Age-Related Differences in Elderly Patients with Atrial Fibrillation

İleri Yaş Atriyal Fibrilasyonlu Hastalarda Yaşa Bağlı Değişiklikler

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Objective: Atrial fibrillation (AF) is the most common cardiac arrhythmia worldwide. Its prevalence increases significantly with age. Therefore, it is particularly important in the elderly population. Despite this, elderly patients have been underrepresented in clinical studies, and optimal medical treatment has been less frequently provided to this group. The aim of this study is to identify age-related patterns in elderly patients and to evaluate their relationship with comorbidities.

Materials and Methods: 118 patients with permanent AF aged ≥75 years (middle-old) and 153 patients with permanent AF aged 65-74 years (youngest-old) were retrospectively evaluated. Demographic, biochemical and echocardiographic parameters were compared between groups.

Results: There were 85 cases (72%) of hypertension, 43 cases (36%) of diabetes mellitus, 56 cases (48%) of coronary artery disease in patients with AF aged ≥75 years. There were 91 cases (60%) of hypertension, 43 cases (28%) of diabetes mellitus, 60 cases (39%) of coronary artery disease in patients with AF aged 65-74 years. Patients with AF aged ≥75 years had higher rates of hypertension, diabetes mellitus and coronary artery disease compared to the patients with AF aged 65-74 years (p=0.021, p=0.092, p=0.108, respectively). However, only hypertension reached statistical significance. Also, creatinine [1.15±0.36 mg/dl vs 1.03±0.23 mg/dl, p=0.003], urea [53.4±29.8 mg/dl vs 41.4±15.5 mg/dl, p<0.001] levels were higher; whereas eGFR [54.9±14.8 ml/min vs 69.5±17.7 ml/min, p<0.001], hemoglobin (11.5±2.1 g/dl vs 12.9±1.8 g/dl, p<0.001) and albumin [3.67±0.54 g/dl vs 4±0.44 g/dl, p=0.003] levels were lower in patients with AF aged ≥75 years compared to the patients with AF aged 65-74 years.

Conclusion: Comorbidities especially hypertension, chronic kidney disease and anemia are more frequently observed in patients with AF as age increases. It is important to recognize that in elderly patients with AF, it is essential to manage not only the arrhythmia itself but also accompanying comorbidities.

Keywords: Atrial fibrillation, Elderly, Geriatric

Amaç: Atriyal fibrilasyon (AF), dünya çapında en sık karşılaşılan kardiyak aritmidir. Yaşla birlikte görülme sıklığı önemli ölçüde artmaktadır. Buna rağmen, yaşlı hastalar klinik çalışmalarda yeterince temsil edilmemekte ve bu gruba optimal medikal tedavi daha seyrek verilmektedir. Bu çalışmanın amacı, AF'si olan yaşlı hastalarda yaşa bağlı değişiklikleri değişiklikleri saptamaktır.

Gereç ve Yöntem: 75 yaş ve üzeri (orta yaşlılar) kalıcı atriyal fibrilasyonu olan 118 hasta ile 65-74 yaş arası (genç yaşlılar) kalıcı atriyal fibrilasyonu olan 153 hasta retrospektif olarak değerlendirildi. Gruplar arasındaki demografik, biyokimyasal ve ekokardiyografik parametreler karşılaştırıldı.

Bulgular: 75 yaş ve üzeri atriyal fibrilasyonlu hastalarda 85 (%72) hipertansiyon, 43 (%36) diyabet mellitus ve 56 (%48) koroner arter hastası vardı. 65-74 yaş arası atriyal fibrilasyonlu hastalarda ise 91 (%60) hipertansiyon, 43 (%28) diyabet mellitus ve 60 (%39) koroner arter hastası vardı. 75 yaş ve üzeri hastalarda, 65-74 yaş arası hastalara kıyasla daha fazla sayıda hipertansiyon, diyabet mellitus ve koroner arter hastalığı vardı (sırasıyla p=0.021, p=0.092, p=0.108). Ancak istatistiksel olarak anlamlılık düzeyine yalnızca hipertansiyon ulaştı. Ayrıca 75 yaş ve üzeri hastalarda kreatinin [1,15±0,36 mg/dl'ye karşı 1,03±0,23 mg/dl, p=0,003] ve üre [53,4±29,8 mg/dl'ye karşı 41,4±15,5 mg/dl, p<0,001] düzeyleri daha yüksek iken; eGFR [54,9±14,8 ml/dk vs 69,5±17,7 ml/dk, p<0,001], hemoglobin (11,5±2,1 g/dl vs 12,9±1,8 g/dl, p<0,001) ve albümin [3,67±0,54 g/dl vs 4±0,44 g/dl, p=0,003] düzeyleri daha düşük saptandı.

