ORIGINAL ARTICLE

The impact of cigarette smoking in predicting stroke using CHADS$_2$ and CHA$_2$DS$_2$-VASc schemas

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Abstract

Objective To determine the impact of smoking status in the prediction of stroke using CHADS$_2$ and CHA$_2$DS$_2$-VASc schemes.

Methods Five hundred twenty-eight consecutive patients with arrhythmic symptoms and without any documented arrhythmia from Queen Mary Hospital, Hong Kong, were followed up to determine the incidence of ischemic stroke, new-onset atrial fibrillation (AF), or all-cause mortality. Smoking status was classified into nonsmokers and smokers. The pairwise comparisons of C-statistics for outcomes were performed.

Results During a median follow-up period of 6.2 years, 65 (12.3%) individuals developed ischemic stroke. Smokers experienced higher annual incidence of stroke, a new-onset AF, and all-cause death compare to nonsmokers, with corresponding hazard ratio (HR) of stroke, AF, and all-cause death being 2.51 (95% confidence intervals, CI 1.36als, CIse death bein 1.15a3.24), and 1.95 (95% CI 1.161.95 (95% CIath being 2.51 (95% confidence corr$_2$ and CHA$_2$DS$_2$-VASc for stroke were 0.60 (95% CI 0.51 for st$p$ = 0.09) and 0.59 (95% CI 0.50 (95%, p = 0.15) respectively, whereas the C-statistics of CHADS$_2$ and CHA$_2$DS$_2$-VASc were 0.66 (95% CI 0.61 were 0p = 0.005), 0.75 (95% CI 0.7 CI 0.7p < 0.0001), respectively among nonsmokers. After incorporating smoking, both the CHADS$_2$-smoking and CHA$_2$DS$_2$-VASc-smoking achieved better C-statistics for new-onset ischemic stroke prediction superior to baseline score systems in male groups.

Conclusion Cigarette smoking status has impact on stroke stratification using CHADS$_2$ and CHA$_2$DS$_2$-VASc scheme. The discrimination of the CHADS$_2$ and CHA$_2$DS$_2$-VASc scheme for stroke can be significantly improved if smoking status is additionally considered.

Keywords Ischemic stroke · Cigarette smoking · Risk prediction · CHADS$_2$ · CHA$_2$DS$_2$-VASc

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Introduction

Stroke that often shows up unnoticed in our life remains a major healthcare problem. Howard et al. forecasted that the number of stroke events will dramatically increase (more than double) from 2010 to 2050, and the increased burden of care of stroke patients on an already stressed healthcare system could be overwhelming [1]. Not only will this burden fall on physicians and hospitals, rather enhance the demand for rehabilitation services and increased nursing home. Therefore, early identification of individual with risk might enable a closer surveillance for the susceptibility of stroke incident and therefore prompt initiation of oral anti-platelet or anticoagulation treatment for stroke prevention.

Generally, current stroke risk stratification schemas such as $CHADS_2$, CHA_2DS_2-VASc, and NICE are validated stratification tools to estimate the risk factor of stroke occurrence used as guideline for oral anticoagulation therapy among non-valvular atrial fibrillation (NVAF) patients [2, 3], though Trousseau score recently appeared for differentiating cancer-associated stroke in patients with cancer [4]. Compared to the $CHADS_2$ score, the CHA_2DS_2-VASc score includes three additional risk factors: female, age 64–75, and vascular disease for ischemic stroke, whereas cigarette smoking status is not considered during risk assessment in all those validation cohorts mentioned above. Cigarette smoking is a well-known risk factor for ischemic stroke and associated with an approximate doubling of risk for ischemic stroke after adjustment for other risk factors [5, 6]. Smoking status relates to atherosclerosis, vascular damage (e.g., endothelial dysfunction), AF incidence (e.g., increased atrial fibrosis), and the incidence of mild cognitive impairment as well [7, 8].

In recent studies, $CHADS_2$ and CHA_2DS_2-VASc scores have been reported with similar (modest) predictive capacity for stroke in general population and non-AF patient populations including the risk of death after stroke, new-onset AF, and stroke in unselected patients [9–11]. However, little is known about the impact of smoking on the incidence of stroke in patients with arrhythmic symptoms but no AF recorded. In the present study, we determined the impact of smoking status for the prediction of stroke using $CHADS_2$ and CHA_2DS_2-VASc schemes.

