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The CHA_2DS_2-VASc score as a predictor of dementia in elderly patients with atrial fibrillation

Skala CHA_2DS_2-VASc jako predyktor demencji wśród chorych w podeszłym wieku z migotaniem przedsionków

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Abstract

Introduction. Many studies suggest that atrial fibrillation (AF) is associated with an increased risk of functional decline and may contribute to the development of dementia. It is not known whether the CHA_2DS_2-VASc scale allows the development of dementia in patients with AF to be predicted.

To assess whether CHA_2DS_2-VASc score can be a predictor of dementia evaluated with Mini-Mental State Examination (MMSE) questionnaire in the elderly patients with atrial fibrillation.

Material and methods. The study included 157 patients (mean age 73.4) with non-valvular atrial fibrillation and no history of stroke. The presence of dementia was defined as the MMSE score of ≤ 23 points.

Results. The univariate analysis revealed that age (b = 0.132, p < 0.001), heart failure (b = 0.786, p = 0.033) and CHA_2DS_2-VASc score were significant determinants of dementia. In multivariate analysis, the CHA_2DS_2-VASc score was proved to be an independent determinant of dementia (β = 0.385, p = 0.003). Prevalence of dementia was one and a half times higher in the group of patients with a CHA_2DS_2-VASc score > 4 points (odds ratio = 0.47) that in the group of patients with CHA_2DS_2-VASc score ≤ 4 points.

Conclusion. The CHA_2DS_2-VASc score is a useful predictor of dementia in the ageing population with atrial fibrillation without clinical stroke.

Key words: atrial fibrillation, cognitive function, cognitive impairment

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Introduction

Atrial fibrillation (AF) is a common arrhythmia that constitutes an independent risk factor for stroke and is associated with increased morbidity and mortality. AF prevalence rises with age and affects up to 9% of the population over 80 years of age [1].

The ageing of the population also leads to an increased risk of cognitive impairment (CI) and dementia [2, 3].

Many studies suggest that AF is associated with an increased risk of CI and functional decline and may contribute to the development of dementia [4]. CI is frequently associated with AF, although the relationship between them remains controversial, especially in the absence of

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stroke. It has been demonstrated that even among patients with AF without clinical stroke, the arrhythmia is still associated with CI and dementia [5].

However, it is not known whether this scale allows the development of dementia in patients with AF to be predicted. How to predict dementia occurrence among AF patients is not clear. There is limited information about the use of $CHADS_2$ and CHA_2DS_2-VASc score to predict dementia

Material and methods

Aim of the study

To assess whether CHA_2DS_2-VASc score can be a predictor of dementia evaluated with Mini-Mental State Examination (MMSE) questionnaire in the elderly patients with atrial fibrillation.

Study design and sample

The study was conducted between January 2015 and September 2016 at the Cardiology Department. It involved 164 patients consecutively admitted to the hospital and selected by the cardiologist based on the inclusion and exclusion criteria.

The inclusion criteria were age > 60 years, a diagnosis of atrial fibrillation (paroxysmal, persistent or permanent), and anticoagulant treatment lasting for at least six months. The exclusion criteria were previous ischemic stroke and a lack of consent to participate in the study. Ultimately, 7 patients were excluded. The study involved 157 patients who were over 60 years of age, were diagnosed with AF and had used oral anticoagulant — either vitamin K antagonist (VKA) or a non-vitamin K oral anticoagulants (NOAC) — for at least six months. The questionnaires were distributed by a specialist cardiac nurse at discharge. All patients were informed of the purpose and nature of this study and provided their written informed consent to be included in it. Based on the MMSE questionnaire score, the study group was divided into the following groups [6]:

- dementia (≤ 23 pts);
- cognitive impairment without dementia (> 23 pts < < 27pts);
- absence of cognitive impairment (≥ 27 pts).

Information concerning the sociodemographic and clinical data come from the hospital registry files.

Ethical consideration

This study was approved by the Bioethical Committee. All qualified patients provided their informed and voluntary consent to participate in the study.

Instrument

We employed the MMSE developed by Folstein et al. [6]. This is a widely used screening test for dementia, whose advantages include the speed of administration and simple interpretation of its results. The MMSE measures cognitive function such as a sense of direction, memory, attention, linguistic function, and visual-spatial abilities, as well as the ability to count, recall things, repeat, and carry out orders. The possible score ranges from 0 to 30, with lower scores indicating more severe cognitive function disorders. Patients with scores ≤ 27 are described as cognitively impaired [6].

