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CHA_2DS_2-VASc score predicts 30-day readmission due to thromboembolic complications following cardioversion of atrial fibrillation: insights from US National Readmissions Database

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Abstract

Purpose Determine whether the CHA_2DS_2-VASc score predicts rates of hospitalization associated with thromboembolic complications (TEC) in the 30, 60, and 90 days following cardioversion (CV) for atrial fibrillation (AF).

Methods The 2014 National Readmissions Database was analyzed to identify readmissions following the index hospitalization for AF and CV. A CHA_2DS_2-VASc score was calculated for each patient from diagnosis codes associated with the index admission. The primary outcome was the incidence of readmission due to TEC in the 30, 60, and 90 days after CV stratified by CHA_2DS_2-VASc scores ≤ 1, 2–3, and ≥ 4; the secondary outcome was specific clinical risk factors independently associated with TEC within 30 days of CV.

Results A total of 109,420 weighted index admissions for AF and CV were identified in between January 1, 2014, and November 30, 2014. Of these, 16,535 (15.1%) had a CHA_2DS_2-VASc score of 0–1, 39,544 (36.1%) had a score of 2–3, and 53,340 (48.8%) had a score of ≥ 4. Readmission due to TEC occurred in 48 (0.29%), 167 (0.42%), and 394 (0.74%) patients with CHA_2DS_2-VASc scores ≤ 1, 2–3, and ≥ 4, respectively, in the 90-day period after CV. The only significant predictor for 30-day TEC-associated readmission after CV was age > 65 years old.

Conclusions This study demonstrated the utility of CHA_2DS_2-VASc score in predicting TEC-associated readmission rate following CV and the temporal relationship of TEC to CV. Patients > 65 years old without other comorbidities may benefit from 30-day OAC following successful CV irrespective of the duration of AF episodes.

Keywords Atrial fibrillation · Cardioversion · Embolic stroke · Epidemiology

1 Introduction

Atrial fibrillation (AF) is the most common arrhythmia with a prevalence of 0.1% in adults < 55 years old compared to 9.0% in adults > 65 years old [1]. Risk factors for AF include obesity, hypertension (HTN), diabetes mellitus (DM), congestive heart failure (CHF), smoking, hyperlipidemia, history of stroke, history of myocardial infarction (MI), and obstructive sleep apnea (OSA) [2]. AF is associated with a fivefold increase in stroke and other thromboembolic (TE) risk [3]. The CHA_2DS_2-VASc score estimates annual stroke risk in patients with non-valvular AF [4, 5].

Current guidelines recommend at least 4 weeks of uninterrupted oral anticoagulation (OAC) after cardioversion (CV) of AF lasting longer than 48 h for all patients regardless of CHA_2DS_2-VASc score, but omitting antithrombotic therapy may be considered in patients at low thromboembolic risk with acute AF lasting less than 48 h [5]. However, prior studies have raised a concern about the safety of withholding OAC in acute AF [6, 7]. A single-center study evaluating the safety of AF CV lasting < 48 h without OAC demonstrated neurological complications in approximately 1% of CV [7]. It is also important to note that in these studies, the 48-h period refers to the time since the patient-reported symptom onset. The safety of acute AF CV without appropriate anticoagulation has not been confirmed in any clinical trial and is based primarily upon expert consensus derived from retrospective studies [8].

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While the CHA_2DS_2-VASc score was first validated in predicting *long-term* thromboembolic risk in non-valvular AF patients [9], the Finnish CardioVersion (FinCV) study demonstrated its predictive value of *short-term* thromboembolic risk following CV [10]. The short-term predictive value of CHA_2DS_2-VASc score has not been replicated in the US population. Using the 2014 US National Readmission Database (NRD), we sought to assess the 30-, 60-, and 90-day readmission rates due to TE after CV stratified by CHA_2DS_2-VASc score. The secondary objective was to identify specific clinical risk factors independently associated with TE within 30 days of AF CV.

