






The CHA₂DS₂-VASc score as a predictor of dementia in elderly patients with atrial fibrillation

Skala CHA₂DS₂-VASc jako predyktor demencji wśród chorych w podeszłym wieku z migotaniem przedsionków

Katarzyna Lomper¹ , Beata Jankowska-Polańska¹ , Joanna Jaroń² ,
Maria Łoboz-Rudnicka² , Krzysztof Dudek³ , Krystyna Łoboz-Grudzień²

¹Department of Clinical Nursing, Faculty of Health Science, Wrocław Medical University, Wrocław, Poland

²T. Marciniak Lower Silesian Specialist Hospital, Wrocław, Poland

³Wrocław University of Science and Technology, Wrocław, Poland

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 CHA₂DS₂-VASc scale allows the development of dementia in patients with AF to be predicted.

To assess whether CHA₂DS₂-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 CHA₂DS₂-VASc score were significant determinants of dementia. In multivariate analysis, the CHA₂DS₂-VASc score was proved to be an independent determinant of dementia ($\beta = 0.385$, $p = 0.003$). Prevalence of dementia was one and a half times higher in the group of patients with a CHA₂DS₂-VASc score > 4 points (odds ratio = 0.47) than in the group of patients with CHA₂DS₂-VASc score ≤ 4 points.

Conclusion. The CHA₂DS₂-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

Folia Cardiologica 2021; 16, 1: 1–7

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

Address for correspondence: Katarzyna Lomper MSc, Katedra Pielęgniarstwa Klinicznego, Wydział Nauk o Zdrowiu, Uniwersytet Medyczny we Wrocławiu, ul. Bartła 5, 51–618 Wrocław, Poland, e-mail: katarzyna.lomper@gmail.com

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 CHADS₂ and CHA₂DS₂-VASc score to predict dementia

Material and methods

Aim of the study

To assess whether CHA₂DS₂-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 < < 27 pts);
- 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 CHA₂DS₂-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, CHA₂DS₂-VASc score) were presented as mean and standard deviations [mean (M) \pm 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 CHA₂DS₂-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 CHA₂DS₂-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 CHA₂DS₂-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 CHA₂DS₂-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)	
CHA₂DS₂-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 ₂ DS 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 dysfunction) ($b = 0,766$, $p = 0,036$) and the CHA₂DS₂-VASc scale ($b = 0.385$; $p = 0.003$). The score on the CHA₂DS₂-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 CHA₂DS₂-VASc scale ($\rho = -0.343$). The percentage of cognitive impairment points consequently increases with increase in the CHA₂DS₂-VASc scores (Figure 1).

The receiver operator characteristic comes for productivity dementia bases on the CHA₂DS₂-VASc scores. CHA₂DS₂-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).

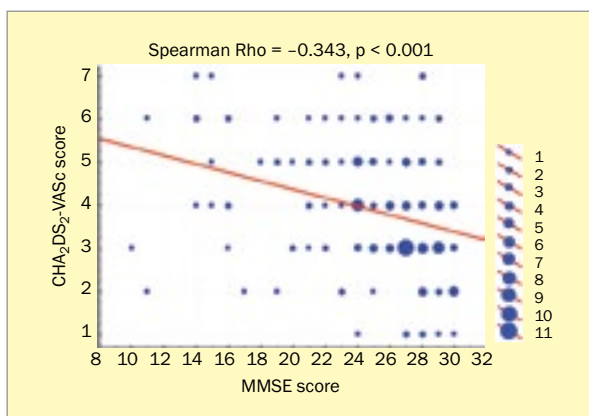


Figure 1. Scatter diagram of Spearman's rank correlation coefficient showing the relationship between the risk of thromboembolic complications measured by the CHA₂DS₂-VASc and the Mini-Mental State Examination (MMSE) score

