$CHADS_2$ and CHA_2DS_2-VASc scores as tools for long-term mortality prognosis in patients with typical atrial flutter after catheter ablation

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KEY WORDS
$CHADS_2$ score, CHA_2DS_2-VASc score, mortality, typical atrial flutter

ABSTRACT

BACKGROUND The $CHADS_2$ and CHA_2DS_2-VASc scores were shown to predict mortality in patients with atrial fibrillation. However, pathophysiology and treatment outcomes of atrial fibrillation and typical atrial flutter (AFL) differ. Consequently, the prognosis of patients with AFL can also be different.

AIMS The aim of the study was to assess $CHADS_2$ and CHA_2DS_2-VASc scores as mortality predictors in patients with typical AFL.

METHODS Large cohort of consecutive patients with typical AFL who underwent catheter ablation was retrospectively analyzed. The $CHADS_2$ and CHA_2DS_2-VASc were calculated using hospital record data. All-cause mortality data was obtained from the registry of national personal identification numbers. The Kaplan–Meier method and multivariable Cox proportional hazard models were applied for survival and hazard ratio analyses, respectively.

RESULTS A total of 469 patients hospitalized for typical AFL ablation were enrolled (mean [SD] age, 63.7 [12.2] years; male sex, 69.1%). Patients were followed from 2 to 12 years resulting in 2974 patient-years of follow-up. The Kaplan–Meier survival analysis revealed a negative impact of each component of the $CHADS_2$ and CHA_2DS_2-VASc scores on survival with the exception of stroke (not significant) and female sex (related to a better survival). Consequently, higher scores were predictive of higher all-cause mortality rates (2.7%–54% at 10 years); the CHA_2DS_2-VASc score was equally predictive as the $CHADS_2$ score.

CONCLUSIONS In patients referred for typical AFL ablation, the $CHADS_2$ score can be applied for prognostic assessment. A successful AFL ablation procedure should not divert the attention from recognizing and addressing other medical issues that have an impact on long-term mortality, which remains very high in this population of patients.

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INTRODUCTION $CHADS_2$ and CHA_2DS_2-VASc scores were developed as stroke risk stratification tools in patients with nonvalvular atrial fibrillation (AF).[1,2] However, several studies have shown that these scores can be also used to predict survival of patients with AF and also of some non-AF patients.[3-8]

The typical atrial flutter (AFL) mechanism includes a reentrant right atrial arrhythmia with the macro reentrant circuit dependent on the cavotricuspid isthmus conduction. The pathophysiology for AFL is different as compared with AF. The success rate of radiofrequency catheter ablation in the management of AFL is much higher compared with AF ablation,[9] and consequently, prognosis of patients with AFL might be significantly different.[10] Data regarding long-term mortality after ablation in patients with typical AFL is limited and conflicting, and the utility of $CHADS_2$ and CHA_2DS_2-VASc scores in the AFL population for mortality assessment has never been studied.

WHAT'S NEW?

The present study is the first to evaluate the long-term prognostic value of the $CHADS_2$ and CHA_2DS_2-VASc scores for the assessment of the mortality risk in a large cohort of patients with typical atrial flutter after radiofrequency catheter ablation. This study shows that the $CHADS_2$ and CHA_2DS_2-VASc scores could be used to predict mortality in patients after radiofrequency catheter ablation for typical atrial flutter. Higher $CHADS_2$ scores were predictive of higher all-cause mortality, ranging from 2.7% to 54% at 10 years. This is the first study to assess the long-term mortality in patients with typical atrial flutter in the Polish population.

METHODS

Population This was a retrospective cohort study including all consecutive patients with typical AFL who underwent radiofrequency catheter ablation in our center between 2006 and 2016. The $CHADS_2$ and CHA_2DS_2-VASc scores (measured at the time of ablation) were calculated for each patient[1,2]; data for these calculations were obtained from the hospital records. Briefly, in these point systems, each capital letter represents one risk factor, 2 points are assigned for stroke / transient ischemic attack in medical history (S_2) or age 75 years or older (A_2), and 1 point is given for age between 65 and 74 years (A), history of hypertension (H), diabetes (D), cardiac failure (C), vascular disease including myocardial infarction, complex aortic plaque, or peripheral artery disease (V), and female sex (Sc).

