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Research Article

Adherence to the Canadian Cardiovascular Society Atrial Fibrillation Guidelines by Family Medicine Groups in Quebec: the I-FACILITER project

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ABSTRACT

Background: The Canadian Cardiovascular Society (CCS) Atrial Fibrillation (AF) guidelines 2014 recommends oral anticoagulation (OAC) for patients with CHADS₂ ≥1 or age ≥65 years and non-vitamin K oral anticoagulants (NOACs) as the preferred medications. We aimed to evaluate adherence to these guidelines by family group practices (FMG) in Quebec.

Methods and results: We completed a cross-sectional evaluation at 15 FMGs. There were 431 patients with non-valvular AF: mean age of 77.3±10.4 years and 52.9% were females. CHADS₂ and HAS-BLED were infrequently documented (47% and 7%, respectively). Most patients (93%) were appropriately anticoagulated (96% for both patients with CHADS₂ ≥1 and patients with age ≥65 years). Sixty-five percent of patients were anticoagulated with warfarin, 28% with NOACs and 21% of patients received a combination of oral anticoagulant (OAC)s and aspirin.

Every decade increase in age was associated with 49% increase in odds of adherence to the guidelines and 26% decrease in odds of NOACs's use. Each point increase in HAS-BLED was associated with 51% decrease in odds of adherence to the guidelines and 36% decrease in odds of NOACs's use. No patient with HAS-BLED of ≥5 received NOAC. Heart failure was associated with a 61% decrease in odds of NOACs's use.

Conclusion: AF management by FMGs could be improved by 1) increasing NOACs uptake, 2) decreasing the combination of OAC with ASA and 3) increasing documentation of stroke and bleeding risks.

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Background

Despite recent Canadian Cardiovascular Society (CCS) Atrial Fibrillation (AF) guidelines emphasizing the importance of oral anticoagulation (OAC), there remained several care gaps noted in the management of Canadians with AF in family practice [1-4]. Notwithstanding the high rates of OAC ($\geq 90\%$) of patients enrolled in these national cohorts, previous authors reported more common use of warfarin than non-vitamin K oral anticoagulants (NOAC), infrequent use of stroke and bleeding risk scores and inappropriate OAC dosing in many patients [1-4]. All of these observational studies were completed prior to 2015, when NOACs were still novel and many primary care physicians (PCP)s might be unfamiliar and uncomfortable with their use [1-4]. The organization of family medicine practice in Quebec has some particularities that differ from the rest of Canada. Since 2005, the Quebec government has established family medicine groups (FMG)s. Each FMG is a group of approximately 12-14 physicians caring for roughly 18,000 patients. In addition to services during regular working hours, FMG also provides weekend services and telephone support. In addition to the regular reimbursement fees for medical services, each FMG receives salary support for nursing and administrative support based on the number of registered patients. These measures aimed to improve accessibility, continuity, and quality of primary practice, in particular for patients with chronic diseases [5]. Considering the above particularities, we aimed to appraise the quality of AF care at Quebec FMGs and to contrast the adherence to the CCS-AF guidelines to the adherence reported elsewhere in Canada. Our secondary objectives were to determine the independent predictors of adherence to CCS-AF guidelines and use of NOACs at Quebec FMGs.

Methods

In 2015, we completed a cross-sectional survey (I-FACILITER) evaluating OAC in patients with AF at 15 FMGs in five Quebec regions (Beauce, Saguenay/Chicoutimi, Montreal, Laval and Trois-Rivières) (List of participating FMGs/Appendix 1). The selection of the FMGs were based on the volume with selection of mainly high-volume regional FMGs. The FMG nurses reviewed the charts of all consecutive patients with non-valvular AF. We included all patients with AF/atrial flutter, regardless of chronicity, etiology, or pattern (persistent or paroxysmal). Each patient was entered only once in the dataset. For patients who presented more than once to the FMG, we retained the most recent data on AF management. We excluded patients with metallic valvular prostheses and moderate/severe mitral stenosis since the AF guidelines focused mainly on non-valvular AF. In addition to general demographic data, collected information included the following: AF history; medical history, history of major bleeding, stroke and bleeding risk assessments, concomitant medications, with a focus on aspirin (ASA) and other antiplatelets, anti-inflammatories and OACs, specialists involved in AF care and warfarin adjustment. (Appendix 2: sample case report). The CHADS₂ and HAS-BLED were calculated by the coordinating center, based on the risk factors noted in the case reports. We reviewed a random sample of 100 clinic charts to ensure the quality of captured data.