A CHA_2DS_2-VASc scale is a tool for assessing the risk of thromboembolic complications in patients with atrial fibrillation. The scale allows the identification of patients with AF who require antiplatelet or anticoagulant therapy. The risk assessment includes factors such as hypertension, old age (age 65 to 74 years or age 75 and older) diabetes mellitus, prior stroke or thromboembolic event, congestive heart failure/LV dysfunction, vascular disease and female sex [1].

Statistical analysis

Statistical analysis of the results was performed with STATISTICA v. 12 (StatSoft, Inc. Tulsa, USA). Quantitative data (age, CHA_2DS_2-VASc score) were presented as mean and standard deviations [mean (M) ± standard deviation (SD)]. Qualitative data (sex, concomitant diseases *etc.*) were shown in contingency tables in the form of size (N) and percentage (%). The independence of qualitative variables from dementia was verified using the chi-square test. The significance of differences between the mean values of quantitative variables in the two groups was verified with the t-test for independent variables. To assess the strength of the correlation between the MMSE score and CHA_2DS_2--VASc score the Spearman's rank correlation coefficient was calculated. Receiver operator characteristic curve analysis was used to establish cut-off values for dementia. The predictors of dementia (univariate analysis) were determined using simple logistic regression and stepwise multiple regression.

Results

The study involved 157 AF patients (including 77 women) aged M = 73.4; SD = 8.3. The mean CHA_2DS_2-VASc score achieved by the patients studied was 3.90 ± 1.46. The participants were categorized by the level of cognitive function. According to the MMSE results, patients were divided into three groups: without cognitive impairment (Group 1; MMSE ≥ 27), with cognitive impairment without

dementia (Group 2; MMSE 24–26) and with dementia (Group 3; MMSE ≤ 23). The groups compared differed in terms of age: the patients in Group 3 were significantly older than those from Group 2 and Group 1 (the mean age in Group 3 was 78.9 ± 7.8, in Group 2 — 75.3 ± 6.6 and in Group 1 — 70.0 ± 6.9, p < 0.001). In addition, Group 3 had the largest percentage of patients aged > 75 (69.0% vs. 64.3% vs. 31.5%, p < 0.001). Furthermore, a statistically significant difference in CHA_2DS_2-VASc score was observed among the groups. Group 3 achieved a result with higher statistical significance than the remaining two groups: 4.48 ± 1.49 Group 3 versus 4.19 ± 1.25 Group 2 versus 3.40 ± 1.40 Group 1; p < 0.001. Statistically significant differences between the studied groups and the occurrence of renal dysfunction were observed — Group 3 was characterized by the highest percentage of patients compared to the other groups (57.1 Group 3 vs. 47.6 Group 2 vs. 32.9 Group 1, p = 0.033). No statistically significant differences were found for the remaining factors included in the study: sex, components of the CHA_2DS_2-VASc scale, duration of atrial fibrillation, type of atrial fibrillation, type of anticoagulant treatment administered and coexisting hyperthyroidism, respiratory system diseases and rheumatic diseases. The results are presented in Table 1.

Table 1. Clinical characteristics of patient groups classified based on cognitive function

Attribute (variable)	Group 1 MMSE ≥ 27 N = 73	Group 2 MMSE 24–26 N = 42	Group 3 MMSE ≤ 23 N = 42	Test result p value
Age	70.0 ± 6.9	75.3 ± 6.6	78.9 ± 7.8	**< 0.001**
Age > 65 years	59 (80.8)	40 (95.2)	41 (97.6)	**0.007**
Age > 75 years	23 (31.5)	27 (64.3)	29 (69.0)	**< 0.001**
Female sex	29 (39.7)	25 (59.5)	23 (54.8)	0.085
City inhabitant	58 (79.5)	31 (73.8)	35 (83.3)	0.558
Comorbidities				
Hypertension	61 (83.6)	32 (76.2)	37 (88.1)	0.342
Diabetes mellitus	15 (20.6)	13 (31.0)	10 (23.8)	0.454
Heart failure	23 (31.5)	13 (31.0)	21 (50.0)	0.098
Ischaemic heart disease	8 (11.0)	6 (14.3)	10 (23.8)	0.179
Hyperthyroidism	10 (13.7)	3 (7.1)	5 (11.9)	0.566
Respiratory system diseases	7 (9.6)	2 (4.8)	5 (11.9)	0.498
Prior vascular diseases	14 (19.2)	9 (21.4)	12 (28.6)	0.501
Rheumatic diseases	9 (12.3)	6 (14.3)	6 (14.3)	0.937
Other diseases	24 (32.9)	20 (47.6)	24 (57.1)	**0.033**
Duration of atrial fibrillation				
Up to 5	50 (68.5)	27 (64.3)	21 (50.0)	0.174
6 to 10 years	10 (13.7)	5 (11.9)	12 (28.6)	
Over 10 years	13 (17.8)	10 (23.8)	9 (21.4)	
Type of atrial fibrillation				
Paroxysmal/persistent	34 (46.6)	21 (50.0)	14 (33.3)	**0.253**
Permanent	39 (53.4)	21 (50.0)	28 (66.7)	
Anticoagulant therapy				
VKA	60 (82.2)	34 (81.0)	33 (78.6)	0.893
NOAC	13 (17.8)	8 (19.0)	9 (21.4)	
CHA_2DS_2-VASc score	3.40 ± 1.40	4.19 ± 1.25	4.48 ± 1.49	**< 0.001**

