. *Ann Thorac Surg*. 2010;89:139–144. doi: 10.1016/j.athoracsur.2009.08.058.
90. Wernovsky G, Ghanayem N, Ohye RG, Bacha EA, Jacobs JP, Gaynor JW, Tabbutt S. Hypoplastic left heart syndrome: consensus and controversies in 2007. *Cardiol Young*. 2007;17(suppl 2):75–86. doi: 10.1017/S1047951107001187.
91. Hoskote A, Li J, Hickey C, Erickson S, Van Arsdell G, Stephens D, Holtby H, Bohn D, Adatia I. The effects of carbon dioxide on oxygenation and systemic, cerebral, and pulmonary vascular hemodynamics after the bidirectional superior cavopulmonary anastomosis. *J Am Coll Cardiol*. 2004;44:1501–1509. doi: 10.1016/j.jacc.2004.06.061.
92. Li J, Hoskote A, Hickey C, Stephens D, Bohn D, Holtby H, Van Arsdell G, Redington AN, Adatia I. Effect of carbon dioxide on systemic oxygenation, oxygen consumption, and blood lactate levels after bidirectional superior cavopulmonary anastomosis. *Crit Care Med*. 2005;33:984–989.
93. Fogel MA, Durning S, Wernovsky G, Pollock AN, Gaynor JW, Nicolson S. Brain versus lung: hierarchy of feedback loops in single-ventricle patients with superior cavopulmonary connection. *Circulation*. 2004;110(suppl 1):II147–II152. doi: 10.1161/01.CIR.0000138346.34596.99.
94. Bradley SM, Atz AM, Simsic JM. Redefining the impact of oxygen and hyperventilation after the Norwood procedure. *J Thorac Cardiovasc Surg*. 2004;127:473–480. doi: 10.1016/j.jtcvs.2003.09.028.
95. Bradley SM, Simsic JM, Atz AM. Hemodynamic effects of inspired carbon dioxide after the Norwood procedure. *Ann Thorac Surg*. 2001;72:2088–2093.
96. Bradley SM, Simsic JM, Mulvihill DM. Hypoventilation improves oxygenation after bidirectional superior cavopulmonary connection. *J Thorac Cardiovasc Surg*. 2003;126:1033–1039. doi: 10.1016/S0022.
97. Bradley SM, Simsic JM, Mulvihill DM. Hyperventilation impairs oxygenation after bidirectional superior cavopulmonary connection. *Circulation*. 1998;98(suppl):II372–II376.
98. Furck AK, Hansen JH, Uebing A, Scheewe J, Jung O, Kramer HH. The impact of afterload reduction on the early postoperative course after the Norwood operation: a 12-year single-centre experience. *Eur J Cardiothorac Surg*. 2010;37:289–295. doi: 10.1016/j.ejcts.2009.07.051.
99. Shekerdemian LS, Shore DF, Lincoln C, Bush A, Redington AN. Negative-pressure ventilation improves cardiac output after right heart surgery. *Circulation*. 1996;94(suppl):II49–II55.
100. Shekerdemian LS, Bush A, Shore DF, Lincoln C, Redington AN. Cardiopulmonary interactions after Fontan operations: augmentation of cardiac output using negative pressure ventilation. *Circulation*. 1997;96:3934–3942.
101. Metzger A, Matsuura T, McKnite S, Marino BS, Nadkarni VM, Yannopoulos D. Intrathoracic pressure regulation improves 24-hour survival in a pediatric porcine model of hemorrhagic shock. *Pediatr Res*. 2011;70:267–271. doi: 10.1203/PDR.0b013e3182275232.
102. Walsh MA, Merat M, La Rotta G, Joshi P, Joshi V, Tran T, Jarvis S, Caldarone CA, Van Arsdell GS, Redington AN, Kavanagh BP. Airway pressure release ventilation improves pulmonary blood flow in infants after cardiac surgery. *Crit Care Med*. 2011;39:2599–2604. doi: 10.1097/CCM.0b013e318228297a.
103. Jolley M, Thiagarajan RR, Barrett CS, Salvin JW, Cooper DS, Rycus PT, Teele SA. Extracorporeal membrane oxygenation in patients undergoing superior cavopulmonary anastomosis. *J Thorac Cardiovasc Surg*. 2014;148:1512–1518. doi: 10.1016/j.jtcvs.2014.04.028.
104. Cullen S, Shore D, Redington A. Characterization of right ventricular diastolic performance after complete repair of tetralogy of Fallot: restrictive physiology predicts slow postoperative recovery. *Circulation*. 1995;91:1782–1789.
105. Gatzoulis MA, Clark AL, Cullen S, Newman CG, Redington AN. Right ventricular diastolic function 15 to 35 years after repair of tetralogy of Fallot: restrictive physiology predicts superior exercise performance. *Circulation*. 1995;91:1775–1781.
106. Norgård G, Gatzoulis MA, Moraes F, Lincoln C, Shore DF, Shinebourne EA, Redington AN. Relationship between type of outflow tract repair and postoperative right ventricular diastolic physiology in tetralogy of Fallot: implications for long-term outcome. *Circulation*. 1996;94:3276–3280.
107. Penny DJ, Hayek Z, Redington AN. The effects of positive and negative extrathoracic pressure ventilation on pulmonary blood flow after the total cavopulmonary shunt procedure. *Int J Cardiol*. 1991;30:128–130.
108. Redington A, Penny D, Rigby M, Hayes A. Antegrade diastolic pulmonary arterial flow as a marker of right ventricular restriction after complete repair of pulmonary atresia with intact septum and critical pulmonary valvar stenosis. *Cardiol Young*. 1992;2:383–386.
109. Guyton AC, Lindsey AW, Gilluly JJ. The limits of right ventricular compensation following acute increase in pulmonary circulatory resistance. *Circ Res*. 1954;2:326–332.
110. Guyton RA, Andrews MJ, Hickey PR, Michaelis LL, Morrow AG. The contribution of atrial contraction to right heart function before and after right ventriculotomy: experimental and clinical observations. *J Thorac Cardiovasc Surg*. 1976;71:1–10.
111. Ayres NA, Miller-Hance W, Fyfe DA, Stevenson JG, Sahn DJ, Young LT, Minich LL, Kimball TR, Geva T, Smith FC, Rychik J; Pediatric Council of the American Society of the Echocardiography. Indications and guidelines for performance of transesophageal echocardiography in the patient with pediatric acquired or congenital heart disease: report from the task force of the Pediatric Council of the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2005;18:91–98. doi: 10.1016/j.echo.2004.11.004.
112. Lang P, Chipman CW, Siden H, Williams RG, Norwood WI, Castaneda AR. Early assessment of hemodynamic status after repair of tetralogy of Fallot: a comparison of 24 hour (intensive care unit) and 1 year postoperative data in 98 patients. *Am J Cardiol*. 1982;50:795–799.
113. Ritter SB. Transesophageal real-time echocardiography in infants and children with congenital heart disease. *J Am Coll Cardiol*. 1991;18:569–580.
114. Smallhorn JF. Intraoperative transesophageal echocardiography in congenital heart disease. *Echocardiography*. 2002;19:709–723.
115. Stümper O, Sutherland GR, Geuskens R, Roelandt JR, Bos E, Hess J. Transesophageal echocardiography in evaluation and management after a Fontan procedure. *J Am Coll Cardiol*. 1991;17:1152–1160.
116. Wolfe LT, Rossi A, Ritter SB. Transesophageal echocardiography in infants and children: use and importance in the cardiac intensive care unit. *J Am Soc Echocardiogr*. 1993;6(pt 1):286–289.
117. Preminger TJ, Sanders SP, van der Velde ME, Castañeda AR, Lock JE. "Intramural" residual interventricular defects after repair of conotruncal malformations. *Circulation*. 1994;89:236–242.
118. Belli E, Houyel L, Serraf A, Lacour-Gayet F, Petit J, Planché C. Transaortic closure of residual intramural ventricular septal defect. *Ann Thorac Surg*. 2000;69:1496–1498.
119. Chaturvedi RR, Shore DF, Lincoln C, Mumby S, Kemp M, Brierly J, Petros A, Gutteridge JM, Hooper J, Redington AN. Acute right ventricular restrictive physiology after repair of tetralogy of Fallot: association with myocardial injury and oxidative stress. *Circulation*. 1999;100:1540–1547.
120. Apitz C, Latus H, Binder W, Uebing A, Seeger A, Bretschneider C, Sieverding L, Hofbeck M. Impact of restrictive physiology on intrinsic diastolic right ventricular function and lusitropy in children and adolescents after repair of tetralogy of Fallot. *Heart*. 2010;96:1837–1841. doi: 10.1136/hrt.2010.203190.
121. Santamore WP, Dell'Italia LJ. Ventricular interdependence: significant left ventricular contributions to right ventricular systolic function. *Prog Cardiovasc Dis*. 1998;40:289–308.
122. Kerstein D, Levy PS, Hsu DT, Hordof AJ, Gersony WM, Barst RJ. Blade balloon atrial septostomy in patients with severe primary pulmonary hypertension. *Circulation*. 1995;91:2028–2035.
123. Sandoval J, Gaspar J, Pulido T, Bautista E, Martínez-Guerra ML, Zeballos M, Palomar A, Gómez A. Graded balloon dilation atrial septostomy in severe primary pulmonary hypertension: a therapeutic alternative for patients nonresponsive to vasodilator treatment. *J Am Coll Cardiol*. 1998;32:297–304.
124. Burrows FA, Williams WG, Teoh KH, Wood AE, Burns J, Edmonds J, Barker GA, Trusler GA, Weisel RD. Myocardial performance after repair of congenital cardiac defects in infants and children: response to volume loading. *J Thorac Cardiovasc Surg*. 1988;96:548–556.
125. Butler J, Rocker GM, Westaby S. Inflammatory response to cardiopulmonary bypass. *Ann Thorac Surg*. 1993;55:552–559.
126. Moat NE, Shore DF, Evans TW. Organ dysfunction and cardiopulmonary bypass: the role of complement and complement regulatory proteins. *Eur J Cardiothorac Surg*. 1993;7:563–573.
127. Seghaye MC, Duchateau J, Grabitz RG, Faymonville ML, Messmer BJ, Buro-Rathsmann K, von Bernuth G. Complement activation

during cardiopulmonary bypass in infants and children: relation to postoperative multiple system organ failure. *J Thorac Cardiovasc Surg*. 1993;106:978–987.
128. Seghaye MC, Grabitz RG, Duchateau J, Busse S, Däbritz S, Koch D, Alzen G, Hörnchen H, Messmer BJ, Von Bernuth G. Inflammatory reaction and capillary leak syndrome related to cardiopulmonary bypass in neonates undergoing cardiac operations. *J Thorac Cardiovasc Surg*. 1996;112:687–697.
129. Burch M, Lincoln C, Carter N, Smith A. Acute sternal opening after cardiac surgery in children: effect on plasma atrial natriuretic peptide. *J Cardiovasc Surg (Torino)*. 1991;32:246–249.
130. Lincoln C, Gibson D, Kay P, Shore D. Delayed sternal closure in neonate. *J Thorac Cardiovasc Surg*. 1990;100:928.
131. McElhinney DB, Reddy VM, Parry AJ, Johnson L, Fineman JR, Hanley FL. Management and outcomes of delayed sternal closure after cardiac surgery in neonates and infants. *Crit Care Med*. 2000;28:1180–1184.
132. Iyer RS, Jacobs JP, de Leval MR, Stark J, Elliott MJ. Outcomes after delayed sternal closure in pediatric heart operations: a 10-year experience. *Ann Thorac Surg*. 1997;63:489–491.
133. Tabbutt S, Duncan BW, McLaughlin D, Wessel DL, Jonas RA, Laussen PC. Delayed sternal closure after cardiac operations in a pediatric population. *J Thorac Cardiovasc Surg*. 1997;113:886–893. doi: 10.1016/S0022-5223(97)70261-7.
134. Baden HP, Morray JP. Drainage of tense ascites in children after cardiac surgery. *J Cardiothorac Vasc Anesth*. 1995;9:720–721.
135. Bokesch PM, Kapural MB, Mossad EB, Cavaglia M, Appachi E, Drummond-Webb JJ, Mee RB. Do peritoneal catheters remove pro-inflammatory cytokines after cardiopulmonary bypass in neonates? *Ann Thorac Surg*. 2000;70:639–643.
136. Stromberg D, Fraser CD Jr, Sorof JM, Drescher K, Feltes TF. Peritoneal dialysis: an adjunct to pediatric postcardiotomy fluid management. *Tex Heart Inst J*. 1997;24:269–277.
137. Chaturvedi RR, Redington AN. Pulmonary regurgitation in congenital heart disease. *Heart*. 2007;93:880–889. doi: 10.1136/hrt.2005.075234.
138. Shekerdemian LS, Bush A, Lincoln C, Shore DF, Petros AJ, Redington AN. Cardiopulmonary interactions in healthy children and children after simple cardiac surgery: the effects of positive and negative pressure ventilation. *Heart*. 1997;78:587–593.
139. Shekerdemian LS, Bush A, Shore DF, Lincoln C, Redington AN. Cardiorespiratory responses to negative pressure ventilation after tetralogy of Fallot repair: a hemodynamic tool for patients with a low-output state. *J Am Coll Cardiol*. 1999;33:549–555.
140. Mildh L, Hiippala A, Rautiainen P, Pettilä V, Sairanen H, Happonen JM. Junctional ectopic tachycardia after surgery for congenital heart disease: incidence, risk factors and outcome. *Eur J Cardiothorac Surg*. 2011;39:75–80. doi: 10.1016/j.ejcts.2010.04.002.
141. Raja P, Hawker RE, Chaikitpinyo A, Cooper SG, Lau KC, Nunn GR, Cartmill TB, Sholler GF. Amiodarone management of junctional ectopic tachycardia after cardiac surgery in children. *Br Heart J*. 1994;72:261–265.
142. Janousek J, Vojtovic P, Hucín B, Tláskal T, Gebauer RA, Gebauer R, Matejka T, Marek J, Reich O. Resynchronization pacing is a useful adjunct to the management of acute heart failure after surgery for congenital heart defects. *Am J Cardiol*. 2001;88:145–152.
143. Kirsh JA, Stephenson EA, Redington AN. Recovery of left ventricular systolic function after biventricular resynchronization pacing in a child with repaired tetralogy of Fallot and severe biventricular dysfunction. *Circulation*. 2006;113:e691–e692. doi: 10.1161/CIRCULATIONAHA.105.580126.
144. Zimmerman FJ, Starr JP, Koenig PR, Smith P, Hijazi ZM, Bacha EA. Acute hemodynamic benefit of multisite ventricular pacing after congenital heart surgery. *Ann Thorac Surg*. 2003;75:1775–1780.
145. Vlahakes GJ, Turley K, Hoffman JI. The pathophysiology of failure in acute right ventricular hypertension: hemodynamic and biochemical correlations. *Circulation*. 1981;63:87–95.
146. Mastropietro CW, Davalos MC, Seshadri S, Walters HL 3rd, Delius RE. Clinical response to arginine vasopressin therapy after paediatric cardiac surgery. *Cardiol Young*. 2013;23:387–393. doi: 10.1017/S1047951112000996.
147. Shekerdemian L. Perioperative manipulation of the circulation in children with congenital heart disease. *Heart*. 2009;95:1286–1296. doi: 10.1136/hrt.2005.069237.
148. Beghetti M, Morris K, Cox P, Bohn D, Adatia I. Inhaled nitric oxide differentiates pulmonary vasospasm from vascular obstruction after surgery for congenital heart disease. *Intensive Care Med*. 1999;25:1126–1130.
149. Adatia I, Atz AM, Jonas RA, Wessel DL. Diagnostic use of inhaled nitric oxide after neonatal cardiac operations. *J Thorac Cardiovasc Surg*. 1996;112:1403–1405. doi: 10.1016/S0022-5223(96)70166-6.
150. Abman SH, Hansmann G, Archer SL, Ivy DD, Adatia I, Chung WK, Hanna BD, Rosenzweig EB, Raj JU, Cornfield D, Stenmark KR, Steinhorn R, Thébaud B, Fineman JR, Kuehne T, Feinstein JA, Friedberg MK, Earing M, Barst RJ, Keller RL, Kinsella JP, Mullen M, Deterding R, Kulik T, Mallory G, Humpl T, Wessel DL; on behalf of the American Heart Association Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; Council on Clinical Cardiology; Council on Cardiovascular Disease in the Young; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Surgery and Anesthesia; and the American Thoracic Society. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society [published correction appears in *Circulation*. 2016;133:e368]. *Circulation*. 2015;132:2037–2099. doi: 10.1161/CIR.0000000000000329.
151. Bando K, Turrentine MW, Sharp TG, Sekine Y, Aufiero TX, Sun K, Sekine E, Brown JW. Pulmonary hypertension after operations for congenital heart disease: analysis of risk factors and management. *J Thorac Cardiovasc Surg*. 1996;112:1600–1607. doi: 10.1016/S0022-5223(96)70019-3.
152. Lindberg L, Olsson AK, Jögi P, Jonmarker C. How common is severe pulmonary hypertension after pediatric cardiac surgery? *J Thorac Cardiovasc Surg*. 2002;123:1155–1163.
153. Loukanov T, Bucsenez D, Springer W, Sebening C, Rauch H, Roesch E, Karck M, Gorenflo M. Comparison of inhaled nitric oxide with aerosolized iloprost for treatment of pulmonary hypertension in children after cardiopulmonary bypass surgery. *Clin Res Cardiol*. 2011;100:595–602. doi: 10.1007/s00392-011-0284-5.
154. Brown KL, Ridout DA, Goldman AP, Hoskote A, Penny DJ. Risk factors for long intensive care unit stay after cardiopulmonary bypass in children. *Crit Care Med*. 2003;31:28–33. doi: 10.1097/01.CCM.0000046068.19048.86.
155. Schulze-Neick I, Li J, Penny DJ, Redington AN. Pulmonary vascular resistance after cardiopulmonary bypass in infants: effect on postoperative recovery. *J Thorac Cardiovasc Surg*. 2001;121:1033–1039. doi: 10.1067/mtc.2001.113747.
156. Fraisse A, Butrous G, Taylor MB, Oakes M, Dilleen M, Wessel DL. Intravenous sildenafil for postoperative pulmonary hypertension in children with congenital heart disease. *Intensive Care Med*. 2011;37:502–509. doi: 10.1007/s00134-010-2065-4.
157. Sanatani S, Wilson G, Smith CR, Hamilton RM, Williams WG, Adatia I. Sudden unexpected death in children with heart disease. *Congenit Heart Dis*. 2006;1:89–97. doi: 10.1111/j.1747-0803.2006.00014.x.
158. Ma M, Gauvreau K, Allan CK, Mayer JE Jr, Jenkins KJ. Causes of death after congenital heart surgery. *Ann Thorac Surg*. 2007;83:1438–1445. doi: 10.1016/j.athoracsur.2006.10.073.
159. Hopkins RA, Bull C, Haworth SG, de Leval MR, Stark J. Pulmonary hypertensive crises following surgery for congenital heart defects in young children. *Eur J Cardiothorac Surg*. 1991;5:628–634.
160. Wheller J, George BL, Mulder DG, Jarmakani JM. Diagnosis and management of postoperative pulmonary hypertensive crisis. *Circulation*. 1979;60:1640–1644.
161. del Nido PJ, Williams WG, Villamater J, Benson LN, Coles JG, Bohn D and Trusler GA. Changes in pericardial surface pressure during pulmonary hypertensive crises after cardiac surgery. *Circulation*. 1987;76:III93-III96.
162. Lincoln CR, Rigby ML, Mercanti C, Al-Fagih M, Joseph MC, Miller GA, Shinebourne EA. Surgical risk factors in total anomalous pulmonary venous connection. *Am J Cardiol*. 1988;61:608–611.
163. Matsumoto M, Naitoh H, Higashi T, Kurasako T, Takatori M, Tada K, Ohba O. Risk factors for pulmonary hypertensive crisis (PHC) following VSD repair in infants [in Japanese]. *Masui*. 1995;44:1208–1212.
164. Miller OI, Tang SF, Keech A, Pigott NB, Beller E, Celermajer DS. Inhaled nitric oxide and prevention of pulmonary hypertension after congenital heart surgery: a randomised double-blind study. *Lancet*. 2000;356:1464–1469. doi: 10.1016/S0140-6736(00)02869-5.
165. Schindler MB, Bohn DJ, Bryan AC, Cutz E, Rabinovitch M. Increased respiratory system resistance and bronchial smooth muscle hypertrophy in children with acute postoperative pulmonary hypertension. *Am J Respir Crit Care Med*. 1995;152(pt 1):1347–1352. doi: 10.1164/ajrccm.152.4.7551393.
166. van Loon RL, Roofthooft MT, Hillege HL, ten Harkel AD, van Osch-Gevers M, Delhaas T, Kapusta L, Strengers JL, Rammeloo L, Clur SA, Mulder BJ, Berger RM. Pediatric pulmonary

