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Assessment of the mean time in the therapeutic INR range and the SAME-TT_2R_2 score in patients with atrial fibrillation and cognitive impairment

Paulina Gorzelak-Pabiś, Sandra Zyzak, Łukasz Krewko, Marlena Broncel

Department of Internal Diseases and Clinical Pharmacology, Medical University of Lodz, Łódź, Poland

KEY WORDS

atrial fibrillation, cognitive impairment, SAME-TT_2R_2, international normalized ratio, vitamin K antagonists

ABSTRACT

INTRODUCTION Most patients with atrial fibrillation (AF) are elderly and may have an increased risk of cognitive disorders. Low mean values of the therapeutic international normalized ratio (INR) range (TTR) (≤60%) are associated with increased risk of stroke, vascular events, and bleeding complications.

OBJECTIVES The aim of the study was to evaluate the efficacy of long-term anticoagulant therapy in patients treated with vitamin K antagonists (VKAs), depending on their cognitive functions. In addition, we used the SAMe-TT_2R_2 risk score to predict the risk of ineffective anticoagulation.

PATIENTS AND METHODS The analysis comprised 154 patients (68 men and 86 women; mean age, 76 ±10 years) with AF and indications for long-term therapy with VKA (CHA_2DS_2-VASc score ≥1, HAS-BLED score <3). Cognitive functions were evaluated using the Mini-Mental State Examination (MMSE) score. The efficacy of VKA therapy was determined by the TTR values from the preceding 6 months of treatment. We used the SAMe-TT_2R_2 score to identify patients who were likely to have poor INR control.

RESULTS Depending on the number of MMSE points, patients treated with VKAs were divided into 2 groups: patients with normal cognitive functions (MMSE score ≥27; n = 62) and those with cognitive impairment (MMSE score <27; n = 42). Despite the fact that all patients had indications for anticoagulant therapy, 50 patients (32%) received no VKAs on admission. The mean TTR value exceeded 60% in 61% of patients with an MMSE score of 27 points or higher, whereas mean TTR value was 28% in patients with an MMSE score of less than 27 (P <0.0001). Patients with a SAMe-TT_2R_2 score of 0 to 1 had higher TTR values than those with a SAMe-TT_2R_2 score of 2 or higher (r = –0.24; P <0.05). The cognitive status was significantly more impaired in patients with persistent and permanent AF compared with patients with paroxysmal AF (MMSE score, 25.8 ±3.7 vs 28.6 ±2; P <0.0001).

CONCLUSIONS Cognitive disorders in patients with AF significantly reduce the efficacy of VKA therapy. The decision to administer VKA treatment should be based not only on the CHA_2DS_2-VASc and HAS-BLED scores, but also on the SAMe-TT_2R_2 score and the evaluation of the patient's cognitive functions.

Correspondence to:
Paulina Gorzelak-Pabiś, MD, Klinika Chorób Wewnętrznych i Farmakologii Klinicznej, Uniwersytet Medyczny w Łodzi, ul. Kniaziewicza 1/5, 91-347 Łódź, Poland, phone: +48 42 251 62 43
e-mail: pau.gorzelak@gmail.com
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INTRODUCTION Atrial fibrillation (AF) is the most common supraventricular arrhythmia, which is associated with a 5-fold higher risk of cerebral stroke and a 3-fold higher risk of congestive heart failure. Nearly 20% of all strokes are caused by cardiogenic embolism associated with AF, and the outcome in these cases is less favorable than that in strokes with different etiology.[1] The incidence of cognitive function disorders and dementia increases with age, and this is similar to a trend observed in the occurrence of AF, where the mean age of patients is from 75 to 85 years and continues to rise.[2] An almost 5-year follow-up of 2837 patients with newly diagnosed AF and no history of stroke showed that dementia developed in 2.7% of patients within a year and in 10.5% of patients within 5 years.[3] Cognitive disorders in AF patients should also be analyzed with regard

to silent cerebral ischemia in the mechanism of systemic microembolism, which, as reported by Georgiadis et al,[4] occurred in 21% of patients with AF and only in 5% of healthy patients.[5,6]

