Research Article AJCRAR (2022) 5:21



# American Journal of Cardiology Research and Reviews (ISSN:2637-4935)



# Failure to Consider Future Atrial Fibrillation Rate Control Needs after Presentation to the Emergency Department with Rapid Rate

Shabnam Tiwari, MD,<sup>2</sup> Katherine White, MD,<sup>1</sup> Shubash Adhikari, MD,<sup>2</sup> Johnathan Cobb, MS4,<sup>1</sup> Johnathan Shakesprere, MS4,<sup>1</sup> Erik Hanson, PharmD,<sup>4</sup> Suzanne Kemper, MPH,<sup>3</sup> Elaine Davis, RN, MBA, EdD,<sup>3</sup> William Carter, MD,<sup>3\*</sup>

<sup>1</sup>West Virginia University Health Sciences Center, Department of Internal Medicine, Charleston Division/Charleston Area Medical Center, Charleston, WV <sup>2</sup>West Virginia University Health Sciences Center, Morgantown, WV <sup>3</sup>Charleston Area Medical Center, Health Education and Research Institute, Charleston, WV <sup>4</sup>University of Charleston School of Pharmacy, Charleston, WV

## **ABSTRACT**

Atrial fibrillation (AF) usually presents to the emergency room (ED) with a rapid ventricular rate, which commonly, but not always, is symptomatic. Rate control is usually easily managed with diltiazem (DTZ) and beta blockers (BBs), typically metoprolol (MTP). Sinus rhythm is frequently restored within 48 hours by means of spontaneous conversion, electrical cardioversion, or medications. However, AF recurs within one year in 60-80% of these subjects. There are little data describing doses of DTZ and MTP used for AF rate control at discharge. A retrospective study of 576 patients presenting with acute AF were evaluated for admission and discharge rate control medications (RCMs). For the 319 (68%) patients with a ventricular rate ≥110bpm the admission and discharge dose of MTP was 61mg and 63mg and DTZ was 195mg and 204mg, respectively. Those who remained in AF had a modest increase in the two medications compared to the patients who converted to sinus rhythm. Current guidelines recommend DTZ up to 300 to 400mg and MTP up to 300mg for rate control for select patients. Concerns about high doses of MTP are mitigated by the MERIT-HF Trial demonstrating improved mortality and symptoms with doses of MTP up to 200mg demonstrating the safety and efficacy of MTP in high risk patients. Lack of follow-up of future AF recurrences is a limitation of the study. For those patients with acute AF and a heart rate (HR) >110bpm, a minimal increase in RCMs for those in AF at discharge was noted.

**Keywords:** atrial fibrillation management, rate control medications

# \*Correspondence to Author:

William H. Carter, MD CHERI Building, Second Floor 3211 MacCorkle Avenue, SE, Charleston, WV 25304 Phone: 304-576-0705

# How to cite this article:

Shabnam Tiwari, Katherine White, Shubash Adhikari, Johnathan Cobb, Johnathan Shakesprere, Erik Hanson, Suzanne Kemper, Elaine Davis, William Carter. Failure to Consider Future Atrial Fibrillation Rate Control Needs after Presentation to the Emergency Department with Rapid Rate. American Journal of Cardiology Research and Reviews, 2022, 5:21.



#### INTRODUCTION

The total cost of non-valvular atrial fibrillation (AF) care was estimated to be \$6.0 billion per year from 2004-2006 in the United States. The majority of this cost was related to inpatient care. [1] Rate control for AF is usually accomplished with the administration of diltiazem (DTZ) and/or beta blockers (BBs), typically metoprolol (MTP). in the emergency department (ED). [2] Conversion to normal sinus rhythm (NSR) typically occurs by means of electrical cardioversion or medications. [2] However, recurrent AF often leads to repeat ED admissions and hospitalizations within one year for non-ablated patients. [3, <sup>4]</sup> The purpose of this study was to evaluate admission and discharge doses of MTP and DTZ for patients presenting to the ED with rapid AF.

