

## Which one is the first choice for rapid ventricular rate atrial fibrillation in emergency department: Metoprolol or Diltiazem? A randomized clinical trial

### Acil serviste hızlı ventriküler hız atriyal fibrilasyonu için ilk tercih hangisidir: Metoprolol veya Diltiazem? Randomize bir klinik çalışma

Mehmet Barış Memiş<sup>1</sup>, Rohat Ak<sup>2</sup>, Tuba Cimilli Öztürk<sup>3</sup>, Özge Onur<sup>4</sup>, Özgür Ordu<sup>5</sup>

<sup>1</sup> Adıyaman Education and Research Hospital, Department of Emergency Medicine, Adıyaman, Turkey

<sup>2</sup> Sancaktepe Şehit Prof. Dr. İlhan Varank Education and Research Hospital, Department of Emergency Medicine, Istanbul, Turkey

<sup>3</sup> Fatih Sultan Mehmet Education and Research Hospital, Department of Emergency Medicine, Istanbul, Turkey

<sup>4</sup> Marmara University Faculty of Medicine, Department of Emergency Medicine, Istanbul, Turkey

<sup>5</sup> Fatih Sultan Mehmet Education and Research Hospital, Department of Cardiology, Istanbul, Turkey

ORCID ID of the authors:

MBM: 0000-0003-3591-2598

RA: 0000-0002-8324-3264

TCÖ: 0000-0002-4760-0076

ÖO: 0000-0002-0110-3533

ÖÖ: 0000-0001-7880-9430

Corresponding author / Sorumlu yazar:  
Rohat Ak

Address / Adres: Sancaktepe Şehit Prof. Dr. İlhan Varank Eğitim ve Araştırma Hastanesi, Acil Tıp Anabilim Dalı, İstanbul, Türkiye  
E-mail: rohatkmd@gmail.com

Ethics Committee Approval: Ethics committee approval was received from Health Sciences University, Fatih Sultan Mehmet Education and Research Hospital Ethical Committee with number of FSM EAH-KAEK 2015/69 in 23 June, 2015. Etik Kurul Onayı: Çalışma için Sağlık Bilimleri Üniversitesi, Fatih Sultan Mehmet Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu 23.07.2015 tarih ve FSM EAH-KAEK 2015/69 sayılı ile onay alınmıştır.

Conflict of Interest: No conflict of interest was declared by the authors.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support. Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 12.07.2018

Accepted / Kabul Tarihi: 06.08.2018

Published / Yayın Tarihi: 11.08.2018

Copyright © 2019 The Author(s)

Published by JOSAM

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License 4.0 (CC BY-NC-ND 4.0) where it is permissible to download, share, remix, transform, and build upon the work provided it is properly cited. The work cannot be used commercially without permission from the journal.



#### Abstract

**Aim:** Atrial fibrillation (AF) is the most common cardiac arrhythmia managed by emergency physicians. Primary goals of treatment are hemodynamic stabilization, ventricular rate control, and prevention of embolic complications. The aim of this study is to compare the drug responses of the patients who presented to the ED with AF with rapid ventricular response (AFRVR), their need for the second dosage and echocardiographic parameters.

**Methods:** This is a prospective, single blind, randomized study. AFRVR patients were randomized and first group was given intravenous 0.25 mg/kg diltiazem as the calcium channel blocker; the second group was given intravenous 5 mg metoprolol. The vital findings and the clinical data of the patients in the 0, 2nd 5th, 15th and 30th minutes were recorded after each treatment. After the initial dosing, the patients having heart rate <110 beat/min in the 30th minutes were regarded as responders to the initial treatment. Nonresponders took second dosage of the same drug. After the rate control of all patients, a cardiologist performed the transthoracic echocardiography (TTE)'s of all participants.

**Results:** Fifty of the patients were given diltiazem, 50 of them were given metoprolol. 45 of them (45%) had no first dose response; whereas 55 (55%) of them had. The rate of incidence for the first dose response in the patients having diltiazem was higher than the patients having metoprolol, which was statistically significant. There is statistically significant difference between rates of the valvular heart disease seen for the patients in responsive /unresponsive groups for both drugs. But diltiazem is more successful in presence of valvular disease than metoprolol.

**Conclusions:** In this study, we found that diltiazem is more effective in the rate control of AFRVR in emergency department. This study showed that most of atrial fibrillation patients have valvular disease, and diltiazem is more effective than metoprolol in these patients. Ejection fraction, cardiac diameters are important in drug response.

