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Atrial fibrillation and CHA_2DS_2VASc score of 1 — is there a problem in clinical practice?

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Aim. To study the incidence of nonvalvular atrial fibrillation (AF) in patients with a CHA_2DS_2VASc score of 1 in actual clinical practice, to determine the major RF for stroke, additional factors for thromboembolic risk modification and the proportion of patients receiving oral anticoagulant therapy.
Material and methods. We performed a retrospective analysis of 6575 medical records of patients hospitalized for five years in a therapeutic inpatient unit. To determine the stroke risk, major and minor modifying factors were assessed.
Results. Of 1160 patients with nonvalvular AF, 93 (8,0%) patients had a CHA_2DS_2VASc score of 1: hypertension (87,1%), heart failure (4,3%), vascular diseases (4,3%), diabetes (2,15%) and age 65-74 years (2,2%); minor modifying factors were as follows: left atrial (LA) dilatation (81,7%), obesity (40,9%), persistent/permanent AF (37,6%), proteinuria (26,9%), chronic kidney disease (3,2%). A combination of minor risk factors was observed in 61,3%, the most common of which were obesity, LA dilatation, persistent/permanent AF. Anticoagulants were prescribed to 72% of patients with a CHA_2DS_2VASc score of 1.
Conclusion. In actual clinical practice, patients with nonvalvular AF with a CHA_2DS_2VASc score of 1 are often found. The most common risk factors for stroke in these patients are hypertension, persistent or permanent AF, LA dilatation, and obesity. The use of anticoagulant therapy in these patients does not contradict current guidelines. However, further prospective follow-up is necessary to determine the effectiveness and safety of this therapy.

Key words: atrial fibrillation, hypertension, CHA_2DS_2VASc score of 1, anticoagulants.

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Atrial fibrillation (AF) is the most common persistent arrhythmia. The AF prevalence in adult population of Western Europe is 3% and it has increased in recent decades [1, 2]. AF significantly increases the thrombotic risk and is the cause of 26% of ischemic strokes, which often leads to disability or death [1].

The anticoagulant therapy is a greatest benefit for patients with AF, which prevents ischemic strokes and systemic embolism [3]. Currently, nonvalvular AF prevails, which is not associated with severe or moderate mitral stenosis and mechanical valve prostheses. To determine the stroke risk in patients with nonvalvular AF, the European Society of Cardiology (ESC) recommends using the CHA_2DS_2VASc score, which considers the main risk factors (RF) for stroke (congestive heart failure, hypertension (HTN), age 65-74 years, age ⩾75 years, diabetes, prior stroke or transient ischemic attack, or systemic embolism, vascular disease (prior myocardial infarction, peripheral artery disease, aortic plaque) and female sex [3, 4]). However, there are other stroke factors that are not included in this score: obesity, cardiac remodeling, chronic kidney disease, obstructive sleep apnea, and others.

Current clinical guidelines recommend use of anticoagulants to prevent thrombotic events, preferably direct oral anticoagulants (DOACs) for patients with nonvalvular AF and CHA_2DS_2VASc score of ⩾2 in men and ⩾3 points in women, regardless of the bleeding risk [3, 4]. If a patient with nonvalvular AF has CHA_2DS_2VASc score of 0, then anticoagulants are not indicated, since the stroke risk is low (IIIB) [3]. Patients with nonvalvular AF and CHA_2DS_2VASc score of 1 (without female sex) have a moderate risk of stroke, and ESC guidelines recommends to consider the anticoagulants for these patients (IIaB) [3]. At the same time, the stroke risk in these patients is relatively low, and with the anticoagulant therapy, risk of bleeding can be higher. Currently, there are no randomized clinical trials in patients with CHA_2DS_2VASc score of 1 (in women — score of 2), and the matter of advisability of using anticoagulants in these patients remains open.