2 Methods

Patients included in this study were extracted from the 2014 US National Readmissions Database (NRD). The Agency for Healthcare Research and Quality (AHRQ) compiles the NRD to estimate national readmission rates and investigate factors associated with readmission [11]. It is derived from the National Inpatient Sample (NIS) [12], the largest all-payer database of hospitalization in the USA, as a sample of all patients in the NIS admitted at least twice in the 2014 calendar year; demographic data is omitted from the NRD to maintain anonymity. The NRD includes variables describing the principal diagnosis of each hospitalization (DX1), other diagnoses billed (DX2-DX30), comorbidity measures (CM) codes, diagnosis-related group (DRG) code for the admission, procedures performed during the hospitalization, patient age, month of discharge, and a unique identifier created to link multiple hospitalizations by the same patient. Diagnoses and procedures are recorded by ICD-9 (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]) code. Demographic data was extracted from the NIS to describe the patients who could be enrolled in the NRD.

Patients aged 18 years and older with an index hospitalization for AF (ICD-9 code 427.31) who underwent any form of CV including electrical and pharmacologic CV (ICD-9 code 99.61, 99.62, and 99.69) between January 1, 2014, and November 30, 2014, were included in this study. The first inpatient AF CV in 2014 was defined as the index CV, regardless of whether this represented the patient's first or subsequent occurrence of AF. Since the shortest follow-up period considered was 30 days, only patients with an index CV between January 1, 2014, and November 30, 2014, were included. Patients with index CV between January 1, 2014, and September 30, 2014; January 1, 2014, and October 31, 2014; and January 1, 2014, and November 30, 2014, were assessed for re-hospitalization rates due to TEC during 90-, 60-, and 30-day follow-up periods, respectively.

The primary study objective was to evaluate the incidence of 30-, 60-, and 90-day readmission for TE events after CV, stratified by CHA_2DS_2-VASc scores, which were calculated for each patient at the index admission. Patients were assigned one point each for comorbid CHF, HTN, DM, or vascular disease and if they were female or 65–74 years old; two points were assigned if age ≥ 75 years old or if the patient had a prior stroke or transient ischemic attack (TIA). Systolic and diastolic heart failure were combined into a single CHF category, consistent with the original CHA_2DS_2-VASc risk prediction model [4, 13]. In the present study, CHA_2DS_2-VASc score was categorized into 3 groups of low (score of 0–1), intermediate (score of 2–3), and high (score of ≥ 4) TE risk. To estimate the risk of TE associated with chronic kidney disease (CKD), we considered a composite of CKD stage 3–5 as one single diagnosis and end-stage renal disease (ESRD) as a separate diagnosis. Stage 3–5 CKD is defined as an estimated glomerular filtration rate (GFR) < 60 ml/min per 1.73 m^2.

Hospitalizations due to TE were defined as re-hospitalizations during the follow-up period which included either an admitting diagnosis or DRG code related to TE; the ICD-9 and DRG codes used to identify TE are listed in Table 4.

The secondary objective was to establish whether any single risk factor of the CHA_2DS_2-VASc score or other clinical variables confer an increased risk of TE-related readmissions following CV during the 30-day follow-up. Clinical variables are not included in the CHA_2DS_2-VASc score tobacco abuse, CKD (stages 3–5, excluding ESRD), and ESRD. The odds ratio (OR) for identified risk factors and 95% confidence intervals (CI) were calculated. Risk factors with a $p < 0.20$ were included as candidate predictors in a multivariate analysis.

NRD-supplied sample weight, stratification, cluster, and domain information were used to calculate national estimates from sample data. Continuous variables were analyzed using ANOVA after meeting normality assumptions tested by the Anderson-Darling test for normality. Categorical variables were analyzed using χ^2 test. Survey-specific methods were used to appropriately estimate variance given the design of the database. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

3 Results

This study identified 47,948 visits representing 109,420 weighted, index admissions for adults with AF treated with CV between January 1, 2014, and November 30, 2014. Of these, 16,535 (15.1%) had a CHA_2DS_2-VASc score of 0–1, 39,544 (36.1%) had a score of 2–3, and 53,340 (48.8%) had a score of ≥ 4. Baseline characteristics, including the rates of comorbidities contributing to the CHA_2DS_2-VASc score, are listed in Table 1. Characteristics of the NIS database include a racial composition of 66% white patients, 15% black patients, 12% Hispanic, and 7% other races. Among hospitalizations eligible for inclusion, 10% were to rural hospitals, 26% to

