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Original Article

Satisfaction With Oral Anticoagulants Among Patients With Atrial Fibrillation: A Prospective Observational Study

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ABSTRACT

Background: Satisfaction with treatment has been identified as an important contributing factor to adherence with oral anticoagulant (OAC) therapy in patients with atrial fibrillation (AF). We aimed to evaluate the satisfaction level of patients with AF regarding OAC use over time, using validated patient-reported outcome instruments, and to identify associated patient characteristics.

Methods: Participants were recruited from specialized AF clinics in Canada. Eligible AF patients who were prescribed OACs were followed for up to 2 years. Participants were interviewed via telephone every 3-4 months using a structured survey. The Treatment Satisfaction Questionnaire for Medication (TSQM II) and the Anti-Clot Treatment Scale (ACTS) were used to measure satisfaction over time.

RÉSUMÉ

Contexte : La satisfaction à l'égard du traitement a été désignée comme un facteur important contribuant à l'adhésion au traitement par anticoagulants oraux (ACO) chez les patients atteints de fibrillation auriculaire (FA). Notre objectif était d'évaluer le degré de satisfaction des patients atteints de FA concernant l'utilisation des ACO au fil du temps, à l'aide d'instruments validés mesurant les résultats signalés par les patients, et de déterminer les caractéristiques connexes des patients.

Méthodologie : Les participants ont été recrutés dans des cliniques spécialisées en FA au Canada. Les patients admissibles atteints de FA qui se sont fait prescrire des ACO ont été suivis pendant une période allant jusqu'à 2 ans. Les participants ont été interrogés par téléphone

Atrial fibrillation (AF) is a major risk factor for ischemic stroke, the second leading cause of death worldwide.[1,2] Oral anticoagulants (OACs) are a central part of stroke risk reduction in patients with AF.[3-5] However, nonadherence to OAC therapy is common and has been significantly associated with poor outcomes such as ischemic stroke, systemic embolism, higher healthcare costs, and a higher mortality rate, compared with those for adherent patients.[6,7]

Patients' satisfaction with therapy has been associated with various outcomes in a range of diseases including adherence to

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Ethics Statement: Ethics approval was granted by the research ethics boards of the University of British Columbia, Interior Health, Fraser Health, Vancouver Island Health, Providence Health, and Vancouver Coastal Health. The research was overseen by all the appropriate research ethics boards in the jurisdictions where it was performed.

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Results: Among the 306 participants, satisfaction scores on the TSQM II and ACTS instruments were high. Unadjusted analyses showed significantly greater satisfaction with the burden of therapy with direct OACs (DOACs) compared to that with warfarin (small-magnitude effect) and greater satisfaction with the convenience of rivaroxaban, compared with that of all other OACs (moderate-magnitude effect). After adjustment for all other variables, vitamin K antagonist therapy was associated with greater global satisfaction than was DOAC treatment. Satisfaction with benefit and burden as measured by the ACTS scale, and global satisfaction on the TSQM II scale, tended to increase over time. Patient factors that were somewhat consistently associated with greater satisfaction were female sex and younger age.

Conclusions: Patients with AF were highly satisfied with their therapy, with few differences among OAC classes and individual OACs. Individual patients may or may not be more satisfied with DOAC than VKA therapy, and regardless of the OAC prescribed, the may require significant support to maintain therapy adherence.

Résultats : Parmi les 306 participants, les taux de satisfaction indiqués par les instruments TSQM II et ACTS étaient élevés. Les analyses non corrigées ont montré une satisfaction liée au fardeau du traitement significativement plus élevée avec les ACO directs qu'avec la warfarine (effet de faible ampleur) et une plus grande satisfaction concernant la commodité du rivaroxaban par rapport à celle de tous les autres ACO (effet de moyenne ampleur). Après ajustement pour tenir compte de toutes les autres variables, le traitement par antivitamines K (AVK) était associé à une plus grande satisfaction globale que le traitement par ACO direct. La satisfaction à l'égard des avantages et du fardeau, mesurée par l'échelle ACTS, et la satisfaction globale sur l'échelle TSQM II, ont eu tendance à augmenter avec le temps. Les facteurs liés aux patients qui ont été associés de manière assez constante à une plus grande satisfaction étaient le sexe féminin et un âge plus jeune.

Conclusions : Les patients atteints de FA étaient très satisfaits de leur traitement, et peu de différences existaient entre les classes d'ACO et les ACO individuels. Chaque patient peut être ou non plus satisfait du traitement par ACO direct que par AVK et, quel que soit l'ACO prescrit, il peut avoir besoin d'un soutien important pour maintenir l'adhésion au traitement.

therapy.[8,9] Studies of patients with AF on OAC therapy have also identified treatment satisfaction as an important psychosocial determinant of adherence to therapy, with a lower level of satisfaction with OAC treatment being a significant predictor of stroke/systemic embolism, mediated by OAC nonadherence and nonpersistence.[7,10-13] In patients with AF on direct OACs (DOACs), a low level of satisfaction with benefits of therapy is independently associated with a 3-fold increase in the incidence of stroke.[11]