In 2019, a document was published containing the opinion of ESC Working Group on Cardiovascular Pharmacotherapy and European Society of Cardiology Council on Stroke [5]. This document contains the decision-making algorithm for the appointment of anticoagulants in patients with CHA_2DS_2VASc score of 1 (without female sex), based on a comparison of the risk for stroke and bleeding. In patients with a HAS-BLED score ⩾2, i.e., if the risk of bleeding prevails over the risk of stroke, the anticoagulants are not indicated. There is a need to correct potentially modifiable RF for bleeding (HTN, use of nonsteroidal anti-inflammatory drugs, alcohol abuse), and then re-evaluate the risk of bleeding and compare with the risk of stroke [5] (Figure 1).

If a patient with CHA_2DS_2VASc score of 1 has a low risk of bleeding (<2 points), then experts recommends an individual risk stratification considering the main and additional risk factors for stroke. In patients with AF, CHA_2DS_2VASc score of 1 and a low risk of bleeding, it is proposed to single out the major factors, which favor oral anticoagulation and additional factors requiring thromboembolic risk modification [5] (Table 1).

At the same time, the following questions remain unclear: (1) how often AF patients with CHA_2DS_2VASc score of 1 are found, (2) what is the incidence of major stroke RF, additional factors for thromboembolic risk modification, and (3) how often these patients use anticoagulants in actual clinical practice.

The aim of this study was to study the incidence of nonvalvular AF in patients with a CHA_2DS_2VASc score of 1 in actual clinical practice, to determine the major RF for stroke, additional factors for thromboembolic risk modification and the proportion of patients receiving oral anticoagulant therapy.

Material and methods

We studied medical records of 6575 patients hospitalized in a period from 2014 to 2018 in the therapeutic and cardiology departments of the university hospital. All data obtained as a result of a retrospective analysis of medical records was entered into a single original MS Excel database developed for this study. From all records of patients with AF, men with CHA_2DS_2VASc score of 1 and women with CHA_2DS_2VASc score of 2 and nonvalvular AF were selected. The prevalence analysis results are presented as n/tot.n (%), where n is the number of patients diagnosed with certain sign, tot.n is the total number of patients who were evaluated for this sign, and % is the percentage of the total number examined. Normally distributed values are presented as mean and standard deviation (M±SD). Statistical analysis was performed using software package StatPlus: mac Pro (AnalystSoft Inc.), version 7.0. The study was supported by a grant from the Russian Science Foundation (№ 17-75-30052).

Results

In the period from 2014 to 2018, 1203 patients with AF were hospitalized, which amounted to 18,3% of the total number of patients (men — 540/1203 (44,9%); women — 663/1203 (55,1%)). The mean age of patients with AF was 69,9±10,6 years. Most patients had a paroxysmal and permanent AF (538 (44,7%) and 456 (37,9%) patients, respectively). Per-

