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Comparison of sustained rate control in atrial fibrillation with rapid ventricular rate: Metoprolol vs. Diltiazem☆

Kristi L. Hargrove, PharmD [a,b,c,d,*], Ellen E. Robinson, PharmD [a,b,c,d], Kathleen A. Lusk, PharmD [a,b,d], Darrel W. Hughes, PharmD [a,b,c], Luke A. Neff, PharmD [a,b,c,d], Amanda L. Fowler, PharmD [a,b,c,d]

[a] University Health, San Antonio, TX 78229, United States
[b] University of Texas Health San Antonio, Pharmacotherapy Education & Research Center, San Antonio, TX 78229, United States
[c] The University of Texas at Austin, College of Pharmacy, Austin, TX 78712, United States
[d] University of the Incarnate Word, Feik School of Pharmacy, San Antonio, TX 78209, United States

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ABSTRACT

Objective: The objective of this study was to compare sustained rate control with intravenous (IV) diltiazem vs. IV metoprolol in acute treatment of atrial fibrillation (AF) with rapid ventricular rate (RVR) in the emergency department (ED).

Methods: This retrospective chart review at a large, academic medical center identified patients with AF with RVR diagnosis who received IV diltiazem or IV metoprolol in the ED. The primary outcome was sustained rate control defined as heart rate (HR) < 100 beats per minute without need for rescue IV medication for 3 h following initial rate control attainment. Secondary outcomes included time to initial rate control, HR at initial control and 3 h, time to oral dose, admission rates, and safety outcomes.

Results: Between January 1, 2016 and November 1, 2018, 51 patients met inclusion criteria (diltiazem $n = 32$, metoprolol $n = 19$). No difference in sustained rate control was found (diltiazem 87.5% vs. metoprolol 78.9%, $p = 0.45$). Time to rate control was significantly shorter with diltiazem compared to metoprolol (15 min vs. 30 min, respectively, $p = 0.04$). Neither hypotension nor bradycardia were significantly different between groups.

Conclusions: Choice of rate control agent for acute management of AF with RVR did not significantly influence sustained rate control success. Safety outcomes did not differ between treatment groups.

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1. Introduction

Atrial fibrillation (AF) is the most common, sustained cardiac arrhythmia encountered in the emergency department (ED) [1,2]. AF accounts for over a half-million ED visits per year - a rising figure as the population continues to age. [1,5] Symptoms include palpitations, angina, dyspnea, and anxiety. [3] Patients experiencing AF with rapid ventricular rate (RVR) require immediate treatment due to increased myocardial oxygen demand, which can lead to myocardial ischemia and acute heart failure. [2,3] Untreated, this stress state can rapidly decompensate into hemodynamic instability. [3]

Achieving heart rate reduction is vital to relieve symptoms and prevent complications in acute AF management. [2,3] Beta-blockers (BB) and calcium channel blockers (CCB) are commonly used to treat AF with RVR, though the optimal acute rate control agent is unclear. The 2014 ACC/AHA/HRS Guideline for the Management of Patients with Atrial Fibrillation recommends either intravenous (IV) BB or non-dihydropyridine CCB for acute management of AF with RVR, without a preference between agents. [4] Additionally, the 2019 focused update did not address any new recommendation regarding acute rate control. [5] Agent efficacy has been compared in only a few studies; therefore, drug choice is most commonly based on physician preference, patient co-morbidities, safety, and home rate control medication. [1-3,6]

Diltiazem is associated with improved early efficacy, however thisdifference does not persist longer than 30 min. [2] Overall, studies have shown similar rate control efficacy between diltiazem and metoprolol at 30 to 60 min after drug administration. [3,7] There is scarce evidence assessing sustained rate control and RVR recurrence longer than 60 min. Assessment of sustained control is important due to potential delays in administration of oral therapy in the ED leading to risk of RVR recurrence based on medication duration. Our study sought to compare sustained rate control success for 3 h after initial control with IV diltiazem or IV metoprolol. The 3 h time frame was chosen due to the pharmacokinetic properties of these agents.

