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Association of Intra-arrest Transport vs Continued On-Scene Resuscitation With Survival to Hospital Discharge Among Patients With Out-of-Hospital Cardiac Arrest

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IMPORTANCE There is wide variability among emergency medical systems (EMS) with respect to transport to hospital during out-of-hospital cardiac arrest (OHCA) resuscitative efforts. The benefit of intra-arrest transport during resuscitation compared with continued on-scene resuscitation is unclear.

OBJECTIVE To determine whether intra-arrest transport compared with continued on-scene resuscitation is associated with survival to hospital discharge among patients experiencing OHCA.

DESIGN, SETTING, AND PARTICIPANTS Cohort study of prospectively collected consecutive nontraumatic adult EMS-treated OHCA data from the Resuscitation Outcomes Consortium (ROC) Cardiac Epidemiologic Registry (enrollment, April 2011-June 2015 from 10 North American sites; follow-up until the date of hospital discharge or death [regardless of when either event occurred]). Patients treated with intra-arrest transport (exposed) were matched with patients in refractory arrest (at risk of intra-arrest transport) at that same time (unexposed), using a time-dependent propensity score. Subgroups categorized by initial cardiac rhythm and EMS-witnessed cardiac arrests were analyzed.

EXPOSURES Intra-arrest transport (transport initiated prior to return of spontaneous circulation), compared with continued on-scene resuscitation.

MAIN OUTCOMES AND MEASURES The primary outcome was survival to hospital discharge, and the secondary outcome was survival with favorable neurological outcome (modified Rankin scale <3) at hospital discharge.

RESULTS The full cohort included 43 969 patients with a median age of 67 years (interquartile range, 55-80), 37% were women, 86% of cardiac arrests occurred in a private location, 49% were bystander- or EMS-witnessed, 22% had initial shockable rhythms, 97% were treated by out-of-hospital advanced life support, and 26% underwent intra-arrest transport. Survival to hospital discharge was 3.8% for patients who underwent intra-arrest transport and 12.6% for those who received on-scene resuscitation. In the propensity-matched cohort, which included 27 705 patients, survival to hospital discharge occurred in 4.0% of patients who underwent intra-arrest transport vs 8.5% who received on-scene resuscitation (risk difference, 4.6% [95% CI, 4.0%- 5.1%]). Favorable neurological outcome occurred in 2.9% of patients who underwent intra-arrest transport vs 7.1% who received on-scene resuscitation (risk difference, 4.2% [95% CI, 3.5%-4.9%]). Subgroups of initial shockable and nonshockable rhythms as well as EMS-witnessed and unwitnessed cardiac arrests all had a significant association between intra-arrest transport and lower probability of survival to hospital discharge.

CONCLUSIONS AND RELEVANCE Among patients experiencing out-of-hospital cardiac arrest, intra-arrest transport to hospital compared with continued on-scene resuscitation was associated with lower probability of survival to hospital discharge. Study findings are limited by potential confounding due to observational design.

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Emergency medical services (EMS) personnel follow established guidelines for the treatment of out-of-hospital cardiac arrest (OHCA).[1-5] If, and when, patients without return of spontaneous circulation (ROSC) are transported to the hospital, however, varies considerably by agency and region.[6] Previous data show wide variability in rates of intra-arrest transport, with some EMS agencies transporting nearly all patients regardless of ROSC, while for others this practice is uncommon if ROSC is not achieved.[6]

Interventional clinical trial data comparing strategies of intra-arrest transport vs the same duration of continued on-scene treatment are lacking. Further evidence is required to determine the potential patient outcomes related to transport with ongoing resuscitation compared with continued efforts on scene, especially given the potential risk to paramedic and public safety that may be attributed to intra-arrest transport.[7]

It is unclear if and to what extent resuscitation quality may be altered by transport to hospital.[8,9] However, in EMS systems where full advanced cardiac life support therapies are available at the scene of the cardiac arrest—the same algorithms that are followed in the emergency department—the mechanism of benefit from intra-arrest transport is debatable. A clinical trial, randomizing to either exclusive on-scene resuscitation or transport to the hospital at a prespecified time (if ROSC is not achieved) would offer the best level of evidence but would require a large sample size and would be limited to a constrained number of intra-arrest transport criteria. Hence, this cohort study used the large population-based cardiac arrest cohort from the Resuscitation Outcomes Consortium (ROC). The primary aim was to determine, among adult patients in refractory arrest, the association of intra-arrest transport compared with continuation of on-scene resuscitation, with respect to survival at hospital discharge.

Key Points

Question Is transport to hospital during adult out-of-hospital cardiac arrest resuscitation compared with continued on-scene treatment associated with a difference in survival to hospital discharge?

Findings In this cohort study that used a time-dependent propensity score–matched analysis including 27 705 patients with out-of-hospital cardiac arrest, intra-arrest transport compared with continued on-scene resuscitation had a probability of survival to hospital discharge of 4.0% vs 8.5%, a difference that was statistically significant.

Meaning These results do not support the practice of routinely transporting patients during resuscitation from out-of-hospital cardiac arrest to the hospital.

Methods

Study Design

We performed a secondary analysis from the ROC Cardiac Epidemiologic Registry-Cardiac Arrest OHCA registry. The registry and secondary analyses were approved by research ethics boards for each participating site, which also waived the requirement for informed consent.[10] These data are publicly available from the National Heart, Lung, and Blood Institute Biologic Specimen and Data Repository Information Coordinating Centre, which can be used to replicate the methods of this investigation.

