Performance of the “CCS Algorithm” in real world patients

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A B S T R A C T

Background: With the publication of the 2014 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation, the Canadian Cardiovascular Society Atrial Fibrillation Guidelines Committee has introduced a new triage and management algorithm; the so-called “CCS Algorithm”. The CCS Algorithm is based upon expert opinion of the best available evidence; however, the CCS Algorithm has not yet been validated. Accordingly, the purpose of this study is to evaluate the performance of the CCS Algorithm in a cohort of real world patients.

Methods: We compared the CCS Algorithm with the European Society of Cardiology (ESC) Algorithm in 172 hospital inpatients who are at risk of stroke due to non-valvular atrial fibrillation in whom anticoagulant therapy was being considered.

Results: The CCS Algorithm and the ESC Algorithm were concordant in 170/172 patients (99% of the time). There were two patients (1%) with vascular disease, but no other thromboembolic risk factors, which were classified as requiring oral anticoagulant therapy using the ESC Algorithm, but for whom ASA was recommended by the CCS Algorithm.

Conclusions: The CCS Algorithm appears to be unnecessarily complicated in so far as it does not appear to provide any additional discriminatory value above and beyond the use of the ESC Algorithm, and its use could result in under treatment of patients, specifically female patients with vascular disease, whose real risk of stroke has been understated by the Guidelines.

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1. Introduction

The Canadian Cardiovascular Society Guidelines Committee has recently published the 2014 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation [1] (the Guidelines). Based upon expert opinion of the best available evidence; however, the CCS Algorithm has not yet been validated. Accordingly, the purpose of this study is to evaluate the performance of the CCS Algorithm in a cohort of real world patients.

Methods: We compared the CCS Algorithm with the European Society of Cardiology (ESC) Algorithm in 172 hospital inpatients who are at risk of stroke due to non-valvular atrial fibrillation in whom anticoagulant therapy was being considered.

Results: The CCS Algorithm and the ESC Algorithm were concordant in 170/172 patients (99% of the time). There were two patients (1%) with vascular disease, but no other thromboembolic risk factors, which were classified as requiring oral anticoagulant therapy using the ESC Algorithm, but for whom ASA was recommended by the CCS Algorithm.

Conclusions: The CCS Algorithm appears to be unnecessarily complicated in so far as it does not appear to provide any additional discriminatory value above and beyond the use of the ESC Algorithm, and its use could result in under treatment of patients, specifically female patients with vascular disease, whose real risk of stroke has been understated by the Guidelines.
recommend no antithrombotic therapy (No Therapy) for all patients with a CHA2DS2-VASc Score ≤ 0, and female patients with a CHA2DS2-VASc Score = 1, and OAC therapy for all other patients (i.e. for all patients with a CHA2DS2-VASc Score of ≥ 1, except for female patients with a CHA2DS2-VASc Score of 1). This ESC Algorithm is simple and familiar, and has been extensively validated.

It is important to acknowledge, that while the new CCS Algorithm is based upon expert opinion of the best available evidence, it has not yet been validated prior to publication. Accordingly, the purpose of this study is to evaluate the performance of the CCS Algorithm in real world patients. Specifically, we intend to compare the CCS Algorithm with the ESC Algorithm in a cohort of patients who are at risk of stroke due to non-valvular atrial fibrillation.

2. Methods

2.1. Participants

Hospital inpatients with documented non-valvular atrial fibrillation/flutter (AF) in whom anticoagulant therapy was being considered were recruited from Kingston General Hospital, located at Queen’s University in Kingston, Ontario. Patients were eligible for the study if they had new onset or known AF that was documented on a 12 Lead ECG. Patients were excluded if they had rheumatic heart disease (moderate or severe mitral stenosis), AF due to a reversible cause (peri-operative, thyrotoxicosis), or conditions other than AF that required anticoagulation (prosthetic heart valves, pulmonary embolism). Patients were also excluded if they had a cognitive impairment that, in the judgment of the investigator, resulted in an inability to follow study procedures, or if they were not fluent in the English language. Ethics approval was obtained from the Research Ethics Board at Queen’s University.

2.2. Data collection

The following details were abstracted from the patient chart and confirmed through verbal interview with the patient: atrial fibrillation history (new onset versus known), atrial fibrillation type (paroxysmal versus persistent), and warfarin use.

After obtaining written informed consent, we then interviewed patients using an iPad questionnaire, “AFib Patient Kiosk” [9]. Individual patients interacted with the iPad directly, and the research assistant remained at the patient’s side to answer questions and to provide assistance where necessary. The order of the questionnaire was standardized. Patients first provided demographic information (age, sex, and ethnicity) using a multiple choice question format. Next, a personal health history was obtained in order to determine the CHA2DS2-VASc Score (congestive heart failure, hypertension, age, diabetes, previous stroke/TIA, vascular disease, and sex) Score.

