The Pharma Innovation Journal 2019; 8(7): 314-316

www.ThePharmaJournal.com

The Pharma Innovation

**ISSN (E): 2277- 7695**
**ISSN (P): 2349-8242**
**NAAS Rating: 5.03**
TPI 2019; 8(7): 314-316

www.thepharmajournal.com
Received: 13-05-2019
Accepted: 17-06-2019

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# Analysis of the hospitalization causes in patients with a permanent form of atrial fibrillation, arterial hypertension, stable coronary artery disease and heart failure

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**Abstract**
Aim of the study was to determine the reasons for hospital admission in patients with a permanent form of atrial fibrillation (AF). We have examined 42 patients with permanent form of AF, arterial hypertension (AH), stable coronary artery disease (SCAD) and heart failure (HF). Results: It was found that in the presence of the previous year admissions, the chances of admission frequencies increased in 82.8 times. Provided that the risk of patient's readmission in presenting of atrial fibrillation-related symptoms (EHRA score) ≥ 1 and New York heart association (NYHA) functional classification of breathlessness (NYHA FC) ≥ 2 increases by 15 times, of unstable angina - by 5,7 times. If the patients have high-sensitivity C-reactive protein (hs-CRP) more than 4.16 mg/L, the risk of readmission increases by 15.0 times. If the patients have interleukins (IL) IL-6 is more than 8.35 pg / mL risk increases by 7.5 times. If patients have IL-10 ≥ 35.3 pg / ml, the risk increases by 15.0 times.

**Keywords:** Atrial fibrillation, arterial hypertension, coronary artery disease, heart failure, causes of readmission

## 1. Introduction
Atrial fibrillation (AF) is new millennium epidemic that affects millions of lives, mostly affecting the middle-aged and elderly [1]. European countries have an aging population that is growing rapidly [2]. This arrhythmia affects over 886,000 new people each year in Europe. By 2030, the number people with AF is expected to increase up to 70 % [3].
Patients with AF have an increases risk for life-threatening complications and other diseases: heat failure (HF) increased by 5 times, stroke increased by 2, 4 times and cardiovascular mortality increased by 2 times [4]. AF increasingly places a critical financial burden on the healthcare system, costing €660 - € 3,286 million annually across European countries [5, 6]. Healthcare resource use in AF patients is high, with up to 40% of AF patients hospitalized each year primarily due to heart failure and arrhythmia recurrence [7, 8]. Hospitalization costs can be 2× higher for persistent AF than paroxysmal AF [8].
Costs for AF management can be divided into 2 groups: direct costs (hospitalization, outpatient and physician visits, prescriptions, laboratory testing, long-term care) and indirect costs (work productivity losses, support provided by caregivers).
Estimate suggested that over the next 12 years, there will be a 70 % increase in the number of people affected by AF, the number medical visits is expected to increase by: 3.5-4 million hospitalizations for AF, 100-120 million outpatient visits [9, 10].
Thus aim of the study was to determine the anamnestic, clinical and laboratory factors which influence the frequency of admission to the cardiological department.

## 2. Materials and Methods
We have examined 42 patients (average age was 68,0 ± 1,2 years) with permanent form of AF, arterial hypertension (AH), coronary artery disease (CAD) and HF who were admitted to the cardiology department. The median follow-up of AF in the examined group is 9,5 years [7,0-13,0]: 3 (7.1 %) patients have had the permanent form AF diagnosed up to 5 years, 18 (42.9 %) patients have suffered from AF up to 10 years, 12 (28.6 %) - up to 15 years, 9 (21.4 %) have had the permanent form of AF more than 15 years. AF was associated with the 1st stage of AH in 21 (50.0 %) cases, the 2nd stage-in 21 (50.0 %). The study excluded patients with the valvular heart disease, the 3d stage of hypertension (systolic BP ≥ 180 mmHg or diastolic BP ≥ 110 mmHg), acute coronary syndrome, myocardial infarction and acute cerebrovascular accident 6 month before our study, heart failure in NYHA functional class IV,

cardiomyopathy, glomerular filtration rate less than 60 ml/min/1.73 m², oncology disease and who taking alcohol and drugs.

Patients were examined by general clinical methods: review of main and additional complains, case history, life history, BMI calculation, measurement of blood pressure, determination of laboratory parameters (complete blood count, urinalysis, biochemiatry, glomerular filtration rate (GFR). Additionally, we determined levels of high-sensitivity C-reactive protein (hs-CRP), interleukin-1 (IL-1), interleukin-6 (IL-6) and interleukin-10 (IL-10) in serum by immunoassay test kits. 12-lead electrocardiography (ECG), 24-hour monitoring of electrocardiogram and blood pressure, transthoracic echocardiography (TTE) were performed for all patients.