Sonuç: AF'li hastalarda yaş ilerledikçe, başta hipertansiyon, kronik böbrek hastalığı ve anemi olmak üzere eşlik eden hastalıklar artmaktadır. Bu hastalarda AF tedavisini optimize etmek yanında, aynı zamanda eşlik eden hastalıkları da yönetmek önemlidir.

Anahtar Kelimeler: Atriyal fibrilasyon, Yaşlanma, Geriatri

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INTRODUCTION

Described as the 'cardiovascular epidemic of the 21st century,' atrial fibrillation (AF), one of the most common arrhythmias, affects 33 million people worldwide, with approximately 5 million new cases added annually (Chugh et al., 2014; Li et al., 2019). Between 2010 and 2060, the number of individuals with AF aged ≥55 years in the European Union is expected to more than double, and the affected population is projected to rise from 8.8 million to 17.9 million (Krijthe et al., 2013).

With regard to the geriatric population; most patients with AF are elderly, and the incidence of AF increases with age (Go et al 2014; Chugh et al., 2014; Heeringa et al., 2006). The Framingham study demonstrated that the incidence of AF increases markedly after the age of 60 (Kannel et al., 1982). As the human body ages, the gene and protein expression levels of contractile proteins and L-type calcium channels decrease, and the size of the left atrium increases, potentially contributing to the development of AF (Chinese Society of Cardiovascular Diseases of Chinese Medical Association, 2003]. In addition, conditions such as systemic inflammation, atrial fibrosis, autonomic nervous system dysfunction and oxidative stress can cause atrial remodeling, creating a proarrhythmic predisposition (Halcox et al., 2017; Siontis et al., 2016).

Epidemiological studies demonstrate that cases of AF increase rapidly after the age of 65, with individuals above this age threshold accounting for the vast majority of AF related complications and hospitalizations (Hindricks et al., 2021; Go et al., 2001). Nevertheless, studies focusing on the elderly patients particularly those aged ≥65 years are limited; there are significant gaps in understanding risk profiles and age-specific disease patterns in the literature (Psaty et al., 1997). In most studies on AF, the subject selection criteria are relatively wide and there is no specific age limit. As a result, the average age of the study group is younger than the average age of the AF population. Whether these data are applicable to the elderly population remains debated (Rich et al., 2016) Therefore, further research is needed on elderly individuals with AF.

Furthermore, some studies showed that elderly patients with AF are less thoroughly evaluated and treated and are less frequently referred to cardiologists (Nieuwlaat et al.,2005; Fumagalli et al., 2012). Although studies have demonstrated that the benefits of oral anticoagulants extend to the elderly patients with AF, real-world data consistently demonstrate that oral anticoagulant prescription rates are inversely proportional to age (Go et al., 2001; Singer et al., 2009; Mant et al., 2007). In addition, advanced age is an independent predictor of reduced medication adherence and early discontinuation (Di Pasquale et al., 2013; Hylek et al., 2007).

Elderly patients with AF face different clinical conditions compared to younger patients. These include increased polypharmacy, frailty and a higher risk of thromboembolic and bleeding events (Psaty et al., 1997). These factors complicate treatment decisions and require individualized treatment approaches (Boriani et al., 2015; Halcox, et al., 2017; Siontis et al., 2016). Thus, there is an urgent need for focused studies on AF in the elderly population. This research is necessary not only to understand age specific risk factors, but also to develop safe and effective preventive and treatment strategies appropriate for these vulnerable patients. We aimed to identify age-stratified patterns and evaluate their associations with comorbidities between patients with permanent AF aged ≥75 years and patients with permanent AF aged 65-74 years.

MATERIALS AND METHODS

Patients ≥65 years of age with permanent AF who presented to the cardiology outpatient clinic for any reason were included in this study. The patients were divided into two groups: 118 patients with permanent AF aged ≥75 years (middle-old) and 153 patients with permanent AF aged 65-74 years (youngest-old).

