



## ARAŞTIRMA / RESEARCH

# Etiology and mortality markers in atrial fibrillation with rapid ventricular response

Hızlı ventrikül yanıtli atriyal fibrilasyonun nedenleri ve mortalite belirteçleri

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### Abstract

**Purpose:** The aim of this study was to obtain data on the causes of rapid rate in the patients with atrial fibrillation (AF), the parameters that may be effective in the decision of antiarrhythmic treatment and short-term mortality during the management of the patients with AF with rapid ventricular response.

**Materials and Methods:** One hundred three patients over 18-year-old were included. Complete blood counts, biochemical and coagulation parameters, venous blood gases of the patients were evaluated. In order to investigate the volume condition, we measure the inferior vena cava (IVC) diameter by bed-side ultrasonography (USG). The mortalities within 15 and 30 days and analyzed the mortality-related parameters of the patients were calculated.

**Results:** Heart failure or hypervolemia are the most common clinical presentation with 15.5% (n=16) of the AF with rapid ventricular response. 14.6% (n=15) of the patients were treated by treating the underlying condition without giving any antiarrhythmics. A statistically significant correlation was found between lactate level and 15-30 day mortality rates. A statistically significant correlation was found between base excess (BE) and 15-30 day mortality rates.

**Conclusion:** The measurement of IVC diameter in the patients may lead the physicians to determine the volume condition of the patients, the lactate levels and BE values to predict the short-term mortality and help to decide whether hospitalize or discharge the patients.

**Keywords:** Atrial fibrillation, etiology, mortality, parameters

### Öz

**Amaç:** Bu çalışmada yüksek ventrikül cevapli atriyal fibrilasyonlu (AF) hastalarda, hız yüksekliğinin nedenleri, antiaritmik tedavi kararı ve kısa dönem mortalitede etkili olabilen bazı belirteçlerin değerlendirilmesi amaçlanmıştır.

**Gereç ve Yöntem:** Kasım 2016- Nisan 2018 tarihleri arasında, acil servise başvuran 18 yaş üstü yüksek ventrikül cevapli 103 AF tiplerindeki hastalar incelendi. Ventrikül hızının etyolojik araştırması için yatak başı ultrason (USG) ile inferior vena kava (IVK) çapları ölçüldü. Hastaların hemogram ve biyokimyasal belirteçler incelendi. 15 ve 30 günlük kısa dönem mortaliteleri sorgulandı. Vakaların mortalite ile ilişkili belirteçler analiz edildi.

**Bulgular:** Yüksek ventrikül cevabının altında yatan ikincil nedenler olarak kalp yetmezliği veya hipervolemi %15.5 (n=16) ile en sık karşılaşılan klinik tabloydu. Hastaların %14.6'sına (n=15) herhangi bir antiaritmik ilaç yapılmadan altta yatan etyolojik neden tedavi edilerek hızının düzeldiği izlendi. Laktat düzeyi ve 15-30 günlük mortalite oranları arasında istatistiksel olarak anlamlı korelasyon bulunmuştur. Baz açığı ve 15-30 günlük mortalite oranları arasında istatistiksel olarak anlamlı korelasyon bulunmuştur.

**Sonuç:** Yüksek ventrikül cevapli AF'li hastalarda, IVK çapı ölçümü hastanın volüm durumunun saptanmasında ve antiaritmik ilaç kararı belirlenmesinde yol gösterici olabilir. Aynı zamanda, bu hastalarda, laktat ve baz açığı değerlerinin bilinmesi, hastaneye yatış veya taburculuk kararı verilirken, kısa dönem mortalitenin öngörülmesi açısından fikir verebilir.

**Anahtar kelimeler:** Atriyal fibrilasyon, etyoloji, mortalite, belirteçler

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## INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia in the society and it is also very common reason to apply to Emergency Department. Its prevalence is gradually increasing. While the prevalence of AF is <0.5% at the ages between 40 and 50, it is about 5-15 % at the age of 80 <sup>1</sup>. AF is associated with thromboembolic conditions such as stroke, heart failure, reduced exercise capacity and dysfunction of left ventricular (LV), impaired quality of life and death <sup>2</sup>.