Study Setting and Data Collection

We used a prospective population-based registry of 10 North American study sites that included consecutive EMS-assessed nontraumatic OHCAs between 2005 and 2015.[10] Trained research personnel at individual sites identified OHCA through dispatch logs, patient care records, defibrillator files, and hospital records. Patient characteristics and time-stamped treatments, interventions, and events were recorded according to standard definitions.[11] Chest compression fraction was measured within the first 10 minutes of the professional resuscitation. There were 2 clinical trials which took place during the study period (participants were included in the registry); one comparing continuous vs interrupted chest compressions and the other comparing 2 antiarrhythmic drugs with placebo for refractory ventricular fibrillation.[12,13] Neither of these trials demonstrated a statistically significant benefit in either group under investigation,[12,13] suggesting that a low risk of bias is introduced from inclusion in observational analyses. The registry collected hospital discharge outcomes of survival for all patients and neurological status for clinical trial–enrolled patients, both of which are ascertained from review of patients' medical records.[13] ROC clinical trial patients have demonstrated similar patient characteristics and outcomes when compared with nonenrolled patients.[14]

EMS Medical Care

Out-of-hospital medical care of the ROC EMS agencies consisted of a coordinated effort between fire department first responders, emergency medical technicians, and paramedics trained in basic life support (BLS) alone or in BLS plus advanced life support (ALS).[1,2] All medical care was carried out per local protocols, including decisions of hospital transport and termination of resuscitation.

Study Population and Primary Exposure

We included consecutive EMS-treated patients with nontraumatic OHCA between April 2011 and June 2015. We included patients as of April 2011 as there were differences in data definitions prior to this date and not after June 2015 as the ROC registry was discontinued (the data used in this study are the most recent data available in this registry). Follow-up for each patient was continued until the date of hospital discharge or death, regardless of when either event occurred. The registry included 192 EMS agencies grouped into 44 treatment regions to achieve a similar number of patients per region and to consolidate overlapping EMS agencies with similar treatment practices. OHCA was defined as persons found apneic and without a pulse who received one of the following interventions: (1) external defibrillation by bystanders or EMS; or (2) chest compressions from EMS.[10] Patients with the following characteristics were excluded: (1) age younger than 18 years; (2) those in whom resuscitative efforts were ceased when a do-not-resuscitate order was discovered; (3) transport was initiated prior to the cardiac arrest; (4) missing time data required to classify as intra-arrest transport or to classify the primary outcome; and, (5) with missing variables required for the propensity score analysis. The primary variable of interest was intra-arrest transport, defined as transport to the hospital initiated prior to any episodes of ROSC. All other patients were classified as receiving on-scene resuscitation.

Outcome Measures and Variable Definitions

The primary end point was survival to hospital discharge. The secondary end point was survival with favorable neurological outcome, defined as a modified Rankin scale of less than 3 at hospital discharge (range: 0, no symptoms or disability; 3, moderate disability, requires some help but able to walk without assistance; 6, death).[11] The definition for ROSC was a palpable pulse for any duration.[11] Time intervals for resuscitation events were calculated between the time that EMS commenced resuscitation and the time the event occurred.

Statistical Analysis

We used R (Foundation for Statistical Computing, Vienna, Austria) for analysis. Categorical variables were reported as counts (frequencies) and continuous variables as means (with standard deviation). Standardized mean differences were used to compare patients excluded due to missing data with the full study cohort. A *P* value of less than .05 was considered a significant result for all analyses.

Primary Analysis

For primary analyses, a time-dependent propensity score analysis was used (based on a model design previously described).[15-17] This methodology accounts for resuscitation time bias in which those eligible for intra-arrest transport have already failed initial resuscitative efforts, which is a predictor of poor outcomes.[18] The linear component of a Cox proportional hazards model was used to generate time-dependent propensity scores for intra-arrest transport assignment (the dependent variable). The following potential confounders of the treatment-outcome relationship were included in the model: patient age, sex, episode location (public vs not), witnessed status (bystander vs EMS vs not witnessed), bystander CPR performed (vs not), interval from 911 call to EMS arrival, initial EMS-recorded rhythm (shockable or nonshockable), etiology (presumed cardiac vs obvious noncardiac cause), ALS unit first on scene (vs not), and treatment region.[11] The proportional hazards assumption was assessed using residual plots. Patients were then paired using a time-dependent, nearest-neighbor, propensity score-matching algorithm using a maximum caliper of 0.01 standard deviations. A given intra-arrest patient (exposed) was matched (1:1) to the closest propensity score within a caliper that was still undergoing on-scene resuscitation (unexposed); ie, at risk of intra-arrest transport regardless of subsequent treatment when the given patient was transported. Exposed patients without possible matches were excluded. In the same fashion, the remaining unexposed patients were then matched with previously matched exposed patients (1 exposed patient could be matched with multiple unexposed patients). Standardized mean differences were calculated (using the stddiff package in R) for patient characteristics. The matched set was used to calculate risk differences (RDs) using the standard method for a difference between proportions, and a modified Poisson regression model with robust standard errors[19,20] was fit to estimate the association between intra-arrest transport and survival to hospital discharge, expressed as a risk ratio (RR). We repeated this analysis for the secondary end point of survival with favorable neurological outcome, including clinical trial-enrolled patients for whom neurological status data were available. We used all available patients from the registry and thus did not perform a power calculation.