hypertension in the Netherlands: epidemiology and characterization during the period 1991 to 2005. *Circulation*. 2011;124:1755–1764. doi: 10.1161/CIRCULATIONAHA.110.969584.
167. Atz AM, Adatia I, Wessel DL. Rebound pulmonary hypertension after inhalation of nitric oxide. *Ann Thorac Surg*. 1996;62:1759–1764.
168. Lavoie A, Hall JB, Olson DM, Wylam ME. Life-threatening effects of discontinuing inhaled nitric oxide in severe respiratory failure. *Am J Respir Crit Care Med*. 1996;153(pt 1):1985–1987. doi: 10.1164/ajrccm.153.6.8665066.
169. Miller OI, Tang SF, Keech A, Celermajer DS. Rebound pulmonary hypertension on withdrawal from inhaled nitric oxide. *Lancet*. 1995;346:51–52.
170. Namachivayam P, Theilen U, Butt WW, Cooper SM, Penny DJ, Shekerdemian LS. Sildenafil prevents rebound pulmonary hypertension after withdrawal of nitric oxide in children. *Am J Respir Crit Care Med*. 2006;174:1042–1047. doi: 10.1164/rccm.200605-694OC.
171. Humpl T, Reyes JT, Erickson S, Armano R, Holtby H, Adatia I. Sildenafil therapy for neonatal and childhood pulmonary hypertensive vascular disease. *Cardiol Young*. 2011;21:187–193. doi: 10.1017/S1047951110001745.
172. Abman SH, Griebel JL, Parker DK, Schmidt JM, Swanton D, Kinsella JP. Acute effects of inhaled nitric oxide in children with severe hypoxemic respiratory failure. *J Pediatr*. 1994;124:881–888.
173. Bull TM, Clark B, McFann K, Moss M; National Institutes of Health/National Heart, Lung, and Blood Institute ARDS Network. Pulmonary vascular dysfunction is associated with poor outcomes in patients with acute lung injury. *Am J Respir Crit Care Med*. 2010;182:1123–1128. doi: 10.1164/rccm.201002-0250OC.
174. Katz R, Pollack M, Spady D. Cardiopulmonary abnormalities in severe acute respiratory failure. *J Pediatr*. 1984;104:357–364.
175. Carmosino MJ, Friesen RH, Doran A, Ivy DD. Perioperative complications in children with pulmonary hypertension undergoing noncardiac surgery or cardiac catheterization. *Anesth Analg*. 2007;104:521–527. doi: 10.1213/01.ane.0000255732.16057.1c.
176. Taylor CJ, Derrick G, McEwan A, Haworth SG, Sury MR. Risk of cardiac catheterization under anaesthesia in children with pulmonary hypertension. *Br J Anaesth*. 2007;98:657–661. doi: 10.1093/bja/aem059.
177. van der Griend BF, Lister NA, McKenzie IM, Martin N, Ragg PG, Sheppard SJ, Davidson AJ. Postoperative mortality in children after 101,885 anesthetics at a tertiary pediatric hospital. *Anesth Analg*. 2011;112:1440–1447. doi: 10.1213/ANE.0b013e318213be52.
178. Haworth SG, Reid L. Structural study of pulmonary circulation and of heart in total anomalous pulmonary venous return in early infancy. *Br Heart J*. 1977;39:80–92.
179. Yamaki S, Tsunemoto M, Shimada M, Ishizawa R, Endo M, Nakayama S, Hata M, Mohri H. Quantitative analysis of pulmonary vascular disease in total anomalous pulmonary venous connection in sixty infants. *J Thorac Cardiovasc Surg*. 1992;104:728–735.
180. Yung D, Widlitz AC, Rosenzweig EB, Kerstein D, Maislin G, Barst RJ. Outcomes in children with idiopathic pulmonary arterial hypertension. *Circulation*. 2004;110:660–665. doi: 10.1161/01.CIR.0000138104.83366.E9.
181. Dimopoulos K, Inuzuka R, Goletto S, Giannakoulas G, Swan L, Wort SJ, Gatzoulis MA. Improved survival among patients with Eisenmenger syndrome receiving advanced therapy for pulmonary arterial hypertension. *Circulation*. 2010;121:20–25. doi: 10.1161/CIRCULATIONAHA.109.883876.
182. Baruteau AE, Serraf A, Lévy M, Petit J, Bonnet D, Jais X, Vouhé P, Simonneau G, Belli E, Humbert M. Potts shunt in children with idiopathic pulmonary arterial hypertension: long-term results. *Ann Thorac Surg*. 2012;94:817–824. doi: 10.1016/j.athoracsur.2012.03.099.
183. Latus H, Apitz C, Schmidt D, Jux C, Mueller M, Bauer J, Akintuerk H, Schneider M, Schranz D. Potts shunt and atrial septostomy in pulmonary hypertension caused by left ventricular disease. *Ann Thorac Surg*. 2013;96:317–319. doi: 10.1016/j.athoracsur.2012.10.069.
184. Rozkovec A, Montanes P, Oakley CM. Factors that influence the outcome of primary pulmonary hypertension. *Br Heart J*. 1986;55:449–458.
185. Hopkins WE, Waggoner AD. Severe pulmonary hypertension without right ventricular failure: the unique hearts of patients with Eisenmenger syndrome. *Am J Cardiol*. 2002;89:34–38.
186. Anand KJ, Hansen DD, Hickey PR. Hormonal-metabolic stress responses in neonates undergoing cardiac surgery. *Anesthesiology*. 1990;73:661–670.
187. Anand KJ, Sippell WG, Aynsley-Green A. Randomised trial of fentanyl anaesthesia in preterm babies undergoing surgery: effects on the stress response. *Lancet*. 1987;1:243–248.
188. Morris K, Beghetti M, Petros A, Adatia I, Bohn D. Comparison of hyperventilation and inhaled nitric oxide for pulmonary hypertension after repair of congenital heart disease. *Crit Care Med*. 2000;28:2974–2978.
189. Nair J, Lakshminrusimha S. Update on PPHN: mechanisms and treatment. *Semin Perinatol*. 2014;38:78–91. doi: 10.1053/j.semperi.2013.11.004.
190. Atsumi N, Gomi S, Kanemoto S, Mihara W, Shigeta O, Terada Y, Jikuya T, Sakakibara Y, Mitsui T, Ninomiya H. Management of postoperative pulmonary hypertensive crisis in children: indication and usefulness of inhaled nitric oxide therapy as a pulmonary vasodilator [in Japanese]. *Nihon Kyobu Geka Gakkai Zasshi*. 1996;44:2123–2129.
191. Moudgil R, Michelakis ED, Archer SL. Hypoxic pulmonary vasoconstriction. *J Appl Physiol (1985)*. 2005;98:390–403.
192. Goldman AP, Delius RE, Deanfield JE, de Leval MR, Sigston PE, Macrae DJ. Nitric oxide might reduce the need for extracorporeal support in children with critical postoperative pulmonary hypertension. *Ann Thorac Surg*. 1996;62:750–755.
193. Murthy KS, Rao SG, Prakash KS, Punnoose A, Benjamin N, Bharati AS, Singh RK, Cherian KM. Inhaled nitric oxide as therapy for pulmonary hypertension in postoperative cases of congenital heart defects. *Indian Heart J*. 1996;48:695–698.
194. Turanlahti MI, Laitinen PO, Sarna SJ, Pesonen E. Nitric oxide, oxygen, and prostacyclin in children with pulmonary hypertension. *Heart*. 1998;79:169–174.
195. Journois D, Pouard P, Mauriat P, Malhère T, Vouhé P, Safran D. Inhaled nitric oxide as a therapy for pulmonary hypertension after operations for congenital heart defects. *J Thorac Cardiovasc Surg*. 1994;107:1129–1135.
196. Khan TA, Schnickel G, Ross D, Bastani S, Laks H, Esmailian F, Marelli D, Beygui R, Shemin R, Watson L, Vartapetian I, Ardehali A. A prospective, randomized, crossover pilot study of inhaled nitric oxide versus inhaled prostacyclin in heart transplant and lung transplant recipients. *J Thorac Cardiovasc Surg*. 2009;138:1417–1424. doi: 10.1016/j.jtcvs.2009.04.063.
197. Berner M, Beghetti M, Ricou B, Rouge JC, Prêtre R, Friedli B. Relief of severe pulmonary hypertension after closure of a large ventricular septal defect using low dose inhaled nitric oxide. *Intensive Care Med*. 1993;19:75–77.
198. Atz AM, Wessel DL. Inhaled nitric oxide in the neonate with cardiac disease. *Semin Perinatol*. 1997;21:441–455.
199. Atz AM, Munoz RA, Adatia I, Wessel DL. Diagnostic and therapeutic uses of inhaled nitric oxide in neonatal Ebstein's anomaly. *Am J Cardiol*. 2003;91:906–908.
200. Adatia I, Lillehei C, Arnold JH, Thompson JE, Palazzo R, Fackler JC, Wessel DL. Inhaled nitric oxide in the treatment of postoperative graft dysfunction after lung transplantation. *Ann Thorac Surg*. 1994;57:1311–1318.
201. Wessel DL, Adatia I, Giglia TM, Thompson JE, Kulik TJ. Use of inhaled nitric oxide and acetylcholine in the evaluation of pulmonary hypertension and endothelial function after cardiopulmonary bypass. *Circulation*. 1993;88(pt 1):2128–2138.
202. Wessel DL, Adatia I. Clinical applications of inhaled nitric oxide in children with pulmonary hypertension. *Adv Pharmacol*. 1995;34:475–504.
203. Limsuwan A, Wanitkul S, Khosithset A, Attanavanich S, Samankatiwat P. Aerosolized iloprost for postoperative pulmonary hypertensive crisis in children with congenital heart disease. *Int J Cardiol*. 2008;129:333–338. doi: 10.1016/j.ijcard.2007.08.084.
204. Journois D, Baufreton C, Mauriat P, Pouard P, Vouhé P, Safran D. Effects of inhaled nitric oxide administration on early postoperative mortality in patients operated for correction of atrioventricular canal defects. *Chest*. 2005;128:3537–3544. doi: 10.1378/chest.128.5.3537.
205. Kelly LK, Porta NF, Goodman DM, Carroll CL, Steinhorn RH. Inhaled prostacyclin for term infants with persistent pulmonary hypertension refractory to inhaled nitric oxide. *J Pediatr*. 2002;141:830–832. doi: 10.1067/mpd.2002.129849.
206. Singh R, Choudhury M, Saxena A, Kapoor PM, Juneja R, Kiran U. Inhaled nitroglycerin versus inhaled milrinone in children with congenital heart disease suffering from pulmonary artery hypertension. *J Cardiothorac Vasc Anesth*. 2010;24:797–801. doi: 10.1053/j.jvca.2009.10.024.
207. Li F, Xia W, Yuan S, Sun R. Acute inhibition of Rho-kinase attenuates pulmonary hypertension in patients with congenital heart disease. *Pediatr Cardiol*. 2009;30:363–366. doi: 10.1007/s00246-008-9315-z.
208. Neutze JM, Ishikawa T, Clarkson PM, Calder AL, Barratt-Boyes BG, Kerr AR. Assessment and follow-up of patients with ventricular septal defect and elevated pulmonary vascular resistance. *Am J Cardiol*. 1989;63:327–331.

209. Weesner KM. Hemodynamic effects of prostaglandin E1 in patients with congenital heart disease and pulmonary hypertension. *Cathet Cardiovasc Diagn*. 1991;24:10–15.
210. Packer M. Vasodilator therapy for primary pulmonary hypertension: limitations and hazards. *Ann Intern Med*. 1985;103:258–270.
211. Stocker C, Penny DJ, Brizard CP, Cochrane AD, Soto R, Shekerdemian LS. Intravenous sildenafil and inhaled nitric oxide: a randomised trial in infants after cardiac surgery. *Intensive Care Med*. 2003;29:1996–2003. doi: 10.1007/s00134-003-2016-4.
212. Zapol WM, Snider MT. Pulmonary hypertension in severe acute respiratory failure. *N Engl J Med*. 1977;296:476–480. doi: 10.1056/NEJM197703032960903.
213. Lammers AE, Haworth SG, Pierce CM. Intravenous sildenafil as an effective treatment of pulmonary hypertensive crises during acute intestinal malabsorption [published correction appears in *Cardiol Young*. 2006;16:328]. *Cardiol Young*. 2006;16:84–86. doi: 10.1017/S1047951105002155.
214. Michelakis E, Tymchak W, Lien D, Webster L, Hashimoto K, Archer S. Oral sildenafil is an effective and specific pulmonary vasodilator in patients with pulmonary arterial hypertension: comparison with inhaled nitric oxide. *Circulation*. 2002;105:2398–2403.
215. Barst RJ, Ivy DD, Gaitan G, Szatmari A, Rudzinski A, Garcia AE, Sastry BK, Pulido T, Layton GR, Serdarevic-Pehar M, Wessel DL. A randomized, double-blind, placebo-controlled, dose-ranging study of oral sildenafil citrate in treatment-naive children with pulmonary arterial hypertension. *Circulation*. 2012;125:324–334. doi: 10.1161/CIRCULATIONAHA.110.016667.
216. Raja SG, Danton MD, MacArthur KJ, Pollock JC. Effects of escalating doses of sildenafil on hemodynamics and gas exchange in children with pulmonary hypertension and congenital cardiac defects. *J Cardiothorac Vasc Anesth*. 2007;21:203–207. doi: 10.1053/j.jvca.2006.02.010.
217. Galiè N, Beghetti M, Gatzoulis MA, Granton J, Berger RM, Lauer A, Chiossi E, Landzberg M; for the Bosentan Randomized Trial of Endothelin Antagonist Therapy-5 (BREATHE-5) Investigators. Bosentan therapy in patients with Eisenmenger syndrome: a multicenter, double-blind, randomized, placebo-controlled study. *Circulation*. 2006;114:48–54. doi: 10.1161/CIRCULATIONAHA.106.630715.
218. Smith AM, Elliot CM, Kiely DG, Channer KS. The role of vasopressin in cardiorespiratory arrest and pulmonary hypertension. *QJM*. 2006;99:127–133. doi: 10.1093/qjmed/hcl009.
219. Currigan DA, Hughes RJ, Wright CE, Angus JA, Soeding PF. Vasoconstrictor responses to vasopressor agents in human pulmonary and radial arteries: an *in vitro* study. *Anesthesiology*. 2014;121:930–936. doi: 10.1097/ALN.0000000000000430.
220. Siehr SL, Feinstein JA, Yang W, Peng LF, Ogawa MT, Ramamoorthy C. Hemodynamic effects of phenylephrine, vasopressin, and epinephrine in children with pulmonary hypertension: a pilot study. *Pediatr Crit Care Med*. 2016;17:428–437. doi: 10.1097/PCC.0000000000000716.
221. Hoeper MM, Galié N, Murali S, Olschewski H, Rubenfire M, Robbins IM, Farber HW, McLaughlin V, Shapiro S, Pepke-Zaba J, Winkler J, Ewert R, Opitz C, Westerkamp V, Vachiéry JL, Torbicki A, Behr J, Barst RJ. Outcome after cardiopulmonary resuscitation in patients with pulmonary arterial hypertension. *Am J Respir Crit Care Med*. 2002;165:341–344. doi: 10.1164/ajrccm.165.3.200109-0130c.
222. Aufderheide TP, Lurie KG. Death by hyperventilation: a common and life-threatening problem during cardiopulmonary resuscitation. *Crit Care Med*. 2004;32(suppl):S345–S351.
223. King R, Esmail M, Mahon S, Dingley J, Dwyer S. Use of nitric oxide for decompensated right ventricular failure and circulatory shock after cardiac arrest. *Br J Anaesth*. 2000;85:628–631.
224. Rubin LJ. Primary pulmonary hypertension. *N Engl J Med*. 1997;336:111–117. doi: 10.1056/NEJM199701093360207.
225. Myles PS, Hall JL, Berry CB, Esmore DS. Primary pulmonary hypertension: prolonged cardiac arrest and successful resuscitation following induction of anesthesia for heart-lung transplantation. *J Cardiothorac Vasc Anesth*. 1994;8:678–681.
226. Haas NA, Schulze-Neick I, Lange PE. Intratracheal prostacyclin for resuscitation in primary pulmonary hypertension. *Lancet*. 1995;346:643.
227. Passarani S, Vignati G, Einaudi A. Eisenmenger syndrome: a case of survival after ventricular tachycardia due to inferior myocardial infarction in a 48-year-old patient with congenital large ventricular septal defect. *Can J Cardiol*. 2004;20:822–824.
228. Arpesella G, Loforte A, Mikus E, Mikus PM. Extracorporeal membrane oxygenation for primary allograft failure. *Transplant Proc*. 2008;40:3596–3597. doi: 10.1016/j.transproceed.2008.06.079.
229. Dhillon R, Pearson GA, Firmin RK, Chan KC, Leanage R. Extracorporeal membrane oxygenation and the treatment of critical pulmonary hypertension in congenital heart disease. *Eur J Cardiothorac Surg*. 1995;9:553–556.
230. Liu KS, Tsai FC, Huang YK, Wu MY, Chang YS, Chu JJ, Lin PJ. Extracorporeal life support: a simple and effective weapon for postcardiotomy right ventricular failure. *Artif Organs*. 2009;33:504–508. doi: 10.1111/j.1525-1594.2009.00734.x.
231. Strueber M, Hoeper MM, Fischer S, Cypel M, Warnecke G, Gottlieb J, Pierre A, Welte T, Haverich A, Simon AR, Keshavjee S. Bridge to thoracic organ transplantation in patients with pulmonary arterial hypertension using a pumpless lung assist device. *Am J Transplant*. 2009;9:853–857. doi: 10.1111/j.1600-6143.2009.02549.x.
232. Marino BS, Kruge LE, Cho CJ, Tomlinson RS, Shera D, Weinberg PM, Gaynor JW, Rychik J. Parachute mitral valve: morphologic descriptors, associated lesions, and outcomes after biventricular repair. *J Thorac Cardiovasc Surg*. 2009;137:385–393.e4. doi: 10.1016/j.jtcvs.2008.09.016.
233. Carabello BA. The current therapy for mitral regurgitation. *J Am Coll Cardiol*. 2008;52:319–326. doi: 10.1016/j.jacc.2008.02.084.
234. Choudhary SK, Talwar S, Dubey B, Chopra A, Saxena A, Kumar AS. Mitral valve repair in a predominantly rheumatic population: long-term results. *Tex Heart Inst J*. 2001;28:8–15.
235. Lee JY, Noh CI, Bae EJ, Yun YS, Lee JR, Kim YJ. Preoperative left ventricular end systolic dimension as a predictor of postoperative ventricular dysfunction in children with mitral regurgitation. *Heart*. 2003;89:1243–1244.
236. Gillespie MJ, Marino BS, Cohen MS, Korteweg AE, Henket M, Gaynor JW, Spray TL, Tabbutt S, Wernovsky G. Risk factors for adverse outcomes after surgery on the systemic atrioventricular valve in 109 children. *Cardiol Young*. 2006;16(suppl 3):35–42.
237. Hoffman TM, Wernovsky G, Atz AM, Kulik TJ, Nelson DP, Chang AC, Bailey JM, Akbary A, Kocsis JF, Kaczmarek R, Spray TL, Wessel DL. Efficacy and safety of milrinone in preventing low cardiac output syndrome in infants and children after corrective surgery for congenital heart disease. *Circulation*. 2003;107:996–1002.
238. Morales DLS, Almond CSD, Jaquiss RDB, Rosenthal DN, Naftel DC, Massicotte MP, Humpl T, Turrentine MW, Tweddell JS, Cohen GA, Kroslowitz R, Devaney EJ, Canter CE, Fynn-Thompson F, Reinhartz O, Imamura M, Ghanayem NS, Buchholz H, Furness S, Mazor R, Gandhi SK, Fraser CD Jr. Bridging children of all sizes to cardiac transplantation: the initial multicenter North American experience with the Berlin Heart EXCOR ventricular assist device. *J Heart Lung Transplant*. 2011;30:1–8. doi: 10.1016/j.healun.2010.08.033.
239. Petit CJ, Ing FF, Mattamal R, Pignatelli RH, Mullins CE, Justino H. Diminished left ventricular function is associated with poor mid-term outcomes in neonates after balloon aortic valvuloplasty. *Catheter Cardiovasc Interv*. 2012;80:1190–1199. doi: 10.1002/ccd.23500.
240. Hraška V, Sinzobahamvya N, Haun C, Photiadis J, Arenz C, Schneider M, Asfour B. The long-term outcome of open valvotomy for critical aortic stenosis in neonates. *Ann Thorac Surg*. 2012;94:1519–1526. doi: 10.1016/j.athoracsur.2012.03.056.
241. Agnoletti G, Raisky O, Boudjemline Y, Ou P, Bonnet D, Sidi D, Vouhé P. Neonatal surgical aortic commissurotomy: predictors of outcome and long-term results. *Ann Thorac Surg*. 2006;82:1585–1592. doi: 10.1016/j.athoracsur.2006.05.049.
242. Hammel JM, Duncan KF, Danford DA, Kutty S. Two-stage biventricular rehabilitation for critical aortic stenosis with severe left ventricular dysfunction. *Eur J Cardiothorac Surg*. 2013;43:143–148. doi: 10.1093/ejcts/ezs197.
243. Hickey EJ, Caldarone CA, Blackstone EH, Williams WG, Yeh T Jr, Pizarro C, Lofland G, Tchervenkov CI, Pigula F, McCrindle BW; Congenital Heart Surgeons' Society. Biventricular strategies for neonatal critical aortic stenosis: high mortality associated with early reintervention. *J Thorac Cardiovasc Surg*. 2012;144:409–417, 417.e1. doi: 10.1016/j.jtcvs.2011.09.076.
244. Alsoufi B, Karamlou T, McCrindle BW, Caldarone CA. Management options in neonates and infants with critical left ventricular outflow tract obstruction [published correction appears in *Eur J Cardiothorac Surg*. 2007;32:558]. *Eur J Cardiothorac Surg*. 2007;31:1013–1021. doi: 10.1016/j.ejcts.2007.03.015.
245. Misumi Y, Hoashi T, Kagisaki K, Yazaki S, Kitano M, Kurosaki K, Shiraishi I, Ichikawa H. The importance of hybrid stage I palliation for neonates with critical aortic stenosis and reduced left ventricular function. *Pediatr Cardiol*. 2015;36:726–731. doi: 10.1007/s00246-014-1074-4.

246. Brown SC, Boshoff D, Eyskens B, Gewillig M. Hybrid approach as bridge to biventricular repair in a neonate with critical aortic stenosis and borderline left ventricle. *Eur J Cardiothorac Surg*. 2009;35:1080–1082. doi: 10.1016/j.ejcts.2009.02.012.
247. Bonow RO, Carabello BA, Chatterjee K, de Leon AC Jr, Faxon DP, Freed MD, Gaasch WH, Lytle BW, Nishimura RA, O'Gara PT, O'Rourke RA, Otto CM, Shah PM, Shanewise JS. 2008 Focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease): endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *Circulation*. 2008;118:e523–e661. doi: 10.1161/CIRCULATIONAHA.108.190748.
248. Gentles TL, French JK, Zeng I, Milsom PF, Finucane AK, Wilson NJ. Normalized end-systolic volume and pre-load reserve predict ventricular dysfunction following surgery for aortic regurgitation independent of body size. *JACC Cardiovasc Imaging*. 2012;5:626–633. doi: 10.1016/j.jcmg.2011.12.021.
249. Tafreshi RI, Shahmohammadi A, Davari PN. Predictors of left ventricular performance after valve replacement in children and adolescents with chronic aortic regurgitation. *Pediatr Cardiol*. 2005;26:331–337. doi: 10.1007/s00246-005-8645-3.
250. Buddhe S, Du W, Walters HL 3rd, Delius R, Pettersen MD. Predictors of left ventricular remodeling after aortic valve replacement in pediatric patients with isolated aortic regurgitation. *Congenit Heart Dis*. 2013;8:167–173. doi: 10.1111/j.1747-0803.2012.00703.x.
251. Ishino K, Alexi-Meskishvili V, Hetzer R. Preoperative extracorporeal membrane oxygenation in newborns with total anomalous pulmonary venous connection. *Cardiovasc Surg*. 1999;7:473–475.
252. Brown KL, Miles F, Sullivan ID, Hoskote A, Verhulst L, Ridout DA, Goldman AP. Outcome in neonates with congenital heart disease referred for respiratory extracorporeal membrane oxygenation. *Acta Paediatr*. 2005;94:1280–1284.
253. Kanter KR. Surgical repair of total anomalous pulmonary venous connection. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2006:40–4.
254. Hancock Friesen CL, Zurakowski D, Thiagarajan RR, Forbess JM, del Nido PJ, Mayer JE, Jonas RA. Total anomalous pulmonary venous connection: an analysis of current management strategies in a single institution. *Ann Thorac Surg*. 2005;79:596–606. doi: 10.1016/j.athoracsur.2004.07.005.
255. Marcondes LD, Galati JC, Jones BO, Konstantinov IE, d'Udekem Y, Brizard CP, Cheung MM. Abnormal left ventricular diastolic function at late follow-up after repair of total anomalous pulmonary venous drainage: the impact of altered ventricular loading in utero. *J Thorac Cardiovasc Surg*. 2014;148:238–244. doi: 10.1016/j.jtcvs.2013.08.045.
256. Maron BJ, Towbin JA, Thiene G, Antzelevitch C, Corrado D, Arnett D, Moss AJ, Seidman CE, Young JB. Contemporary definitions and classification of the cardiomyopathies: an American Heart Association Scientific Statement from the Council on Clinical Cardiology, Heart Failure and Transplantation Committee; Quality of Care and Outcomes Research and Functional Genomics and Translational Biology Interdisciplinary Working Groups; and Council on Epidemiology and Prevention. *Circulation*. 2006;113:1807–1816. doi: 10.1161/CIRCULATIONAHA.106.174287.
257. Kirk R, Dipchand AI, Rosenthal DN, Addonizio L, Burch M, Chrisant M, Dubin A, Everitt M, Gajarski R, Mertens L, Miyamoto S, Morales D, Pahl E, Shaddy R, Towbin J, Weintraub R. The International Society for Heart and Lung Transplantation guidelines for the management of pediatric heart failure: executive summary [published correction appears in *J Heart Lung Transplant*. 2014;42:1104]. *J Heart Lung Transplant*. 2014;33:888–909. doi: 10.1016/j.healun.2014.06.002.
258. Rivenes SM, Kearney DL, Smith EO, Towbin JA, Denfield SW. Sudden death and cardiovascular collapse in children with restrictive cardiomyopathy. *Circulation*. 2000;102:876–882.
259. Walsh MA, Grenier MA, Jefferies JL, Towbin JA, Lorts A, Czosek RJ. Conduction abnormalities in pediatric patients with restrictive cardiomyopathy. *Circ Heart Fail*. 2012;5:267–273. doi: 10.1161/CIRCHEARTFAILURE.111.964395.
260. Webber SA, Lipshultz SE, Sleeper LA, Lu M, Wilkinson JD, Addonizio LJ, Canter CE, Colan SD, Everitt MD, Jefferies JL, Kantor PF, Lamour JM, Margossian R, Pahl E, Rusconi PG, Towbin JA; Pediatric Cardiomyopathy Registry Investigators. Outcomes of restrictive cardiomyopathy in childhood and the influence of phenotype: a report from the Pediatric Cardiomyopathy Registry. *Circulation*. 2012;126:1237–1244. doi: 10.1161/CIRCULATIONAHA.112.104638.
261. Towbin JA. Left ventricular noncompaction: a new form of heart failure. *Heart Fail Clin*. 2010;6:453–469. doi: 10.1016/j.hfc.2010.06.005.
262. Pignatelli RH, McMahon CJ, Dreyer WJ, Denfield SW, Price J, Belmont JW, Craigen WJ, Wu J, El Said H, Bezold LI, Clunie S, Fernbach S, Bowles NE, Towbin JA. Clinical characterization of left ventricular noncompaction in children: a relatively common form of cardiomyopathy. *Circulation*. 2003;108:2672–2678. doi: 10.1161/01.CIR.0000100664.10777.B8.
263. Hanke SP, Gardner AB, Lombardi JP, Manning PB, Nelson DP, Towbin JA, Jefferies JL, Lorts A. Left ventricular noncompaction cardiomyopathy in Barth syndrome: an example of an undulating cardiac phenotype necessitating mechanical circulatory support as a bridge to transplantation. *Pediatr Cardiol*. 2012;33:1430–1434. doi: 10.1007/s00246-012-0258-z.
264. Brescia ST, Rossano JW, Pignatelli R, Jefferies JL, Price JF, Decker JA, Denfield SW, Dreyer WJ, Smith O, Towbin JA, Kim JJ. Mortality and sudden death in pediatric left ventricular noncompaction in a tertiary referral center. *Circulation*. 2013;127:2202–2208. doi: 10.1161/CIRCULATIONAHA.113.002511.
265. Jefferies JL, Towbin JA. Dilated cardiomyopathy. *Lancet*. 2010;375:752–762. doi: 10.1016/S0140-6736(09)62023-7.
266. James CA, Calkins H. Update on arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C). *Curr Treat Options Cardiovasc Med*. 2013;15:476–487. doi: 10.1007/s11936-013-0251-8.
267. Miyake CY, Teele SA, Chen L, Motonaga KS, Dubin AM, Balasubramanian S, Balise RR, Rosenthal DN, Alexander ME, Walsh EP, Mah DY. In-hospital arrhythmia development and outcomes in pediatric patients with acute myocarditis. *Am J Cardiol*. 2014;113:535–540. doi: 10.1016/j.amjcard.2013.10.021.
268. Wilmot I, Morales DL, Price JF, Rossano JW, Kim JJ, Decker JA, McGarry MC, Denfield SW, Dreyer WJ, Towbin JA, Jefferies JL. Effectiveness of mechanical circulatory support in children with acute fulminant and persistent myocarditis. *J Card Fail*. 2011;17:487–494. doi: 10.1016/j.cardfail.2011.02.008.
269. Teele SA, Allan CK, Laussen PC, Newburger JW, Gauvreau K, Thiagarajan RR. Management and outcomes in pediatric patients presenting with acute fulminant myocarditis. *J Pediatr*. 2011;158:638–643.e1. doi: 10.1016/j.jpeds.2010.10.015.
270. Rajagopal SK, Almond CS, Laussen PC, Rycus PT, Wypij D, Thiagarajan RR. Extracorporeal membrane oxygenation for the support of infants, children, and young adults with acute myocarditis: a review of the Extracorporeal Life Support Organization registry. *Crit Care Med*. 2010;38:382–387. doi: 10.1097/CCM.0b013e3181bc8293.
271. Van Hare G. Supraventricular tachycardia. In: *Clinical Pediatric Arrhythmia*. Philadelphia, PA: Saunders; 1999:97–120.
272. Ludomirsky A, Garson A Jr. Supraventricular tachycardia. In: Gillette PC, Garson A Jr. *Pediatric Arrhythmias: Electrophysiology and Pacing*. Philadelphia, PA: Saunders; 1990:380–426.
273. Ganz LI, Friedman PL. Supraventricular tachycardia. *N Engl J Med*. 1995;332:162–173. doi: 10.1056/NEJM199501193320307.
274. Fisher DJ, Gross DM, Garson A Jr. Rapid sinus tachycardia: differentiation from supraventricular tachycardia. *Am J Dis Child*. 1983;137:164–166.
275. Lesh MD, Kalman JM, Saxon LA, Dorostkar PC. Electrophysiology of "incisional" reentrant atrial tachycardia complicating surgery for congenital heart disease. *Pacing Clin Electrophysiol*. 1997;20(pt 2):2107–2111.
276. Gikonyo BM, Dunnigan A, Benson DW Jr. Cardiovascular collapse in infants: association with paroxysmal atrial tachycardia. *Pediatrics*. 1985;76:922–926.
277. Zampi JD, Hirsch JC, Gurney JG, Donohue JE, Yu S, LaPage MJ, Hanauer DA, Charpie JR. Junctional ectopic tachycardia after infant heart surgery: incidence and outcomes. *Pediatr Cardiol*. 2012;33:1362–1369. doi: 10.1007/s00246-012-0348-y.
278. Hoffman TM, Bush DM, Wernovsky G, Cohen MI, Wieand TS, Gaynor JW, Spray TL, Rhodes LA. Postoperative junctional ectopic tachycardia in children: incidence, risk factors, and treatment. *Ann Thorac Surg*. 2002;74:1607–1611.
279. Batra AS, Chun DS, Johnson TR, Maldonado EM, Kashyap BA, Maiers J, Lindblade CL, Rodefeld M, Brown JW, Hubbard JE. A prospective analysis of the incidence and risk factors associated with junctional ectopic tachycardia following surgery for congenital heart disease. *Pediatr Cardiol*. 2006;27:51–55. doi: 10.1007/s00246-005-0992-6.
280. Walsh EP, Saul JP, Sholler GF, Triedman JK, Jonas RA, Mayer JE, Wessel DL. Evaluation of a staged treatment protocol for rapid automatic