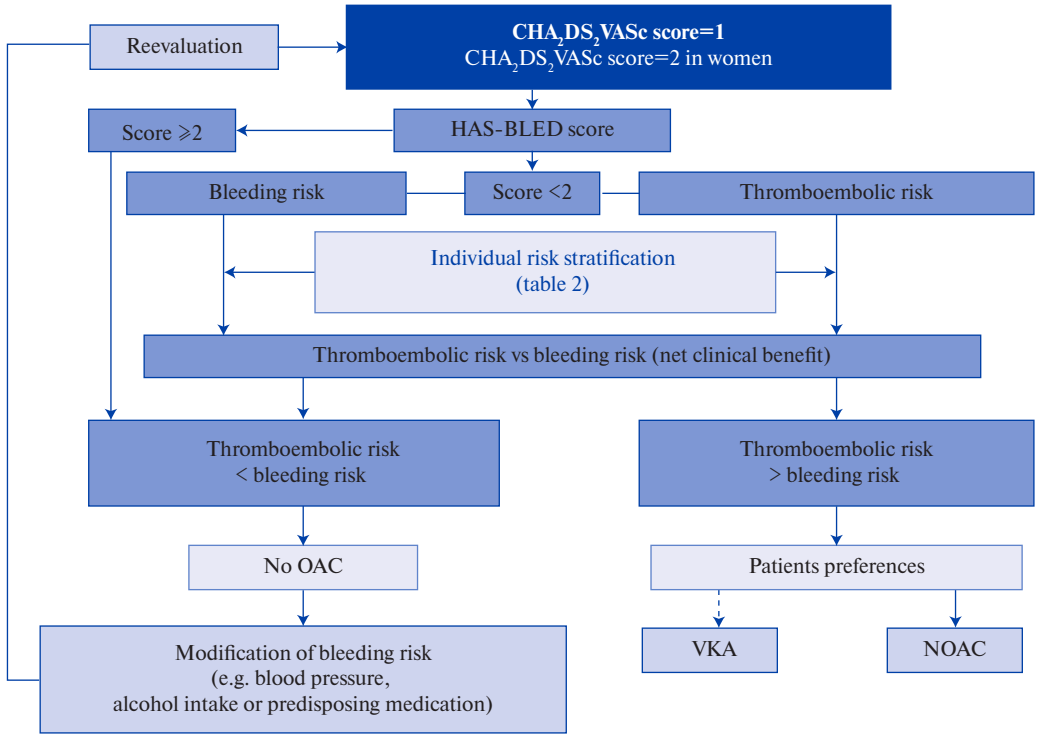

Figure 1. Decision tree for oral anticoagulation in patients with AF and CHA_2DS_2-VASc score of 1 [5].

sistent and long-standing persistent AF were found less frequently (201 (16,7%) and 8 (0,7%) patients, respectively). Valvular AF (mechanical valve prosthesis, moderate and severe mitral stenosis) were found in 43 (3,6%) patients, nonvalvular AF — in 1160 (96,4%) patients. The mean CHA_2DS_2VASc score was 4,3±1,9, HAS-BLED — 1,5±0,9. Among patients with nonvalvular AF, there were 93 (8,0%) men with CHA_2DS_2VASc score of 1 and women with CHA_2DS_2VASc score of 2. The most common single RF was HTN — 81 (87,1%) patients, less common — vascular diseases and diabetes (Table 2).

When analyzing the patients with AF and HTN as the single RF for stroke, it was found that the majority of them (n=70; 86,4%) at the hospitalization had controlled HTN and received antihypertensive therapy: beta-blockers — 49 (52,7%), angiotensin converting enzyme inhibitors — 38 (30,1%) or angiotensin II receptor blockers — 28 (30,1%).

An analysis of additional RF for thromboembolic events in patients with AF and CHA_2DS_2VASc score of 1 [5] revealed the following most common factors: left atrial (LA) dilatation — 76 (81,7%), which was more common in men; obesity — 38 (40,9%); persistent/permanent AF — 35 (37,6%). The combination of several additional RF for thromboembolism in AF patients was recorded in 57 patients (61,3%). In women, the most common were the combination of obesity and LA dilatation (n=14; 24,6%), while in men — permanent/persistent AF and LA dilatation (Table 3).

Table 1
Individual risk stratification factors in patients with AF and CHA_2DS_2-VASc score of 1 (without female sex) [5]

Favors oral anticoagulation (in case of low bleeding risk)
Age (>65 years)
Type II diabetes mellitus
Atrial fibrillation (not atrial flutter)
Persistent/permanent atrial fibrillation
Additional factors for thromboembolic risk modification
Obesity (body mass index ⩾30 kg/m^2)
Proteinuria (>150 mg/24 h or equivalent)
eGFR (<45 ml/h)
NT-proBNP (>1400 ng/l)
Positive cardiac troponin T and I
Enlarged LA volume (⩾73 ml) or diameter (⩾4,7 cm)
LAA emptying velocity (<20 cm/s)
ABC (age/biomarker/clinical history) score

Abbreviations: BMI — body mass index, LA — left atrium, eGFR — estimated glomerular filtration rate, AF — atrial fibrillation.

Despite the minimum CHA_2DS_2VASc score, 48 (51,6%) patients received anticoagulant therapy before hospitalization and 67 (72,0%) patients were

Table 2

RF for stroke in patients with nonvalvular AF and CHA_2DS_2-VASc score of 1 in men and of 2 in women

Parameter	Men 47/526 (8,9%)	Women 46/634 (7,3%)	Overall 93/1160 (8,0%)
Hypertension	41/47 (87,2%)	40/46 (87,0%)	81/93 (87,1%)
Age 65-74 years	1/47 (2,1%)	1/46 (2,2%)	2/93 (2,15%)
Diabetes	0/47 (0%)	2/46 (4,3%)	2/93 (2,15%)
CHF (congestive or LVEF ⩽40%)	3/47 (6,4%)	1/46 (2,2%)	4/93 (4,3%)
Vascular diseases (prior myocardial infarction, peripheral artery disease, aortic plaque)	2/47 (4,3%)	2/46 (4,3%)	4/93 (4,3%)

Abbreviations: CHF — chronic heart failure, LVEF — left ventricular ejection fraction, MI — myocardial infarction.