Secondary Analyses

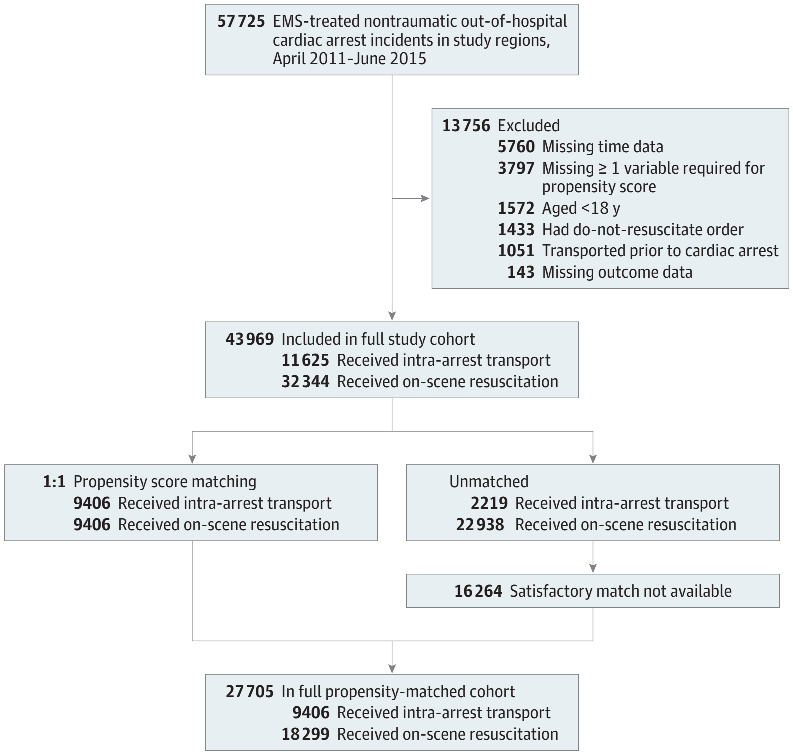
To investigate whether the association between to hospital discharge and intra-arrest transport varied depending on the time of transport, we repeated the analysis and included an interaction term between the intra-arrest transport variable and the time of matched exposure to transport. We then repeated the analysis within 5-minute time-based epochs defined by the time of matching. Because of the potential for type I error due to multiple comparisons, findings for analyses of secondary end points and subgroup analyses should be interpreted as exploratory.

We examined subgroups based on several categories: by EMS level of care (ALS first, BLS first then ALS, BLS only), EMS-witnessed status, initial cardiac rhythm, treatment with a mechanical CPR device, and study site. In addition, we created subgroups based on the universal termination of resuscitation rule[21,22]: (1) patients with EMS-witnessed arrests or initial shockable rhythm; and (2) patients with arrests that were not EMS witnessed and had initial nonshockable rhythms. All patients in this analysis were without a pulse. The initial cardiac rhythm category was used instead of grouping by any shock delivered (as stipulated in the rule) so that patients would not require reclassification at different time junctures of the resuscitation. Comparisons of subgroups were performed using robust Wald tests for interaction terms in the Poisson regression models.

Sensitivity Analyses

The primary analysis was repeated with the 1:1 propensity-matched cohort. Although a smaller cohort, as these patients were matched first, the comparator groups were more closely aligned. Second, although the treatment region was included in the propensity score, we repeated the primary analysis with a random-effects Poisson regression model fit by maximum likelihood with site as a random effect. In a third sensitivity analysis, we repeated the primary analysis and included cases that were excluded due to missing data and conducted multiple imputation using 5 hot-deck imputations based on all variables used in the analysis.

Figure 1. Flow of Participants in a Study of Intra-arrest Transport vs On-Scene Resuscitation in Patients With Out-of-Hospital Cardiac Arrest



EMS indicates emergency medical system. Unmatched on-scene resuscitation patients were matched with the best possible intra-arrest transport patient within 1 caliper. Of the 9406 intra-arrest transport patients in the full matched set, 6025 were matched with 1 on-scene resuscitation patient, 1024 were matched with 2 on-scene resuscitation patients, and the remaining 2357 were matched with 3 or more on-scene resuscitation patients.

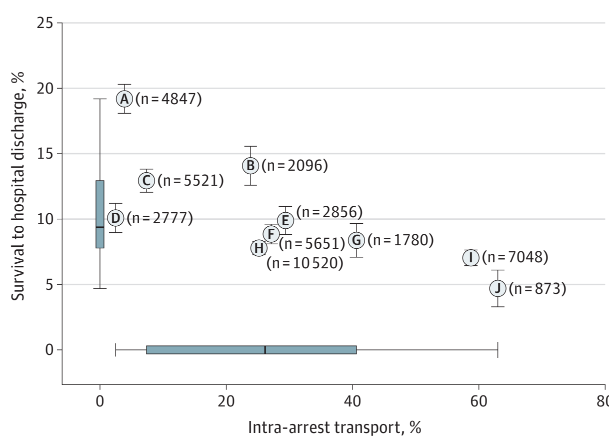
Results

Characteristics of Study Patients

A total of 57 725 consecutive OHCAs were treated by EMS in the study regions (**Figure 1**) between April 2011 and June 2015 (inclusive). eTable 1 in the Supplement shows characteristics of patients excluded due to missing data. After exclusions, 43 969 patients were included in this study, of whom 11 625 (26%) underwent intra-arrest transport and 32 344 (74%) were treated with on-scene resuscitation until ROSC or termination of resuscitation. **Figure 2** demonstrates the variability among the 10 study sites with respect to intra-arrest transport and overall survival to hospital discharge. The median duration of transport from the scene to the hospital was similar between study sites (eTable 2 in the Supplement), with an overall median of 9.9 minutes (interquartile range [IQR], 6.8-13.4).