Patients and methods

Design and sampling

The cohort study was established in Hong Kong and approved by the local ethics committee, and individual informed consent was obtained from all subjects. The study design has been reported in detail elsewhere [12]. In brief, 743 consecutive patients were referred to the cardiac clinic of Queen Mary Hospital, Hong Kong for assessment of palpitation, dizziness, and/or syncope.

Data collection and clinical evaluation

For each patient, demographics at baseline, detailed medical history, medication use, and cardiovascular diseases were recorded. Thorough clinical examination, standard 12-lead electrocardiogram, Holter, and conventional echocardiographic examination were performed. Left ventricular ejection fraction was measured by echocardiography using a biplane modified Simpson's method with the GE Vivid 7 (GE Healthcare, Milwaukee, Wisconsin). Blood samples were obtained by venipuncture on the same day of the procedure after a 12-h overnight fast and drew into standardized tubes that were delivered to the laboratory within a few minutes. Fasting blood glucose, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, and renal function tests were performed using standard laboratory methods. Diabetes was considered present if fasting blood glucose 126 mg/dl or low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, and renal function tests were performed using standard laboratory methods. Diabetes was considered present if the fasting blood glucose was higher than 126 mg/dl or the subject was taking antidiabetic medication. Hypertension was defined as systolic and diastolic blood pressures are higher than 140 mmHg and 90 mmHg, respectively, or if the subject was taking antihypertensive medication. Heart failure and history of stroke/TIA in medical record, and vascular diseases including myocardial infarction, peripheral artery disease, and complex aortic plaque were evaluated [3].

Smoking status

Smoking status was classified as follows: Nonsmokers were defined as former smokers and individuals who never smoked. Current-smokers were defined as those who have been smoking at least one cigarette per day [13]. We also grouped current smokers according to their cigarettes consumption, as follows: < 10, 10–19, and ≥ 20 cigarettes/day.

Risk score calculation

The $CHADS_2$ score was calculated as the following: 1 point was assigned to chronic heart failure, hypertension (HT), age over 75 years, and diabetes mellitus (DM), respectively; 2 points was assigned to the history of stroke. The CHA_2DS_2-VASc score is a modification of the $CHADS_2$ score by adding 1 point each for three additional risk factors: vascular disease (V), age of 65 to 74 years (A), and gender of female (as a sex category). The $CHADS_2$-S or CHA_2DS_2-VASc-S score adds smoking (S) to the previous scores. The maximum $CHADS_2$,

CHA_2DS_2-VASc, $CHADS_2$-S, and CHA_2DS_2-VASc-S were 6, 9, 7, and 10 respectively.

Follow-up and end point

Patients were followed up to determine the incidence of the primary end point of ischemic stroke, new-onset AF, or all-cause mortality. Information on the end points was collected from hospital databases and responses to questionnaires by patients themselves or their family members. The new occurrence of clinical AF was defined as the presence of AF documented by resting 12-lead ECGs. Ischemic stroke was defined as a neurological deficit of sudden onset that persisted for more than 24 h in the absence of intracerebral and subarachnoid hemorrhage, and that could not be explained by other causes (trauma, infection, and vasculitis). Stroke was confirmed by computerized axial tomography or magnetic resonance imaging of the brain. Death events were determined by a query of computerized social security death records and the medical records.

Statistical analyses

The baseline information is summarized as mean ± standard deviation for continuous variables and as frequencies for discrete variables. Comparisons between the smoker and non-smoker groups were performed using Student us$t$ test. Categorical variables were summarized as percentages and compared with the chi-square or Fisherrized as perc. Hazard ratios (HRs) and their 95% confidence intervals (CIs) were computed by means of time-dependent Cox regression models. To predict stroke or AF and death, the discriminatory power toward $CHADS_2$ and CHA_2DS_2-VASc was quantified by determining the area under the receiver operator characteristic (ROC). The pairwise comparisons of ROC curves for each outcome were performed. Data were analyzed with SPSS 15.0 (SPSS, Inc. Chicago, IL) and MedCalc Statistical Software11.4 (MedCalc Software bvba, Ostend, Belgium). A p value < 0.05 was considered nominally significant. Ideal prediction yields a C-statistics of 1.00, whereas a value of < 0.5 reflects that prediction is no better than chance.