**Keywords:** Atrial fibrillation, Diltiazem, Metoprolol, Rate control

#### Öz

**Amaç:** Atriyal fibrilasyon (AF), acil hekimleri tarafından yönetilen en yaygın kardiyak aritmidir. Tedavinin primer hedefleri hemodinamik stabilizasyon, ventriküler hız kontrolü ve embolik komplikasyonların önlenmesidir. Bu çalışmanın amacı, acil servise hızlı ventrikül yanıtı AF ile başvuran hastaların hız yanıtlarını, ikinci doz ilaç gerkesimlerini ve ekokardiyografik bulgularını incelemektir.

**Yöntemler:** Bu prospektif, tek kör, randomize bir çalışmadır. Hızlı ventrikül yanıtı AF hastaları randomize edildi ve ilk gruba kalsiyum kanal blokleri olarak intravenöz 0,25 mg / kg diltiazem verildi; ikinci gruba intravenöz 5 mg metoprolol verildi. Her tedaviden sonra 0, 2, 5, 15 ve 30. dakikalardaki hastaların vital bulguları ve klinik verileri kaydedildi. İlk dozlamadan sonra 30. dakikada kalp atış hızı <110 atım / dk olan hastalar ilk tedaviye yanıt alınmış olarak kabul edildi. Cevap vermeyenler aynı ilacın ikinci dozunu aldı. Tüm hastalara hız kontrolünden sonra bir kardiyolog tarafından transtorasik ekokardiyografi yapıldı.

**Bulgular:** Hastaların 50'sine diltiazem, 50'sine metoprolol verildi. 45'inin (%45) ilk doz cevabı yoktu; 55'inde ilk doz cevabı (%55) vardı. Diltiazem alan hastalarda ilk doz cevap oranı, metoprolol alanlara göre istatistiksel olarak yüksek bulundu. Her iki ilaç için cevap veren / cevapsız gruplarda görülen kapak kalp hastalığı oranları arasında istatistiksel olarak anlamlı fark vardı. Ancak diltiazem, valvüler hastalık varlığında metoprololdan daha başarılı bulundu.

**Sonuçlar:** Çalışmamızda, acil serviste hızlı ventrikül yanıtı AF kontrolünde diltiazemin daha etkili olduğunu bulduk. Bu çalışmada atriyal fibrilasyon hastalarının çoğunun valvüler hastalığı olduğunu ve bu hastalarda diltiazemin metoprololdan daha etkili olduğunu göstermiştir. Ejeksiyon fraksiyonu, kardiyak çaplar ilaç yanıtında önemlidir.

**Anahtar kelimeler:** Atriyal fibrilasyon, Diltiazem, Metoprolol, Hız kontrolü

## Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia in emergency department (ED) clinical practice. AF is associated with the increase in the incidence of mortality, stroke and other thromboembolic events, congestive heart failure and hospitalization, disturbed life quality, decreased exercise capacity and left ventricular dysfunction [1]. The left ventricular dysfunction is generally caused by the rapid ventricular rate, loss of atrial contractility and left ventricular filling pressure after the increased diastole. In accordance with the current guidelines, for the ventricular rate control, beta blockers or nondihydropyridine derivative calcium channel blockers are recommended as the chronic rate limiting treatment for the paroxysmal, persistent or permanent AF diseases.

Although the chronic AF maintenance treatments are standard in the guidelines, there are no wide ranged studies carried out in the ED for the patients who present with symptomatic disease and need the rate control. In patients with mild to moderate symptoms, slowing the rate often results in significant improvement or even resolution of symptoms. According to the current recommendations, it is effective to use esmolol, propranolol and metoprolol as the beta blocker for the intravenous therapy of AF with rapid ventricular response and diltiazem as the calcium channel blocker. However there is no prospective and extensive research carried out on the ED patients in relation to the 1st line medication for the acute rate control treatment and which patient responses to which treatment; the recommendations are weak evidentially.

The primary aim of this study is to compare the drug responses of the patients who presented to the ED with AF with rapid ventricular response and their need for the second dosage. The secondary purpose of this study is to determine whether there is a relation between the rate control responses to the medication groups and echocardiographic parameters.