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* Corresponding author at: Department of Pharmacotherapy and Pharmacy Services, University Health, 4502 Medical Drive, San Antonio, TX 78229, United States.
E-mail address: kristi.hargrove@uhs-sa.com (K.L. Hargrove).

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2. Methods

2.1. Study design

This was a single center, retrospective chart review conducted at University Hospital in San Antonio, Texas, a 716-bed, safety net, academic hospital with approximately 94,000 ED visits per year. The study was approved by the University of Texas Health Science Center at San Antonio Institutional Review Board. Patients were identified using International Classification of Diseases (ICD) 9th and 10th Revision codes for AF with RVR then cross referenced with pharmacy billing data for IV diltiazem and IV metoprolol between January 1, 2016 and November 1, 2018.

2.2. Patients

A random sample of 100 eligible patients per drug group were screened for inclusion criteria. Adults aged 18 years and older who were treated with IV diltiazem or IV metoprolol for acute AF with RVR in the ED and achieved rate control within 30 min were included. Rapid ventricular rate was defined as HR > 120 bpm and rate control was defined as HR < 100 bpm to align with prior studies. [2,3,7] Exclusion criteria included: initial HR > 220 bpm, systolic blood pressure (SBP) < 90 mmHg, alternative initial drug treatment, receipt of both IV diltiazem and IV metoprolol to achieve initial rate control, acute decompensated heart failure, incarceration, and pregnancy.

2.3. Methods and measurements

Baseline data collected from the electronic medical record included patient demographics, new onset or chronic AF, applicable past medical history, baseline vital signs, and reported home medications. The administration of the first metoprolol or diltiazem dose was marked as time zero with subsequent documented time points thereafter. A single investigator identified patients and collected data using a standardized data collection form. This investigator was aware of the study group during data collection. Periodic check-ins were conducted with co-investigators to support consistency and discuss unforeseen data collection challenges. Collected data was transcribed and maintained in a REDCap database hosted at University of Texas Health Science Center. [8]

2.4. Outcomes

The primary outcome was sustained rate control defined as HR < 100 bpm without need for rescue IV medication for 3 h from initial rate control. Multiple doses of a single medication could be used for initial control defined within 30 min of initial dose. Secondary outcomes included time to initial rate control (documented every 5 min), median initial dose administered, HR at initial control and 3 h follow-up, conversion to oral medication, time to oral dose, and disposition. Missing vital sign values were addressed by using a carry forward method of last known value. Hypotension (SBP < 90 mmHg), bradycardia (HR < 60 bpm), fluid bolus (≥500 mL crystalloid) administration, and diuretic use were assessed up to 24 h after rate control. Thirty-day hospital readmission was also collected to assess safety.

2.5. Analysis

Data were analyzed using JMP 11.0.0 (Copyright 2013, SAS Institute, Cary, NC). Chi-squared or Fisher's exact test were used to compare nominal data. Wilcoxon rank sum test was used to compare non-normal parametric data, and Student's *t*-test was used for normal, parametric data. An alpha level of ≤0.05 was used to determine statistical significance.

3. Results

After initial review of 573 visits meeting the ICD codes, 300 patients with AF with RVR received IV diltiazem or IV metoprolol in the ED. A random sample of 100 patients per medication group were screened for inclusion and exclusion criteria which yielded 51 patients (diltiazem $n = 32$ and metoprolol $n = 19$). The most common reason for exclusion was lack of rate control at 30 min ($n = 116$) (Fig. 1).