For statistical analysis of the result we used biometric analysis methodology support by STATISTICA v.6.1 and MedCalc Statical Software v.11.5.0. software. Normal distribution was analyzed by the mean value (M) and mean error (m). Non-normal distribution was analyzed by median (Me) and quartiles (LQ-HQ). Comparison of relative values was performed according to the Pearson Chi-square ($\chi^2$) and Fisher exact two-tailed (FET) criteria and the average values were compared to Student T-test and Mann-Whitney U-test. The existence of interrelationships between the data under investigation were established on the basis of the correlation analysis with the calculation of the Spearman rank correlation coefficients (Rs). In order to detect the predictors of rhythm disturbances we used the method of logistic regression and calculated the Odds ratio (OR) and ROC-analysis (Receiver Operating Characteristic) with constructing characteristic curves and plotting the area under the curve (AUC), sensitivity and specificity with 95% confidence intervals (CI). The difference was considered significant at $p< 0, 05$ (5%).

## 3. Results and Discussion

In our study the group consisted of 42 patients, the ratio of men and women among patients with permanent form of AF, AH, CAD and HF was 1:1, smokers-15 (35, 7%). The ratios of the patients admitted to the cardiology department previous year can be presented as follows: only once-16/42 (38.1%), twice-5/42 (11.9%), thrice-1/42 (2.4%). The patients who hadn't been admitted earlier (till 2018) compiled 20/42 (47.6%). The main causes of admission to the cardiology department were hypertensive crisis or unstable angina-6/42 (14.3%), hear failure-14/42 (33.3%). AF was associated with hypertensive crisis and unstable angina in 10/42 (23.8%) cases, hypertensive crisis and HF–1/42 (2.3%), unstable angina and HF–3/42 (7.1%) cases. The simultaneous manifestation of the three emergences states (hypertensive crisis, unstable angina and HF) was founded in 3 patients (7.1%).

Among the 42 patients implicated in the study, 14 (33.3%) were readmitted in the cardiology hospital during the year (A group) (Figure 1). Among them were 6 men (49.9%) and 8 women (51.1%). The main reason for admission to the hospital in group A was progression of HF in 2 (14.3%) patients or the adaption of antiarrhythmic drug treatment in 12 (85.7%) patients. 2 (4.8%) patients out of 42 died due to a sudden cardiac death. 28/42 (66,7%) (group B) patients were not admitted during the year.

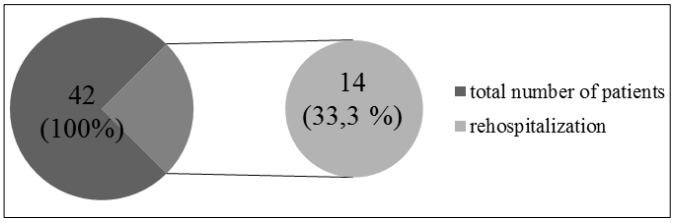


**Fig 1:** Number of patients undergone readmission

We compared the both research groups and identified the indicators that were significantly different and could affected readmission. Such indicators were the frequency of the hospitalization during the previous year, the number of hypertensive crises and unstable angina as the main causes of hospitalization, New York heart association (NYHA) functional classification of breathlessness in angina pectoris patients and atrial fibrillation-related symptoms (EHRA score) as well (Table. 1)

**Table 1:** Risk factor prevalence among patients of study groups

| Indicators | | A group (n=14) | B group (n=28) | Significant differences between groups |
|---|---|---|---|---|
| Admission frequency for the previous year: | 0 | 0 | 20 (71.4%) | $\chi^2$=20.68; $p$<0.001 |
| | 1 | 9 (64.3%) | 7 (25.0%) | |
| | 2 | 4 (28.6%) | 1 (3.6%) | |
| | 3 | 1 (7.1%) | 0 | |
| Hypertensive crisis | | 11 (78.6%) | 9 (32.1%) | p=0.008 * |
| Angina pectoris | | 11 (78.6%) | 11 (39.3%) | p=0.023 * |
| NYHA: | 2 | 1 (7.1%) | 15 (53.6%) | p=0.006 * |
| | 3 | 13 (92.9%) | 13 (46.4%) | |
| EHRA: | 1 points | 1 (7.1%) | 15 (53.6%) | $\chi^2$=8.75; p=0.013 |
| | 2 points | 10 (71.4%) | 9 (32.1%) | |
| | 3 points | 3 (21.4% | 4 (14.3%) | |

Explanatory note: * -according to FET
FET – Fisher exact two-tailed
NYHA- New York heart association (NYHA) functional classification of breathlessness
EHRA - atrial fibrillation-related symptoms

It was established a direct correlation between readmission and the case frequency of admission to the cardiology department during the year preceded the year of study (rs = +0.70; $p< 0.001$), an EHRA scale symptoms score (rs = +0.38; p = 0.012), NYHA FC (rs = +0.45; p = 0.003) and the presence of unstable angina (rs = +0.37; p = 0.016).