Table 1 Characteristics of study population at index hospitalization

Characteristic	$CHADS_2$-VASc 0–1 $n = 16,535$		$CHADS_2$-VASc 2–3 $n = 39,544$		$CHADS_2$-VASc ≥ 4 $n = 53,340$		*p* value
Age (Q1-Q3)	56	(48–61)	65	(59–71)	77	(71–83)	< 0.0001
Female	1883	(11.4%)	12207	(30.9%)	30221	(56.7%)	< 0.0001
Comorbidities							
CKD Stage III-V	268	(1.6%)	2443	(6.2%)	8971	(16.8%)	< 0.0001
ESRD	174	(1.1%)	984	(2.5%)	1716	(3.2%)	< 0.0001
CHF	1548	(9.4%)	12723	(32.2%)	33717	(63.2%)	< 0.0001
Diabetes	442	(2.7%)	8229	(20.8%)	23397	(43.9%)	< 0.0001
Hypertension	5353	(32.4%)	27688	(70%)	47590	(89.2%)	< 0.0001
Tobacco use	2774	(16.8%)	5285	(13.4%)	3600	(6.8%)	< 0.0001
Vascular disease	925	(5.6%)	12947	(32.7%)	35507	(66.6%)	< 0.0001

CKD, chronic kidney disease, *ESRD*, end-stage renal disease, *CHF*, congestive heart failure

urban non-teaching hospitals, and 64% to urban teaching hospitals.

The total incidence of TE-related first readmissions following CV was 48 (0.29%) for CHA_2DS_2-VASc 0–1 patient, 167 (0.42%) for CHA_2DS_2-VASc score 2–3 patients, and 394 (0.74%) for CHA_2DS_2-VASc ≥ 4 patients ($p < 0.0001$ for trend) during a mean follow-up duration of 86.0 days. Rates of TE-associated readmission 30, 60, and 90 days after CV, stratified by CHA_2DS_2-VASc score, are depicted in Fig. 1; rates of TE and population at risk are listed in Table 2. In patients with 60 or 90 days of follow-up, TE were elevated in the first 30 days after CV, then decreased in days 31–60 and 61–90 ($p = 0.003$) across all risk groups stratified by CHA_2DS_2-VASc score. Among all cardioverted patients, the median time to re-hospitalization for TE was 35 days after discharge (IQR 16–59). Furthermore, across all time periods, TE risk increased with increasing CHA_2DS_2-VASc risk group.

Within 30 days of CV, the only significant clinical factor for readmission due to TE was age ≥ 65 (OR 3.21, 95% CI 2.00, 5.15) (Table 3). Female sex, CHF, and hypertension all trended towards significance but did not reach statistical significance in predicting TE readmission. Notably, neither CKD stages 3–5 nor ESRD was associated with readmission for TE. In a multivariate analysis, age remained a significant predictor for TEC ($p < 0.0001$); CHF was not a significant predictor for TEC ($p = 0.2885$) (Table 4).

4 Discussion

This study demonstrated the following: (1) readmission due to TE following CV is relatively rare in this cohort; (2) the CHA_2DS_2-VASc score is a significant predictor of TE-associated readmission following CV; (3) the readmission rate for TE was highest in the first 30 days, then decreased in the second and third 30-day periods following CV; and (4) age ≥ 65 is independently associated with readmission due to TE within 30 days of CV.

While the CHA_2DS_2-VASc score has been validated in predicting *long-term* TE risk in non-valvular AF patients in general, this study also revealed its predictive value of *short-*