A cardiologist (TH) examined all case reports to determine adherence to the CCS-AF guidelines 2014 and to identify justifications for non-adherence to these guidelines [6]. Adherence was determined as OAC for all patients with CHADS₂ ≥ 1 or age ≥ 65 years unless presence of

valid contra-indications. Valid reasons for withholding OAC were recent or active bleeding diathesis, increased bleeding risk and patient refusal. This cross-sectional study was part of a knowledge translation initiative known as I-FACILITER whereby the FMGs received two on-site workshops with dissemination of the CCS-AF 2014 guidelines at the first session and feedback of the local performance in terms of adherence to the guidelines at the second session. Workshops were organized regionally and moderated by a regional cardiologist (TH, IG, MM, DD, MB, MAB and RB).

The study was approved by the McGill Health Center Ethic Boards and the medical directors of all participating FMGs.

Definitions of clinical variables collected

Kidney disease: most recent (within one-year) estimated glomerular filtration of less than 60 cc/min.

Liver disease: abnormal liver enzymes (more than 3 times of upper limit of normal values) or liver disease documented in clinical charts.

Major bleeding: bleeding requiring hospitalization and/or transfusion.

Statistical analyses

All data were analyzed NCSS version 12, 2018. Categorical variables were reported as proportions, continuous variables were reported as with standard deviations (median for duration of AF due to its right skewed distribution). We used the CHADS₂ and HAS-BLED calculated by the coordinating centers for all analyses. We completed multivariate logistic regressions to determine independent predictors for adherence to the guidelines and use of NOACs. We selected variables for both models based on their univariate correlation with the above variables of interests (all variables with p-values of 0.25 and less). For sensitivity analyses, we forced the variable "referral to cardiologist" in both models. All p-values less than 0.05 were considered significant.

Results

We described the characteristics of patients stratified by adherence to CCS-AF guidelines in (Table 1). Most patients were elderly (mean age of 77 years) and more than half were females. Approximately 40% of patients had paroxysmal AF and a very small minority (less than 2%) had pure atrial flutter. Only 43% and 7% of patients had CHADS₂ and HAS-BLED scores documented in their clinic charts. The mean CHADS₂ and HAS-BLED scores (as calculated by the coordinating center) were similar at 2.4. Close to a third of patients suffered from heart failure, diabetes mellitus and renal disease while 75% were hypertensive. Less than 5% had prior major bleeding, prior cancer and peptic ulcer disease. The majority of patients were referred to cardiologists (81%) and only 1% was referred to internists. Excluding patients with valid contra-indications and/or refusal, most patients who should have been on OAC according to guidelines were appropriately anticoagulated (96.4% for patients of 65 years and older and 95.8% for patients with CHADS₂ ≥ 1). Patients who were not anticoagulated according to guidelines were younger and with lower proportion of CHADS₂ ≥ 1 . There were notable regional variations in rates of appropriate OAC (87%-98%) and for NOAC (15%-42%) (Figure 2). We compared the characteristics of patients anticoagulated with warfarin and NOACs in (Table 2). Patients anticoagulated with warfarin had more high-risk features including older age, higher CHADS₂ and

HASBLED scores, more heart failure and kidney diseases. Patients treated with NOACs had more paroxysmal AF and AF of more recent onset.

We reported the independent predictors of adherence to guidelines and NOACs in (Tables 3 and 4), respectively. Increased age was associated with increased probability of adherence to guidelines and decreased odds of NOACs treatment. For every decade of increase in age, there was an approximate increase of 49% in odds of adherence to the CCS-AF guidelines and a decrease of 24% odds in use of NOACs. HAS-BLED score was also an independent determinant of decreased adherence to the CCS-AF guidelines and lesser use of NOACs. Every point increase in HAS-BLED reduces by 54% the odds of adherence to the CCS-AF guidelines and by 36% the odds of NOACs use. The use of NOAC declined from 47.9% in patients with HAS-BLED of 0 to 22.9% in patients with HAS-BLED of 4. No patient with HAS-BLED of ≥ 5 received NOAC (89% of these patients were appropriately anticoagulated). Patients with heart failure were 60% less likely to

receive NOACs. CHADS₂ was associated with a borderline significant 25% less odds of receiving NOAC with each increase in point of CHADS₂ (p: 0.050).

