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Intravenous diltiazem versus metoprolol for acute rate control of atrial fibrillation with rapid ventricular response in the emergency department: a retrospective cohort study

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Abstract

Background

Intravenous diltiazem and metoprolol are both used for acute rate control of atrial fibrillation with rapid ventricular response, but comparative real-world evidence is limited. We compared their effectiveness and safety in the emergency department and assessed how robust any difference was to missing outcome data and confounding.

Methods

This single-center retrospective cohort study included adults with atrial fibrillation with rapid ventricular response treated with intravenous diltiazem or metoprolol in a tertiary-care emergency department in Saudi Arabia between January 2022 and August 2025. The primary outcome was heart rate < 100 beats/min at 1 hour. Differences were expressed as absolute risk differences with 95% confidence intervals (CIs). Robustness was assessed with complete-case, best-/worst-case bounding, and multivariable analyses.

Results

Of 293 patients, 147 received diltiazem and 146 received metoprolol. One-hour rate control was achieved in 30.6% versus 19.2% (risk difference 11.4 percentage points, 95% CI 1.5–21.1). One-hour heart rate was missing in 15.6% and 30.1% of patients, respectively. The difference was not robust: the complete-case risk difference was 8.8 percentage points (95% CI − 3.4 to 20.5), bounding risk differences ranged from − 18.7 to 27.1 percentage points, and the adjusted odds ratio was 0.84 (95% CI 0.34–2.06). Thirty-minute rate control was 32.7% versus 13.0% (risk difference 19.6 percentage points, 95% CI 10.1–28.8). Hypotension and bradycardia were uncommon, and 90-day emergency department return was similar (35.4% vs. 35.6%).

Conclusions

Diltiazem was associated with higher unadjusted early rate control, but this difference was sensitive to differential missing data and was not supported by complete-case or adjusted analyses. Neither agent was shown to be superior; a randomized trial with standardized weight-based dosing is needed.

Background

Atrial fibrillation (AF) is the most common sustained cardiac dysrhythmia and is associated with substantial morbidity, mortality, and healthcare utilization [1–4]. AF with rapid ventricular response (RVR) is an important emergency department (ED) presentation because excessive ventricular rates may

reduce cardiac output and precipitate hemodynamic instability, particularly in patients with underlying cardiac dysfunction [1, 2]. AF also increases the risk of thromboembolic complications and imposes a substantial healthcare burden through hospitalizations, ED visits, and associated costs [1–3].

Management of AF with RVR is guided by hemodynamic status, left ventricular systolic function, comorbidities, and clinical context. Current guidelines recommend beta-blockers or nondihydropyridine calcium-channel blockers, such as diltiazem or verapamil, for acute rate control in hemodynamically stable patients, with the latter recommended when left ventricular ejection fraction is > 40% [1, 2]. Immediate synchronized electrical cardioversion is recommended for hemodynamic instability attributable to AF [1, 2].

Several studies have compared intravenous diltiazem and metoprolol for acute rate control in AF with RVR, with variable findings [5–11]. Some have suggested more rapid early rate control with diltiazem, although differences at later timepoints have been less consistent [7–11]. Weight-based dosing of both agents has also been evaluated [5, 6].

Despite this evidence, uncertainty remains because of heterogeneity in patient populations, outcome definitions, assessment timepoints, and dosing regimens [5–16]. Real-world weight-based dosing also varies and may influence treatment response [5, 6]. Further evaluation of comparative effectiveness and dosing patterns in routine ED practice is therefore warranted.

Accordingly, this study aimed to compare the effectiveness and safety of intravenous diltiazem and metoprolol for acute rate control of AF with RVR in the ED, with additional evaluation of serial hemodynamic response, weight-based dosing, additional rate-control therapy, and short- and medium-term clinical outcomes.

Methods

Study Design and Participants

This single-center retrospective cohort study included adults aged ≥ 18 years presenting to a tertiary-care ED between January 2022 and August 2025 with electrocardiogram-confirmed AF and ventricular rate > 100 beats/min who received intravenous diltiazem or metoprolol as the initial rate-control strategy. Treatment was at clinician discretion. Patients with hemodynamic instability requiring immediate cardioversion, Wolff–Parkinson–White syndrome, no post-treatment vital-sign documentation, or intentional co-administration of both agents were excluded. The study was approved by the Institutional Review Board of King Abdullah International Medical Research Center (protocol no. 0000011624), with a waiver of informed consent because of the retrospective design. The study was conducted in accordance with the Declaration of Helsinki and is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline; the completed checklist is provided in Additional file 2.