Results

Baseline characteristics and risk scores by smoking

A total of 743 consecutive patients were admitted for the study, and 215 were excluded due to any documented high-grade atrioventricular block and/or sustained cardiac arrhythmias including AF during resting ECG and 24-h ECGs, the presence of any implantable pacemaker or cardioverter defibrillators, hyperthyroidism, major valvular heart diseases, or

incomplete clinical or follow-up data. As a result, a total of 528 Chinese and other Asian participants, including 145 smokers and 383 nonsmokers, were registered for clinical trial and follow-up studies. The participants have an average age of 68.5 years and 46.2% were male; 45.3% had hypertension; 17.1% had diabetes mellitus; 18.5% had coronary artery disease (CAD).

The mean age of the smokers was 67 years. The percentage of smokers in male group was higher than in female group. Among the smoker's group, 48.3% of them received antiplatelet administration. The nonsmokers had an average age of 66 years and 32.0% of them had antiplatelet therapy. The prevalence of CAD is higher among smokers than nonsmokers. There is a higher portion of smokers than nonsmokers who have $CHADS_2$ score equal or more than 2. There is no difference between the CHA_2DS_2-VASc scores of smokers and nonsmokers across different strata (Table 1).

However, based on the CHA_2DS_2-VASc scores, the proportions of cigarette smokers with CHA_2DS_2-VASc score of 0 and 1 were heterogeneously distributed ($p = 0.048$) with 38% smokers in the score of 0 and with 24% smokers in the score of 1. The proportions of cigarette smokers with CHA_2DS_2-VASc score of 3 and ≥ 4 were also heterogeneously distributed ($p = 0.040$) with 38% smokers in the score of 3 and with 19% smokers in the score of ≥ 4. Whereas, there was no significant heterogeneity of cigarette smoking in $CHADS_2$ score of 0 and 1, and 1 and ≥ 2 in this population ($p = 0.77$, 0.058 respectively).

Comparison of hazard ratios by smoking

During the median follow-up period of 6.2 years, 65 (12.3%) developed ischemic stroke, 89 (16.8%) were newly diagnosed with AF, and 89 (16.8%) died in the study groups.

Table 2 shows the annual events rates in this population and hazard ratios for outcomes by smoking status. The risk of the endpoints was significantly higher among smokers during follow-up, with corresponding HR for stroke, new-onset AF, and death being 2.51 (95% CI 1.36% CIt, $p = 0.003$), 1.93 (95% CI 1.153), $1.9 p = 0.01$), and 1.95 (95% CI 1.16 1.95 ($p = 0.01$), respectively.

Comparison of annual event rates by risk scores and smoking

Higher incidence of annual risk of stroke was observed in CHA_2DS_2-VASc score of 0 than that of 1 (0.85 vs. 0.57, $p = 0.048$), although all patients with higher $CHADS_2$ or CHA_2DS_2-VASc scores were more likely to suffer from ischemic stroke.

Figure 1 shows annual event rates according to different risk stratification in nonsmokers and smokers. There was significantly different risk trend of ischemic stroke between the

Table 1 Baseline characteristics and risk scores by cigarette smoking

	Total population (n = 528)	Nonsmokers (n = 383)	Smokers (n = 145)	p
Mean age (SD, years)	66.7 ± 10.2	65.7 ± 9.9	68.9 ± 10.4	0.004*
Age ≥ 75, n (%)	138 (26.1)	84 (21.9)	54 (37.3)	0.001*
Age 65–70, n (%)	159 (30.1)	121 (31.6)	38 (26.3)	0.005*
Male, n (%)	230 (43.7)	113 (29.6)	117 (80.5)	0.000*
CHF, n (%)	--	--	--	
HT, n (%)	239 (45.3)	171 (44.8)	68 (46.6)	0.74
DM, n (%)	90 (17.1)	59 (15.5)	31 (21.2)	0.16
CAD, n (%)	92 (17.5)	57 (14.8)	35 (24.6)	0.02*
Pre stroke /TIA, n (%)	---	---	---	
Echo				
LAD (mm)	3.8 ± 0.8	3.8 ± 0.8	3.9 ± 0.8	0.38
LVEF (%)	65.8 ± 8.1	66.1 ± 7.8	64.8 ± 8.6	0.13
Anyantiplatelet therapy, n (%)	195 (36.9)	122 (32.0)	73 (48.3)	0.001*
$CHADS_2$ score				0.03*
0	215 (40.6)	162 (42.2)	53 (36.4)	0.49
1	180 (34.1)	138 (36.1)	42 (28.8)	0.32
≥ 2	133 (25.1)	83 (21.6)	50 (34.7)	0.03
$CHA_2DS_2\text{-}VASc$ score				
0	48 (9.1)	30 (7.7)	18 (12.7)	0.19
1	142 (26.9)	107 (28.1)	34 (23.7)	0.49
≥ 2	338 (62)	246 (69.2)	93 (63.6)	0.94