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

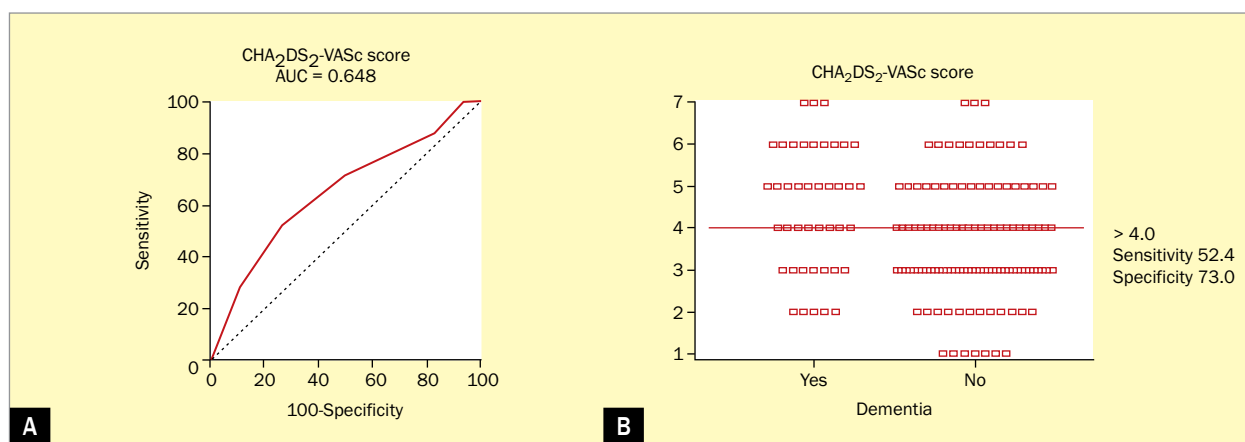


Figure 2A, B. The receiver operator characteristic (ROC) curve, sensitivity and specificity of the test concerning the prevalence of dementia at CHA₂DS₂-VASc cut-off score > 4; AUC – area under the curve

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 CHA₂DS₂-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 CHADS₂ and CHA₂DS₂-VASc score in predicting cognitive impairment in patients with AF. However, the number of studies concerned with the relationship between the CHADS₂ or CHA₂DS₂-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 CHADS₂ 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 CHADS₂ 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 CHADS₂ and CHA₂DS₂-VASc scores were significant predictors

of developing dementia during a 14-year follow-up in AF subjects. However, the CHA₂DS₂-VASc score was better than CHADS₂ in predicting dementia [17].

In summary, the presented study shows a statistically significant correlation between the risk of thromboembolic complications measured with the CHA₂DS₂-VASc scale and the score on the MMSE scale. The logistic regression analysis has shown that the CHA₂DS₂-VASc scale is an independent and statistically significant determinant in patients with dementia, which correlates with the MMSE score.

Conclusion

The CHA₂DS₂-VASc score is a useful predictor of dementia. Patients with a CHA₂DS₂-VASc score > 4 are 1.5 times more likely to develop dementia than the population with a lower score.

Acknowledgements

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 CHA₂DS₂-VASc pozwala na przewidywanie rozwoju demencji u pacjentów z AF.

Celem było wskazanie, czy wynik w CHA₂DS₂-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 CHA₂DS₂-VASc były istotnymi determinantami demencji. W analizie wieloczynnikowej wynik w skali CHA₂DS₂-VASc okazał się niezależnym predyktorem demencji ($\beta = 0,385$; $p = 0,003$). Częstość występowania demencji była półtora razy większa w grupie chorych z wynikiem w CHA₂DS₂-VASc przekraczającym 4 punkty (iloraz szans = 0,47) niż w grupie chorych z wynikiem w CHA₂DS₂-VASc mniejszym lub równym 4 punktom.