Data regarding outcomes (all-cause mortality), as of February 2019, was obtained from the government-maintained database of national personal identification numbers (PESEL).

Ablation Radiofrequency ablation was performed according to an established technique.[11,12] Briefly, a multipolar halo catheter (Cordis Webster, Diamond Bar, California, United States, United States) was used to record the right atrial activation sequence around the tricuspid annulus and a decapolar catheter was inserted within the coronary sinus. An irrigated ablation catheter with a 3.5-mm tip (ThermoCool F curve, Cordis Webster) was used for creating an ablation line in the cavotricuspid isthmus. Stepwise withdrawal of the ablation catheter was performed after each 1-minute delivery of radiofrequency in order to create coalescent point-by-point ablation lesions from the tricuspid annulus to the inferior vena cava. An SR0 long sheath (Abbot, Abbott Park, Illinois, United States) was used in case of difficulty in reaching the ventricular side of the cavotricuspid isthmus. Atrial flutter noninducibility with right atrial and coronary sinus burst pacing (200–300 bpm) and bidirectional cavotricuspid isthmus block confirmed with atrial activation mapping were used as the ablation endpoints.

Statistical analysis The Kaplan–Meier analysis was used to estimate the survival functions for the endpoint (all-cause mortality). Univariate and multivariable Cox proportional hazard regression models were used to describe the effect of predictors on survival. The results of Cox models were presented as hazard ratios along with tests of significance and 95% CIs. There were no significant violations of the proportional hazard assumption that underlies the Cox models. Statistical analysis was performed with the R software, version 3.2 (R Foundation for Statistical Computing, Vienna, Austria). A *P* value of less than 0.05 was considered significant.

TABLE 1 Basic clinical characteristics of the study group

Variable	AFL ablation (n = 469)
Age, y, mean (SD)	63.7 (12.2)
Male sex	324 (69.1)
LVEF, %, mean (SD)	50.9 (14.9)[a]
LVEDD, mm, mean (SD)	54.1 (8.4)[a]
Comorbidities	
Heart failure	146 (31.1)
Vascular disease	81 (17.3)
Diabetes mellitus	109 (23.2)
Hypertension	351 (74.8)
Stroke	16 (3.4)
Atrial fibrillation	185 (39.4)

Data are presented as number (percentage) unless otherwise indicated.

a Echo data available for 173 patients (37%)

Abbreviations: AFL, atrial flutter; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end diastolic diameter

RESULTS A total of 469 consecutive patients with symptomatic typical AFL were enrolled and analyzed. Clinical characteristics of the study population are presented in TABLE 1. Patients were followed from 2 to 12 years, resulting in 2974 patient-years of follow-up and mean follow-up of 6.3 years. The Kaplan–Meier survival analysis revealed a negative impact of each component of the $CHADS_2$ and CHA_2DS_2-VASc scores on survival with the exception of stroke, which was not significant, and female sex, which was related to a better survival (FIGURES 1 and 2). Consequently, higher $CHADS_2$ and CHA_2DS_2-VASc scores were predictive of worse long-term survival (FIGURE 3). The mortality rates for $CHADS_2$ score at 10 years were 2.75% for 0 points, 21.4% for 1 point, 42.9% for 2 points, and 54.2% for 3 or more points. The mortality rates for the CHA_2DS_2-VASc score at 10 years

TABLE 2 Predictors of all-cause mortality in the multivariate Cox proportional hazards analysis

Variable	All-cause mortality after AFL ablation			
	$CHADS_2$		CHA_2DS_2-VASc	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
CHF	2.29 (1.56–3.38)	<0.001	1.95 (1.31–2.91)	0.001
Hypertension	1.08 (0.64–1.81)	0.77	0.99 (0.59–1.66)	0.972
Age ≥75 y	2.94 (1.99–4.34)	<0.001	4.23 (2.59–6.92)	<0.001
Diabetes	1.93 (1.30–2.85)	0.001	1.38 (1.24–2.7)	0.002
Stroke	1.53 (0.48–4.89)	0.47	1.51 (0.46–4.9)	0.494
Female sex	–	–	0.51 (0.32–0.82)	0.006
Vascular disease	–	–	1.75 (1.14–2.69)	0.01
Age, 65–74 y	–	–	2.34 (1.43–3.85)	0.001