junctional tachycardia after operation for congenital heart disease. *J Am Coll Cardiol*. 1997;29:1046–1053.
281. Pfammatter JP, Paul T, Ziemer G, Kallfelz HC. Successful management of junctional tachycardia by hypothermia after cardiac operations in infants. *Ann Thorac Surg*. 1995;60:556–560. doi: 10.1016/0003-4975(95)00425-K.
282. Chrysostomou C, Sanchez-de-Toledo J, Wearden P, Jooste EH, Lichtenstein SE, Callahan PM, Suresh T, O'Malley E, Shiderly D, Haney J, Yoshida M, Orr R, Munoz R, Morell VO. Perioperative use of dexmedetomidine is associated with decreased incidence of ventricular and supraventricular tachyarrhythmias after congenital cardiac operations. *Ann Thorac Surg*. 2011;92:964–972. doi: 10.1016/j.athoracsur.2011.04.099.
283. Saul JP, Scott WA, Brown S, Marantz P, Acevedo V, Etheridge SP, Perry JC, Triedman JK, Burriss SW, Cargo P, Graepel J, Koskelo EK, Wang R; for the Intravenous Amiodarone Pediatric Investigators. Intravenous amiodarone for incessant tachyarrhythmias in children: a randomized, double-blind, antiarrhythmic drug trial. *Circulation*. 2005;112:3470–3477. doi: 10.1161/CIRCULATIONAHA.105.534149.
284. Jacobs I, Nadkarni V, Bahr J, Berg RA, Billi JE, Bossaert L, Cassan P, Coovadia A, D'Este K, Finn J, Halperin H, Handley A, Herlitz J, Hickey R, Idris A, Kloeck W, Larkin GL, Mancini ME, Mason P, Mears G, Monsieurs K, Montgomery W, Morley P, Nichol G, Nolan J, Okada K, Perlman J, Shuster M, Steen PA, Sterz F, Tibballs J, Timerman S, Truitt T, Zideman D; ILCOR Task Force on Cardiac Arrest and Cardiopulmonary Resuscitation Outcomes. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Councils of Southern Africa). *Circulation*. 2004;110:3385–3397. doi: 10.1161/01.CIR.0000147236.85306.15.
285. Panidis IP, Morganroth J. Sudden death in hospitalized patients: cardiac rhythm disturbances detected by ambulatory electrocardiographic monitoring. *J Am Coll Cardiol*. 1983;2:798–805.
286. Young KD, Gausche-Hill M, McClung CD, Lewis RJ. A prospective, population-based study of the epidemiology and outcome of out-of-hospital pediatric cardiopulmonary arrest. *Pediatrics*. 2004;114:157–164.
287. Hickey RW, Cohen DM, Strausbaugh S, Dietrich AM. Pediatric patients requiring CPR in the prehospital setting. *Ann Emerg Med*. 1995;25:495–501.
288. Mogayzel C, Quan L, Graves JR, Tiedeman D, Fahrenbruch C, Herndon P. Out-of-hospital ventricular fibrillation in children and adolescents: causes and outcomes. *Ann Emerg Med*. 1995;25:484–491.
289. Herlitz J, Engdahl J, Svensson L, Young M, Angquist KA, Holmberg S. Characteristics and outcome among children suffering from out of hospital cardiac arrest in Sweden. *Resuscitation*. 2005;64:37–40. doi: 10.1016/j.resuscitation.2004.06.019.
290. Smith B, Rea T, Eisenberg M. Ventricular fibrillation in pediatric cardiac arrest. *Acad Emerg Med*. 2006;13:525–529.
291. Donoghue AJ, Nadkarni V, Berg RA, Osmond MH, Wells G, Nesbitt L, Stiell IG; CanAm Pediatric Cardiac Arrest Investigators. Out-of-hospital pediatric cardiac arrest: an epidemiologic review and assessment of current knowledge. *Ann Emerg Med*. 2005;46:512–522. doi: 10.1016/j.annemergmed.2005.05.028.
292. Nadkarni VM, Larkin GL, Peberdy MA, Carey SM, Kaye W, Mancini ME, Nichol G, Lane-Truitt T, Potts J, Ornato JP, Berg RA; National Registry of Cardiopulmonary Resuscitation Investigators. First documented rhythm and clinical outcome from in-hospital cardiac arrest among children and adults. *JAMA*. 2006;295:50–57. doi: 10.1001/jama.295.1.50.
293. Samson RA, Nadkarni VM, Meaney PA, Carey SM, Berg MD, Berg RA; American Heart Association National Registry of CPR Investigators. Outcomes of in-hospital ventricular fibrillation in children. *N Engl J Med*. 2006;354:2328–2339. doi: 10.1056/NEJMoa052917.
294. Reis AG, Nadkarni V, Perondi MB, Grisi S, Berg RA. A prospective investigation into the epidemiology of in-hospital pediatric cardiopulmonary resuscitation using the international Utstein reporting style. *Pediatrics*. 2002;109:200–209.
295. Chiang CE, Roden DM. The long QT syndromes: genetic basis and clinical implications. *J Am Coll Cardiol*. 2000;36:1–12.
296. Schwartz PJ. The congenital long QT syndromes from genotype to phenotype: clinical implications. *J Intern Med*. 2006;259:39–47. doi: 10.1111/j.1365-2796.2005.01583.x.
297. Ali RH, Zareba W, Moss AJ, Schwartz PJ, Benhorin J, Vincent GM, Locati EH, Priori S, Napolitano C, Towbin JA, Hall WJ, Robinson JL, Andrews ML, Zhang L, Timothy K, Medina A. Clinical and genetic variables associated with acute arousal and nonarousal-related cardiac events among subjects with long QT syndrome. *Am J Cardiol*. 2000;85:457–461.
298. Arnestad M, Crotti L, Rognum TO, Insolia R, Pedrazzini M, Ferrandi C, Vege A, Wang DW, Rhodes TE, George AL Jr, Schwartz PJ. Prevalence of long-QT syndrome gene variants in sudden infant death syndrome. *Circulation*. 2007;115:361–367. doi: 10.1161/CIRCULATIONAHA.106.658021.
299. Roden DM. Acquired long QT syndromes and the risk of proarrhythmia. *J Cardiovasc Electrophysiol*. 2000;11:938–940.
300. Wen ZC, Chen SA, Tai CT, Chiang CE, Chiou CW, Chang MS. Electrophysiological mechanisms and determinants of vagal maneuvers for termination of paroxysmal supraventricular tachycardia. *Circulation*. 1998;98:2716–2723.
301. Sreeram N, Wren C. Supraventricular tachycardia in infants: response to initial treatment. *Arch Dis Child*. 1990;65:127–129.
302. Overholt ED, Rheuban KS, Gutgesell HP, Lerman BB, DiMarco JP. Usefulness of adenosine for arrhythmias in infants and children. *Am J Cardiol*. 1988;61:336–340.
303. Losek JD, Endom E, Dietrich A, Stewart G, Zempsky W, Smith K. Adenosine and pediatric supraventricular tachycardia in the emergency department: multicenter study and review. *Ann Emerg Med*. 1999;33:185–191.
304. Adamson PC, Rhodes LA, Saul JP, Dick M 2nd, Epstein MR, Moate P, Boston R, Schreiner MS. The pharmacokinetics of esmolol in pediatric subjects with supraventricular arrhythmias. *Pediatr Cardiol*. 2006;27:420–427. doi: 10.1007/s00246-006-1162-1.
305. Trippel DL, Wiest DB, Gillette PC. Cardiovascular and antiarrhythmic effects of esmolol in children. *J Pediatr*. 1991;119(pt 1):142–147.
306. Artman M, Grayson M, Boerth RC. Propranolol in children: safety-toxicity. *Pediatrics*. 1982;70:30–31.
307. Yabek SM, Berman W Jr, Dillon T. Electrophysiologic effects of propranolol on sinus node function in children. *Am Heart J*. 1982;104:612–616.
308. Burri S, Hug MI, Bauersfeld U. Efficacy and safety of intravenous amiodarone for incessant tachycardias in infants. *Eur J Pediatr*. 2003;162:880–884. doi: 10.1007/s00431-003-1302-z.
309. Celiker A, Ceviz N, Ozme S. Effectiveness and safety of intravenous amiodarone in drug-resistant tachyarrhythmias of children. *Acta Paediatr Jpn*. 1998;40:567–572.
310. Figa FH, Gow RM, Hamilton RM, Freedom RM. Clinical efficacy and safety of intravenous amiodarone in infants and children. *Am J Cardiol*. 1994;74:573–577.
311. Laird WP, Snyder CS, Kertesz NJ, Friedman RA, Miller D, Fenrich AL. Use of intravenous amiodarone for postoperative junctional ectopic tachycardia in children. *Pediatr Cardiol*. 2003;24:133–137. doi: 10.1007/s00246-002-0276-3.
312. Perry JC, Knilans TK, Marlow D, Denfield SW, Fenrich AL, Friedman RA. Intravenous amiodarone for life-threatening tachyarrhythmias in children and young adults. *J Am Coll Cardiol*. 1993;22:95–98.
313. Soult JA, Muñoz M, Lopez JD, Romero A, Santos J, Tovaruela A. Efficacy and safety of intravenous amiodarone for short-term treatment of paroxysmal supraventricular tachycardia in children. *Pediatr Cardiol*. 1995;16:16–19. doi: 10.1007/BF02310328.
314. Mandel WJ, Laks MM, Obayashi K, Hayakawa H, Daley W. The Wolff-Parkinson-White syndrome: pharmacologic effects of procaine amide. *Am Heart J*. 1975;90:744–754.
315. Bauernfeind RA, Swiryn S, Petropoulos AT, Coelho A, Gallastegui J, Rosen KM. Concordance and discordance of drug responses in atrioventricular reentrant tachycardia. *J Am Coll Cardiol*. 1983;2:345–350.
316. Benson DW Jr, Dunnigan A, Green TP, Benditt DG, Schneider SP. Periodic procainamide for paroxysmal tachycardia. *Circulation*. 1985;72:147–152.
317. Komatsu C, Ishinaga T, Tateishi O, Tokuhisa Y, Yoshimura S. Effects of four antiarrhythmic drugs on the induction and termination of paroxysmal supraventricular tachycardia. *Jpn Circ J*. 1986;50:961–972.
318. Boahene KA, Klein GJ, Yee R, Sharma AD, Fujimura O. Termination of acute atrial fibrillation in the Wolff-Parkinson-White syndrome by procainamide and propafenone: importance of atrial fibrillatory cycle length. *J Am Coll Cardiol*. 1990;16:1408–1414.
319. Rhodes LA, Walsh EP, Saul JP. Conversion of atrial flutter in pediatric patients by transesophageal atrial pacing: a safe, effective, minimally invasive procedure. *Am Heart J*. 1995;130:323–327.
320. Gandhi SK, Bromberg BI, Mallory GB, Huddleston CB. Atrial flutter: a newly recognized complication of pediatric lung transplantation. *J*

Thorac Cardiovasc Surg. 1996;112:984–991. doi: 10.1016/S0022-5223(96)70099-5.
321. Mandapati R, Byrum CJ, Kavey RE, Smith FC, Kveselis DA, Hannan WP, Brandt B 3rd, Gaum WE. Procainamide for rate control of postsurgical junctional tachycardia. *Pediatr Cardiol*. 2000;21:123–128.
322. Wang JN, Wu JM, Tsai YC, Lin CS. Ectopic atrial tachycardia in children. *J Formos Med Assoc*. 2000;99:766–770.
323. Epstein ML, Kiel EA, Victorica BE. Cardiac decompensation following verapamil therapy in infants with supraventricular tachycardia. *Pediatrics*. 1985;75:737–740.
324. Kirk CR, Gibbs JL, Thomas R, Radley-Smith R, Qureshi SA. Cardiovascular collapse after verapamil in supraventricular tachycardia. *Arch Dis Child*. 1987;62:1265–1266.
325. Benson DW Jr, Smith WM, Dunnigan A, Sterba R, Gallagher JJ. Mechanisms of regular, wide QRS tachycardia in infants and children. *Am J Cardiol*. 1982;49:1778–1788.
326. Kugler JD, Danford DA. Management of infants, children, and adolescents with paroxysmal supraventricular tachycardia. *J Pediatr*. 1996;129:324–338.
327. Perry JC, Fenrich AL, Hulse JE, Triedman JK, Friedman RA, Lamberti JJ. Pediatric use of intravenous amiodarone: efficacy and safety in critically ill patients from a multicenter protocol. *J Am Coll Cardiol*. 1996;27:1246–1250.
328. Schwartz PJ, Ackerman MJ. The long QT syndrome: a transatlantic clinical approach to diagnosis and therapy. *Eur Heart J*. 2013;34:3109–3116. doi: 10.1093/eurheartj/eht089.
329. Moss AJ, Zareba W, Hall WJ, Schwartz PJ, Crampton RS, Benhorin J, Vincent GM, Locati EH, Priori SG, Napolitano C, Medina A, Zhang L, Robinson JL, Timothy K, Towbin JA, Andrews ML. Effectiveness and limitations of beta-blocker therapy in congenital long-QT syndrome. *Circulation*. 2000;101:616–623.
330. Homme JH, White RD, Ackerman MJ. Management of ventricular fibrillation or unstable ventricular tachycardia in patients with congenital long-QT syndrome: a suggested modification to ACLS guidelines. *Resuscitation*. 2003;59:111–115.
331. Bacha EA, Zimmerman FJ, Mor-Avi V, Weinert L, Starr JP, Sugeng L, Lang RM. Ventricular resynchronization by multisite pacing improves myocardial performance in the postoperative single-ventricle patient. *Ann Thorac Surg*. 2004;78:1678–1683. doi: 10.1016/j.athoracsur.2004.04.065.
332. Béland MJ, Hesslein PS, Finlay CD, Faerron-Angel JE, Williams WG, Rowe RD. Noninvasive transcutaneous cardiac pacing in children. *Pacing Clin Electrophysiol*. 1987;10:1262–1270.
333. Kiserud T, Acharya G. The fetal circulation. *Prenat Diagn*. 2004;24:1049–1059. doi: 10.1002/pd.1062.
334. Clyman RI. Ductus arteriosus: current theories of prenatal and postnatal regulation. *Semin Perinatol*. 1987;11:64–71.
335. Legato MJ. Cellular mechanisms of normal growth in the mammalian heart, II: a quantitative and qualitative comparison between the right and left ventricular myocytes in the dog from birth to five months of age. *Circ Res*. 1979;44:263–279.
336. Colan SD, Parness IA, Spevak PJ, Sanders SP. Developmental modulation of myocardial mechanics: age- and growth-related alterations in afterload and contractility. *J Am Coll Cardiol*. 1992;19:619–629.
337. Thornburg KL, Morton MJ. Filling and arterial pressures as determinants of left ventricular stroke volume in fetal lambs. *Am J Physiol*. 1986;251(pt 2):H961–H968.
338. Zaritsky A, Chernow B. Use of catecholamines in pediatrics. *J Pediatr*. 1984;105:341–350.
339. Rozé JC, Tohier C, Maingueneau C, Lefèvre M, Mouzard A. Response to dobutamine and dopamine in the hypotensive very preterm infant. *Arch Dis Child*. 1993;69(1 Spec No):59–63.
340. Fabiato A. Calcium-induced release of calcium from the cardiac sarcoplasmic reticulum. *Am J Physiol*. 1983;245:C1–14.
341. Mirro R, Brown DR. Parenteral calcium treatment shortens the left ventricular systolic time intervals of hypocalcemic neonates. *Pediatr Res*. 1984;18:71–73.
342. Venkataraman PS, Wilson DA, Sheldon RE, Rao R, Parker MK. Effect of hypocalcemia on cardiac function in very-low-birth-weight preterm neonates: studies of blood ionized calcium, echocardiography, and cardiac effect of intravenous calcium therapy. *Pediatrics*. 1985;76:543–550.
343. Jarmakani JM, Nakazawa M, Nagatomo T, Langer GA. Effect of hypoxia on mechanical function in the neonatal mammalian heart. *Am J Physiol*. 1978;235:H469–H474.
344. Bove EL, Stammers AH. Recovery of left ventricular function after hypothermic global ischemia: age-related differences in the isolated working rabbit heart. *J Thorac Cardiovasc Surg*. 1986;91:115–122.
345. Daly DM. Interactions between respiration and circulation. In: Cerniack NS, Widdicombe JG, eds. *Handbook of Physiology: The Respiratory System (Vol 2)*. Bethesda, MD: American Physiological Society; 1986: 529–594.
346. Leung MP, Chau KT, Hui PW, Tam AY, Chan FL, Lai CL, Yeung CY. Necrotizing enterocolitis in neonates with symptomatic congenital heart disease. *J Pediatr*. 1988;113:1044–1046.
347. Andropoulos DB, Hunter JV, Nelson DP, Stayer SA, Stark AR, McKenzie ED, Heinle JS, Graves DE, Fraser CD Jr. Brain immaturity is associated with brain injury before and after neonatal cardiac surgery with high-flow bypass and cerebral oxygenation monitoring. *J Thorac Cardiovasc Surg*. 2010;139:543–556. doi: 10.1016/j.jtcvs.2009.08.022.
348. Miller SP, McQuillen PS, Hamrick S, Xu D, Glidden DV, Charlton N, Karl T, Azakie A, Ferriero DM, Barkovich AJ, Vigneron DB. Abnormal brain development in newborns with congenital heart disease. *N Engl J Med*. 2007;357:1928–1938. doi: 10.1056/NEJMoa067393.
349. Licht DJ, Shera DM, Clancy RR, Wernovsky G, Montenegro LM, Nicolson SC, Zimmerman RA, Spray TL, Gaynor JW, Vossough A. Brain maturation is delayed in infants with complex congenital heart defects. *J Thorac Cardiovasc Surg*. 2009;137:529–536. doi: 10.1016/j.jtcvs.2008.10.025.
350. Rudolph AM. Aortopulmonary transposition in the fetus: speculation on pathophysiology and therapy. *Pediatr Res*. 2007;61:375–380. doi: 10.1203/pdr.0b013e318030d5b9.
351. Donofrio MT, Bremer YA, Schieken RM, Gennings C, Morton LD, Eidem BW, Cetta F, Falkensammer CB, Huhta JC, Kleinman CS. Autoregulation of cerebral blood flow in fetuses with congenital heart disease: the brain sparing effect. *Pediatr Cardiol*. 2003;24:436–443. doi: 10.1007/s00246-002-0404-0.
352. Kaltman JR, Di H, Tian Z, Rychik J. Impact of congenital heart disease on cerebrovascular blood flow dynamics in the fetus. *Ultrasound Obstet Gynecol*. 2005;25:32–36. doi: 10.1002/uog.1785.
353. Srivastava D. Making or breaking the heart: from lineage determination to morphogenesis. *Cell*. 2006;126:1037–1048. doi: 10.1016/j.cell.2006.09.003.
354. Francis F, Meyer G, Fallet-Bianco C, Moreno S, Kappeler C, Socorro AC, Tuy FP, Beldjord C, Chelly J. Human disorders of cortical development: from past to present. *Eur J Neurosci*. 2006;23:877–893. doi: 10.1111/j.1460-9568.2006.04649.x.
355. Hoch RV, Rubenstein JL, Pleasure S. Genes and signaling events that establish regional patterning of the mammalian forebrain. *Semin Cell Dev Biol*. 2009;20:378–386. doi: 10.1016/j.semcdb.2009.02.005.
356. Kostovic I, Vasung L. Insights from *in vitro* fetal magnetic resonance imaging of cerebral development. *Semin Perinatol*. 2009;33:220–233. doi: 10.1053/j.semperi.2009.04.003.
357. Shillingford AJ, Ittenbach RF, Marino BS, Rychik J, Clancy RR, Spray TL, Gaynor JW, Wernovsky G. Aortic morphometry and microcephaly in hypoplastic left heart syndrome. *Cardiol Young*. 2007;17:189–195. doi: 10.1017/S1047951107000248.
358. Mahle WT, Tavani F, Zimmerman RA, Nicolson SC, Galli KK, Gaynor JW, Clancy RR, Montenegro LM, Spray TL, Chiavacci RM, Wernovsky G, Kurth CD. An MRI study of neurological injury before and after congenital heart surgery. *Circulation*. 2002;106(suppl 1):I109–I114.
359. McQuillen PS, Barkovich AJ, Hamrick SE, Perez M, Ward P, Glidden DV, Azakie A, Karl T, Miller SP. Temporal and anatomic risk profile of brain injury with neonatal repair of congenital heart defects. *Stroke*. 2007;38(suppl):736–741. doi: 10.1161/01.STR.0000247941.41234.90.
360. McQuillen PS, Goff DA, Licht DJ. Effects of congenital heart disease on brain development. *Prog Pediatr Cardiol*. 2010;29:79–85. doi: 10.1016/j.ppedcard.2010.06.011.
361. Tagin MA, Woolcott CG, Vincer MJ, Whyte RK, Stinson DA. Hypothermia for neonatal hypoxic ischemic encephalopathy: an updated systematic review and meta-analysis. *Arch Pediatr Adolesc Med*. 2012;166:558–566. doi: 10.1001/archpediatrics.2011.1772.
362. Shankaran S, Laptook AR, Ehrenkranz RA, Tyson JE, McDonald SA, Donovan EF, Fanaroff AA, Poole WK, Wright LL, Higgins RD, Finer NN, Carlo WA, Duara S, Oh W, Cotten CM, Stevenson DK, Stoll BJ, Lemons JA, Guillet R, Jobe AH; National Institute of Child Health and Human Development Neonatal Research Network. Whole-body hypothermia for neonates with hypoxic-ischemic encephalopathy. *N Engl J Med*. 2005;353:1574–1584. doi: 10.1056/NEJMcps050929.

