Assessment of the CHA$_2$DS$_2$-VASc Score for the Prediction of Death in Elderly Patients With Coronary Artery Disease and Atrial Fibrillation

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Purpose: Coronary artery disease (CAD) and atrial fibrillation (AF) often coexist and lead to a much higher risk of mortality in the elderly population. The aim of this study was to investigate whether the CHA$_2$DS$_2$-VASc score could predict the risk of death in elderly patients with CAD and AF.

Methods: Hospitalized patients aged ≥65 years with a diagnosis of CAD and AF were recruited consecutively. Patients were divided into 5 groups according to the CHA$_2$DS$_2$-VASc score (≤2, =3, =4, =5, and ≥6). At least a 1-year follow-up was carried out for the assessment of all-cause death.

Results: A total of 1,579 eligible patients were recruited, with 582 all-cause deaths (6.86 per 100 patient-years) occurring during a follow-up of at least 1 year. With the increase in the CHA$_2$DS$_2$-VASc score, the 1-year and 5-year survival rate decreased (96.4% vs. 95.7% vs. 94.0% vs. 86.5% vs. 85.7%, respectively, $P < 0.001$; 78.4% vs. 68.9% vs. 64.6% vs. 55.5% vs. 50.0%, respectively, $P < 0.001$). Compared with the patients with CHA$_2$DS$_2$-VASc score <5, for patients with CHA$_2$DS$_2$-VASc score ≥5, the adjusted hazard ratio for death was 1.78 (95% CI: 1.45–2.18, $P < 0.001$). The predictive values of the CHA$_2$DS$_2$-VASc score ≥5 for in-hospital (C-index = 0.66, 95% CI: 0.62–0.69, $P < 0.001$), 1-year (C-index = 0.65, 95% CI: 0.63–0.67, $P < 0.001$) and 5-year (C-index = 0.60, 95% CI: 0.59–0.61, $P < 0.001$) death were in comparable.

Conclusion: In elderly patients with concomitant CAD and AF, the CHA$_2$DS$_2$-VASc score can be used to predict death with moderate accuracy.

Keywords: elderly, atrial fibrillation, coronary artery disease, death, CHA$_2$DS$_2$-VASc score

INTRODUCTION

Coronary artery disease (CAD) is the most common cardiovascular disease, while atrial fibrillation (AF) is the most common cardiac arrhythmia (1). The prevalence of both CAD and AF increases monotonically with age (2, 3). CAD and AF often coexist and interact with each other (4). CAD is a leading cause of morbidity and mortality in elderly adults (5). Elderly patients are more likely than

their younger counterparts to present with comorbidities (6–9), contributing to worse outcomes. Patients with AF are relatively older and have higher risk of stroke, which may contribute to increased mortality (10–16). Furthermore, AF is a well-established marker of poor short- and long-term prognosis in patients with acute myocardial infarction (AMI) (11, 12, 17, 18) and is associated with a large increase in overall mortality (15, 19). Therefore, the coexistence of CAD and AF might lead to a much higher risk of mortality in the elderly population.

The CHA$_2$DS$_2$-VASc score [congestive heart failure, hypertension, age ≥75 years (doubled), diabetes, stroke/transient ischemic attack/thromboembolism (doubled), vascular disease (prior myocardial infarction, peripheral artery disease, or aortic plaque), age 65–74 years, sex category (female)] has been used for the assessment of thromboembolic (TE) risk and the guidance of antithrombotic treatment in patients with AF (20). In addition, this simple and well-established scoring system has been shown to predict the risk for other conditions beyond its original designations (20–26).

In the presence of comorbidities of CAD and AF, advancing age further elevates the risk of TE complications and death. Evaluating the risk of death from TE in an elderly population with CAD and AF is important, because a competing-risk setting taking careful consideration of the interplay between the mortality of elderly individuals with CAD and AF, and mortality of ischemic stroke/TE is needed to provide meaningful risk assessments. However, how to assess the relationship between the mortality of ischemic stroke/TE and the high mortality of the elderly population is still unclear. Therefore, we aimed to evaluate whether the CHA$_2$DS$_2$-VASc score can predict the risk of death in elderly CAD and AF patients and be used as an indicator of treatment and prognosis.