CHF indicates congestive heart failure; *HT*, hypertension; *DM*, diabetes mellitus; *CAD*, coronary artery disease; *TIA*, transient ischemic attack; *LAD*, left atrial dimension; *LVEF*, left ventricular ejection fraction; *CHADS2*, C congestive heart failure; *H*, hypertension; *A*, age >75; *D*, diabetes mellitus and *S*, prior stroke or transient ischemic attack; *CHA2DS2-VASc, C*, congetive heart failure; *H*, hypertension, *A2*, age 65 to 74 years and age ≥ 75 years; *D*, diabetes mellitus, and *S*, prior stroke or transient ischemic attack; *VA*, vascular disease; *Sc*, sex category. *$p < 0.05$

two groups. Nonsmoker group with higher risk score experienced higher cumulative event rate stratified by either $CHADS_2$ or CHA_2DS_2-VASc score. Moreover, no ischemic stroke events were recorded with CHA_2DS_2-VASc score of 0. However, smoker group with lower risk score suffered from higher risk trend of ischemic stroke during follow-up.

The impact of smoking on stroke prediction by comparison of ROC

We further performed receiver-operating characteristic analysis to determine the prediction for ischemic stroke, new-onset AF, and death using $CHADS_2$ and CHA_2DS_2-VASc among

nonsmokers and smokers. Table 3 presents the comparison of the two scoring systems for ischemic stroke, new-onset AF, and death. Among smokers, predictivity performance of the two schemes for ischemic stroke and death was poorer than that among nonsmokers. The area under the curve of $CHADS_2$ and CHA_2DS_2-VASc for ischemic stroke among smokers were 0.60 (95% CI 0.5–0.69, $p = 0.09$) and 0.59 (95% CI 0.50–0.68, $p = 0.15$), respectively. Whereas, the area under the curve of $CHADS_2$ and CHA_2DS_2-VASc for ischemic stroke among nonsmokers were 0.66 (95% CI 0.61 Ifor is $p = 0.005$), 0.75 (95% CI 0.75), 0.7$p< 0.0001$), respectively. Figure 2 shows that nonsmokers had a higher area under the curve of $CHADS_2$ and CHA_2DS_2-VASc for stroke compared

Table 2 Events rates by smoking status and hazard ratios for outcomes

	Event rate (%/year)		p value		HR (95% CI)	p value
	Nonsmokers		Smokers			
Ischemic stroke	0.042		0.069	0.002	2.51 (1.36–4.64)	0.003*
New-onset AF	0.059		0.112	0.01	1.93 (1.15–3.24)	0.01*
Death	0.065		0.113	0.02	1.95 (1.16–2.27)	0.01*

*Log-rank *p* value for nonsmokers versus smokers, *CI* confidence interval

Fig. 1 Annual event rates according to risk stratification in nonsmokers and smokers. **a** Cumulative event rate of patients with or without smoking by $CHADS_2$ score. **b** Cumulative event rate of patients with or without smoking by CHA_2DS_2-VASc score
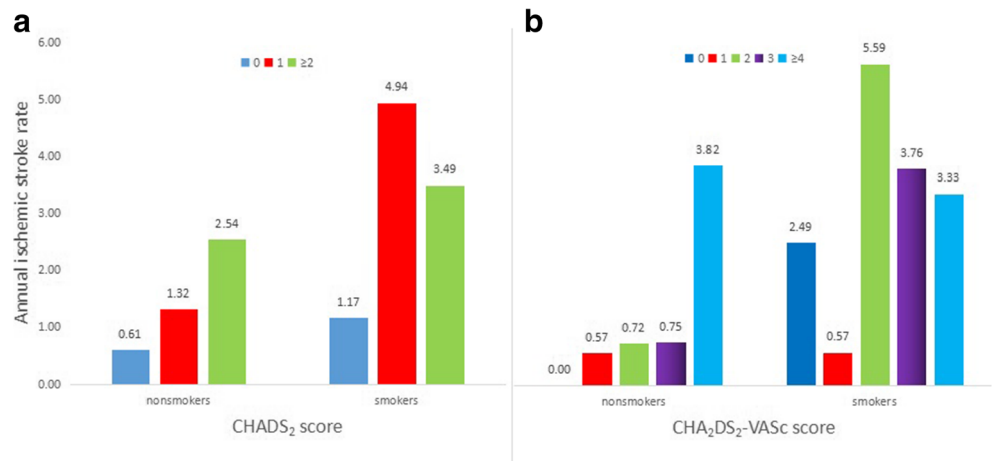
to smokers subjects. Moreover, CHA_2DS_2-VASc score had also better performance than $CHADS_2$ among nonsmokers.