## Materials and methods

### Study Design

This prospective, single blind, randomized study was carried out between 25.07.2015 and 25.11.2015 in the ED of Fatih Sultan Mehmet Research and Training Hospital, Istanbul, Turkey. Approval of the study was obtained from our hospital's Institutional Review Board. All the enrolled patients received information about the study and gave written informed consent. The study was conducted in accordance with the Declaration of Helsinki. The study was done and is reported according to the CONSORT (Consolidated Standards of Reporting Trials) Group.

### Study Setting and Selection of Participants

A convenience sample of ED patients who are >18 years old with AF with rapid ventricular response were evaluated in accordance with the inclusion criteria for the study. The patients who are hemodynamically stable and requiring rate control by medical treatment were included to the study and randomized after signing the consent form. Exclusion criteria were : <18 years old, systolic blood pressure < 90 mmHg, pulse < 60beat/min, temperature > 38°C, hemoglobin < 11.0 g/dL, Wolf Parkinson White Syndrome in ECG, 2nd or 3rd degree AV block, unstable clinics, having mental fog, being allergic to

diltiazem and metoprolol (which is known), having contraindication to use calcium channel blocker or beta blocker due to any reason, usage of a beta blocker or diltiazem or any other AV nodal blocking agent, a history of cocaine or methamphetamine use in the 24 hours before arrival, having severe heart failure or pulmonary edema, being with suspected acute coronary syndrome, not consenting participation to the study, pregnancy and lactation period.

### Interventions

After the identification of patients according to inclusion and exclusion criteria, patients' data were collected prospectively. All patients were monitorized in the observation room, 12 lead ECG was reviewed by an Emergency Medicine Specialist in charge for any contraindication to have any medication and the requirement of rate control.

Block randomization method was used for allocation of patients due to the small sample size. The first group (Group 1) was given intravenous 0.25 mg/kg (to a maximum dose of 30 mg) diltiazem (Diltizem-L®) as the calcium channel blocker by slow push in 2 minutes; the second group (Group 2) was given intravenous 5 mg metoprolol (Beloc®) by slow push in 2 minutes. The vital findings and the clinical data of the patients in the 0, 2nd 5th, 15th and 30th minutes were recorded after each treatment. After the initial dosing, the patients having heart rate <110 beat/min(bpm) in the 30th minutes were regarded as responders to the initial treatment. The patients who aren't responding the first dosage or having a decrease in heart rate firstly and afterward an increase as being >110 bpm in 30th minutes dedicated as unresponder and 2nd dosage of the same drug was given. The patients of Group 1 received intravenous 0.35mg/kg diltiazem (to a maximum dose of 30 mg) in 2 minutes; whereas the patients of Group 2 received intravenous 5 mg metoprolol in 2 minutes. After the application of the second dose, the patients having the heart rate 110 bpm in the 30th minute were regarded as responder to 2nd dose. The patients of Group 1 who did not respond the total dose were given diltiazem 5-15mg /hour by intravenous infusion and the patients of Group 2 were given metoprolol 5 mg as the 3rd dose in 2 minutes if still unresponder after 3rd dose of metoprolol, esmolol (Brevibloc ®) infusion was started. After the rate control of all patients, a cardiologist performed the transthoracic echocardiography (TTE)'s of all participants. PHILIPS EPIQ7 echocardiography device was used for examinations. The sizes of right, left atrium and ventricle, the heart valve motion and function disorders, the ejection fractions were recorded.

### Outcome Measures

The primary efficacy outcome measure was HR < 100 bpm within 60 min of 1st or second dose drug administrations. The primary safety outcome measures were HR < 60 bpm, any complicating heart rhythm as 2nd or third degree heart block and SBP < 90 mm Hg.

### Sample Size and Data Analyses

The standard deviations used to calculate the sample size were based on the study by Demircan et al and Fromm et al [2,3]. We estimated a sample size of 92 patients assigned in a 1:1 ratio to receive diltiazem and metoprolol would achieve 80% power to detect noninferiority using a one-sided, two-sample test.

As the data collected during the study were evaluated, IBM SPSS Statistics 22 (IBM SPSS, Turkey) was used for the statistical analyses. For the evaluation of the data, Shapiro Wilks was used to see the compliance of the parameters with the normal distribution. Besides the descriptive statistical methods (Mean, Standard Deviation, Frequency), Mann Whitney U test was used for the comparisons between the two groups of the parameters which did not present normal distribution in the comparison of the quantitative data. Continuity (Yates) Correction and Fisher's Exact test was used for the comparison of qualitative data. Significance level was  $p < 0.05$ .