MMSE — Mini-Mental State Examination; VKA — vitamin K antagonist; NOAC — non-vitamin K oral anticoagulants

Table 2. Values of the logistic regression coefficient for the predictors of dementia analysed

Attribute (variable)	Univariate analysis		Multivariate analysis	
	b	p value	beta	p value
Age	**0.132**	**< 0.001**	–	–
> 65 years	1.891	0.071	–	–
> 75 years	**1.065**	**0.006**	–	–
Female sex	0.313	0.387	–0.225	0.599
City inhabitant	0.379	0.420	–	–
Hypertension	0.560	0.293	–	–
Diabetes mellitus	–0.029	0.944	–	–
Heart failure	**0.786**	**0.033**	–	–
Ischaemic heart disease	0.813	0.078	–	–
Hyperthyroidism	0.058	0.917	–	–
Respiratory system diseases	0.465	0.430	–	–
Prior vascular diseases (atherosclerosis)	0.470	0.256	–	–
Rheumatic diseases	0.031	0.952	–	–
Other diseases	**0.766**	**0.036**	–	–
Duration of atrial fibrillation	0.272	0.209	0.242	0.318
Permanent atrial fibrillation	0.606	0.108	0.424	0.295
Anticoagulant treatment with NOAC	0.200	0.655	0.684	0.169
CHA_2DS_2-VASc score	**0.386**	**0.003**	**0.385**	**0.003**

NOAC — non-vitamin K oral anticoagulants

Next, logistic regression analysis of predictors for dementia was conducted. Significant determinants of dementia in the univariate logistic regression analysis were: age (b = 0.132; p < 0.001) — especially among patients aged > 75 (b = 1.065; p = 0.006), heart failure (b = 0.786; p = 0.033), other diseases (renal disfunction) (b = 0,766, p = 0,036) and the CHA_2DS_2-VASc scale (b = 0.385; p = 0.003). The score on the CHA_2DS_2-VASc scale was found to be a significant independent determinant of cognitive impairment with dementia in the multivariate logistic regression analysis (b = 0.385; p = 0.003). The results are presented in Table 2.

We found a statistically significant negative moderate correlation between the score on the MMSE scale and the risk of thromboembolic complications assessed with the CHA_2DS_2-VASc scale (*rho* = –0.343). The percentage of cognitive impairment points consequently increases with increase in the CHA_2DS_2-VASc scores (Figure 1).

The receiver operator characteristic comes for productivity dementia bases on the CHA_2DS_2-VASc scores. CHA_2DS_2-VASc scores ≥ 4 identified by the ROC (sensitivity 52.4%; specificity 73.0%, area under the cut-off AUC 0.648) were associated with a higher rate of dementia. (Figure 2).

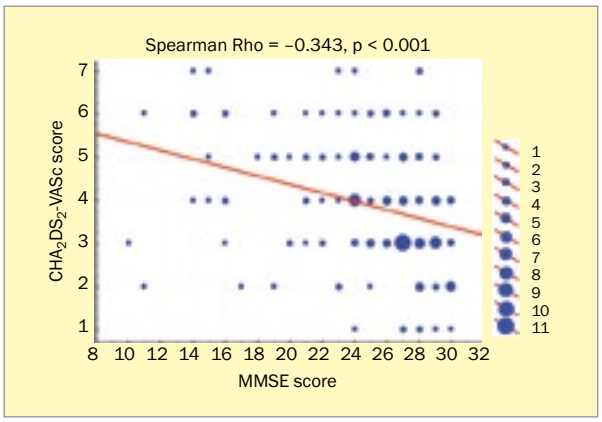

Figure 1. Scatter diagram of Spearman's rank correlation coefficient showing the relationship between the risk of thromboembolic complications measured by the CHA_2DS_2-VASc and the Mini-Mental State Examination (MMSE) score