The CHA_2DS_2-VASc score, which includes the most common risk factors for cerebral stroke and embolism observed in everyday clinical practice (congestive heart failure/left ventricular dysfunction, hypertension, age from 65 to <75 years, age ≥75 years, diabetes, stroke, and female sex), was developed to assess the risk of thromboembolic complications in patients with AF.[7,8] The evaluation of the risk of hemorrhagic complications with the use of the HAS-BLED score (hypertension, abnormal renal and/or liver function, previous stroke, bleeding history, labile international normalized ratios, older age, drugs/alcohol concomitantly) is also recommended in all patients with AF. Caution should be exercised in patients with a score of 3 or higher, and potentially reversible risk factors for bleeding should be reduced and corrected in these patients.[9] Oral anticoagulants should be administered to AF patients with a medium or high risk of stroke and thromboembolic complications (CHA_2DS_2-VASc ≥2), and the most common oral anticoagulants are vitamin K antagonists (VKAs), such as acenocoumarol or warfarin.[10]

Stroke prevention associated with VKA therapy is effective only if the individual average time of the international normalized ratio in the therapeutic range (TTR) is high and exceeds 60%.[11] However, the therapy is difficult because it requires regular monitoring of antithrombotic effect, a narrow therapeutic window, and numerous drug interactions with food and other medications. Moreover, the fact that the incidence of cognitive functions increases among elderly people makes the therapy even more challenging. Therefore, it seems particularly important to choose an adequate therapy for patients who require antithrombotic treatment.[11,12]

A new 8-point score, SAMe-TT_2R_2, was introduced in 2013 to identify patients with a high risk of inadequate response to VKA therapy. Patients with a score of 0 to 1 should receive VKA treatment, while a score of 2 or higher suggests the use of non-VKA oral anticoagulants as an alternative, considering the high probability of inadequate response to VKAs.[13]

The aim of the study was to assess the efficacy of antithrombotic treatment in patients with AF and dementia using the mean time in the therapeutic INR range (TTR) during 6 consecutive months of therapy. Moreover, the risk of VKA treatment ineffectiveness was evaluated in all patients according to the new SAMe-TT_2R_2 score.

PATIENTS AND METHODS

The study comprised 154 patients with AF, with indications for oral antithrombotic therapy (CHA_2DS_2-VASc ≥1, HAS-BLED <3). All patients came from Łódź, a large city in central Poland, who were treated in the Department of Internal Diseases and Clinical Pharmacology, Medical University of Lodz, and the Department of Internal Diseases, Władysław Biegański Hospital in Łódź, in the years from 2013 to 2015. In patients on chronic VKA treatment (n = 104), the TTR from the previous 6 months was calculated. Cognitive skills were assessed with the Polish version of the corrected Mini-Mental State Examination (MMSE). The probability of stabilized anticoagulation effect during VKA treatment was assessed using the SAMe-TT_2R_2 score.

Assessment of thromboembolic complications: CHA_2DS_2-VASc score Indications for VKA treatment were determined on the basis of the 6-point CHA_2DS_2-VASc score. A score of 1 or higher indicated the need for treatment with oral antithrombotic medications.

Assessment of the bleeding risk: the HAS-BLED score The HAS-BLED score was calculated in all patients included in the study. A score of 3 points or higher indicated a significantly higher risk of bleeding.

Mini Mental State Examination It is one of the most commonly used screening tests for evaluating mental capacity. The time of examination does not exceed 10 minutes. The maximum score is 30 points: 27–30 points indicate normal cognition; 24–26 points, mild cognitive impairment; <24 points, dementia (20–23 points, mild dementia; 10–19 points, moderate dementia; and 0–9 points, severe dementia). In order to objectify the results, MMSE scores were corrected using Mungas adjustments (ie, correction for age and educational level).[14]

Efficacy of vitamin-K antagonist treatment: time in the therapeutic INR range The effectiveness of VKA therapy was determined with the use of TTR, which is the percent of INR results within the therapeutic range (for patients with AF, 2.0–3.0) in a given time interval. A TTR exceeding 60% was considered to indicate effective treatment.

SAMe-TT_2R_2 score The SAMe-TT_2R_2 score is an 8-point score for the assessment of the probability of stabilized anticoagulation during VKA treatment. The components of the score are presented in detail in TABLE 1.