Demographic, echocardiographic and biochemical parameters were compared between groups.

A person aged ≥65 years is referred to as 'elderly' (Orimo et al., 2006). Patients were classified into Group 1 (youngest-old), ages 65-74 years; Group 2 (middle-old), ranging from ages 75-84 years; and Group 3 (oldest-old), aged ≥85 years. (Lee et al., 2018)
Permanent AF was defined as AF for which no further attempts at restoration of sinus rhythm are planned, after a shared decision between the patient and doctor (Gelder et al., 2024).
The estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft-Gault formula (Cockcroft et al., 1976; Coresh et al., 2006). Diabetes mellitus (DM) was described as HbA1c level ≥6.5%, fasting blood glucose level ≥126 mg/dl, 2 hour postprandial blood glucose level ≥200 mg/dl or use of insulin or oral antidiabetic treatment (American Diabetes Association, 2010). Hypertension (HT) was described as higher systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg or the use of antihypertensive treatment (Williams et al., 2018). Coronary artery disease (CAD) was described as coronary artery stenosis ≥50% confirmed by coronary angiography or coronary computed tomography, previous history of percutaneous coronary intervention or myocardial infarction (Li et al., 2019).

Statistical analysis and ethical aspects

SPSS version 13.0 (SPSS Inc., IBM, Chicago, IL, USA) program was used for statistical data processing. Kolmogorov-Smirnov test was used to analyze the distribution of the parameters. Normally distributed variables were expressed as ''mean±standard deviation'' and Non-normally distributed variables were expressed as median (25th–75th percentiles)''. Categorical variables were presented as percentages and frequencies. Categorical variables were tested with the Chi-square test. Normally distributed continuous variables were evaluated with two-tailed Student's T-test and abnormally distributed parameters with Mann Whitney U test. A value $p<0.05$ was considered statistically significant.

This retrospective study was approved by the Ethics Committee of Balıkesir University (11.10.2023 date and 2023/137 number) according to the Declaration of Helsinki.

RESULTS

A total of 118 patients with permanent AF aged ≥75 years and 153 patients with permanent AF aged 65-74 years were enrolled in this study.

When demographic/clinical characteristics were evaluated; the mean age was 76.7±1.7 years in patients with AF aged ≥75 years and 70±3 years in patients with AF aged 65-74 years. 47 (40%) were male and 71 (60%) were female in patients with AF aged ≥75 years. 61 (40%) were male and 92 (60%) were female in patients with permanent AF aged 65-74 years. There was no significant difference in gender between the groups (p=0.548). However, the number of females was higher than males in both groups. The mean BMI was 27.6±4 kg/m^2 in patients with AF aged ≥75 years and 28±4.1 kg/m^2 in patients with AF aged 65-74 years. There was no significant difference between the groups (p=0.573).

When comorbidities were evaluated; there were 85 cases (72%) of HT, 43 cases (36%) of DM, 56 cases (48%) of CAD in patients with AF aged ≥75 years. There were 91 cases (60%) of HT, 43 cases (28%) of DM, 60 cases (39%) of CAD in patients with AF aged 65-74 years. Patients with AF aged ≥75 years had more HT, DM and CAD compared to the patients with AF aged 65-74 years (p=0.021, p=0.092, p=0.108, respectively). However, only HT reached statistical significance.
Regarding echocardiographic parameters; ejection fraction values were similar between groups [55 (50-60) vs 55 (50-60), p=0.635]. Demographic/clinical characteristics, Baseline characteristics and echocardiographic parameters of the groups are presented in Table 1.

Regarding laboratory parameters; creatinine [1.15±0.36 mg/dl vs 1.03±0.23 mg/dl, p=0.003], urea [53.4±29.8 mg/dl vs 41.4±15.5 mg/dl, p<0.001] levels were higher; while eGFR [54.9±14.8 ml/min vs 69.5±17.7 ml/min, p<0.001], hemoglobin [11.5±2.1 g/dl vs 12.9±1.8 g/dl, p<0.001] and albumin [3.67±0.54

g/dl vs 4±0.44 g/dl, p=0.003] levels were lower in patients with AF aged ≥75 compared with patients with AF aged 65-74 years.