Table 1 shows patient characteristics of the full study cohort, dichotomized by whether the patient was treated with intra-arrest transport or on-scene resuscitation until termination of resuscitation or ROSC. Survival to hospital discharge was 3.8% for patients who received intra-arrest transport and 12.6% for those who received on-scene resuscitation (**Table 2**). Overall, the mean (SD) duration of attempted out-of-hospital resuscitation was 21.8 (11.8) minutes. A total of 17 468 (40%) achieved out-of-hospital ROSC, and 18 373 (42%) had medical care terminated in the out-of-hospital setting. Among those treated with intra-arrest transport 1834/11 625 (16%) achieved ROSC prior to hospital arrival. Of the 446 intra-arrest transport survivors, 265 (59%) achieved ROSC between the times

Figure 2. Relationship Between Overall Survival by Study Site and the Proportion of Patients Treated With Intra-arrest Transport Using the Full Study Cohort (N = 43 969)



Study sites are ordered by overall survival, from A to J. Numbers in parentheses indicate the number of patients from each study site; error bars indicate 95% CIs for the proportion of survival at hospital discharge. Box plots display the median (solid line in the box), interquartile range (ends of the box), and range (whiskers) of unadjusted study site proportions for survival and intra-arrest transport. Point locations for E and F are minimally adjusted to avoid overlap.

Table 1. Patient Characteristics of the Full Study Cohort and Full Propensity-Matched Cohort[a]

	Full study cohort			Full propensity-matched cohort[b]		
	No. (%)			No. (%)		
	Intra-arrest transport (n = 11 625)	On-scene resuscitation (n = 32 344)	Absolute difference (95% CI)[c]	Intra-arrest transport (n = 9406)[d]	On-scene resuscitation (n = 18 299)[e]	Standard mean difference[f]
Sex						
Women	3943 (33.9)	12 141 (37.5)	−3.6 (−4.6 to −2.6)	3213 (34.2)	6551 (35.8)	0.034
Men	7682 (66.1)	20 203 (62.5)	3.6 (2.6 to 4.6)	6193 (65.8)	11 748 (64.2)	0.034
Age, mean (SD), y	63.9 (17.2)	67.1 (17.0)	−3.2 (−3.6 to −2.8)	64.2 (17.2)	66.8 (16.7)	0.156
Private location	9125 (78.5)	28 624 (88.5)	−10.0 (−10.8 to −9.2)	7537 (80.1)	15 509 (84.8)	0.122
Witness status						
Bystander	4609 (39.6)	12 129 (37.5)	2.1 (1.1 to 3.2)	3692 (39.3)	7239 (39.6)	
EMS	2035 (17.5)	2705 (8.4)	9.1 (9.9 to 8.4)	1557 (16.6)	2021 (11.0)	0.167
None	4981 (42.8)	17 510 (54.1)	−11.3 (−12.3 to −10.2)	4157 (44.2)	9039 (49.4)	
Bystander CPR	4509 (47.0)[g]	15 014 (50.7)[g]	−7.6 (−8.7 to −6.6)	3706 (47.2)[g]	8163 (50.1)[g]	0.059
Dispatch to EMS interval, mean (SD), min	5.8 (2.8)	5.9 (3.0)	−0.1 (−0.2 to −0.03)	5.8 (2.8)	5.9 (2.7)	0.024
EMS level of care						
BLS only[h]	473 (4.1)	674 (2.1)	2.0 (1.6 to 2.4)	450 (4.8)	235 (1.3)	
ALS[h]						0.272
Administered first	7252 (62.4)	12 320 (38.1)	24.3 (23.3 to 25.3)	5603 (59.6)	9709 (53.1)	
Administered later	3900 (33.5)	19 350 (59.8)	−26.3 (−27.3 to −25.3)	3353 (35.6)	8355 (45.7)	
Initial cardiac rhythm						
VF/VT	3028 (26.0)	6541 (20.2)	5.8 (4.9 to 6.7)	2401 (25.5)	4045 (22.1)	
PEA	3424 (29.5)	7445 (23.0)	6.4 (5.5 to 7.4)	2673 (28.4)	4758 (26.0)	
Asystole	4856 (41.8)	16 737 (51.7)	−10.0 (−11.0 to −8.9)	4039 (42.9)	8756 (47.8)	0.122
No shock advised	317 (2.7)	1621 (5.0)	−2.3 (−2.7 to −1.9)	293 (3.1)	740 (4.0)	
Presumed cardiac etiology	10 897 (93.7)	30 028 (92.8)	0.9 (0.4 to 1.4)	8810 (93.7)	17 213 (94.1)	0.017
Chest compression fraction, mean (SD)	0.81 (0.13)	0.83 (0.12)	−0.02 (−0.02 to −0.02)	0.81 (0.13)	0.82 (0.12)	0.119
Out-of-hospital resuscitation duration, mean (SD), min[i]	29.3 (11.4)	19.1 (10.7)	10.2 (10.0 to 10.4)	29.1 (11.1)	22.9 (11.1)	0.552
ROC study site[j]						
A	188 (3.9)	4659 (96.1)		178 (23.8)	569 (76.2)	
B	500 (23.9)	1596 (76.1)		427 (26.3)	1199 (73.7)	
C	407 (7.4)	5114 (92.6)		392 (25.4)	1152 (74.6)	
D	69 (2.5)	2708 (97.5)		64 (23.6)	207 (76.4)	
E	810 (28.4)	2046 (71.6)		673 (26.2)	1896 (73.8)	
F	1589 (28.1)	4062 (71.9)		1395 (30.9)	3116 (69.1)	0.396
G	723 (40.6)	1057 (59.4)		512 (36.4)	895 (63.6)	
H	2649 (25.2)	7871 (74.8)		2371 (29.4)	5693 (70.6)	
I	4140 (58.7)	2908 (41.3)		2996 (49.1)	3109 (50.9)	
J	550 (63.0)	323 (37.0)		398 (46.2)	463 (53.8)	