To account for the potential effect of cigarette smoking for predicting stroke incidence using $CHADS_2$ and CHA_2DS_2-VASc schemas, we excluded female who seldom smoked. After incorporating smoking, $CHADS_2$-S was better predictor for ischemic stroke compared to baseline $CHADS_2$ ($p = 0.006$) in male groups. Similarly, CHA_2DS_2-VASc-S achieved better C-Statistic compared to baseline CHA_2DS_2-VASc score ($p = 0.01$, Fig 3) in male groups. The C-statistics with 95% confidence interval (95% CI) for that respective scores were $CHADS_2$ 0.59 (95% CI 0.522–0.667, $p = 0.10$); $CHADS_2$-S 0.67 (95% CI 0.596–0.736, $p = 0.004$); CHA_2DS_2-VASc 0.63 (95% CI 0.556–0.699, $p = 0.03$); and CHA_2DS_2-VASc-S 0.68 (95% CI 0.605–0.744, $p = 0.002$) in male groups.

Discussion

In this study, we have demonstrated that cigarette smoking has impact on stroke risk stratification using $CHADS_2$ and CHA_2DS_2-VASc schemes in patients with arrhythmic symptoms without documented AF. The relatively poorer performance of the risk scores was shown in smokers. The area

under the ROC curve for CHA_2DS_2-VASc scores was significantly higher in nonsmokers than in smokers (0.75 vs. 0.59, $p<0.05$). After incorporating smoking, risk factor for ischemic stroke, to both the $CHADS_2$-S and CHA_2DS_2-VASc-S score, we can get superior estimates in the risk prediction of ischemic stroke in male groups. Our results suggest that cigarette smoking status should be additionally considered when estimating the risk of ischemic stroke.

To our knowledge, this is the important study for the prediction of ischemic stroke among patients with arrhythmic symptoms without documented AF on presentation stratified by cigarette smoking. Previous studies have addressed the cigarette smoking as an independent risk factor for initial and recurrent ischemic stroke [14–16]. In addition, spousal smoking poses important stroke risks for never-smokers and former smokers (HR 1.42, 1.72, respectively) [17]. In the present study, HR for ischemic stroke among smoking patients is compared with non-smoking counterparts ranged from 1.36 to 4.64 (HR = 2.51, $p = 0.003$), which reaffirms that patients with cigarette smoking represent a "high-risk" population. Indeed, smoking continued to be a strong independent predictor for stroke occurrence [18], major adverse cardiac, and cerebrovascular events (MACCE) (OR = 2.34, 95% CI 1.49–3.68) after adjustment for clinical and angiographic variables in patients

Table 3 Comparison of ROC by smoking

| Events	Parameter	C-statistics (95% CI)			
		Nonsmokers	p	Smokers	p
Stroke	$CHADS_2$	0.66 (0.61–0.71)	0.005*	0.60 (0.51–0.69)	0.09
	CHA_2DS_2-VASc	0.75 (0.70–0.80)	0.0001*	0.59 (0.50–0.68)	0.15
AF	$CHADS_2$	0.65 (0.59–0.70)	0.0003*	0.65 (0.55–0.73)	0.01*
	CHA_2DS_2-VASc	0.70 (0.65–0.75)	< 0.0001*	0.68 (0.59–0.76)	0.0016*
Death	$CHADS_2$	0.61 (0.55–0.66)	0.02*	0.60 (0.51–0.69)	0.06
	CHA_2DS_2-VASc	0.70 (0.65–0.75)	< 0.0001*	0.60 (0.51–0.69)	0.08