METHODS

Patients

From January 2010 to December 2017, patients aged ≥65 years with a diagnosis of both CAD and AF who were hospitalized in the Department of Cardiology, Chinese PLA General Hospital, were recruited consecutively. This study complied with the Declaration of Helsinki and was approved by the institutional ethics committee of the General Hospital of the People's Liberation Army. CAD was defined as stable coronary artery disease (SCAD, including stable angina, previous myocardial infarction and ischemic cardiomyopathy) and acute coronary syndrome (ACS, including unstable angina and acute myocardial infarction). AF was defined as an irregular rhythm recorded in a standard 12-lead electrocardiogram, including discrete P waves and their replacement with irregular chaotic oscillatory atrial activity (F waves) in the setting of irregular QRS complexes. Body mass index (BMI) was categorized according to the distribution of BMI among the patients and the WHO criteria (27). In line with the epidemiological evidence, a BMI from 22 to <25 kg/m^2 was used as the reference group. On defining the different classification of HF, we summarized the left ventricular ejection fraction (LVEF) data of the included CAD and AF patients. Patients with HF were stratified into 3 groups according to the

criteria that LVEF <40% represents heart failure with reduced ejection fraction (HFrEF), LVEF ≥50% represents heart failure with preserved ejection fraction (HFpEF), and LVEF ranges from 40 to 50 represents heart failure with mid-range ejection fraction (HFmrEF).

Data Collection, Follow-Up and Death Definitions

Baseline demographics and clinical characteristics in the hospital were extracted from the electronic health records system. The components of the CHA$_2$DS$_2$-VASc score were collected to retrospectively assess the risk of mortality. The CHA$_2$DS$_2$-VASc score was calculated as congestive heart failure (1 point), aged 65–74 years (1 point), hypertension (1 point), diabetes (1 point), vascular disease (prior myocardial infarction, peripheral artery disease, or aortic plaque; 1 point), female sex (1 point), aged 75 years or older (2 points) and stroke/transient ischemic attack/thromboembolism (2 points) (28, 29).

Participants were followed-up until Dec 31st, 2019. The follow-up protocol included a combination of hospital medical record reviews, telephone contacts with patients or family members and death certificate reviews. All deaths were independently adjudicated in a blinded manner by 2 members of the event adjudication committee. All-cause death was classified using the tenth revision of the International Classification of Disease and confirmed through death certificates using personal identity card numbers. Cardiac death was defined as death attributable to fatal myocardial infarction, sudden cardiac death or stroke. Apart from cardiac death, non-cardiac death included deaths from malignancies, infections, respiratory, trauma/accidental or other non-vascular deaths. If the cause of death could not be determined from the available evidence, death was classified as undetermined.