2.2.1. Statistical analysis

Statistical analysis was performed using SPSS (version 17, SPSS Inc., Chicago, IL) and statistical significance was established a-priori at α = 0.05. Descriptive data in addition to the CHA2DS2-VASc Score were tabulated for the study cohort. The sample was further divided based upon the presence or absence of vascular disease and was analyzed with one way ANOVA or Chi-square analysis dependent upon the data type.

3. Results

Fig. 2 represents a schematic of the study design. A total of 436 consecutive hospital inpatients were screened for entry into the study between May, 2012 and August, 2012. Of those, 220 patients did not meet eligibility criteria and were excluded, leaving 216 patients who were eligible for inclusion in the study. Reasons for exclusion included AF due to a reversible cause (n = 51), presence of other conditions that required anticoagulation with warfarin (n = 41), cognitive impairment (n = 99) and communication difficulties (n = 29). Thirty patients declined to participate in the study, and 14 patients withdrew from the study part way through completing the questionnaire, leaving 172 patients on whom the primary analysis was performed.

3.1. Patient characteristics

The patient characteristics of the study participants are reported in Table 1. The average age of the study participants was 73 ± 12 years.
78% of patients had a known history of AF, and 59% of patients were already on warfarin. The mean CHA2DS2-VASc Score was 3.5 ± 2.0, representing an annual absolute risk of stroke of 6.3%.

### 3.2. Patient classification

Table 2 illustrates the classification of patients using either the ESC Algorithm or the CCS Algorithm. 10 out of 172 patients (5.8%) had a CHA2DS2-VASc Score of 0, while there was one female patient (0.6%) with a CHA2DS2-VASc Score of 1. Accordingly 11 out of 172 patients (6%) were allocated to No Therapy using the ESC Algorithm. Conversely, 161 out of 172 patients (94%) have a CHA2DS2-VASc Score ≥ 1 (excluding the single female patient with a CHA2DS2-VASc Score of 1), and were therefore allocated to therapy with OAC. Progressing through the CCS Algorithm, 131 out of 172 patients (76%) were aged ≥ 65 years, and were therefore allocated to therapy with the ESC Algorithm. 11 patients (6%) were allocated to No Therapy using the CCS Algorithm. 10 out of 172 patients (5.8%) had a CHA2DS2-VASc Score = 0.

10 versus 70 ± 13 years, representing an annual absolute risk of stroke of 6.3%.

Table 3 presents the contingency table results. 159 out of 172 patients (92%) were recommended OAC therapy by both the ESC Algorithm and the CCS Algorithm. 11 out of 172 patients (6%) were recommended No Therapy by both the ESC Algorithm and the CCS Algorithm. 11 out of 172 patients (6%) were recommended No Therapy by the CCS Algorithm, 131 out of 172 patients (76%) were aged ≥ 65 years of age, while 28 out of the remaining 40 patients (16%) had one or more of the following “CHDS” risk factors: prior stroke or TIA, hypertension, heart failure or diabetes mellitus. Accordingly 159 out of 172 patients (92%) were allocated to therapy with OAC using the CCS Algorithm. 2 out of 172 patients (1%) had vascular disease as their sole thromboembolic risk factor, and these two patients were allocated to therapy with ASA using the CCS Algorithm. 11 patients (6%) were allocated to No Therapy using the CCS Algorithm, of which one patient was female.

The patient characteristics were then analyzed by vascular disease status (see Table 4). Patients with vascular disease were older (75 ± 10 versus 70 ± 13 years, p = 0.007) than patients without vascular disease, and there was a trend towards a greater proportion of patients with vascular disease being aged ≥ 75 years (54% versus 41%, p = 0.076). Patients with vascular disease were more likely to have a history of heart failure (33% versus 12%, p = 0.001), and the mean CHA2DS2-VASc Score was significantly higher in patients with vascular disease than in patients without vascular disease (4.4 ± 1.9 versus 2.8 ± 1.7, p < 0.001).

### 4. Discussion

The Canadian Cardiovascular Society Atrial Fibrillation Guidelines Committee has introduced the “CCS Algorithm” in the 2014 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. This represents an attempt to further refine the risk stratification, and treatment of patients with non-valvular atrial fibrillation. The CCS Algorithm has not yet been validated prior to publication, and as such, we set out to evaluate the performance of the CCS Algorithm in real world patients by comparing the CCS Algorithm with the ESC Algorithm in a cohort of patients who are at risk of stroke due to non-valvular atrial fibrillation. The results of our study show that, for the vast majority (99%) of patients, there is no difference in recommended therapy between the CCS Algorithm and the ESC Algorithm.