#### **METHODS**

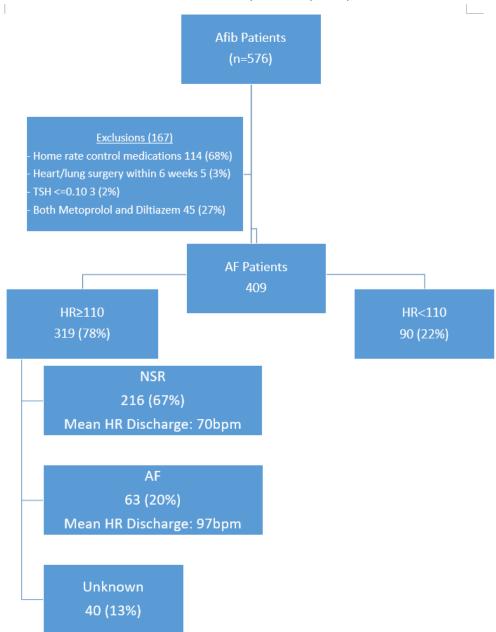
A retrospective, single tertiary care center review of MTP or DTZ used on admission and discharge from either the ED or hospital for patients with a primary diagnosis of AF. Chart review was performed on 576 patients. Those with a rapid

ventricular rate ≥ 110bpm were considered the study group. Patients with acute coronary syndrome, acute angina, heart failure, stroke, syncope, were below age 20 and over age 90, or several clinical comorbidities that put patients at a higher embolic risk, were excluded. Patients who received both MTP and DTZ and any new or increased rhythm control medications with rate control properties, other than MTP or DTZ alone, were also excluded. The rate slowing effect of metoprolol succinate and tartrate appears to be equally potent, thus we considered both as MTP when reporting the results.

Data analysis was performed using SAS (Version 9.3). Descriptive statistics for individual data elements included means and standard deviations for continuous variables and proportions and frequencies for categorical variables. Comparisons were performed using Chi-square or Fisher's exact tests for categorical variables and t-tests for continuous variables to determine statistically significant differences. Statistical significance was defined as P < 0.05.

**Table 1:** Baseline clinical presentation of patients with HR >110. (n=319)

	Total (N=319)
Age, years (±SD)	64 (±12.4)
Gender, Male (%)	163 (51%)
Mean HR (Range 110-215)	143 (±21)
ВМІ	32.0±8
<u>Co-morbidities</u>	
Heart Failure (%)	26 (8%)
Diabetes (%)	80 (26%)
Hypertension (%)	203 (65%)
Prior ablation (%)	42 (13%)
Type of Atrial fibrillation	
First episode (%)	139 (44%)
Known paroxysmal (%)	148 (46%)
Persistent (%)	32 (10%)
Ejection Fraction (±SD)	51.4 (±8.9)
Patient Management	
Admitted to hospital	246 (77%)
Discharged from ED	72 (23%)



**Figure 1:** Flowchart. Abbreviations:  $AF = atrial \ fibrillation$ ,  $HR = heart \ rate$ ,  $NSR = normal \ sinus \ rhythm$ .

#### RESULTS

Of the 576 adult patients screened, 167 (29%) were predominately excluded due to the use of new or increased doses of non DTZ or MTP medications with rate controlling properties. (Figure 1). A HR  $\geq$  110bpm on admission was observed in 319/409 (78%) patients with a mean ventricular rate of 143bpm (range 110-215). Baseline clinical characteristics are illustrated in Table 1. Upon discharge, for those patients with a HR  $\geq$ 110bmp, 63 (20%) remained in AF and 216/319 (68%) converted to NSR, either in the ED or hospital.

Admission and discharge dosages of MTP and DTZ for both those who converted to NSR and those who remained in AF are illustrated in Figure 2. Overall mean dose from admission to discharge for those patients with a HR ≥110bpm showed only a small increase in either MTP (P=0.37) or DTZ (P=0.35) (Figure 2). No increase in RCMs for either MTP (P=0.53) or DTZ (p=0.55) from admission to discharge was noted for those patients who converted to NSR in the ED or hospital. Those who persisted in AF after admission received only a small increase in RCMs, either MTP (P=0.22) or DTZ (P=0.08). (Figure 3)