Data Collection and Outcomes

Demographic, clinical, laboratory, and treatment data were extracted from electronic medical records. Heart rate (HR) and systolic blood pressure (SBP) were recorded at baseline and 15, 30, 60, 120, and 240 min after treatment.

The primary outcome was rate-control success, defined a priori as HR < 100 beats/min at 1 h [10, 13, 15]. Secondary outcomes included rate-control success at 30 min and 4 h, HR reduction, serial HR and SBP, additional rate-control therapy, cardioversion, hypotension (SBP < 90 mmHg), bradycardia (HR < 60 beats/min), intensive care unit (ICU) transfer, discharge home, new anticoagulation, and unplanned ED return within 90 days. Additional rate-control therapy was defined as administration of any additional rate-control agent during the ED visit.

Weight-Based Dosing

Diltiazem dose was normalized to body weight and categorized using a prespecified ± 20% margin around the 0.25 mg/kg initial bolus: <0.20, 0.20–0.30, or > 0.30 mg/kg. Weight-adjusted metoprolol dosing was calculated when data were available.

Statistical Analysis

Continuous variables were compared using independent-samples *t*-tests or Mann–Whitney *U* tests and categorical variables using χ^2 or Fisher's exact tests, as appropriate.

Three complete-case multivariable logistic regression models evaluated 1-h rate-control success, additional rate-control therapy, and 90-day ED return. The first two models adjusted for treatment, baseline HR, age, sex, heart failure, ischemic heart disease, chronic kidney disease, and time to treatment. The 90-day return model included treatment, baseline HR, age, sex, heart failure, new-onset AF, elevated B-type natriuretic peptide (BNP > 100 pg/mL), time to treatment, and prior anticoagulation. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC-ROC).

Between-group differences for binary outcomes were expressed as absolute risk differences (RDs; diltiazem minus metoprolol) with Newcombe hybrid-score 95% confidence intervals (CIs), and for continuous outcomes as mean differences with 95% CIs. In the primary analysis, patients without a documented 1-h HR were classified as not achieving rate control. Because missingness differed between groups and was unlikely to be random, robustness was assessed with (1) a complete-case analysis and (2) a best-/worst-case bounding analysis in which all patients with a missing 1-h HR were classified as successes in one treatment group and failures in the other. The unadjusted odds ratio (OR) with 95% CI was also reported for the primary outcome. Secondary and subgroup analyses were

exploratory, without adjustment for multiple comparisons. Tests were two-sided, with $p < 0.05$ considered statistically significant.

All eligible patients during the study period were included, and no a priori sample-size calculation was performed. With 147 and 146 patients, the study had 80% power (two-sided α = 0.05) to detect an absolute difference of approximately 14 percentage points in 1-h rate-control success, assuming a success rate of 19.2% with metoprolol. Smaller but potentially clinically relevant differences therefore could not be excluded.

Use of Generative Artificial Intelligence

Claude (Anthropic) was used to improve the language and readability of the manuscript. The authors reviewed and edited all output and take full responsibility for the content of this article.

Results

Patient Characteristics

A total of 293 patients met the inclusion criteria: 147 received diltiazem and 146 received metoprolol. Patients receiving diltiazem were younger, had higher baseline HRs, and had lower rates of ischemic heart disease, chronic kidney disease, and prior anticoagulation use, as well as lower BNP and blood urea nitrogen (BUN) levels. Other baseline characteristics were generally comparable between groups (Table 1).

Table 1
Baseline characteristics of study patients.