Statistical analysis The results were expressed as a mean value ± SD (for quantitative variables) and the index structure (for qualitative variables). Statistical significance between the study groups was determined using the nonparametric Mann–Whitney test. A *P* value of less than 0.05 was considered to be statistically significant. The χ^2 test of independence was used to compare qualitative variables, and the Fisher exact test was used in the case of noncompliance with the assumptions of the χ^2 test. The Spearman's rank correlation coefficient was used to describe

TABLE 1 Components of the SAMe-TT_2R_2 score

Parameter	Points
Sex (female)	1
Age (<60 years)	1
Medical history (2 or more of the following diseases: hypertension, diabetes, myocardial infarction, peripheral arterial disease, congestive heart failure, history of stroke, pulmonary disease, hepatic or renal disease)	1
Treatment (interacting medications)	1
Tobacco use (within 2 years)	2
Race (non-Caucasian)	2

correlation power between age and the $CHAD_2VASc_2$-VASc and HAS-BLED scores as well as between SAMe-TT_2R_2, MMSE, and TTR scores.

All analyses were conducted with the STATISTICA v 12.5 software (StatSoft, Inc., Kraków, Poland). The study was approved by the Ethics Committee of the Medical University of Lodz (consent number, RNN/660/13/KB).

RESULTS The study included 154 patients with AF (86 women, 68 men; age, 46–96 years; mean age, 76 ±10 years). The average MMSE score of the studied patients was 26 ±4 points. Despite indications for antithrombotic therapy, 50 patients (32%) were not receiving VKA treatment at the time of admission (23 women, 27 men; age, 53–91 years; mean age, 78 ±10 years). In this group, there were 58% patients with an MMSE score of less than 27 points, and 40% patients with an MMSE score of less than 24 points.

A group of patients with AF receiving VKA treatment was subject to a detailed analysis. This group comprised 104 patients (63 women, 41 men; age, 46–96 years; mean age, 75 ±10 years), and the average MMSE score was 27 ±4 points.

The MMSE score of 27 or higher was observed in 60% of the patients (n = 62) from the group on VKA treatment, whereas cognitive impairment was reported for 40% of the patients (n = 42), including 15% of the patients (n = 14) with an MMSE score of less than 24 points. No significant differences in age were found between the group with normal cognitive functions and the that with an MMSE score of less than 27 points.

Patients receiving VKA treatment who were younger than 70 years constituted 31% of the group (32 patients). The mean MMSE score in this group of patients was 28 ±3 points; the mean TTR value was 51% ±32%, and 56% of the patients had a TTR value of less than 60%. Patients receiving VKA treatment who were older than 70 years constituted 69% of the group (72 patients). The mean MMSE score in this group was 26 ±3; the mean TTR value was 51% ±28%, and 54% of the patients had a TTR value of less than 60%. The TTR value was significantly higher in the group of patients with good cognitive skills as compared with the group with an MMSE score of less than 27 (61% ±27% vs 38% ±25%; P <0.0001).

Paroxysmal AF was most frequent in the group of patients with normal cognitive skills, while persistent or permanent AF was predominant in the group with cognitive impairment, along with a higher number of brain-related incidents.

The most common causes for hospital admission in patients with an MMSE score of less than 27 included exacerbation of cardiac insufficiency symptoms, infections, dyspnea, general health deterioration, and increased blood pressure. Most of the patients with normal MMSE scores were admitted due to AF-related symptoms. The mean CHA_2DS_2-VASc score was higher in patients with an MMSE score of less than 27 and reached 5 ±2 points as compared with patients with an MMSE exceeding 27, whose score was 4 ±2 (P <0.05).

The CHA_2DS_2-VASc and HAS-BLED scores of our patients increased with age (r = 0.45, P <0.0001 and r = 0.23, P <0.05, respectively). Acenocoumarol was administered in most patients (61%) with both an MMSE score of 27 points or higher and an MMSE score of less than 27 points. A more frequent use of medications interacting with VKAs was noted in patients with cognitive impairment compared with those with normal cognitive skills (52% vs 39%). No significant relationship between the TTR value and the amount of received medications interacting with VKAs was shown in the group with normal MMSE scores (r = –0.01; P >0.05) or the group with MMSE scores of less than 27 (r = 0.16; P >0.05). Digoxin, sulfonylureas, and thyroxine were the most common drugs interacting with VKAs. Detailed characteristics of patients during VKA therapy are shown in TABLE 1.

