Critical Review Form
Therapy

PGY-4

HYPERLINK "http://pmid.us/35623182"Hasbrouck M, Nguyen TT. Acute management of atrial fibrillation in congestive heart failure with reduced ejection fraction in the emergency department. Am J Emerg Med. 2022 Aug;58:39-42.

Objectives: **"to compare the incidence of adverse effects in a larger HFrEF [heart failure with reduced ejection fraction] patient population whose AF [atrial fibrillation] with RVR [rapid ventricular response] was treated with IV diltiazem or metoprolol in the ED." (p. 39)**

Methods: **This single-center, retrospective study was conducted in the ED of Virginia Commonwealth Medical Center in Richmond, VA between January 1, 2018 and December 31, 2019. Patients aged 18 years or older presenting with AF with RVR for which IV diltiazem or metoprolol was ordered within 12 hours of arrival with a formal echocardiogram documenting an EF ≤ 40% during the same encounter were eligible for inclusion. Exclusion criteria were pregnancy, incarceration, and repeat encounters for the same patient.**

The primary outcome was adverse events, defined as hypotension (SBP < 90 mmHg requiring a fluid bolus or vasopressors) or bradycardia (HR < 60 bpm) within 60 minutes of ED intervention, or worsening heart failure symptoms (increase in O2 requirement by at least 2 liters or requirement of an inotrope) within 48 hours of ED intervention. Secondary outcomes included rate control failure, admission level of care, ED length of stay, hospital length of stay, and in-hospital mortality.

Out of 169 patients screened, 125 met inclusion criteria with 57 (45.6%) receiving diltiazem and 68 (54.4%) receiving metoprolol. The mean age was 62 years and 76% were male. The mean EF was 16%.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis?**	
1.	Were patients randomized?	No. This was a retrospective, observational study in which initial treatment group was determined by the treating clinician. This study is hence at high risk of selection bias.
2.	Was allocation concealed? In other words, was it possible to subvert the randomization process to ensure that a patient would be "randomized" to a particular group?	N/A

3.	Were patients analyzed in the groups to which they were randomized?	Uncertain. This was not a randomized trial, and patients were analyzed based on whether they received IV metoprolol or diltiazem. The authors make no mention of patients receiving both agents and how they were handled in the analysis.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Somewhat. Patients in the diltiazem group were somewhat younger than those in the metoprolol group (mean 59 vs 65 years), were more likely to have combined systolic and diastolic heart failure (47% vs. 38%), were less likely to have a past history of AF (63% vs. 76%), were less likely to be on a home beta blocker (58% vs. 81%), and had higher mean initial diastolic blood pressure (100 vs. 90 mmHg).
B.	**Did experimental and control groups retain a similar prognosis after the study started?**	
1.	Were patients aware of group allocation?	Yes. While patients and clinicians were aware of treatments being given, this was a retrospective study and hence was unlikely to be influenced by performance bias.
2.	Were clinicians aware of group allocation?	See above.
3.	Were outcome assessors aware of group allocation?	Yes. The authors make no mention of blinding of outcome assessors, raising the risk of observer bias.
4.	Was follow-up complete?	Yes. All outcomes were measured during the hospitalization; hence outcomes were available for all patients enrolled.
II.	**What are the results ?**	
1.	How large was the treatment effect?	● For the composite primary adverse event outcome, there was no statistically significant difference in the diltiazem or metoprolol groups (32% vs. 21%, p = 0.217). ○ There was a statistically significant increased risk of worsening CHF symptoms in the diltiazem group (33% vs. 15%, p = 0.019). ● There was no difference in rate control failure (51% vs. 62%, p = 0.277), although patients receiving diltiazem had a lower mean HR at 60 minutes (109 bpm vs. 117 bpm, p = 0.028).

		• There was no difference in admission level of care, ED length of stay, hospital length of stay, or in-hospital mortality.
2.	How precise was the estimate of the treatment effect?	See above. The authors do not report actual **effect sizes** or associated **confidence intervals**.
III.	**How can I apply the results to patient care?**	
1.	Were the study patients similar to my patient?	Likely yes. This was a fairly recent study conducted at a large, urban ED in the US. It is likely that the patient population and treatments were similar with those in our institution (external validity).
2.	Were all clinically important outcomes considered?	Yes. The authors considered a broad array of patient-centered outcomes.
3.	Are the likely treatment benefits worth the potential harm and costs?	Uncertain. While this study found no statistically significant difference in the primary composite outcome of adverse events, this was a relatively small study and was underpowered to detect a potentially clinically significant difference. The study is further limited by its retrospective, observational design.

Limitations:

1. **This was a retrospective, observational study at high risk of selection bias; further, there was no blinding of patients, clinicians, or outcome assessors.**
2. **There were several significant differences in baseline prognostic factors, including higher rates of combined heart failure in the diltiazem group.**
3. **The authors do not report actual effect sizes or associated confidence intervals.**
4. **The study was underpowered to detect potentially clinically significant differences in the composite of adverse outcomes.**

Bottom Line:

This single-center, retrospective, observational study comparing IV diltiazem and metoprolol for the management of AF with RVR in patients with concomitant systolic heart failure found no statistically significant difference in the primary composite outcome of clinically significant hypotension, bradycardia, or worsening heart failure (32% vs. 21%, p = 0.217). There was a statistically significant increased risk of worsening CHF symptoms in the diltiazem group (33% vs. 15%, p = 0.019). The

study was underpowered to detect as potentially clinically significant difference in the primary outcome and was a high risk of selection bias.