Abbreviations: ALS, advanced life support; BLS, EMS unit with basic life support training; CPR, cardiopulmonary resuscitation; EMS, emergency medical system; PEA, pulseless electrical activity; ROC, Resuscitation Outcomes Consortium; VF/VT, ventricular fibrillation or pulseless ventricular tachycardia.

[a] Of the 9406 exposed patients in the matched set, 6025 were matched with 1 unexposed patient, 1024 were matched with 2 unexposed patients, and the remaining were matched with at least 3 unexposed patients. All proportions were rounded to 1 decimal place (indicating totals may not sum to exactly 100%).

[b] Propensity score matching was conducted using patient age, sex, episode location, witnessed status (bystander vs EMS vs not witnessed), bystander CPR, interval from 9-1-1 call to EMS arrival, initial shockable rhythm, presumed cardiac etiology, ALS unit first on scene, and treatment region.

[c] Absolute differences were calculated as a percent for categorical data and as mean differences for continuous data.

[d] Intra-arrest patients in the propensity score cohort were categorized as exposed.

[e] On-scene resuscitation patients in the propensity score cohort (categorized as unexposed) indicate that this was the treatment strategy at the time of matching; 11.9% of patients later underwent intra-arrest transport.

[f] The standard mean difference was calculated for variables used in the propensity score.

[g] The denominator indicates the number of cardiac arrests not witnessed by EMS.

[h] Indicates an EMS unit with ALS or BLS level of training.

[i] Measured from the commencement of professional resuscitation until either ROSC, termination, or arrival at the hospital.

[j] Indicates percent of a row's total.

Table 2. Patient Outcomes of the Full Study Cohort and Full Propensity-Matched Cohort

	Full study cohort			Full propensity-matched cohort[a]		
	No. (%)			No. (%)		
	Intra-arrest transport (n = 11 625)	On-scene resuscitation (n = 32 344)	Absolute difference (95% CI)[b]	Intra-arrest transport (n = 9406)	On-scene resuscitation (n = 18 299)[c]	Absolute difference (95% CI), %
Primary end point						
Survival to hospital discharge	446 (3.8)	4072 (12.6)	−8.8 (−8.3 to −9.3)	372 (4.0)	1557 (8.5)	−4.6 (−5.1 to −4.0)
Secondary end point						
Survival with favorable neurological outcome	162 (2.6)[d]	2000 (10.2)[d]	−7.6 (−8.2 to −7.0)	148 (2.9)[d]	733 (7.1)[d]	−4.2 (−4.9 to −3.5)
Additional end points						
Out-of hospital return of spontaneous circulation	1834 (15.8)	15 634 (48.3)	−32.6 (−33.4 to −31.7)	1522 (16.2)	7199 (39.3)	−23.2 (−24.2 to −22.1)
Interval, mean (SD), min[e]	32.9 (11.4)	23.3 (10.1)	9.6 (9.4 to 9.8)	33.0 (11.5)	25.3 (10.1)	7.7 (7.4 to 8.0)
Out-of-hospital termination of resuscitation	29 (0.2)	18344 (56.7)	−56.5 (−57.0 to −55.9)	25 (0.3)	9937 (54.3)	−54.0 (−54.8 to −53.3)
Interval, mean (SD), min[f]	35.4 (14.8)	23.9 (11.0)	11.5 (11.2 to 11.8)	36.1 (15.3)	26.1 (10.0)	10.0 (9.7 to 10.3)
Survival to hospital admission[g]	2226 (19.1)	9950 (30.8)	−11.6 (−12.5 to −10.7)	1815 (19.3)	4532 (24.8)	−5.5 (−6.5 to −4.5)
Hospital stay, mean (SD), d	5.4 (7.3)	6.6 (10.5)	−1.2 (−1.4 to −0.99)	5.4 (7.3)	6.6 (10.3)	−1.2 (−1.4 to −0.97)

[a] Propensity score matching was conducted using patient age, sex, episode location, witnessed status (bystander vs EMS vs not witnessed), bystander cardiopulmonary resuscitation, interval from 9-1-1 call to emergency medical systems arrival, initial shockable rhythm, presumed cardiac etiology, advanced life support unit first on scene, and treatment region. Patients in the intra-arrest transport group were categorized as exposed, and those in the on-scene resuscitation group were categorized as unexposed.