The presence of more active chronic systemic inflammation in patients with AF, AH, HF compared with relatively healthy persons has been established. The average levels of these parameters in patients with rhythm disturbances by type of

continuous AF were significantly higher in comparison with relatively healthy persons: levels hs-CRP (4.12 mg / L [3.51; 6.77] vs 2.98 mg / L [2.21; 3.43], $p< 0.001$), IL-1 (11.21 pg / mL [4.64; 17.24] vs 3.48 pg / mL [1.19; 6.06], $p< 0.001$), IL-6 (7.09 pg / mL [5.88; 13.77] vs. 5.03 pg / mL [3.16; 7.51], $p< 0.001$), IL-10 (33.04 pg / ml [15.91; 35.54] vs 11,14 pg / ml [1.71; 21.91], $p< 0.001$).

The analysis of hs-CRP and cytokine parameters in the study groups showed a direct relationship between the severity of chronic inflammation and patients' readmission frequency: hs-CRP (rs = +0.54; $p< 0.001$), IL-6 (rs = +0.31; p = 0.044), IL-10 (rs = +0.45; p=0.003).

Through the ROC analysis, optimal cut off points were determined for the studied parameters that identify the relative risk of readmission: cases of the admission in anamnesis area under the ROC curve (AUC = 0.892; 95% CI 0.757 – 0.966; sensitivity = 100%; specificity = 71.4%), the presence of unstable angina (AUC=0.696; 95% CI 0.535 – 0.828; sensitivity = 78.6%; specificity = 60.7%), EHRA ≥ 1 score (AUC=0.716; 95% CI 0.555 – 0.844; sensitivity = 92.9%; specificity = 53.6%), NYHA FC ≥ 2 (AUC=0.732; 95% CI 0.573-0.857; sensitivity = 92.9%; specificity = 53.6%), levels of hs-CRP ≥ 4.16 mg/L in serum concentration (AUC=0.832; 95% CI 0.684- 0.929; sensitivity = 85.7%; specificity = 71.4%), IL-6 ≥ 8.35 pg / ml in serum concentration (AUC=0.691; 95% CI 0.530 – 0.824; sensitivity = 71.4%; specificity = 75.0%), IL-10 ≥ 35.3 pg / ml in serum concentration (AUC=0.774; 95% CI 0.619 – 0.888; sensitivity = 64.3%; specificity = 89.3%).

According to the results of one-factor logit-regression analysis, it was found that in the presence of the previous year admissions, the chances of admission frequencies in patients with a permanent form of AF, HA and HF significantly increased by 82.8 times (OR = 82.8; 95% CI 3.4-2011.3), and the probability of such event achieved Pmax. = 63.9%. Provided that the patient has EHRA ≥ 1 and NYHA FC ≥ 2, the risk increases by 15 times (HR= 15.0; 95% CI 1.6-139.9); with unstable angina - by 5.7 times (OR = 5.7; 95% CI 1.2-26.2), reaching 50% probability. If the concentration of hs-CRP in serum is determined more than 4.16 mg / L, the risk of readmission increases by 15.0 times (OR = 15.0; 95% CI 2.6-87.2); the probability of the event is 60%. In IL-6 serum concentration composing more than 8.35 pg / mL the risk probability increases in 7.5 times (HR = 7.5; 95% CI 1.7-33.1), reaching 58.8%. In conditions of an increase of IL-10 ≥ 35.3 pg / ml, the risk increases by 15.0 times (OR = 15.0; 95% CI 2.8-79.9); the event probability reaches 75%.

## 4. Conclusion

The study found that patients with permanent form AF, AH, SCAD and HF admitting to the cardiology department repeatedly increase the social and economic burden.

It was established a direct correlation between readmission and the case frequency of readmission to the cardiology department during the year preceded the year of study, an EHRA scale symptoms score, NYHA FC and the presence of unstable angina.

Through the ROC analysis, optimal cut off points were determined for the studied parameters identifing the relative risk of readmission: number of the readmissions in anamnesis, the presence of unstable angina, EHRA ≥ 1 score, NYHA FC ≥ 2, levels of hs-CRP ≥ 4.16 mg / L, IL-6 ≥ 8.35 pg / ml and IL-10 ≥ 35.3 pg / ml in serum.

According to the results of one-factor logit-regression analysis, it was found that in the presence of the previous year admissions, the chances of admission frequencies in patients with a permanent form of AF, HA and HF significantly increased by 82.8 times, and the probability of such event achieved Pmax. = 63.9%. Provided that the patients have EHRA ≥ 1 and FC CH for NYHA ≥ 2, the risk increases by 15 times; with presence of unstable angina - by 5.7 times, reaching 50%. If the concentration of hs-CRP in serum is determined more than 4.16 mg / L, the risk of readmission increases by 15.0 times; the probability of the event is 60%. Provided that the level of IL-6 in serum is more than 8.35 pg / mL the risk probability of readmission increases by 7.5 times, reaching 58.8%. If IL-10 increases more than 35.3 pg / ml, the risk increases by 15.0 times; the probability of the event is 75%.

If IL-6 serum concentration composing more than 8.35 pg / mL the risk probability increases in 7.5 times (HR = 7.5; 95% CI 1.7-33.1), reaching 58.8%. In conditions of an increase of IL-10 ≥ 35.3 pg / ml, the risk increases by 15.0 times (OR = 15.0; 95% CI 2.8-79.9); the event probability reaches 75%.

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