We examined the use of ASA and OAC in (Figure 1). Overall, 93.0% were anticoagulated and 21% of these patients received additional ASA. Forty-nine percent were treated with warfarin alone and 16% with a combination of warfarin and ASA. Close to a quarter of patients were treated with NOACs and 5% with a combination of NOACs and ASA. None of the patients who received the combination of OAC, and ASA had any reason justifying this combination (such as recent stent implantation or acute coronary syndrome). Five percent of patients were prescribed ASA alone, while 0.5% of patients were taking another anti-platelet, and 1.5% of patients did not receive any OAC or anti-platelet without any valid justification. We observed marked regional variations in uses of OAC (from 88% to 98%) and NOAC (from 15% to 43%). (Figure 2).

Table 1: Characteristics of patients stratified by adherence to the CCS Atrial Fibrillation Management Guidelines 2014.

Clinical Characteristics	All patients N=431 (%)	Adherent N=410 (%)	Non-adherent N=21 (%)	p-values*
Mean age, years	77.3 $\pm$ 10.3	77.7 $\pm$ 10.0	70.4 $\pm$ 9.5	0.03
Female	228 (52.9)	220 (53.7)	8 (38.1)	0.24
Median duration of AF, years, (Q1:Q3)	4.0 (1.0, 8.0)	3.5 (0.0,6.3)	4.0 (1.0,8.0)	0.84
Age ≥ 65 years old	406 (94.2)	392 (95.6)	14 (66.7)	0.02
Age ≥ 75 years old	285 (66.1)	281 (68.6)	4 (19.0)	0.001
CHADS ₂ ≥ 1	416 (96.5)	405 (98.7)	11 (52.4)	<0.001
Paroxysmal AF	173 (40.1)	164 (40.0)	9 (42.9)	0.96
Atrial flutter only	8 (1.8)	7 (1.7)	1 (4.8)	0.22
Mean CHADS ₂ score	2.4 $\pm$ 1.3	2.4 $\pm$ 1.3	2.0 $\pm$ 1.5	0.22
Mean HAS-BLED score	2.4 $\pm$ 1.0	2.4 $\pm$ 1.0	2.5 $\pm$ 1.2	0.58
Prior major bleeding	19 (4.4)	18 (4.4)	1 (4.8)	0.94
History of heart failure	137 (31.8)	129 (31.5)	8 (38.1)	0.69
Hypertension	324 (75.1)	310 (75.6)	14 (66.7)	0.51
Diabetes mellitus	131 (30.4)	125 (30.5)	6 (28.6)	0.85
Prior stroke/transient ischemic attack	72 (16.7)	70 (17.0)	2 (9.1)	0.37
Prior peptic ulcer disease	17 (3.9)	17 (4.1)	0 (0.0)	0.34
Kidney disease	112 (25.9)	105 (25.6)	7(33.3)	0.44
Liver disease	11 (2.6)	11 (2.7)	0 (0.0)	0.45
Excessive alcohol use	17 (3.9)	16 (3.9)	1 (4.8)	0.84
Prior cancer	23 (5.3)	23 (5.6)	0 (0.0)	0.27
Cognitive impairment	20 (4.6)	18 (4.4)	2 (9.5)	0.28
Referral to cardiology/internist	361 (83.8)	344 (83.9)	17 (81.0)	0.79

*: Comparison between patients whose treatment adhered or not to the CCS-AF Guidelines 2014.

AF: Atrial fibrillation; Q1, Q3: First quartile, third quartile.

[†]: Defined as ≥ 15 drinks/week and ≥ 12 drinks/week for men and women respectively <http://educalcoool.qc.ca/>

CHADS₂: The Congestive Heart Failure, Hypertension, Age, Diabetes, Stroke/Transient Ischemic Attack.

HAS-BLED: Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly (> 65 Years), Drugs/Alcohol.

Table 2: Characteristics of patients stratified by anticoagulants.