Table 3

Additional factors for thromboembolic risk modification in patients with nonvalvular AF and CHA_2DS_2-VASc score of 1 in men and of 2 in women

Parameter	Men	Women	Overall
LA dilatation (⩾73 ml or ⩾4,7 cm)	46/47 (97,9%)	30/46 (65,2%)	76/93 (81,7%)
Obesity (BMI ⩾30 kg/m^2)	20/47 (42,6%)	18/46 (39,1%)	38/93 (40,9%)
Persistent/permanent AF	23/47 (48,9%)	12/46 (26,1%)	35/93 (37,6%)
Proteinuria (>150 mg/day)	12/47 (25,5%)	13/46 (28,3%)	25/93 (26,9%)
CKD (GFR <45 ml/min/1,73 m^2)	1/47 (2,1%)	2/46 (4,3%)	3/93 (3,2%)
Combination of additional factors	32/93 (68,1%)	25/93 (54,3%)	57/93 (61,3%)
Obesity+LA dilatation	6/32 (18,8%)	8/25 (32,0%)	14/57 (24,6%)
Persistent/permanent AF+LA dilatation	7/32 (21,9%)	2/25 (8,0%)	9/57 (15,8%)
Persistent/permanent AF+obesity	0/32 (0,0%)	1/25 (4,0%)	1/57 (1,8%)
Obesity+proteinuria	0/32 (0,0%)	1/25 (4,0%)	1/57 (1,8%)
Proteinuria+LA dilatation	0/32 (0,0%)	4/25 (16,0%)	4/57 (7,0%)
Persistent/permanent AF+LA dilatation+proteinuria	4/32 (12,5%)	1/25 (4,0%)	5/57 (8,8%)
Obesity+proteinuria+LA dilatation	5/32 (15,6%)	2/25 (8,0%)	7/57 (12,3%)
Persistent/permanent AF+obesity+LA dilatation	6/32 (18,8%)	2/25 (8,0%)	8/57 (14,0%)
Obesity+LA dilatation+CKD	1/32 (3,2%)	1/25 (4,0%)	2/57 (3,5%)
Persistent/permanent AF+obesity+LA dilatation+proteinuria	3/32 (9,4%)	2/25 (8,0%)	5/57 (8,8%)
Persistent/permanent AF+LA dilatation+proteinuria	0/32 (0,0%)	1/25 (4,0%)	1/57 (1,8%)

Abbreviations: CKD — chronic kidney disease, AF — atrial fibrillation, LA — left atrium, BMI — body mass index.

recommended anticoagulant therapy after hospitalization. Two (2,2%) patients, in addition to AF, had other indications for anticoagulant therapy (pulmonary embolism, intracardiac thrombus). Among the RF for thromboembolic events in patients receiving anticoagulants, HTN was more common, and among the additional RF — LA dilatation (Table 4).

Bleeding risk analysis revealed 2 men with HAS-BLED score of 2 and 5 women with HAS-BLED score ⩾2; all other patients had score <2. The drugs prescribed for patients with AF and CHA_2DS_2VASc score of 1 in men and of 2 in women were as follows: warfarin — 18/67 (26,9%), apixaban — 40/67 (59,7%), dabigatran — 6/67 (8,9%) and rivaroxaban — 3/67 (4,5%).

Discussion

ESC guidelines (2016) recommends consideration of anticoagulants in patients with nonvalvular AF and CHA_2DS_2VASc score of 1 in men and of 2 in women (IIaB) [3]. It has been established that even a single RF for stroke in AF patients increases the thromboembolic risk. In a study by Lip GYH, et al. (2015), it was found that CHA_2DS_2VASc score of 1 (without female sex) increases the stroke risk by 3,01 times and death by 3,12 times [6]. Anticoagulant therapy reduces the incidence of stroke and systemic emboli in patients with nonvalvular AF and CHA_2DS_2VASc score of 1 [7].