[b] Absolute differences were calculated as a percent for categorical data and as mean differences for continuous data.

[c] On-scene resuscitation patients in the propensity score cohort indicate that this was the treatment strategy at the time of matching; 11.9% of patients later underwent intra-arrest transport.

[d] The denominator indicates patients with data available for neurological outcomes. For the full study cohort the denominator was 6223 for intra-arrest transport and 19 636 for on-scene resuscitation, and for the full propensity-matched cohort, the denominator was 5066 for intra-arrest transport and 10 317 for on-scene resuscitation.

[e] Measured from the commencement of professional resuscitation until time of return of spontaneous circulation.

[f] Measured from the commencement of professional resuscitation until time of out-of-hospital termination of resuscitation. For the intra-arrest transport patients, this only applies to those who had termination of resuscitation after leaving the scene but before arriving to the hospital.

[g] Patient survived until hospital admission from the emergency department.

of scene departure and hospital arrival. Of intra-arrest transport survivors who were transported after 30 minutes, 61% achieved ROSC prior to hospital arrival.

Primary Analysis

Using a propensity score, 9406/11 625 of the exposed patients (81%) were matched in a 1:1 ratio to unexposed patients (eTable 3 in the Supplement). Remaining unexposed patients were then resampled and an additional 8893 unexposed patients were matched, resulting in a total of 27 705 unique patients in the full propensity-matched cohort analysis (9406 exposed and 18 299 unexposed patients; Table 1). The median time of matching was 18.4 minutes (IQR, 12.5-24.9). The assumptions of the proportional hazards model were met. Overall, survival to hospital discharge was lower among patients treated with intra-arrest transport (372/9406 [4.0%]) compared with continued on-scene resuscitation (1557/18 299 [8.5%]), and the risk difference was 4.6% (95% CI, 4.0-5.1) with an adjusted risk ratio of 0.48 (95% CI, 0.43-0.54) (**Figure 3**; eTable 4 in the Supplement). Among the 15 383 matched patients with available neurological outcome data, survival with favorable neurological outcome was lower among patients treated with intra-arrest transport (148/5066 [2.9%]) compared with continued-on scene resuscitation (733/10 317 [7.1%]), and the risk difference was 4.2% (95% CI, 3.5-4.9) with an adjusted risk ratio of 0.60 (95% CI, 0.47-0.76).

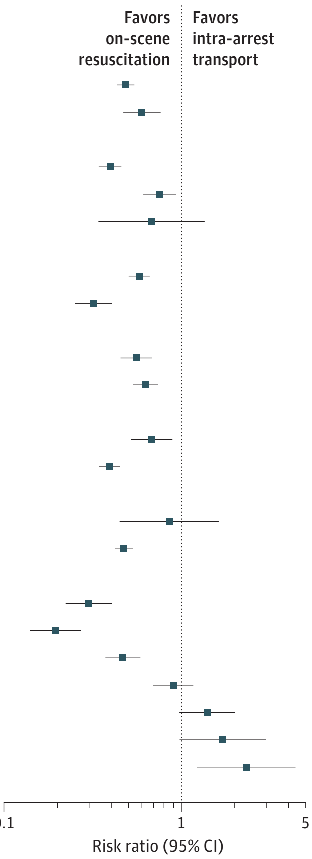
Secondary Analyses

The interaction term between exposure status and the time of matching was statistically significant (P = .001), indicating that the association of intra-arrest transport and survival to hospital discharge varied depending on the timing of transport. Figure 3 displays the association of intra-arrest transport and survival to hospital discharge within time-based epochs defined by the time between start of EMS resuscitation and time of matching.

Intra-arrest transport was significantly associated with a lower probability of survival to hospital discharge within the subgroups of ALS first, ALS second, EMS witnessed, not EMS witnessed, initial shockable cardiac rhythm, and initial nonshockable cardiac rhythm. The combined categories of (1) EMS-witnessed or an initial shockable rhythm, and (2) not EMS-witnessed and initial nonshockable rhythm both showed a significant association between intra-arrest transport and a lower probability of survival to hospital discharge. There was no significant association seen in the BLS-only and mechanical CPR-treated subgroups; however, these analyses were limited by a low sample size. Within subgroups defined by study site (eTable 5 in the Supplement), intra-arrest transport was associated with a significantly lower probability of survival to hospital discharge for 7 sites, neutral results were observed for 2 subgroups (both with point estimates favoring on-scene resuscitation), and intra-arrest transport was associated with

Figure 3. Adjusted Analyses Examining the Association of Intra-arrest Transport and Survival Among the Full Propensity-Matched Cohort and Subgroups