Characteristic	Diltiazem (*n* = 147)	Metoprolol (*n* = 146)	*p*-Value
Demographics			
Age, years	56.5 ± 15.4	60.9 ± 15.3	**0.015**
Male sex	59 (40.1)	75 (51.4)	0.070
Weight, kg	82.3 ± 19.0	81.3 ± 16.6	0.902
Comorbidities			
Hypertension	79 (53.7)	95 (65.1)	0.064
Diabetes mellitus	65 (44.2)	70 (47.9)	0.601
Prior atrial fibrillation	65 (44.2)	62 (42.5)	0.853
Heart failure	20 (13.6)	27 (18.5)	0.327
Ischemic heart disease	17 (11.6)	31 (21.2)	**0.038**
Chronic kidney disease	3 (2.0)	13 (8.9)	**0.020**
Thyroid disease	13 (8.8)	10 (6.8)	0.676
COPD	3 (2.0)	3 (2.1)	1.000
Previous stroke	6 (4.1)	3 (2.1)	0.505
Smoking	7 (4.8)	10 (6.8)	0.607
Prior medications			
Prior anticoagulation	38 (25.9)	56 (38.4)	**0.030**
Presenting vital signs			
Heart rate, beats/min	128.1 ± 34.8	119.4 ± 30.9	**0.015**
Systolic blood pressure, mmHg	134.0 ± 22.2	133.7 ± 22.2	0.720
Diastolic blood pressure, mmHg	86.6 ± 18.4	83.1 ± 16.7	0.140
Oxygen saturation, %	96.7 ± 7.5	97.7 ± 2.2	0.400
Laboratory values			
BNP, pg/mL	47.3 [19.2–135.5]	69.9 [33.6–139.0]	**0.034**
BUN, mmol/L	4.8 [3.7–6.1]	5.7 [4.2–7.2]	**< 0.001**
Potassium, mmol/L	4.2 [4.0–4.5]	4.3 [4.0–4.7]	0.171
INR	1.1 [1.0–1.1]	1.1 [1.0–1.2]	0.058

Characteristic	Diltiazem (*n* = 147)	Metoprolol (*n* = 146)	*p*-Value
Demographics			
Sodium, mmol/L	138.0 [136–140]	138.0 [136–139]	0.685

Data are presented as mean ± SD, *n* (%), or median [IQR], as appropriate. *p*-Values represent between-group comparisons using the independent-samples *t*-test or Mann–Whitney *U* test for continuous variables and the χ^2 test or Fisher's exact test for categorical variables, as appropriate. Available-case data were used; denominators may vary because of missing data. Bold *p*-values indicate statistical significance at $p < 0.05$. BNP, B-type natriuretic peptide; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; INR, international normalized ratio; IQR, interquartile range; SD, standard deviation.

Primary Outcome

Rate-control success (HR < 100 beats/min at 1 h) occurred in 45/147 patients (30.6%) receiving diltiazem and 28/146 (19.2%) receiving metoprolol ($p = 0.033$; Table 2; Additional file 1: Figure S1), corresponding to an absolute RD of 11.4 percentage points (95% CI 1.5–21.1) and an unadjusted OR of 1.86 (95% CI 1.08–3.19).

One-hour HR measurements were unavailable for 23/147 patients (15.6%) in the diltiazem group and 44/146 (30.1%) in the metoprolol group and were classified as not achieving rate control in the primary analysis. In the complete-case analysis ($n = 124$ and $n = 102$, respectively), success was 36.3% versus 27.5% (RD 8.8 percentage points, 95% CI − 3.4 to 20.5; OR 1.51, 95% CI 0.85–2.66). In the bounding analysis, the RD ranged from − 18.7 percentage points (95% CI − 29.3 to − 7.5) when all missing outcomes were assumed to favor metoprolol to 27.1 (95% CI 16.5 to 36.9) when all were assumed to favor diltiazem, indicating that the direction of the treatment effect depended on the unobserved outcomes (Table 2).

Table 2
Primary, secondary, and safety outcomes with between-group differences.

Outcome	Diltiazem (*n* = 147)	Metoprolol (*n* = 146)	Difference (95% CI)	*p*-Value
Primary outcome				
Rate control at 1 h (HR < 100 beats/min)	45/147 (30.6)	28/146 (19.2)	11.4 (1.5 to 21.1)	0.033
Complete-case analysis [a]	45/124 (36.3)	28/102 (27.5)	8.8 (− 3.4 to 20.5)	0.20
Bounding: missing favor metoprolol [b]	45/147 (30.6)	72/146 (49.3)	−18.7 (− 29.3 to − 7.5)	—
Bounding: missing favor diltiazem [b]	68/147 (46.3)	28/146 (19.2)	27.1 (16.5 to 36.9)	—
Secondary efficacy outcomes				
Rate control at 30 min (HR < 100 beats/min)	48/147 (32.7)	19/146 (13.0)	19.6 (10.1 to 28.8)	< 0.001
Rate control at 4 h (HR < 100 beats/min)	44/147 (29.9)	32/146 (21.9)	8.0 (− 2.0 to 17.8)	0.152
Absolute HR reduction at 1 h, beats/min	18.9 ± 42.1	12.4 ± 36.4	6.5 (− 3.7 to 16.7)	0.258
HR reduction at 1 h, %	13.1 ± 25.2	9.9 ± 25.3	3.2 (− 3.4 to 9.8)	0.221
Additional rate-control therapy	88 (59.9)	62 (42.5)	17.4 (6.0 to 28.2)	0.004
Cardioversion	18 (12.2)	14 (9.6)	2.7 (− 4.6 to 10.0)	0.588
Safety outcomes				
Hypotension (SBP < 90 mmHg)	1 (0.7)	0 (0.0)	0.7 (− 1.9 to 3.8)	1.000
Bradycardia (HR < 60 beats/min)	2 (1.4)	0 (0.0)	1.4 (− 1.4 to 4.8)	0.481
Disposition and follow-up				
ICU transfer	0 (0.0)	10 (6.8)	−6.8 (− 12.1 to − 2.8)	0.004
Discharged home from ED	110 (74.8)	114 (78.1)	−3.3 (− 12.9 to 6.5)	0.604
New anticoagulation initiated in ED	65 (44.2)	89 (61.0)	−16.7 (− 27.6 to − 5.3)	0.006

