Management and comorbidities of atrial fibrillation in patients admitted in cardiology service in Kosovo-a single-center study

Kosovo'da kardiyoloji servisine başvuran hastalarda atriyal fibrilasyonun komorbiditeleri ve takibi-Tek merkezli çalışma

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ABSTRACT

Objective: Atrial fibrillation (AF) is the most important risk factor for ischemic stroke. Anticoagulation therapy can substantially decrease the risk of stroke in patients with AF. The aim of our study was to investigate the patient's comorbidities and management of patients with AF on the discharge.
Methods: From 5382 consecutive patients admitted in our institution between January 2005 and March 2008, 525 (mean age 66.4±11.4 years, 53.3% male) had AF upon discharge, who were included in this retrospective study. Patients were divided in two groups according to prescription of anticoagulation therapy at discharge. Continuous data were compared between groups using a two-tailed unpaired Student t test. Discrete variables were compared using Chi-square test or Fisher's exact probability test as appropriate. Logistic regression analysis was used to identify the independent clinical and echocardiographic predictors of prescribing oral anticoagulation therapy.
Results: Associated comorbidities of AF in our patients were: ischemic heart disease (21.4%), hypertensive heart disease (27.44%), valvular heart disease (17.4%), congestive heart failure (47%), chronic obstructive pulmonary disease (6.7%), and diabetes 14.3%). Of 525 patients 76% were discharged on beta-blockers, 67% on angiotensin converting enzyme inhibitors, 23% on digoxin, 16% on calcium antagonists, 67% on diuretics, 72% on aspirin, and 27% on oral anticoagulant (OAC) therapy, 11% were with both antithrombotics. Multivariate analysis showed that the under-prescription of OAC therapy in patients with AF was independently associated with elder age (OR=0.916, 95%CI 0.891-0.942, p<0.001), non-enlarged left atrium (OR=1.148, 95%CI 1.100-1.198, p<0.001) and good left ventricular ejection fraction (OR=0.970, 95%CI 0.948-0.993, p=0.011).
Conclusions: Patients with atrial fibrillation were mainly with ischemic, hypertensive heart disease and congestive heart failure. Our study, suggests underuse of anticoagulation therapy. The independent predictors of under prescription of anticoagulants in patients with atrial fibrillation were elder age, non-enlarged left atrium, and good left ventricular ejection fraction. Medical treatment with other groups of drugs for atrial fibrillation and comorbidities seems to be according to current guidelines. *(Anadolu Kardiyol Derg 2010; 10: 36-40)*
Key words: Atrial fibrillation, anticoagulation, predictive models, logistic regression analysis

ÖZET

Amaç: Atriyal fibrilasyon (AF) iskemik inmenin en önemli risk faktörüdür. Antikoagülasyon tedavisi atriyal fibrilasyonlu hastalarda inme riskini büyük oranda azaltabilir. Bizim çalışmamızın amacı, taburcu olan AF'li hastaların takibi ve hastaların komorbiditesini araştırmak idi.
Yöntemler: Ocak 2005 ve Mart 2008 tarihleri arasında kurumumuza başvuran 5382 ardışık hastadan, bu retrospektif çalışmaya dahil edilen 525'i (ortalama yaş 66.4±11.4 yaş, %53.3 erkek) taburcu edilirken atriyal fibrilasyonlu idi. Hastalar taburcu olurken antikoagülasyon tedavi reçetesine göre iki gruba ayrıldı. Eşleştirilmemiş Student t testi kullanılarak sürekli veriler gruplar arasında karşılaştırıldı. Uygunluklarına göre kategorik değişkenler, Ki-kare testi ya da Fisher'in kesin olasılık testi kullanılarak karşılaştırıldı. Oral antikoagülasyon tedavisinin reçetelenmesinin bağımsız klinik ve ekokardiyografik belirleyicilerini tanımlamak için lojistik regresyon analizi kullanıldı.
Bulgular: Hastalarımızda atriyal fibrilasyonla ilgili komorbiditeler: İskemik kalp hastalığı (%21.4), hipertansif kalp hastalığı (%27.4), valvüler kalp hastalığı (%17.4), kongestif kalp yetersizliği (%47), kronik obstrüktif pulmoner hastalık (%6.7) ve diyabettir (%14.3). Hastların %76'sı beta-blokerlerle, %67 anjiyotensin dönüştürücü enzim inhibitörlerle, %23 digoksinle, %16 kalsiyum antagonistleri ile %67 diüretik ilaçlarla, ve %72 aspirinle ve 27% oral antikoagülasyon tedavisi (OAK) ile taburcu edildi, %11 ise her iki antitrombotiği alıyordu.