Statistical Analysis

The patients were divided into CHA$_2$DS$_2$-VASc score groups (≤2, =3, =4, =5, and ≥6) according to whether they had died by the end of follow-up. Baseline demographic and clinical characteristics were summarized using medians and interquartile ranges (IQRs) for continuous measures and percentages for categorical measures. The comparison of the data was performed using the chi-square test for categorical variables and Mann–Whitney U-test for continuous variables. Univariate and multivariate Cox regression models were used to explore the risk factors associated with mortality. According to the CHA$_2$DS$_2$-VASc score, Kaplan–Meier curves with the log-rank test were used to compare survival. The calibration of the CHA$_2$DS$_2$-VASc score was assessed with the Hosmer-Lemeshow goodness-of-fit test (HL), which may determine the degree of agreement between the observed event rate and the predicted one over a series of scores. A significant value of $P < 0.05$ represents a lack of fit. The concordance index (C-index) was conducted to determine the discrimination of and the diagnostic value of the CHA$_2$DS$_2$-VASc score for death. All analysis were performed with the R 4.0.1 Statistical Package (the R foundation for Statistical Computing, Vienna, Austria) and SPSS v.24.0 (Statistical Package for Social Science; IBM, Chicago, IL, USA).
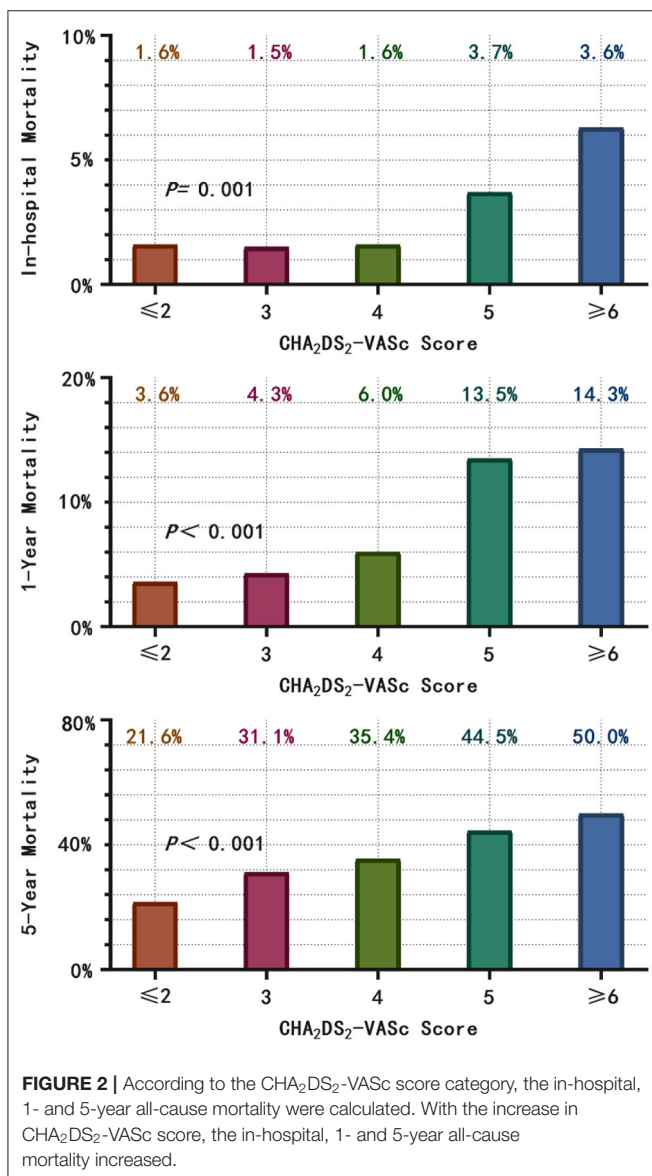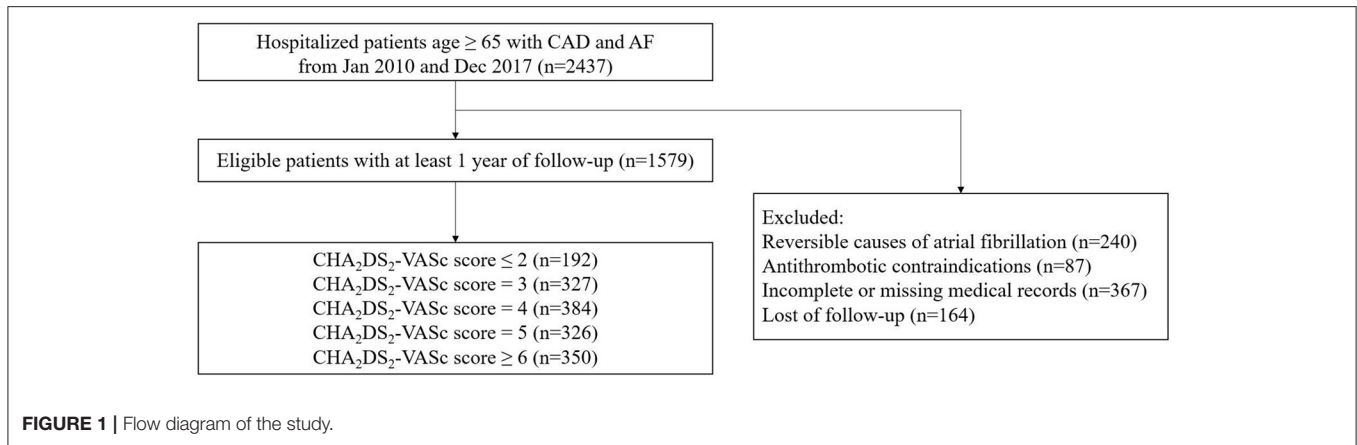
RESULTS

Baseline Characteristics

Follow-up data were available for 1,579 patients (with a total of 1,579 patients for 1-year and 910 for 5-year follow-up). The baseline characteristics according to the CHA$_2$DS$_2$-VASc score are shown in **Table 1**. The mean CHA$_2$DS$_2$-VASc score was 4.3 ± 1.6 (median 4.0, interquartile range 3.0–5.0). We divided the cohort into five quintiles based on the CHA$_2$DS$_2$-VASc score: ≤2 ($n = 192$), 3 ($n = 327$), 4 ($n = 384$), 5 ($n = 326$), and ≥6 ($n = 350$) (**Figure 1**). Patients with a higher CHA$_2$DS$_2$-VASc score were more likely to be women, older and with cardiovascular diseases,

such as AMI and heart failure (HF). The proportion of patients with HF was 38.3% (602/1579) in the whole study. Among the patients with HF, LVEF data were retrieved in 581 patients, with 114 of HFrEF (19.6%), 81 of HFmrEF (13.9%) and 386 of HFpEF (66.4%). The rate of comorbidities, such as hypertension, diabetes, prior transient ischemic attack (TIA)/stroke, peripheral arterial disease (PAD), chronic kidney disease (CKD) and HF, increased with the increasing CHA$_2$DS$_2$-VASc score. In terms of treatment, diuretics, calcium channel blockers (CCBs) and renin angiotensin system inhibitors (RASI) were used more frequently in elderly patients with AF and CAD with a higher CHA$_2$DS$_2$-VASc score (**Table 1**). The application of oral anticoagulants

TABLE 1 | Baseline characteristics of elderly patients with CAD and AF according to the CHA$_2$DS$_2$-VASc score.