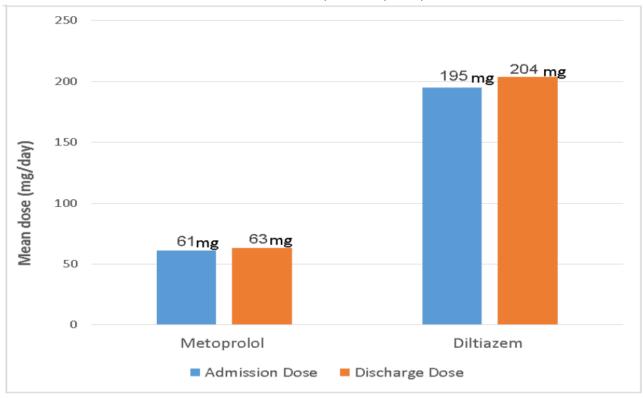
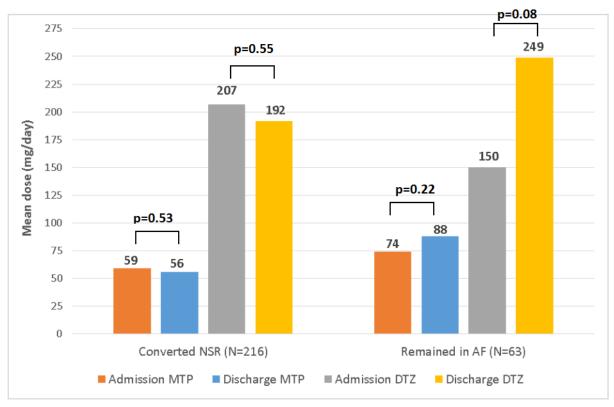
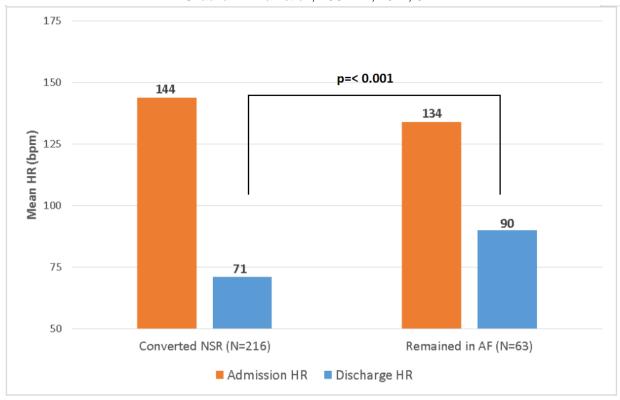


Figure 2: Mean dose RCMs on admission and discharge for all patients with admit HR  $\geq$ 110. (n=319) Abbreviations: mg = milligram.



**Figure 3:** Mean MTP or DTZ on admission and discharge for patients with admit HR  $\geq$ 110 and either converted to NSR (n= 216) or remained in AF (n=63). *Abbreviations: DTZ = diltiazem, MTP = metoprolol, NSR = normal sinus rhythm.* 

At the time of discharge, ventricular rate slowed those who remained in AF, the rate slowed to 71bpm for those who converted to NSR, while only 90bpm at rest (P=<0.001). (Figure 4)



**Figure 4:** Mean resting HR on admission and discharge for patients with admit HR ≥110 and either converted to NSR (n= 216) or remained in AF (n=63). *Abbreviations: HR* = *heartrate, NSR* = *normal sinus rhythm.* 

#### DISCUSSION

To our knowledge this is the only reported population with careful analysis of admission and discharge RCMs for patients presenting to the ED with rapid AF. Those patients with a rapid ventricular rate ≥ 110bpm were considered the study group. The average discharge doses of MTP 63mg/day and DTZ 204mg/day were well below the recommended doses for rate control of AF, especially considering the average admission AF rate was 143bpm. Doses of MTP up to 400mg/day and DTZ up to 360mg/day are acceptable upper limits of dosing for occasional patients. <sup>[2]</sup> Obviously many patients would not need these upper limits for adequate rate control.

In the MERIT-HF Trial where a target dose of up to 200mg/day of MTP was evaluated, patient survival significantly increased and perceived side effects were similar to placebo. Thus, it appears likely that most patients who return to NSR could tolerate higher discharge doses of BBs. Although BBs are not traditionally

considered rhythm control medications some randomized trials report decreased recurrent AF with BBs after the establishment of NSR. [5-6] The AFFIRM Study reported the effectiveness of combined BBs, CCBs, and digoxin as effective rate control combinations. [7] This regimen may be considered if there are concerns about undue adverse side effects from a higher dose of one of the RCMs.

AF will frequently revert to NSR usually within 24 hours regardless of management, especially with recent AF onset of short duration. [8-9] It is well known that conversion to NSR without additional RCMs will slow ventricular rate. This study demonstrated rate slowing from 144bpm to 71bpm at time of discharge for the 2/3s of those who converted to NSR as opposed to rate slowing from 134bpm and 90bpm for those who remained in AF at discharge. The difference in HR between those who converted to NSR and those who remained in AF at discharge was significant (P = < 0.001).