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Çok değişkenli analiz atriyal fibrilasyonlu hastalarda OAK tedavinin daha az reçetelenmesinin ileri yaş (OR=0.916, %95GA 0.891-0.942, p<0.001), büyümemiş sol atriyum (OR=1.148, %95GA 1.100-1.198, p<0.001) ve iyi sol ventriküler ejeksiyon fraksiyonundan (OR=0.970, %95GA 0.948-0.993, p=0.011) bağımsız olduğunu gösterdi.
Sonuçlar: Atriyal fibrilasyonlu hastalar çoğunlukla, iskemik, hipertansif kalp hastalığı ve doğuştan kalp hastalığı olanlardı. Bizim çalışmamız, antikogülasyon tedavisinin az kullanıldığını akla getirdi. İleri yaş, büyümemiş sol atriyum, iyi sol ventrikül ejeksiyon fraksiyonu atriyal fibrilasyonlu hastalarda antikoagülasyon reçetesinin daha az kullanılmasının bağımsız belirleyicileridir. Atriyal fibrilasyon ve komorbiditeler için diğer ilaç gruplarıyla tıbbi tedavi güncel kılavuzlara uygun olduğu saptanmıştır. *(Anadolu Kardiyol Derg 2010; 10: 36-40)*
Anahtar kelimeler: Atriyal fibrilasyon, antikogülasyon, tahmini modeller, lojistik regresyon analizi

Introduction

Atrial fibrillation (AF) is the most common arrhythmia and is an important risk factor for stroke (1). The risk of stroke in patients with AF is increased by three to seven-fold compared to those without AF (2) and it is increased in the presence of comorbidities (3). The use of oral anticoagulant (OAC) therapy has been shown to reduce markedly the rate of ischemic stroke in patients with AF (4, 5) and also to reduce poststroke mortality in patients with stroke and AF (6). The major risk associated with the use of OAC therapy is bleeding, which limits its use in general practice. The major bleeding episodes occur significantly more frequently in patients receiving warfarin compared to those with aspirin, even the use of warfarin was shown to be more effective (3). It is evident that the OAC therapy is underused in patients with AF, even in developed Western countries (7-10). The most suggested factors influencing underuse of OAC therapy were shown to be: the clinical perception that the patients will not comply with the treatment, advanced age, rural location and walking ability (11-13). However, it was shown that the treatment of AF with OAC therapy was increased over last years (14).

The aim of our study was to investigate the patient characteristics, comorbidities and management of patients with AF admitted in Service of Cardiology in Kosovo.

Methods

Of 5382 consecutive patients discharged from our Service, between January 2005 and February 2007, 525 had AF at discharge, and were included in this retrospective study.

Data collection

Trained research medical students studied the information from the hospital medical records in the hospital archive. Demographic data were obtained from all patients: these included age, gender, laboratory data, electrocardiogram (ECG), and the prevalence of comorbidities such as congestive heart failure, diabetes, hypertensive heart disease, valvular heart disease and chronic obstructive pulmonary disease. Routine biochemical measurements were performed. In all patients the measurements of fasting blood glucose, cholesterol, triglycerides, urea, creatinine, erythrocytes, leucocytes, hemoglobin, hematocrit and erythrocyte sedimentation were performed.

The prescribed drugs on discharge, including OAC therapy were also evidenced.

Echocardiographic examinations

Echocardiographic examination was performed with Philips E-33 (Philips Medical Systems, Netherlands), equipped with multifrequence probe. The left ventricular (LV) end-diastolic dimension, LV end-systolic dimension, interventricular septal thickens, LV posterior wall thickness, left atrium dimension, aortic root dimension, fractional shortening (FS) and ejection fraction (EF) were evidenced in all patients. The structure of heart valves and their changes were evauaded using two-dimensional echocardiography, while the scale of the valvular abnormalities, including systolic pulmonary artery pressure were assessed by Doppler echocardiography.

Statistical analysis

All analyses were performed using Statview 4.5 software (Abacus Concepts, Berkley, CA, USA).