363. Broitman E, Ambalavanan N, Higgins RD, Vohr BR, Das A, Bhaskar B, Murray K, Hintz SR, Carlo WA; National Institute of Child Health and Human Development Neonatal Research Network. Clinical data predict neurodevelopmental outcome better than head ultrasound in extremely low birth weight infants. *J Pediatr*. 2007;151:500–5, 505.e1. doi: 10.1016/j.jpeds.2007.04.013.
364. Beca J, Gunn JK, Coleman L, Hope A, Reed PW, Hunt RW, Finucane K, Brizard C, Dance B, Shekerdemian LS. New white matter brain injury after infant heart surgery is associated with diagnostic group and the use of circulatory arrest. *Circulation*. 2013;127:971–979. doi: 10.1161/CIRCULATIONAHA.112.001089.
365. Diaz LK, Jones L. Sedating the child with congenital heart disease. *Anesthesiol Clin*. 2009;27:301–319. doi: 10.1016/j.anclin.2009.05.003.
366. Naguib AN, Tobias JD, Hall MW, Cismowski MJ, Miao Y, Barry N, Preston T, Galantowicz M, Hoffman TM. The role of different anesthetic techniques in altering the stress response during cardiac surgery in children: a prospective, double-blinded, and randomized study. *Pediatr Crit Care Med*. 2013;14:481–490. doi: 10.1097/PCC.0b013e31828a742c.
367. Gupta P, Whiteside W, Sabati A, Tesoro TM, Gossett JM, Tobias JD, Roth SJ. Safety and efficacy of prolonged dexmedetomidine use in critically ill children with heart disease. *Pediatr Crit Care Med*. 2012;13:660–666. doi: 10.1097/PCC.0b013e318253c7f1.
368. Lam F, Bhutta AT, Tobias JD, Gossett JM, Morales L, Gupta P. Hemodynamic effects of dexmedetomidine in critically ill neonates and infants with heart disease. *Pediatr Cardiol*. 2012;33:1069–1077. doi: 10.1007/s00246-012-0227-6.
369. Lam F, Ransom C, Gossett JM, Kelkhoff A, Seib PM, Schmitz ML, Bryant JC, Frazier EA, Gupta P. Safety and efficacy of dexmedetomidine in children with heart failure. *Pediatr Cardiol*. 2013;34:835–841. doi: 10.1007/s00246-012-0546-7.
370. Chrysostomou C, Komarlu R, Lichtenstein S, Shiderly D, Arora G, Orr R, Wearden PD, Morell VO, Munoz R, Jooste EH. Electrocardiographic effects of dexmedetomidine in patients with congenital heart disease. *Intensive Care Med*. 2010;36:836–842. doi: 10.1007/s00134-010-1782-z.
371. Hammer GB, Drover DR, Cao H, Jackson E, Williams GD, Ramamoorthy C, Van Hare GF, Niksch A, Dubin AM. The effects of dexmedetomidine on cardiac electrophysiology in children. *Anesth Analg*. 2008;106:79–83. doi: 10.1213/01.ane.0000297421.92857.4e.
372. Chrysostomou C, Schulman SR, Herrera Castellanos M, Cofer BE, Mitra S, da Rocha MG, Wisemandle WA, Gramlich L. A phase II/III, multicenter, safety, efficacy, and pharmacokinetic study of dexmedetomidine in preterm and term neonates. *J Pediatr*. 2014;164:276–282.e1. doi: 10.1016/j.jpeds.2013.10.002.
373. Du Y, Chen YJ, He B, Wang YW. The effects of single-dose etomidate versus propofol on cortisol levels in pediatric patients undergoing urologic surgery: a randomized controlled trial. *Anesth Analg*. 2015;121:1580–1585. doi: 10.1213/ANE.0000000000000981.
374. van den Heuvel I, Wurmb TE, Böttiger BW, Bernhard M. Pros and cons of etomidate: more discussion than evidence? *Curr Opin Anaesthesiol*. 2013;26:404–408. doi: 10.1097/ACO.0b013e328362a84c.
375. Dewhirst E, Naguib A, Tobias JD. Chest wall rigidity in two infants after low-dose fentanyl administration. *Pediatr Emerg Care*. 2012;28:465–468. doi: 10.1097/PEC.0b013e3182535a2a.
376. Bovill JG. Intravenous anesthesia for the patient with left ventricular dysfunction. *Semin Cardiothorac Vasc Anesth*. 2006;10:43–48. doi: 10.1177/108925320601000108.
377. Green SM, Krauss B. Clinical practice guideline for emergency department ketamine dissociative sedation in children. *Ann Emerg Med*. 2004;44:460–471. doi: 10.1016/S0196064404006365.
378. Green SM, Roback MG, Krauss B, Brown L, McGlone RG, Agrawal D, McKee M, Weiss M, Pitetti RD, Hostetler MA, Wathen JE, Treston G, Garcia Pena BM, Gerber AC, Losek JD, Emergency Department Ketamine Meta-Analysis Study Group. Predictors of airway and respiratory adverse events with ketamine sedation in the emergency department: an individual-patient data meta-analysis of 8,282 children. *Ann Emerg Med*. 2009;54:158–168.e4. doi: 10.1016/.annemergmed.2008.12.011.
379. Wathen JE, Roback MG, Mackenzie T, Bothner JP. Does midazolam alter the clinical effects of intravenous ketamine sedation in children? A double-blind, randomized, controlled, emergency department trial. *Ann Emerg Med*. 2000;36:579–588. doi: 10.1067/mem.2000.111131.
380. Sherwin TS, Green SM, Khan A, Chapman DS, Dannenberg B. Does adjunctive midazolam reduce recovery agitation after ketamine sedation for pediatric procedures? A randomized, double-blind, placebo-controlled trial. *Ann Emerg Med*. 2000;35:229–238.
381. Chidambaran V, Costandi A, D'Mello A. Propofol: a review of its role in pediatric anesthesia and sedation. *CNS Drugs*. 2015;29:543–563. doi: 10.1007/s40263-015-0259-6.
382. Srinivasan M, Turmelle M, Depalma LM, Mao J, Carlson DW. Procedural sedation for diagnostic imaging in children by pediatric hospitalists using propofol: analysis of the nature, frequency, and predictors of adverse events and interventions. *J Pediatr*. 2012;160:801–806.e1. doi: 10.1016/j.jpeds.2011.11.003.
383. Ellenbogen KA, Thames MD, DiMarco JP, Sheehan H, Lerman BB. Electrophysiological effects of adenosine in the transplanted human heart: evidence of supersensitivity. *Circulation*. 1990;81:821–828.
384. Kudenchuk PJ, Cobb LA, Copass MK, Cummins RO, Doherty AM, Fahrenbruch CE, Hallstrom AP, Murray WA, Olsufka M, Walsh T. Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. *N Engl J Med*. 1999;341:871–878. doi: 10.1056/NEJM199909163411203.
385. Dorian P, Cass D, Schwartz B, Cooper R, Gelaznikas R, Barr A. Amiodarone as compared with lidocaine for shock-resistant ventricular fibrillation [published correction appears in *N Engl J Med* 2002;347:955]. *N Engl J Med*. 2002;346:884–890. doi: 10.1056/NEJMoa013029.
386. Valdes SO, Donoghue AJ, Hoyme DB, Hammond R, Berg MD, Berg RA, Samson RA; American Heart Association Get With The Guidelines-Resuscitation Investigators. Outcomes associated with amiodarone and lidocaine in the treatment of in-hospital pediatric cardiac arrest with pulseless ventricular tachycardia or ventricular fibrillation. *Resuscitation*. 2014;85:381–386. doi: 10.1016/j.resuscitation.2013.12.008.
387. Fishberger SB, Hannan RL, Welch EM, Rossi AF. Amiodarone for pediatric resuscitation: a word of caution. *Pediatr Cardiol*. 2009;30:1006–1008. doi: 10.1007/s00246-009-9470-x.
388. Tabbutt S, Nicolson SC, Adamson PC, Zhang X, Hoffman ML, Wells W, Backer CL, McGowan FX, Tweddell JS, Bokesch P, Schreiner M. The safety, efficacy, and pharmacokinetics of esmolol for blood pressure control immediately after repair of coarctation of the aorta in infants and children: a multicenter, double-blind, randomized trial. *J Thorac Cardiovasc Surg*. 2008;136:321–328. doi: 10.1016/j.jtcvs.2007.09.086.
389. Chang PM, Silka MJ, Moromisato DY, Bar-Cohen Y. Amiodarone versus procainamide for the acute treatment of recurrent supraventricular tachycardia in pediatric patients. *Circ Arrhythm Electrophysiol*. 2010;3:134–140. doi: 10.1161/CIRCEP.109.901629.
390. McGovern B, Garan H, Ruskin JN. Precipitation of cardiac arrest by verapamil in patients with Wolff-Parkinson-White syndrome. *Ann Intern Med*. 1986;104:791–794.
391. Srinivasan V, Morris MC, Helfaer MA, Berg RA, Nadkarni VM; American Heart Association National Registry of CPR Investigators. Calcium use during in-hospital pediatric cardiopulmonary resuscitation: a report from the National Registry of Cardiopulmonary Resuscitation. *Pediatrics*. 2008;121:e1144–e1151. doi: 10.1542/peds.2007-1555.
392. de Mos N, van Litsenburg RR, McCrindle B, Bohn DJ, Parshuram CS. Pediatric in-intensive-care-unit cardiac arrest: incidence, survival, and predictive factors. *Crit Care Med*. 2006;34:1209–1215. doi: 10.1097/01.CCM.0000208440.66756.C2.
393. Moler FW, Donaldson AE, Meert K, Brilli RJ, Nadkarni V, Shaffner DH, Schleien CL, Clark RS, Dalton HJ, Statler K, Tieves KS, Hackbarth R, Pretzlaff R, van der Jagt EW, Pineda J, Hernan L, Dean JM; Pediatric Emergency Care Applied Research Network. Multicenter cohort study of out-of-hospital pediatric cardiac arrest. *Crit Care Med*. 2011;39:141–149. doi: 10.1097/CCM.0b013e3181fa3c17.
394. Giglia TM, Massicotte MP, Tweddell JS, Barst RJ, Bauman M, Erickson CC, Feltes TF, Foster E, Hinoki K, Ichord RN, Kreutzer J, McCrindle BW, Newburger JW, Tabbutt S, Todd JL, Webb CL; on behalf of the American Heart Association Congenital Heart Defects Committee of the Council on Cardiovascular Disease in the Young, Council on Cardiovascular and Stroke Nursing, Council on Epidemiology and Prevention, and Stroke Council. Prevention and treatment of thrombosis in pediatric and congenital heart disease: a scientific statement from the American Heart Association [published correction appears in *Circulation*. 2014;129:e23]. *Circulation*. 2013;128:2622–2703. doi: 10.1161/01.cir.0000436140.77832.7a.
395. Kessel AD, Kline M, Zinger M, McLaughlin D, Silver P, Sweberg TM. The impact and statistical analysis of a multifaceted anticoagulation strategy in children supported on ECMO: performance and pitfalls. *J Intensive Care Med*. 2017;32:59–67. doi: 10.1177/0885066615601977.
396. Field D, Elbourne D, Hardy P, Fenton AC, Ahluwalia J, Halliday HL, Subhedar N, Heinonen K, Aikio O, Grieve R, Truesdale A, Tomlin K,

Normand C, Stocks J; INNOVO Trial Collaborating Group. Neonatal ventilation with inhaled nitric oxide vs. ventilatory support without inhaled nitric oxide for infants with severe respiratory failure born at or near term: the INNOVO multicentre randomised controlled trial. *Neonatology*. 2007;91:73–82. doi: 10.1159/000097123.

397. Taylor MB, Laussen PC. Fundamentals of management of acute postoperative pulmonary hypertension. *Pediatr Crit Care Med*. 2010;11(suppl):S27–S29. doi: 10.1097/PCC.0b013e3181c769a4.
398. de Caen AR, Maconochie IK, Aickin R, Atkins DL, Biarent D, Guerguerian AM, Kleinman ME, Kloeck DA, Meaney PA, Nadkarni VM, Ng KC, Nuthall G, Reis AG, Shimizu N, Tibballs J, Veliz Pintos R; on behalf of the Pediatric Basic Life Support and Pediatric Advanced Life Support Chapter Collaborators. Part 6: pediatric basic life support and pediatric advanced life support: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations [published correction appears in *Circulation*. 2016;134:e121]. *Circulation*. 2015;132(suppl 1):S177–S203. doi: 10.1161/CIR.0000000000000275.
399. Mackie AS, Gauvreau K, Booth KL, Newburger JW, Laussen PC, Roth SJ. Hemodynamic correlates of serum cortisol in neonates after cardiopulmonary bypass. *Pediatr Crit Care Med*. 2011;12:297–303. doi: 10.1097/PCC.0b013e3181f36929.
400. Verweij EJ, Hogenbirk K, Roest AA, van Brempt R, Hazekamp MG, de Jonge E. Serum cortisol concentration with exploratory cut-off values do not predict the effects of hydrocortisone administration in children with low cardiac output after cardiac surgery. *Interact Cardiovasc Thorac Surg*. 2012;15:685–689. doi: 10.1093/icvts/ivs292.
401. Shore S, Nelson DP, Pearl JM, Manning PB, Wong H, Shanley TP, Keyser T, Schwartz SM. Usefulness of corticosteroid therapy in decreasing epinephrine requirements in critically ill infants with congenital heart disease. *Am J Cardiol*. 2001;88:591–594.
402. Suominen PK, Dickerson HA, Moffett BS, Ranta SO, Mott AR, Price JF, Heinle JS, McKenzie ED, Fraser CDJ, Chang AC. Hemodynamic effects of rescue protocol hydrocortisone in neonates with low cardiac output syndrome after cardiac surgery. *Pediatr Crit Care Med*. 2005;6:655-659 10.1097/01.PCC.0000185487.69215.29.
403. Pasquali SK, Hall M, Li JS, Peterson ED, Jaggers J, Lodge AJ, Marino BS, Goodman DM, Shah SS. Corticosteroids and outcome in children undergoing congenital heart surgery: analysis of the Pediatric Health Information Systems Database. *Circulation*. 2010;122:2123–2130. doi: 10.1161/CIRCULATIONAHA.110.948737
404. Mastropietro CW, Barrett R, Davalos MC, Zidan M, Valentine KM, Delius RE, Walters HL 3rd. Cumulative corticosteroid exposure and infection risk after complex pediatric cardiac surgery. *Ann Thorac Surg*. 2013;95:2133–2139. doi: 10.1016/j.athoracsur.2013.02.026.
405. Schroeder VA, Pearl JM, Schwartz SM, Shanley TP, Manning PB, Nelson DP. Combined steroid treatment for congenital heart surgery improves oxygen delivery and reduces postbypass inflammatory mediator expression. *Circulation*. 2003;107:2823–2828. doi: 10.1161/01.CIR.0000070955.55636.25.
406. Clarizia NA, Manlhiot C, Schwartz SM, Sivarajan VB, Maratta R, Holtby HM, Gruenwald CE, Caldarone CA, Van Arsdell GS, McCrindle BW. Improved outcomes associated with intraoperative steroid use in high-risk pediatric cardiac surgery. *Ann Thorac Surg*. 2011;91:1222–1227. doi: 10.1016/j.athoracsur.2010.11.005.
407. Pasquali SK, Li JS, He X, Jacobs ML, O'Brien SM, Hall M, Jaquiss RD, Welke KF, Peterson ED, Shah SS, Gaynor JW, Jacobs JP. Perioperative methylprednisolone and outcome in neonates undergoing heart surgery. *Pediatrics*. 2012;129:e385-e391. doi: 10.1542/peds.2011-2034
408. Brady WJ, Swart G, DeBehnke DJ, Ma OJ, Aufderheide TP. The efficacy of atropine in the treatment of hemodynamically unstable bradycardia and atrioventricular block: prehospital and emergency department considerations. *Resuscitation*. 1999;41:47–55.
409. Jones P, Peters MJ, Pinto da Costa N, Kurth T, Alberti C, Kessous K, Lode N, Dauger S. Atropine for critical care intubation in a cohort of 264 children and reduced mortality unrelated to effects on bradycardia. *PLoS One*. 2013;8:e57478. doi: 10.1371/journal.pone.0057478.
410. Barrington KJ. The myth of a minimum dose for atropine. *Pediatrics*. 2011;127:783–4. doi: 10.1542/peds.2010-1475.
411. Vogt W, Läer S. Drug use patterns for the prevention of paediatric low cardiac output syndrome in Europe. *Intensive Care Med*. 2011;37:1390–1391. doi: 10.1007/s00134-011-2266-5.
412. Li J, Zhang G, Holtby H, Humpl T, Caldarone CA, Van Arsdell GS, Redington AN. Adverse effects of dopamine on systemic hemodynamic status and oxygen transport in neonates after the Norwood procedure. *J Am Coll Cardiol*. 2006;48:1859–1864. doi: 10.1016/j.jacc.2006.07.038.
413. Perondi MB, Reis AG, Paiva EF, Nadkarni VM, Berg RA. A comparison of high-dose and standard-dose epinephrine in children with cardiac arrest. *N Engl J Med*. 2004;350:1722–1730. doi: 10.1056/NEJMoa032440.
414. Fukushige J, Takahashi N, Igarashi H, Nakayama H, Inoue K, Hijii T. Perinatal management of congenital complete atrioventricular block: report of nine cases. *Acta Paediatr Jpn*. 1998;40:337–340.
415. Tibballs J, Carter B, Kiraly NJ, Ragg P, Clifford M. External and internal biphasic direct current shock doses for pediatric ventricular fibrillation and pulseless ventricular tachycardia. *Pediatr Crit Care Med*. 2011;12:14–20. doi: 10.1097/PCC.0b013e3181dbb4fc.
416. Egan JR, Clarke AJ, Williams S, Cole AD, Ayer J, Jacobe S, Chard RB, Winlaw DS. Levosimendan for low cardiac output: a pediatric experience. *J Intensive Care Med*. 2006;21:183–187. doi: 10.1177/0885066606287039.
417. Lechner E, Hofer A, Leitner-Peneder G, Freynschlag R, Mair R, Weinzettel R, Rehak P, Gombotz H. Levosimendan versus milrinone in neonates and infants after corrective open-heart surgery: a pilot study. *Pediatr Crit Care Med*. 2012;13:542–548. doi: 10.1097/PCC.0b013e3182455571.
418. Vogt W, Läer S. Treatment for paediatric low cardiac output syndrome: results from the European EuLoCOS-Paed survey. *Arch Dis Child*. 2011;96:1180–1186. doi: 10.1136/archdischild-2011-300370.
419. Tanaka K, Kitahata H, Kawahito S, Nozaki J, Tomiyama Y, Oshita S. Phenylephrine increases pulmonary blood flow in children with tetralogy of Fallot. *Can J Anaesth*. 2003;50:926–929. doi: 10.1007/BF03018741.
420. Neumar RW, Otto CW, Link MS, Kronick SL, Shuster M, Callaway CW, Kudenchuk PJ, Ornato JP, McNally B, Silvers SM, Passman RS, White RD, Hess EP, Tang W, Davis D, Sinz E, Morrison LJ. Part 8: adult advanced cardiovascular life support: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2010;122(suppl 3):S729–S767. doi: 10.1161/CIRCULATIONAHA.110.970988.
421. Link MS, Berkow LC, Kudenchuk PJ, Halperin HR, Hess EP, Moitra VK, Neumar RW, O'Neil BJ, Paxton JH, Silvers SM, White RD, Yannopoulos D, Donnino MW. Part 7: adult advanced cardiovascular life support: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132(suppl 2):S444–S464. doi: 10.1161/CIR.0000000000000261.
422. Duncan JM, Meaney P, Simpson P, Berg RA, Nadkarni V, Schexnayder S; National Registry of CPR Investigators. Vasopressin for in-hospital pediatric cardiac arrest: results from the American Heart Association National Registry of Cardiopulmonary Resuscitation. *Pediatr Crit Care Med*. 2009;10:191–195. doi: 10.1097/PCC.0b013e31819a36f2.
423. Mastropietro CW, Rossi NF, Clark JA, Chen H, Walters H 3rd, Delius R, Lieh-Lai M, Sarnaik AP. Relative deficiency of arginine vasopressin in children after cardiopulmonary bypass. *Crit Care Med*. 2010;38:2052–2058. doi: 10.1097/CCM.0b013e3181eed91d.
424. Matok I, Rubinshtein M, Levy A, Vardi A, Leibovitch L, Mishali D, Barzilay Z, Paret G. Terlipressin for children with extremely low cardiac output after open heart surgery. *Ann Pharmacother*. 2009;43:423–429. doi: 10.1345/aph.1L199.
425. Alten JA, Borasino S, Toms R, Law MA, Moellinger A, Dabal RJ. Early initiation of arginine vasopressin infusion in neonates after complex cardiac surgery. *Pediatr Crit Care Med*. 2012;13:300–304. doi: 10.1097/PCC.0b013e31822f1753.
426. Maltz LA, Klugman D, Spaeder MC, Wessel DL. Off-label drug use in a single-center pediatric cardiac intensive care unit. *World J Pediatr Congenit Heart Surg*. 2013;4:262–266. doi: 10.1177/2150135113481042.
427. Rosa RC, Rosa RF, Zen PR, Paskulin GA. Congenital heart defects and extracardiac malformations [article in English, Portuguese]. *Rev Paul Pediatr*. 2013;31:243–251.
428. Kazim R, Quaegebeur JM, Sun LS. The association of tracheal anomalies and tetralogy of Fallot. *J Cardiothorac Vasc Anesth*. 1996;10:589–592.
429. Kazim R, Berdon WE, Montoya CH, Quaegebeur JM, Sun LS. Tracheobronchial anomalies in children with congenital cardiac disease. *J Cardiothorac Vasc Anesth*. 1998;12:553–555.
430. Akpek EA, Mutlu H, Kayhan Z. Difficult intubation in pediatric cardiac anesthesia. *J Cardiothorac Vasc Anesth*. 2004;18:610–612.
431. Pfammatter JP, Casaulta C, Pavlovic M, Berdat PA, Frey U, Carrel T. Important excess morbidity due to upper airway anomalies in the perioperative course in infant cardiac surgery. *Ann Thorac Surg*. 2006;81:1008–1012. doi: 10.1016/j.athoracsur.2005.09.015.