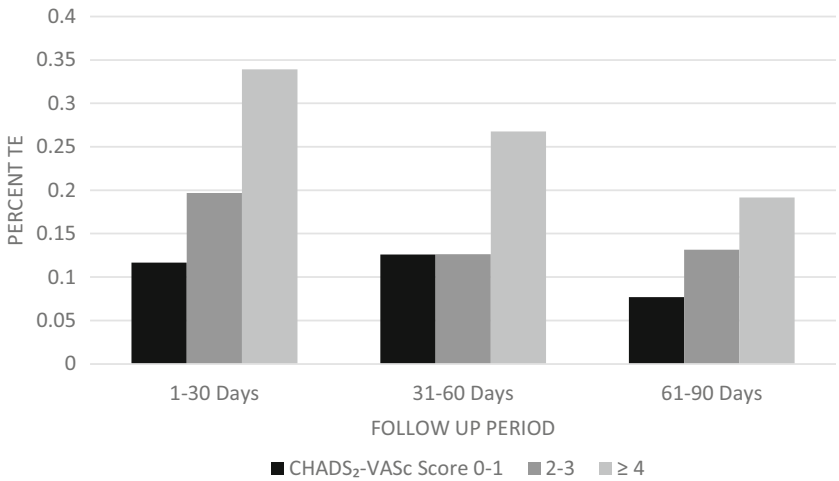

Fig. 1 Percent of cardioverted patients readmitted due to thromboembolic complications by $CHADS_2$-VASc score

Table 2 Readmission rate due to thromboembolic complications by CHA2DS2-VASc score, expressed as (number of events) / (population at risk). Denominators in each column vary because patients with index cardioversion between January 1, 2014, and September 30, 2014, were followed for 90 days, patients with index cardioversion between January 1, 2014, and October 31, 2014, were followed for 60 days, and patients with index cardioversion between January 1, 2014, and November 30, 2014, were followed for 30 days

$CHADS_2$-VASc score	Overall		1–30 days		31–60 days		61–90 days	
0–1	48/16443	(0.29)	19/16443	(0.12)	19/15130	(0.13)	10/13637	(0.07)
2–3	167/39348	(0.42)	78/39348	(0.20)	46/36184	(0.13)	43/32441	(0.13)
≥ 4	394/53340	(0.74)	181/53340	(0.34)	130/48556	(0.27)	83/43186	(0.19)

term TE episodes necessitating hospitalization following AF CV. This finding is consistent with the FinCV study, which showed the CHA_2DS_2-VASc score as a valuable predictor of TE after CV of acute AF episodes < 48 h without anticoagulation [10]. That study followed a 3143 cohort of Finnish patients and concluded that a higher CHA_2DS_2-VASc score was adversely associated with TE in patients over a 30-day follow-up period.

The most unique aspect of this study is the very large and diverse study population sampled from the NRD database. To our knowledge, the total 109,420 cardioversions recorded in the NRD represents the largest sample that has been specifically examined with regard to AF CV and its associated TE complications. The FinCV study was drawn from 3 hospitals in Finland, a county with a relatively homogenous population predominantly comprised of northern European descendants. In contrast, the NRD is drawn from the NIS, 15% black patient admissions, 12% Hispanic, and 7% other races. Additionally, whereas the hospitals in the FinCV were all large referral centers, the present study evaluated cardioversions performed at all nonfederal American hospitals; the NIS is drawn from 10% rural hospitals, 26% urban non-teaching hospitals, and 64% urban teaching hospitals.

Cardioversion is known to transiently depress atrial contractility, decrease left atrial and left atrial appendage flow velocities, and increase the likelihood of thrombus formation, with the duration of depressed contractility correlating with the duration of AF [14]. Even in individuals with acute AF, echocardiographic studies have demonstrated spontaneous echo contrast and left atrial thrombus [15]. The temporal relationship between CV- and TE-associated readmission observed in the current study highlights AF patients' time-dependent risk for early TE post-CV.

Table 3 Risk factors for TE within 30 days of cardioversion (results expressed as odds ratio and 95% confidence interval)

Risk factor	OR (95% CI)	
Congestive heart failure	1.392	(0.95, 2.05)
Hypertension	1.299	(0.80, 2.10)
Age ≥ 65	3.21	(2.00, 5.15)
Diabetes	1.021	(0.67, 1.55)
Prior stroke	0.964	(0.31, 3.01)
Vascular disease	1.056	(0.73, 1.53)
Female sex	1.227	(0.86, 1.76)
End-stage renal disease	0.657	(0.15, 2.97)

Previous studies have reported a transient but marked elevation in stroke and TE rate (0.4–1.61%) soon after CV [9, 16]. Possible explanations for the transient increase in TE risk include atrial stunning, blood stasis, and increased von Willebrand Factor [14]. Von Willebrand Factor can remain elevated up to 30 days following CV [17]. In contrast to the established relationship between CV and TE risk, the temporal relationship between AF episode and TE risk is less clear despite the widely available implantable cardiac devices with continuous AF monitoring capabilities [16, 18]. Building upon the FinCV study, our study highlights the temporal relationship of AF CV and elevated TE risk in a larger, more heterogeneous US population.