ROC receiver operating characteristic curve; *$p < 0.05$
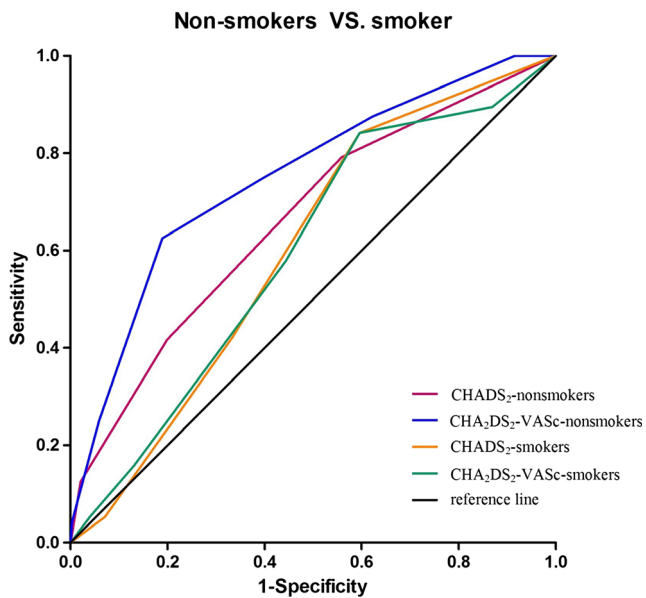
Fig. 2 Receive-operating characteristic (ROC) curves for the performance of $CHADS_2$ and CHA_2DS_2-VASc scores in predicting stroke according to cigarette smoking

treated with drug-eluting stents [19]. By contrast, nonsmoking was a significant prognostic factor of favorable outcomes after ischemic stroke, and long-time smoking had a negative effect on stroke severity [20, 21].

On the other hand, lower score did not correspond to lower annual stroke rate when stratified by CHA_2DS_2-VASc score among all patients (0.85 in CHA_2DS_2-VASc score of 0, 0.57 in CHA_2DS_2-VASc score of 1) [12]. By contrast, we observed that the risk of stroke during follow-up increased with $CHADS_2$ score, as it was double for patients with $CHADS_2$ score of 1 compared with score of 0. This may be partially due to the heterogeneity of cigarette smoking, with higher
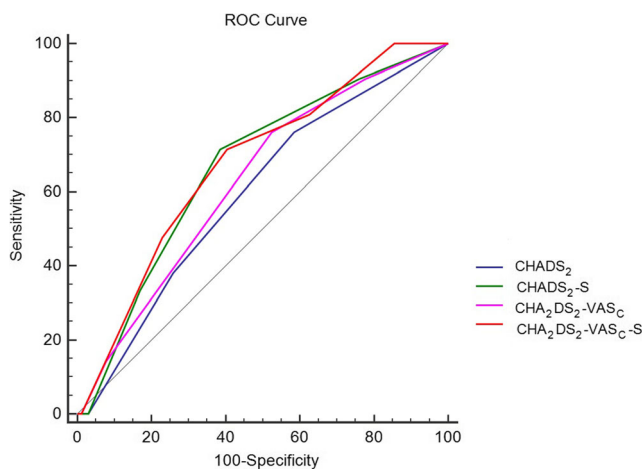
Fig. 3 Receiver-operating characteristic (ROC) curves of $CHADS_2$, CHA_2DS_2-VASc, and combined smoking scores for prediction of new-onset ischemic stroke

proportion of cigarette smoking in CHA_2DS_2-VASc score of 0 compared with those in the score of 1. There was no significant heterogeneity of cigarette smoking in $CHADS_2$ score of 0 and 1 in this population ($p = 0.77$). As a confounding factor, the heterogeneity of smoking maybe had some effect on the prediction performance of CHA_2DS_2-VASc schema. Indeed, during the subgroup analysis of smokers was excluded whereas nonsmokers with higher risk score experienced higher cumulative event rate and no ischemic stroke events were recorded with CHA_2DS_2-VASc score of 0 during follow-up. On the contrary, smokers with lower risk score suffered from higher ischemic stroke.

