THERAPEUTICAL CONSIDERATIONS IN ASSOCIATED ATRIAL FIBRILLATION AND HEART FAILURE

O. Mitu\textsuperscript{2}, F. Mitu\textsuperscript{2,4}, S. Constantin\textsuperscript{1}, Elena Cojocaru\textsuperscript{3}, Maria-Magdalena Leon\textsuperscript{2,4}

University of Medicine and Pharmacy “Grigore T. Popa” - Iasi
Faculty of Medicine
1. Ph.D. student
2. Discipline of Medical Semiology
3. Department of Pathology
4. Clinical Rehabilitation Hospital Iasi

THERAPEUTICAL CONSIDERATIONS IN ASSOCIATED ATRIAL FIBRILLATION AND HEART FAILURE (Abstract): Atrial fibrillation is a supraventricular tachyarrhythmia very common in medical practice, often associated with heart failure. Pathophysiological relationship between atrial fibrillation and heart failure is in the attention of numerous case studies, being incomplete elucidated. **Material and methods:** We made a retrospective study on patients with both diseases, hospitalized in Cardiovascular Rehabilitation Hospital, Iasi, during 01.01.2013 - 31.12.2013. The obtained data allowed the classification of patients according to gender distribution, age groups, area of origin, clinical aspects, and association with other diseases, instituted treatment and appreciation of CHADS2 score. Data interpretation was performed with appropriate statistical methods. **Results:** We found a higher frequency of the disease among male patients, male: female ratio being 2:1; the most of the patients lived in urban area. The pick of diseases incidence was in patients over 65 years with a total percentage of 70.84% of cases. We noted that the most common symptoms were exertional dyspnea (in all patients), palpitations, dizziness, headache, fatigue, asthenia, dyspnea at rest and pain / chest pressure. In our study, the majority of patients received the beta-blocker - digoxin combination (46 patients, 40 patients respectively). **Conclusions:** The co-existence of the two disorders could be explained by identifying common risk factors. Beta blockers should be the first therapeutic option in patients with chronic heart failure and atrial fibrillation because they have the effect of controlling heart rate and improve survival in patients with these disorders. Meanwhile, digoxin is a drug, only certain conditions of high accuracy monitoring; whose major clinical indications are heart failure and atrial rhythm disturbances. **Keywords:** ATRIAL FIBRILLATION, HEART FAILURE, DIGOXIN, BETA-BLOCKER

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia very common in medical practice, which consists of a disorganized cardiac electrical activity and progressive deterioration of atrial electromechanical function (1, 2, 3).

Heart failure (HF) is symptomatic in about 30% of patients with AF, and AF is also found in approximately 30-40% of patients with symptoms of HF (4, 5, 6). Pathophysiological relationship between AF and HF was in the spotlight of numer-
usaha studies, as it has not been fully elucidated. In patients with chronic HF and AF, beta blockers should be the first therapeutic option because their effect are related to heart rate control and the improvement of survival in patients suffering from these disorders (7, 8). Meanwhile, digoxin is an effective drug, safe only during an accurate monitoring, whose major clinical indications are HF and atrial rhythm disturbances (9, 10). In combination of the two, digoxin has electrophysiological effects which decrease the atrioventricular node level, making it potentially useful in controlling heart rate (11, 12, 13).

MATERIAL AND METHODS

We present a retrospective study on patients with associated pathology - AF an HF that aims to highlight clinical and laboratory aspects, the type of treatment instituted, the occurrence of side effects and the assessment of the CHADS2 score (Cardiac failure-Hypertension-Age- Diabetes-Stroke double), in order to evaluate the risk of stroke and thromboembolism in this class of patients. During 01.01.2013 - 31.12.2013, we recorded a number of 2279 hospitalizations at Rehabilitation Hospital - Cardiovascular Rehabilitation Clinic, Iasi. Within these, 72 were related to the above mentioned pathologies. Our data allowed the classification of patients according to gender distribution, age, area of origin, clinical aspects, association with other diseases, type of instituted treatment and appreciation of CHADS2 score. Data interpretation was performed with appropriate statistical methods.

RESULTS AND DISCUSSION

CHADS2 score. We conducted the evaluation of CHADS2 score in order to assess the risk of ischemic stroke events and thromboembolic phenomena, namely of the need for an anticoagulant therapy, considering the following criteria:
- 2 points for a history of stroke or ischemic transient pathology;
- 1 point for each of the following: age over 75 years, hypertension, diabetes, heart failure.

A score of 0 represents a low risk of stroke or thromboembolism, a score of 1-2 represents a moderate risk and a risk higher than 2 is translated into an increased risk of presenting these complications (fig.1).

![Fig. 1. Distribution of cases according to CHADS2 score;](image_url)
The distribution by area of origin. The classification of patients based on the area of origin was as follows: urban 54.2%, rural 45.8% (fig. 2).