Readmission due to TE following CV proved to be relatively rare in this cohort, particularly in patients with a CHA_2DS_2-VASc score of 0 or 1. There are multiple plausible explanations for this observation. First, many patients with transient ischemic attack and stroke with a minor neurological deficit are treated on an outpatient basis [19]. Therefore, this study does not reflect the totality of the healthcare burden associated with TE events following AF CV. Moreover, since the CHA_2DS_2-VASc score is also associated with the severity of the stroke, the ratio of outpatient to inpatient management of TE events is expected to be higher among patients with low CHA_2DS_2-VASc score [20]. Second, many patients with a pre-existing diagnosis of AF and high CHA_2DS_2-VASc score are expected to be on chronic OAC, which likely attenuated elevated TE risk following AF CV. Third, patients with a CHA_2DS_2-VASc score of 0 or 1 may be truly at low risk of any TE risk post-CV regardless of the duration of AF episode and OAC status. Although we have no data on OAC status in this database, it is highly plausible that many patients with CHA_2DS_2-VASc score of 0 or 1 were discharged without OAC due to perceived low TE risk, particularly among those with AF episode < 48 h. Despite the heterogeneity of OAC status, this cohort of low CHA_2DS_2-VASc score of 0 or 1 exhibited extremely low readmission rate associated with TE events.

Table 4 ICD and DRG codes used in analysis

Condition	Code type	Code
Atrial fibrillation	ICD-9 diagnosis	427.31
Cardioversion	ICD-9 procedural	99.61, 99.62, 99.69
Cardioversion, electrical	ICD-9 procedural	99.61, 99.62
Congestive heart failure	ICD-9 diagnosis	398.91, 428.0, 428.1, 428.20, 428.21, 428.22, 428.23, 428.30, 428.31, 428.32, 428.33 428.40, 428.41, 428.42, 428.43, 428.9
Hypertension	ICD-9 diagnosis	401.0, 401.1, 401.9 402.00, 402.01, 402.10, 402.11, 402.90, 402.91 403.00, 403.01, 403.10, 403.11, 403.90, 403.91 404.00, 404.01, 404.02, 404.03, 404.10, 404.11, 404.12, 404.13, 404.90, 404.91, 404.92, 404.93 405.01, 405.09, 405.11, 405.19, 405.91, 405.99
Diabetes mellitus	ICD-9 diagnosis	250.00, 250.01, 250.02, 250.03, 250.10, 250.11, 250.12, 250.13, 250.20, 250.21, 250.22, 250.23, 250.30, 250.31, 250.32, 250.33, 250.40, 250.41, 250.42, 250.43, 250.50, 250.51, 250.52, 250.53, 250.60, 250.61, 250.62, 250.63, 250.70, 250.71, 250.72, 250.73, 250.80, 250.81, 250.82, 250.83, 250.90, 250.91, 250.92, 250.93, 357.2, 362.01, 362.02, 362.03, 362.04, 362.05, 362.06, 362.07, 366.41
[Stroke	ICD-9 diagnosis	434.00, 434.01, 434.10, 434.11, 434.90, 434.91, 435.0, 435.1, 435.2, 435.3, 435.8, 435.9, v1254
Vascular disease	ICD-9 diagnosis	410.0, 410.1, 410.2, 410.3, 410.4, 410.5, 410.6, 410.7, 410.8, 410.9, 412, 413.0, 413.1, 413.9, 414.00, 414.01, 414.02, 414.03, 414.04, 414.05, 414.06, 414.07, 414.10, 414.11, 414.12, 414.19, 414.2, 414.3, 414.8, 414.9 433.00, 433.01, 433.10, 433.11, 433.20, 433.21, 433.30, 433.31, 433.80, 433.81, 433.90, 433.91, 436, 437.0, 437.1, 437.2, 437.3, 437.4, 437.8, 437.9, 438.10, 438.11, 438.12, 438.19, 438.20, 438.21, 438.22, 438.30, 438.31, 438.32, 438.40, 438.41, 438.42, 438.50, 438.51, 438.52, 438.53, 438.6, 438.7, 438.81, 438.82, 438.83, 438.84, 438.85, 438.89, 438.9 440.0, 440.1, 440.20, 440.21, 440.22, 440.23, 440.24, 440.29, 440.30, 440.31, 440.32, 440.4, 440.8, 440.9 447.1, 557.0, 557.1, 557.9
Chronic kidney disease, stage I	ICD-9 diagnosis	585.1
Chronic kidney disease, stage II	ICD-9 diagnosis	585.2
Chronic kidney disease, stage III	ICD-9 diagnosis	585.3
Chronic kidney disease, stage IV	ICD-9 diagnosis	585.4
Chronic kidney disease, stage V	ICD-9 diagnosis	585.5
End-stage renal disease	ICD-9 diagnosis	585.6
Chronic kidney disease, stage unspecified	ICD-9 diagnosis	585.9
Tobacco use	ICD-9 diagnosis	305.10, 305.11, 305.12
Transient ischemic attack	ICD-9 diagnosis	435.9
Acute ischemic stroke with use of thrombolytic agent with major complication or comorbidity	DRG Code	61