Outcome	Diltiazem (*n* = 147)	Metoprolol (*n* = 146)	Difference (95% CI)	*p*-Value
Primary outcome				
90-day ED return	52 (35.4)	52 (35.6)	−0.2 (− 11.1 to 10.6)	1.000

Data are presented as *n* (%) or mean ± SD. Rate-control success was defined as HR < 100 beats/min at the specified post-treatment timepoint. For the primary 1-h analysis, patients without a documented 1-h HR measurement were classified as not achieving rate control. Differences are diltiazem minus metoprolol: absolute RDs in percentage points with Newcombe 95% CIs for binary outcomes, and mean differences with 95% CIs for continuous outcomes (calculated among patients with a documented 1-h HR). [a] Complete-case analysis restricted to patients with a documented 1-h HR. [b] Bounding analysis: all patients with a missing 1-h HR (diltiazem 23, metoprolol 44) classified as successes in one group and failures in the other. Categorical outcomes were compared using the χ^2 test or Fisher's exact test, as appropriate; continuous outcomes were compared using the Mann–Whitney *U* test. CI, confidence interval; ED, emergency department; HR, heart rate; ICU, intensive care unit; SBP, systolic blood pressure; SD, standard deviation.

Secondary Outcomes

Rate-control success at 30 min was higher with diltiazem (32.7% vs. 13.0%; RD 19.6 percentage points, 95% CI 10.1–28.8), whereas success at 4 h was similar (29.9% vs. 21.9%; RD 8.0, 95% CI − 2.0 to 17.8). Additional rate-control therapy was more frequent with diltiazem (59.9% vs. 42.5%; RD 17.4, 95% CI 6.0–28.2). Hypotension (RD 0.7, 95% CI − 1.9 to 3.8) and bradycardia (RD 1.4, 95% CI − 1.4 to 4.8) were uncommon. ICU transfer occurred in 0% versus 6.8% (RD − 6.8, 95% CI − 12.1 to − 2.8), while 90-day ED return was similar (35.4% vs. 35.6%; RD − 0.2, 95% CI − 11.1 to 10.6). Serial HR and SBP trajectories are shown in Fig. 1. Other secondary outcomes are presented in Table 2 and Additional file 1: Figures S1 and S3.

Exploratory subgroup analyses are shown in Fig. 2 and Additional file 1: Figure S4; formal treatment-by-subgroup interaction testing was not performed.

Diltiazem Weight-Based Dosing

Among 145 patients with dosing data, 49.7% received diltiazem 0.20–0.30 mg/kg, 31.7% received < 0.20 mg/kg, and 18.6% received > 0.30 mg/kg. One-hour success was numerically highest with 0.20–0.30 mg/kg (36.1% vs. 26.1% and 25.9%, respectively), although differences were not statistically significant (Table 3; Additional file 1: Figure S2).

Table 3
Diltiazem weight-based dosing analysis (*n* = 145).

Diltiazem dose category	*n* (%)	Rate control at 1 h, *n* (%)	*p*-Value [a]
Below target range (< 0.20 mg/kg)	46 (31.7)	12/46 (26.1)	0.243
Target range (0.20–0.30 mg/kg)	72 (49.7)	26/72 (36.1)	Reference
Above target range (> 0.30 mg/kg)	27 (18.6)	7/27 (25.9)	0.356
Overall	145 (100)	45/145 (31.0)	—

Rate-control success was defined as HR < 100 beats/min at 1 h after treatment initiation. The prespecified target-dose range was 0.20–0.30 mg/kg, corresponding to ± 20% of the recommended 0.25 mg/kg initial intravenous diltiazem bolus. [a] *p*-Values compare the below-target and above-target groups separately with the target-range group. Among 145 patients with available dose and body-weight data, the median administered dose was 0.236 mg/kg (IQR 0.174–0.282), and the mean absolute dose was 19.2 ± 8.8 mg. Patients without a documented 1-h HR measurement were classified as not achieving rate-control success, consistent with the primary analysis. HR, heart rate; IQR, interquartile range.