432. Odegard KC, DiNardo JA, Kussman BD, Shukla A, Harrington J, Casta A, McGowan FX Jr, Hickey PR, Bacha EA, Thiagarajan RR, Laussen PC. The frequency of anesthesia-related cardiac arrests in patients with congenital heart disease undergoing cardiac surgery. *Anesth Analg*. 2007;105:335–343. doi: 10.1213/01.ane.0000268498.68620.39.
433. Ramamoorthy C, Haberkern CM, Bhananker SM, Domino KB, Posner KL, Campos JS, Morray JP. Anesthesia-related cardiac arrest in children with heart disease: data from the Pediatric Perioperative Cardiac Arrest (POCA) registry. *Anesth Analg*. 2010;110:1376–1382. doi: 10.1213/ANE.0b013e3181c9f927.
434. Gupta P, Kuperstock JE, Hashmi S, Arnolde V, Gossett JM, Prodhan P, Venkataraman S, Roth SJ. Efficacy and predictors of success of noninvasive ventilation for prevention of extubation failure in critically ill children with heart disease. *Pediatr Cardiol*. 2013;34:964–977. doi: 10.1007/s00246-012-0590-3.
435. Green DW, Bristow AS, Fisher M. Comparison of i.v. glycopyrrolate and atropine in the prevention of bradycardia and arrhythmias following repeated doses of suxamethonium in children. *Br J Anaesth*. 1984;56:981–985.
436. Shaw CA, Kelleher AA, Gill CP, Murdoch LJ, Stables RH, Black AE. Comparison of the incidence of complications at induction and emergence in infants receiving oral atropine vs no premedication. *Br J Anaesth*. 2000;84:174–178.
437. Zimmerman G, Steward DJ. Bradycardia delays the onset of action of intravenous atropine in infants. *Anesthesiology*. 1986;65:320–322.
438. Jones P, Dauger S, Peters MJ. Bradycardia during critical care intubation: mechanisms, significance and atropine. *Arch Dis Child*. 2012;97:139–144. doi: 10.1136/adc.2010.210518.
439. Marsch SC, Steiner L, Bucher E, Pargger H, Schumann M, Aebi T, Hunziker PR, Siegemund M. Succinylcholine versus rocuronium for rapid sequence intubation in intensive care: a prospective, randomized controlled trial. *Crit Care*. 2011;15:R199. doi: 10.1186/cc10367.
440. Chambers D, Paulden M, Paton F, Heirs M, Duffy S, Hunter JM, Sculpher M, Woolacott N. Sugammadex for reversal of neuromuscular block after rapid sequence intubation: a systematic review and economic assessment. *Br J Anaesth*. 2010;105:568–575. doi: 10.1093/bja/aeq270.
441. Albanese CT, Nour BM, Rowe MI. Anesthesia blocks nonshivering thermogenesis in the neonatal rabbit. *J Pediatr Surg*. 1994;29:983–986.
442. Plattner O, Semsroth M, Sessler DI, Papousek A, Klasen C, Wagner O. Lack of nonshivering thermogenesis in infants anesthetized with fentanyl and propofol. *Anesthesiology*. 1997;86:772–777.
443. Palmisano BW, Fisher DM, Willis M, Gregory GA, Ebert PA. The effect of paralysis on oxygen consumption in normoxic children after cardiac surgery. *Anesthesiology*. 1984;61:518–522.
444. Weiss M, Dullenkopf A, Fischer JE, Keller C, Gerber AC; European Paediatric Endotracheal Intubation Study Group. Prospective randomized controlled multi-centre trial of cuffed or uncuffed endotracheal tubes in small children. *Br J Anaesth*. 2009;103:867–873. doi: 10.1093/bja/aep290.
445. Fonte M, Oulego-Erroz I, Nadkarni L, Sánchez-Santos L, Iglesias-Vásquez A, Rodríguez-Núñez A. A randomized comparison of the GlideScope videolaryngoscope to the standard laryngoscopy for intubation by pediatric residents in simulated easy and difficult infant airway scenarios. *Pediatr Emerg Care*. 2011;27:398–402. doi: 10.1097/PEC.0b013e318217b550.
446. Apfelbaum JL, Hagberg CA, Caplan RA, Blitt CD, Connis RT, Nickinovich DG, Hagberg CA, Caplan RA, Benumof JL, Berry FA, Blitt CD, Bode RH, Cheney FW, Connis RT, Guidry OF, Nickinovich DG, Ovassapian A; American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology*. 2013;118:251–270. doi: 10.1097/ALN.0b013e31827773b2.
447. Sunder RA, Haile DT, Farrell PT, Sharma A. Pediatric airway management: current practices and future directions. *Paediatr Anaesth*. 2012;22:1008–1015. doi: 10.1111/pan.12013.
448. Hellström-Westas L, Hanséus K, Jögi P, Lundström NR, Svenningsen N. Long-distance transports of newborn infants with congenital heart disease. *Pediatr Cardiol*. 2001;22:380–384. doi: 10.1007/s002460010254.
449. Bronicki RA. Venous oximetry and the assessment of oxygen transport balance. *Pediatr Crit Care Med*. 2011;12(suppl):S21–S26. doi: 10.1097/PCC.0b013e3182211667.
450. Checchia PA, Bronicki RA. The Pediatric Cardiac Intensive Care Society evidence-based review and consensus statement on monitoring of hemodynamics and oxygen transport balance. *Pediatr Crit Care Med*. 2011;12(suppl):S1. doi: 10.1097/PCC.0b013e318220e64f.
451. Fletcher R, Jonson B, Cumming G, Brew J. The concept of deadspace with special reference to the single breath test for carbon dioxide. *Br J Anaesth*. 1981;53:77–88.
452. Burrows FA. Physiologic dead space, venous admixture, and the arterial to end-tidal carbon dioxide difference in infants and children undergoing cardiac surgery. *Anesthesiology*. 1989;70:219–225.
453. Fletcher R. Relationship between alveolar deadspace and arterial oxygenation in children with congenital cardiac disease. *Br J Anaesth*. 1989;62:168–176.
454. Benjamin JT, Romp RL, Carlo WA, Schelonka RL. Identification of serious congenital heart disease in neonates after initial hospital discharge. *Congenit Heart Dis*. 2007;2:327–331. doi: 10.1111/j.1747-0803.2007.00120.x.
455. Yeager SB, Horbar JD, Greco KM, Duff J, Thiagarajan RR, Laussen PC. Pretransport and posttransport characteristics and outcomes of neonates who were admitted to a cardiac intensive care unit. *Pediatrics*. 2006;118:1070–1077. doi: 10.1542/peds.2006-0719.
456. Orr RA, Felmet KA, Han Y, McCloskey KA, Dragotta MA, Bills DM, Kuch BA, Watson RS. Pediatric specialized transport teams are associated with improved outcomes. *Pediatrics*. 2009;124:40–48. doi: 10.1542/peds.2008-0515.
457. Ramnarayan P, Thiru K, Parslow RC, Harrison DA, Draper ES, Rowan KM. Effect of specialist retrieval teams on outcomes in children admitted to paediatric intensive care units in England and Wales: a retrospective cohort study. *Lancet*. 2010;376:698–704. doi: 10.1016/S0140-6736(10)61113-0.
458. Meckler GD, Lowe C. To intubate or not to intubate? Transporting infants on prostaglandin E1. *Pediatrics*. 2009;123:e25–e30. doi: 10.1542/peds.2008-0641.
459. Lewis AB, Freed MD, Heymann MA, Roehl SL, Kensey RC. Side effects of therapy with prostaglandin E1 in infants with critical congenital heart disease. *Circulation*. 1981;64:893–898.
460. Singh GK, Fong LV, Salmon AP, Keeton BR. Study of low dosage prostaglandin: usages and complications. *Eur Heart J*. 1994;15:377–381.
461. Kramer HH, Sommer M, Rammos S, Krogmann O. Evaluation of low dose prostaglandin E1 treatment for ductus dependent congenital heart disease. *Eur J Pediatr*. 1995;154:700–707.
462. Browning Carmo KA, Barr P, West M, Hopper NW, White JP, Badawi N. Transporting newborn infants with suspected duct dependent congenital heart disease on low-dose prostaglandin E1 without routine mechanical ventilation. *Arch Dis Child Fetal Neonatal Ed*. 2007;92:F117–F119.
463. Cabrera AG, Prodhan P, Cleves MA, Fiser RT, Schmitz M, Fontenot E, McKamie W, Chipman C, Jaquiss RD, Imamura M. Interhospital transport of children requiring extracorporeal membrane oxygenation support for cardiac dysfunction. *Congenit Heart Dis*. 2011;6:202–208. doi: 10.1111/j.1747-0803.2011.00506.x.
464. Clement KC, Fiser RT, Fiser WP, Chipman CW, Taylor BJ, Heulitt MJ, Moss M, Fasules JW, Faulkner SC, Imamura M, Fontenot EE, Jaquiss RD. Single-institution experience with interhospital extracorporeal membrane oxygenation transport: a descriptive study. *Pediatr Crit Care Med*. 2010;11:509–513. doi: 10.1097/PCC.0b013e3181c515ca.
465. Coppola CP, Tyree M, Larry K, DiGeronimo R. A 22-year experience in global transport extracorporeal membrane oxygenation. *J Pediatr Surg*. 2008;43:46–52. doi: 10.1016/j.jpedsurg.2007.09.021.
466. Drew BJ, Califf RM, Funk M, Kaufman ES, Krucoff MW, Laks MM, Macfarlane PW, Sommargren C, Swiryn S, Van Hare GF. Practice standards for electrocardiographic monitoring in hospital settings: an American Heart Association scientific statement from the Councils on Cardiovascular Nursing, Clinical Cardiology, and Cardiovascular Disease in the Young: endorsed by the International Society of Computerized Electrocardiology and the American Association of Critical-Care Nurses [published correction appears in *Circulation*. 2005;111:378]. *Circulation*. 2004;110:2721–2746. doi: 10.1161/01.CIR.0000145144.56673.59.
467. American Society of Anesthesiologists. Standards, guidelines, statements and other documents. 2013. http://www.asahq.org/quality-and-practice-management/standards-and-guidelines. Accessed April 23, 2013.
468. Sivarajan VB, Bohn D. Monitoring of standard hemodynamic parameters: heart rate, systemic blood pressure, atrial pressure, pulse oximetry, and end-tidal CO_2. *Pediatr Crit Care Med*. 2011;12(suppl):S2–S11. doi: 10.1097/PCC.0b013e318220e7ea.

469. Young D, Griffiths J. Clinical trials of monitoring in anaesthesia, critical care and acute ward care: a review. *Br J Anaesth*. 2006;97:39–45. doi: 10.1093/bja/ael107.
470. Reich DL, Kahn RA, Mittnacht AJ, Leibowitz AB, Stone ME, Eisenkraft JB, eds. *Monitoring in Anesthesia and Perioperative Care*. Cambridge, United Kingdom: Cambridge University Press; 2011.
471. Tibby SM, Hatherill M, Marsh MJ, Murdoch IA. Clinicians' abilities to estimate cardiac index in ventilated children and infants. *Arch Dis Child*. 1997;77:516–518.
472. Wernovsky G, Wypij D, Jonas RA, Mayer JE Jr, Hanley FL, Hickey PR, Walsh AZ, Chang AC, Castañeda AR, Newburger JW, Wessel DL. Postoperative course and hemodynamic profile after the arterial switch operation in neonates and infants: a comparison of low-flow cardiopulmonary bypass and circulatory arrest. *Circulation*. 1995;92:2226–2235.
473. Stocker CF, Shekerdemian LS, Nørgaard MA, Brizard CP, Mynard JP, Horton SB, Penny DJ. Mechanisms of a reduced cardiac output and the effects of milrinone and levosimendan in a model of infant cardiopulmonary bypass. *Crit Care Med*. 2007;35:252–259. doi: 10.1097/01.CCM.0000251123.70632.4E.
474. Ziemer G, Karck M, Müller H, Luhmer I. Staged chest closure in pediatric cardiac surgery preventing typical and atypical cardiac tamponade. *Eur J Cardiothorac Surg*. 1992;6:91–95.
475. Bronicki RA, Herrera M, Mink R, Domico M, Tucker D, Chang AC, Anas NG. Hemodynamics and cerebral oxygenation following repair of tetralogy of Fallot: the effects of converting from positive pressure ventilation to spontaneous breathing. *Congenit Heart Dis*. 2010;5:416–421. doi: 10.1111/j.1747-0803.2010.00445.x.
476. Shekerdemian LS, Schulze-Neick I, Redington AN, Bush A, Penny DJ. Negative pressure ventilation as haemodynamic rescue following surgery for congenital heart disease. *Intensive Care Med*. 2000;26:93–96.
477. Morales DLS, Carberry KE, Heinle JS, McKenzie ED, Fraser CD Jr, Diaz LK. Extubation in the operating room after Fontan's procedure: effect on practice and outcomes. *Ann Thorac Surg*. 2008;86:576–582. doi: 10.1016/j.athoracsur.2008.02.010.
478. Lofland GK. The enhancement of hemodynamic performance in Fontan circulation using pain free spontaneous ventilation. *Eur J Cardiothorac Surg*. 2001;20:114–119.
479. Mora GA, Pizarro C, Jacobs ML, Norwood WI. Experimental model of single ventricle: influence of carbon dioxide on pulmonary vascular dynamics. *Circulation*. 1994;90(pt 2):II43–II46.
480. Checchia PA, Bronicki RA, Goldstein B. Review of inhaled nitric oxide in the pediatric cardiac surgery setting. *Pediatr Cardiol*. 2012;33:493–505. doi: 10.1007/s00246-012-0172-4.
481. Vogt W, Läer S. Prevention for pediatric low cardiac output syndrome: results from the European survey EuLoCOS-Paed. *Paediatr Anaesth*. 2011;21:1176–1184. doi: 10.1111/j.1460-9592.2011.03683.x.
482. Van Saet A, De Wildt SN. Prevention of low cardiac output syndrome in children: where is the evidence? *Paediatr Anaesth*. 2011;21:1173–1175. doi: 10.1111/j.1460-9592.2011.03700.x.
483. Osthaus WA, Boethig D, Winterhalter M, Huber D, Goerler H, Sasse M, Sümpelmann R. First experiences with intraoperative levosimendan in pediatric cardiac surgery. *Eur J Pediatr*. 2009;168:735–740. doi: 10.1007/s00431-008-0834-7.
484. Momeni M, Rubay J, Matta A, Rennotte MT, Veyckemans F, Poncelet AJ, Clement de Clety S, Anslot C, Joomye R, Detaille T. Levosimendan in congenital cardiac surgery: a randomized, double-blind clinical trial. *J Cardiothorac Vasc Anesth*. 2011;25:419–424. doi: 10.1053/j.jvca.2010.07.004.
485. Ricci Z, Garisto C, Favia I, Vitale V, Di Chiara L, Cogo PE. Levosimendan infusion in newborns after corrective surgery for congenital heart disease: randomized controlled trial. *Intensive Care Med*. 2012;38:1198–1204. doi: 10.1007/s00134-012-2564-6.
486. Hamilton MA, Cecconi M, Rhodes A. A systematic review and meta-analysis on the use of preemptive hemodynamic intervention to improve postoperative outcomes in moderate and high-risk surgical patients. *Anesth Analg*. 2011;112:1392–1402. doi: 10.1213/ANE.0b013e3181eeaae5.
487. Aya HD, Cecconi M, Hamilton M, Rhodes A. Goal-directed therapy in cardiac surgery: a systematic review and meta-analysis. *Br J Anaesth*. 2013;110:510–517. doi: 10.1093/bja/aet020.
488. Morrison LJ, Neumar RW, Zimmerman JL, Link MS, Newby LK, McMullan PW Jr, Hoek TV, Halverson CC, Doering L, Peberdy MA, Edelson DP; on behalf of the American Heart Association Emergency Cardiovascular Care Committee, Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Peripheral Vascular Disease. Strategies for improving survival after in-hospital cardiac arrest in the United States: 2013 consensus recommendations: a consensus statement from the American Heart Association. *Circulation*. 2013;127:1538–1563. doi: 10.1161/CIR.0b013e31828b2770.
489. Burstein DS, Rossi AF, Jacobs JP, Checchia PA, Wernovsky G, Li JS, Pasquali SK. Variation in models of care delivery for children undergoing congenital heart surgery in the United States. *World J Pediatr Congenit Heart Surg*. 2010;1:8–14. doi: 10.1177/2150135109360915.
490. Burstein DS, Jacobs JP, Li JS, Sheng S, O'Brien SM, Rossi AF, Checchia PA, Wernovsky G, Welke KF, Peterson ED, Jacobs ML, Pasquali SK. Care models and associated outcomes in congenital heart surgery. *Pediatrics*. 2011;127:e1482-e1489. doi: 10.1542/peds.2010-2796.
491. Hickey PA, Gauvreau K, Tong E, Schiffer NP, Connor JA. Pediatric cardiovascular critical care in the United States: nursing and organizational characteristics. *Am J Crit Care*. 2012;21:242–250. doi: 10.4037/ajcc2012853.
492. Gaies MG, Clarke NS, Donohue JE, Gurney JG, Charpie JR, Hirsch JC. Personnel and unit factors impacting outcome after cardiac arrest in a dedicated pediatric cardiac intensive care unit. *Pediatr Crit Care Med*. 2012;13:583–588. doi: 10.1097/PCC.0b013e318238b272.
493. Hickey PA, Gauvreau K, Curley MA, Connor JA. The effect of critical care nursing and organizational characteristics on pediatric cardiac surgery mortality in the United States. *J Nurs Adm*. 2013;43:637–644. doi: 10.1097/NNA.0000000000000005.
494. Hickey PA, Pasquali SK, Gaynor JW, He X, Hill KD, Connor JA, Gauvreau K, Jacobs ML, Jacobs JP, Hirsch-Romano JC. Critical care nursing's impact on pediatric patient outcomes. *Ann Thorac Surg*. 2016;102:1375–1380. doi: 10.1016/j.athoracsur.2016.03.019.
495. Usuku H, Nakayama M, Sumida H, Yamamuro M, Izumiya Y, Suzuki S, Kusuhara K, Ueno H, Sugiyama S, Yoshimura M, Ogawa H. Pump failure death and sudden cardiac death in patients with cardiac dysfunction: a search for prognostic predictive factors: a long-term follow-up study. *J Cardiol*. 2010;55:55–64. doi: 10.1016/j.jjcc.2009.08.005.
496. Lara TM, Hajjar LA, de Almeida JP, Fukushima JT, Barbas CS, Rodrigues AR, Nozawa E, Feltrim MI, Almeida E, Coimbra V, Osawa E, Ianotti RdM, Leme AC, Jatene FB, Auler-Jr JO, Galas FR. High levels of B-type natriuretic peptide predict weaning failure from mechanical ventilation in adult patients after cardiac surgery. *Clinics (Sao Paulo)*. 2013;68:33–38.
497. Huang SC, Wu ET, Ko WJ, Lai LP, Hsu J, Chang CI, Chiu IS, Wang SS, Wu MH, Lin FY, Chen YS. Clinical implication of blood levels of B-type natriuretic peptide in pediatric patients on mechanical circulatory support. *Ann Thorac Surg*. 2006;81:2267–2272. doi: 10.1016/j.athoracsur.2005.12.061.
498. Amirnovin R, Keller RL, Herrera C, Hsu JH, Datar S, Karl TR, Adatia I, Oishi P, Fineman JR. B-type natriuretic peptide levels predict outcomes in infants undergoing cardiac surgery in a lesion-dependent fashion. *J Thorac Cardiovasc Surg*. 2013;145:1279–1287. doi: 10.1016/j.jtcvs.2012.07.067.
499. Balasubramanyan N, Havens PL, Hoffman GM. Unmeasured anions identified by the Fencl-Stewart method predict mortality better than base excess, anion gap, and lactate in patients in the pediatric intensive care unit. *Crit Care Med*. 1999;27:1577–1581.
500. Cheung PY, Chui N, Joffe AR, Rebeyka IM, Robertson CM; Western Canadian Complex Pediatric Therapies Project, Follow-up Group. Postoperative lactate concentrations predict the outcome of infants aged 6 weeks or less after intracardiac surgery: a cohort follow-up to 18 months. *J Thorac Cardiovasc Surg*. 2005;130:837–843. doi: 10.1016/j.jtcvs.2005.04.029.
501. Molina Hazan V, Gonen Y, Vardi A, Keidan I, Mishali D, Rubinshtein M, Yakov Y, Paret G. Blood lactate levels differ significantly between surviving and nonsurviving patients within the same Risk-Adjusted Classification for Congenital Heart Surgery (RACHS-1) group after pediatric cardiac surgery. *Pediatr Cardiol*. 2010;31:952–960. doi: 10.1007/s00246-010-9724-7.
502. Charpie JR, Dekeon MK, Goldberg CS, Mosca RS, Bove EL, Kulik TJ. Serial blood lactate measurements predict early outcome after neonatal repair or palliation for complex congenital heart disease. *J Thorac Cardiovasc Surg*. 2000;120:73–80. doi: 10.1067/mtc.2000.106838.
503. Hannan RL, Ybarra MA, White JA, Ojito JW, Rossi AF, Burke RP. Patterns of lactate values after congenital heart surgery and timing of cardiopulmonary support. *Ann Thorac Surg*. 2005;80:1468–1473. doi: 10.1016/j.athoracsur.2005.04.050.

504. Kalyanaraman M, DeCampli WM, Campbell AI, Bhalala U, Harmon TG, Sandiford P, McMahon CK, Shore S, Yeh TS. Serial blood lactate levels as a predictor of mortality in children after cardiopulmonary bypass surgery. *Pediatr Crit Care Med*. 2008;9:285–288. doi: 10.1097/PCC.0b013e31816c6f31.
505. Thayssen P, Klarholt E. Relation between caval and pulmonary artery oxygen saturation in children. *Br Heart J*. 1980;43:574–578.
506. Dueck MH, Klimek M, Appenrodt S, Weigand C, Boerner U. Trends but not individual values of central venous oxygen saturation agree with mixed venous oxygen saturation during varying hemodynamic conditions. *Anesthesiology*. 2005;103:249–257.
507. Rossi AF, Sommer RJ, Lotvin A, Gross RP, Steinberg LG, Kipel G, Golinko RJ, Griepp RB. Usefulness of intermittent monitoring of mixed venous oxygen saturation after stage I palliation for hypoplastic left heart syndrome. *Am J Cardiol*. 1994;73:1118–1123.
508. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M; Early Goal-Directed Therapy Collaborative Group. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med*. 2001;345:1368–1377. doi: 10.1056/NEJMoa010307.
509. Oliveira C, Oliveira DF, Gottschald AC, Moura JG, Costa G, Ventura A, Fernandes J, Vaz FC, Carcillo J, Rivers E, Troster E. ACCM/PALS haemodynamic support guidelines for paediatric septic shock: an outcomes comparison with and without monitoring central venous oxygen saturation. *Intensive Care Med*. 2008;34:1065–1075. doi: 10.1007/s00134-008-1085-9
510. Rao RP, Danduran MJ, Frommelt PC, Ghanayem NS, Berger S, Simpson PM, Yan K, Hoffman GM. Measurement of regional tissue bed venous weighted oximetric trends during exercise by near infrared spectroscopy. *Pediatr Cardiol*. 2009;30:465–471. doi: 10.1007/s00246-009-9393-6.
511. Rao RP, Danduran MJ, Hoffman GM, Ghanayem NS, Berger S, Frommelt PC. Cerebral hemodynamics in the presence of decreased systemic venous compliance in patients with Fontan physiology may limit anaerobic exercise capacity. *Pediatr Cardiol*. 2010;31:208–214. doi: 10.1007/s00246-009-9585-0.
512. Danduran MJ, Dixon JE, Rao RP. Near infrared spectroscopy describes physiologic payback associated with excess postexercise oxygen consumption in healthy controls and children with complex congenital heart disease. *Pediatr Cardiol*. 2012;33:95–102. doi: 10.1007/s00246-011-0097-3.
513. Rao RP, Danduran MJ, Loomba RS, Dixon JE, Hoffman GM. Near-infrared spectroscopic monitoring during cardiopulmonary exercise testing detects anaerobic threshold. *Pediatr Cardiol*. 2012;33:791–796. doi: 10.1007/s00246-012-0217-8.
514. Bhalala US, Nishisaki A, McQueen D, Bird GL, Morrison WE, Nadkarni VM, Nathan M, Starr JP. Change in regional (somatic) near-infrared spectroscopy is not a useful indicator of clinically detectable low cardiac output in children after surgery for congenital heart defects. *Pediatr Crit Care Med*. 2012;13:529–534. doi: 10.1097/PCC.0b013e3182389531.
515. Li J, Van Arsdell GS, Zhang G, Cai S, Humpl T, Caldarone CA, Holtby H, Redington AN. Assessment of the relationship between cerebral and splanchnic oxygen saturations measured by near-infrared spectroscopy and direct measurements of systemic haemodynamic variables and oxygen transport after the Norwood procedure. *Heart*. 2006;92:1678–1685. doi: 10.1136/hrt.2005.087270.
516. McQuillen PS, Nishimoto MS, Bottrell CL, Fineman LD, Hamrick SE, Glidden DV, Azakie A, Adatia I, Miller SP. Regional and central venous oxygen saturation monitoring following pediatric cardiac surgery: concordance and association with clinical variables. *Pediatr Crit Care Med*. 2007;8:154–160. doi: 10.1097/01.PCC.0000257101.37171.BE.
517. Dent CL, Spaeth JP, Jones BV, Schwartz SM, Glauser TA, Hallinan B, Pearl JM, Khoury PR, Kurth CD. Brain magnetic resonance imaging abnormalities after the Norwood procedure using regional cerebral perfusion. *J Thorac Cardiovasc Surg*. 2005;130:1523–1530. doi: 10.1016/j.jtcvs.2005.07.051.
518. Kussman BD, Wypij D, Laussen PC, Soul JS, Bellinger DC, DiNardo JA, Robertson R, Pigula FA, Jonas RA, Newburger JW. Relationship of intraoperative cerebral oxygen saturation to neurodevelopmental outcome and brain magnetic resonance imaging at 1 year of age in infants undergoing biventricular repair. *Circulation*. 2010;122:245–254. doi: 10.1161/CIRCULATIONAHA.109.902338.
519. Ortmann LA, Fontenot EE, Seib PM, Eble BK, Brown R, Bhutta AT. Use of near-infrared spectroscopy for estimation of renal oxygenation in children with heart disease. *Pediatr Cardiol*. 2011;32:748–753. doi: 10.1007/s00246-011-9960-5.
520. Owens GE, King K, Gurney JG, Charpie JR. Low renal oximetry correlates with acute kidney injury after infant cardiac surgery. *Pediatr Cardiol*. 2011;32:183–188. doi: 10.1007/s00246-010-9839-x.
521. Papadea C, Foster J, Grant S, Ballard SA, Cate JC 4th, Southgate WM, Purohit DM. Evaluation of the i-STAT Portable Clinical Analyzer for point-of-care blood testing in the intensive care units of a university children's hospital. *Ann Clin Lab Sci*. 2002;32:231–243.
522. Karon BS, Scott R, Burritt MF, Santrach PJ. Comparison of lactate values between point-of-care and central laboratory analyzers. *Am J Clin Pathol*. 2007;128:168–171. doi: 10.1309/HBQEFDPH34MKK5GP.
523. Klugman D, Berger JT. Echocardiography as a hemodynamic monitor in critically ill children. *Pediatr Crit Care Med*. 2011;12(suppl):S50–S54. doi: 10.1097/PCC.0b013e3182211c17.
524. Longjohn M, Wan J, Joshi V, Pershad J. Point-of-care echocardiography by pediatric emergency physicians. *Pediatr Emerg Care*. 2011;27:693–696. doi: 10.1097/PEC.0b013e318226c7c7.
525. Mertens L, Seri I, Marek J, Arlettaz R, Barker P, McNamara P, Moon-Grady AJ, Coon PD, Noori S, Simpson J, Lai WW; Writing Group of the American Society of Echocardiography; European Association of Echocardiography; Association for European Pediatric Cardiologists. Targeted neonatal echocardiography in the neonatal intensive care unit: practice guidelines and recommendations for training. *J Am Soc Echocardiogr*. 2011;24:1057–1078. doi: 10.1016/j.echo.2011.07.014.
526. Sehgal A, McNamara PJ. Does point-of-care functional echocardiography enhance cardiovascular care in the NICU? *J Perinatol*. 2008;28:729–735. doi: 10.1038/jp.2008.100.
527. Booth KL, Roth SJ, Thiagarajan RR, Almodovar MC, del Nido PJ, Laussen PC. Extracorporeal membrane oxygenation support of the Fontan and bidirectional Glenn circulations. *Ann Thorac Surg*. 2004;77:1341–1348. doi: 10.1016/j.athoracsur.2003.09.042.
528. Gandhi NN, Hartman ME, Williford WL, Peters MA, Cheifetz IM, Turner DA. Successful use of extracorporeal membrane oxygenation for pH1N1-induced refractory hypoxemia in a child with hypoplastic left heart syndrome. *Pediatr Crit Care Med*. 2011;12:e398–e401. doi: 10.1097/PCC.0b013e3181fe3189.
529. Chang YH, Kim H, Sung SC, Lee HD. Temporary fenestration using venoatrial extracorporeal membrane oxygenation after the Fontan operation. *Ann Thorac Surg*. 2012;93:2068–2069. doi: 10.1016/j.athoracsur.2011.11.020.
530. Nielsen JC, Seiden HS, Nguyen K, Vlahakis SA, Ravishankar C. Extracorporeal membrane oxygenation for pneumonitis after a Glenn palliation. *Perfusion*. 2002;17:457–458. doi: 10.1191/0267659102pf616cr.
531. Guntheroth WG. Sensitivity and specificity of echocardiographic evidence of tamponade: implications for ventricular interdependence and pulsus paradoxus. *Pediatr Cardiol*. 2007;28:358–362. doi: 10.1007/s00246-005-0807-9.
532. Berman W Jr, Fripp RR, Rubler M, Alderete L. Hemodynamic effects of ketamine in children undergoing cardiac catheterization. *Pediatr Cardiol*. 1990;11:72–76. doi: 10.1007/BF02239565.
533. Hart BB, Stanford GG, Ziegler MG, Lake CR, Chernow B. Catecholamines: study of interspecies variation. *Crit Care Med*. 1989;17:1203–1222.
534. Fisher DG, Schwartz PH, Davis AL. Pharmacokinetics of exogenous epinephrine in critically ill children. *Crit Care Med*. 1993;21:111–117.
535. Morray JP, Lynn AM, Mansfield PB. Effect of pH and PCO2 on pulmonary and systemic hemodynamics after surgery in children with congenital heart disease and pulmonary hypertension. *J Pediatr*. 1988;113:474–479.
536. McLellan MC, Gauvreau K, Connor JA. Validation of the Cardiac Children's Hospital Early Warning Score: an early warning scoring tool to prevent cardiopulmonary arrests in children with heart disease. *Congenit Heart Dis*. 2014;9:194–202. doi: 10.1111/chd.12132.
537. Furck AK, Uebing A, Hansen JH, Scheewe J, Jung O, Fischer G, Rickers C, Holland-Letz T, Kramer HH. Outcome of the Norwood operation in patients with hypoplastic left heart syndrome: a 12-year single-center survey. *J Thorac Cardiovasc Surg*. 2010;139:359–365. doi: 10.1016/j.jtcvs.2009.07.063.
538. Ghanayem NS, Hoffman GM, Mussatto KA, Cava JR, Frommelt PC, Rudd NA, Steltzer MM, Bevandic SM, Frisbee SS, Jaquiss RD, Litwin SB, Tweddell JS. Home surveillance program prevents interstage mortality after the Norwood procedure. *J Thorac Cardiovasc Surg*. 2003;126:1367–1377.
539. Siehr SL, Norris JK, Bushnell JA, Ramamoorthy C, Reddy VM, Hanley FL, Wright GE. Home monitoring program reduces interstage mortality after the modified Norwood procedure. *J Thorac Cardiovasc Surg*. 2014;147:718–23.e1. doi: 10.1016/j.jtcvs.2013.04.006.