Abbreviations: CHF, congestive heart failure; HR, hazard ratio; others, see TABLE 1

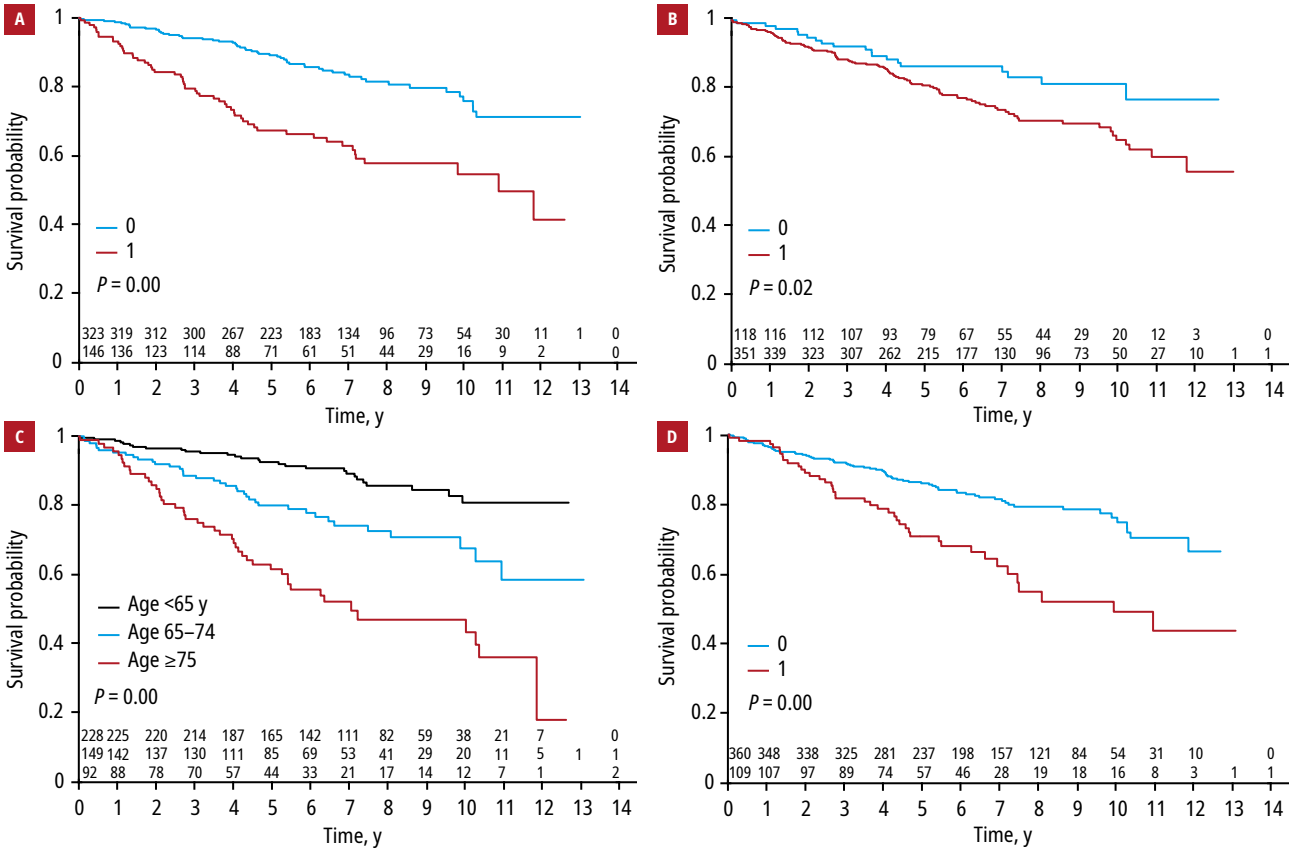

FIGURE 1 Kaplan–Meier survival curves for all-cause mortality with regard to 4 components of the $CHADS_2$ and CHA_2DS_2-VASc scores: congestive heart failure (**A**), arterial hypertension (**B**), different age categories (**C**), and diabetes mellitus (**D**). Blue line denotes the absence of a component (0); red line denotes the presence of a component (1).