Characteristics	CHA$_2$DS$_2$-VASc ≤2 (n = 192)	CHA$_2$DS$_2$-VASc = 3 (n = 327)	CHA$_2$DS$_2$-VASc = 4 (n = 384)	CHA$_2$DS$_2$-VASc = 5 (n = 326)	CHA$_2$DS$_2$-VASc ≥6 (n = 350)	P-value
Demographics						
Age, yrs, median (IQR)	72 (67–78)	76 (71–81)	77 (73–83)	79 (75–84)	80 (77–84)	<0.001
Male, n (%)	179 (90.2)	231 (70.6)	204 (53.1)	137 (42.0)	145 (41.4)	<0.001
BMI, kg/m^2, median (IQR)	24 (22–27)	25 (23–27)	25 (23–27)	25 (22–27)	24 (22–27)	0.143
Medical history, n (%)						
Hypertension	65 (33.9)	239 (73.1)	289 (75.3)	273 (83.7)	318 (90.9)	<0.001
Diabetes	4 (2.1)	47 (14.4)	106 (27.6)	131 (40.2)	195 (55.7)	<0.001
Previous myocardial infarction	2 (1.0)	23 (7.0)	47 (12.2)	54 (16.6)	71 (20.3)	<0.001
Prior TIA/stroke	0 (0.0)	5 (1.5)	51 (13.3)	103 (31.6)	276 (78.9)	<0.001
Peripheral arterial disease	3 (1.6)	32 (9.8)	73 (19.0)	88 (27.0)	134 (38.3)	<0.001
COPD	6 (3.1)	10 (3.1)	21 (5.5)	11 (3.4)	10 (2.9)	0.314
Hyperlipidemia	46 (24.0)	62 (19.0)	74 (19.3)	73 (22.4)	90 (25.7)	0.152
Chronic kidney disease	6 (3.1)	26 (8.0)	44 (11.5)	42 (12.9)	47 (13.4)	0.001
Liver disease	16 (8.3)	31 (9.5)	35 (9.1)	23 (7.1)	31 (8.9)	0.829
Malignancy	24 (12.5)	30 (9.2)	49 (12.8)	41 (12.6)	50 (14.3)	0.361
Clinical presentation, n (%)						
SCAD	104 (54.2)	188 (57.5)	217 (56.5)	171 (52.5)	177 (50.6)	0.342
ACS	88 (45.8)	139 (42.5)	167 (43.5)	155 (47.5)	173 (49.4)	0.342
Unstable angina	87 (45.3)	130 (39.8)	144 (37.5)	125 (38.3)	121 (34.6)	0.170
Acute myocardial infarction	1 (0.5)	11 (3.4)	27 (7.0)	31 (9.5)	54 (15.4)	<0.001
Heart failure	15 (7.8)	54 (16.5)	152 (39.6)	159 (48.8)	222 (63.4)	<0.001
In-hospital treatment, n (%)						
Diuretic	56 (29.2)	150 (45.9)	230 (59.9)	217 (66.6)	264 (75.4)	<0.001
Statins	162 (84.4)	275 (84.1)	315 (82.0)	276 (84.7)	297 (84.9)	0.842
CCB	57 (29.7)	192 (58.7)	206 (53.6)	187 (57.4)	226 (64.6)	<0.001
β-blockers	147 (76.6)	246 (75.2)	298 (77.6)	263 (80.7)	272 (77.7)	0.566
RASI	56 (29.2)	187 (57.2)	218 (56.8)	207 (63.5)	232 (66.3)	<0.001
Antiplatelet therapy						
Aspirin	162 (84.4)	249 (76.1)	289 (75.3)	242 (74.8)	259 (74.0)	0.074
P2Y$_{12}$ receptor inhibitors	126 (65.6)	198 (60.6)	237 (61.7)	191 (58.6)	224 (64.0)	0.471
Anticoagulation						
Warfarin	26 (13.5)	59 (18.0)	68 (17.7)	59 (18.1)	54 (15.4)	0.575
NOACs	28 (14.6)	42 (12.8)	46 (12.0)	40 (12.3)	29 (8.3)	0.197
Amiodarone	64 (33.3)	96 (29.4)	83 (21.6)	79 (24.2)	98 (28.0)	0.740
PCI with drug-eluting stent	24 (12.5)	36 (11.0)	50 (13.0)	30 (9.2)	30 (8.6)	0.264