Thus, the majority of patients who converted to NSR and have the resultant rate control may appear not to need RCMS as long as recurrence is not common, which however unfortunately, is not the case. Most patients who convert to NSR do not have comorbidities allowing successful correction risk factors, such as obesity or alcohol to prevent the known high incidence of recurrent AF within one year. [3, 4]

For the majority of AF patients presenting with a rapid rate on admission, and receive minimal or no increase in RCMs it appears probable that AF ventricular rate, when it recurs, will probably be rapid and frequently need treatment in the ED or in the hospital as opposed to outpatient adjustments.

It is possible discharge order sets may lead to more logical choices of a discharge RCM strategy. If AF recurs with a well-controlled rate it may be more likely to be treated cost-effectively as an outpatient. This may possibly decrease the cost of AF management. Numerous studies have demonstrated strategy trials can decrease cost, improve outcomes, and increase patient satisfaction. [11]

It is well documented that rapid AF may be asymptomatic <sup>[12]</sup>. It is well established that chronic asymptomatic tachycardia of any type may lead to severe cardiomyopathy that can be reversed with rate slowing. <sup>[12]</sup> Guidelines now accept a HR < 110bpm as adequate rate control for most AF patients. <sup>[2]</sup> Even modest higher rates are associated with adverse outcomes, <sup>[13]</sup> which however, may be an association and not causation.

Strengths mentioned for this study include it being a large series of consecutive patients with a focus on management of rapid AF after presentation to the ED, but also incorporated outcomes of those admitted for hospital management. The high frequency of hospitalizations from the ED reflects that of the US and thus the study is generalizable to many AF patients.

Noted limitations reported only the AF management of one center and is not reflective necessarily of widespread practice. There were limitations in distinguishing by chart review between

first episode, known paroxysmal, or persistent AF. Likewise the timing of intravenous RCM before discharge may be suspect. Follow-up post discharge was unavailable to evaluate subsequent long term outcomes for patients who received low dose RCMs at discharge after presenting with rapid AF.

In conclusion, the vast majority, 68%, of the 319 patients admitted to the ED with acute AF and a HR ≥110bpm converted to sinus rhythm. Since recurrence of AF over the next year is known to be common, it seems likely when AF recurs the ventricular rate will be rapid and symptomatic, often leading to expensive ED or hospital care.

# **ACKNOWLEDGEMENTS**

The authors would like to acknowledge Mariam Rauf, MD for her work on the project and Stephanie Thompson, PhD for editing the final manuscript.

## **REFERENCES**

- [1] Patel NJ, Deshmukh A, Pant S, Singh V, Patel N, Arora S, Shah N, Chothani A, Savani GT, Mehta K, Parikh V, Rathod A, Badheka AO, Lafferty J, Kowalski M, Mehta JL, Mitrani RD, Viles-Gonzalez JF, Paydak H. Contemporary trends of hospitalization for atrial fibrillation in the United States, 2000 through 2010: implications for healthcare planning. Circulation. 2014 Jun 10;129(23):2371-9. doi: 10.1161/CIRCULATIONAHA.114.008201. Epub 2014 May 19. PMID: 24842943.
- [2] January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG, Tchou PJ, Tracy CM, Yancy CW; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 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 Dec 2;64(21):e1-76. doi: 10.1016/j.jacc.2014.03.022. Epub 2014 Mar 28. Erratum in: J Am Coll Cardiol. 2014 Dec 2;64(21):2305-7. PMID: 24685669.
- [3] Lafuente-Lafuente C, Valembois L, Bergmann JF, Belmin J. Antiarrhythmics for maintaining sinus rhythm after cardioversion of atrial fibrillation. Cochrane Database Syst Rev. 2015 Mar 28;(3):CD005049. doi: 10.1002/14651858.CD005049.pub4. Update in:

- Cochrane Database Syst Rev. 2019 Sep 04;9:CD005049. PMID: 25820938.
- [4] Gwag HB, Chun KJ, Hwang JK, Park SJ, Kim JS, Park KM, On YK. Which antiarrhythmic drug to choose after electrical cardioversion: A study on non-valvular atrial fibrillation patients. PLoS One. 2018 May 22;13(5):e0197352. doi: 10.1371/journal.pone.0197352. eCollection 2018. PMID:29787592; PMCID: PMC5963785.
- [5] Hjalmarson A, Goldstein S, Fagerberg B, Wedel H, Waagstein F, Kjekshus J, Wikstrand J, El Allaf D, Vítovec J, Aldershvile J, Halinen M, Dietz R, Neuhaus KL, Jánosi A, Thorgeirsson G, Dunselman PH, Gullestad L, Kuch J, Herlitz J, Rickenbacher P, Ball S, Gottlieb S, Deedwania P. Effects of controlled-release metoprolol on total mortality, hospitalizations, and well-being in patients with heart failure: the Metoprolol CR/XL Randomized Intervention Trial in congestive heart failure (MERIT-HF). MERIT-HF Study Group. JAMA. 2000 Mar 8;283(10):1295-302. PMID:10714728.
- [6] Kühlkamp V, Schirdewan A, Stangl K, Homberg M, Ploch M, Beck OA. Use of metoprolol CR/XL to maintain sinus rhythm after conversion from persistent atrial fibrillation: a randomized, double-blind, placebo-controlled study. J Am Coll Cardiol. 2000 Jul;36(1):139-46. doi: 10.1016/s0735-1097(00)00693-8. PMID: 10898425.
- [7] Valembois L, Audureau E, Takeda A, Jarzebowski W, Belmin J, Lafuente-Lafuente C. Antiarrhythmics for maintaining sinus rhythm after cardioversion of atrial fibrillation. Cochrane Database Syst Rev. 2019 Sep 4;9(9):CD005049. doi: 10.1002/14651858.CD005049.pub5. PMID: 31483500; PMCID: PMC6738133.
- [8] Olshansky B, Rosenfeld LE, Warner AL, Solomon AJ, O'Neill G, Sharma A, Platia E, Feld GK, Akiyama T, Brodsky MA, Greene HL; AFFIRM Investigators. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study: approaches to control rate in atrial fibrillation. J Am Coll Cardiol. 2004 Apr 7;43(7):1201-8. doi: 10.1016/j.jacc.2003.11.032. PMID: 15063 430.

- [9] Danias PG, Caulfield TA, Weigner MJ, Silverman DI, Manning WJ. Likelihood of spontaneous conversion of atrial fibrillation to sinus rhythm. J Am Coll Cardiol. 1998 Mar 1;31(3):588-92. doi: 10.1016/s0735-1097(97)00534-2. PMID: 95026 40.
- [10] Pluymaekers NAHA, Dudink EAMP, Luermans JGLM, Meeder JG, Lenderink T, Widdershoven J, Bucx JJJ, Rienstra M, Kamp O, Van Opstal JM, Alings M, Oomen A, Kirchhof CJ, Van Dijk VF, Ramanna H, Liem A, Dekker LR, Essers BAB, Tijssen JGP, Van Gelder IC, Crijns HJGM; RACE 7 ACWAS Investigators. Early or Delayed Cardioversion in Recent-Onset Atrial Fibrillation. N Engl J Med. 2019 Apr 18;380(16):1499-1508. doi: 10.1056/NEJMoa1900353. Epub 2019 Mar 18. PMID: 30883054.
- [11] Bellew SD, Bremer ML, Kopecky SL, Lohse CM, Munger TM, Robelia PM, Smars PA. Impact of an Emergency Department Observation Unit Management Algorithm for Atrial Fibrillation. J Am Heart Assoc. 2016 Feb 8;5(2):e002984. doi: 10.1161/JAHA.115.002984. PMID: 26857070; PMCID: PMC4802469.
- [12] Huizar JF, Ellenbogen KA, Tan AY, Kaszala K. Arrhythmia-Induced Cardiomyopathy: JACC State-of-the-Art Review. J Am Coll Cardiol. 2019 May 14;73(18):2328-2344. doi: 10.1016/j.jacc. 2019.02.045. PMID: 31072578; PMCID: PMC 6538508.
- [13] Steinberg BA, Kim S, Thomas L, Fonarow GC, Gersh BJ, Holmqvist F, Hylek E, Kowey PR, Mahaffey KW, Naccarelli G, Reiffel JA, Chang P, Peterson ED, Piccini JP; Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT AF) Investigators and Patients. Increased Heart Rate Is Associated With Higher Mortality in Patients With Atrial Fibrillation (AF): Results From the Outcomes Registry for Better Informed Treatment of AF (ORBIT-AF). J Am Heart Assoc. 2015 Sep 14;4(9):e002031. doi: 10.1161/JAHA.115.002031. PMID: 26370445; PMCID: PMC4599492.