### Results

Between July 2015 and November 2015, of 114 patients who were initially evaluated, 100 met all the inclusion criteria and enrolled in the study (Figure 1).

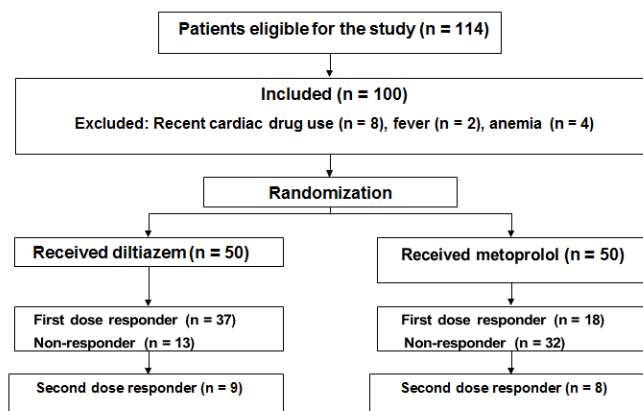


Figure 1: Patient enrollment chart

The study was carried out with 100 patients consisting of 55 male (55%) and 45 female (45%) between 25.07.2015-25.11.2015. The demographic data of the patients, the vital signs, their comorbid diseases and the drugs/medication they use are summarized in Table 1. There is no statistical difference between two groups.

Fifty of the patients (50%) were given diltiazem, 50 of them (50%) were given metoprolol. 45 of them (45%) had no first dose response; whereas 55 (55%) of them had. 48 of them (48%) had the second dose; whereas 52 of them (52%) did not need the 2nd dose. It was determined that there was 1 patient in Group 1 and 2 patients in Group 2 who responded in the 5th minute after the first dose however had heart rate increasing as being  $>110$ beat/min between the 5th and 30th minutes following. Those patients had the 2nd dose medication and were included in the group 'not responding the first dose'. 31 patients (64.6%) having the second dose did not respond to the second dose, however the rate was decreased for 17 patients (35.4%) by the 2nd dose. The total response was not seen in 28 of the patients (28%), whereas the total response was determined in 72 of them (72%). The rate of incidence for the first dose response in the patients having diltiazem was (74%) and higher than the patients having metoprolol (36%), which was statistically significant ( $p:0.001$ ;  $p<0.01$ ). The rate of incidence for the second dose response in the patients having diltiazem was (60%) higher than the patients having metoprolol (24.2%), which was statistically significant ( $p:0.038$ ;  $p<0.05$ ).

The rate of incidence for the total response in the patients having diltiazem was 92% and higher than the patients

having metoprolol (52%), which was statistically significant ( $p:0.001$ ;  $p<0.01$ ). The responses of the patients in accordance with the medication given were summarized in the Table 2.

Ejection fraction (EF) values of the patients having medication response in Group 1 were significantly higher than the patients not having total medication response ( $p:0.001$ ;  $p<0.01$ ). The left atrium anterior- posterior diameter mean of the females responding to the treatment was significantly lower than the female not responding to the treatment ( $p:0.043$ ;  $p<0.05$ ). In accordance with the total response, there was no statistically significant difference between left atrium anterior posterior diameters of the males ( $p>0.05$ ). In the same patient group, the left ventricular systole diameters of the patients not having total response were significantly higher than the patients "having total response" ( $p:0.003$ ;  $p<0.01$ ), and their left ventricular diastole diameters were significantly higher than "the patients not having total response" ( $p:0.013$ ;  $p<0.05$ ). Total echocardiographic findings of Group 1 are summarized in the Table 3. The evaluation of the echocardiographic findings according to the total responses of the patients having metoprolol (Group 2) is summarized in the Table 4.

Table1: Distribution of the general features in relation to the patients

	Diltiazem Mean±SD	Metoprolol Mean±SD	P
Age (year)	74.18±11.73	73.36±13.54	0.75
Heart rate	141.08±11.57	136.98±10.39	0.07
Respiration rate	20.66±3.55	20.52±2.38	0.82
Systolic blood pressure (mmHg)	149.5±23.21	155.38±22.28	0.20
Diastolic blood pressure (mmHg)	77.64±10.21	78.86±11.88	0.58
Temperature	36.1±0.19	36.1±0.22	0.96
Mean arterial pressure	101.58±12.71	104.35±14.58	0.31

Table 2: The evaluation of the first, second and total dose responses of the patients in accordance with the medication given