Multivariable Analysis

Complete-case multivariable analyses included 159 patients (Table 4). Treatment group was not independently associated with 1-h rate-control success (adjusted OR 0.841, 95% CI 0.344–2.056; $p = 0.704$), additional rate-control therapy (adjusted OR 1.512, 95% CI 0.699–3.267; $p = 0.293$), or 90-day ED return (adjusted OR 1.150, 95% CI 0.476–2.778; $p = 0.756$). Higher baseline HR was associated with lower odds of 1-h success ($p = 0.011$), and longer time to treatment was associated with higher odds of 90-day ED return ($p = 0.009$).

Table 4
Multivariable logistic regression analyses of clinical outcomes.

Model/Predictor	Adjusted OR	95% CI	*p*-Value
Model 1: Rate control at 1 h (*n* = 159; 38 events; AUC-ROC = 0.674)			
Diltiazem (reference: metoprolol)	0.841	0.344–2.056	0.704
Baseline heart rate, per beat/min	0.984	0.971–0.996	**0.011**
Model 2: Additional rate-control therapy (n = 159; 75 events; AUC-ROC = 0.680)			
Diltiazem (reference: metoprolol)	1.512	0.699–3.267	0.293
Baseline heart rate, per beat/min	1.010	0.999–1.021	0.078
Model 3: 90-day unplanned ED return (n = 159; 45 events; AUC-ROC = 0.670)			
Diltiazem (reference: metoprolol)	1.150	0.476–2.778	0.756
Time to treatment, per minute	1.004	1.001–1.007	**0.009**

Adjusted ORs were estimated using multivariable logistic regression. Metoprolol was the reference treatment group. Models 1 and 2 included treatment group, baseline HR, age, sex, heart failure, ischemic heart disease, chronic kidney disease, and time to treatment. Model 3 included treatment group, baseline HR, age, sex, heart failure, new-onset AF, elevated BNP, time to treatment, and prior anticoagulation. ORs for baseline HR and time to treatment are expressed per 1 beat/min and 1 min increase, respectively. Analyses were restricted to complete cases. Given the limited number of outcome events relative to the number of covariates, adjusted estimates should be interpreted as exploratory. Bold *p*-values indicate statistical significance at $p < 0.05$. AF, atrial fibrillation; AUC-ROC, area under the receiver operating characteristic curve; BNP, B-type natriuretic peptide; CI, confidence interval; ED, emergency department; OR, odds ratio.

Discussion

In this retrospective cohort of 293 ED patients with AF-RVR, diltiazem was associated with higher unadjusted rate-control success at 30 min and 1 h than metoprolol, whereas outcomes were similar at later timepoints. However, the 1-h difference was not robust: it was attenuated, with a CI including no difference, in the complete-case analysis; its direction depended on assumptions about missing outcomes in the bounding analysis; and it was not maintained after multivariable adjustment. Accordingly, these data do not establish that either agent provides superior rate control. Adverse events were uncommon, and 90-day ED return rates were similar between groups.

The higher unadjusted early rate-control success with diltiazem is broadly consistent with previous studies. Demircan et al. and Fromm et al. reported greater early HR reduction with diltiazem [9, 10], while Martindale et al. reported findings favoring calcium-channel blockers for acute rate control [11]. More

recent systematic reviews and meta-analyses have generally reported greater rate-control success with diltiazem, although study populations, dosing regimens, outcome definitions, and assessment timepoints have varied [17–19]. At later timepoints, differences have been less consistent: Hargrove et al. found no significant difference in sustained rate control [13], whereas Moskowitz et al. reported different treatment responses in a critically ill population [12]. These differences highlight the importance of clinical setting and patient characteristics when comparing studies.