Data are presented as the median (IQR), n (%), or n/N (%). CAD, Coronary artery disease; AF, Atrial fibrillation; BMI, Body mass index; TIA, Transient ischemic attack; COPD, Chronic obstructive pulmonary disease; SCAD, Stable coronary artery disease; ACS, Acute coronary syndrome; CCB, Calcium channel blocker; RASI, Renin angiotensin system inhibitors; NOACs, Nonvitamin K antagonist oral anticoagulants; PCI, Percutaneous coronary intervention.
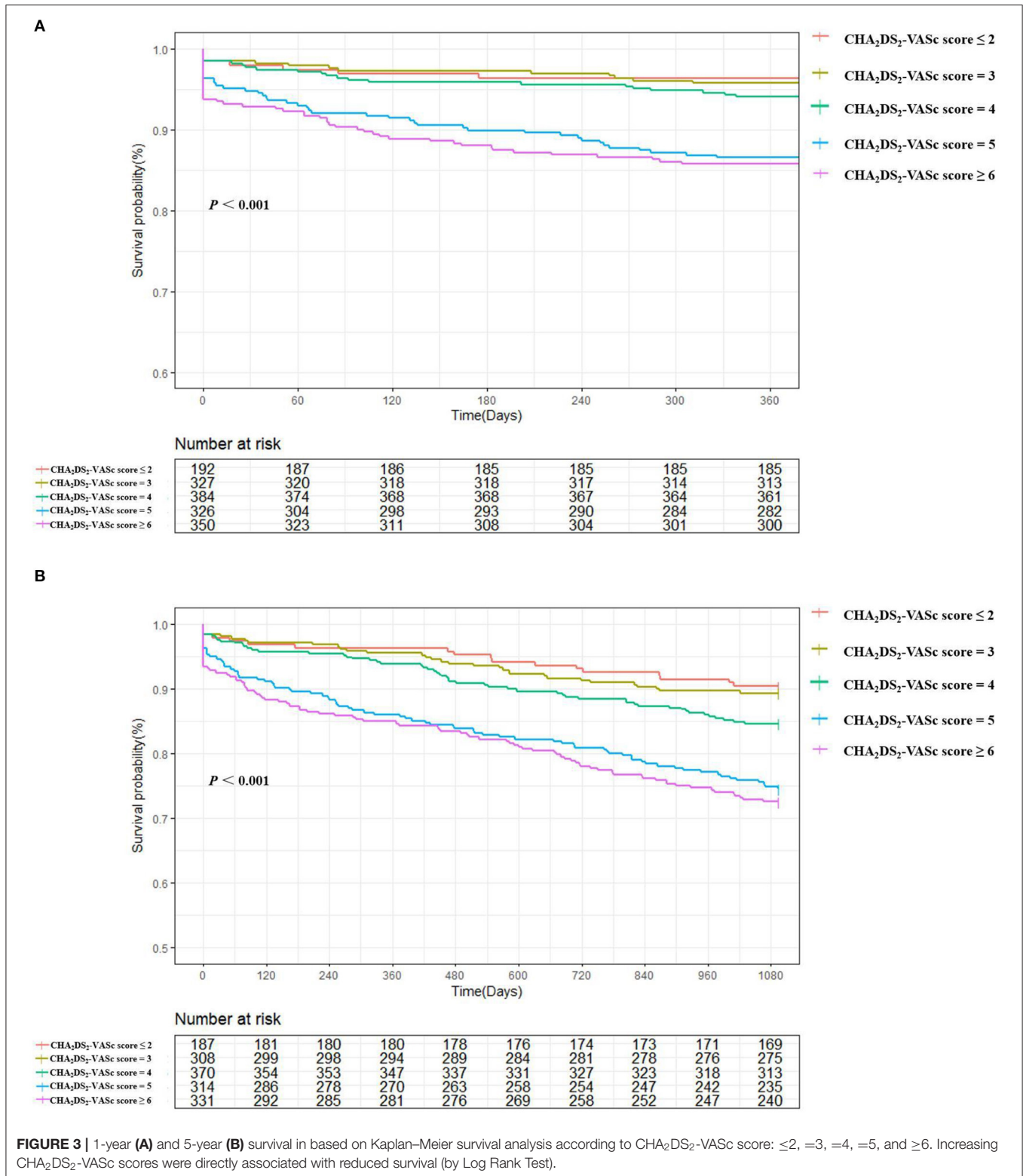
FIGURE 1 | Flow diagram of the study.

FIGURE 2 | According to the CHA$_2$DS$_2$-VASc score category, the in-hospital, 1- and 5-year all-cause mortality were calculated. With the increase in CHA$_2$DS$_2$-VASc score, the in-hospital, 1- and 5-year all-cause mortality increased.

(OACs) and oral antiplatelets (aspirin and P2Y$_{12}$ inhibitors) in all patients were 27.1% and 83.3%, respectively. With the increase of CHA$_2$DS$_2$-VASc score, no significant difference was found for the proportion of patients administrated with OACs (CHA$_2$DS$_2$-VASc score $\leq$2: 27.1%, score = 3: 28.4%, score = 4: 29.2%, score = 5: 27.3%, and score $\geq$6: 23.4%, P = 0.475) or oral antiplatelet (score $\leq$2: 85.9%, score = 3: 81.3%, score = 4: 81.8%, score = 5: 82.8%, and score $\geq$6: 85.7%, P = 0.404).