Current cohort study was conducted for the first time in the Russian population and it was found that

Table 4

Risk factors for thromboembolic events in patients with AF and CHA_2DS_2-VASc score of 1 in men and of 2 in women who received anticoagulant therapy

Parameter	Men	Women	Overall
Number of patients receiving anticoagulants	30/47 (63,8%)	37/46 (80,4%)	67/93 (72,0%)
Hypertension	25/30 (83,3%)	33/37 (89,2%)	58/67 (86,6%)
CHF (congestive or LVEF ⩽40%)	3/30 (10,0%)	1/37 (2,7%)	4/67 (6,0%)
Vascular diseases (prior myocardial infarction, peripheral artery disease, aortic plaque)	2/30 (6,7%)	2/37 (5,4%)	4/67 (6,0%)
Age 65-74 years	0/30 (0,0%)	1/37 (2,7%)	1/67 (1,5%)
LA dilatation (⩾73 ml or 47 mm)	27/30 (90,0%)	24/37 (64,9%)	51/67 (76,1%)
Persistent/permanent AF	19/30 (63,3%)	11/37 (29,7%)	30/67 (44,8%)
Obesity (BMI ⩾30 kg/m^2)	14/30 (46,7%)	15/37 (40,5%)	29/67 (43,3%)
Proteinuria (>150 mg/day)	10/30 (33,3%)	10/37 (27,0%)	20/67 (29,9%)

Abbreviations: CHF — chronic heart failure, LVEF — left ventricular ejection fraction, MI — myocardial infarction, LA — left atrium, BMI — body mass index.

out of 1160 patients hospitalized with nonvalvular AF, there were 8% of patients with CHA_2DS_2VASc score of 1. The proportion of such patients among outpatient population with AF is 15% [8]. Such a difference is due to the fact that hospitalized patients with AF are often older than outpatients and often have comorbidities.

We found that the most common single RF for stroke was HTN (87,1%), other RF were much less common. According to Chao T-F, et al. (2015), among population with CHA_2DS_2VASc score of 1, patients were more likely to have a single RF for stroke — age 65-74 years or HTN [9]. ESC/ESH Guidelines for the management of HTN (2018) note that stroke prevention with oral anticoagulants should be considered in AF patients with hypertension, even when HTN is the single additional RF (IIa, B) [10]. In a study by Chao T-F, et al. (2015), it was shown that in patients with AF and HTN as a single RF, the frequency of thromboembolic events per 100 patient years is 2,2 in men and 1,9 in women [9]. HTN is of particular importance as a stroke RF in patients older than 50 years [11]. A meta-analysis of 9 clinical trials conducted in 2020 showed that HTN and inadequate control of office blood pressure are predictors of stroke and systemic embolism [12]. Therefore, when considering anticoagulants to AF patients, non-taking into account this important predictor of stroke, in our opinion, is not justified.

In a study conducted in Taiwan, it was found that age 65-74 years or type 2 diabetes are the most significant RF of thromboembolic events; the incidence of strokes or systemic embolism in such patients is on average 3 per 100 patient years [9]. However, in our study, there were little number of patients with type 2 diabetes or 65-74 years of age without additional RF for stroke (without comorbidities). This is probably due to the special characteristics of in-patient population, and the race has lower value.

Currently, there are no data from randomized clinical trials indicating the need for anticoagulant therapy in AF patients and CHA_2DS_2VASc score of 1. At the same time, patients with CHA_2DS_2VASc score of 1 were included in the RE-LY and ARISTOTLE studies [13, 14].

When considering the anticoagulants to AF patients with CHA_2DS_2VASc score of 1, the risks of thrombosis and bleeding should be evaluated [5]. The bleeding frequency in patients with HAS-BLED score of 2 (1,88-3,20% per year) exceeds the thrombotic risk in patients with AF and CHA_2DS_2VASc score of 1 (0,6%-1,3% per year) [5]. According to study by Sulzgruber P, et al. (2019), anticoagulants should not be used in patients with CHA_2DS_2VASc score of 1 and HAS-BLED score ⩾2 [5]. With a low bleeding risk (HAS-BLED score <2) and CHA_2DS_2VASc score of 1, additional RF may affect the considering anticoagulants (Table 1).