Since smokers had a higher risk of stroke events rate, how to improve risk stratification is an important issue. In the present study, both the C-statistics of $CHADS_2$ and CHA_2DS_2-VASc in smokers were poorer than that in nonsmoking population. Moreover, CHA_2DS_2-VASc score performed better than $CHADS_2$ among nonsmokers in predicting ischemic stroke assessed by the C-statistics, which suggested that cigarette smoking has impact on stroke risk stratification.

Existing schemes to predict ischemic stroke do not include cigarette smoking as an independent predictor for stroke events. Even it has been underrepresented in clinical trials and entirely absent from the completed double-blind trial of factors associated with ischemic stroke [22, 23], indeed, revised schemes must be comprehensive enough to incorporate all the independent variables that contribute importantly to the risk factors of stroke. Recently, efforts to improve risk stratification have been made. For example, the CHA_2DS_2-VASc-HS or CHA_2DS_2-VASc-HSF score, which includes hyperlipidemia (HL) and smoking (S) or family history(F), is found to be the best score scheme to predict CAD severity in comparison to ROC curves, such as a score > 2 may predict CAD severity [24, 25]. Therefore, further investigation is needed to develop more accurate stroke risk stratification scheme by incorporating cigarette smoking status to $CHADS_2$ or CHA_2DS_2-VASc score schema.

In the present study, when additional smoking status was considered, we found that CHA_2DS_2-VASc score offered excellent predictability for stroke in nonsmokers and limited predictability in smokers (C-statistics 0.75 vs. 0.59, respectively). Additionally, real low risk of stroke (i.e., those entirely free of stroke events at 6.2 ± 1.3 years) can be identified by CHA_2DS_2-VASc score in nonsmokers. Our novel data suggests that incorporating smoking as a risk factor for ischemic stroke, to both the $CHADS_2$ and CHA_2DS_2-VASc score, resulted in superior estimates for the risk prediction of ischemic stroke in male groups.

Conclusion

In this population of patients that were referred for assessment of palpitation, dizziness, and/or syncope, smokers experienced

higher hazard ratio (HR) of stroke, AF, and all-cause death. The discrimination of the CHADS$_2$ and CHA$_2$DS$_2$-VASc scheme for stroke can be significantly improved when smoking status was additionally considered. Future studies are warranted to determine the smoking-specific risk stratification.