540. Petit CJ, Fraser CD, Mattamal R, Slesnick TC, Cephus CE, Ocampo EC. The impact of a dedicated single-ventricle home-monitoring program on interstage somatic growth, interstage attrition, and 1-year survival. *J Thorac Cardiovasc Surg*. 2011;142:1358–1366. doi: 10.1016/j.jtcvs.2011.04.043.
541. Hansen JH, Furck AK, Petko C, Buchholz-Berdau R, Voges I, Scheewe J, Rickers C, Kramer HH. Use of surveillance criteria reduces interstage mortality after the Norwood operation for hypoplastic left heart syndrome. *Eur J Cardiothorac Surg*. 2012;41:1013–1018. doi: 10.1093/ejcts/ezr190.
542. Schidlow DN, Anderson JB, Klitzner TS, Beekman RH 3rd, Jenkins KJ, Kugler JD, Martin GR, Neish SR, Rosenthal GL, Lannon C; JCCHD National Pediatric Cardiology Quality Improvement Collaborative. Variation in interstage outpatient care after the Norwood procedure: a report from the Joint Council on Congenital Heart Disease National Quality Improvement Collaborative. *Congenit Heart Dis*. 2011;6:98–107. doi: 10.1111/j.1747-0803.2011.00509.x.
543. Pasquali SK. Reexamining interstage home monitoring after the Norwood operation. *Circulation*. 2015;132:475–478. doi: 10.1161/CIRCULATIONAHA.115.017682.
544. Oster ME, Ehrlich A, King E, Petit CJ, Clabby M, Smith S, Glanville M, Anderson J, Darbie L, Beekman RH 3rd. Association of interstage home monitoring with mortality, readmissions, and weight gain: a multicenter study from the National Pediatric Cardiology Quality Improvement Collaborative. *Circulation*. 2015;132:502–508. doi: 10.1161/CIRCULATIONAHA.114.014107.
545. Donoghue A, Berg RA, Hazinski MF, Praestgaard AH, Roberts K, Nadkarni VM; American Heart Association National Registry of CPR Investigators. Cardiopulmonary resuscitation for bradycardia with poor perfusion versus pulseless cardiac arrest. *Pediatrics*. 2009;124:1541–1548. doi: 10.1542/peds.2009-0727.
546. Berg MD, Schexnayder SM, Chameides L, Terry M, Donoghue A, Hickey RW, Berg RA, Sutton RM, Hazinski MF. Part 13: pediatric basic life support: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2010;122(suppl 3):S862–S875. doi: 10.1161/CIRCULATIONAHA.110.971085.
547. Fitzgerald KR, Babbs CF, Frissora HA, Davis RW, Silver DI. Cardiac output during cardiopulmonary resuscitation at various compression rates and durations. *Am J Physiol*. 1981;241:H442–H448.
548. Kattwinkel J, Perlman JM, Aziz K, Colby C, Fairchild K, Gallagher J, Hazinski MF, Halamek LP, Kumar P, Little G, McGowan JE, Nightengale B, Ramirez MM, Ringer S, Simon WM, Weiner GM, Wyckoff M, Zaichkin J. Part 15: neonatal resuscitation: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care [published correction appears in *Circulation*. 2011;124:e406]. *Circulation*. 2010;122(suppl 3):S909–S919. doi: 10.1161/CIRCULATIONAHA.110.971119.
549. Dorfsman ML, Menegazzi JJ, Wadas RJ, Auble TE. Two-thumb vs. two-finger chest compression in an infant model of prolonged cardiopulmonary resuscitation. *Acad Emerg Med*. 2000;7:1077–1082.
550. Whitelaw CC, Slywka B, Goldsmith LJ. Comparison of a two-finger versus two-thumb method for chest compressions by healthcare providers in an infant mechanical model. *Resuscitation*. 2000;43:213–216.
551. Idris AH, Guffey D, Aufderheide TP, Brown S, Morrison LJ, Nichols P, Powell J, Daya M, Bigham BL, Atkins DL, Berg R, Davis D, Stiell I, Sopko G, Nichol G; Resuscitation Outcomes Consortium (ROC) Investigators. Relationship between chest compression rates and outcomes from cardiac arrest. *Circulation*. 2012;125:3004–3012. doi: 10.1161/CIRCULATIONAHA.111.059535.
552. Kim H, Hwang SO, Lee CC, Lee KH, Kim JY, Yoo BS, Lee SH, Yoon JH, Choe KH, Singer AJ. Direction of blood flow from the left ventricle during cardiopulmonary resuscitation in humans: its implications for mechanism of blood flow. *Am Heart J*. 2008;156:1222.e1–1222.e7. doi: 10.1016/j.ahj.2008.09.003.
553. Haas T, Voelckel WG, Wenzel V, Antretter H, Dessl A, Lindner KH. Revisiting the cardiac versus thoracic pump mechanism during cardiopulmonary resuscitation. *Resuscitation*. 2003;58:113–116.
554. Higano ST, Oh JK, Ewy GA, Seward JB. The mechanism of blood flow during closed chest cardiac massage in humans: transesophageal echocardiographic observations. *Mayo Clin Proc*. 1990;65:1432–1440.
555. Sutton RM, Niles D, Nysaether J, Arbogast KB, Nishisaki A, Maltese MR, Bishnoi R, Helfaer MA, Nadkarni V, Donoghue A. Pediatric CPR quality monitoring: analysis of thoracic anthropometric data. *Resuscitation*. 2009;80:1137–1141. doi: 10.1016/j.resuscitation.2009.06.031.
556. Niles DE, Sutton RM, Nadkarni VM, Glatz A, Zuercher M, Maltese MR, Eilevstjønn J, Abella BS, Becker LB, Berg RA. Prevalence and hemodynamic effects of leaning during CPR. *Resuscitation*. 2011;82(suppl 2):S23–S26. doi: 10.1016/S0300-9572(11)70147-2.
557. Sutton RM, Maltese MR, Niles D, French B, Nishisaki A, Arbogast KB, Donoghue A, Berg RA, Helfaer MA, Nadkarni V. Quantitative analysis of chest compression interruptions during in-hospital resuscitation of older children and adolescents. *Resuscitation*. 2009;80:1259–1263. doi: 10.1016/j.resuscitation.2009.08.009.
558. Zuercher M, Hilwig RW, Ranger-Moore J, Nysaether J, Nadkarni VM, Berg MD, Kern KB, Sutton R, Berg RA. Leaning during chest compressions impairs cardiac output and left ventricular myocardial blood flow in piglet cardiac arrest. *Crit Care Med*. 2010;38:1141–1146. doi: 10.1097/CCM.0b013e3181ce1fe2.
559. Sutton RM, Niles D, Nysaether J, Stavland M, Thomas M, Ferry S, Bishnoi R, Litman R, Allen J, Srinivasan V, Berg RA, Nadkarni VM. Effect of residual leaning force on intrathoracic pressure during mechanical ventilation in children. *Resuscitation*. 2010;81:857–860. doi: 10.1016/j.resuscitation.2010.03.015.
560. Kern KB, Hilwig RW, Berg RA, Sanders AB, Ewy GA. Importance of continuous chest compressions during cardiopulmonary resuscitation: improved outcome during a simulated single lay-rescuer scenario. *Circulation*. 2002;105:645–649.
561. Miller AC, Rosati SF, Suffredini AF, Schrump DS. A systematic review and pooled analysis of CPR-associated cardiovascular and thoracic injuries. *Resuscitation*. 2014;85:724–731. doi: 10.1016/j.resuscitation.2014.01.028.
562. Bush CM, Jones JS, Cohle SD, Johnson H. Pediatric injuries from cardiopulmonary resuscitation. *Ann Emerg Med*. 1996;28:40–44.
563. Paradis NA, Martin GB, Rivers EP, Goetting MG, Appleton TJ, Feingold M, Nowak RM. Coronary perfusion pressure and the return of spontaneous circulation in human cardiopulmonary resuscitation. *JAMA*. 1990;263:1106–1113.
564. Asim K, Gokhan E, Ozlem B, Ozcan Y, Deniz O, Kamil K, Murat Z, Aydın C, Selman Y. Near infrared spectrophotometry (cerebral oximetry) in predicting the return of spontaneous circulation in out-of-hospital cardiac arrest. *Am J Emerg Med*. 2014;32:14–17. doi: 10.1016/j.ajem.2013.09.010.
565. Ahn A, Nasir A, Malik H, D'Orazi F, Parnia S. A pilot study examining the role of regional cerebral oxygen saturation monitoring as a marker of return of spontaneous circulation in shockable (VF/VT) and non-shockable (PEA/Asystole) causes of cardiac arrest. *Resuscitation*. 2013;84:1713–1716. doi: 10.1016/j.resuscitation.2013.07.026.
566. Kerber RE, Carter J, Klein S, Grayzel J, Kennedy J. Open chest defibrillation during cardiac surgery: energy and current requirement. *Am J Cardiol*. 1980;46:393–396.
567. Cheskes S, Schmicker RH, Christenson J, Salcido DD, Rea T, Powell J, Edelson DP, Sell R, May S, Menegazzi JJ, Van Ottingham L, Olsufka M, Pennington S, Simonini J, Berg RA, Stiell I, Idris A, Bigham B, Morrison L; Resuscitation Outcomes Consortium (ROC) Investigators. Perishock pause: an independent predictor of survival from out-of-hospital shockable cardiac arrest. *Circulation*. 2011;124:58–66. doi: 10.1161/CIRCULATIONAHA.110.010736.
568. Hoogendijk MG, Schumacher CA, Belterman CN, Boukens BJ, Berdowski J, de Bakker JM, Koster RW, Coronel R. Ventricular fibrillation hampers the restoration of creatine-phosphate levels during simulated cardiopulmonary resuscitations. *Europace*. 2012;14:1518–1523. doi: 10.1093/europace/eus078.
569. Berg RA, Hilwig RW, Kern KB, Ewy GA. Precountershock cardiopulmonary resuscitation improves ventricular fibrillation median frequency and myocardial readiness for successful defibrillation from prolonged ventricular fibrillation: a randomized, controlled swine study. *Ann Emerg Med*. 2002;40:563–570.
570. Sherbino J, Verbeek PR, MacDonald RD, Sawadsky BV, McDonald AC, Morrison LJ. Prehospital transcutaneous cardiac pacing for symptomatic bradycardia or bradyasystolic cardiac arrest: a systematic review. *Resuscitation*. 2006;70:193–200. doi: 10.1016/j.resuscitation.2005.11.019.
571. Quan L, Graves JR, Kinder DR, Horan S, Cummins RO. Transcutaneous cardiac pacing in the treatment of out-of-hospital pediatric cardiac arrests. *Ann Emerg Med*. 1992;21:905–909.
572. White JD. Transthoracic pacing in cardiac asystole. *Am J Emerg Med*. 1983;1:264–266.
573. Ornato JP, Carveth WL, Windle JR. Pacemaker insertion for prehospital bradyasystolic cardiac arrest. *Ann Emerg Med*. 1984;13:101–103.
574. Niemann JT, Adomian GE, Garner D, Rosborough JP. Endocardial and transcutaneous cardiac pacing, calcium chloride, and epinephrine in postcountershock asystole and bradycardias. *Crit Care Med*. 1985;13:699–704.

575. Dalsey WC, Syverud SA, Hedges JR. Emergency department use of transcutaneous pacing for cardiac arrests. *Crit Care Med*. 1985;13:399–401.
576. Knowlton AA, Falk RH. External cardiac pacing during in-hospital cardiac arrest. *Am J Cardiol*. 1986;57:1295–1298.
577. Hedges JR, Syverud SA, Dalsey WC, Feero S, Easter R, Shultz B. Prehospital trial of emergency transcutaneous cardiac pacing. *Circulation*. 1987;76:1337–1343.
578. Barthell E, Troiano P, Olson D, Stueven HA, Hendley G. Prehospital external cardiac pacing: a prospective, controlled clinical trial. *Ann Emerg Med*. 1988;17:1221–1226.
579. Cummins RO, Graves JR, Larsen MP, Hallstrom AP, Hearne TR, Ciliberti J, Nicola RM, Horan S. Out-of-hospital transcutaneous pacing by emergency medical technicians in patients with asystolic cardiac arrest. *N Engl J Med*. 1993;328:1377–1382. doi: 10.1056/NEJM199305133281903.
580. Ornato JP, Peberdy MA. The mystery of bradyasystole during cardiac arrest. *Ann Emerg Med*. 1996;27:576–587.
581. Salem MR, Khorasani A, Saatee S, Crystal GJ, El-Orbany M. Gastric tubes and airway management in patients at risk of aspiration: history, current concepts, and proposal of an algorithm. *Anesth Analg*. 2014;118:569–579. doi: 10.1213/ANE.0b013e3182917f11.
582. Marill KA, Greenberg GM, Kay D, Nelson BK. Analysis of the treatment of spontaneous sustained stable ventricular tachycardia. *Acad Emerg Med*. 1997;4:1122–1128.
583. Chen YS, Lin JW, Yu HY, Ko WJ, Jerng JS, Chang WT, Chen WJ, Huang SC, Chi NH, Wang CH, Chen LC, Tsai PR, Wang SS, Hwang JJ, Lin FY. Cardiopulmonary resuscitation with assisted extracorporeal life-support versus conventional cardiopulmonary resuscitation in adults with in-hospital cardiac arrest: an observational study and propensity analysis. *Lancet*. 2008;372:554–561. doi: 10.1016/S0140-6736(08)60958-7.
584. Thiagarajan RR, Laussen PC, Rycus PT, Bartlett RH, Bratton SL. Extracorporeal membrane oxygenation to aid cardiopulmonary resuscitation in infants and children. *Circulation*. 2007;116:1693–1700. doi: 10.1161/CIRCULATIONAHA.106.680678.
585. Thiagarajan RR, Brogan TV, Scheurer MA, Laussen PC, Rycus PT, Bratton SL. Extracorporeal membrane oxygenation to support cardiopulmonary resuscitation in adults. *Ann Thorac Surg*. 2009;87:778–785. doi: 10.1016/j.athoracsur.2008.12.079.
586. Huang SC, Wu ET, Chen YS, Chang CI, Chiu IS, Wang SS, Lin FY, Ko WJ. Extracorporeal membrane oxygenation rescue for cardiopulmonary resuscitation in pediatric patients. *Crit Care Med*. 2008;36:1607–1613. doi: 10.1097/CCM.0b013e318170b82b.
587. Shin TG, Jo IJ, Sim MS, Song YB, Yang JH, Hahn JY, Choi SH, Gwon HC, Jeon ES, Sung K, Lee YT, Choi JH. Two-year survival and neurological outcome of in-hospital cardiac arrest patients rescued by extracorporeal cardiopulmonary resuscitation. *Int J Cardiol*. 2013;168:3424–3430. doi: 10.1016/j.ijcard.2013.04.183.
588. Morris MC, Wernovsky G, Nadkarni VM. Survival outcomes after extracorporeal cardiopulmonary resuscitation instituted during active chest compressions following refractory in-hospital pediatric cardiac arrest. *Pediatr Crit Care Med*. 2004;5:440–446.
589. Lasa JJ, Rogers RS, Localio R, Shults J, Raymond T, Gaies M, Thiagarajan R, Laussen PC, Kilbaugh T, Berg RA, Nadkarni V, Topjian A. Extracorporeal cardiopulmonary resuscitation (E-CPR) during pediatric in-hospital cardiopulmonary arrest is associated with improved survival to discharge: a report from the American Heart Association's Get With The Guidelines-Resuscitation (GWTG-R) registry. *Circulation*. 2016;133:165–176. doi: 10.1161/CIRCULATIONAHA.115.016082.
590. Dalton HJ, Siewers RD, Fuhrman BP, Del Nido P, Thompson AE, Shaver MG, Dowhy M. Extracorporeal membrane oxygenation for cardiac rescue in children with severe myocardial dysfunction. *Crit Care Med*. 1993;21:1020–1028.
591. Chan T, Thiagarajan RR, Frank D, Bratton SL. Survival after extracorporeal cardiopulmonary resuscitation in infants and children with heart disease. *J Thorac Cardiovasc Surg*. 2008;136:984–992. doi: 10.1016/j.jtcvs.2008.03.007.
592. del Nido PJ, Dalton HJ, Thompson AE, Siewers RD. Extracorporeal membrane oxygenator rescue in children during cardiac arrest after cardiac surgery. *Circulation*. 1992;86(suppl):II300–II304.
593. Alsoufi B, Al-Radi OO, Nazer RI, Gruenwald C, Foreman C, Williams WG, Coles JG, Caldarone CA, Bohn DG, Van Arsdell GS. Survival outcomes after rescue extracorporeal cardiopulmonary resuscitation in pediatric patients with refractory cardiac arrest. *J Thorac Cardiovasc Surg*. 2007;134:952–959.e2. doi: 10.1016/j.jtcvs.2007.05.054.
594. Duncan BW, Bohn DJ, Atz AM, French JW, Laussen PC, Wessel DL. Mechanical circulatory support for the treatment of children with acute fulminant myocarditis. *J Thorac Cardiovasc Surg*. 2001;122:440–448. doi: 10.1067/mtc.2001.115243.
595. Sivarajan VB, Best D, Brizard CP, Shekerdemian LS, d'Udekem Y, Butt W. Duration of resuscitation prior to rescue extracorporeal membrane oxygenation impacts outcome in children with heart disease. *Intensive Care Med*. 2011;37:853–860. doi: 10.1007/s00134-011-2168-6.
596. Tajik M, Cardarelli MG. Extracorporeal membrane oxygenation after cardiac arrest in children: what do we know? *Eur J Cardiothorac Surg*. 2008;33:409–417. doi: 10.1016/j.ejcts.2007.12.018.
597. Allan CK, Thiagarajan RR, Armsby LR, del Nido PJ, Laussen PC. Emergent use of extracorporeal membrane oxygenation during pediatric cardiac catheterization. *Pediatr Crit Care Med*. 2006;7:212–219. doi: 10.1097/01.PCC.0000200964.88206.B0.
598. Posner JC, Osterhoudt KC, Mollen CJ, Jacobstein CR, Nicolson SC, Gaynor JW. Extracorporeal membrane oxygenation as a resuscitative measure in the pediatric emergency department. *Pediatr Emerg Care*. 2000;16:413–415.
599. Jen HC, Shew SB. Hospital readmissions and survival after non-neonatal pediatric ECMO. *Pediatrics*. 2010;125:1217–1223. doi: 10.1542/peds.2009-0696.
600. Karamlou T, Vafaeezadeh M, Parrish AM, Cohen GA, Welke KF, Permut L, McMullan DM. Increased extracorporeal membrane oxygenation center case volume is associated with improved extracorporeal membrane oxygenation survival among pediatric patients. *J Thorac Cardiovasc Surg*. 2013;145:470–475. doi: 10.1016/j.jtcvs.2012.11.037.
601. Freeman CL, Bennett TD, Casper TC, Larsen GY, Hubbard A, Wilkes J, Bratton SL. Pediatric and neonatal extracorporeal membrane oxygenation: does center volume impact mortality? *Crit Care Med*. 2014;42:512–519. doi: 10.1097/01.ccm.0000435674.83682.96.
602. Sakamoto T, Morimura N, Nagao K, Asai Y, Yokota H, Nara S, Hase M, Tahara Y, Atsumi T; SAVE-J Study Group. Extracorporeal cardiopulmonary resuscitation versus conventional cardiopulmonary resuscitation in adults with out-of-hospital cardiac arrest: a prospective observational study. *Resuscitation*. 2014;85:762–768. doi: 10.1016/j.resuscitation.2014.01.031.
603. Teele SA, Salvin JW, Barrett CS, Rycus PT, Fynn-Thompson F, Laussen PC, Thiagarajan RR. The association of carotid artery cannulation and neurologic injury in pediatric patients supported with venoarterial extracorporeal membrane oxygenation. *Pediatr Crit Care Med*. 2014;15:355–361. doi: 10.1097/PCC.0000000000000103.
604. Su L, Spaeder MC, Jones MB, Sinha P, Nath DS, Jain PN, Berger JT, Williams L, Shankar V. Implementation of an extracorporeal cardiopulmonary resuscitation simulation program reduces extracorporeal cardiopulmonary resuscitation times in real patients. *Pediatr Crit Care Med*. 2014;15:856–860. doi: 10.1097/PCC.0000000000000234.
605. Barrett CS, Bratton SL, Salvin JW, Laussen PC, Rycus PT, Thiagarajan RR. Neurological injury after extracorporeal membrane oxygenation use to aid pediatric cardiopulmonary resuscitation. *Pediatr Crit Care Med*. 2009;10:445–451. doi: 10.1097/PCC.0b013e318198bd85.
606. Morris MC, Ittenbach RF, Godinez RI, Portnoy JD, Tabbutt S, Hanna BD, Hoffman TM, Gaynor JW, Connelly JT, Helfaer MA, Spray TL, Wernovsky G. Risk factors for mortality in 137 pediatric cardiac intensive care unit patients managed with extracorporeal membrane oxygenation. *Crit Care Med*. 2004;32:1061–1069.
607. Hintz SR, Benitz WE, Colby CE, Sheehan AM, Rycus P, Van Meurs KP; ELSO Registry. Utilization and outcomes of neonatal cardiac extracorporeal life support: 1996-2000. *Pediatr Crit Care Med*. 2005;6:33–38. doi: 10.1097/01.PCC.0000149135.95884.65.
608. Duncan BW, Ibrahim AE, Hraska V, del Nido PJ, Laussen PC, Wessel DL, Mayer JE Jr, Bower LK, Jonas RA. Use of rapid-deployment extracorporeal membrane oxygenation for the resuscitation of pediatric patients with heart disease after cardiac arrest. *J Thorac Cardiovasc Surg*. 1998;116:305–311.
609. Bautista-Hernandez V, Thiagarajan RR, Fynn-Thompson F, Rajagopal SK, Nento DE, Yarlagadda V, Teele SA, Allan CK, Emani SM, Laussen PC, Pigula FA, Bacha EA. Preoperative extracorporeal membrane oxygenation as a bridge to cardiac surgery in children with congenital heart disease. *Ann Thorac Surg*. 2009;88:1306–1311. doi: 10.1016/j.athoracsur.2009.06.074.
610. Sherwin ED, Gauvreau K, Scheurer MA, Rycus PT, Salvin JW, Almodovar MC, Fynn-Thompson F, Thiagarajan RR. Extracorporeal membrane oxygenation after stage 1 palliation for hypoplastic left heart syndrome. *J*