Patients with AF were divided in two groups according to OAC prescription or lack of prescription at discharge. Data are presented as mean±standard deviation or percentages. Continuous data were compared between groups using a two-tailed unpaired Student *t* test. Discrete variables were compared using Chi-square test or Fisher's exact probability test as appropriate. Logistic regression model was used to identify the independent clinical and echocardiographic predictors of OAC prescription. Dependent variable was OAC prescription at discharge and we included in logistic regression model only independent variables that were significantly different in univariate analysis: age, left atrium size, LV ejection fraction (LV diastolic and systolic dimensions were used to calculate ejection fraction) and arterial hypertension. P value less than 0.05 indicated statistical significance.

Results

Of 5382 consecutive patients discharged from our Service, between January 2005 and March 2008, 525 patients had AF (9.75%). The mean age of study population was 66.4±11.4 years (range 16-95 years). There were 280 (53.3%) males and 245 (46.7%) females (Table 1).

Associated comorbidities of AF in our patients were: ischemic heart disease (21.4%), hypertensive heart disease (27.44%), valvular heart disease (17%), congestive heart failure (39%), chronic obstructive pulmonary disease (6%), and diabetes 14.3%), (Fig. 1, Table 1), whereas the frequency of smokers was 36.3%. From the patients with valvular heart diseases, the AF was attributed to mitral stenosis as a main cause in 30% of

patients, mitral regurgitation-25%, combined mitral valve stenosis and regurgitation in 8%, aortic stenosis-17%, aortic regurgitation-28%, and combined aortic stenosis and regurgitation in 5% of patients with valvular heart disease.

From laboratory analyses of patient population with atrial fibrillation the urea and creatinine were found increased (11±8 mmol/L and 118±67 μmol/L, respectively), whereas the mean values of other blood analyses were within normal values (Table 1).

In our study population, the echocardiography showed enlarged LV end-systolic dimension (40.5±10.0 mm), reduced LV systolic function (EF=48±12%) and enlarged left atrium (4.7±2.7 cm) (Table 1).

Of 525 patients 76% were discharged on beta-blockers, 67% on angiotensin-converting enzyme (ACE) inhibitors, 23% on digoxin, 16% on calcium antagonists, 67% on diuretics, 72% on aspirin, and 27% on anticoagulation therapy, 11% were with both antithrombotics, whereas in 12% of patients there were no prescription of any antithrombotic drug (Fig. 2).

According to the prescribed OAC therapy, the study patients were divided into two groups: Group 1 (patients with AF and with prescribed OAC therapy) and Group 2 (patients with AF and no OAC therapy prescription). The age of patients was significantly lower (p<0.001) and the arterial hypertension as a comorbidity was significantly less frequent (p=0.049) in patients in whom the OAC therapy was prescribed (Table 1), whereas sex, smoking, diabetes, coronary artery disease, fasting glycemia, urea, creatinine and hemoglobin blood levels did not differsignificantly between groups.

