Assessment of adherence to antithrombotic therapy in patients with atrial fibrillation during the COVID-19 pandemic

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ABSTRACT
Introduction: Despite epidemiological evidence linking COVID-19 with cardiovascular diseases, little is known about whether and how coronavirus infection (CVI) influences atrial fibrillation (AF), the most prevalent arrhythmia in clinical practice.

Materials and Methods: We examined 621 patients with AF using the Morisky-Green scale (MMAS-4) criteria to assess adherence to antithrombotic therapy. They received inpatient treatment during the COVID-19 pandemic.

Results: A total of 118 patients out of 621 underwent CVI. Most patients had mild (33.9%) and moderate (49.15%) CVI. We managed to confirm the data of studies by foreign authors, according to which treatment with anticoagulants for at least 1 month reduces the severity of coronavirus infection, as well as protects against thrombotic complications.

Conclusion: It is necessary to improve the management of AF, especially if someone was infected with COVID-19. The susceptibility to AF is increased in the acute phase of COVID-19 infection. Personal electrocardiogram devices as well as remote monitoring (teleconsultations) could optimise the care of such patients.

KEYWORDS:
Atrial fibrillation, Morisky-Green scale, COVID-19, antithrombotic therapy

INTRODUCTION
COVID-19 has a diverse clinical picture. Uncontrolled diabetes, hypertension, obesity, old age, as well as male gender are considered to be risk factors, predisposing to severe COVID-19 and cardiovascular diseases as well.[1] Atrial fibrillation (AF) is one of the most important medical and socially significant problems, associated with increased mortality, stroke, left ventricular (LV) dysfunction and other thromboembolic complications. The mortality rate in patients with AF doubles regardless of the presence of other known risk factors. Only antithrombotic therapy is known to reduce AF-related mortality.[2-4]

AF is one of the most common cardiac arrhythmias and occurs in the general population in 1 to 2% of cases, and the frequency of AF increases with age. Multicentre studies have revealed that the prevalence of this pathology among people at the age below 60 years is ~ 0.5%; at the age of 60 years-5%, > 75 years - >10%. It has also been shown that AF is more common in men than in women. Paroxysms of AF account for >1/3 of hospital admissions due to cardiac arrhythmias, including in connection with an increase in the life expectancy of the population, there is an increase in the prevalence of AF by an average of 13% over the past 20 years.[5]

COVID-19 has become a rapidly growing epidemiological problem worldwide. The clinical manifestations of the disease are quite diverse and depend, mainly, on the patient's age and concomitant diseases. Patients with arrhythmias, coronary heart disease, heart failure, and CV risk factors (male gender, elderly age, diabetes mellitus [DM], arterial hypertension [AH], obesity and cerebrovascular diseases) have a higher risk of death in the course of this disease. The COVID-19 pandemic dictates the need to create new conditions for providing specialised care to patients with cardiac arrhythmias and conduction disorders.[6,7]

PURPOSE OF THE STUDY
To assess the adherence to antithrombotic therapy in patients with AF during the COVID-19 pandemic. Determine the relationship between oral anticoagulants and the severity of coronavirus infection in patients with fibrillation.

MATERIALS AND METHODS
The study included 621 patients with AF who received inpatient treatment. The mean age of the patients was 68.73 (range from 25 to 93 years). Among the patients, there were 259 men (41.71%), mean age 66.38 + 2.05 years, 362 women (58.29%), mean age 70.42 + 1.5 years. Adherence to antithrombotic therapy was assessed on the basis of the Morisky-Green scale (MMAS-4) criteria.8 The MMAS-4 questionnaire consists of four questions (Table I).

The MMAS-4 is often used in scientific research as the main tool and as a reference for comparison in the development of

Table I: Morisky-Green (self-reporting Medication-taking) scale

Questions	Risk level depending on patient response	
	Patient answered "Yes"	Risk level
1. Do you ever forget to take your medicine?	0 times	High
2. Are you careless at times about taking your medicine?		
3. When you feel better do you sometimes stop taking your medicine?	1 time	Medium
	2 times	
4. Sometimes if you feel worse when you take the medicine, do you stop taking it?	3 times	Low
	4 times	

Table II: Patients' adherence to medication (antiarrhythmic drugs and anticoagulants)

Commitment assessment	Number of patients (n/%)		
	Men	Women	Total
1 Not committed to therapy (1 to 2 points)	69 (11.11%)	75 (12.08%)	144 (23.19%)
2 Not committed enough (3 points)	58 (9.34%)	72 (11.59%)	130 (20.93%)
3 Committed to therapy (4 points)	132 (21.26%)	215 (34.62%)	347 (55.88%)
p value	≤ 0.05	≤ 0.05	≤ 0.05

Table III: Severity of coronavirus infection in patients with atrial fibrillation

№	Degree of severity	Total (%)
1	Asymptomatic form	4.2%
2	Mild	33.9%
3	Moderate	49.1%
4	Severe	12.8%
	p value	≤0.05

new, more detailed, and specialised scales. The MMAS-4 questionnaire was developed in 1985 and published in 1986. The MMAS-4 is a reliable and effective method of identifying patients at risk of non-compliance with the treatment regimen. And it can still be used in a doctor's daily medical practice to support treatment adherence in patients with atrial fibrillation.

