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Title: Geographic and temporal variation in the treatment and outcomes of atrial fibrillation: a population-based analysis of national quality indicators

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Reviewer 1: Dr. François Madore

Institution: Hôpital du Sacré-Coeur de Montréal
General comments (author response in bold)

Summary

Chew et al. investigated the variation in AF quality indicators developed by the Canadian Cardiovascular Society in a population-based cohort of adults with incident nonvalvular AF in Alberta. The authors assessed the geographic and temporal variation in anticoagulation prescription, ischemic stroke and major bleeding outcomes following AF diagnosis. They observed that there was substantial regional variation observed in OAC initiation, but not ischemic stroke or major bleeding. The authors conclude that the large geographic variation in OAC prescription provides an opportunity for additional study into patient, provider and health-system factors that contribute to variation and drive disparities in high-quality and equitable care in AF.

General comments

The study addresses significant and clinically relevant health issues: management of AF and insufficient uptake of evidence-based AF therapies into routine clinical practice. This study provides interesting data on geographic and temporal trends in anticoagulation prescription, ischemic stroke and major bleeding outcomes. The manuscript is generally well written and clearly presented. It follows most of STROBE guidelines.

Thank you.

Specific comments

1) Methods – Pampalon deprivation index. A short description should be provided in the manuscript as this index may not be known to the average reader.

We have provided additional details of the Pampalon deprivation index. These details are included in Supplemental eMethods 1, given the word count limitations of the CMAJ Open. We would be happy to move the additional description into the main text if preferred by the Editors. The supplemental eMethods include the following:

“As a comprehensive indicator of socioeconomic status, we used the Pampalon deprivation index, which is a small-area based composite index derived from census data that includes employment status, income, education, marital status, single parent status or living alone. The material index reflects deprivation of wealth, goods and conveniences, and the social index reflects deprivation of relationships among individuals in the family, the workplace, and the community. Each index stratifies each dissemination area (i.e. smallest standard census area) into quintiles, from 1 (least deprived) to 5 (most deprived). Deprivation scores were obtained from the Institut National de Santé Publique du Quebec and assigned to individuals in the cohort based on postal code.”

2) Methods – NVAF diagnosis: Was an echocardiogram required for inclusion in the cohort to differentiate NVAF from valvular AF?

We did not have echocardiographic data available for linkage to the administrative datasets. To differentiate valvular from non-valvular AF, we used administrative definitions of valvular AF.

3) Methods – were patients at high bleeding risk excluded from the study (for instance, patients with a diagnosis of GI bleeding in the years prior to the index date)?

No, we did not exclude high bleeding risk patients from the study as these exclusion criteria were not applied in the Quality Indication definitions provided by the Canadian Cardiovascular Society. We have clarified this in the methods as follows:

“To be consistent with the definitions of AF quality indicators developed and updated by the Canadian Cardiovascular Society, we did not exclude high bleeding risk patients from the study.”

4) Methods – it would be interesting to provide basic demographic information on the geographic regions. For instance, what is the proportion of indigenous people, the proportion of the population living in rural vs urban area for each region? What is the number of physicians in the region, the distribution of sub-specialists, the number of health centers in each region, etc. This information could be informative and could be provided as supplemental material.

Additional information is provided via an interactive map that visualizes the geographic variation of AF quality indicators and additional HSA characteristics (<https://bit.ly/3fOXJq3>). These HSA characteristics include social vulnerability indicators, visible minorities, employment, income, other socioeconomic indicators, and rural/urban status. We did not collect information regarding the distribution of subspecialists providing AF care across the province.

5) Methods – Is information available on subspecialty care (i.e. whether or not the patient was cared for by a cardiologist or general internist or by primary care physicians)?

No, information regarding subspecialty access or primary care attachment was not available for this study.

6) Methods – Is information available on filled prescriptions for other medications (other than OAC) for participants over the same period? This would help to evaluate whether the patients who did not receive AOC were simply lost to follow-up.

We did not collect data on other filled prescriptions for other medications, but based on health encounters (inpatient – DAD, outpatient – NACRS, and physician claims), 0.6% (N=394) were lost to follow up based on emigration out of the province and 10.2% (N=6,565) were deceased within a 1 year. We have included this information in the results as follows:

“Following index diagnosis of NVAF, 3,035 (4.7%) of the cohort were excluded prior to endpoint ascertainment of OAC initiation or prescription as they died within 90 days of NVAF diagnosis. Among patients surviving beyond the 90-day exclusion period, 10.2% (N=6,565) died within 1 year and 0.6% (N=394) emigrated out of the province and were lost to follow up.”