Wniosek. Skala CHA₂DS₂-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

Folia Cardiologica 2021; 16, 1: 1–8

References

1. Camm AJ, Kirchhof P, Lip GYH, et al. European Heart Rhythm Association, European Association for Cardio-Thoracic Surgery. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J*. 2010; 31(19): 2369–2429, doi: [10.1093/eurheartj/ehq278](https://doi.org/10.1093/eurheartj/ehq278), indexed in Pubmed: [20802247](https://pubmed.ncbi.nlm.nih.gov/20802247/).
2. Kalantarian S, Stern TA, Mansour M, et al. Cognitive impairment associated with atrial fibrillation: a meta-analysis. *Ann Intern Med*. 2013; 158(5 Pt 1): 338–346, doi: [10.7326/0003-4819-158-5-201303050-00007](https://doi.org/10.7326/0003-4819-158-5-201303050-00007), indexed in Pubmed: [23460057](https://pubmed.ncbi.nlm.nih.gov/23460057/).
3. Marzona I, O'Donnell M, Teo K, et al. Increased risk of cognitive and functional decline in patients with atrial fibrillation: results of the ONTARGET and TRANSCEND studies. *CMAJ*. 2012; 184(6): E329–E336, doi: [10.1503/cmaj.111173](https://doi.org/10.1503/cmaj.111173), indexed in Pubmed: [22371515](https://pubmed.ncbi.nlm.nih.gov/22371515/).
4. Bunch TJ, Crandall BG, Weiss JP, et al. Patients treated with catheter ablation for atrial fibrillation have long-term rates of death, stroke, and dementia similar to patients without atrial fibrillation. *J Cardiovasc Electrophysiol*. 2011; 22(8): 839–845, doi: [10.1111/j.1540-8167.2011.02035.x](https://doi.org/10.1111/j.1540-8167.2011.02035.x), indexed in Pubmed: [21410581](https://pubmed.ncbi.nlm.nih.gov/21410581/).
5. Forti P, Forti P, Maioli F, et al. Atrial fibrillation and risk of dementia in non-demented elderly subjects with and without mild cognitive impairment. *Neurol Res*. 2006; 28(6): 625–629, doi: [10.1179/016164106X130461](https://doi.org/10.1179/016164106X130461), indexed in Pubmed: [16945214](https://pubmed.ncbi.nlm.nih.gov/16945214/).
6. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975; 12(3): 189–198, doi: [10.1016/0022-3956\(75\)90026-6](https://doi.org/10.1016/0022-3956(75)90026-6).
7. Kilander L, Andrén B, Nyman H, et al. Atrial fibrillation is an independent determinant of low cognitive function: a cross-sectional study in elderly men. *Stroke*. 1998; 29(9): 1816–1820, doi: [10.1161/01.str.29.9.1816](https://doi.org/10.1161/01.str.29.9.1816), indexed in Pubmed: [9731601](https://pubmed.ncbi.nlm.nih.gov/9731601/).
8. Tatemichi TK, Desmond DW, Stern Y, et al. Cognitive impairment after stroke: frequency, patterns, and relationship to functional abilities. *J Neurol Neurosurg Psychiatry*. 1994; 57(2): 202–207, doi: [10.1136/jnnp.57.2.202](https://doi.org/10.1136/jnnp.57.2.202), indexed in Pubmed: [8126506](https://pubmed.ncbi.nlm.nih.gov/8126506/).
9. Levent C, Hatice K, Aziz G, et al. Double-edged blade, hemorrhagic or cardioembolic cognitive impairment. *J Geriatr Cardiol*. 2016; 13(8): 724–726, doi: [10.11909/j.issn.1671-5411.2016.08.012](https://doi.org/10.11909/j.issn.1671-5411.2016.08.012), indexed in Pubmed: [27781064](https://pubmed.ncbi.nlm.nih.gov/27781064/).
10. Farina E, Magni E, Ambrosini F, et al. Neuropsychological deficits in asymptomatic atrial fibrillation. *Acta Neurol Scand*. 1997; 96(5): 310–316, doi: [10.1111/j.1600-0404.1997.tb00289.x](https://doi.org/10.1111/j.1600-0404.1997.tb00289.x), indexed in Pubmed: [9405001](https://pubmed.ncbi.nlm.nih.gov/9405001/).
11. Forti P, Maioli F, Pisacane N, et al. Atrial fibrillation and risk of dementia in non-demented elderly subjects with and without mild cognitive impairment (MCI). *Arch Gerontol Geriatr*. 2007; 44(Suppl 1): 155–165, doi: [10.1016/j.archger.2007.01.023](https://doi.org/10.1016/j.archger.2007.01.023), indexed in Pubmed: [17317449](https://pubmed.ncbi.nlm.nih.gov/17317449/).
12. Barber M, Tait RC, Scott J, et al. Dementia in subjects with atrial fibrillation: hemostatic function and the role of anticoagulation. *J Thromb Haemost*. 2004; 2(11): 1873–1878, doi: [10.1111/j.1538-7836.2004.00993.x](https://doi.org/10.1111/j.1538-7836.2004.00993.x), indexed in Pubmed: [15550013](https://pubmed.ncbi.nlm.nih.gov/15550013/).
13. Bellomo A, De Benedetto G, Fossati C, et al. Atrial fibrillation (AF) and cognitive impairment in the elderly: a case-control study. *Arch Gerontol Geriatr*. 2012; 55(2): 247–250, doi: [10.1016/j.archger.2011.07.017](https://doi.org/10.1016/j.archger.2011.07.017), indexed in Pubmed: [21940057](https://pubmed.ncbi.nlm.nih.gov/21940057/).
14. Hart RG, Pearce LA, Rothbart RM, et al. Stroke with intermittent atrial fibrillation: incidence and predictors during aspirin therapy. *Stroke Prevention in Atrial Fibrillation Investigators*. *J Am Coll Cardiol*. 2000; 35(1): 183–187, doi: [10.1016/s0735-1097\(99\)00489-1](https://doi.org/10.1016/s0735-1097(99)00489-1), indexed in Pubmed: [10636278](https://pubmed.ncbi.nlm.nih.gov/10636278/).
15. Knecht S, Oelschläger C, Duning T, et al. Atrial fibrillation in stroke-free patients is associated with memory impairment and hippocampal atrophy. *Eur Heart J*. 2008; 29(17): 2125–2132, doi: [10.1093/eurheartj/ehn341](https://doi.org/10.1093/eurheartj/ehn341), indexed in Pubmed: [18667399](https://pubmed.ncbi.nlm.nih.gov/18667399/).
16. Chou RH, Chiu CC, Huang CC, et al. Prediction of vascular dementia and Alzheimer's disease in patients with atrial fibrillation or atrial flutter using CHADS₂ score. *J Chin Med Assoc*. 2016; 79(9): 470–476, doi: [10.1016/j.jcma.2016.02.007](https://doi.org/10.1016/j.jcma.2016.02.007), indexed in Pubmed: [27234974](https://pubmed.ncbi.nlm.nih.gov/27234974/).
17. Liao JN, Chao TF, Liu CJ, et al. Risk and prediction of dementia in patients with atrial fibrillation – a nationwide population-based cohort study. *Int J Cardiol*. 2015; 199: 25–30, doi: [10.1016/j.ijcard.2015.06.170](https://doi.org/10.1016/j.ijcard.2015.06.170), indexed in Pubmed: [26173170](https://pubmed.ncbi.nlm.nih.gov/26173170/).