Discussion

It has been reported that AF may be associated with a higher risk of cognitive impairment. One important explanation is the increased incidence of stroke. AF is

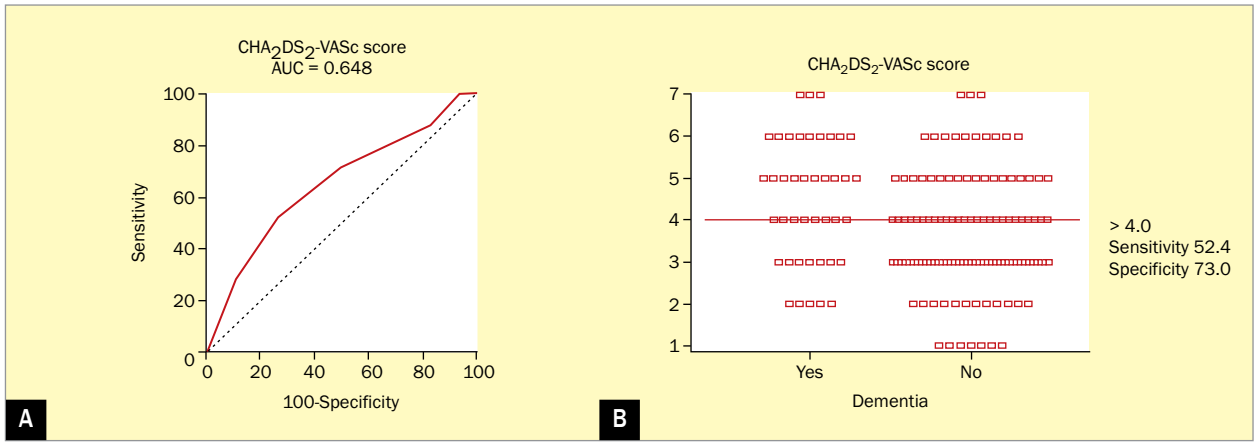

Figure 2A, B. The receiver operator characteristic (ROC) curve, sensitivity and specificity of the test concerning the prevalence of dementia at CHA_2DS_2-VASc cut-off score > 4; AUC — area under the curve

a well — known risk factor of clinical and silent cerebral infarctions. It is not difficult to connect AF with post-stroke dementia. Multiple episodes of subclinical strokes may be a cause of CI [7, 8]. The authors' interest is in the population with AF without stroke or transient ischemic attack (TIA). What is the possible link between AF and dementia?

The subject literature offers information on cognitive impairment in patients with AF and a history of stroke, but there have been few studies on patients who did not suffer a stroke. A correlation between AF and cognitive impairment has been established, but more research is required to examine the exact mechanism of this relationship. Much controversy exists as to what factors mediate the development of CI or dementia in this group of patients [2, 3]. Several mechanisms have been proposed to explore the relationship between AF and CI or dementia. One possible explanation is the presence of other risk factors for dementia such as age, hypertension, heart failure, diabetes mellitus, metabolic syndrome and hypercholesterolemia [9].

A meta-analysis conducted by Kalantarian et al. [2] summarizes data from prospective and non-prospective observational studies has suggested that AF is associated with a high risk of CI and dementia, with or without a history of clinical stroke.

Marzona et al. [3] conducted a post-hoc analysis of the trials ONTARGET and TRANSCEND that incorporated 31 506 patients (1016 with AF at baseline) and proved that cognitive and functional decline are important consequences of AF, even in the absence of overt stroke. In a study by Farina et al. [10], which excluded patients with a history of stroke by detailed imaging, an association between AF and cognitive impairment was shown.

Forti et al. reported that AF was not significantly associated with dementia. In a population of patients with mild cognitive impairment (MCI), atrial fibrillation was significantly associated with conversion to dementia [hazard ratio (HR): 4.63; 95% confidence interval: 1.72–12.46], whilst no significant association with AF was found in the group without cognitive impairment (HR: 1.10; 95% confidence interval: 0.40–3.03). The authors concluded that atrial fibrillation may be a predictor of conversion to dementia in patients with MCI [11].

Our data also showed a significant correlation between AF and dementia in the non-stroke population (26.75% dementia). It should be emphasised that all patients were administered anticoagulant treatment. Recent publications suggest that warfarin use may reduce the incidence of dementia in AF patients [12].

Our findings are consistent with those found in the available literature. Bellomo et al. [13] performed a detailed geriatric assessment of two groups of ageing patients (mean age 71.76) with atrial fibrillation and normal sinus rhythm (control group) and demonstrated that patients with AF who completed the MMSE questionnaire more often obtained a score suggesting cognitive impairment than the controls (31% vs. 26%). It was also shown that AF may have an influence on the progression to dementia, even when a patient had no history of stroke [13].