There are, however, two key patient populations that distinguish the CCS Algorithm from the ESC Algorithm; patients with vascular disease but no other thromboembolic risk factors (CHA2DS2-VASc Score = 1), and female patients with vascular disease, but no other thromboembolic risk factors (CHA2DS2-VASc Score = 2).

In our cohort of patients, there were only two patients (1%) with vascular disease but no other thromboembolic risk factors. We found that patients with vascular disease were older, and were more likely to have a history of heart failure than patients without vascular disease. These results are concordant with the Danish National Patient Registry [10], where only 508 out of the 87,202 patients (0.6%) were identified as having vascular disease without any other thromboembolic risk factors. In this same study, patients with vascular disease were found to be older, and were more likely to have heart failure, hypertension, diabetes, and previous thromboembolism. As a result, in patients with atrial fibrillation, it is very unlikely that vascular disease will occur in isolation of other thromboembolic risk factors.

The Guidelines Committee authors recommended the use of ASA for patients with vascular disease without any other thromboembolic risk factors.

### Table 1

**Patient characteristics.**

| Demographics | n = 172 |
|--------------|--------|
| Age (years)  | 73 ± 12 |
| Ethnicity    |       |
| Caucasian    | 164 (95%) |
| Atrial fibrillation history |       |
| New onset    | 38 (22%) |
| Known        | 134 (78%) |
| Atrial fibrillation type |       |
| Paroxysmal   | 62 (36%) |
| Persistent   | 72 (42%) |
| Permanent    | 52 (30%) |
| Warfarin     | 102 (59%) |
| CHA2DS2-VASc score mean | 3.5 ± 2.0 |
| Congestive heart failure | 37 (22%) |
| Hypertension | 102 (59%) |
| Age ≥ 75     | 81 (47%) |
| Diabetes mellitus | 49 (29%) |
| Stroke, TIA or thromboembolism | 38 (22%) |
| Vascular disease | 79 (46%) |
| Coronary artery disease | 70 (41%) |
| Angina       | 32 (19%) |
| Previous myocardial infarction | 42 (24%) |
| Previous PCI | 20 (12%) |
| Previous CAGB | 22 (13%) |
| Peripheral arterial disease | 26 (15%) |
| Age 65–74    | 50 (29%) |
| Female sex   | 56 (34%) |

### Table 2

**Patient classification using the ESC Algorithm (CHA2DS2-VASc Score) and the “CCS Algorithm”.

| Therapy          | n (%) | Male | Female |
|------------------|-------|------|--------|
| OAC              | 161 (94%) | 106  | 55     |
| No therapy       | 11 (6%)   | 10   | 1      |

**CCS Algorithm (progressing through algorithm)**

| Age ≥ 65 | OAC | 131 (76%) | 82 | 49 |
| CHDS     | OAC | 28 (16%)  | 22 | 6  |
| Vascular disease | ASA  | 2 (1%)  | 2  | 0  |

No therapy

| No therapy | OAC | 11 (6%) | 10 | 1 |

*OAC = oral anticoagulant therapy.

CHDS = CHF, Htn, diabetes, stroke/TIA.

A excluding female patients with a CHA2DS2-VASc Score of 1.

B including female patients with a CHA2DS2-VASc Score of 1.
risk to justify the use of OAC in preference to ASA. This position is sup-
ported by the Guidelines. Arguably these female patients are at suf-
ciently high risk (1.6% annual stroke risk [7]), for which OAC is currently recommended by the Guidelines.

Further, use of the CCS Algorithm could increase in major bleeding. As such the routine use of apixaban, in preference to ASA, in female patients with vascular disease, but no other thromboembolic risk factors is actually 2.0 \times 10^{-3}.

The importance of the authors, it is ill advised to recommend ASA in preference to apixaban for patients (male or female, but especially female) with vascular disease as their sole thromboembolic risk factor.

This study was conducted on hospital inpatients. As such the findings of this study may not be able to be extrapolated to the outpatient setting. However, the results of the Danish National Patient Registry [7] appear to be concordant with the results of the present study, and therefore, the results of this study can likely be extrapolated to the entire atrial fibrillation population.

5. Conclusion

The CCS Algorithm, as proposed by the CCS AF Guideline Committee, does not appear to be any better in the real world setting than simply using the ECS Algorithm. Unlike the CCS Algorithm, the ESC Algorithm is familiar to most clinicians, and can be easily remembered and employed to dichotomize patients into Low Risk (CHA2DS2-VASc Score = 0), and female patients with a CHA2DS2-VASc Score = 1) for thromboembolism, who require No Therapy, or High Risk (CHA2DS2-VASc Score ≥ 1, except for female patients with a CHA2DS2-VASc Score of 1) for thromboembolism, who do require OAC Therapy. In the opinion of the authors, it is ill advised to recommend ASA in preference to apixaban for patients (male or female, but especially female) with vascular disease as their sole thromboembolic risk factor.