Association Between CHA$_2$DS$_2$-VASc Score and Mortality

A total of 582 patients died, with a mortality of 6.86 per 100 patient-years. The causes of death were cardiovascular in 152 patients (26.1%), non-cardiovascular in 247 patients (42.5%) and undetermined in 183 patients (31.4%). The in-hospital, 1-year and 5-year all-cause mortality were 3.0%, 8.7%, and 24.4%, respectively, and higher CHA$_2$DS$_2$-VASc scores were associated with a significantly higher mortality (**Figure 2**). The survival rate according to Kaplan–Meier analysis suggested that with the increase in the CHA$_2$DS$_2$-VASc score, the 1-year and 5-year survival rates decreased (96.4% vs. 95.7% vs. 94.0% vs. 86.5% vs. 85.7%, respectively, P < 0.001; 78.4% vs. 68.9% vs. 64.6% vs. 55.5% vs. 50.0%, respectively, P < 0.001) (**Figure 3**).

Compared with the patients with CHA$_2$DS$_2$-VASc scores <5, the patients with CHA$_2$DS$_2$-VASc scores $\geq$5 had higher risk of death (HR: 2.01, 95% CI: 1.65–2.45, P < 0.001). Multivariable Cox regression analysis demonstrated that CHA$_2$DS$_2$-VASc score $\geq$5 could independently predict mortality with the adjustment of the risk variables not included in the CHA$_2$DS$_2$-VASc score (adjusted HR: 1.78, 95% CI: 1.45–2.18, P < 0.001) (**Table 2**). Moreover, all types of HF could significantly predict the risk of death, with HFrEF contributing the most (adjusted HR for HFrEF: 2.06, 95%CI: 1.52–2.79, P < 0.001); for HFmrEF: 1.74, 95% CI: 1.24–2.45, P = 0.001; for HFpEF: 1.38, 95% CI: 1.13–1.69, P = 0.002, respectively).

FIGURE 3 | 1-year **(A)** and 5-year **(B)** survival in based on Kaplan–Meier survival analysis according to CHA$_2$DS$_2$-VASc score: $\leq$2, =3, =4, =5, and $\geq$6. Increasing CHA$_2$DS$_2$-VASc scores were directly associated with reduced survival (by Log Rank Test).

Prediction of the CHA$_2$DS$_2$-VASc Score for Mortality

In elderly patients with CAD and AF, CHA$_2$DS$_2$-VASc score $\geq$5 had a modest predictive ability for all-cause death in-hospital (C-index = 0.66, 95% CI: 0.62–0.69, P < 0.001), during 1-year (C-index = 0.65, 95% CI: 0.63–0.67, P < 0.001), and 5-year (C-index = 0.60, 95% CI: 0.59–0.61, P < 0.001) follow-ups. The diagnostic statistics for the CHA$_2$DS$_2$-VASc

TABLE 2 | Predictors of mortality in elderly patients with CAD and AF by Cox regression analysis.

Variables	Univariate analysis			#Multivariate analysis		
	HR	95% CI	P	HR	95% CI	P
Age	1.09	1.07–1.10	<0.001	1.08	1.06–1.09	<0.001
*BMI<18.5	1.84	1.34–2.51	<0.001	1.72	1.25–2.35	0.001
*BMI≥30	0.89	0.63–1.24	0.486	1.01	0.73–1.41	0.936
Previous AMI	1.62	1.31–1.99	<0.001	1.33	1.08–1.65	0.008
AMI	2.44	1.90–3.13	<0.001	2.08	1.62–2.67	<0.001
HF	2.30	1.95–2.71	<0.001	1.42	1.18–1.72	<0.001
HFrEF	2.29	1.78–2.94	<0.001	2.06	1.52–2.79	<0.001
HFmrEF	2.13	1.57–2.89	<0.001	1.74	1.24–2.45	0.001
HFpEF	1.54	1.29–1.84	<0.001	1.38	1.13–1.69	0.002
Diabetes	1.27	1.07–1.51	0.006	1.11	0.92–1.33	0.296
Prior TIA/stroke	1.28	1.08–1.52	0.005	1.05	0.90–1.14	0.487
PAD	1.90	1.59–2.64	<0.001	1.03	0.81–1.28	0.351
CKD	2.03	1.63–2.54	<0.001	2.04	1.42–2.94	<0.001
COPD	1.87	1.30–2.69	0.001	1.78	1.43–2.23	<0.001
Malignancy	1.69	1.36–2.09	<0.001	1.49	1.20–1.85	<0.001
CHA$_2$DS$_2$-VASc Score <5	1.0 (Reference)	1.0 (Reference)				
CHA$_2$DS$_2$-VASc Score ≥5	2.01	1.65–2.45	<0.001	†1.78	1.45–2.18	<0.001