	No. of events/patients			
	On-scene resuscitation	Intra-arrest transport	Risk ratio (95% CI)	Interaction *P* value
Full cohort	1557/18 299	372/9406	0.48 (0.43-0.54)	
Neurological outcome	733/10 317	148/5066	0.60 (0.47-0.76)	
EMS level of care				
ALS first	936/9709	213/5603	0.40 (0.34-0.46)	
ALS second	599/8355	143/3353	0.75 (0.61-0.93)	.001
BLS only	22/235	16/450	0.68 (0.34-1.35)	
EMS witnessed				.001
Yes	313/2021	98/1557	0.58 (0.50-0.66)	
No	1244/16 278	274/7849	0.32 (0.25-0.41)	
Initial shockable rhythm				.38
Yes	1101/4045	230/2401	0.55 (0.45-0.68)	
No	456/14 254	142/7005	0.63 (0.53-0.74)	
EMS witnessed or shockable				.001
Yes	1272/5727	293/3753	0.68 (0.52-0.89)	
No	285/12 572	79/5653	0.39 (0.34-0.45)	
Mechanical chest compressions				.08
Yes	47/832	19/505	0.85 (0.45-1.62)	
No	1510/17 467	353/8901	0.47 (0.42-0.53)	
Time-based epochs. min				
0-5	490/1319	49/411	0.30 (0.22-0.41)	
5-10	472/2013	45/849	0.20 (0.14-0.27)	
10-15	341/3619	96/1757	0.47 (0.37-0.59)	
15-20	145/3815	86/2031	0.90 (0.69-1.17)	.001
20-25	65/3322	51/1837	1.40 (0.97-2.01)	
25-30	27/2112	25/1220	1.70 (0.97-2.98)	
>30	17/2099	20/1301	2.31 (1.22-4.38)	



The primary outcome for all analyses is survival to hospital discharge, with the exception of the "neurological outcome" subgroup, for which the outcome variable is survival with favorable neurological outcome, defined as Modified Rankin Scale score <3. The *P* value for interaction is between intra-arrest transport and a subgroup. Time-based epochs include intra-arrest transport patients who were transported during that time interval (measured from the onset of EMS-commenced resuscitation) and the on-scene resuscitation patients whom they were matched to. The right end points are included in the time interval. ALS indicates advanced life support; BLS, basic life support; EMS, emergency medical systems.

a significantly higher probability of survival to hospital discharge for 1 site. There was statistically significant interaction for EMS level of care (*P* = .001), EMS witnessed status (*P* = .001), the combination of EMS-witnessed or shockable initial rhythm (*P* = .001), and study site (*P* < .001). There were no subgroup differences detected according to initial shockable rhythm (*P* = .38) or mechanical chest compression use (*P* = .08).

Sensitivity Analyses

The analysis of the 1:1 propensity-matched cohort (eTable 3 in the Supplement) was consistent with the primary analysis that survival to hospital discharge was lower among patients treated with intra-arrest transport compared with continued on-scene resuscitation (372/9406 [4.0%] vs 763/9406 [8.1%]; adjusted risk ratio, 0.49 [95% CI, 0.43-0.55]). The analysis with adjustment for site as a random effect (adjusted risk ratio, 0.46 [95% CI, 0.41-0.52]; estimated SD for random effects, 1.01) and the analysis with multiple imputation that incorporated the 9700 cases excluded due to missing data (adjusted risk ratio, 0.48 [95% CI, 0.43-0.54]) were both also consistent with the primary analysis.

Discussion

In this large multicenter time-dependent propensity score–matched cohort study of patients experiencing out-of-hospital cardiac arrest, intra-arrest transport to the hospital compared with continued on-scene treatment was significantly associated with a lower probability of survival to hospital discharge. Likewise, intra-arrest transport was significantly associated with a lower probability of survival to hospital discharge with favorable neurological outcome.

Consistent with a previous analysis, these data demonstrate a marked heterogeneity in intra-arrest transport practices across EMS systems.[6] Although important differences in management may be expected between systems with variable structure and history,[23,24] all EMS systems in this study had the same basic structure (strengthening internal validity) with protocols based on American Hospital Association guidelines and response teams with BLS-trained and ALS-trained personnel (without out-of-hospital physicians).[25,26] Given the statistically significant association between intra-arrest transport and lower survival to hospital discharge and the variability in resuscitation practices across ROC sites, the current results provide a potential explanation, in part, for why survival may differ markedly across the network sites.[27] Overall, despite more favorable characteristics among those treated with intra-arrest transport, intra-arrest transport was significantly associated with adverse outcomes, supporting a strategy that EMS dedicate effort and expertise on scene rather than prioritizing transport to hospital. The majority of survivors treated with intra-arrest transport achieved ROSC prior to arriving at the hospital, raising questions about the hospital-based contributions to intra-arrest transport survivors.

This analysis examined subgroups for which early hospital transport might be considered potentially advantageous (ie, those with favorable phenotypes such as shockable rhythms or EMS-witnessed arrests). Despite smaller sample sizes, the significant adverse association between intra-arrest transport and outcomes was consistent with the primary analysis. When examining subgroups defined by EMS level of care, outcomes among ALS-treated subgroups were consistent with the primary analysis. The analysis did not detect a significant association within the BLS-only subgroup, however this subgroup was limited by a small sample size.