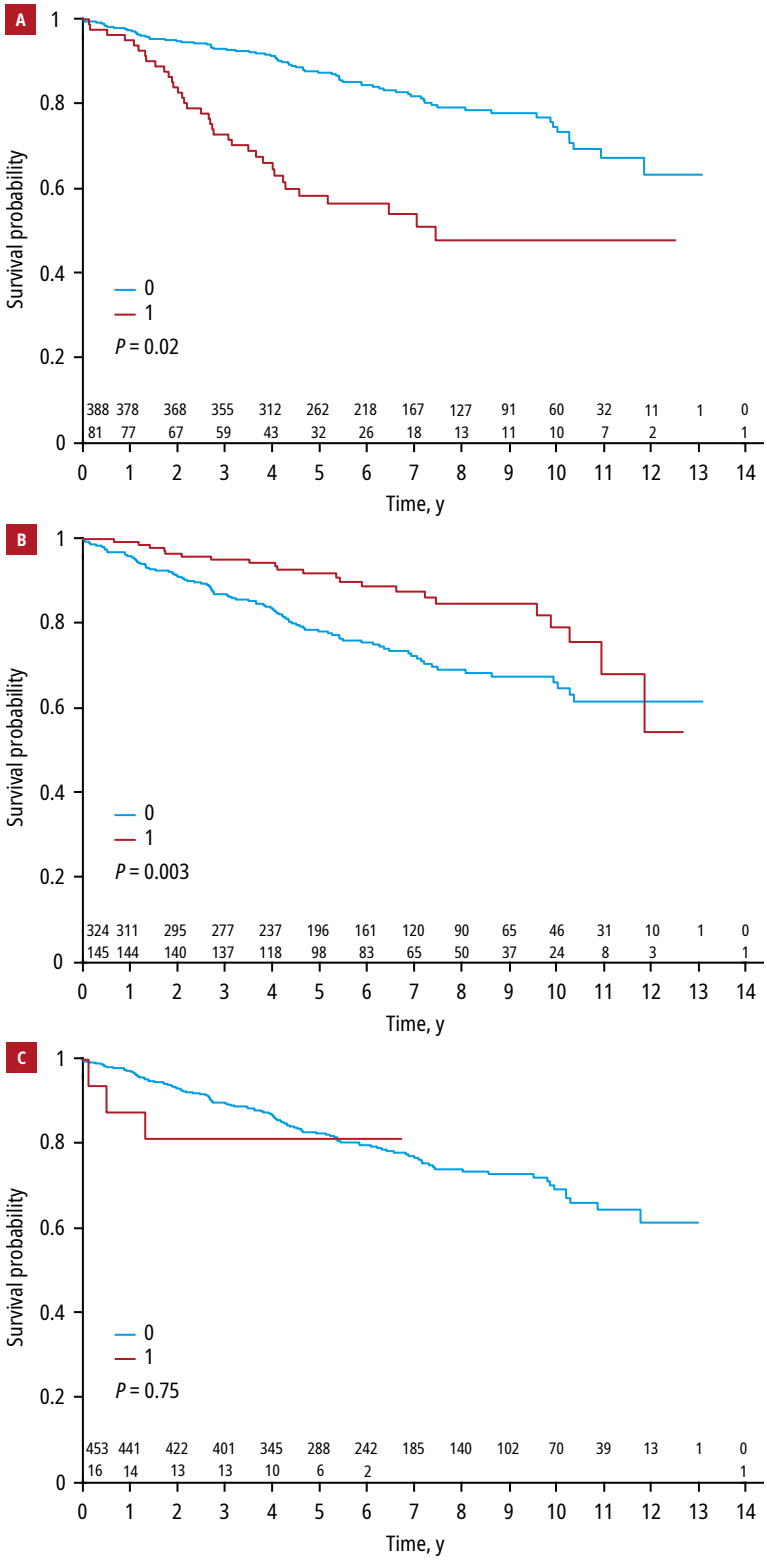

FIGURE 2 Kaplan–Meier survival curves for all-cause mortality with regard to 3 components of the $CHADS_2$ and the CHA_2DS_2-VASc scores: vascular disease (**A**), female sex (**B**), and stroke (**C**). Blue line denotes the absence of a component (0); red line denotes the presence of a component (1).

were 0% for 0 points, 11.0% for 1 point, 31.6% for 2 points, 31.9% for 3 points, 61.3% for 4 points, and 48.0% for 5 or more points.