Clinical Characteristics	All anticoagulated patients N=401 (%)	Warfarin N=280 (%)	NOACs N=121 (%)	p-values*
Mean age, years	77.6±10.1	79.0 ±10.0	74.3±9.5	0.009
Median duration of AF, years, (Q1:Q3)	4.0 (1,8)	4.0 (2,9)	3.0 (1,7)	0.06
Female	212 (52.4)	146 (52.1)	66 (54.5)	0.67
Age ≥65 years old	366 (91.3)	262 (93.6)	104 (86.0)	0.02
Age ≥75 years old	261 (65.0)	199 (71.1)	62 (51.2)	<0.001
CHADS ₂ ≥1	379 (94.5)	270 (96.4)	109 (90.0)	0.02
Paroxysmal AF	162 (39.7)	103 (36.7)	59.5 (49.2)	0.01
Atrial flutter only	6 (1.5)	4 (1.4)	2 (1.7)	0.99
Mean CHADS ₂ score	2.4±1.3	2.5±1.3	2.1±1.3	0.007
Mean HAS-BLED score	2.4±1.0	2.5±1.0	2.1±1.0	<0.001
Prior major bleeding	16 (4.0)	11 (3.9)	5 (4.1)	0.93
History of heart failure	126 (31.4)	105 (37.5)	21 (17.4)	<0.001
Hypertension	306 (76.3)	221 (78.9)	85 (70.2)	0.08
Diabetes Mellitus	124 (30.9)	81 (28.9)	43 (35.5)	0.18
Prior stroke/transient ischemic attack	67 (16.7)	47 (16.8)	20 (16.5)	1.0
Prior peptic ulcer disease	15 (3.7)	8 (2.9)	7 (5.8)	0.16
Kidney Disease	104 (25.9)	87 (31.2)	17 (14.2)	<0.001
Liver Disease	11 (2.7)	7 (2.5)	4 (3.3)	0.64
Excessive alcohol use [‡]	14 (3.5)	7 (2.5)	7 (5.8)	0.10
Prior cancer	23 (5.7)	17 (6.1)	6 (5.0)	0.66
Referral to cardiologist/internist	341 (83.8)	233 (83.2)	108 (89.3)	0.22

*: Comparison between patients anticoagulated with warfarin and with NOACs

AF: Atrial fibrillation, NOACs: Non-vitamin K oral antagonists, Q1, Q3: First quartile, third quartile.

[‡]: Defined as ≥15 drinks/week and ≥12 drinks/week for men and women respectively <http://educalcoo.qc.ca/>

CHADS₂: The Congestive Heart Failure, Hypertension, Age, Diabetes, Stroke/Transient Ischemic Attack.

HAS-BLED: Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly (> 65 Years), Drugs/Alcohol.

Table 3: Independent predictors of adherence to the CCS-AF guidelines

Variables	Odds Ratios	95% Confidence Intervals	p-values
Age (per decade increase)	1.49	1.01-2.22	0.04
HAS-BLED	0.46	0.25-0.84	0.01
Female sex	2.29	0.15-1.43	0.76
CHADS ₂	1.56	0.92-2.67	0.10
Duration of AF	1.02	0.92-1.22	0.75
Referral to cardiologist/internist	1.47	0.37-5.77	0.58

AF: Atrial Fibrillation

CHADS₂: The Congestive Heart Failure, Hypertension, Age, Diabetes Mellitus, Prior Stroke/Transient Ischemic Attack Score to predict Stroke risk in patients with atrial fibrillation

HAS-BLED: The Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Bleeding Risk Score.

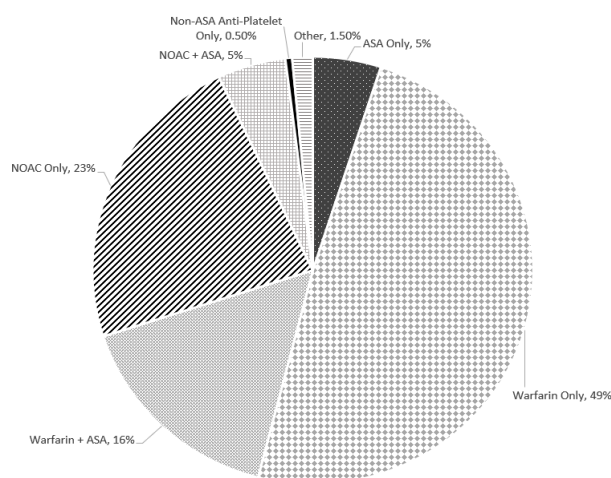
Table 4: Independent predictors of anticoagulation with non-vitamin K oral antagonists

Variables	Odds Ratios	95% Confidence Intervals	p-values
Age (per decade increase)	0.74	0.55-0.90	0.005
HAS-BLED	0.64	0.43-0.95	0.03
Heart failure	0.39	0.20-0.74	0.003
CHADS ₂	0.74	0.54-1.00	0.05
Female sex	0.75	0.45-1.27	0.29
Duration of AF	1.00	0.96-1.04	0.96
Paroxysmal AF	0.66	0.40-1.11	0.67
Referral to cardiologist/internist	0.68	0.32-1.46	0.33