Distribution of patients by gender. Analyzing the data from figure 3 we can see a higher frequency of the diseases among male patients, male: female ratio being 2:1. In terms of AF, the literature mentions that men are affected more often than women, and in terms of HF, gender ratio is approximately equal (fig. 3).

Distribution of cases by age groups. We calculated the mean age of incidence of the associated pathologies that was 69 years. We noted that our results were consistent with the literature data according to which the prevalence increases in patients older than 65 years (14, 15). Indeed, in our study the pick of incidence was in patients over 65 years, with a total percentage of 70.84% of cases, more precisely on the segment 65-75 years being registered the highest percentage of 37.50% of total cases. The lowest age recorded in this study was 53 years, and the highest was 83 years (fig. 4).

Family history (HCA). HCA study revealed a number of 27 patients, 12 females and 15 males, who had a first degree relative suffering from heart disease (fig. 5).

Risk Factors. Regarding the usual risk factors, we noted a number of 15 patients affected by chronic alcohol consumption, a number of 24 smokers, and 12 who were smokers and affected by chronic alcohol consumption.

Distribution of patients by symptoms. We noted that the most common symptoms are exertional dyspnea (in all patients),
palpitations, dizziness, headache, fatigue, asthenia, rest dyspnea and pain/chest pressure (fig. 6).

Classification of patients according to the type of AF is shown in fig. 7, and according to NYHA class in fig. 8. Associated pathology is also an important element in calculating the risk, in assessing the prognosis of these patients and in choosing an appropriate treatment (fig. 9).

Fig. 6. Dominant symptoms in patients

Fig. 7. The presence of different forms of AF
The instituted treatment. The classes of drugs that were used for the treatment were diuretics, converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, antiarrhythmics, anticoagulants and antiplatelet agents, nitrates, statins, fibrates and other cardiac preparations. Beta blocker class was represented by carvedilol (22 patients), bisoprolol (14 patients), nebivolol (6 patients), betaxolol (4 patients). Digoxin was administered intermittently 5 days per week, with two-day break, in maintenance doses ranging between 0.25 and 0.50 mg / day, *per os* in a single dose in most patients. Patients over 70 years, those with reduced muscle mass, those with variations in potassium, calcium or magnesium levels, patients with hypothyroidism required caution and special care regarding dose adjustment, more precisely a decrease to 0.125 mg / day to avoid toxic effects. In patients with HF or left ventricular dysfunction involving AF, digoxin can be used as first-line agent for heart rate control. We also know that treatment is made intermittent in patients with NYHA class I, first using other therapeutic classes such as diuretics, while in
those with NYHA class II or III we begin the initial treatment with digoxin, especially in cases with association of the two diseases (16).

We noted that 33 patients had an increased risk of ischemic stroke or thromboembolism, having a CHADS2 score higher than 2; most of them were male patients (18 versus 15). Most of the patients had a score of 2, thus having a moderate risk to develop these complications.

Guidelines ACC/AHA/ESC (American College of Cardiology/American Heart Association/European Society of Cardiology) recommends beta-blockers or non-dihydropyridine calcium blockers as first-line agents for frequency control in AF (17). These agents take action quickly and are effective in reducing heart rate at rest and during exercise in patients with AF. In addition, in AFFIRM study beta-blockers proved to be superior to calcium channel blockers (18, 19).

Studies have shown that beta-blocker carvedilol is effective in these patients, but sometimes we do not get a satisfactory response in heart rate control because of the fact that beta-blocker doses should be higher (20, 21). Digoxin is less effective in controlling ventricular rate compared with beta-blockers in patients with AF, both because it acts slowly, taking about 60 minutes, and because it has a weak action as a blocking agent of atrioventricular node. In addition, it is not effective in controlling heart rate during exercise and can be used only for sedentary patients (22, 23). Combining the two, beta blocker and digoxin, is therefore a solution to get the desired result both in sedentary patients and in those who exercise. In our study, patients received the beta-blocker - digoxin combination (46 patients, 40 patients respectively). We should mention that there were no adverse effects registered during hospitalization.

**CONCLUSIONS**

Patients who have AF and associated HF are a challenge for the treating physician due to the limitations imposed by their treatment, due to the intricate hemodynamic stress, due to the mechanism of the two diseases, and the unfavorable prognosis of this association. Our epidemiological data showed that patients with this pathology were male, from urban areas, older than 65 years. The major challenges in the treatment of these pathologies are getting sinus rhythm and heart rate control. Beta blockers should be the first therapeutic option in patients with chronic heart failure and atrial fibrillation because they have the effect of controlling heart rate and improve survival in patients with these disorders. Meanwhile, digoxin is a drug, very efficient in conditions of high accuracy monitoring whose major clinical indications are heart failure and atrial rhythm disturbances. In our study, the majority of patients received the beta-blocker - digoxin combination as a solution to get the desired results both in sedentary patients and in those who exercise.

**REFERENCES**