The MMAS-4 questionnaire consists of four questions. To determine whether the patient skips taking medications, if he feels good or bad, whether he forgets to take medications, and whether he is attentive to the recommended time for taking medications. The MMAS-4 is used in the standard examination of patients with various chronic diseases to identify potentially non-adherent patients.[9,10] Each question was asked to choose a positive or negative answer (yes/no). Each negative answer was rated at 1 point. Patients who score 4 points, are considered to be committed to therapy, 1 to 2 points-not committed, and 3 points-insufficiently committed, with the risk of moving to the group of those who are not committed to treatment. There was a weak direct correlation between oral anticoagulant use and the severity of CVI. 118 out of 621 patients with AF had CVI. They were asymptomatic (4.2%), mild (33.9%) and moderate (49.1%) severity in severity. The share of patients with severe illnesses was 12.8%.

The statistical analysis was carried out according to the Mann-Whitney criteria.

The relevance of the problem of studying AF, is related to the fact that this violation of the heart rhythm is one of the causes of heart failure, increased mortality, stroke, and other thromboembolic complications, hospitalisations, deterioration of the quality of life and reduced exercise tolerance. Mortality in this group of patients is doubled regardless of the presence of other known risk factors. Since patients have been receiving antithrombotic therapy for a long time, we decided to evaluate their adherence to therapy and the severity of their COVID–19 history against the background of chronic therapeutic anticoagulation.[11,12]

RESULTS
We found that 23.19% of patients are not committed to therapy, 20.93% are insufficiently committed and only 55.88% of patients are committed to therapy.

The MMAS-4 rating scale for adherence to therapy, depending on gender, is presented in Table II. 144 patients did not adhere to therapy. Looking at the sex distribution, more women were non-adherent to therapy (12.08% against 11.11% of men). Insufficient adherence was found in 130 patients, where the proportion of women also prevailed over men (11.59% vs. 9.34%, respectively).

Consequently, in 55.88% of patient's adherence to therapy was established, and in women, the percentage of adherence also prevailed in comparison with males (34.62% vs. 21.26%).

The majority of patients taking long-term antithrombotic therapy had mild (33.9%) and moderate (49.15%) CVI. The proportion of patients with severity was only 12.71%. A weak

direct correlation was determined between the intake of oral anticoagulants and the severity of CVI (Table III). This confirms the data of studies by foreign authors [5,6,7], according to which treatment with anticoagulants for at least 1 month reduces mortality, the severity of the transferred coronavirus infection and can protect against thrombotic complications.

DISCUSSION

Patient adherence assessment is a large sample of patients, which allows us to evaluate the psychometric properties of the MMAS-4 questionnaire. Thus, this analysis can help us understand the MMAS-4 as a measure of medication adherence. The advantage of this questionnaire is that it is a brief measure of medication adherence. It is used in both research and medical practice more frequently.[16,17]

Studies have shown that 87.9% of patients required mandatory anticoagulant therapy, but only 69.2% of patients out of the total number of patients with AF take it. The indicators obtained in our work on the adherence of patients with AF to therapy, also confirm the data of foreign studies. They published the problem of insufficient patient adherence to treatment. This leads to a decrease in the therapeutic effect, significantly increases the development of complications of the underlying disease, and also leads to a decrease in the patient's quality of life and an increase in government costs for treatment.[18]

It is necessary to take measures to improve the management of this pathology: actively conduct sanitary-and educational work (thereby reducing risk factors for the development of the disease, such as alcohol consumption, control and treatment of major diseases); explain what complications can lead to insufficient adherence to the prescribed therapy.[19]

As in the acute phase of COVID-19 infection, the susceptibility to AF is increased and a worsening of existing AF likely, utilisation of personal electrocardiogram devices as well as remote monitoring (teleconsultations) could optimise care of patients with AF and those with a high risk for developing AF.[20]

LIMITATIONS

Although our study helped answer our research question, it has some limitations. The main limit is that the study is retrospective. The difficulty was that we were not allowed to determine adherence to antithrombotic therapy during the immediate hospital stay. In addition, we could not assess other properties of the measure, such as group validity and sensitivity to changes in medication adherence over time. This limitation is also evident in some studies.[13,14]

Another limitation was that all patients considered received therapy at the same hospital. Accordingly, the full range of medication adherence that is theoretically possible with this study method was not obtained. There is a difficulty regarding the extent to which the climate of different medical facilities affects adherence in patients with atrial fibrillation. Researchers in China, who used a similar methodology, came up against a similar limitation.[15]

We would also like to note that the translation of the article into English was performed not by a professional translator or a native speaker, but by a person with a high level of English.

The results we obtained are nevertheless valid for answering our research question since the data on adherence to therapy and the correlation between anticoagulant intake and disease severity were statistically significant.

We hope the limitations mentioned above will serve as recommendations for how the next study on a similar topic should be conducted.

CONCLUSION

Even a mild degree of infection caused by COVID-19 can cause thrombotic complications, especially in patients suffering from atrial fibrillation (AF). So, according to the results of our study, the Morisky-Green scale (MMAS-4) questionnaire can be recommended as a screening of adherence to therapy in patients with AF to identify potentially unaffected patients in everyday clinical practice due to its statistical significance. Thus, this method will reduce the risk of thrombotic complications in patients with COVID-19. We would like to note that the appointment of anticoagulants can reduce the severity of the coronavirus infection and protect these patients from thrombotic complications.

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