Groups were similar in terms of glucose [128.1±42.7 mg/dl vs 120.3±40.3 mg/dl, p=0.129], total cholesterol [166.1±46.8 mg/dl vs 174.5±39 mg/dl, p=0.136], triglycerides [97 (71-153) mg/dl vs 111 (85-155) mg/dl, p=0.070], LDL cholesterol [97±35.3 mg/dl vs 101.7±29 mg/dl, p=0.260] and HDL cholesterol [45 (38-51) mg/dl vs 45 (39-54) mg/dl, p=0.206] levels. Laboratory parameters of the groups are presented in Table 2.

Table 1. Baseline characteristics and echocardiographic parameters of the groups

	Patients with AF aged ≥75 years (n=118)	**Patients with AF aged 65-74 years (n=153)**	***p***
Age (years)	76.7±1.7	70±3	<0.001
Gender (Male/Female)	47/71 (40%-60%)	61/92 (40%-60%)	0.548
Body mass index (kg/m^2)	27.6±4	28±4.1	0.573
Hypertension	85 (72%)	91 (60%)	0.021
Diabetes mellitus	43 (36%)	43 (28%)	0.092
Coronary artery disease	56 (48%)	60 (39%)	0.108
Ejection fraction (%)	55 (50-60)	55 (50-60)	0.635

Table 2. Laboratory parameters of the groups

	Patients with AF aged ≥75 years (n=118)	**Patients with AF aged 65-74 years (n=153)**	***p***
Glucose (mg/dl)	128.1±42.7	120.3±40.3	0.129
Hemoglobin (g/dl)	11.5±2.1	12.9±1.8	<0.001
Creatinine (mg/dl)	1.15±0.36	1.03±0.23	0.003
Urea (mg/dl)	53.4±29.8	41.4±15.5	<0.001
eGFR (ml/min)	54.9 ±14.8	69.5±17.7	<0.001
Total Cholesterol (mg/dl)	166.1±46.8	174.5±39	0.136
Triglyceride (mg/dl)	97 (71-153)	111 (85-155)	0.070
LDL Cholesterol (mg/dl)	97±35.3	101.7±29	0.260
HDL Cholesterol (mg/dl)	45 (38-51)	45 (39-54)	0.206
Albumin (g/dl)	3.67±0.54	4±0.44	0.003

eGFR: Estimated glomerular filtration rate, LDL: Low density lipoprotein, HDL: High density lipoprotein

DISCUSSION

In elderly adults, the number of AF cases increases with age. Despite the strong association between AF and aging, elderly patients have not been adequately included in clinical studies; therefore, there are limited data on the characteristics of these elderly patients (Rich et al., 2016; Psaty et al., 1997). Also, the rates of optimal medical treatment provided by healthcare professionals for patients are low due to additional comorbidities associated with aging (Go et al., 2001; Singer et al.,2009; Mant et al., 2007). Our study aimed to shed light on the differences between age groups (group 1: youngest-old, ages 65-74 years and group 2: middle-old, ages 75-84 years) in elderly patients with AF.

Several comorbidities, such as HT and chronic kidney disease (CKD), and anemia were more prevalent in patients with AF aged ≥75 years compared to the patients with AF aged 65-74 years. Although the number of DM and CAD cases was higher in patients with AF aged ≥75 years, it did not reach statistical significance. In addition, the number of females was higher than that of males in both groups.

Although no significant difference was found between the groups in terms of gender; in our study, the number of females was greater than the number of males in both groups. Li et al. showed that the prevalence of AF in older females is higher than that in males (Li et al., 2019). Feinberg et al. demonstrated that males are more common than females before the age of 75 and after 75 years old, the ratio of female patients with AF increased (Feinberg et al., 1995) in a study conducted in Switzerland, the prevalence of AF among females under 80 is lower than that of males, and females over 80 are higher than males (Andersson et al., 2013). Other studies have demonstrated that the prevalence of female patients in the age group >75 years old is twice that of males [Fang et al., 2005). This shows that gender differences in AF may vary with age. The higher prevalence of AF in older females may be related to changes in hormonal levels especially estrogen, autonomic dysfunction and increased comorbidities in older females. Gender-related differences are still open to further debate. It is important to pay more attention to older women with AF.

