



## Article Appraisal

**Article:** "Diltiazem vs Metoprolol in the Management of Atrial Fibrillation or Flutter with Rapid Ventricular Rate in the Emergency Department." Fromme, Christian, et al. April 2015. The Journal of Emergenc Medicine. Vol. No. pp1-18.

**Date of Journal Club:** Oct 1, 2015

**Resident Reviewer Name(s) and Residency Affiliation:** Robert Brunelle (R3) CCFP-EM

**Faculty Methodology/Bio-statistics Resource Person:** Dr. Corinne Hohl

---

### Background and Study Objective(s):

Both diltiazem and metoprolol are commonly used to treat atrial fibrillation and flutter with rapid ventricular response in the emergency department. This study aimed to compare the effectiveness of diltiazem with metoprolol for rate control in the ED.

### Study Design:

This was a prospective, double blind, randomized control trial, designed as a non-inferiority study. A convenience sample was enrolled as only patients presenting during hours in which a pharmacist was in house were included in the study. It was estimated that a sample size of 200 patients would achieve 80% power to detect noninferiority with a margin of equivalence of -10. The study was registered with clinicaltrials.gov.

### Inclusion:

- adult patients 18 years and older
- 12-lead ECG showing atrial fibrillation or atrial flutter with a ventricular rate of greater than or equal to 120bpm
- systolic blood pressure of greater than or equal to 90mm Hg

### Exclusion:

- systolic blood pressure less than 90mm Hg
- ventricular rate greater than or equal to 120bpm
- QRS greater than 0.100s
- second or third degree AV block
- temperature greater than 38.0 degrees Celcius
- acute ST elevation myocardial infarction
- known history of New York Heart Association Class IV heart failure
- active wheezing with a history of bronchial asthma or chronic obstructive pulmonary disease
- prehospital administration of diltiazem or other AV nodal blocking agent
- history of cocaine or methamphetamine use in the 24hrs prior to arrival
- history of sick sinus or preexcitation syndrome

- history of anemia with hemoglobin less than 11.0g/dL
- pregnancy, breastfeeding

2 Treatment arms (N = 52)

- metoprolol 0.15mg/kg IV to a max dose of 10mg , may repeat at 15min at 0.25mg/kg to a max dose of 10mg
- diltiazem 0.25mg/kg IV to a maximum of 30mg, may repeat at 15min at 0.35mg/kg to a max dose of 30mg

Primary Efficacy Outcome:

- Rate less than 100bpm within 30min

Primary Safety Outcomes:

- Rate less than 60bpm
- SBP < 90mm Hg

## Results:

- In the first five minutes, 50.0% of the diltiazem group and 10.7% of the metoprolol group reached the target heart rate
- By thirty minutes, 95.8% of the diltiazem group and 46.4% of the metoprolol group met the primary efficacy outcome
- Five metoprolol patients and one diltiazem patient became hypotensive ( $p = 0.199$ )
- Bradycardia occurred in one diltiazem patient ( $p = 0.462$ )
- In a Cox regression model, patients receiving diltiazem were 4.66 times (95% confidence interval 2.09 to 10.36;  $p = 0.0001$ ) more likely to reach target heart rate than were patients receiving metoprolol
- The study was stopped after only 25% enrollment when the safety monitoring team observed that significantly more patients in one study group were reaching the desired endpoint.

## Validity of Results:

- The study design was designed as non-inferiority but insufficiently powered to actually show this.
- There was no intention to treat analysis.
- There may be selection bias in that recruitment occurred only during daytime hours.
- Stopping the study early may have overestimated the treatment effects (“Problems of stopping trials early.”

Guyatt et al. BMJ 2012;344:e3863)

## Generalizability of Results:

The results of this study are applicable to the management of patients in atrial fibrillation or flutter with rapid ventricular response. This is a common ED presenting complaint, and both diltiazem and metoprolol are recommended as first-line agents by the Canadian Cardiovascular Society. The results give a clear edge to diltiazem in achieving rate control without an increase in adverse events. However, the trial was stopped early, and non-inferiority was not demonstrated as per the initial study design.

## The Bottom Line:

Both metoprolol and diltiazem appear safe in the treatment of atrial fibrillation and flutter with RVR, but further study is needed to compare the two agents in terms of efficacy.