*Compared to the reference value of BMI 22 -<25 kg/m^2. #Adjusted by the risk factors with a statistically significant P-value <0.05 after the univariate analysis. †Adjusted by the risk factors not included in the CHA$_2$DS$_2$-VASc score with a statistically significant P value <0.05 after the univariate analysis. CI, Confidence interval; BMI, Body mass index; AMI, Acute myocardial infarction; HF, Heart failure; HFrEF, Heart failure with reduced ejection fraction; HFmrEF, Heart failure with mid-range ejection fraction; HFpEF, Heart failure with preserved ejection fraction; AF, Atrial fibrillation; TIA, Transient ischemic attack; PAD, Peripheral arterial disease; CKD, Chronic kidney disease; COPD, Chronic obstructive pulmonary disease.

TABLE 3 | Statistics of the CHA$_2$DS$_2$-VASc Score for the prediction of death.

	CHA$_2$DS$_2$-VASc score ≥ 5					
	HL-p	C-index (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
All death	0.28	0.60 (0.59–0.61)	52.6 (48.4–56.7)	67.1 (64.1–70.0)	48.3 (44.3–52.2)	70.8 (67.8–73.7)
In SCAD	0.86	0.59 (0.57–0.60)	48.2 (42.4–54.0)	68.5 (64.4–72.3)	45.0 (39.5–50.6)	71.1 (67.1–74.9)
In ACS	0.94	0.61 (0.60–0.63)	57.2 (51.2–63.0)	65.4 (60.7–70.0)	51.6 (45.9–57.2)	70.3 (65.6–74.7)
In hospital death	0.57	0.66 (0.62–0.69)	70.8 (55.7–82.6)	58.1 (55.5–60.5)	5.0 (3.6–7.0)	98.4 (97.3–99.1)
In SCAD	0.65	0.63 (0.58–0.68)	62.5 (40.8–80.4)	63.4 (60.0–66.6)	4.7 (2.7–7.8)	98.3 (96.7–99.2)
In ACS	0.93	0.68 (0.64–0.73)	79.2 (57.3–92.1)	57.7 (54.0–61.4)	6.1 (3.8–9.4)	98.8 (97.0–99.5)
1-year death	0.97	0.65 (0.63–0.67)	68.1 (59.6–75.6)	59.6 (57.0–62.2)	13.9 (11.5–16.8)	95.1 (93.4–96.4)
In SCAD	0.57	0.62 (0.58–0.65)	59.4 (46.4–71.2)	64.4 (61.0–67.8)	11.9 (8.6–16.1)	95.2 (92.9–96.8)
In ACS	0.11	0.67 (0.64–0.70)	75.3 (63.6–84.4)	60.1 (56.2–63.9)	17.5 (13.6–22.3)	95.6 (93.0–97.3)
5-year death	0.51	0.60 (0.59–0.61)	57.0 (51.9–62.0)	60.0 (56.0–63.9)	47.4 (42.8–52.1)	68.8 (64.6–72.7)
In SCAD	0.29	0.58 (0.57–0.60)	51.1 (43.7–58.3)	66.6 (62.8–70.1)	30.3 (25.4–35.7)	82.7 (79.2–85.7)
In ACS	0.52	0.61 (0.60–0.63)	60.7 (53.5–67.5)	62.9 (58.6–67.0)	37.9 (32.6–43.5)	81.1 (76.9–84.7)

HL-p, Hosmer–Lemeshow goodness-of-fit test p-value; C-index, Concordance index; CI, Confidence interval; SCAD, Stable coronary artery disease; ACS, Acute coronary artery disease; PPV, Positive predictive value; NPV, Negative predictive value; CAD, Coronary heart disease; AF, Atrial fibrillation.

score of in-hospital, 1-year death, 5-year death and all death are displayed in **Table 3**. We also performed the internal validation by dividing the patients into those with SCAD and those with ACS. The performance of the CHA$_2$DS$_2$-VASc score ≥5 was comparable between the patients with SCAD and ACS for predicting in-hospital death, 1-year or 5-year death, with a moderate higher C-index in ACS patients (**Table 3**).

DISCUSSION

In this cohort study, the main findings were that (1) the CHA$_2$DS$_2$-VASc score was a significant predictor of death in elderly patients with CAD and AF, and the mortality generally increased with the increasing CHA$_2$DS$_2$-VASc score, exhibiting a clear dose-response relationship; (2) CHA$_2$DS$_2$-VASc score independently and strongly predicted the in-hospital, 1- and

5-year death in elderly patients with CAD and AF. To our knowledge, this is the first study to evaluate the predictive ability of the CHA$_2$DS$_2$-VASc score for death in elderly patients with CAD and AF. This study could facilitate risk stratification and improve the prevention of death associated with comorbid CAD and AF in elderly patients.