Strengths and limitations

The present study was comprised of a single-center design with a relatively small sample size, and therefore the results might differ if a larger population were used. The study was based on patients who were admitted for assessment of palpitation, dizziness, and/or syncope, which may be observer bias. Therefore, the results need to be reaffirmed in a more representative large patient population.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Howard G, Goff DC (2012) Population shifts and the future of stroke: forecasts of the future burden of stroke. Ann N Y Acad Sci 1268:14–20
2. Stroke Risk in Atrial Fibrillation Working G (2008) Comparison of 12 risk stratification schemes to predict stroke in patients with nonvalvular atrial fibrillation. Stroke 39(6):1901–1910
3. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ (2010) Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest 137(2):263–272
4. Hasegawa Y, Setoguchi T, Sakaida T, Iuchi T (2020) Utility of a scoring system for differentiating cancer-associated stroke from cryptogenic stroke in patients with cancer. Neurol Sci 41:1245–1250
5. Goldstein LB, Bushnell CD, Adams RJ et al (2011) Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 42(2):517–584
6. Goldstein LB, Adams R, Alberts MJ, Appel LJ, Brass LM, Bushnell CD, Culebras A, DeGraba T, Gorelick PB, Guyton JR, Hart RG, Howard G, Kelly-Hayes M, Nixon JV, Sacco RL, American Heart Association, American Stroke Association Stroke Council (2006) Primary prevention of ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council: cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation 113(24):e873–e923
7. Aune D, Schlesinger S, Norat T, Riboli E (2018) Tobacco smoking and the risk of atrial fibrillation: a systematic review and meta-analysis of prospective studies. Eur J Prev Cardiol 25(13):1437–1451
8. Hu M, Yin H, Shu X, Jia Y, Leng M, Chen L (2019) Multi-angles of smoking and mild cognitive impairment: is the association mediated by sleep duration? Neurol Sci 40(5):1019–1027
9. Biancari F, Asim Mahar MA, Kangasniemi OP (2013) CHADS2 and CHA2DS2-VASc scores for prediction of immediate and late stroke after coronary artery bypass graft surgery. J Stroke Cerebrovasc Dis 22(8):1304–1311
10. Chan YH, Yiu KH, Lau KK, Yiu YF, Li SW, Lam TH, Lau CP, Siu CW, Tse HF (2014) The CHADS2 and CHA2DS2-VASc scores predict adverse vascular function, ischemic stroke and cardiovascular death in high-risk patients without atrial fibrillation: role of incorporating PR prolongation. Atherosclerosis 237(2):504–513
11. Mitchell LB, Southern DA, Galbraith D et al (2014) Prediction of stroke or TIA in patients without atrial fibrillation using CHADS2 and CHA2DS2-VASc scores. Heart 100(19):1524–1530
12. Zuo ML, Liu S, Chan KH et al (2013) The CHADS2 and CHA 2DS 2-VASc scores predict new occurrence of atrial fibrillation and ischemic stroke. J Interv Card Electrophysiol 37(1):47–54
13. Bossard M, Granger CB, Tanguay JF, Montalescot G, Faxon DP, Jolly SS, Widimsky P, Niemela K, Steg PG, Natarajan MK, Gao P, Fox KAA, Yusuf S, Mehta SR (2017) Double-dose versus standard-dose clopidogrel according to smoking status among patients with acute coronary syndromes undergoing percutaneous coronary intervention. J Am Heart Assoc 6(11)
14. Kelly TN, Gu D, Chen J et al (2008) Cigarette smoking and risk of stroke in the Chinese adult population. Stroke 39(6):1688–1693
15. Hankey GJ (2005) Preventable stroke and stroke prevention. J Thromb Haemost 3(8):1638–1645
16. Goldstein LB, Adams R, Alberts MJ et al (2006) Primary prevention of ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council: cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: the American Academy of Neurology affirms the value of this guideline. Stroke 37(6):1583–1633
17. Glymour MM, Defries TB, Kawachi I, Avendano M (2008) Spousal smoking and incidence of first stroke: the Health and Retirement Study. Am J Prev Med 35(3):245–248
18. Glymour MM, Avendano M (2009) Can self-reported strokes be used to study stroke incidence and risk factors?: evidence from the health and retirement study. Stroke 40(3):873–879
19. Sherif MA, Nienaber CA, Toelg R et al (2011) Impact of smoking on the outcome of patients treated with drug-eluting stents: 1-year

results from the prospective multicentre German Drug-Eluting Stent Registry (DES.DE). Clin Res Cardiol 100(5):413–423

20. Kumagai N, Origasa H, Nagao T, Takekawa H, Okuhara Y, Yamaguchi T (2013) Prognostic significance of smoking in patients with acute ischemic stroke within 3 months of onset. J Stroke Cerebrovasc Dis 22(6):792–798

21. Edjoc RK, Reid RD, Sharma M, Fang J, Registry of the Canadian Stroke N (2013) The prognostic effect of cigarette smoking on stroke severity, disability, length of stay in hospital, and mortality in a cohort with cerebrovascular disease. J Stroke Cerebrovasc Dis 22(8):e446–e454

22. Kornej J, Hindricks G, Kosiuk J, Arya A, Sommer P, Husser D, Rolf S, Richter S, Piorkowski C, Gaspar T, Lip GYH, Bollmann A (2013) Renal dysfunction, stroke risk scores (CHADS2, CHA2DS2-VASc, and R2CHADS2), and the risk of thromboembolic events after catheter ablation of atrial fibrillation: the Leipzig Heart Center AF Ablation Registry. Circ Arrhythm Electrophysiol 6(5):868–874

23. Hart RG, Pearce LA, McBride R, Rothbart RM, Asinger RW (1999) Factors associated with ischemic stroke during aspirin therapy in atrial fibrillation: analysis of 2012 participants in the SPAF I-III clinical trials. The Stroke Prevention in Atrial Fibrillation (SPAF) Investigators. Stroke 30(6):1223–1229

24. Cetin M, Cakici M, Zencir C et al (2014) Prediction of coronary artery disease severity using CHADS2 and CHA2DS2-VASc scores and a newly defined CHA2DS2-VASc-HS score. Am J Cardiol 113(6):950–956

25. Modi R, Patted SV, Halkati PC, Porwal S, Ambar S, MR P, Metgudmath V, Sattur A (2017) CHADS-VASc-HSF score - new predictor of severity of coronary artery disease in 2976 patients. Int J Cardiol 228:1002–1006