Table 4 (continued)

Condition	Code type	Code
Acute ischemic stroke with use of thrombolytic agent with complication or comorbidity	DRG code	61
Acute ischemic stroke with use of rhrombolytic agent without complication or comorbidity	DRG code	63
Intracranial hemorrhage or cerebellar infarct with major complication or comorbidity	DRG code	64
Intracranial hemorrhage or cerebellar infarct with complication or comorbidity or TPA within 24 h	DRG Code	65
Intracranial hemorrhage or cerebellar infarct without complication or comorbidity	DRG code	66
Nonspecific CVA and precerebral occlusion without infarction with major complication or comorbidity	DRG code	67
Nonspecific CVA and precerebral occlusion without infarction without major complication or comorbidity	DRG code	68
Transient ischemia	DRG code	69
Nonspecific cerebrovascular disorder with major complication or comorbidity	DRG code	70
Nonspecific cerebrovascular disorder with complication or comorbidity	DRG code	71
Nonspecific cerebrovascular disorder without complication or comorbidity	DRG code	72

In this study, among all patients, only age ≥ 65 was an independent risk factor for readmission for TE within 30 days of CV. Numerous studies have identified an association between age and stroke, both in the presence and absence of AF [1, 3, 21]. This finding may have an important clinical implication in assessing the risk/benefit of 30-day OAC in male patients ≥ 65 years old after AF CV regardless of AF duration.

Several factors inherent to the NRD limited this study. The most important limitations were the lack of medication data, specifically the periprocedural use of parenteral or oral antithrombotic therapy, and duration of AF prior to CV in the NRD. The lack of medication data precluded analysis of OAC status and its impact on post-CV TE-related re-hospitalization.

This study may have also been limited by possible undercoding of comorbidities. The NRD relies on hospitals' coding of patient comorbidities and outcomes data. Also, since the database only includes re-hospitalized patients, patients with the less severe manifestation of TE that do not require hospitalization are not included in the NRD database. As previously mentioned, the ratio of outpatient to inpatient management of TE events is expected to be variable according to the CHA_2DS_2-VASc score and stroke severity, and inclusion of TE events sufficiently severe to necessitate hospitalization may have underestimated the event rate in patients with low CHA_2DS_2-VASc score.

Despite these limitations, this large-scale database involving more than 100,000 index admissions demonstrated the utility of CHA_2DS_2-VASc score in predicting TE-associated readmission rate following CV and the temporal relationship of TE to CV. It is the first study to establish these findings in the large US cohort. Although there are important limitations to this database, this analysis provides at least a conservative estimate of TE-related admission following CV and is reflective of routine clinical care outside of specific clinical trials.

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