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The Predictive Ability of the $CHADS_2$ and CHA_2DS_2-VASc Scores for Bleeding Risk in Atrial Fibrillation: The $MAQI^2$ Experience☆

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ABSTRACT

Introduction: Guidelines recommend the assessment of stroke and bleeding risk before initiating warfarin anticoagulation in patients with atrial fibrillation. Many of the elements used to predict stroke also overlap with bleeding risk in atrial fibrillation patients and it is tempting to use stroke risk scores to efficiently estimate bleeding risk. Comparison of stroke risk scores to bleeding risk scores to predict bleeding has not been thoroughly assessed.

Methods: 2600 patients followed at seven anticoagulation clinics were followed from October 2009-May 2013. Five risk models ($CHADS_2$, CHA_2DS_2-VASc, $HEMORR_2HAGES$, HAS-BLED and ATRIA) were retrospectively applied to each patient. The primary outcome was the first major bleeding event. Area under the ROC curves were compared with C statistic and net reclassification improvement (NRI) analysis was performed.

Results: 110 patients experienced a major bleeding event in 2581.6 patient-years (4.5%/year). Mean follow up was 1.0 ± 0.8 years. All of the formal bleeding risk scores had a modest predictive value for first major bleeding events (C statistic 0.66-0.69), performing better than $CHADS_2$ and CHA_2DS_2-VASc scores (C statistic difference 0.10 - 0.16). NRI analysis demonstrated a 52-69% and 47-64% improvement of the formal bleeding risk scores over the $CHADS_2$ score and CHA_2DS_2-VASc score, respectively.

Conclusions: The $CHADS_2$ and CHA_2DS_2-VASc scores did not perform as well as formal bleeding risk scores for prediction of major bleeding in non-valvular atrial fibrillation patients treated with warfarin. All three bleeding risk scores (HAS-BLED, ATRIA and $HEMORR_2HAGES$) performed moderately well.

Introduction

Atrial fibrillation (AF) is known to significantly increase the risk of stroke and thromboembolism, leading to significant morbidity and mortality. For over 40 years, warfarin has been used to reduce the risk by up to 60% [1]. However, the beneficial effects of warfarin must be balanced with the increased risk of major bleeding [2]. Guidelines recommend taking into account both thromboembolic and bleeding risk when considering stroke prevention therapy for AF [3]. Prediction of thromboembolic risk is predominately performed using the $CHADS_2$ or CHA_2DS_2-VASc risk scoring systems [4,5].

Multiple scoring systems have been proposed to predict the risk of major bleeding in AF populations, including the $HEMORR_2HAGES$, HAS-BLED and ATRIA scores [6–8]. Choosing the most effective scoring system has been the topic of debate in the literature [9–13]. Additionally, use of bleeding risk assessment tools, especially the HAS-BLED score, has been endorsed by several guidelines for management of AF [14–16].

With overlap of some of the risks factors for stoke or bleeding in the risk prediction rules, the $CHADS_2$ scoring system has been associated with an increased risk of both stroke and bleeding in patients with AF [17–19]. In this study, we retrospectively compared the $CHADS_2$ and

Abbreviations: ACS, Anticoagulation clinics; AF, Atrial Fibrillation; BCBSM/BCN, Blue Cross Blue Shield of Michigan/Blue Care Network; $MAQI^2$, Michigan Anticoagulation Quality Improvement Initiative; NRI, Net Reclassification Improvement; ROC, Receiver Operator Curve; TTR, Time in Therapeutic Range.

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CHA_2DS_2-VASc stroke scores to the $HEMORR_2HAGES$, HAS-BLED and ATRIA bleeding scoring systems for predicting major bleeding in a contemporary, "real-world" population of non-valvular AF patients treated with warfarin.

Methods

$MAQI^2$ Collaborative

The Michigan Anticoagulation Quality Improvement Initiative ($MAQI^2$) is a Blue Cross Blue Shield of Michigan/Blue Care Network (BCBSM/BCN) sponsored continuous quality improvement consortium. Full details of the $MAQI^2$ consortium have previously been published [20,21]. Briefly, the aim of the $MAQI^2$ collaborative is to describe anticoagulation care across the state, identify best practices and procedures associated with best outcomes, and to partner in quality improvement projects. The collaborative was formed in 2008 with initial patient enrollment starting in October 2009. As a BCBSM/BCN-funded quality improvement collaborative, selected anticoagulation clinics (ACS) in the state of Michigan were invited to participate. Participating clinics are provided reimbursement by BCBSM/BCN to cover the costs of participation in $MAQI^2$, including data abstraction and associated quality improvement efforts. All data abstractors undergo training and each center undergoes regular audits to ensure high quality data collection. Data collected is verified by random audits to ensure agreement with pre-defined data element definitions, including the primary outcomes for this study.