Groups were similar at baseline except AF history, past medical history, and home medications (Table 1). A significantly higher number of patients in the diltiazem group were diagnosed with new onset AF (diltiazem 53.1% vs. metoprolol 21.1%, $p = 0.04$). Concurrent hypothyroidism was more frequent in the diltiazem group (diltiazem 21.9% vs. metoprolol 0%, $p = 0.04$). A higher number of patients in the metoprolol group were on metoprolol as a home medication (diltiazem 28.1% vs. metoprolol 68.4%, $p = 0.008$). Diltiazem use as a home medication was low in both groups (diltiazem 6.3% vs. metoprolol 5.3%, $p = 1.0$)

The primary outcome of sustained rate control did not differ between groups (diltiazem 87.5% vs. metoprolol 78.9%, $p = 0.45$) (Table 2). Median time to initial rate control was significantly shorter with diltiazem than metoprolol (diltiazem 15 min vs. metoprolol 30 min, $p = 0.04$). Two patients in the diltiazem group (6.3%) required a second dose to obtain initial control while 8 patients (42.1%) in the metoprolol group required repeat dosing (a second or third dose). Mean first dose was 23.6 mg in the diltiazem group and 5.6 mg in the metoprolol group. Median weight-based first doses for diltiazem and metoprolol were 0.24 mg/kg (0.23–0.28) and 0.05 mg/kg (0.04–0.07), respectively. The median HR at control was 89 bpm in the diltiazem group compared to 92 bpm in the metoprolol group ($p = 0.10$). Heart

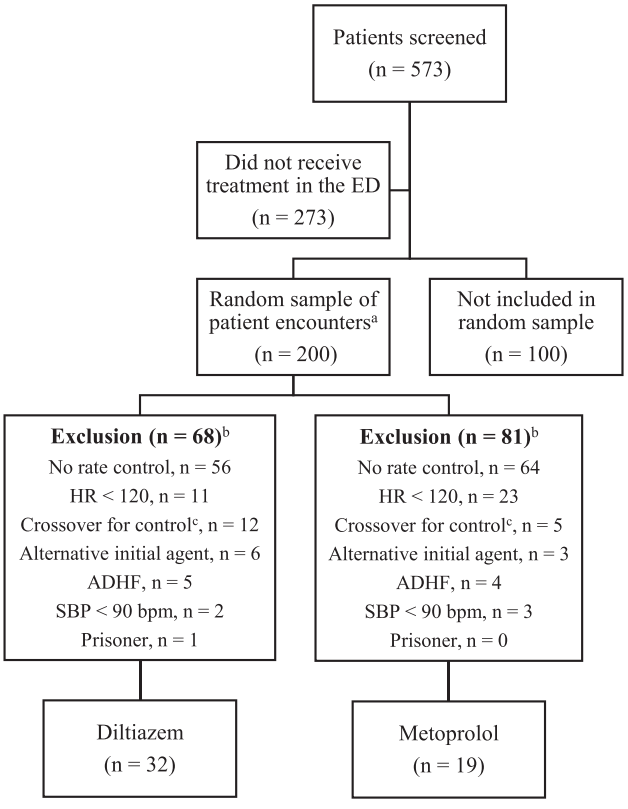

Fig. 1. Patient Enrollment Flowchart. [a]One-hundred patients from each group (diltiazem and metoprolol) were randomly assessed for inclusion. [b]Patients could qualify for more than one exclusion criteria. [c]Crossover defined as receipt of both IV diltiazem and IV metoprolol to achieve initial rate control. ADHF = acute decompensated heart failure, BPM = beats per minute, ED = emergency department, HR = heart rate, SBP = systolic blood pressure.

Table 1
Baseline characteristics.