It is common to see patients with AF with rapid ventricular response and these patients have an extended stay in the Emergency Department. To control the heart rate and for effective treatment it is essential to determine the underlying etiologic factors, the choice of anti-arrhythmic drugs, measuring the volume load and perfusion conditions of the patients. Determination the volume condition by the caval index with the bedside ultrasonography may give enlightening information in terms of the necessity of diuretic treatment <sup>3,4</sup>. The determination of the patients' perfusion findings and some parameters are needed to prediction of the short-term mortality to make the decision for discharging the patient.

In this study, we aim to obtain some parameters to facilitate the choice of antiarrhythmic drugs in the emergency department, to shorten the duration spend in the emergency department and to help predicting the short-term mortality in the determination of the patients to discharge in the patients with atrial fibrillation rapid ventricular response.

## MATERIALS AND METHODS

After getting the approval of Cukurova University's ethics committee on January 13<sup>th</sup>, 2017 (decision number 60) for our prospective study, the patients, over 18 years old, with atrial fibrillation with rapid ventricular response who applied to Emergency Department of University Faculty of Medicine between November 2016 and April 2018 who agreed to involve the study by sign were investigated. The patients who were diagnosed with AF but who were noticed not to have rapid ventricular response the patients under 18 years old and the patients who did not give approval were excluded from the study.

## Procedure

During patient's care in emergency department following test were carried out; complete blood count white blood cell (WBC) , hematocrit ( HCT) , hemoglobine(HGB), red cell distribution width (RDW) , biochemical parameters (Glucose, Blood Urea Nitrogen (BUN) , creatinine, sodium, potassium, alanin aminotransferaz (ALT) , aspartate transaminaz (AST), Tiroid Stimulating Hormone (TSH) , Creatinine Kinase Myocardial Band ( CK-MB, Troponin), lactate levels, coagulation parameters , prothrombin time (PTT) , International Ratio (INR) and venous blood gases of the patients were checked. (Arterial blood gas was only evaluated in the patients who needed it for the oxygenation)

In order to investigate the volume condition of the patients, the device which is branded Sonosite M Turbo was used in the measurement of the Inferior Vena Cava (IVC) diameter. In the measurement of IVC diameter, the collapse condition of IVC during inhaling and exhaling was evaluated and the patients' estimated CVP (central venous pressure) conditions were evaluated.

For the measurement of IVC, the widest diameter during the expiratory in the B-Mode of USG was taken as a base. The measurement was made from 2 cm distal of the entry point to the right atrium. The outcome points of the study were determined as the hospitalization in the services of hospitals and in the intensive care units and the mortality within 15 and 30 days. Patients who did not need hospitalization or were discharged early from the hospital were interviewed by phone call and they were informed about the out-of-hospital prognosis (mortality within 15 and 30 days was questioned).

## Statistical analysis

SPSS version 15.0 program was used for data analysis. The suitability of the variables to normal distribution was examined by histogram graphs and Kolmogorov-Smirnov test. Mann Whitney U Test was used to evaluate the normal distribution between the groups.

## RESULTS

57 (55.3%) male patients and 46 (44.7%) female patients, 103 in total, were included in the study. The mean age of the patients was found as 66.7 ±15.1 year. When the complaints of the patients who participated in our study were considered, it was

found out that 37.9% of the patients applied to the hospital for palpitation, the most common reason (50.5%) for applying the hospital were the other cardiac symptoms (dyspnea, chest pain) among the patients. The types and rates of the patients with AF with rapid ventricular response were determined by reviewing the medical history and old recordings. Permanent AF was detected among the types of AF with the highest rate (49.5%).