Two separate sources of uncertainty limit interpretation of the unadjusted difference. First, 1-h HR was missing nearly twice as often after metoprolol (30.1% vs. 15.6%). Missingness was unlikely to be random: patients who responded may have been monitored less closely, or nonresponders may have moved to other care pathways before repeat measurement. Classifying missing values as failures therefore penalizes the group with more missing data, and the bounding analysis showed that plausible assumptions about these patients yield estimates ranging from a clear metoprolol advantage to a clear diltiazem advantage. Second, treatment was not randomly allocated. Diltiazem-treated patients were younger, had higher baseline HR, and less often had ischemic heart disease or chronic kidney disease. After adjustment, diltiazem was not associated with 1-h rate-control success (adjusted OR 0.841, 95% CI 0.344–2.056), and the point estimate reversed direction, whereas higher baseline HR was associated with lower odds of success (OR 0.984 per 1 beat/min increase, 95% CI 0.971–0.996). Because both the complete-case and adjusted analyses failed to support the primary result, the unadjusted estimate should not be used to guide agent selection.

Diltiazem dosing also varied substantially. Among patients with available dose and weight data, 49.7% received the prespecified target range of 0.20–0.30 mg/kg, whereas 31.7% received < 0.20 mg/kg and 18.6% received > 0.30 mg/kg. One-hour rate-control success was numerically highest within the target range (36.1%), but differences between dosing categories were not statistically significant. Similar variability in diltiazem dosing has been described previously [5, 20]. Because dosing was not randomized, these findings do not establish a dose–response relationship but support further evaluation of standardized weight-based dosing strategies.

Hypotension and bradycardia were uncommon, and post-treatment SBP did not differ significantly between groups. Given the small number of events, however, the study was not sufficiently powered to establish equivalent safety. The higher unadjusted ICU-transfer rate in the metoprolol group should likewise not be interpreted as a treatment effect because ICU transfer was not included in the adjusted models and may have been influenced by baseline differences, illness severity, ventricular function, and clinician treatment selection.

New anticoagulation was more frequent in the metoprolol group (61.0% vs. 44.2%), but formal CHA_2DS_2-VASc scores were not systematically available; therefore, this finding should be considered descriptive rather than an effect of the rate-control agent. Ninety-day ED return rates were similar between groups (35.4% vs. 35.6%), and treatment group was not independently associated with return. Although longer

time to treatment was associated with slightly higher odds of 90-day return, the small effect size and observational design preclude causal interpretation.

Overall, the unadjusted findings resemble previous studies and meta-analyses reporting greater early rate-control success with diltiazem [11, 17–19], but in this cohort the association did not withstand sensitivity and adjusted analyses. Given that AF-RVR is common and both agents are widely available, these results should not be interpreted as favoring one agent. A pragmatic randomized trial with standardized weight-based dosing, protocolized HR measurement, and complete outcome ascertainment is needed.

Limitations

This study has several limitations. Its retrospective, single-center design limits causal inference and generalizability, and clinician-directed treatment selection introduces potential confounding by indication. Residual confounding remains possible, particularly because left ventricular ejection fraction was not systematically incorporated despite its potential influence on treatment selection.

One-hour HR measurements were missing more frequently in the metoprolol group than in the diltiazem group (30.1% vs. 15.6%), and missingness was unlikely to be random. Missing measurements were classified as not achieving rate control in the primary analysis; however, the complete-case analysis produced an attenuated difference with a CI that included zero, and the bounding analysis showed that the direction of the effect depended on the unobserved outcomes. The primary result should therefore be regarded as uncertain. Missing measurements may also have affected estimates at other timepoints.

The adjusted analyses were restricted to complete cases and included relatively few outcome events for the number of covariates; therefore, these estimates should be considered exploratory. Diltiazem dosing was observational and clinician-determined, limiting causal conclusions regarding dosing categories. Finally, the small number of adverse events limited safety comparisons, CHA_2DS_2-VASc scores were unavailable, and 90-day ED returns were captured only at the index institution.

Conclusions

In this retrospective cohort of patients with AF-RVR, diltiazem was associated with higher unadjusted early rate-control success than metoprolol, but this difference was sensitive to differential missing outcome data and was not supported by complete-case or multivariable analyses. The study therefore does not establish the superiority of either agent. Adverse events and 90-day ED return rates were similar. Variation in diltiazem dosing and the uncertainty inherent in this observational comparison support a prospective randomized evaluation using standardized weight-based dosing.