	Diltiazem (n = 32)	Metoprolol (n = 19)	p-value
Age, years^	62.2 ± 13.9	62.9 ± 13.2	0.85
Male, n (%)	">21 (65.6)	9 (47.4)	0.25
Caucasian, n (%)	16 (50)	6 (31.6)	0.34
BMI ≥ 30, n (%)	18 (56.3)	14 (73.3	0.24
New onset AF, n (%)	17 (53.1)	4 (21.1)	0.04
Baseline vitals			
HR, bpm*	140 (128–151)	136 (126–149)	0.35
SBP, mmHg^	142 ± 20	137 ± 17	0.02
DBP, mmHg^	93 ± 21	83 ± 15	0.07
Past medical history, n (%)			
AF	15 (46.9)	15 (79)	0.02
Hypertension	21(65.6)	16 (84.2)	0.2
CHF	8 (25)	4 (21.1)	1
Diabetes	9 (28.1)	6 (31.6)	1
Hyperthyroidism	0 (0)	1 (5.3)	0.38
Hypothyroidism	7 (21.9)	0 (0)	0.04
Home medications, n (%)			
Metoprolol	9 (28.1)	13 (68.4)	0.008
Carvedilol	4 (12.5)	2 (10.5)	1
Diltiazem	2 (6.3)	1 (5.3)	1
Verapamil	1 (3.1)	0 (0)	1
Other	16 (50)	3 (15.8)	–

AF = atrial fibrillation, BMI = body mass index, CHF = congestive heart failure, DBP = diastolic blood pressure, HR = heart rate, SBP = systolic blood pressure.
^ mean ± SD.
* median (IQR).

rates at 15, 30, and 45 min after rate control were significantly lower for diltiazem than metoprolol (87 bpm vs. 92 bpm, $p < 0.01$; 86 bpm vs. 94 bpm, $p < 0.01$; 89 bpm vs. 92 bpm, $p = 0.04$, respectively)

Table 2
Primary and secondary outcomes.

Primary	Diltiazem (n = 32)	Metoprolol (n = 19)	p-value
Sustained rate control, n (%)	28 (87.5)	15 (78.9)	0.45
Secondary			
Time to rate control, min*	15 (10–25)	30 (10−30)	0.04
Patients requiring repeat dosing to obtain control, n (%)+	2 (6.3%)	8 (42.1%)	–
Mean first dose, mg^	23.6 ± 6.9	5.6 ± 2.6	–
Median weight-based first dose, mg/kg*	0.24 (0.23–0.28)	0.05 (0.04–0.07)	–
Median HR at control, bpm*	89 (81–93)	92 (89–96)	0.10
Median HR after control achieved, bpm*			
15 min	87 (81–93)	92 (89–99)	<0.01
30 min	86 (77–93)	94 (89–105)	<0.01
45 min	89 (80–94)	92 (89–105)	0.04
60 min	88 (82–94)	90 (88–105)	0.44
90 min	91 (85–99)	90 (84–97)	0.75
120 min	98 (86–107)	88 (84–102)	0.35
180 min	95 (83–110)	92 (81–109)	0.61
Conversion to PO, n (%)	24 (75%)	13 (68)	0.75
Time to PO agent, min*	168 (32–334)	80 (28–258)	0.33
PO agent, n (%)			<0.0001
Diltiazem	19 (79.2)	0 (0)	
Metoprolol	4 (16.7)	12 (92.3)	
Carvedilol	1 (4.2)	1 (7.7)	
Disposition, n (%)			0.01
Admitted	29 (90.6)	11 (57.9)	
Discharged	3 (9.4)	8 (42.1)	

bpm = beats per minute, HR = heart rate, PO = oral, min = minutes.
^ mean ± SD.
* median (IQR).
+ diltiazem up to 2 total doses, metoprolol 2 or 3 total doses.

Transition to an oral agent occurred in 75% of patients in the diltiazem group and 68% in the metoprolol group ($p = 0.75$). Median time to oral agent administration was 168 min for diltiazem compared to 80 min in the metoprolol group ($p = 0.33$). Choice of oral agent was found to be significantly different (Table 2). Oral diltiazem was continued in 79.2% of patients in the diltiazem group vs. zero patients in the metoprolol group. Oral metoprolol was continued in 92.3% of patients in the metoprolol group vs. 16.7% of the diltiazem group. A higher number of patients in the diltiazem group were admitted (diltiazem 90.6% vs. metoprolol 57.9%, $p = 0.01$).