HT is a strong predictor of AF. HT leads to left atrial enlargement and fibrotic remodeling of the atrium. In addition, HT damages the blood vessel walls, leading to atherosclerosis and increased arterial stiffness, which can trigger AF. The Framingham Heart Study showed that HT increases the risk of developing AF by 1.42 times in males and 1.56 times in females (Benjamin et al., 1994) Similarly, the ARIC Study demonstrated that the risk of AF is almost twice as high in patients with systolic blood pressure ≥160 mm Hg compared to those with blood pressure <120 mmHg (Huxley et al., 2011). Patients with AF aged ≥75 years had more HT compared to the patients with AF aged 65-74 years in our study.

DM promotes atrial remodeling related to AF through autonomic dysfunction, oxidative stress and systemic inflammation (Movahed et al., 2005). Huxley et al. showed the results of meta-analysis and systematic review evaluating the association between DM and AF. Overall, DM was related to a 39% increased risk of AF (Huxley et al., 2011). Elizabeth Caroline Palaparthi et al. showed that DM was more common in patients with AF (Palaparthi et al., 2025). Patients with AF aged ≥75 years had more DM compared to the patients with AF aged 65-74 years in our study. However, this result did not reach statistical significance. This situation may be due to lower sample size of the study.

CAD related myocardial ischemia triggers structural remodeling and atrial electrical instability. In the EORP-AF study, patients with AF aged ≥75 years had more common CAD (Fumagalli et al, 2015). Although the number of CAD cases was higher in patients with AF aged ≥75 years, it did not reach statistical significance. This situation may be due to low study population.

Serum albumin levels are used in the monitoring of nutritional status, renal and liver disease (Weaving et al., 2016). Low albumin levels are associated with poor nutritional states; chronic illnesses such as liver and renal dysfunction and infections (Harrison et al., 2017). Chronic diseases may reduce albumin levels in any age groups. Some studies support a negative relationship between serum albumin and age. Cooper et al found that a small but consistent negative association was found for those aged over 70. In elderly patients, hypoalbuminemia may be a result of a combination of age and comorbidities (Cooper et al., 1989). In our study, albumin levels were also found to be significantly lower in elderly patients with AF aged ≥75 years. This situation, similar to the studies above, may be related to an increase in chronic diseases with aging.

There is a bidirectional relationship between CKD and AF. Renal dysfunction not only

predisposes to AF through electrolyte imbalances and fluid overload, but AF itself can also worsen renal failure through thromboembolism and impaired hemodynamics (Bansal et al., 2013; Zimmerman et al., 2014). GFR values are important in initiating and adjusting the dosage of novel oral anticoagulant therapy used to prevent stroke in patients with AF. Oral anticoagulant was used less frequently in elderly patients (Fumagalli et al., 2015). One of the most important reasons for this is lower eGFR and increased comorbidities associated with advanced age may be responsible for underprescription of optimal medical therapies (Hess et al., 2013).

Compared to younger patients, chronic inflammation and additional diseases that may be associated with atrial fibrosis tend to be more cumulative and chronic in elderly patients (Movahed et al., 2005; Al Chekakie et al., 2010). These differences highlight the importance of age specific diagnostic, screening strategies and treatment.

Limitations

There were several limitations in this study. First, this retrospective study was conducted on a small number of patients at a single center. Prospective and multicenter studies are needed to verify these results. Secondly, in our study we did not include the third group of elderly classification, namely those aged 85 and over, due to the low number of patients. Third, follow-up, mortality, morbidity rates and medication use were not included in this study. Also, it should also be remembered that patient characteristics may differ in different regions and races.

CONCLUSION

The study shows that patients with AF aged ≥75 years had a statistically higher comorbidity burden especially HT, CKD and anemia compared to the patients with AF aged 65-74 years. DM and CAD were more common in patients with AF aged ≥75 years, but the differences were not statistically significant. Accordingly, the approach of patients with AF should change across different stages of life. The finding of this study that additional comorbidities are more frequently observed in AF patients with aging emphasizes that not only should AF treatment be optimized, but these additional comorbidities should also be treated. Furthermore, there is a need for future studies to evaluate and develop age-specific preventive, screening and treatment strategies suitable for the vulnerable body profile of the elderly.

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Availability of Data and Materials: The datasets from the current study can be obtained on request from the corresponding author.

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