Relationship between cognitive impairment and time in the therapeutic INR range Low MMSE scores were correlated with a low TTR value (r = 0.40; P <0.0001). The mean TTR value for patients with an MMSE score of 27 or higher was 61% ±27%, and for patients with an MMSE of less than 24, it was 28% ±26%. Even mild cognitive impairment (MMSE, 24–26) was associated with a low TTR value (43% ±23%). Data are shown in FIGURE 1.

In the group of patients with an MMSE score of less than 27, a significant INR values (46%) did not achieve the values indicating therapeutic success (TABLE 2). The cognitive status of patients with persistent and permanent AF was significantly lower compared with patients with paroxysmal AF (25.8 ±3.7 vs 28.6 ±2; P <0.0001).

Analysis of the SAMe-TT_2R_2 risk score for predicting the quality of anticoagulation control High TTR values were associated with a small number of points in the SAMe-TT_2R_2 risk score (r = –0.24; P <0.05). The mean TTR value for patients with a SAMe-TT_2R_2 score of 0 to 1 was 64% ±26% and for those with a SAMe-TT_2R_2 score of 2 or higher, it was 50% ±28% (FIGURE 2). Patients with normal cognitive skills had a lower SAMe-TT_2R_2 score compared with patients with an MMSE score of

TABLE 2 Characteristics of the study group during therapy with vitamin K antagonist

Variable	MMSE ≥27 n = 62	MMSE <27 n = 42	*P* value
age, y	73 ±9	77 ±11	NS
age <70 years	35 (22)	24 (10)	NS
sex, female/male, n	38/24	29/13	NS
CHA_2DS_2-VASc	4 ±2	5 ±2	<0.05
HAS-BLED	2 ±1	2 ±1	NS
SAMe-TT_2R_2	2 ±1	3 ±1	<0.05
stroke/TIA	11 (7)	19 (8)	NS
atrial fibrillation			
paroxysmal	52 (32)	19 (8)	<0.05
persistent	35 (22)	57 (24)	
permanent	13 (8)	24 (10)	
comorbidities			
heart failure	53 (33)	93 (39)	<0.0001
systemic hypertension	90 (56)	86 (36)	NS
diabetes mellitus	29 (18)	29 (12)	NS
treatment of AF			
acenocoumarol	66 (41)	52 (22)	NS
warfarin	34 (21)	48 (20)	
BMI	29 ±7	28 ±5	NS
smoking	18 (11)	21 (9)	NS
AST	27 ±20	30 ±20	NS
ALT	26 ±24	21 ±12	NS
creatinine (eGFR, ml/min/1.73 m^2)	1.1 ±0.3 (63 ±21)	1.1 ±0.4 (63 ±21)	NS
drug interactions			
amiodarone	8 (5)	7 (3)	NS
allopurinol	3 (2)	13 (5)	NS
sulfonylureas	10 (6)	17 (7)	NS
nonsteroidal anti-inflammatory drugs	0	7 (3)	NS
digoxin	16 (10)	38 (16)	NS
thyroxine	11 (7)	19 (8)	NS

Data are presented as percentage (number) of patients or mean ± SD.

a *P* value of less than 0.05 is considered significant.

Abbreviations: AF, atrial fibrillation; ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; eGFR, estimated glomerular filtration rate; MMSE, Mini-Mental State Examination; TTR, time in the therapeutic range

TABLE 3 Mean time in the therapeutic range (TTR) and values of international normalized ratio (INR) in patients with atrial fibrillation treated with vitamin K antagonists, depending on the Mini-Mental State Examination (MMSE) result

Parameter	MMSE ≥27 n = 62	MMSE <27 n = 42	*P* value
average TTR	61 ±27	38 ±26	<0.0001
TTR >60	61 (38)	28 (12)	<0.0001
INR <2	18 (11)	46 (19)	<0.05
INR 2–3	59 (37)	26 (11)	
INR >3	22 (14)	28 (12)	

Data are presented as percentage (number) of patients or mean ± SD.

a *P* value of less than 0.05 is considered significant.

less than 27 (r = –0.32; P <0.05). Data are presented in FIGURE 3.

DISCUSSION Supposedly, cognitive function impairment may affect the efficacy of anticoagulant treatment. However, there are scarce data regarding the effect of this type of disorder on TTR values, particularly among the Polish population.