	Diltiazem n (%)	Metoprolol n (%)	p
First dose response	57 (74%)	18 (36%)	0.001**
Second dose response	9 (60%)	8 (24.2%)	0.038*
Total response	46 (92%)	26 (52%)	0.001**

Continuity (Yates) Correction, \* $p<0.05$ , \*\* $p<0.01$

Table 3: The evaluation of the echocardiographic findings according to the total responses of the patients having diltiazem

Diltiazem	Total Response		p
	Exist (n=46)	None (n=4)	
	Avg±SD (Median)	Avg±SD (Median)	
EF	55.43±8.42 (60)	23.75±10.31 (22.5)	0.001**
Right atrium anterior posterior diameter(cm)	4.83±0.87 (4.8)	5.1±0.54 (5.35)	0.215
Left atrium anterior posterior diameter(cm)	4.42±0.53 (4.45)	4.88±0.39 (5)	0.076
Left atrium anterior posterior diameter(cm) for females	4.37±0.47 (4.3)	5.10±0.14 (5.1)	0.043*
Left atrium anterior posterior diameter (cm) for males	4.47±0.60 (4.5)	4.65±0.49 (4.6)	0.675
Right ventricular diastolic diameter(cm)	2.92±0.37 (2.9)	3.1±0.27 (3)	0.297
Left ventricular systolic diameter(cm)	3.35±0.64 (3.2)	5±0.83 (4.95)	0.003**
Left ventricular diastolic diameter(cm)	5.25±19.57 (4.3)	5.35±0.37 (5.5)	0.013*
Left ventricular diastolic diameter(cm) for females	4.40±0.73 (4.3)	5.55±0.07 (5.5)	0.074
Left ventricular diastolic diameter(cm) for males	4.40±0.58 (4.3)	5.15±0.49 (5.15)	0.084

Mann Whitney U Test, \* $p<0.05$ , \*\* $p<0.01$ , EF: Ejection fraction

Table 4: The evaluation of the echocardiographic findings according to the total responses of the patients having metoprolol

Metoprolol	Total Response		p
	Exist (n=26)	None (n=24)	
	Avg±SD (Median)	Avg±SD (Median)	
EF	59.62±1.96 (60)	47.08±7.79 (45)	0.001**
Right atrium anterior posterior diameter(cm)	4.31±0.89 (4.25)	5.22±0.51 (5.2)	0.001**
Left atrium anterior posterior diameter(cm)	3.92±0.36 (3.9)	4.53±0.42 (4.5)	0.001**
Left atrium anterior posterior diameter(cm) for females	3.93±0.23 (3.9)	4.50±0.43 (4.3)	0.003**
Left atrium anterior posterior diameter(cm) for males	3.91±0.42 (3.9)	4.54±0.42 (4.6)	0.001**
Right ventricular diastolic diameter(cm)	2.51±0.39 (2.35)	3.01±0.31 (3)	0.001**
Left ventricular systolic diameter(cm)	2.86±0.71 (2.7)	3.67±0.44 (3.6)	0.001**
Left ventricular diastolic diameter(cm)	4.07±0.69 (4.1)	4.52±0.7 (4.5)	0.004**
Left ventricular diastolic diameter(cm) for females	4.01±0.76 (4.1)	4.68±0.74 (4.8)	0.026*
Left ventricular diastolic diameter(cm) for males	4.10±0.67 (4.1)	4.42±0.69 (4.5)	0.044*

Mann Whitney U Test, \* $p<0.05$ , \*\* $p<0.01$ , EF: Ejection fraction

There is statistically significant difference between rates of the valvular heart disease seen for the patients in responsive /unresponsive groups for both drugs (Table 5). But diltiazem is more successful in presence of valvular disease than metoprolol. No hemodynamic instability observed among the patients within the study.

Table 5: The evaluation of rates of echocardiographic valvular heart disease for the patients having diltiazem/ metoprolol according to the total responses

		Response positive	Response negative	
Diltiazem	Valvular disease positive (44)	90.90%	9.09%	P<0.01
	Valvular disease neg (6)	100%	-	
Metoprolol	Valvular disease positive (34)	35.29%	64.70%	
	Valvular disease neg (16)	87.5%	12.5%	

Continuity (Yates) Correction, \*\*p<0.01

## Discussion

In this study, we found that diltiazem is more effective in the rate control of rapid ventricular rate atrial fibrillation in emergency department. This study showed that most of atrial fibrillation patients have valvular disease, and diltiazem is more effective than metoprolol in these patients. Ejection fraction, cardiac diameters are important in drug response and especially metoprolol response is dependent on the diameters of heart chambers.