Similarly, the multivariable Cox proportional hazard analysis showed an independent predictive value of 3 components of the $CHADS_2$ score (C, A, and D) and 6 components of the CHA_2DS_2-VASc score (C, A_2, D and V, A and Sc) (TABLE 2).

The CHA_2DS_2-VASc score did not show superiority over the simpler $CHADS_2$ score, with the C statistic of 0.778 and 0.748, respectively.

DISCUSSION

The present study is the first to evaluate the long-term prognostic value of the $CHADS_2$ and CHA_2DS_2-VASc scores to assess risk of death in a large cohort of patients with typical AFL. The main finding of the study was that these scores can be used to predict mortality in patients after ablation for typical AFL.

Long-term mortality in patients with atrial flutter

While there is an abundance of data concerning prognosis after atrial fibrillation (AF) ablation, data on long-term mortality in patients after typical AFL ablation are relatively sparse. Several studies suggested that patients with AFL are at a higher risk of death than patients with AF. One study reports that AFL ablation might lead to decrease in mortality in these patients.[13] A meta-analysis of 37 studies including 3433 patients, albeit with a mean (SD) follow-up of only 12.1 (0.6) months and including highly selected low-risk patients, reported all-cause mortality rate of only 3.3%.[14] This is similar to our results for 1-year mortality in low-mid $CHADS_2$ (0–1 points) and CHA_2DS_2-VASc (1–3 points) scores. However, in a study by Expósito et al[15] with a longer follow-up of 5 years, and nonselected population, the all-cause mortality rate was 15.8% (19 out of 188 patients) and in a study by Seara et al[16] with a follow-up of 5.9 years, the mortality rate was 18.4% (75 out of 408 patients). In the current study, which is the longest follow-up study to evaluate outcomes after typical AFL ablation, the total mortality rate was 23.9%. These long-term follow-up results suggest that despite successful ablation of AFL, patients are still at a high risk of death in the subsequent years. This warrants risk stratification in this population.

$CHADS_2$ and CHA_2DS_2-VASc for mortality prediction

The $CHADS_2$ and CHA_2DS_2-VASc scores were not primarily designed to predict mortality, yet their popularity and ease of application make it attractive and justified to test their usefulness not only for the assessment of the risk of stroke. Consequently, several studies have tested the scores in the context of predicting mortality in both AF and non-AF populations.[3-8,14] For example, Lahewala et al[5] found a strong association between the CHA_2DS_2-VASc score and in-hospital mortality ranging from 0.2% for 0 points to 3.2% for 6 points or more, Poçi et al[3] and Crandall et al[17] have applied the $CHADS_2$ score to non-AF patients with coronary heart disease and found that it predicts mortality during both acute coronary