7) Methods – Is information available on prescription of Aspirin or other platelet aggregation inhibitors (e.g. clopidogrel, ticlopidine, etc.)?

No, we did not collect this data. We have now acknowledged this limitation in the manuscript as follows:

“Furthermore, we did not collect data on concomitant use of antiplatelet agents which may influence stroke and bleeding risk.”

8) Results: the authors could consider adding a flow diagram of participants (Included/excluded participants, high-risk/moderate risk, etc.).

A flow diagram of participants is now included as Supplemental Figure S1.

9) Results/discussion: how can the authors explain that they did not observe significant variation in the risk of ischemic stroke or major bleeds despite variation in the use of OAC. Some hypotheses should be added and discussed.

Additional discussion regarding the absence of variation in ischemic stroke / major bleeds is now included in the manuscript as follows:

“Second, we did not detect geographic variation in ischemic stroke risk or major hemorrhage may be partially attributed to the administrative definitions to identify study outcomes. Consistent with the national quality indicator definitions, the one-year ischemic stroke risk was reported for all patients with incident AF, regardless of CHADS2 score. The one-year assessment of stroke outcome may not be long enough to observe the downstream effects of the observed variation in OAC initiation. Other potential reasons for the disconnect between process (OAC prescription) and outcomes measure may also reflect the small sample size of clinical events in some of the geographic areas, region differences in coding practices, or unmeasured clinical practice factors such as improved management of AF comorbidities that interact with stroke and bleeding risk.”

Reviewer 2: Dr. Suzan Abou-Raya

Institution: Faculty of Medicine, University of Alexandria

General comments (author response in bold)

This is a well-written article on the important issue of temporal variation in the initiation treatment and of atrial fibrillation.

Thank you.

1. Abbreviations such as OAC, DOAC & CHADS2 score should be written out in full at the beginning

OAC and DOAC abbreviations are written out in full when first described in the text. The full components of the CHADS2 score (and administrative definitions) are described in Supplemental Table S1. We have made the following amends to the manuscript:

Introduction: “High-quality evidence guides AF management, including use of oral anticoagulation (OAC) to reduce the risk of ischemic stroke.”

Methods: “We also determined the proportion of OAC persistence at 1 year where persistence was defined as a minimum of 6 months of ongoing prescription fills of any OAC (including warfarin and direct oral anticoagulations (DOACs)). As the introduction of DOACs (dabigatran, rivaroxaban, apixaban, and edoxaban) may have influenced.”

2. In the Methods section- do authors have data on the level of education of patients?

Our primary indicator for socioeconomic status was the Pampalon Deprivation Index (material and social deprivation), which is included in the baseline characteristics table. However, for descriptive purposes, additional information is

provided in the online interactive map that visualizes the geographic variation of AF quality indicators and additional HSA characteristics (<https://bit.ly/3fOXJq3>). Specifically, the proportion of individuals with secondary (high) school or diploma equivalent is provided by HSA geographic unit.

3. In the Results section- on page 8, lines 14 & 15 - should be rephrased to make more sense

The results section has been rephrased as follows:

“Over the 8-year study period, the unadjusted proportions of OAC initiation are described by regional HSA for NVAF patients at high risk of stroke (Figure 1) and moderate risk of stroke (Figure 2). Crude OAC initiation proportions ranged from 22.6% (95% confidence interval (CI) 14.6 - 30.5%) to 71.2% (95% CI 60.0 - 82.3%) among high stroke risk NVAF, and 22.7% (95% CI 13.2 - 32.2%) to 55.8% (95% CI 47.2 - 64.3%) among moderate stroke risk NVAF.”

Reviewer 3: Dr. Yi-Ting Lin

Institution: Department of Family Medicine

General comments (author response in bold)

Chew et al. investigated the geographic variation in the quality of atrial fibrillation in Alberta, Canada. The researchers demonstrated less than 60% oral anticoagulation treatment among incident atrial fibrillation patients, presenting large geographic variation in oral anticoagulation prescription. This descriptive research demonstrated a comprehensive study design and delicate result to present Alberta's overall oral anticoagulation prescription pattern. I have no major comments in this paper.

Thank you.