AF is one of the most frequently seen arrhythmias in practice and associated with mortality, stroke and other thromboembolic events, left ventricular dysfunction and heart failure, decreased exercise capacity and the disturbed life quality [4].

Diltiazem and metoprolol used frequently for rate control of atrial fibrillation those have effects on slowing the AV nodal conduction and extending the AV nodal refractory period. In accordance with 2014 AHA Guideline these medications are recommended as the class I for the acute rate control of AF [5-7]. However, there is no recommendation which of the medications is required to be preferred primarily. The number of the randomized prospective studies on the issue is limited and the studies carried out are mostly related to the chronic therapy and complications of AF. Due to the lack of the studies on the emergency practices, it is not known which one has the priority in the emergency intervention.

There are only 2 studies carried out with small patient groups for comparison the rate control of these two medications in the emergency room in the literature. However, there is no structural evaluation of the heart by means of echocardiography in both studies [2,3].

The first study is carried out by Demircan et al [2] with 40 patients. The study shows that both medications are safe for the rate control however the patients with diltiazem have more rapid responses.

According to the study carried out by Christian Fromm et al, diltiazem is more effective in achieving heart rate in ED patients with rapid ventricular rate atrial fibrillation and there is no increase incidence of adverse effects beside metoprolol [3].

The rate control was maintained for 74% of the patients having diltiazem as rate-limiting agent for the first dose in our study, whereas the ratio was 36% among the patients having metoprolol; the difference is statistically significant. The ratios increased to 92% and 52% after the second dose. In the study by

Fromm et al, 50% of the patients having diltiazem and 10.7% of the patients having metoprolol reached the target heart rate which is <100/min at the 5th minute and 95.8% of the group with diltiazem and 46.4% of the group with metoprolol at the 30th minute [3]. These findings are correlated with each other.

Martindale et al reviewed the literature to compare the efficacy of calcium channel blockers to  $\beta$ -blockers for acute rate control of atrial fibrillation with rapid ventricular response in the emergency department setting. Of the 1003 studies yielded by our initial search, two met inclusion criteria; and they reported that on the basis of the paucity of available evidence, diltiazem may be more effective than metoprolol in achieving rapid rate control, but high-quality randomized studies are needed at 2015. But none of the studies searched underlying heart condition effect for response to drugs [8].

In the study by Salih A et al [9], it is determined that 71% of the patients with AF have LV dilatation, 27% have LV function depletion and 26% have left ventricular hypertrophy.

In our study, we found that EF value is one of the determinant factors to maintain the rate control (p:0.001; p<0.01). As responses to the treatment are analyzed it is seen that there is no significant difference in the atrium diameters as diltiazem is concerned, however both diameters of the atrium are statistically significantly low in the patients giving response as metoprolol (p:0.001; p<0.01). There is statistically significant difference measured between the left ventricular systolic and diastolic in the use of diltiazem for the ventricular diameters, whereas the difference is statistically significant in both ventricle in the use of metoprolol.

Approximately 30% of the patients with AF have valvular heart disease [10,11]. AF due to LAD might be the early stage symptom of mitral stenosis and/or coronary failure.

More importantly as the patients in the diltiazem group are evaluated in accordance with the total response there is no statistically significant difference in terms of rate of incidence for valvular disease seen in the echocardiography (p>0.05), whereas the rate of incidence for valvular diseases of the patients not responding the medication in the metoprolol group is significantly high (91.7%, 46.2%, p:0.002; p<0.01). According to our study the use of beta blocker, in case of structural heart disease should be discussed due to the facts that the lower atrium diameters and compact valvular system are more important parameters for beta blocker response. The emergency department studies on this subject are limited. Kannel et al [12] found risk of AF for the patients having valvular disease history increased 1.8 times in males and 3.4 times in females. In the study carried out by Andrew et al, it is recommended that beta blockers and non dihydropyridine group calcium channel blockers are to be used as the primary medication for the patients with AF and valvular disease [13]. Moreover, Wang TJ et al show that there is increase in the AF risk due to the left atrial dilatation in obese patients [14]. There is no study in the literature showing the superiority of diltiazem or metoprolol used for the rate control in the patients having AF and valvular heart disease. In this study we show that diltiazem is more effective than the metoprolol for the rate control in the patients having AF and valvular heart disease.