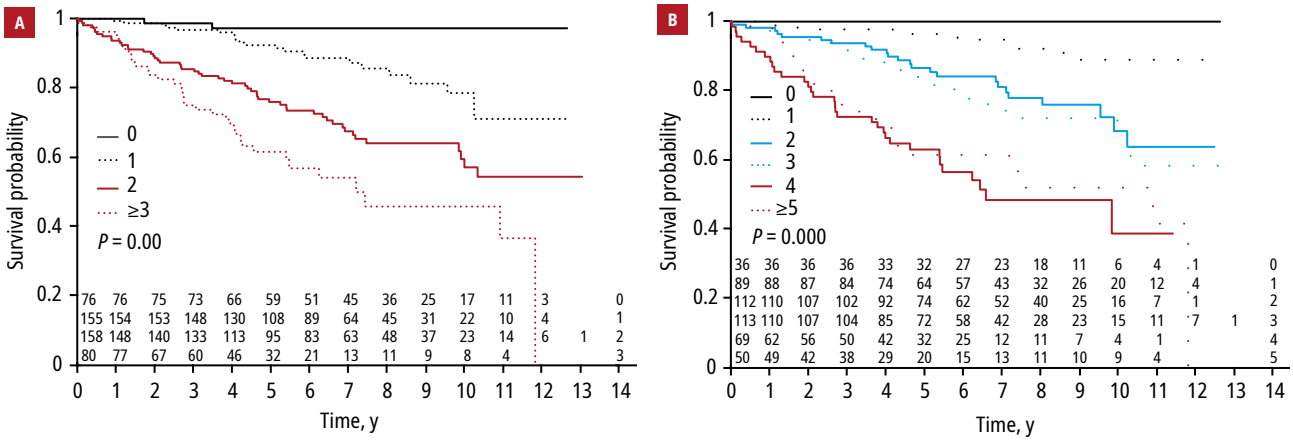

FIGURE 3 Kaplan–Meier survival curves for all-cause mortality with regard to the number of points assigned based on the $CHADS_2$ (**A**) and CHA_2DS_2-VASc (**B**) scores

syndromes and stable angina, while Svendsen et al[7] reported that the $CHADS_2$ and CHA_2DS_2-VASc scores are associated with an increased risk of death in patients paced for sick sinus syndrome. Importantly, this association was not related to the presence of AF in the population of patients with a pacemaker. Our results corroborate and expand these observations by showing that $CHADS_2$ and CHA_2DS_2-VASc scores can be used to predict mortality also in patients after ablation for typical AFL. The risk factors – components of these scores were found important also in multivariable analysis both by us and by others. We found that age, heart failure, and diabetes were independently related to mortality (TABLE 2). The same factors were found as mortality predictors by Seara et al[16] in patients with AFL and by Svendsen et al[7] in patients with sick sinus syndrome. The most potent mortality predictor in our cohort, that is, chronological age, although inferior to biological age, is still very informative about general health. It reflects length of exposure to multiple risk factors and environment. We believe that the strong impact of age in our study reflects the burden of comorbidities that accumulate with age and that are not included in the $CHADS_2$ and CHA_2DS_2-VASc scores. The lack of significant impact of stroke on prognosis might be related to long-term anticoagulation and a small number of events (only 16 strokes in our cohort). Although hypertension and stroke did not have an independent predictive power, trend analysis suggests a similar impact (higher hazard ratio) to that of the other variables and seem valuable when included in the score, as each additional score point resulted in an increased risk.

An analysis of an extensive set of clinical, biochemical, and other variables could probably provide basis for a score dedicated to patients with AFL with a better predictive power than $CHADS_2$, which is based on a limited set of data. However, the need for additional information, such as results of laboratory tests or echocardiography, or access to a computer for difficult calculations would significantly limit the impact of such a score. Moreover, from a practical point of view, new prognostic scores tend to have limited popularity, which further limits their usefulness.[18] In contrast, $CHADS_2$ is already widely known and straightforward, both in out-patient and in-hospital settings as the required data is readily available. This makes our results more pertinent to clinical practice.

Limitations Our study has some limitations. It was a single-center retrospective study. An analysis of the cause of death was not performed; however, data from other studies point to the usual causes of death in patients with AFL with a similar contribution of cardiovascular diseases as in the general Polish population.[15,16,19] The impact of AF on prognosis in patients with AFL was not studied, mainly due to the lack of reliable means to verify the AF diagnosis, which in our experience, is not uncommonly erroneous in patients with AFL due to many similarities between these 2 arrhythmias. However, we used information on unconfirmed AF diagnosis obtained from the available medical documentation and we performed the Kaplan–Meier analysis, which showed that AF had no influence on long-term mortality in patients with AFL (Supplementary material, *Figure S1*).

Conclusions It seems that in patients referred for typical AFL ablation, the $CHADS_2$ and/or CHA_2DS_2-VASc scores can be applied to assess prognosis. A successful AFL ablation procedure should not divert the attention from recognizing and addressing other medical issues that have an impact on long-term mortality, which is very high in this particular population.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/kardiologiapolska.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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