The present study provides evidence that cognitive impairment in patients with AF worsens control of VKA therapy as compared with patients with normal cognitive functions. It was additionally shown that even mild impairment (MMSE score, 26–24 points) was associated with the predominance of the TTR value of less than 60%. Importantly, the mean age of patients with an MMSE score of 27 or less was not significantly higher than in the group of patients with normal cognitive functions. The prevalence of dementia is known to increase with age from about 5% in patients aged 70 years or older to nearly 40% among those at the age of 90 years.[15,16] This may confirm the effect of AF alone on the occurrence of cognitive disorders.

In patients with an MMSE score of less than 27, who did not maintain a TTR exceeding 60%, most measurements of INR values were below the therapeutic values. Therefore, it is likely that a higher percentage of cerebral events was also observed in these patients as compared with those with normal cognitive functions (19% vs 11%). Additionally, we observed no significant effect of drugs interacting with VKA on TTR values either in patients with cognitive impairment or in those without such an impairement. This led us to assume that poor control of VKA therapy was associated with deterioration of cognitive functions.

Despite indications for anticoagulant treatment, 32% of the patients (58% of whom were patients with an MMSE score of less than 27 points, including 40% with an MMSE score of less than 24 points) were not treated with VKAs on admission. The withdrawal from VKA therapy was mainly caused by the lack of possibility to adequately monitor the anticoagulant treatment or the lack of consent to apply the anticoagulant therapy including therapy with non-vitamin K oral anticoagulants.

The outcomes of the prospective multicenter GARFIELD-AF registry,[17] which compares stroke prevention in AF patients among the European countries, unequivocally indicated that the frequency of using VKAs in patients with AF in Poland is lower than that in other European countries (41.7% in Cohort 1 and 36.9% in Cohort 2 in Poland vs 55.5% in Cohort 1 and 41.9% in Cohort 2 in other European countries). Moreover, both in Poland and in other European countries, antithrombotic treatment seems to be administered in too many patients with a low risk of stroke, whereas it is less frequently applied in patients with a higher risk of stroke.[17]

The results of our study have been confirmed by ACTIVE-W,[18] a large clinical study conducted

FIGURE 1 Relationship between the time in the therapeutic INR range (TTR) and the Mini-Mental State Examination (MMSE) score

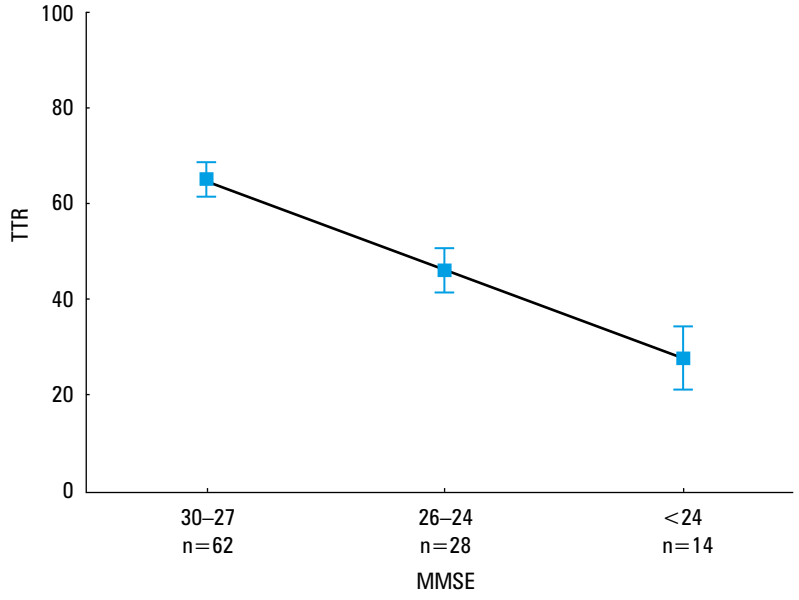


FIGURE 2 Relationship between the time in the therapeutic INR range (TTR) and the SAMe-TT_2R_2 risk score for prediction of the effectiveness of anticoagulant treatment