Antiarrhythmic agents that were used in the patients and the rates of them are given in Table 2. 14.6%(n=15) of patients were treated for the secondary cause of high rate and no antiarrhythmic agent was needed. The short-term mortality rates

within 15 and 30 days of the patients who were included in our study were reviewed. In this prospective analysis, it was found that 13.6% (n=14) of the patients died within 15 days and 15.5% (n=16) of the patients died within 30 days. The underlying etiological causes of rapid ventricular response were given in Table 4. While no reason for increasing the rate was found in 38% of the patients, some other causes such as hypervolemia, anemia etc. were detected in the other patients. The other variables were compared according to the mortality rate within 30 days of the patients who participated in our study. Table 5 shows the statistically significant parameters in patients who developed mortality within 30 days

**Table 1. AF\* types of the patients who participated in the study**

AF Type	n	%
New onset AF	32	(31.1)
Paroxysmal AF	3	(2.9)
Persistent AF	8	(7.8)
Long-standing persistent AF	9	(8.7)
Permanent AF	51	(49.5)

\*In the measurable data, mean±SD is presented instead of n and median is presented instead of %. \*AF: Atrial Fibrillation

**Table 2. The medicines that were used to slow the AF in the patients**

Treatment for rate control	n	%
Treatment only for the underlying cause	15	(14.6)
Beta Blocker	15	(14.6)
Calcium Channel Blocker	2	(1.9)
Digoxine	32	(31.1)
Amiodarone	18	(17.5)
2 or more medicines	21	(20.4)

**Table 3. The patients' mortality rates within 15 and 30 days**

Mortality rate	n	%
15 days	14	(13.6)
30 days	16	(15.5)

**Table 4. Clinical conditions accompanying rapid rate**

Secondary cause of rapid ventricular response	n	%
Idiopathic	38	(36.9)
Hypervolemia and/or CHF*	16	(15.5)
Hypovolemia	14	(13.6)
Anemia	3	(2.9)
Fever	5	(4.9)
Hypoxia	7	(6.8)
Hyperthyroidism	2	(1.9)
Pain	2	(1.9)
More than one cause	16	(15.6)

\*CHF: Congestive Heart Failure

**Table 5. The comparison of the other variables according to the 30-day mortality of the patients**

	Mortality within 30 days						p*
	Exitus within 30 days			Alive			
	Mean ± SD	Median		Mean±SD	Median		
Oxygen saturation (%)	89.8	±9.5	92	94.6	±5.4	96	0,015
Glasgow Coma Scale	12.9	±3.0	15	14.8	±0.8	15	<0,001
Base Excess	-4.3	±5.2	-3.7	-1.0	±3.2	-0.9	0,008
BUN (mg/dl)	51.5	±27.8	48.5	23.5	±15	19	<0,001
Creatinine (mg/dl)	3.4	±4.7	2	1.1	±0.8	0,9	0,001
Hemoglobin (g/dl)	10.2	±3.1	9.5	12.9	±3.7	12,6	0,002
Hematocrit (%)	31.9	±9.3	32.2	38.4	±8.5	39	0,007
Troponin (ng/L)	0.5	±0.9	0.1	0.1	±0.3	0	0,001
Duration of the stay in the emergency service (minutes)	328.6	±118.1	345	310.6	±358.9	240	0,047
Lactate (mmol/L)	2.6	±1.3	2.4	1.9	±0.8	1.7	0,029

\*Mann whitney u test, SD: Standard deviation, S.: Score

## DISCUSSION

Atrial fibrillation is a kind of arrhythmia the etiology of which cannot be elucidated fully yet, the prevalence of which increases in parallel with the age and which can cause serious mortality and morbidity in patients. It is the most common arrhythmia among the elderly and 70% of the patients are above the age of 65<sup>5</sup>. In our study we investigate the underlying conditions that may cause the high rate in AF. Detection and treatment of etiological factors such as hypervolemia, hypovolemia, shock, fever, anemia etc. significantly affect the duration of hospital stay, morbidity and mortality rates, especially in patients with chronic AF.