Abbreviations

AF, atrial fibrillation; AUC-ROC, area under the receiver operating characteristic curve; BNP, B-type natriuretic peptide; BUN, blood urea nitrogen; CI, confidence interval; ED, emergency department; HR, heart rate; ICU, intensive care unit; OR, odds ratio; RD, risk difference; RVR, rapid ventricular response; SBP, systolic blood pressure; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of King Abdullah International Medical Research Center, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia (IRB no. 0000011624). The requirement for informed consent was waived by the Institutional Review Board because of the retrospective design and the use of de-identified data.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available because they contain patient health information, but de-identified data and analysis code are available from the corresponding author on reasonable request, subject to institutional and IRB approval.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MA and SAA conceived and designed the study and drafted the manuscript. HA, DA and SBS collected and curated the data. FFA, AA, AHH, MAA and LA critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Figures

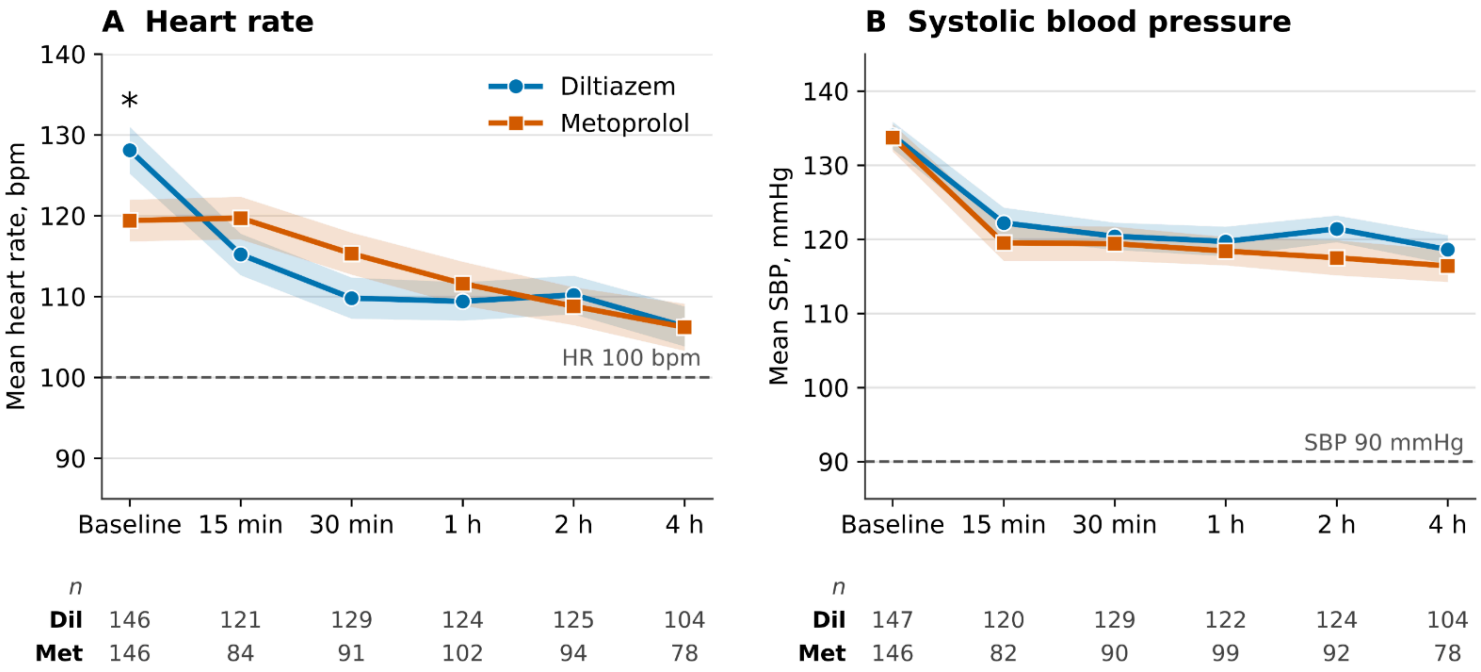

Figure 1

Serial heart rate and systolic blood pressure trajectories after treatment. (A) Mean heart rate and (B) mean systolic blood pressure at baseline and 15 min, 30 min, 1 h, 2 h, and 4 h after treatment initiation. Shaded areas represent ±1 SEM. Dashed reference lines indicate HR 100 beats/min (panel A) and SBP 90 mmHg (panel B). An asterisk indicates a between-group difference with $p < 0.05$ (Mann–Whitney *U* test). The number of patients with a recorded value at each timepoint is shown beneath each panel. HR, heart rate; SBP, systolic blood pressure; SEM, standard error of the mean.