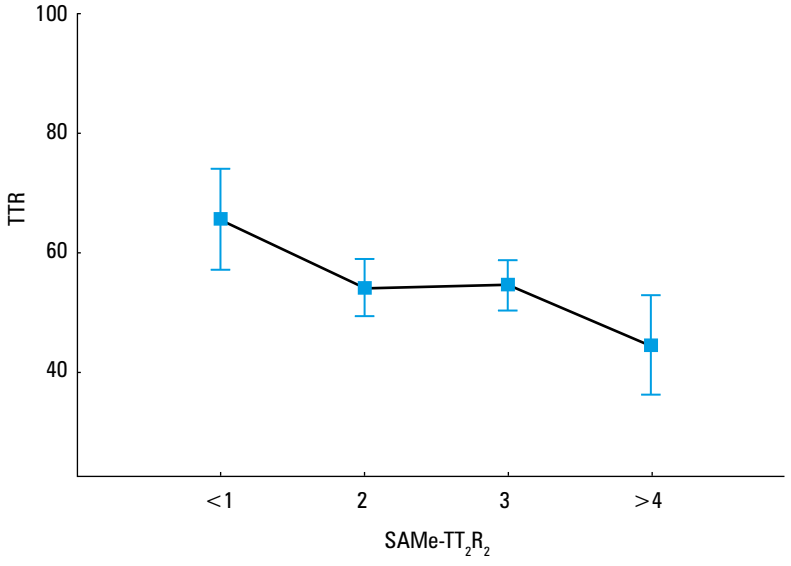
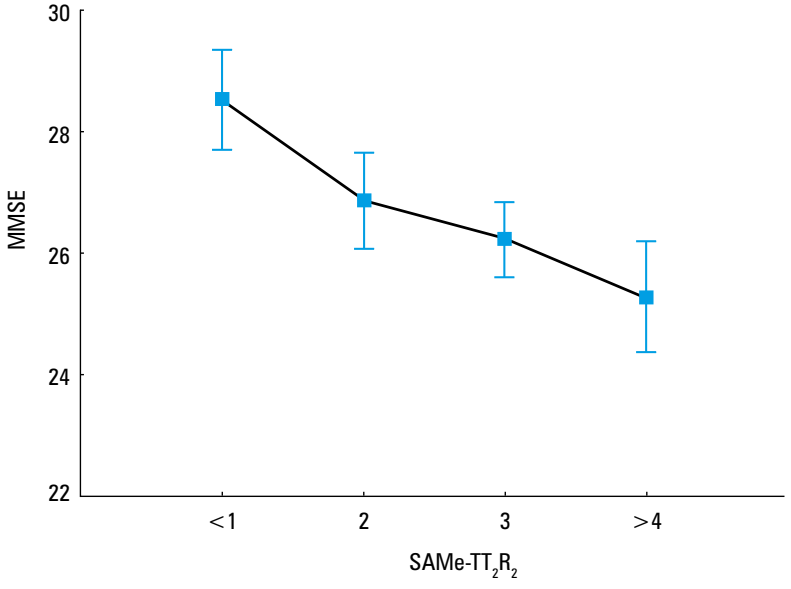


FIGURE 3 Relationship between the Mini-Mental State Examination (MMSE) score and the SAMe-TT_2R_2 risk score for prediction of the effectiveness of anticoagulant treatment



in a group of 2510 patients in 27 countries and comprising 194 people with cognitive impairment and 171 people with dementia. The study showed that cognitive impairment significantly reduced TTR values. Additionally, those patients had a higher risk of cardiovascular events and significant bleeding.[18]

On the one hand, it is clear that the prevalence of cognitive impairment increases with age. However, on the other hand, AF itself seems to be an independent risk factor for the occurrence of cognitive disorders.[19,20] The Rotterdam population study conducted in a group of 6584 participants aged from 55 to 106 years demonstrated that AF increases the risk of developing mild cognitive impairment (MMSE score <26 points) as well as symptomatic dementia of the Alzheimer type, particularly in patients younger than 70 years of age. Moreover, the Intermountain Heart Collaborative Study,[21] which comprised 37 000 patients, revealed a relationship between AF and all types of dementia. Interestingly, the effect of AF on the development of cognitive impairment was independent of the simultaneous occurrence of neurological events, including cerebral stroke.[19]

While analyzing the types of AF in our study groups, a more frequent occurrence of persistent or permanent AF was observed in the group of patients with an MMSE score of less than 27 points (80%) as compared with those with an MMSE score of 27 points or higher, in whom sinus rhythm prevailed (52%). Similar results were noted in a study by Wożakowska-Kapłon et al[22] in a group of Polish patients. The authors demonstrated that permanent AF in patients above 65 years of age deteriorated cognitive functions in comparison with individuals with sinus rhythm: 24.8 ±3.1 vs 27.1 ±2.6 (P <0.05). Patients with optimal control of the ventricular rate achieved higher MMSE scores, as opposed to patients with a poorly controlled ventricular rhythm.[23,24] The Framingham Offspring Study[25] showed that, irrespective of age, education, cardiovascular risk factors, diagnostic tests used or the threshold for recognizing cognitive impairment, AF contributed to a significant deterioration in cognitive functions as compared with individuals with sinus rhythm.