The treatment strategies can be summarized as anticoagulation, rhythm and rate control. In addition to these three treatment strategies, the underlying cause of high rate should be investigated in patients especially with Atrial Fibrillation with rapid ventricular response<sup>6</sup>. If AF depends on an underlying secondary cause, AF with rapid ventricular response can be named as Complex Atrial Fibrillation<sup>6</sup>. In Complex AFs, it is known that the treatments which only focus on AF may give harm to the patients<sup>6</sup>. 63.1% of the patients with AF with rapid ventricular response were accompanied with clinical features such as hypovolemia 13.6% (n=14), heart failure-hypervolemia 15.5% (n=16), hypoxic

respiratory failure 6.8% (n=7), fever 4.9% (n=5), anemia 2.9% (n=3), hyperthyroidism 1.9% (n=2) while no secondary clinical feature was detected in 36.9% (n=38) of the patients. The mean age of the patient group in our study was 66.7 and comorbidity rate was high. The secondary reason which was thought to be the cause of rapid rate in 14.6% (n=15) of our patients was treated and the rate control was maintained without giving any antiarrhythmic agent. In the study of Brit Long et al., it was expressed that there might be other reason or reasons underlying rapid ventricular response in the patients with especially permanent AF who applied to emergency departments and these patients should be treated as the patients with sinus tachycardia<sup>6</sup>. With the treatment strategy in this article, the control of the rate was achieved by combining the treatment of the underlying cause with antiarrhythmic treatment in 86.3% (n=88) of the total patient group in our study.

Atrial fibrillation alone increases the risk of mortality regardless of all causes<sup>7</sup>. This rise in the mortality may be resulting from cardiovascular diseases or other causes rather than AF<sup>7</sup>. Non-valvular AF is responsible for 15-25% of all stroke events and at least half of cardio embolic paralysis are resulting from AF. In our study, it was observed that patients who applied to our emergency department with TIA and paralysis were more mortal than those who did not apply with the complaint of TIA and stroke<sup>7</sup>.

In our study, parameters that can predict the short-term mortality (within 15 and 30 days) of the patients with AF with rapid ventricular response and which may be effective in the decision of the physician about hospitalization or discharge were investigated.

The lactate levels of the patients who were mortal within 15 and 30 days were found to be statistically and significantly higher than those who were alive ( $p:0,029$ ). Many studies have reported that high lactate level can be considered as a useful indicator for determining the severity of disease and mortality rates<sup>8-9</sup>. The mortality rate within 15 day in the patients who were included in our study was 13.6% ( $n=14$ ) and the mortality rate within 30 days was 15.5% ( $n=16$ ). Lactate shows hypoperfusion<sup>10</sup>. It is controversial whether lactate increases as the secondary to AF with rapid ventricular response, or whether hyperlactatemia is the underlying cause of high rate.

Base excess (BE) shows extra acid or base in the blood that is caused by the defect in the metabolic system. It is an indicator of metabolic condition. The conducted studies presented that base deficit is associated with mortality in patients with acute renal failure, trauma, and shock<sup>9-11-12</sup>. In patients with acute pancreatitis, the base deficit should be  $> 4$  mEq / L at 48<sup>th</sup> hour and this is among the Ranson criteria and it is associated with increased mortality in acute pancreatitis<sup>13</sup>. There are many studies related to base excess and mortality in trauma patients, intensive care patients<sup>13</sup>. In our study, the base excess was found to be significantly higher in patients who were mortal within 15 and 30 days compared to the ones who were alive ( $p:0,008$ ).

Among the hospitalization criteria in patients with rapid ventricular response are patients with severe bradycardia after cardioversion, maintenance of antiarrhythmic medicine therapy, presence of active ischemia, significant hypotension, severe heart failure, acute renal failure, and rapid delivery of AF via an accessory pathway<sup>6</sup>. Although hyperlactatemia or increased base excess in the AF guidelines is not considered as an indicator for the hospitalization of the patient who applied to the emergency department with AF with rapid ventricular response, the fact that these values were found to be significantly higher in patients who were mortal in short-term lead to the conclusion that these values can be used as a poor prognostic marker in the decision of hospitalization. High lactate level and increased base excess may encourage the clinician to hospitalize the patients<sup>11</sup>.