Patient Selection

Between October 2009 and December 2012, 2600 new patients with non-valvular AF were enrolled in $MAQI^2$. Patients were identified at the time of ACS enrollment in this inception cohort and clinical data was abstracted from the individual ACS database and hospital or group medical records.

Risk Stratification

The $CHADS_2$, CHA_2DS_2-VASc, $HEMORR_2HAGES$, HAS-BLED and ATRIA scoring systems were retrospectively calculated and patients were grouped into low, intermediate and high risk as noted in Table 1 [4–8,10,19,22]. Presence of an aortic plaque was not available and not included in the calculation of vascular disease for the CHA_2DS_2-VASc score. Genetic factors associated with increased risk for bleeding were not available and not included in the calculation of the $HEMORR_2HAGES$ score. Labile INR was not included in the HAS-BLED score as this data was not available at the time of warfarin initiation. Time in the therapeutic range (TTR) was calculated using the Rosendaal method [23].

Study Endpoints

The primary endpoint was occurrence of first major bleeding event. Major bleeding was defined according to the International Society of Thrombosis and Haemostasis consensus, which includes fatal bleeding, bleeding into a critical organ, overt bleeding requiring transfusion of 2+ units of red blood cells or an overt bleed causing a hemoglobin fall of 2+ g/dL [24].

Statistical Analysis

Because of censored data, the association of patient demographics and comorbidities with the bleeding outcome was evaluated by using Cox regression analysis. We determined the cumulative incidence of first major bleeding in all patients. Patients were stratified according to the various risk scoring systems. Kaplan-Meier analysis was performed to determine the likelihood of a major bleeding event at 1 year, as well as to generate the individual bleeding risks at 1 year for the various bleeding risk scores. For the dichotomous categorical bleeding risk analysis, multiple analyses were performed. Based on the accepted low/moderate/high risk cut offs, we compared low/moderate vs high and low vs moderate/high. We also used the median bleeding risk score of all patients to create low and high risk bleeding groups.

Table 1
Bleeding Risk Scores.

Risk Elements	$CHADS_2$	CHA_2DS_2-VASc	$HEMORR_2HAGES$	HAS-BLED	ATRIA
CHF	1 point	1 point	-	-	-
HTN	1 point	1 point	1 point	1 point	1 point
Age	1 point (≥75)	2 points (≥75) 1 point (65-74)	1 point (>75)	1 point (>65)	2 points (≥75)
DM	1 point	1 point			
Prior Stroke or TIA	2 points	2 points	1 point	1 point	
CAD, PAD or Aortic plaque	-	1 point	-	-	-
Female Gender	-	1 point	-	-	-
Chronic Liver Disease or Cirrhosis	-	-	1 point	1 point	-
Chronic Renal Insufficiency	-	-	1 point	1 point	3 points
Heavy Alcohol Use	-	-	1 point	1 point	-
Malignancy	-	-	1 point	-	-
Thrombocytopenia or Antiplatelet Use	-	-	1 point	-	-
Prior Bleeding Event	-	-	2 point	-	1 point
Anemia	-	-	1 point	-	3 points
History of Falls	-	-	1 point	-	-
Genetic Factors	-	-	1 point	-	-
Prior Bleeding Event or Anemia	-	-	-	1 point	-
TTR < 60%	-	-	-	1 point	-
Use of ASA, clopidogrel, prasugrel, ticagrelor or NSAIDs	-	-	-	1 point	-
Low	0-1	0-1	0-1	0	0-3
Intermediate	2	2	2-3	1-2	4
High	3+	3+	4+	3+	5-10

CHF – congestive heart failure, HTN – hypertension (>140/90 or use of antihypertensive medications), DM – diabetes mellitus, TIA – transient ischemic attack, CAD – coronary artery disease, PAD – peripheral artery disease, ASA – aspirin, TTR – time in therapeutic range, NSAIDs – non-steroidal anti-inflammatory drugs.