AF: Atrial Fibrillation

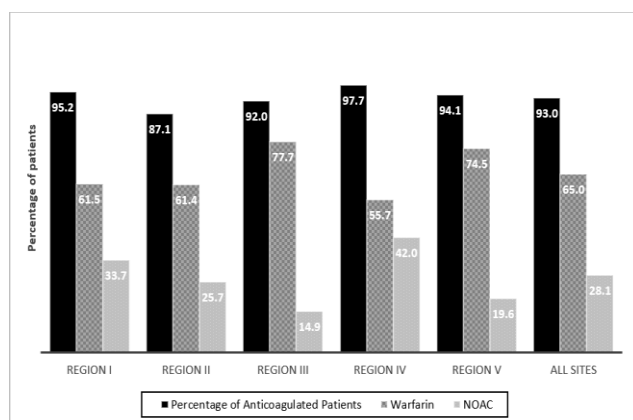
CHADS₂: The Congestive Heart Failure, Hypertension, Age, Diabetes Mellitus, Prior Stroke/Transient Ischemic Attack Score to predict Stroke risk in patients with atrial fibrillation

HAS-BLED: The Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Bleeding Risk Score.

**Figure 1:** Overall use of anticoagulants and anti-platelets

NOACS: Non-vitamin K oral anticoagulants

ASA: Aspirin

**Figure 2:** Regional variation of anticoagulation

Discussion

Rates of anticoagulation and use of NOAC

Although there were a few prior evaluations of OAC use within Canadian primary practices, there had been no formal evaluation of adherence to the CCS-AF guidelines within integrated multi-disciplinary public funded systems of primary care such as the FMGs in Quebec [1, 3, 4]. Hereby, we reported a cross-sectional survey of OAC at 15 Quebec FMGs (involving approximately 200 PCPs). We showed remarkably high rates of AC in patients who should be anticoagulated according to the CCS-AF guidelines. However, there were a few notable care gaps which merit attention and remedial such as 1) use of warfarin in the majority of patients, 2) combination of OAC and ASA and 3) infrequent documentation of stroke and bleeding risks by PCP. The high adherence rate to the CCS-AF guidelines in our cohort (95% in patients with CHADS₂ ≥ 1 and age of ≥ 65 years) compared favorably with the reported rates in other Canadian primary practices (55% by Valentini et al., 89% by Angaran et al.) [4, 7]. The dominance of warfarin use in our cohort (65%) was markedly higher than those previously reported (54% in CONNECT-AF and 24% in QUESTION-AF [2, 4]. This was possibly in part due to Quebec's ministry of health reimbursement restrictions in effect in 2015 (NOACs reimbursed only if intolerance/allergy to warfarin, difficult follow-up, and labile international normalized ratio). The recent modification of the provincial reimbursement of NOACs in 2018 (allowing NOAC to be used as first-line medication for AF) may increase their future use in Quebec [8]. The remarkable variations in rates of anticoagulation rates and use of NOACs were noteworthy. The region with the highest rate of appropriate use of OAC also had the highest rate of NOAC use. Qualitative studies with focus groups in regions with high/low adherence rates to the guidelines may provide invaluable insights and help to optimize AC in primary care practices.

Documentation of stroke and bleeding risk scores

The infrequent evaluation of stroke and bleeding risk scores at the FMGs mirrored the results of previous studies [4, 7]. Use of CHADS₂ and

HASBLED risk scores remained suboptimal in Canadian practices despite their endorsement by the CCC guidelines since 2010 [9]. It was possible that the PCPs did not re-calculate these risk scores if this had been done by other health care providers (consultations or prior hospitalizations); however, this was not documented in the clinic charts. Development of user-friendly tools which can be more easily applied in busy family practices (such as automated calculation of CHADS₂, HAS-BLED scores by electronic medical records or risk scoring by nurses/other allied health professionals) are needed.