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Conflicts of interest

LaHaye: Has received speaker fees from Bristol-Myers Squibb and Pfizer.
Olesen: Has received speaker fees from Bristol-Myers Squibb and Boehringer Ingelheim, and funding for research from the Lundbeck Foundation, Bristol-Myers Squibb, and The Capital Region of Denmark, Foundation for Health Research.
Lacombe: None declared.

References

[1] Verma A, Cairns JA, Mitchell LB, et al. 2014 focused update of the Canadian Cardiovascular Society Guidelines for the management of atrial fibrillation. Can J Cardiol 2014;30:1114–30.
[2] Cairns JA, Connolly S, McMurty S, et al. Canadian Cardiovascular Society atrial fibrillation Guidelines 2010: prevention of stroke and systemic thromboembolism in atrial fibrillation and flutter. Can J Cardiol 2011;27:74–90.
[3] Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: JAMA 2001;285:2864–70.
[4] Skanes AC, Healey JS, Cairns JA, et al. Focused 2012 update of the Canadian Cardiovascular Society atrial fibrillation guidelines: recommendations for stroke prevention and rate/rhythm control. Can J Cardiol 2012;28:125–36.
[5] Lip GYH, Nieuwlaat R, Pisters R, Lane DA, Crijns HJGM. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach. Chest 2010;137:263–72.
[6] Olesen JB, Torp-Pedersen C, Hansen ML, Lip GYH. The value of the CHA2DS2-VASc score for refining stroke risk stratification in patients with atrial fibrillation with a CHADS2 score 0–1: a nationwide cohort study. Thromb Haemost 2012;107:1072–9.
[7] Olesen JB, Lip GY, Hansen ML, et al. Validation of risk stratification schemes for predicting stroke and thromboembolism in patients with atrial fibrillation: nation-wide cohort study. BMJ 2011;342:d124.
[8] Camm AJ, Lip GYH, De Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. Eur Heart J 2012;33:2719–47.
[9] Clinical Support Systems. ‘AppFib Patient Kiosk’ iPad application available at the iTunes App Store. February 23, 2012.
[10] Olesen JB, Lip GYH, Lane DA, et al. Vascular disease and stroke risk in atrial fibrillation: a nationwide cohort study. Am J Med 2012;125:e13–23.
[11] Connolly SJ, Eikelboom J, Joyner C, et al. Apixaban in patients with atrial fibrillation. N Engl J Med 2011;364:806–17.

Table 4

Patient characteristics by vascular disease status.

| Vascular disease | Absent (n = 93) | Present (n = 79) | p Value |
|------------------|----------------|-----------------|---------|
| Demographics     |                |                 |         |
| Age (years)      | 70 ± 13        | 75 ± 10         | 0.007*  |
| Ethnicity        |                |                 |         |
| Caucasian        | 88 (95%)       | 76 (96%)        | 0.624   |
| Paroxysmal       | 41 (44%)       | 21 (27%)        | 0.027*  |
| Persistent       | 13 (14%)       | 7 (9%)          |         |
| Permanant        | 20 (22%)       | 32 (41%)        |         |
| Warfarin         | 52 (56%)       | 50 (63%)        | 0.326   |
| CHA2DS2-VASc mean| 2.8 ± 1.7      | 4.4 ± 1.9       | -0.001* |
| Congestive heart failure | 11 (12%) | 26 (33%) | 0.001* |
| Hypertension     | 51 (55%)       | 51 (65%)        | 0.196   |
| Diabetes mellitus| 38 (41%)       | 43 (54%)        | 0.076   |
| Stroke, TIA or thromboembolism | 20 (22%) | 18 (23%) | 0.840   |
| Vascular disease | 79 (100%)      |                 |         |
| Coronary artery disease | 70 (89%) |            |         |
| Angina           | 32 (41%)       |                 |         |
| Previous myocardial infarction | – | 42 (53%) |         |
| Previous PCI     | 20 (25%)       |                 |         |
| Previous CABG    | 22 (28%)       |                 |         |
| Peripheral arterial disease | 26 (33%) |            |         |
| Age ≥ 75         | 38 (41%)       | 43 (54%)        | 0.076   |
| Age 65–74        | 27 (29%)       | 23 (30%)        | 0.991   |
| Female sex       | 31 (33%)       | 25 (32%)        | 0.814   |