We detected LA dilatation in 81,7% of patients with AF and CHA_2DS_2VASc score of 1. This fact should be taken into account, since LA remodeling is an additional factor for thromboembolic risk modification and is easily diagnosed with ultrasound. It is known that LA dilation is a result of not only HTN, but also obesity, and in our study, obesity was detected in 40,9% of patients. LA dilatation favors a persistent and permanent AF, which we found in 37,6% of patients. In 61,3% of patients, a combination of several additional thromboembolic risk modification factors was observed. The most common were combinations of LA dilatation with obesity or with a permanent/persistent AF.

In our study, an analysis of LA appendage peak flow velocity was not performed. However, it was previously established that a decrease of this parameter (<20 cm/sec) is a risk of stroke [15]. Slowing blood flow contributes to blood clot formation in LA appendage, and such patients have a very high risk of cerebral embolism (up to 16% per year) [16]. At the same time, 50% of patients with a thrombus in LA or its appendage have a low CHA_2DS_2VASc score and the risk of cardioembolic events in such patients can be underestimated [16].

According to the meta-analysis of 8 largest studies, CHA_2DS_2VASc score of 1 significantly increases the risk of thromboembolic events, and the age of patients (65-74 years) is of the greatest importance, therefore, these patients should receive anticoagulants [17]. Moreover, the authors believe that even in patients with CHA_2DS_2VASc score of 1 and comorbidity as the single additional RF (HTN, type 2 diabetes, heart failure and atherosclerosis-related diseases), anticoagulants, especially DOACs, are indicated [17].

Our study revealed that 72,0% of patients with CHA_2DS_2VASc score of 1 after hospitalization were prescribed anticoagulants, and most did not have other indications for anticoagulant therapy (pulmonary embolism, deep vein thrombosis, intracardiac trombus). The most common single RF for stroke in these patients was HTN (86,6%). In addition, many of these patients had additional factors for thromboembolic risk modification (LA dilatation, permanent and persistent AF, obesity, and kidney disease).

When choosing management strategy of patients with CHA_2DS_2VASc score of 1, additional RFs in favor of anticoagulants and low risk of bleeding, the matter should be discussed with the patient and jointly resolved [5]. If it is decided not to use anticoagulants, then in such patients it is necessary to monitor and annually calculate CHA_2DS_2VASc score, since the age of patients increases and comorbidities may develop, that is, additional RFs for stroke [11]. If there is CHA_2DS_2VASc score $\geqslant 2$ (without female sex), anticoagulants should be prescribed unless contraindicated, regardless of the HAS-BLED score [3].

Study limitations. We conducted a study of patients hospitalized with nonvalvular AF, which does not fully reflect the incidence of patients with CHA_2DS_2VASc score of 1 in the population; most subjects were not examined for such additional factors of thromboembolic risk modification as the levels of NT-proBNP, troponin T or I, and LA appendage peak flow velocity.

Conclusion

1. Among hospitalized patients, 8,0% had nonvalvular AF and CHA_2DS_2VASc score of 1.
2. The most common single RF for stroke in patients with nonvalvular AF and CHA_2DS_2VASc score of 1 was HTN (87,1%).
3. LA dilatation, obesity, permanent or persistent AF are the most common factors for thromboembolic risk modification; 61,3% of patients have a combination of several additional factors.
4. Anticoagulants were prescribed for 72,0% of patients with CHA_2DS_2VASc score of 1; most of these patients had HTN.

Thus, the problem of detecting and treating patients with nonvalvular AF and CHA_2DS_2VASc score of 1 is relevant in actual clinical practice; such patients are not uncommon, and the most frequent RFs for stroke in these patients are HTN, persistent or permanent AF, LA dilatation, and obesity. Most patients with CHA_2DS_2VASc score of 1 have indications for the oral anticoagulant therapy, and further prospective studies are necessary to determine the effectiveness and safety of this strategy.

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