PCPs appeared to base their decision of OAC and thus choice of drug on their intuitive appraisal of bleeding risk in our study. HAS-BLED, as calculated by the coordinating center, was a powerful determinant of both adherence to guidelines and use of NOACs. Patients with higher HAS-BLED scores were less likely to be treated according to guidelines and with NOACs. On the other hand, CHADS₂ did not correlate with adherence to the CCS-AF guidelines. These findings suggested that fear of major bleeding prevailed over fear of stroke in the decisions of the PCPs. HAS-BLED score was also an independent predictor of reduced odds of choosing NOACs for anticoagulating patients with AF. The PCPs appeared to favor the use of warfarin in patients perceived at increased bleeding risks. PCPs might not be aware that NOACs have similar and/or less bleeding rates than warfarin. Introduction of idarucizumab as a specific antidote for dabigatran and the upcoming availability of an antidote for the anti-Xa agents may alleviate PCP's avoidance of NOACs in patients with increased bleeding risk [10, 11]. CHADS₂ was borderline correlated with reduced odds of use of NOAC in our cohort. This finding may be real and may have been limited by the reduced power of our relatively small sample size to confirm the statistical significance. Paradoxically, PCPs may have been preferring warfarin over NOAC despite the superiority of NOAC over warfarin to prevent ischemic strokes [12, 13].

Combination of Aspirin and OAC

One in five patients was treated with a combination of OAC and ASA. Combining OAC and ASA increases the bleeding risk without necessarily increasing the protection against a coronary or cerebrovascular event. The CCS-AF guidelines 2014 recommend against this treatment strategy, even in patients with coronary/peripheral vascular diseases except for in patients with recent acute coronary syndromes or coronary stents [6]. PCPs may not be aware about these CCS-AF recommendations.

Other predictors of adherence to the CCS AF guidelines and use of NOAC

Age was associated with improved adherence to the CCS-AF guidelines. Similar to previous report of Gupta et al., increase in age was associated with decreased use of NOACs in our cohort [14]. Our finding inferred that although Quebec PCPs were comfortable with OAC in older patients, they were potentially at less ease in using NOACs in elderly. The independent association of HF with decreased use of NOACs was unexpected and difficult to explain. It was possible that this finding was due to chance or that PCPs may not want to modify OAC when patients were followed by HF clinics. Another possible reason for the lower use of NOAC in patients with HF may be due to impaired renal function in many of these patients. Surveys of HF clinics are needed to evaluate their management of AF patients.

Limitations

Our study had few noteworthy limitations. Although we required consecutive enrolment of patients with AF, we did not verify whether the FMG nurses complied with this obligation. The FMG nurses may have entered preferentially patients whose OAC was adherent to the guidelines. Second, the participating FMGs were potentially more motivated practices whose patient care may be more optimal than other FMGs in Quebec. Third, although we reviewed 25% of clinic charts to ensure accuracy of the case reports, we did not perform 100% data audits. Fourth, we identified referral to cardiologist/internist without capturing the reason for referral. It was possible that patients were referred to cardiologist/internist for reasons other than for AF management. Finally, the study was completed prior to release of the more recent CCS AF 2016 and CCS AF 2018 guidelines [15, 16]. Nevertheless, since there was no notable difference between the CCS AF 2016 and the CCC AF 2014 concerning the anticoagulation in primary care practice, we believe that our findings can still be relevant [6, 15, 16].

Conclusion

Considering the growing burdens of AF and preventable strokes in an increasingly older population, we need to remediate the identified care gaps in a timely manner. It is crucial to enhance awareness of CCS-AF guidelines in FMGs since 85% of OAC prescriptions in Canada were by PCPs [17]. More widespread dissemination of the most recent CCS-AF guidelines is needed to 1) decrease the inappropriate combination of AC and aspirin, 2) to optimize OAC in patients with acceptable bleeding risks and to augment systematic use of stroke and bleeding risk scores in primary care practices [15]. Since cardiologist referral was not associated with improved adherence to guidelines and choice of OAC, other means to disseminate these guidelines (such as more continuous medical education to PCPs, review of clinic charts of patients with AF....) should be considered. Automated electronic calculation of stroke and bleeding risk scores would optimize identification and management of patients with AF at high risk of major adverse events. Finally, future qualitative studies with focus groups of regions with high/low adherence rates to the guidelines may provide invaluable insights and help to optimize AC in primary care practices.

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Disclosure of conflict of interest

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Abbreviations

OAC: Oral anticoagulation

AF: Atrial fibrillation

ASA: aspirin

CHADS₂: The Congestive Heart Failure, Hypertension, Age, Diabetes,

Stroke/Transient Ischemic Attack.

FMG: Family Group Practice

HAS-BLED: Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly (> 65 Years), Drugs/Alcohol.

HF: Heart Failure

NOAC: Non-vitamin K Oral Anticoagulant

PCP: Primary Care Physician

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