Safety outcomes were assessed for hemodynamic instability and/or worsening heart failure (Table 3). Hemodynamic instability as defined by hypotension (diltiazem 3.1% vs. metoprolol 10.5%, $p = 0.54$) and bradycardia (diltiazem 15.6% vs. metoprolol 10.5%, $p = 0.70$) occurred infrequently overall, and differences were not statistically significant. Worsening heart failure, as assessed by diuretic use (diltiazem 28.1% vs. metoprolol 15.8%, $p = 0.05$) and 30-day readmission (diltiazem 12.5% vs. metoprolol 21.1%, $p = 0.45$), were also not statistically significant in either group.

4. Discussion

The optimal first line agent for rate control in acute treatment of AF with RVR is unclear, and current guidelines give no preference between BB or non-dihydropyridine CCB. Onset and duration of action are important considerations for acute rate control medication choice. A faster onset presents more rapid efficacy while longer duration confers sustained control. Diltiazem has a faster onset of 3–5 min, but a shorter duration (1 to 3 h) compared to metoprolol (onset up to 20 min and duration up to 6 to 8 h). [9,10] Current literature shows similar rate control efficacy up to 60 min following drug administration of BB or CCB; giving insight to the effect of agent onset on rate control. [2,3,6,7] The 3 h time frame in our study was chosen to account for expected duration of action of IV diltiazem and IV metoprolol in continued ED rate control where practical barriers in the transition to oral therapy are present.

A 2005 study by Demirican and colleagues prospectively examined effectiveness of diltiazem 0.25 mg/kg IV (maximum 25 mg) vs. metoprolol 0.15 mg/kg IV (maximum 10 mg) for 20 patients with new onset AF with RVR for up to 20 min. [3] The study found rate control success (defined as HR < 100 or decrease by 20%) was higher in the diltiazem group at 2 min, but similar to metoprolol at 20 min (diltiazem 90% vs. metoprolol 80%, $p > 0.05$). The authors concluded diltiazem and metoprolol showed similar efficacy for rate control. In 2015, Fromm and colleagues sought to test prior findings by prospectively comparing diltiazem 0.25 mg/kg IV (maximum 30 mg) and metoprolol 0.15 mg/kg IV (maximum 10 mg) for acute rate control efficacy up to 30 min in 52 new onset and chronic AF patients. [2] Data was collected at 5-min intervals and showed a higher percentage of patients reached goal HR with diltiazem vs. metoprolol at each time point. At 30 min, 95.8% of diltiazem patients vs. 46.4% of metoprolol patients ($p < 0.0001$) achieved rate control. The authors concluded diltiazem was more effective than metoprolol in achieving rate control in ED patients with AF with RVR.

Table 3
Safety outcomes.

	Diltiazem (n = 32)	Metoprolol (n = 19)	p-value
SBP < 90 mmHg, n (%)	1 (3.1)	2 (10.5)	0.54
HR < 60 bpm, n (%)	5 (15.6)	2 (10.5)	0.70
Fluid bolus, n (%)[a]	11 (34.4)	6 (31.6)	1
Diuretic use, n (%)	9 (28.1)	3 (15.8)	0.50
30-day readmission, n (%)	4 (12.5)	4 (21.1)	0.45

[a] Fluid bolus ≥ 500 mL IV crystalloid, bpm = beats per minute, HR = heart rate, SBP = systolic blood pressure.

In our study, no difference was found in the primary outcome of sustained rate control efficacy 3 h after administration of IV diltiazem or IV metoprolol. In addition, initial rate control was overall less successful compared to prior studies. Medication dosing could have contributed to these findings. Though Demirican and Fromm showed greater success with weight-based dosing of both medications, our institution routinely uses flat dose metoprolol and weight-based diltiazem dosing. [2,3] This strategy resulted in a median weight-based dose in the metoprolol group of 0.05 mg/kg; a much lower dose than studied previously which could have led to the reduced efficacy observed in the metoprolol group. The diltiazem median dose, however, was 0.24 mg/kg which more accurately reflects studied doses and does not explain the low incidence of rate control success with diltiazem. In addition, only 6.3% of patients in the diltiazem group required a second dose to obtain initial control while 42.1% of patients in the metoprolol group required one or two additional doses. It should be noted, the need for repeat dosing in the metoprolol group could also be related to the lower weight-based doses these patients received.