Thorac Cardiovasc Surg. 2012;144:1337–1343. doi: 10.1016/j.jtcvs.2012.03.035
611. Hoskote A, Bohn D, Gruenwald C, Edgell D, Cai S, Adatia I, Van Arsdell G. Extracorporeal life support after staged palliation of a functional single ventricle: subsequent morbidity and survival. *J Thorac Cardiovasc Surg*. 2006;131:1114–1121. doi: 10.1016/j.jtcvs.2005.11.035.
612. Debrunner MG, Porayette P, Breinholt JP 3rd, Turrentine MW, Cordes TM. Midterm survival of infants requiring postoperative extracorporeal membrane oxygenation after Norwood palliation. *Pediatr Cardiol*. 2013;34:570–575. doi: 10.1007/s00246-012-0499-x.
613. Newburger JW, Sleeper LA, Bellinger DC, Goldberg CS, Tabbutt S, Lu M, Mussatto KA, Williams IA, Gustafson KE, Mital S, Pike N, Sood E, Mahle WT, Cooper DS, Dunbar-Masterson C, Krawczeski CD, Lewis A, Menon SC, Pemberton VL, Ravishankar C, Atz TW, Ohye RG, Gaynor JW; for the Pediatric Heart Network Investigators. Early developmental outcome in children with hypoplastic left heart syndrome and related anomalies: the Single Ventricle Reconstruction Trial. *Circulation*. 2012;125:2081–2091. doi: 10.1161/CIRCULATIONAHA.111.064113.
614. Ravishankar C, Zak V, Williams IA, Bellinger DC, Gaynor JW, Ghanayem NS, Krawczeski CD, Licht DJ, Mahony L, Newburger JW, Pemberton VL, Williams RV, Sananes R, Cook AL, Atz T, Khaikin S, Hsu DT; Pediatric Heart Network Investigators. Association of impaired linear growth and worse neurodevelopmental outcome in infants with single ventricle physiology: a report from the Pediatric Heart Network Infant Single Ventricle Trial. *J Pediatr*. 2013;162:250–256.e2. doi: 10.1016/j.jpeds.2012.07.048.
615. Roeleveld PP, Wilde Rd, Hazekamp M, Rycus PT, Thiagarajan RR. Extracorporeal membrane oxygenation in single ventricle lesions palliated via the hybrid approach. *World J Pediatr Congenit Heart Surg*. 2014;5:393–397. doi: 10.1177/2150135114526420.
616. Rood KL, Teele SA, Barrett CS, Salvin JW, Rycus PT, Fynn-Thompson F, Laussen PC, Thiagarajan RR. Extracorporeal membrane oxygenation support after the Fontan operation. *J Thorac Cardiovasc Surg*. 2011;142:504–510. doi: 10.1016/j.jtcvs.2010.11.050.
617. Berg RA, Sutton RM, Holubkov R, Nicholson CE, Dean JM, Harrison R, Heidemann S, Meert K, Newth C, Moler F, Pollack M, Dalton H, Doctor A, Wessel D, Berger J, Shanley T, Carcillo J, Nadkarni VM; Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network and for the American Heart Association's Get With the Guidelines-Resuscitation (formerly the National Registry of Cardiopulmonary Resuscitation) Investigators. Ratio of PICU versus ward cardiopulmonary resuscitation events is increasing. *Crit Care Med*. 2013;41:2292–2297. doi: 10.1097/CCM.0b013e31828cf0c0.
618. Donoghue AJ, Nadkarni VM, Elliott M, Durbin D; American Heart Association National Registry of Cardiopulmonary Resuscitation Investigators. Effect of hospital characteristics on outcomes from pediatric cardiopulmonary resuscitation: a report from the National Registry of Cardiopulmonary Resuscitation. *Pediatrics*. 2006;118:995–1001. doi: 10.1542/peds.2006-0453.
619. Bennett D, Marcus R, Stokes M. Incidents and complications during pediatric cardiac catheterization. *Paediatr Anaesth*. 2005;15:1083–1088. doi: 10.1111/j.1460-9592.2005.01677.x.
620. Odegard KC, Bergersen L, Thiagarajan RR, Clark L, Shukla A, Wypij D, Laussen PC. The frequency of cardiac arrests in patients with congenital heart disease undergoing cardiac catheterization. *Anesth Analg*. 2014;118:175–182.
621. Mori Y, Nakazawa M, Yagihara T. Complications of pediatric cardiac catheterization and system of catheterization laboratories minimizing complications–a Japanese multicenter survey. *J Cardiol*. 2010;56:183–188. doi: 10.1016/j.jjcc.2010.05.001.
622. Bergersen L, Marshall A, Gauvreau K, Beekman R, Hirsch R, Foerster S, Balzer D, Vincent J, Hellenbrand W, Holzer R, Cheatham J, Moore J, Lock J, Jenkins K. Adverse event rates in congenital cardiac catheterization: a multi-center experience. *Catheter Cardiovasc Interv*. 2010;75:389–400. doi: 10.1002/ccd.22266.
623. Mehta R, Lee KJ, Chaturvedi R, Benson L. Complications of pediatric cardiac catheterization: a review in the current era. *Catheter Cardiovasc Interv*. 2008;72:278–285. doi: 10.1002/ccd.21580.
624. Bhanji F, Donoghue AJ, Wolff MS, Flores GE, Halamek LP, Berman JM, Sinz EH, Cheng A. Part 14: education: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132(suppl 2):S561–S573. doi: 10.1161/CIR.0000000000000268.
625. Sutton RM, Nadkarni V, Abella BS. "Putting it all together" to improve resuscitation quality. *Emerg Med Clin North Am*. 2012;30:105–122. doi: 10.1016/j.emc.2011.09.001.
626. Sutton RM, Niles D, Meaney PA, Aplenc R, French B, Abella BS, Lengetti EL, Berg RA, Helfaer MA, Nadkarni V. Low-dose, high-frequency CPR training improves skill retention of in-hospital pediatric providers. *Pediatrics*. 2011;128:e145–e151. doi: 10.1542/peds.2010-2105.
627. Sutton RM, Niles D, Meaney PA, Aplenc R, French B, Abella BS, Lengetti EL, Berg RA, Helfaer MA, Nadkarni V. "Booster" training: evaluation of instructor-led bedside cardiopulmonary resuscitation skill training and automated corrective feedback to improve cardiopulmonary resuscitation compliance of pediatric basic life support providers during simulated cardiac arrest. *Pediatr Crit Care Med*. 2011;12:e116–e121. doi: 10.1097/PCC.0b013e3181e91271.
628. Olivieri LJ, Su L, Hynes CF, Krieger A, Alfares FA, Ramakrishnan K, Zurakowski D, Marshall MB, Kim PC, Jonas RA, Nath DS. "Just-in-time" simulation training using 3-D printed cardiac models after congenital cardiac surgery. *World J Pediatr Congenit Heart Surg*. 2016;7:164–168. doi: 10.1177/2150135115623961.
629. Sutton RM, French B, Niles DE, Donoghue A, Topjian AA, Nishisaki A, Leffelman J, Wolfe H, Berg RA, Nadkarni VM, Meaney PA. 2010 American Heart Association recommended compression depths during pediatric in-hospital resuscitations are associated with survival. *Resuscitation*. 2014;85:1179–1184. doi: 10.1016/j.resuscitation.2014.05.007.
630. Sutton RM, Niles D, French B, Maltese MR, Leffelman J, Eilevstjønn J, Wolfe H, Nishisaki A, Meaney PA, Berg RA, Nadkarni VM. First quantitative analysis of cardiopulmonary resuscitation quality during in-hospital cardiac arrests of young children. *Resuscitation*. 2014;85:70–74. doi: 10.1016/j.resuscitation.2013.08.014.
631. Sutton RM, French B, Nishisaki A, Niles DE, Maltese MR, Boyle L, Stavland M, Eilevstjønn J, Arbogast KB, Berg RA, Nadkarni VM. American Heart Association cardiopulmonary resuscitation quality targets are associated with improved arterial blood pressure during pediatric cardiac arrest. *Resuscitation*. 2013;84:168–172. doi: 10.1016/j.resuscitation.2012.08.335.
632. Ornato JP, Peberdy MA, Reid RD, Feeser VR, Dhindsa HS; NRCPR Investigators. Impact of resuscitation system errors on survival from in-hospital cardiac arrest. *Resuscitation*. 2012;83:63–69. doi: 10.1016/j.resuscitation.2011.09.009.
633. Cheng A, Brown LL, Duff JP, Davidson J, Overly F, Tofil NM, Peterson DT, White ML, Bhanji F, Bank I, Gottesman R, Adler M, Zhong J, Grant V, Grant DJ, Sudikoff SN, Marohn K, Charnovich A, Hunt EA, Kessler DO, Wong H, Robertson N, Lin Y, Doan Q, Duval-Arnould JM, Nadkarni VM; International Network for Simulation-Based Pediatric Innovation, Research, & Education (INSPIRE) CPR Investigators. Improving cardiopulmonary resuscitation with a CPR feedback device and refresher simulations (CPR CARES Study): a randomized clinical trial. *JAMA Pediatr*. 2015;169:137–144. doi: 10.1001/jamapediatrics.2014.2616.
634. Kurosawa H, Ikeyama T, Achuff P, Perkel M, Watson C, Monachino A, Remy D, Deutsch E, Buchanan N, Anderson J, Berg RA, Nadkarni VM, Nishisaki A. A randomized, controlled trial of in situ pediatric advanced life support recertification ("pediatric advanced life support reconstructed") compared with standard pediatric advanced life support recertification for ICU frontline providers. *Crit Care Med*. 2014;42:610–618. doi: 10.1097/CCM.0000000000000024.
635. Allan CK, Pigula F, Bacha EA, Emani S, Fynn-Thompson F, Thiagarajan RR, Imprescia A, Hayes G, Weinstock P. An extracorporeal membrane oxygenation cannulation curriculum featuring a novel integrated skills trainer leads to improved performance among pediatric cardiac surgery trainees. *Simul Healthc*. 2013;8:221–228. doi: 10.1097/SIH.0b013e31828b4179.
636. Burkhart HM, Riley JB, Lynch JJ, Suri RM, Greason KL, Joyce LD, Nuttall GA, Stulak J, Schaff HV, Dearani JA. Simulation-based postcardiotomy extracorporeal membrane oxygenation crisis training for thoracic surgery residents. *Ann Thorac Surg*. 2013;95:901–906. doi: 10.1016/j.athoracsur.2012.12.015.
637. Sanchez-Glanville C, Brindle ME, Spence T, Blackwood J, Drews T, Menzies S, Lopushinsky SR. Evaluating the introduction of extracorporeal life support technology to a tertiary-care pediatric institution: smoothing the learning curve through interprofessional simulation training. *J Pediatr Surg*. 2015;50:798–804. doi: 10.1016/j.jpedsurg.2015.02.037.
638. Ad Hoc Committee on Cardiopulmonary Resuscitation. Cardiopulmonary resuscitation: statement by the Ad Hoc Committee on Cardiopulmonary Resuscitation of the Division of Medical Sciences, National Academy of Sciences–National Research Council. *JAMA*. 1966;198:372–379. doi: 10.1001/jama.1966.03110170084023.
639. Negovsky VA, Gurvitch AM. Post-resuscitation disease: a new nosological entity: its reality and significance. *Resuscitation*. 1995;30:23–27.

640. Neumar RW, Nolan JP, Adrie C, Aibiki M, Berg RA, Böttiger BW, Callaway C, Clark RS, Geocadin RG, Jauch EC, Kern KB, Laurent I, Longstreth WT Jr, Merchant RM, Morley P, Morrison LJ, Nadkarni V, Peberdy MA, Rivers EP, Rodriguez-Nunez A, Sellke FW, Spaulding C, Sunde K, Vanden Hoek T. Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication: a consensus statement from the International Liaison Committee on Resuscitation (American Heart Association, Australian and New Zealand Council on Resuscitation, European Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Asia, and the Resuscitation Council of Southern Africa); the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; and the Stroke Council. *Circulation*. 2008;118:2452–2483. doi: 10.1161/CIRCULATIONAHA.108.190652.

641. Nolan JP, Neumar RW, Adrie C, Aibiki M, Berg RA, Böttiger BW, Callaway C, Clark RS, Geocadin RG, Jauch EC, Kern KB, Laurent I, Longstreth WT, Merchant RM, Morley P, Morrison LJ, Nadkarni V, Peberdy MA, Rivers EP, Rodriguez-Nunez A, Sellke FW, Spaulding C, Sunde K, Hoek TV. Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication: a scientific statement from the International Liaison Committee on Resuscitation; the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; the Council on Stroke. *Resuscitation*. 2008;79:350–379. doi: 10.1016/j.resuscitation.2008.09.017.

642. Hagihara A, Hasegawa M, Abe T, Nagata T, Wakata Y, Miyazaki S. Prehospital epinephrine use and survival among patients with out-of-hospital cardiac arrest. *JAMA*. 2012;307:1161–1168. doi: 10.1001/jama.2012.294.

643. Tang W, Weil MH, Sun S, Noc M, Yang L, Gazmuri RJ. Epinephrine increases the severity of postresuscitation myocardial dysfunction. *Circulation*. 1995;92:3089–3093.

644. Kern KB. Postresuscitation myocardial dysfunction. *Cardiol Clin*. 2002;20:89–101.

645. Hildebrand CA, Hartmann AG, Arcinue EL, Gomez RJ, Bing RJ. Cardiac performance in pediatric near-drowning. *Crit Care Med*. 1988;16:331–335.

646. Jones AE, Shapiro NI, Kilgannon JH, Trzeciak S; Emergency Medicine Shock Research Network (EMSHOCKNET) Investigators. Goal-directed hemodynamic optimization in the post-cardiac arrest syndrome: a systematic review. *Resuscitation*. 2008;77:26–29. doi: 10.1016/j.resuscitation.2007.10.021.

647. Karanjia N, Geocadin RG. Post-cardiac arrest syndrome: update on brain injury management and prognostication. *Curr Treat Options Neurol*. 2011;13:191–203. doi: 10.1007/s11940-011-0112-2.

648. Kern KB, Hilwig RW, Berg RA, Rhee KH, Sanders AB, Otto CW, Ewy GA. Postresuscitation left ventricular systolic and diastolic dysfunction: treatment with dobutamine. *Circulation*. 1997;95:2610–2613.

649. Kilgannon JH, Roberts BW, Reihl LR, Chansky ME, Jones AE, Dellinger RP, Parrillo JE, Trzeciak S. Early arterial hypotension is common in the post-cardiac arrest syndrome and associated with increased in-hospital mortality. *Resuscitation*. 2008;79:410–416. doi: 10.1016/j.resuscitation.2008.07.019.

650. Checchia PA, Sehra R, Moynihan J, Daher N, Tang W, Weil MH. Myocardial injury in children following resuscitation after cardiac arrest. *Resuscitation*. 2003;57:131–137.

651. Cobb LA, Fahrenbruch CE, Walsh TR, Copass MK, Olsufka M, Breskin M, Hallstrom AP. Influence of cardiopulmonary resuscitation prior to defibrillation in patients with out-of-hospital ventricular fibrillation. *JAMA*. 1999;281:1182–1188.

652. Lister G, Pérez Fontán JJ. Can resuscitation jeopardize survival? *N Engl J Med*. 2004;350:1708–1709. doi: 10.1056/NEJMp048055.

653. Lindner KH, Dirks B, Strohmenger HU, Prengel AW, Lindner IM, Lurie KG. Randomised comparison of epinephrine and vasopressin in patients with out-of-hospital ventricular fibrillation. *Lancet*. 1997;349:535–537. doi: 10.1016/S0140-6736(97)80087-6.

654. Pellis T, Weil MH, Tang W, Sun S, Xie J, Song L, Checchia P. Evidence favoring the use of an alpha2-selective vasopressor agent for cardiopulmonary resuscitation. *Circulation*. 2003;108:2716–2721. doi: 10.1161/01.CIR.0000096489.40209.DD.

655. Shaffner DH, Eleff SM, Brambrink AM, Sugimoto H, Izuta M, Koehler RC, Traystman RJ. Effect of arrest time and cerebral perfusion pressure during cardiopulmonary resuscitation on cerebral blood flow, metabolism, adenosine triphosphate recovery, and pH in dogs. *Crit Care Med*. 1999;27:1335–1342.

656. Donnino MW, Miller J, Goyal N, Loomba M, Sankey SS, Dolcourt B, Sherwin R, Otero R, Wira C. Effective lactate clearance is associated with improved outcome in post-cardiac arrest patients. *Resuscitation*. 2007;75:229–234. doi: 10.1016/j.resuscitation.2007.03.021.

657. Jefferies JL, Morales DL. Mechanical circulatory support in children: bridge to transplant versus recovery. *Curr Heart Fail Rep*. 2012;9:236–243. doi: 10.1007/s11897-012-0103-y.

658. Mackling T, Shah T, Dimas V, Guleserian K, Sharma M, Forbess J, Ardura M, Gross-Toalson J, Lee Y, Journeycake J, Barnes A. Management of single-ventricle patients with Berlin Heart EXCOR Ventricular Assist Device: single-center experience. *Artif Organs*. 2012;36:555–559. doi: 10.1111/j.1525-1594.2011.01403.x.

659. Warnes CA, Williams RG, Bashore TM, Child JS, Connolly HM, Dearani JA, del Nido P, Fasules JW, Graham TP Jr, Hijazi ZM, Hunt SA, King ME, Landzberg MJ, Miner PD, Radford MJ, Walsh EP, Webb GD. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to develop guidelines on the management of adults with congenital heart disease). *Circulation*. 2008;118:e714–e833. doi: 10.1161/CIRCULATIONAHA.108.190690.

660. Fraser CD Jr, Jaquiss RD, Rosenthal DN, Humpl T, Canter CE, Blackstone EH, Naftel DC, Ichord RN, Bomgaars L, Tweddell JS, Massicotte MP, Turrentine MW, Cohen GA, Devaney EJ, Pearce FB, Carberry KE, Kroslowitz R, Almond CS; Berlin Heart Study Investigators. Prospective trial of a pediatric ventricular assist device. *N Engl J Med*. 2012;367:532–541. doi: 10.1056/NEJMoa1014164.

661. Cabrera AG, Sundareswaran K, Samayoa AX, Farrar DJ, Frazier OH, Morales DLS. 338 Outcomes of pediatric patients supported by the Heartmate II LVAD in the USA. *J Heart Lung Transplant*. 2012;31(suppl):S120. doi: 10.1016/j.healun.2012.01.347.

662. Morales DL, Adachi I, Heinle JS, Fraser CD Jr. A new era: use of an intracorporeal systemic ventricular assist device to support a patient with a failing Fontan circulation. *J Thorac Cardiovasc Surg*. 2011;142:e138–e140. doi: 10.1016/j.jtcvs.2011.05.018.

663. Miera O, Potapov EV, Redlin M, Stepanenko A, Berger F, Hetzer R, Hübler M. First experiences with the HeartWare ventricular assist system in children. *Ann Thorac Surg*. 2011;91:1256–1260. doi: 10.1016/j.athoracsur.2010.12.013.

664. Crews KA, Kaiser SL, Walczak RJ, Jaquiss RD, Lodge AJ. Bridge to transplant with extracorporeal membrane oxygenation followed by HeartWare ventricular assist device in a child. *Ann Thorac Surg*. 2013;95:1780–1782. doi: 10.1016/j.athoracsur.2012.09.088.

665. Copeland JG, Copeland H, Gustafson M, Mineburg N, Covington D, Smith RG, Friedman M. Experience with more than 100 total artificial heart implants. *J Thorac Cardiovasc Surg*. 2012;143:727–734. doi: 10.1016/j.jtcvs.2011.12.002.

666. Wang S, Wu JY, Guo ZJ, Li CS. Effect of rescue breathing during cardiopulmonary resuscitation on lung function after restoration of spontaneous circulation in a porcine model of prolonged cardiac arrest. *Crit Care Med*. 2013;41:102–110. doi: 10.1097/CCM.0b013e318265792b.

667. Richards EM, Rosenthal RE, Kristian T, Fiskum G. Postischemic hyperoxia reduces hippocampal pyruvate dehydrogenase activity. *Free Radic Biol Med*. 2006;40:1960–1970. doi: 10.1016/j.freeradbiomed.2006.01.022.

668. Zwemer CF, Whitesall SE, D'Alecy LG. Cardiopulmonary-cerebral resuscitation with 100% oxygen exacerbates neurological dysfunction following nine minutes of normothermic cardiac arrest in dogs [published correction appears in *Resuscitation*. 1994;27:267]. *Resuscitation*. 1994;27:159–170.

669. Kuisma M, Boyd J, Voipio V, Alaspää A, Roine RO, Rosenberg P. Comparison of 30 and the 100% inspired oxygen concentrations during early post-resuscitation period: a randomised controlled pilot study. *Resuscitation*. 2006;69:199–206. doi: 10.1016/j.resuscitation.2005.08.010.

670. Bennett KS, Clark AE, Meert KL, Topjian AA, Schleien CL, Shaffner DH, Dean JM, Moler FW; Pediatric Emergency Care Medicine Applied Research Network. Early oxygenation and ventilation measurements after pediatric cardiac arrest: lack of association with outcome. *Crit Care Med*. 2013;41:1534–1542. doi: 10.1097/CCM.0b013e318287f54c.

671. Guerra-Wallace MM, Casey FL 3rd, Bell MJ, Fink EL, Hickey RW. Hyperoxia and hypoxia in children resuscitated from cardiac arrest. *Pediatr Crit Care Med*. 2013;14:e143–e148. doi: 10.1097/PCC.0b013e3182720440.