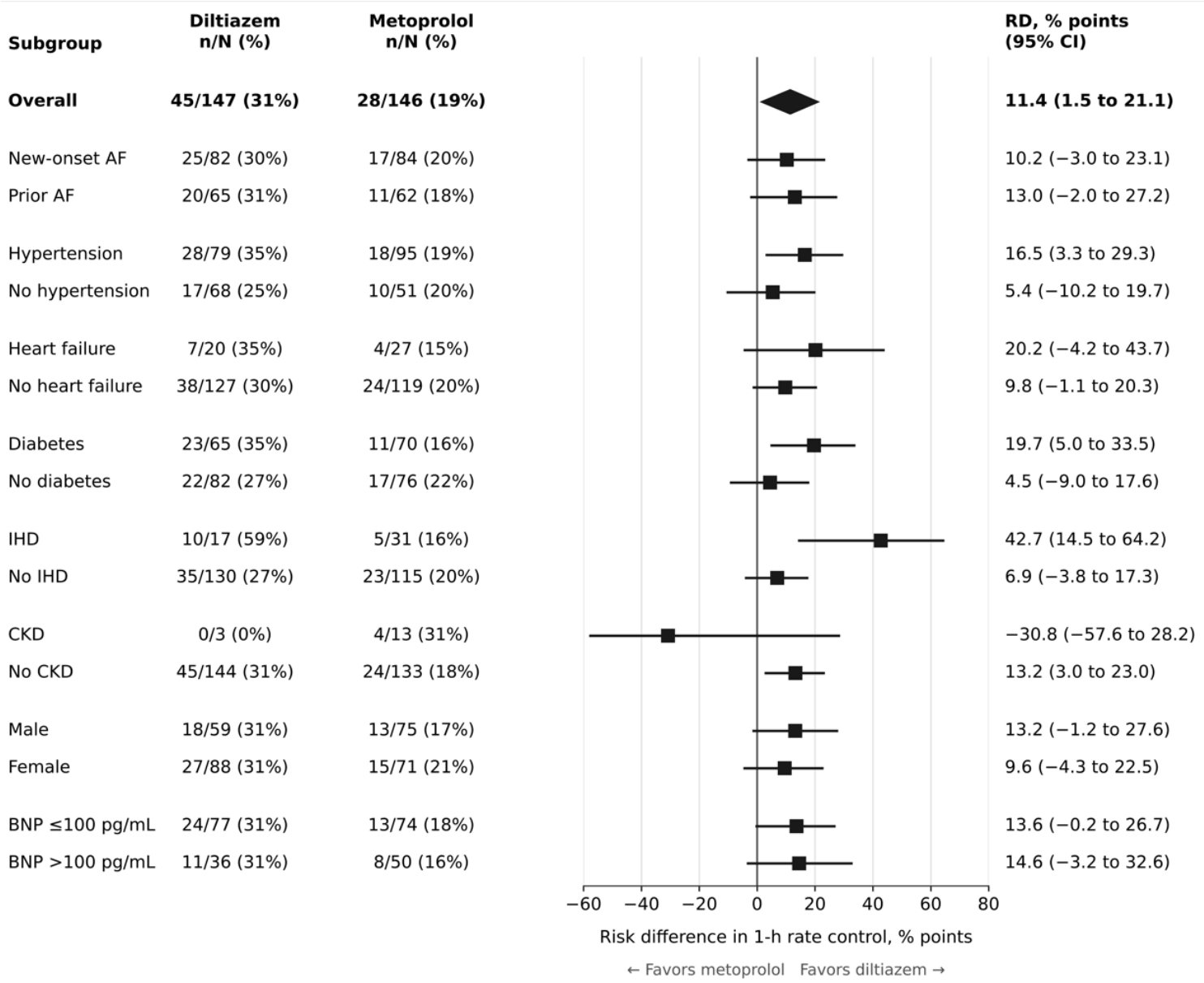

Figure 2

Subgroup analysis of 1-hour rate-control success by treatment group. Squares (diamond for the overall cohort) show the absolute risk difference (RD; diltiazem minus metoprolol) in the proportion of patients achieving HR <100 beats/min at 1 h; horizontal lines show Newcombe 95% confidence intervals. Patients without a documented 1-h HR were classified as not achieving rate control, consistent with the primary analysis. Subgroup analyses were exploratory and unadjusted, formal treatment-by-subgroup interaction testing was not performed, and estimates in small subgroups (e.g., chronic kidney disease, ischemic heart disease) are imprecise. AF, atrial fibrillation; BNP, B-type natriuretic peptide; CKD, chronic kidney disease; HR, heart rate; IHD, ischemic heart disease.

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