Knowing which patient should be given fluid or which patient will be contraindicated in emergency critical care units is an issue that can compel the doctors in the emergency departments. Intravascular volume condition can be determined by physical examination, evaluation of vital signs, measurement of biochemical markers, tissue perfusion, sonographic evaluation of CVP or IVC diameter<sup>3</sup>. There are several methods being used to detect intravascular volume. Among these, IVC diameter measurement has been reported to reliably reflect volume condition<sup>3-14</sup> although there are also studies demonstrating quite the contrary<sup>3-15</sup>. However, a meta-analysis dated 2011 showed moderate evidence for the measurement of IVC diameter in determining normovolemic and hypovolemic condition, and for this purpose, further studies were needed to determine the exact role of IVC diameter measurement for this purpose<sup>3</sup>. No comprehensive study examining the role of IVC diameter in treatment and intravascular volume monitoring exist in the literature. Besides, various study groups used different methods in the measurement of IVC diameter<sup>12</sup>. Secondary causes or causes of tachycardia should definitely be considered in patients who applied to the emergency service with AF with rapid ventricular response. The adverse effect to antiarrhythmic agents increased 5.7 times in the patients with Complex AF<sup>6</sup>. This adverse effect increases up to 11.7 times if rate and rhythm are treated without treating the underlying cause<sup>6</sup>. This kind of patients may need relative tachycardia for the compensation of the secondary cause<sup>6</sup>. Determining the intravascular volume becomes more of an issue while investigating the secondary cause. The usage of bedside USG has become widespread in emergency departments and volume assessment with IVC is quite noninvasive, fast and practical for the physicians in the emergency departments compared to CVP catheter<sup>3-14</sup>. The physicians in the emergency departments gain experience in determining the diameter and collapsibility of inferior vena cava day by day.

In this study, we tried to determine the underlying causes of rapid ventricular rate, especially in patients with hypovolemia and hypervolemia. 13.6% ( $n=14$ ) of the patients were hypovolemic and 15.5% ( $n=16$ ) were hypervolemic. Determining the volume condition before making the treatment decision to control the rate in these patients may reduce unnecessary antiarrhythmic treatment, especially in hypovolemic patients. However, not only the IVC

diameter itself but also some other parameters such as the physical examination, the clinical condition of the patient, chest radiography, PaO<sub>2</sub>/FiO<sub>2</sub>, urine output and renal function should be evaluated<sup>16</sup>.

Limitations of our study are being conducted in only one centre with limited number of patients and the possibility of the physician's subjective decision when determining the secondary cause of AF.

Especially in patients with chronic AF with rapid ventricular rate, the etiological factors that may cause high rate. When the rate controlled by antiarrhythmic drugs without determining these etiological factors makes it difficult to determine the underlying cause. This turns into a burden on both the clinicians and the patients.

IVC diameter can guide the physicians to decide on antiarrhythmic treatment and to determine volume condition in the patients with AF with rapid ventricular response. While making the decision of hospitalization and discharge of these patients, it should be taken into consideration that the knowledge of lactate and base deficit values as well as the traditional hospitalization indications may support the physician as a guiding marker for predicting short-term mortality.

**Yazar Katkıları:** Çalışma konsepti/Tasarımı: GS, ÖT, AAA; Veri toplama: GS, ÖT, AAA; Veri analizi ve yorumlama: GS, ÖT, AAA; Yazı taslağı: GS, ÖT, AAA; İçerigin eleştirel incelenmesi: GS, ÖT, AAA; Son onay ve sorumluluk: GS, ÖT, AAA; Teknik ve malzeme desteği: AAA; Süpervizyon: -; Fon sağlama (mevcut ise): yok.

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