Time to rate control was significantly shorter in the diltiazem group which affirms the early efficacy of diltiazem observed in prior studies and aligns with the expected drug onset. [2,3] Of note, more patients in the diltiazem group presented with new onset AF. This may reflect physician preference for diltiazem in new onset patients to utilize the drug with data to support early efficacy. On the contrary, the majority of patients in the metoprolol group were on metoprolol at home, corresponding to the higher rate of chronic AF in this group. This emphasizes that in patients with a history of AF, physicians at our institution, similar to other institutions, favor the IV formulation of a patient's home rate control medication. [1,6] In addition, significantly more patients in the diltiazem group were admitted. This is likely related to the diltiazem group's higher percentage of new onset AF requiring further assessment and work-up for underlying cause.

Timely transition to an oral rate control medication is essential for successful sustained rate control. Practical barriers in the ED can lead to delay in oral medication administration, adding importance to maintaining control with the initial IV medication. In our study, not all patients were transitioned to an oral medication by ED team prior to admission. In some cases, patients were discharged prior to administration of an oral dose or transitioned to oral maintenance medication after admission. In other cases, the authors anecdotally observed documentation that AF with RVR was attributed to an acute underlying condition and continued rate control was not warranted once the underlying cause was treated. The median time to transition was earlier in the metoprolol group with time to oral dose nearly half of that in the diltiazem group. Most patients were given an oral medication in the same class as the IV agent that achieved rate control. Earlier administration in the metoprolol group may be due to greater availability of metoprolol dosage forms in the ED automated dispensing machines. In addition, there was high variability in time to oral dose which precludes conclusions of how time to oral transition may have contributed to the primary outcome and likely led to the lack of statistical significance in this outcome.

Safety is another important consideration in medication choice. [6] In this study, bradycardia and hypotension were assessed for safety after acute treatment and were found to be similar. Adverse effects occurred infrequently and neither hypotension nor bradycardia were found to be significantly different. Overall, fluid bolus administration was higher than the observed rate of hypotension. This finding is likely confounded by fluid boluses given for treatment of underlying causes that led to AF with RVR rather than a clear marker of clinically relevant hypotension due to medication administration to treat AF with RVR.

In addition to hemodynamic effects, acute heart failure exacerbation is a commonly cited concern with non-dihydropyridine CCB use, though acute use of BB can pose a similar risk. [11] A retrospective study by Hirschy and colleagues assessed efficacy and safety of BB and CCB for acute AF with RVR treatment in patients with heart failure with reduced ejection fraction (HFrEF) history. [11] Notably, rate control was achieved in less than two thirds of both groups. Doses administered were lower than weight-based doses evaluated in prior prospective trials and likely contributed to drug efficacy. Worsening heart failure incidence was not found to be significantly different. Authors concluded diltiazem use did not increase adverse events in patients with HFrEF. In our study, worsening heart failure was assessed through diuretic use and 30-day readmission for HF. Both outcomes occurred at low frequency in the total population though only a subset of patients had a baseline history of HFrEF (approximately 25% of total population). In addition, diuretic use could be confounded by use in patients where AF with RVR was incited by volume overload secondary to HF. Therefore, the risk of worsening heart failure cannot be ruled out from our investigation.

One limitation to our study was the higher than expected exclusion frequency of patients who did not achieve initial rate control at 30 min. Two-thirds of screened patients met this exclusion, which is discordant with many prior studies, but similar to the more recent Hirschy study. [11] The resulting low sample size reduced study power to detect the primary outcome and limits secondary outcome evaluation. Further limitations included those inherent to the retrospective design. Treatment bias was seen based on home medications and physician preference. The choice to re-dose was at the discretion of treating physicians; therefore, patients may not have received further IV rate control medications despite intermittent HR excursions above goal. In addition, data collection relied on medical record documentation in which data may have been omitted and readmission rates could only be assessed within our own health system.