Pulse deficit in the peripheral arteries, which is associated with inadequate left ventricular diastolic filling and, in consequence, with a decrease in the minute heart volume leading to cerebral blood flow impairment and ischemia of the central nervous system is regarded as the cause of cognitive decline in those patients with AF in whom no ischemic foci have been observed in brain imaging examinations.[26] Additionally, Stefansdottir et al[27] showed that patients with AF had lower total brain volume compared with subjects without AF (P <0.001). Moreover, brain volume was lower in patients with persistent and permanent AF in comparison with patients with paroxysmal AF; it also decreased with AF duration.[27]

The above studies demonstrate that the causes of AF-related cognitive impairment are complex, and that adequate antithrombotic treatment as well as control of ventricular rate can efficiently prevent deterioration of cognitive function.

In 2013, a new 8-point score, SAMe-TT_2R_2, was developed, which allowed clinicians to identify patients with a high risk of inadequate INR control. This score enables physicians to recognize patients who will be efficiently treated with VKA (SAMe-TT_2R_2 score, 0–1) as well as those (SAMe-TT_2R_2 score ≥2) in whom additional procedures should be undertaken to achieve an acceptable response to anticoagulant treatment.[28]

In our study, patients who achieved a SAMe-TT_2R_2 score of 0 to 1 were characterized by a better INR control, and in the majority of the cases, they had a TTR value exceeding 60%, whereas patients with a SAMe-TT_2R_2 score of 2 or higher had poor INR control and their TTR value did not exceed 60%.

In our study, we also analyzed whether the MMSE score would affect the SAMe-TT_2R_2 score in a way similar to the TTR. We showed that patients with cognitive impairment had higher SAMe-TT_2R_2 scores than subjects with an MMSE score of 27 or higher.

A large prospective "real-world" study comprising 459 patients with AF, in whom the baseline SAMe-TT_2R_2 score was evaluated before the initiation of therapy with acenocoumarol, and the efficacy of therapy was assessed after 6 months by calculating TTR, allowed clinicians to identify patients who would not show adequate response to VKA therapy. Patients with the SAMe-TT_2R_2 score of 0 to 1 achieved a mean TTR of 67% ±18%, while those with a score of 2 or higher had a mean TTR of 61% ±16% (P <0.001).[29] Through the implementation of the SAMe-TT_2R_2 score to everyday clinical practice, it is possible to identify patients in whom VKA therapy will not be effective.

In summary, the decision on the choice of thromboembolism prevention should be made by balancing the risk of stroke against the risk of major bleeding complications, particularly in the group of patients with cognitive impairment. Non-VKA oral anticoagulants (dabigatran, riwaroxaban, apixaban, and edoxaban), which do not require INR monitoring, may be a therapeutic option for those patients.[30] However, this therapy cannot be applied in each patient because elderly patients with renal dysfunction need a more intensive care during therapy with non-VKA oral anticoagulants because of a higher risk of bleeding complications. For non-VKA oral anticoagulants, no routine monitoring is mandatory. Therefore, the level of treatment satisfaction and efficacy will be unknown until an adverse event occurs.

Conclusions First, cognitive impairment in patients with AF is associated with inefficacy of anticoagulant treatment with VKAs. Second, patients with a SAMe-TT_2R_2 score of 0 to 1 achieved a mean TTR exceeding 60%, while patients with

a score of 2 or higher had poorer INR control and achieved a mean TTR of less than 60%. Third, patients with persistent and permanent AF achieved a worse MMSE score as compared with patients with paroxysmal AF. Finally, the decision to introduce VKA therapy should be based not only on the assessment of CHA_2DS_2-VASc and HAS-BLED scores but also on the SAMe-TT_2R_2 score and the evaluation of cognitive functions using the simplest and fastest tool, namely, the MMSE score.

Contribution statement PG-P conceived the idea of the study. PG-P, SZ, ŁK, and MB contributed to the design of the research. All authors were involved in data collection. All authors were involved in drafting the article. PG-P, SZ, and ŁK analyzed the data. MB coordinated funding for the project. All authors edited and approved the final version of the manuscript.