672. Del Castillo J, López-Herce J, Matamoros M, Cañadas S, Rodriguez-Calvo A, Cechetti C, Rodriguez-Núñez A, Alvarez AC; Iberoamerican Pediatric Cardiac Arrest Study Network RIBEPCI. Hyperoxia, hypocapnia and hypercapnia as outcome factors after cardiac arrest in children. *Resuscitation*. 2012;83:1456–1461. doi: 10.1016/j.resuscitation.2012.07.019.
673. Ferguson LP, Durward A, Tibby SM. Relationship between arterial partial oxygen pressure after resuscitation from cardiac arrest and mortality in children. *Circulation*. 2012;126:335–342. doi: 10.1161/CIRCULATIONAHA.111.085100.
674. Sundgreen C, Larsen FS, Herzog TM, Knudsen GM, Boesgaard S, Aldershvile J. Autoregulation of cerebral blood flow in patients resuscitated from cardiac arrest. *Stroke*. 2001;32:128–132.
675. Beckstead JE, Tweed WA, Lee J, MacKeen WL. Cerebral blood flow and metabolism in man following cardiac arrest. *Stroke*. 1978;9:569–573.
676. Buunk G, van der Hoeven JG, Meinders AE. Cerebrovascular reactivity in comatose patients resuscitated from a cardiac arrest. *Stroke*. 1997;28:1569–1573.
677. Roine RO, Launes J, Nikkinen P, Lindroth L, Kaste M. Regional cerebral blood flow after human cardiac arrest: a hexamethylpropyleneamine oxime single photon emission computed tomographic study. *Arch Neurol*. 1991;48:625–629.
678. Han BK, Towbin RB, De Courten-Myers G, McLaurin RL, Ball WS Jr. Reversal sign on CT: effect of anoxic/ischemic cerebral injury in children. *AJR Am J Roentgenol*. 1990;154:361–368. doi: 10.2214/ajr.154.2.2105031.
679. Tardieu M, Devictor D, Wood C, Navelet Y, Pariente D, Huault G, Landrieu P. Prognostic factors in cerebral hypoxic-ischemias in infants less than a year old [in French]. *Arch Fr Pediatr*. 1987;44:833–838.
680. Starling RM, Shekdar K, Licht D, Nadkarni VM, Berg RA, Topjian AA. Early head CT findings are associated with outcomes after pediatric out-of-hospital cardiac arrest. *Pediatr Crit Care Med*. 2015;16:542–548. doi: 10.1097/PCC.0000000000000404.
681. Nelson TR, Fowlkes JB, Abramowicz JS, Church CC. Ultrasound biosafety considerations for the practicing sonographer and sonologist. *J Ultrasound Med*. 2009;28:139–150.
682. Bisschops LL, Hoedemaekers CW, Simons KS, van der Hoeven JG. Preserved metabolic coupling and cerebrovascular reactivity during mild hypothermia after cardiac arrest. *Crit Care Med*. 2010;38:1542–1547. doi: 10.1097/CCM.0b013e3181e2cc1e.
683. Astudillo R, van der Linden J, Ekroth R, Wesslén O, Hallhagen S, Scallan M, Shore D, Lincoln C. Absent diastolic cerebral blood flow velocity after circulatory arrest but not after low flow in infants. *Ann Thorac Surg*. 1993;56:515–519.
684. Doepp Connolly F, Reitemeier J, Storm C, Hasper D, Schreiber SJ. Duplex sonography of cerebral blood flow after cardiac arrest: a prospective observational study. *Resuscitation*. 2014;85:516–521. doi: 10.1016/j.resuscitation.2013.12.021.
685. Fink EL, Panigrahy A, Clark RS, Fitz CR, Landsittel D, Kochanek PM, Zuccoli G. Regional brain injury on conventional and diffusion weighted MRI is associated with outcome after pediatric cardiac arrest. *Neurocrit Care*. 2013;19:31–40. doi: 10.1007/s12028-012-9706-0.
686. Shellhaas RA, Chang T, Tsuchida T, Scher MS, Riviello JJ, Abend NS, Nguyen S, Wusthoff CJ, Clancy RR. The American Clinical Neurophysiology Society's guideline on continuous electroencephalography monitoring in neonates. *J Clin Neurophysiol*. 2011;28:611–617. doi: 10.1097/WNP.0b013e31823e96d7.
687. van Rooij LG, Toet MC, van Huffelen AC, Groenendaal F, Laan W, Zecic A, de Haan T, van Straaten IL, Vrancken S, van Wezel G, van der Sluijs J, Ter Horst H, Gavilanes D, Laroche S, Naulaers G, de Vries LS. Effect of treatment of subclinical neonatal seizures detected with aEEG: randomized, controlled trial. *Pediatrics*. 2010;125:e358–e366. doi: 10.1542/peds.2009-0136.
688. Abend NS, Dlugos DJ, Clancy RR. A review of long-term EEG monitoring in critically ill children with hypoxic-ischemic encephalopathy, congenital heart disease, ECMO, and stroke. *J Clin Neurophysiol*. 2013;30:134–142. doi: 10.1097/WNP.0b013e3182872af9.
689. Abend NS, Topjian A, Ichord R, Herman ST, Helfaer M, Donnelly M, Nadkarni V, Dlugos DJ, Clancy RR. Electroencephalographic monitoring during hypothermia after pediatric cardiac arrest. *Neurology*. 2009;72:1931–1940. doi: 10.1212/WNL.0b013e3181a82687.
690. Williams K, Jarrar R, Buchhalter J. Continuous video-EEG monitoring in pediatric intensive care units. *Epilepsia*. 2011;52:1130–1136. doi: 10.1111/j.1528-1167.2011.03070.x.
691. Hosain SA, Solomon GE, Kobylarz EJ. Electroencephalographic patterns in unresponsive pediatric patients. *Pediatr Neurol*. 2005;32:162–165. doi: 10.1016/j.pediatrneurol.2004.09.008.
692. Jette N, Claassen J, Emerson RG, Hirsch LJ. Frequency and predictors of nonconvulsive seizures during continuous electroencephalographic monitoring in critically ill children. *Arch Neurol*. 2006;63:1750–1755. doi: 10.1001/archneur.63.12.1750.
693. Abend NS, Dlugos DJ. Nonconvulsive status epilepticus in a pediatric intensive care unit. *Pediatr Neurol*. 2007;37:165–170. doi: 10.1016/j.pediatrneurol.2007.05.012.
694. Alehan FK, Morton LD, Pellock JM. Utility of electroencephalography in the pediatric emergency department. *J Child Neurol*. 2001;16:484–487. doi: 10.1177/088307380101600704.
695. Tay SK, Hirsch LJ, Leary L, Jette N, Wittman J, Akman CI. Nonconvulsive status epilepticus in children: clinical and EEG characteristics. *Epilepsia*. 2006;47:1504–1509. doi: 10.1111/j.1528-1167.2006.00623.x.
696. Saengpattrachai M, Sharma R, Hunjan A, Shroff M, Ochi A, Otsubo H, Cortez MA, Carter Snead O 3rd. Nonconvulsive seizures in the pediatric intensive care unit: etiology, EEG, and brain imaging findings. *Epilepsia*. 2006;47:1510–1518. doi: 10.1111/j.1528-1167.2006.00624.x.
697. DeLorenzo RJ, Waterhouse EJ, Towne AR, Boggs JG, Ko D, DeLorenzo GA, Brown A, Garnett L. Persistent nonconvulsive status epilepticus after the control of convulsive status epilepticus. *Epilepsia*. 1998;39:833–840.
698. Jaitly R, Sgro JA, Towne AR, Ko D, DeLorenzo RJ. Prognostic value of EEG monitoring after status epilepticus: a prospective adult study. *J Clin Neurophysiol*. 1997;14:326–334.
699. Wijdicks EF, Hijdra A, Young GB, Bassetti CL, Wiebe S; Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: prediction of outcome in comatose survivors after cardiopulmonary resuscitation (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2006;67:203–210. doi: 10.1212/01.wnl.0000227183.21314.cd.
700. Roest A, van Bets B, Jorens PG, Baar I, Weyler J, Mercelis R. The prognostic value of the EEG in postanoxic coma. *Neurocrit Care*. 2009;10:318–325. doi: 10.1007/s12028-008-9178-4.
701. Synek VM. Prognostically important EEG coma patterns in diffuse anoxic and traumatic encephalopathies in adults. *J Clin Neurophysiol*. 1988;5:161–174.
702. Young GB, McLachlan RS, Kreeft JH, Demelo JD. An electroencephalographic classification for coma. *Can J Neurol Sci*. 1997;24:320–325.
703. Nishisaki A, Sullivan J 3rd, Steger B, Bayer CR, Dlugos D, Lin R, Ichord R, Helfaer MA, Nadkarni V. Retrospective analysis of the prognostic value of electroencephalography patterns obtained in pediatric in-hospital cardiac arrest survivors during three years. *Pediatr Crit Care Med*. 2007;8:10–17. doi: 10.1097/01.pcc.0000256621.63135.4b.
704. Kessler SK, Topjian AA, Gutierrez-Colina AM, Ichord RN, Donnelly M, Nadkarni VM, Berg RA, Dlugos DJ, Clancy RR, Abend NS. Short-term outcome prediction by electroencephalographic features in children treated with therapeutic hypothermia after cardiac arrest. *Neurocrit Care*. 2011;14:37–43. doi: 10.1007/s12028-010-9450-2.
705. Watzman HM, Kurth CD, Montenegro LM, Rome J, Steven JM, Nicolson SC. Arterial and venous contributions to near-infrared cerebral oximetry. *Anesthesiology*. 2000;93:947–953.
706. Kurth CD, Levy WJ, McCann J. Near-infrared spectroscopy cerebral oxygen saturation thresholds for hypoxia-ischemia in piglets. *J Cereb Blood Flow Metab*. 2002;22:335–341. doi: 10.1097/00004647-200203000-00011.
707. Lee JK, Yang ZJ, Wang B, Larson AC, Jamrogowicz JL, Kulikowicz E, Kibler KK, Mytar JO, Carter EL, Burman HT, Brady KM, Smielewski P, Czosnyka M, Koehler RC, Shaffner DH. Noninvasive autoregulation monitoring in a swine model of pediatric cardiac arrest. *Anesth Analg*. 2012;114:825–836. doi: 10.1213/ANE.0b013e31824762d5.
708. Saugstad OD, Ramji S, Soll RF, Vento M. Resuscitation of newborn infants with 21% or 100% oxygen: an updated systematic review and meta-analysis. *Neonatology*. 2008;94:176–182. doi: 10.1159/000143397.
709. Davis PG, Tan A, O'Donnell CP, Schulze A. Resuscitation of newborn infants with 100% oxygen or air: a systematic review and meta-analysis. *Lancet*. 2004;364:1329–1333. doi: 10.1016/S0140-6736(04)17189-4.
710. Jaskiewicz JA, McCarthy CA, Richardson AC, White KC, Fisher DJ, Dagan R, Powell KR; Febrile Infant Collaborative Study Group. Febrile infants at low risk for serious bacterial infection: an appraisal of the Rochester criteria and implications for management. *Pediatrics*. 1994;94:390–396.
711. Hickey RW, Kochanek PM, Ferimer H, Graham SH, Safar P. Hypothermia and hyperthermia in children after resuscitation from cardiac arrest. *Pediatrics*. 2000;106(pt 1):118–122.

712. Bembea MM, Nadkarni VM, Diener-West M, Venugopal V, Carey SM, Berg RA, Hunt EA; American Heart Association National Registry of Cardiopulmonary Resuscitation Investigators. Temperature patterns in the early postresuscitation period after pediatric inhospital cardiac arrest. *Pediatr Crit Care Med*. 2010;11:723–730. doi: 10.1097/PCC.0b013e3181dde659.
713. Laptook A, Tyson J, Shankaran S, McDonald S, Ehrenkranz R, Fanaroff A, Donovan E, Goldberg R, O'Shea TM, Higgins RD, Poole WK; National Institute of Child Health and Human Development Neonatal Research Network. Elevated temperature after hypoxic-ischemic encephalopathy: risk factor for adverse outcomes. *Pediatrics*. 2008;122:491–499. doi: 10.1542/peds.2007-1673.
714. Laptook AR, McDonald SA, Shankaran S, Stephens BE, Vohr BR, Guillet R, Higgins RD, Das A; Extended Hypothermia Follow-up Subcommittee of the National Institute of Child Health and Human Development Neonatal Research Network. Elevated temperature and 6- to 7-year outcome of neonatal encephalopathy. *Ann Neurol*. 2013;73:520–528. doi: 10.1002/ana.23843.
715. Bernard SA, Gray TW, Buist MD, Jones BM, Silvester W, Gutteridge G, Smith K. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med*. 2002;346:557–563. doi: 10.1056/NEJMoa003289.
716. The Hypothermia After Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest [published correction appears in *N Engl J Med*. 2002;346:1756]. *N Engl J Med*. 2002;346:549–556.
717. Gluckman PD, Wyatt JS, Azzopardi D, Ballard R, Edwards AD, Ferriero DM, Polin RA, Robertson CM, Thoresen M, Whitelaw A, Gunn AJ. Selective head cooling with mild systemic hypothermia after neonatal encephalopathy: multicentre randomised trial. *Lancet*. 2005;365:663–670. doi: 10.1016/S0140-6736(05)17946-X.
718. Moler FW, Silverstein FS, Holubkov R, Slomine BS, Christensen JR, Nadkarni VM, Meert KL, Clark AE, Browning B, Pemberton VL, Page K, Shankaran S, Hutchison JS, Newth CJ, Bennett KS, Berger JT, Topjian A, Pineda JA, Koch JD, Schleien CL, Dalton HJ, Ofori-Amanfo G, Goodman DM, Fink EL, McQuillen P, Zimmerman JJ, Thomas NJ, van der Jagt EW, Porter MB, Meyer MT, Harrison R, Pham N, Schwarz AJ, Nowak JE, Alten J, Wheeler DS, Bhalala US, Lidsky K, Lloyd E, Mathur M, Shah S, Wu T, Theodorou AA, Sanders RC Jr, Dean JM; THAPCA Trial Investigators. Therapeutic hypothermia after out-of-hospital cardiac arrest in children. *N Engl J Med*. 2015;372:1898–1908. doi: 10.1056/NEJMoa1411480.
719. Fink EL, Clark RS, Kochanek PM, Bell MJ, Watson RS. A tertiary care center's experience with therapeutic hypothermia after pediatric cardiac arrest. *Pediatr Crit Care Med*. 2010;11:66–74. doi: 10.1097/PCC.0b013e3181c58237.
720. Doherty DR, Parshuram CS, Gaboury I, Hoskote A, Lacroix J, Tucci M, Joffe A, Choong K, Farrell R, Bohn DJ, Hutchison JS; Canadian Critical Care Trials Group. Hypothermia therapy after pediatric cardiac arrest. *Circulation*. 2009;119:1492–1500. doi: 10.1161/CIRCULATIONAHA.108.791384.
721. Fink EL, Kochanek PM, Clark RS, Bell MJ. How I cool children in neurocritical care. *Neurocrit Care*. 2010;12:414–420. doi: 10.1007/s12028-010-9334-5.
722. Topjian A, Dominguez T, Boyce J, Ichord R, MA H and Nadkarni V. Surface cooling induced therapeutic hypothermia following pediatric cardiac arrest. *Circulation*. 2007;116(suppl):II_945.
723. Kasner SE, Wein T, Piriyawat P, Villar-Cordova CE, Chalela JA, Krieger DW, Morgenstern LB, Kimmel SE, Grotta JC. Acetaminophen for altering body temperature in acute stroke: a randomized clinical trial. *Stroke*. 2002;33:130–134.
724. Koennecke HC, Leistner S. Prophylactic antipyretic treatment with acetaminophen in acute ischemic stroke: a pilot study. *Neurology*. 2001;57:2301–2303.
725. Polderman KH. Application of therapeutic hypothermia in the intensive care unit: opportunities and pitfalls of a promising treatment modality, part 2: practical aspects and side effects. *Intensive Care Med*. 2004;30:757–769.
726. Shankaran S, Pappas A, Laptook AR, McDonald SA, Ehrenkranz RA, Tyson JE, Walsh M, Goldberg RN, Higgins RD, Das A; NICHD Neonatal Research Network. Outcomes of safety and effectiveness in a multicenter randomized, controlled trial of whole-body hypothermia for neonatal hypoxic-ischemic encephalopathy. *Pediatrics*. 2008;122:e791–e798. doi: 10.1542/peds.2008-0456.
727. Thoresen M, Whitelaw A. Cardiovascular changes during mild therapeutic hypothermia and rewarming in infants with hypoxic-ischemic encephalopathy. *Pediatrics*. 2000;106(pt 1):92–99.
728. Gebauer CM, Knuepfer M, Robel-Tillig E, Pulzer F, Vogtmann C. Hemodynamics among neonates with hypoxic-ischemic encephalopathy during whole-body hypothermia and passive rewarming. *Pediatrics*. 2006;117:843–850. doi: 10.1542/peds.2004-1587.
729. Buratti S, Lampugnani E, Tuo P, Moscatelli A. Congenital diaphragmatic hernia repair during whole body hypothermia for neonatal hypoxic ischemic encephalopathy. *J Perinatol*. 2012;32:981–984. doi: 10.1038/jp.2012.29.
730. Shah SK, Khan AM, Cox CS Jr. Pulmonary hypertensive crisis requiring ECMO associated with re-warming from whole body hypothermia for hypoxic ischemic encephalopathy: clinical observations from a case series. *Eur J Pediatr Surg*. 2010;20:205–206. doi: 10.1055/s-0029-1241872.
731. Sarkar S, Barks JD, Bhagat I, Dechert R, Donn SM. Pulmonary dysfunction and therapeutic hypothermia in asphyxiated newborns: whole body versus selective head cooling. *Am J Perinatol*. 2009;26:265–270. doi: 10.1055/s-0028-1103154.
732. Lebiedz P, Meiners J, Samol A, Wasmer K, Reinecke H, Waltenberger J, Eckardt L. Electrocardiographic changes during therapeutic hypothermia. *Resuscitation*. 2012;83:602–606. doi: 10.1016/j.resuscitation.2011.11.016.
733. Aktas MK, Aguila A. Successful therapeutic hypothermia in patients with congenital long QT syndrome. *Ann Noninvasive Electrocardiol*. 2011;16:100–103. doi: 10.1111/j.1542-474X.2010.00400.x.
734. Gunn AJ, Gluckman PD, Gunn TR. Selective head cooling in newborn infants after perinatal asphyxia: a safety study. *Pediatrics*. 1998;102(pt 1):885–892.
735. Tiainen M, Parikka HJ, Mäkijärvi MA, Takkunen OS, Sarna SJ, Roine RO. Arrhythmias and heart rate variability during and after therapeutic hypothermia for cardiac arrest. *Crit Care Med*. 2009;37:403–409. doi: 10.1097/CCM.0b013e31819572c4.
736. Yanta J, Guyette FX, Doshi AA, Callaway CW, Rittenberger JC; Post Cardiac Arrest Service. Renal dysfunction is common following resuscitation from out-of-hospital cardiac arrest. *Resuscitation*. 2013;84:1371–1374. doi: 10.1016/j.resuscitation.2013.03.037.
737. Bellomo R, Ronco C, Kellum J, Mehta R, Palevsky P; Acute Dialysis Quality Initiative Workgroup. Acute renal failure: definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care*. 2004;8:R204–R212.
738. Krawczeski CD, Goldstein SL, Woo JG, Wang Y, Piyaphanee N, Ma Q, Bennett M, Devarajan P. Temporal relationship and predictive value of urinary acute kidney injury biomarkers after pediatric cardiopulmonary bypass. *J Am Coll Cardiol*. 2011;58:2301–2309. doi: 10.1016/j.jacc.2011.08.017.
739. Brienza N, Giglio MT, Dalfino L. Protocoled resuscitation and the prevention of acute kidney injury. *Curr Opin Crit Care*. 2012;18:613–622. doi: 10.1097/MCC.0b013e32835944d6.
740. Joannidis M, Druml W, Forni LG, Groeneveld AB, Honore P, Oudemans-van Straaten HM, Ronco C, Schetz MR, Woittiez AJ; Critical Care Nephrology Working Group of the European Society of Intensive Care Medicine. Prevention of acute kidney injury and protection of renal function in the intensive care unit: expert opinion of the Working Group for Nephrology, ESICM [published correction appears in *Intensive Care Med*. 2010;36:727]. *Intensive Care Med*. 2010;36:392–411. doi: 10.1007/s00134-009-1678-y.
741. Goldstein SL, Currier H, Graf JM, Cosio CC, Brewer ED, Sachdeva R. Outcome in children receiving continuous venovenous hemofiltration. *Pediatrics*. 2001;107:1309–1312.
742. Selewski DT, Jordan BK, Askenazi DJ, Dechert RE, Sarkar S. Acute kidney injury in asphyxiated newborns treated with therapeutic hypothermia. *J Pediatr*. 2013;162:725–729.e1. doi: 10.1016/j.jpeds.2012.10.002.
743. Susantitaphong P, Alfayez M, Cohen-Bucay A, Balk EM, Jaber BL. Therapeutic hypothermia and prevention of acute kidney injury: a meta-analysis of randomized controlled trials. *Resuscitation*. 2012;83:159–167. doi: 10.1016/j.resuscitation.2011.09.023.
744. Losek JD. Hypoglycemia and the ABC'S (sugar) of pediatric resuscitation. *Ann Emerg Med*. 2000;35:43–46.
745. Srinivasan V, Spinella PC, Drott HR, Roth CL, Helfaer MA, Nadkarni V. Association of timing, duration, and intensity of hyperglycemia with intensive care unit mortality in critically ill children. *Pediatr Crit Care Med*. 2004;5:329–336.

746. Van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, Vlasselaers D, Ferdinande P, Lauwers P, Bouillon R. Intensive insulin therapy in critically ill patients. *N Engl J Med*. 2001;345:1359–1367. doi: 10.1056/NEJMoa011300.
747. Van den Berghe G, Wilmer A, Hermans G, Meersseman W, Wouters PJ, Milants I, Van Wijngaerden E, Bobbaers H, Bouillon R. Intensive insulin therapy in the medical ICU. *N Engl J Med*. 2006;354:449–461. doi: 10.1056/NEJMoa052521.
748. The NICE-SUGAR Study Investigators. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med*. 2009;360:1283–1297. doi: 10.1056/NEJMoa0810625.
749. Marik PE, Preiser JC. Toward understanding tight glycemic control in the ICU: a systematic review and metaanalysis. *Chest*. 2010;137:544–551. doi: 10.1378/chest.09-1737.
750. Polito A, Thiagarajan RR, Laussen PC, Gauvreau K, Agus MS, Scheurer MA, Pigula FA, Costello JM. Association between intraoperative and early postoperative glucose levels and adverse outcomes after complex congenital heart surgery. *Circulation*. 2008;118:2235–2242. doi: 10.1161/CIRCULATIONAHA.108.804286.
751. Mesotten D, Gielen M, Sterken C, Claessens K, Hermans G, Vlasselaers D, Lemiere J, Lagae L, Gewillig M, Eyskens B, Vanhorebeek I, Wouters PJ, Van den Berghe G. Neurocognitive development of children 4 years after critical illness and treatment with tight glucose control: a randomized controlled trial. *JAMA*. 2012;308:1641–1650. doi: 10.1001/jama.2012.12424.
752. Agus MS, Steil GM, Wypij D, Costello JM, Laussen PC, Langer M, Alexander JL, Scoppettuolo LA, Pigula FA, Charpie JR, Ohye RG, Gaies MG; SPECS Study Investigators. Tight glycemic control versus standard care after pediatric cardiac surgery. *N Engl J Med*. 2012;367:1208–1219. doi: 10.1056/NEJMoa1206044.
753. Macrae D, Grieve R, Allen E, Sadique Z, Morris K, Pappachan J, Parslow R, Tasker RC, Elbourne D; CHiP Investigators. A randomized trial of hyperglycemic control in pediatric intensive care [published correction appears in *N Engl J Med*. 2014;370:1469]. *N Engl J Med*. 2014;370:107–118. doi: 10.1056/NEJMoa1302564.
754. Vannucci RC, Vannucci SJ. Hypoglycemic brain injury. *Semin Neonatol*. 2001;6:147–155. doi: 10.1053/siny.2001.0044.
755. Salhab WA, Wyckoff MH, Laptook AR, Perlman JM. Initial hypoglycemia and neonatal brain injury in term infants with severe fetal acidemia. *Pediatrics*. 2004;114:361–366.
756. Yanpeng L, Greisen G. Analysis of the risk of brain damage in asphyxiated infants. *J Perinat Med*. 1996;24:581–589.
757. Mir NA, Faquih AM, Legnain M. Perinatal risk factors in birth asphyxia: relationship of obstetric and neonatal complications to neonatal mortality in 16,365 consecutive live births. *Asia Oceania J Obstet Gynaecol*. 1989;15:351–357.
758. Vespa P, McArthur DL, Stein N, Huang SC, Shao W, Filippou M, Etchepare M, Glenn T, Hovda DA. Tight glycemic control increases metabolic distress in traumatic brain injury: a randomized controlled within-subjects trial. *Crit Care Med*. 2012;40:1923–1929. doi: 10.1097/CCM.0b013e31824e0fcc.
759. Duning T, van den Heuvel I, Dickmann A, Volkert T, Wempe C, Reinholz J, Lohmann H, Freise H, Ellger B. Hypoglycemia aggravates critical illness-induced neurocognitive dysfunction. *Diabetes Care*. 2010;33:639–644. doi: 10.2337/dc09-1740.
760. Hékimian G, Baugnon T, Thuong M, Monchi M, Dabbane H, Jaby D, Rhaoui A, Laurent I, Moret G, Fraisse F, Adrie C. Cortisol levels and adrenal reserve after successful cardiac arrest resuscitation. *Shock*. 2004;22:116–119.
761. Pene F, Hyvernat H, Mallet V, Cariou A, Carli P, Spaulding C, Dugue MA, Mira JP. Prognostic value of relative adrenal insufficiency after out-of-hospital cardiac arrest. *Intensive Care Med*. 2005;31:627–633. doi: 10.1007/s00134-005-2603-7.
762. Kim JJ, Lim YS, Shin JH, Yang HJ, Kim JK, Hyun SY, Rhoo I, Hwang SY, Lee G. Relative adrenal insufficiency after cardiac arrest: impact on postresuscitation disease outcome. *Am J Emerg Med*. 2006;24:684–688. doi: 10.1016/j.ajem.2006.02.017.
763. Miller JB, Donnino MW, Rogan M, Goyal N. Relative adrenal insufficiency in post-cardiac arrest shock is under-recognized. *Resuscitation*. 2008;76:221–225. doi: 10.1016/j.resuscitation.2007.07.034.
764. de Jong MF, Beishuizen A, de Jong MJ, Girbes AR, Groeneveld AB. The pituitary-adrenal axis is activated more in non-survivors than in survivors of cardiac arrest, irrespective of therapeutic hypothermia. *Resuscitation*. 2008;78:281–288. doi: 10.1016/j.resuscitation.2008.03.227.
765. Kim JJ, Hyun SY, Hwang SY, Jung YB, Shin JH, Lim YS, Cho JS, Yang HJ, Lee G. Hormonal responses upon return of spontaneous circulation after cardiac arrest: a retrospective cohort study. *Crit Care*. 2011;15:R53. doi: 10.1186/cc10019.
766. Mentzelopoulos SD, Malachias S, Chamos C, Konstantopoulos D, Ntaidou T, Papastylianou A, Kolliantzaki I, Theodoridi M, Ischaki H, Makris D, Zakynthinos E, Zintzaras E, Sourlas S, Aloizos S, Zakynthinos SG. Vasopressin, steroids, and epinephrine and neurologically favorable survival after in-hospital cardiac arrest: a randomized clinical trial. *JAMA*. 2013;310:270–279. doi: 10.1001/jama.2013.7832.
767. Millar KJ, Thiagarajan RR, Laussen PC. Glucocorticoid therapy for hypotension in the cardiac intensive care unit. *Pediatr Cardiol*. 2007;28:176–182. doi: 10.1007/s00246-006-0053-9.
768. Plumpton KR, Anderson BJ, Beca J. Thyroid hormone and cortisol concentrations after congenital heart surgery in infants younger than 3 months of age. *Intensive Care Med*. 2010;36:321–328. doi: 10.1007/s00134-009-1648-4.
769. Wald EL, Preze E, Eickhoff JC, Backer CL. The effect of cardiopulmonary bypass on the hypothalamic-pituitary-adrenal axis in children. *Pediatr Crit Care Med*. 2011;12:190–196. doi: 10.1097/PCC.0b013e3181f36d17.
770. Morrison LJ, Kierzek G, Diekema DS, Sayre MR, Silvers SM, Idris AH, Mancini ME. Part 3: ethics: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2010;122(suppl 3):S665–S675. doi: 10.1161/CIRCULATIONAHA.110.970905.
771. Mancini ME, Diekema DS, Hoadley TA, Kadlec KD, Leveille MH, McGowan JE, Munkwitz MM, Panchal AR, Sayre MR, Sinz EH. Part 3: ethical issues: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132(suppl 2):S383–S396. doi: 10.1161/CIR.0000000000000254.
772. Boyle D, Carlo WA, Goldsmith J, Halamek L, Perlman J, Wiswell TE, Kattwinkel J, Engle W, Gonzalez JL, Singhal N, Nightengale B, Myers T; American Academy of Pediatrics Neonatal Resuscitation Program Steering Committee. Born-Alive Infants Protection Act of 2001, Public Law No. 107-207. *Pediatrics*. 2003;111:680–681.
773. American Academy of Pediatrics Committee on Bioethics. Ethics and the care of critically ill infants and children. *Pediatrics*. 1996;98:149–152.
774. American Academy of Pediatrics Committee on Bioethics. Guidelines on foregoing life-sustaining medical treatment. *Pediatrics*. 1994;93:532–536.
775. Nondiscrimination on the basis of handicap: procedures and guidelines relating to health care for handicapped infants: HHS: final rules. *Fed Regist*. 1984;49:1622–1654.
776. Kopelman LM. Are the 21-year-old Baby Doe rules misunderstood or mistaken? *Pediatrics*. 2005;115:797–802. doi: 10.1542/peds.2004-2326.

Cardiopulmonary Resuscitation in Infants and Children With Cardiac Disease: A Scientific Statement From the American Heart Association

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Circulation. published online April 23, 2018;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539