Despite its limitations, our study is unique in that the observation time frame extended beyond that of prior studies, and it evaluated sustained efficacy while assessing multiple safety outcomes including hemodynamic parameters and worsening heart failure. Overall, the study aimed to examine longer rate control endpoints while considering multiple factors that may be weighed in a physician's choice of acute rate control agent for AF with RVR.

5. Conclusion

Atrial fibrillation with RVR is an important and common diagnosis in the ED. Successful acute treatment is vital to prevent complications such as myocardial ischemia, heart failure, and hemodynamic instability. Though limited by sample size, our study found no difference in sustained rate control for 3 h between diltiazem and metoprolol in real-world practice. In accordance with prior studies, our study showed significantly earlier rate control achievement with diltiazem. Safety outcomes were similar between groups as assessed by hemodynamic parameters and heart failure exacerbation. Further prospective studies should be conducted to explore sustained rate control in this patient population.

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None.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Martindale JL, deSouza IS, Silverberg M, et al. Beta-blockers versus calcium channel blockers for acute rate control of atrial fibrillation with rapid ventricular response: a systematic review. Euro J Emerg Med. 2015;22:150–4. https://doi.org/10.1097/MEJ.0000000000000227.

[2] Fromm C, Suau SJ, Cohen V, et al. Diltiazem vs. metoprolol in the management of atrial fibrillation or flutter with rapid ventricular rate in the emergency department. J Emerg Med. 2015;49(2):175–82. https://doi.org/10.1016/j.jemermed.2015.01.014.

[3] Demirican C, Cikriklar HI, Engindeniz Z, et al. Comparison of intravenous diltiazem and metoprolol in the management of rapid ventricular rate in atrial fibrillation. Emerg Med J. 2005;22(6):411–4 22/6/411 [pii].

[4] January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2014;64(21):e1–76. https://doi.org/10.1016/j.jacc2014.03.022.

[5] January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Associate Task force on Clinical Practice Guidelines and the Heart Rhythm Society. Circulation. 2019;140:e125–51. https://doi.org/10.1161/CIR.0000000000000665.

[6] Hines MC, Reed BN, Ivaturi V, et al. Diltiazem versus metoprolol for rate control in atrial fibrillation with rapid ventricular response in the emergency department. Am J Health-Syst Pharm. 2016;73(24):2068–76. https://doi.org/10.2146/ajhp160126.

[7] Scheuermeyer FX, Grafstein E, Stentstrom R, et al. Safety and efficacy of calcium channel blockers versus beta-blockers for rate control in patients with atrial fibrillation and no acute underlying medical illness. Acad Emerg Med. 2013;20(3):222–30. https://doi.org/10.1111/acem.12091.

[8] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic database capture (REDCap): a metadata-driven methodology and workflow process for providing translational research informatics support. J Biormed Inform. 2009;42:377–81.

[9] Dias VC, Weir SJ, Ellenbogen KA. Pharmacokinetics and pharmacodynamics of intravenous diltiazem in patients with atrial fibrillation or atrial flutter. Circulation. 1992;86(5):1421–8. https://doi.org/10.1161/01.cir.86.5.1421.

[10] Benfield P, Clissold SP, Brogden RN. Metoprolol. Drugs. 1986;31(5):376–429. https://doi.org/10.2165/00003495-198631050-00002.

[11] Hirschy R, Ackerbauer KA, Peksa GD, et al. Metoprolol vs. diltiazem in the acute management of atrial fibrillation in patients with heart failure with reduced ejection fraction. Am J Emerg Med. 2019;37(1):80–4. https://doi.org/10.1015/j.ajem.2018.04.062.