In a secondary analysis, the association of intra-arrest transport and survival to hospital discharge varied within differing times of matched exposure. The following differing strata, defined by exposure match time, were explored: (1) within the first 15 minutes intra-arrest transport was associated with significantly decreased survival; (2) between 15 and 30 minutes results were neutral; (3) but the greater than 30-minute strata showed a significant association with improved survival. These findings raise the possibility that the overall association of intra-arrest transport and worse outcomes may be driven by a detrimental effect of intra-arrest transport early in the resuscitation, with benefit from intra-arrest transport after 30 minutes. However, patients who received intra-arrest transport were treated with significantly longer attempts of out-of-hospital resuscitation. This may lead to a particularly important bias when comparing patients within time-based strata late in the resuscitation: those chosen for intra-arrest transport underwent a median of 10 additional minutes of resuscitation attempts while en route to hospital (and likely further efforts in hospital); whereas patients who received on-scene resuscitation were likely declared dead soon after (given the mean duration until termination of 26 minutes). Furthermore, of those who received intra-arrest transport after 30 minutes and who survived, two-thirds were successfully resuscitated prior to hospital arrival.

There are several possible explanations for the overall adverse association of transport prior to ROSC. Although there are novel hospital-based resuscitation strategies (such as extracorporeal CPR[28]) that may ultimately advance resuscitation in select subgroups, in many settings, conventional advanced life support resuscitation can be fully implemented in the out-of-hospital setting so that there is no clear hospital-based advantage. Thus the logistical obstacle of moving the patient with ongoing resuscitation may impair or delay best practices including CPR quality. Extrication and transport may impair quality of manual compression, which has been demonstrated in some studies[8,29]; whereas it was not observed in another EMS.[9] Data on chest compression fraction or other measures of CPR quality during the extrication period were not available. The physical tasks of patient movement may also interfere or delay resuscitative maneuvers such as defibrillation or drug delivery. Transport during an active resuscitation may also produce a cognitive distraction and inhibit a paramedic's ability to deliver high-quality resuscitative efforts and treat possible reversible causes.

The study cohort did not contain data on hospital-based invasive resuscitative techniques such as extracorporeal CPR,[28] intra-arrest coronary angiography,[30] or advanced monitoring techniques.[31] However, it is likely that the majority of patients in the cohort who arrived at the hospital without a pulse were treated with continued standard management by advanced cardiac life support. Likely only a small number of patients with ongoing resuscitation at the hospital would have been considered eligible for novel invasive treatments,[32,33] though these select patients groups in refractory arrest may benefit from early transport for hospital-based invasive strategies. Data are not currently available to inform this hypothesis. Based on data from this study, caution may be warranted with regards to changes in EMS policy favoring routine intra-arrest transport for the purpose of extracorporeal CPR candidacy assessment at the hospital as most will likely prove ineligible, and overall survival statistics may actually worsen. Rather, in settings evaluating extracorporeal CPR provision for OHCA, systems might consider applying eligibly criteria prior to transport, which may mitigate these risks. Further study is required to determine the efficacy of intra-arrest transport plus extracorporeal CPR compared with exclusive on-scene resuscitation.[34] Alternatively, out-of-hospital on-scene initiation of extracorporeal CPR may benefit from access to mechanical perfusion without the risks of hospital transport.[35]

Limitations

This study has several limitations. First, results of this investigation are limited to association, not causation. Ideally the results should be validated in a randomized evaluation. Second, although these data originated from a North American collaboration with wide variability in transport practices, external validity may not be generalizable to systems with differing patient characteristics and medical management (including physician-based EMS systems). Specifically, as out-of-hospital ALS was utilized in the majority of patients, the results may not be valid in BLS-only resuscitations. Third, these results cannot be extended to patients treated with mechanical CPR (because of the low prevalence in the study sample) or for those treated with novel invasive resuscitative techniques. Fourth, other characteristics of rescue personnel or patients not available for this analysis may have influenced the probability of both intra-arrest transport and outcomes. EMS personnel may have used certain patient characteristics to estimate benefit from intra-arrest transport (leading to confounding by indication). Intra-arrest transport may also have been associated with more aggressive resuscitative efforts by rescuers (intra-arrest transport patients had longer durations of resuscitation attempted in the out-of-hospital setting, in addition to further hospital-based efforts). Fifth, these results are subject to prognostication bias; patients with unfavorable phenotypes may have had resuscitation terminated early, without adequate opportunity to achieve ROSC. Sixth, the analysis design compared those transported at a certain time juncture with those not transported at that juncture. For this reason, 12% of patients in the unexposed group actually underwent intra-arrest transport at a later time point, which may have affected the ability to see the true association. Seventh, misclassification of time data may have affected the results. Eighth, in the full propensity-matched set, not all individual variables were aligned between groups; exposed patients demonstrated more favorable prognostic features (were younger, more with initial shockable rhythms in public locations and EMS witnessed), which may have biased the results toward intra-arrest transport. Ninth, 9 of the 10 site-based subgroups had point estimates suggesting a harmful association of intra-arrest transport; whereas 1 subgroup had point estimates in the direction of protection (although the low sample sizes for this subgroup may have made the result less reliable). It is possible that within certain system characteristics, intra-arrest transport may be of benefit. Tenth, it was assumed that missing data was missing at random, which may not have been the case. Eleventh, the data from this study were collected from 2011 to 2015, and it is uncertain whether these results are fully applicable to out-of-hospital resuscitation and in-hospital post cardiac arrest care in 2020.

Conclusions

Among patients experiencing out-of-hospital cardiac arrest, intra-arrest transport to hospital compared with continued on-scene treatment was associated with lower probability of survival to hospital discharge. Study findings are limited by potential confounding due to observational design.

ARTICLE INFORMATION

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