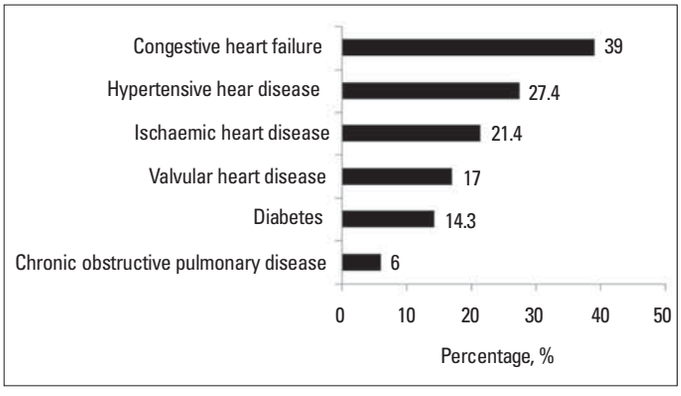

Figure 1. Comorbidities of atrial fibrillation in the study patients

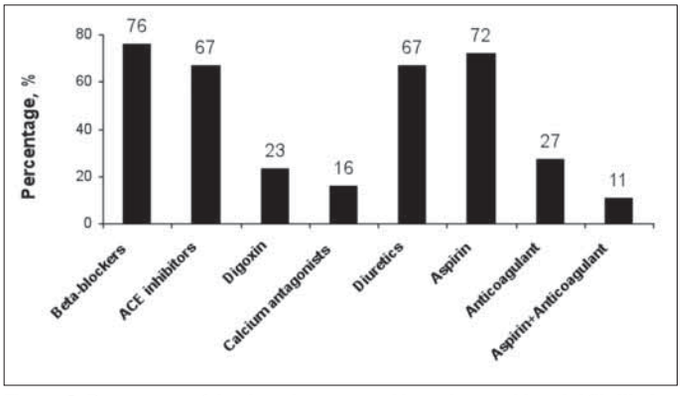

Figure 2. Percentage of the drug therapy used in patients with atrial fibrillation
ACE - angiotensin-converting enzyme

From echocardiographic variables, left atrium was larger (p<0.001), LV end-diastolic and end-systolic dimensions were higher (p<0.001 and p<0.001, respectively), whereas FS and EF were lower in the Group 1 as compared with Group 2 (p=0.006, and, p=0.004, respectively) (Table 1).

Multivariate analysis showed that the lack of prescription of anticoagulants in patients with AF was independently associated with older age (OR=0.916, 95%CI 0.891-0.942, p<0.001), non-enlarged left atrium (OR=1.148, 95%CI 1.100-1.198, p<0.001) and good LV ejection fraction (OR=0.970, 95%CI 0.948-0.993, p=0.011) (Table 2).

Discussion

By our knowledge, this is the first study conducted in Kosovo about the prevalence, comorbidities and quality of treatment of AF.

Table 1. Clinical and biochemical data of patients with atrial fibrillation discharged from the Service of Cardiology, who were prescribed (Group 1) or were not prescribed anticoagulation therapy (Group 2)

Variables	All (n=525)	Group 1 (n = 142)	Group 2 (n = 383)	p*
Female gender, %	46.7	47.2	48.8	0.768
Age, years	66.4±11.4	60.8±12.0	68.5±10.0	<0.001
Smoking, %	36.3	35.2	37.2	0.684
Diabetes, %	14.3	13.9	14.7	0.590
Arterial hypertension, %	27.4	21.8	30.7	0.049
Coronary artery disease, %	21.4	18.4	22.5	0.338
Fast glycemia, mmol/L	6.80±3.70	6.,77±4.70	6.82±3.30	0.876
Urea, mmol/L	11.0±8.4	5.83±0.5	8.99±0.50	0.117
Creatinine, μmol/L	118.0±67.4	118.7±80.00	117.9±62.0	0.912
Hemoglobin	106.4±31.9	109.1±32.8	103.2±30.6	0.353
Aortic root dimension, mm	33.8±4.8	33.9±5.0	33.8±4.7	0.839
Left atrium dimension, mm	47.0±27.1	51.3±11.1	43.5±7.4	<0.001
LV end-diastolic dimension, mm	54.7±8.9	58.0±10.3	53.3±7.9	<0.001
LV end-systolic dimension, mm	40.5±10.0	44.6±11.7	38.8.±8.6	<0.001
Shortening fraction, %	25.9±8.2	24.1±8.1	26.7±8.1	0.006
Ejection fraction, %	48.0±12.2	45.2±12.5	49.2±11.9	0.004

Data are presented as mean ± standard deviation or percentages
*- two-tailed unpaired Student t test and Chi-square test
LV - left ventricle

Table 2. Results of logistic regression analysis in predicting non-prescribing anticoagulation therapy in patients with atrial fibrillation discharged from the Service of Cardiology

Variables	Odds ratio (95% CI)	p
Age	0.916 (0.891-0.942)	<0.001
Left atrium	1.148 (1.100-1.198)	<0.001
Left ventricular ejection fraction	0.970 (0.948-0.993)	0.011
Arterial hypertension	0.866 (0.479-1.568)	0.636

The main finding of our study was the low use of OAC therapy (in less than 1/3 of patients discharged with primary or secondary diagnosis of AF). Aspirin was used in 2/3 of our patients. While there was a considerable number of patients (1/10 of studied patients) that did not receive any antithrombotic drug, and in almost all of these cases gastrointestinal diseases or recent bleedings were the main reasons. These results should be interpreted in demographic, economic and historical perspectives as well as by our clinical practices in our centre.