### Limitations

The study was conducted with the patients presented with rapid ventricular rate atrial fibrillation to the emergency department and underlying problems those may cause the acceleration of AF were tried to be excluded, but the patients with thyroid dysfunction might be included in the study due to the limited laboratory opportunities in the emergency department. The study team were not blind except the cardiologist who examined echocardiography. Regardless of the control of the pharmacy records via electronic system, there are patients whose records are not available and the usage and time of previous antiarrhythmic drug were reported as the patient said. Moreover, the long term drug compliance of the patients is unknown. The short term results of the patients are analyzed; there is no information about their subsequent follow-ups and treatment. Our study is limited with the patient group recognized as stable. Patients with known decompensated heart failure were excluded from the study. An inclusion bias may be consisted due to convenience sampling. The cardiologist who make echocardiography was studying between 08:00- 17:00 hours, Monday to Friday.

### Conclusion

In this study we have determined that the stable patients having symptomatic atrial fibrillation with rapid ventricular response without any underlying correctable reason have better response to diltiazem as rate controlling treatment, especially for the patients with coexisting valvular disease. We did not determine any difference between the two medications in terms of their side-effects.

### References

1. "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." *Journal of the American College of Cardiology* 64.21 2014:e1-e76.
2. Demircan C, Cikrikler HI, Engindeniz Z, Cebicci H, Atar N, Guler V, et al. Comparison of the effectiveness of intravenous diltiazem and metoprolol in the management of rapid ventricular rate in atrial fibrillation. *Emergency Medicine Journal*. 2005;22:411-4.
3. Fromm C, Suau SJ, Cohen V, Likourezos A, Jellinek-Cohen S, Rose J, et al. Diltiazem vs. Metoprolol in the Management of Atrial Fibrillation or Flutter with Rapid Ventricular Rate in the Emergency Department. *The Journal of emergency medicine*. 2015;49:175-82.
4. AFFIRM Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med*. 2002;347:1825-33.
5. Farshi R, Kistner D, Sarma JS, Longmate JA, Singh BN. Ventricular rate control in chronic atrial fibrillation during daily activity and programmed exercise: a crossover open-label study of five drug regimens. *Journal of the American College of Cardiology*. 1999;33(2):304-10.
6. Steinberg JS, Katz RJ, Bren G, Buff LA, Varghese PJ. Efficacy of oral diltiazem to control ventricular response in chronic atrial fibrillation at rest and during exercise. *Journal of the American College of Cardiology*. 1987;9(2):405-11.
7. Olshansky B, Rosenfeld LE, Warner AL, Solomon AJ, O'Neill G, Sharma A, et al. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study: Approaches to control rate in atrial fibrillation. *Journal of the American College of Cardiology*. 2004;43(7):1201-8.
8. Martindale JL, Silverberg M, Freedma, J, Sinert R.  $\beta$ -Blockers versus calcium channel blockers for acute rate control of atrial fibrillation with rapid ventricular response: a systematic review. *European Journal of Emergency Medicine*. 2015;22:150-4.
9. Salih S, Showlag MS, Al-Qahtan MA, Taha A, Yousuf M, Abdullah M. Clinical characteristics of patients with atrial fibrillation at a tertiary care hospital in the central region of Saudi Arabia. *Journal of Family and Community Medicine*. 2011;18:80.
10. Gudbjartsson DF, Holm H, Gretarsdottir S, Thorleifsson G, Walters GB, Thorgeirsson G, et al. A sequence variant in ZFX3 on 16q22 associates with atrial fibrillation and ischemic stroke. *Nature genetics*. 2009;41:876-8.
11. Watson T, Shantsila E, Lip GY. Mechanisms of thromboembolism in atrial fibrillation: Virchow's triad revisited. *Lancet*. 2009;373:155-66.
12. Kannel WB, Benjamin EJ. Status of the epidemiology of atrial fibrillation. *The Medical clinics of North America*. 2008;92:17-40.

13. Darby AE, Di Marco JP. Management of atrial fibrillation in patients with structural heart disease. *Circulation*. 2012;125:945-57.

14. Wang TJ, Parise H, Levy D, D'Agostino RB, Wolf PA, Vasan RS, et al. Obesity and the risk of new-onset atrial fibrillation. *JAMA*. 2004;292:2471-7.