AF is the most common arrhythmia, with high incidence and prevalence, and is associated with an increased risk of all-cause death and stroke (30, 31). CAD, especially AMI, will also lead to other complications and increase the risk of death (32). Age is an obvious risk factor for patients with CAD and AF (31, 33), and elderly individuals are more likely to have coexisting CAD and AF, thus the risk of death in elderly patients with CAD and AF is higher. In addition to the assessment of thromboembolic risk in patients with AF, the CHA$_2$DS$_2$-VASc score has been shown to predict the adverse outcomes for other cardiovascular conditions, such as chest pain (25), ACS (21, 22), AMI (24), HF (20), pulmonary emboli (23), and ACS undergoing percutaneous coronary intervention (PCI) (26). Therefore, we believe that the CHA$_2$DS$_2$-VASc score is a feasible predictor of prognosis in elderly patients with CAD and AF. The sensitivity of the CHA$_2$DS$_2$-VASc score was higher than specificity for the prediction of death in-hospital or within 1-year. It indicated that the CHA$_2$DS$_2$-VASc score could effectively evaluate the mortality of elderly patients with CAD and AF in-hospital or within 1 year follow-up in the study. When the CHA$_2$DS$_2$-VASc score is ≥ 5, the probability of death within 1 year will increase significantly. Additionally, with the increase in the CHA$_2$DS$_2$-VASc score, the in-hospital, 1- and 5-year mortality also increased. These results indicate that the CHA$_2$DS$_2$-VASc score could predict the prognosis of elderly patients with CAD and AF.

The risk factors for death in elderly patients with CAD and AF were assessed for the first time in this cohort. We found that in addition to the CHA$_2$DS$_2$-VASc score, the independent risk factors for all-cause death in elderly patients with CAD and AF included BMI <18.5 kg/m^2, previous or current AMI, CKD, COPD, and malignancy. Similar risk factors for death were also found in AF patients in the ROCKET-AF study (34) and the GARFIELD-AF global prospective registry (35), suggesting that overall mortality due to AF is tightly linked to the same risk factors and comorbidities. Our results also emphasized the prognostic importance of underweight (BMI <18.5 kg/m^2) in the elderly population. We found that BMI <18.5 kg/m^2 was a significant predictor of overall mortality, which probably reflects the known association between a decrease in BMI and an increase in mortality in CAD patients, regardless of the baseline BMI value (36). Further studies are needed to better understand the impact of the combination of risk factors on mortality in the elderly population.

The combination of AF and CAD is a common and complex clinical condition in which to address anticoagulation therapy (37), especially in elderly patients. Taking OACs can reduce the risk of embolism, but it also increases the risk of bleeding. Therefore, whether to take OACs should be judged by the patient's health situation (38). If AF develops during the first year after ACS and there is an indication for thromboembolic prevention with anticoagulation, OACs should be started. In stable CAD patients with AF, oral anticoagulation is necessary when the CHA$_2$DS$_2$-VASc score is ≥ 2 (39). Elderly patients requiring anticoagulation for AF are at higher risk of adverse outcomes, but also have a higher absolute benefit from OAC (40). However, in our study, the application rate of OACs was only 27.1%, and it did not increase with the CHA$_2$DS$_2$-VASc score, suggesting that the application of OACs in elderly patients with CAD and AF was not sufficient, which might attribute to the increasing risk of death in patients with higher value of CHA$_2$DS$_2$-VASc score. Previous studies have found that the application of OACs in the elderly population was insufficient (41). Therefore, the use of OACs in elderly patients with CAD and AF should be increased, and further studies are needed to verify whether the application of OAC could decrease the mortality in these patients.

Several limitations of this study warrant consideration. The present study was an observational real-world study in which we did not exclude severely ill patients (who are typically excluded from clinical trials), thus, the mortality in elderly patients with CAD and AF might be higher than expected in clinical trials. Data on the clinical parameters and drug therapies were obtained from electronic health record. Although the data was validated and found to be highly accurate, not all clinical characteristics could be verified. While we tried to make adjustment for the clinically relevant parameters, it is impossible to adjust for all variables that may affect the outcomes. In addition, the study was based on a single-center cohort, and the findings should be validated in large multicenter cohorts.

CONCLUSION

The CHA$_2$DS$_2$-VASc score could independently predict all-cause death in the elderly patients with concomitant CAD and AF.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institutional Ethics Committee of the General Hospital of the People's Liberation Army. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

TY, JM, and YZha: study concept and design. YW, JL, LD, LQ, HY, WG, XF, GW, ZW, RD, and YZou: acquisition of data. GW, YW, LQ, LD, and TY: analysis and interpretation of data.

GW, YW, LD, LQ, and TY: drafting of the manuscript. TY and JM: critical revision of the manuscript for important intellectual content. All authors contributed to the article and approved the submitted version.

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