The age of our study population was lower than the age of patients in most of previous studies (6, 7, 10, 15-18). This can be explained by the low mean age of Kosovo population. In fact, Kosovo has the youngest population in Europe and among youngest in the world. In addition, in the recent history, in Kosovo war, health system was disrupted, destroyed and in many respect suffered form various difficulties in providing basic health care for its population. Therefore, probability was high for many patients to went unrecognized for many years and thus to be left untreated for many forms of diseases such are valvular diseases, arterial hypertension, ischemic heart disease and other diseases that are known to increase the incidence of AF. Thus, this recent historical fact may have contributed to development of preconditions for AF in younger age than usually.

We have found that the congestive heart failure was the most frequent comorbidity in patients with AF, followed by hypertensive heart disease, ischemic heart disease, valvular heart disease and diabetes. The high frequency of congestive heart failure in our patients is in line with the findings of the most previous investigators (15, 19, 20), except a study by Lip et al (18) that found lower rate of heart failure. However, the patient population that was selected for that study was from the general medicine ward, whereas our study was done in tertiary health care, where the most patients with signs of congestive heart failure are referred for the treatment in Kosovo. The arterial hypertension and ischemic heart disease are the most frequent comorbidities in our patients, as was the case in patients included in previous studies (15, 19-21).

The oral anticoagulation therapy in patients with atrial fibrillation

AF increases four to five fold the risk of stroke and thromboembolism (22, 23) and despite the evident benefit from results of randomized clinical trials (5, 24-29) and from actual clinical guidelines (30) today OAC therapy often is prescribed sub optimally in clinical practice, even in Western countries (13, 18, 31-39). However, recent reports have shown that in hospitalized (39) and ambulatory (40, 41) patients with AF, warfarin was prescribed in about half of the patients with AF. But in one study (41) more than 30% of patients received neither aspirin nor warfarin.

Compared with these studies, our patients received OAC therapy in lower percentage. This difference may be explained by several factors. Our study population had lower prevalence of coronary heart disease, diabetes, and arterial hypertension compared with similar previous studies. The low prevalence of these factors may have labeled many of our patients at low or medium risk for thromboembolic event and thus according to current guideline many of them were eligible to receive only aspirin. In addition, poor transportation means, poverty, especially among older population and reduced communication possibilities to follow-up the INR values may have inclined many physicians for the safety reasons to prescribe less often OAC. However, it remains through quality control measures to improve prescription of therapy for AF according to current guidelines and to investigate in-depth the patterns of prescription of OAC in different population subsets with AF.

Approximately one tenth of our patients did not receive any of antithrombotic therapy, which is comparable or better than in some of previously published studies. Nevertheless, the devastating effect of thromboembolic complication demands to correctly identify absolute contraindications for OAC especially for high-risk patients and thus decreases as much as possible the rate of patients that do not receive any form of antithrombotic drugs. Various other drugs prescribed in our study patients for comorbidities, such as beta-blockers, ACE inhibitors, digoxin, calcium antagonists and diuretics, demonstrates similar pattern of drugs prescribed with other comparable studies.

Multivariate analysis showed that the under-prescription of OAC therapy in patients with AF was independently associated with older age, non-enlarged left atrium, and good left ventricular ejection fraction. Indeed, all these factors may have contributed importantly in the assessment for prescribing OAC. This result may emphasize the specificity of local conditions and clinical judgment of physician. Namely, for older people in Kosovo with extremely low incomes it is particularly difficult to regularly visit doctor or perform required blood analysis. On the other hand, smaller left atrium dimensions and higher ejection fraction may have been presented more in low-or medium-risk patients and thus inclined physicians to prescribe less OAC.

Study limitations

Our study has several limitations. This is a retrospective study and thus has all statistical drawbacks inherent with this method. We could not collect the data about the post-discharge period in order to follow-up the adhesiveness of OAC therapy during this period. These dates would have provided additional information about the quality of the treatment of AF patients through the pattern of OAC use and follow-up consultations.

Conclusion

Patients discharged from our centre with atrial fibrillation were mainly with ischemic, hypertensive heart disease and congestive heart failure. Our study, as many previous studies, suggests underuse of anticoagulation therapy. The independent predictors of under prescription of anticoagulants in patients with atrial fibrillation were older age, non-enlarged left atrium, and good left ventricular ejection fraction. Medical treatment with other groups of drugs for atrial fibrillation and comorbidities seems to be according to current guidelines.

Conflict of interest: None declared

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