We analysed cognitive function depending on the type of AF: paroxysmal, persistent or permanent. No differences were found with regard to the types of AF and their impact on the severity of cognitive impairment. The literature on the subject indicates there are no differences between those in complications such as stroke [14]. There are only several papers analysing dementia prevalence depending on AF type. The study by Knecht et al. [15] demonstrated a lack of any association between type of AF (paroxysmal/persistent) and cognitive function. However, a downward trend in performance was observed in patients with chronic AF in tasks related to memorizing and learning ($p = 0.0062$).

Therefore, it is very important to assess cognitive function in patients with AF. This leads to the question of whether dementia in patients with AF is mediated through an increased risk of stroke or whether other factors are responsible. What could be the value of a CHA_2DS_2-VASc evaluation in predicting dementia? Which non-stroke patients with AF stroke should undergo an assessment of cognitive function?

There has been growing interest in the role of $CHADS_2$ and CHA_2DS_2-VASc score in predicting cognitive impairment in patients with AF. However, the number of studies concerned with the relationship between the $CHADS_2$ or CHA_2DS_2-VASc score and cognitive impairment is limited [16, 17].

In a population-based cohort study (Taiwan cohort) Chou et al. [16] investigated the correlation between the $CHADS_2$ score and the future risk for vascular dementia or Alzheimer's disease (mean follow up 3.71 ± 2.78 years, 38.2% with previous stroke/TIA) and showed that $CHADS_2$ score is a useful predictor of the development of vascular dementia, as well as Alzheimer's disease in patients with AF. Liao et al. in the study using the Taiwan AF cohort of 332 665 patients with AF (32.3% with the previous cerebral vascular incident and no history of dementia) showed that both $CHADS_2$ and CHA_2DS_2-VASc scores were significant predictors of developing dementia during a 14-year follow-up in AF subjects. However, the CHA_2DS_2-VASc score was better than $CHADS_2$ in predicting dementia [17].

In summary, the presented study shows a statistically significant correlation between the risk of thromboembolic complications measured with the CHA_2DS_2-VASc scale and the score on the MMSE scale. The logistic regression analysis has shown that the CHA_2DS_2-VASc scale is an independent and statistically significant determinant in patients with dementia, which correlates with the MMSE score.

Conclusion

The CHA_2DS_2-VASc score is a useful predictor of dementia. Patients with a CHA_2DS_2-VASc score > 4 are 1.5 times more likely to develop dementia than the population with a lower score.

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We want to thank all of the participants in this study.

Conflicts of interest

The author reports no conflicts of interest in this work.

Streszczenie

Wstęp. Wiele badań wskazuje na związek między migotaniem przedsionków (AF) a zwiększonym ryzykiem pogorszenia się funkcji poznawczych. Nie wiadomo, czy skala CHA_2DS_2-VASc pozwala na przewidywanie rozwoju demencji u pacjentów z AF.

Celem było wskazanie, czy wynik w CHA_2DS_2-VASc może być predyktorem demencji ocenianej za pomocą kwestionariusza *Mini-Mental State Examination* (MMSE) wśród chorych z AF w podeszłym wieku.

Materiał i metody. Badaniem objęto 157 pacjentów (średnia wieku 73,4 roku) z niezastawkowym AF bez historii udaru mózgu w wywiadzie. Obecność demencji zdefiniowano jako wynik w MMSE mniejszy lub równy 23 punktom.

Wyniki. Analiza jednoczynnikowa wykazała, że wiek (b = 0,132; p < 0,001), niewydolność serca (b = 0,786; p = 0,033) oraz wynik w CHA_2DS_2-VASc były istotnymi determinantami demencji. W analizie wieloczynnikowej wynik w skali CHA_2DS_2-VASc okazał się niezależnym predyktorem demencji (β = 0,385; p = 0,003). Częstość występowania demencji była półtora razy większa w grupie chorych z wynikiem w CHA_2DS_2-VASc przekraczającym 4 punkty (iloraz szans = 0,47) niż w grupie chorych z wynikiem w CHA_2DS_2-VASc mniejszym lub równym 4 punktom.

Wniosek. Skala CHA_2DS_2-VASc jest przydatnym narzędziem predykcyjnym demencji w starzejącej się populacji z AF bez historii udaru mózgu.

Słowa kluczowe: migotanie przedsionków, funkcje poznawcze, upośledzenie funkcji poznawczych

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