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Ocena średniego czasu INR w zakresie terapeutycznym i skali SAM-TT_2R_2 u pacjentów z migotaniem przedsionków i zaburzeniami funkcji poznawczych

Paulina Gorzelak-Pabiś, Sandra Zyzak, Łukasz Krewko, Marlena Broncel

Klinika Chorób Wewnętrznych i Farmakologii Klinicznej. Uniwersytet Medyczny w Łodzi, Łódź

SŁOWA KLUCZOWE

antagoniści witaminy K, międzynarodowy współczynnik znormalizowany, migotanie przedsionków, SAME-TT_2R_2, zaburzenia funkcji poznawczych

STRESZCZENIE

WPROWADZENIE Większość pacjentów z migotaniem przedsionków (*atrial fibrillation* – AF) jest w podeszłym wieku i ma zwiększone ryzyko występowania zaburzeń funkcji poznawczych. Niskie wartości średniego czasu INR w zakresie terapeutycznym (*time in the therapeutic range* – TTR) (≤60%) wiążą się ze zwiększonym ryzykiem udaru mózgu, incydentów naczyniowych i powikłań krwotocznych.

CELE Celem pracy była ocena skuteczności długoterminowej terapii przeciwzakrzepowej antagonistami witaminy K (*vitamin K antagonists* – VKA) u pacjentów z AF w zależności od poziomu funkcji poznawczych. Dodatkowo za pomocą skali SAMe-TT_2R_2 oceniono ryzyko nieskutecznej antykoagulacji.

PACJENCI I METODY Analizie poddano 154 pacjentów (68 mężczyzn i 86 kobiet, średni wiek 76 ±10 lat) z AF i wskazaniami do przewlekłego leczenia VKA (CHA_2DS_2-VASc ≥1, HAS-BLED <3). Zdolności poznawcze oceniono za pomocą krótkiej skali oceny stanu umysłowego (Mini-Mental State Examination – MMSE). Skuteczność terapii VKA obliczono przy użyciu wskaźnika TTR z ostatnich 6 miesięcy terapii. Skali SAMe-TT_2R_2 użyto w celu identyfikacji pacjentów obarczonych ryzykiem nieskutecznej kontroli wskaźnika INR.

WYNIKI W zależności od uzyskanej punktacji w skali MMSE pacjentów w trakcie terapii VKA podzielono na dwie grupy: z prawidłowymi funkcjami poznawczymi (MMSE ≥27, n = 62) oraz z ich zaburzeniami (MMSE <27, n = 42). Pomimo wskazań do terapii przeciwzakrzepowej u wszystkich chorych, w momencie przyjęcia 50 (32%) pacjentów nie miało włączonej terapii VKA. Średnia wartość wskaźnika TTR wynosiła >60% u 61% pacjentów z wynikiem MMSE ≥27 punktów, podczas gdy u pacjentów z wynikiem MMSE <27 średnia wartość wskaźnika TTR wyniosła 28% (p <0,0001). U pacjentów, którzy uzyskali w skali SAMe-TT_2R_2 wynik 0–1, stwierdzono wyższą wartość wskaźnika TTR niż u chorych z wynikiem ≥2 (r = –0.24; p <0,05). Funkcje poznawcze w grupie pacjentów z przetrwałym i utrwalonym AF były istotnie bardziej zaburzone w porównaniu z grupą chorych z napadowym AF (MMSE: 25,8 ±3,7 *vs* 28,6 ±2; p <0,0001).

WNIOSKI Zaburzenia funkcji poznawczych u pacjentów z AF istotnie obniżają skuteczność terapii przeciwzakrzepowej z użyciem VKA. Decyzja o wdrożeniu leczenia VKA powinna być oparta nie tylko o ocenę skali CHA_2DS_2-VASc i HAS-BLED, ale również skali SAMe-TT_2R_2 oraz o ocenę funkcji poznawczych.

Adres do korespondencji:
lek. Paulina Gorzelak-Pabiś,
Klinika Chorób Wewnętrznych
i Farmakologii Klinicznej,
Uniwersytet Medyczny w Łodzi,
ul. Kniaziewicza 1/5, 91-347 Łódź,
tel.: 42 251 62 43,
e-mail: pau.gorzelak@gmail.com
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