Reasons for lack of satisfaction include factors related to the patient, and to the OAC itself, such as the need for routine blood-work monitoring, treatment-associated bleeding, drug and dietary interactions, dosing schedule, and cost.[14,15] A pool of evidence has shown that simplified dosage regimens are associated with higher patient satisfaction, including in patients with AF on OACs.[8,16]

Several studies have measured satisfaction with OACs in patients who have AF.[7,10-13,17-25] However, most of these studies have one or more limitation—small sample size, lack of (or short-duration) longitudinal observation, retrospective design, use of unvalidated instruments, and exclusion of certain OACs. The purpose of our study was to prospectively evaluate the satisfaction level of AF patients with anticoagulation treatment overtime using patient-reported outcome measures to identify patients at risk of poor adherence and to assist in the development of interventions to improve satisfaction and adherence.

Methods

Design

A multicentre, prospective, longitudinal cohort study was conducted at British Columbia's 5 specialized AF clinics. Ethics approval was granted by the research ethics boards of the University of British Columbia, Interior Health, Fraser Health, Vancouver Island Health, Providence Health, and Vancouver Coastal Health.

Sampling strategy

Patients with AF attending the study clinics who were prescribed OAC therapy (warfarin, dabigatran, rivaroxaban, or apixaban) for stroke prevention were eligible. Edoxaban was not available in Canada at the time of data collection. Patients were excluded if they declined to provide consent, were unable to participate in study activities due to either cognitive impairment or other reasons identified by the referring clinician, or had a planned temporary course of OAC (eg, for cardioversion). Clinicians identified eligible patients and provided them with the study information sheet. Those interested were referred to the study coordinator, who contacted them either in person or by phone following their clinic visit. Recruitment and data collection were refined through an initial pilot study of 59 participants.

Data collection

Participants' demographic and clinical data were collected during the baseline visit. Patients were then interviewed every 3-4 months (similar to the normal frequency of clinic follow-ups) for 2 years, until OAC discontinuation or loss to follow-up. Follow-up data were collected by telephone interviews using a structured survey, conducted in English, by trained research assistants who were pharmacists or pharmacists-in-training and were not involved in the participants' care. The survey included several validated questionnaires and additional questions developed by the study team based on their clinical and research experience with AF patients. All interviewers were trained by the study coordinator (A.K.), observed for their first interview, and given feedback before conducting interviews independently.

Data collection commenced in January 2015 and continued until January 2018. The following were noted in every interview: changes in OAC therapy since the preceding visit, satisfaction level with therapy, and occurrence of clinical events (eg, bleeding, stroke, hospitalization).

Outcome measures

Satisfaction with medication was measured using 2 instruments: the Treatment Satisfaction Questionnaire for Medication Version 2 (TSQM-II) and the Anti-Clot Treatment Scale (ACTS).[26,27] The TSQM is a validated and widely used instrument measuring satisfaction with medication on 4 subscales: side effects, effectiveness, convenience, and global (score range: 0-100).[26] The ACTS is a validated anticoagulation-specific instrument with 2 subscales that are scored on a 5-point Likert scale; a 12-item burden subscale (score range: 12-60), and a 3-item benefit subscale (score range: 3-15). The burden subscale was reverse-coded per the ACTS coding instructions, so that higher scores indicated greater satisfaction on all scales.[26,27]

Analysis

Patients were included in the analysis if they completed at least one study follow-up visit and provided complete baseline and follow-up satisfaction data.

Univariate analyses of demographic characteristics were reported using means and standard deviations (SDs) for continuous variables, and frequencies and percentages for categorical variables. The mean and SD of patient satisfaction scores over the follow-up period were reported for every subscale and also stratified by OAC. Unadjusted relationships between average satisfaction and OAC were explored using the analysis of variance test followed by post hoc pairwise *t*-tests with Bonferroni's correction to explore differences. The standardized mean difference (SMD; Cohen's d) was calculated for significant differences with effect size values of 0.2-0.5, 0.5-0.8, and > 0.8, deemed to be small, moderate, and large, respectively.[28,29]

Linear regression models were used to study the relationship between patient factors and therapy satisfaction. Given the repeated data structure, we used a generalized estimating equation (GEE) technique to account for the dependencies among data collected from each patient over time.[30] A separate, independent model was constructed for each satisfaction subscale as the outcome. Dependent variables considered for inclusion in the models were patients' stroke and bleeding risk scores, AF subtype, OAC drug class at study enrolment ("index OAC"), AF severity, race, education, marital status, income, level of support available, the occurrence of bleeding, and time (indicated by visit number). All adjusted estimates were reported with 95% confidence intervals (CIs) and the associated *P* values.

Stroke and bleeding risks were assessed using the CHA_2DS_2-VASc stroke risk score: **C**ongestive Heart Failure-1, **H**ypertension-1, **A**ge $\geq$ 75 Years-2, **D**iabetes Mellitus-1, History of **S**troke-2, **V**ascular Disease-1) Age 65 to 74 years-1, Female sex category-1, and the HAS-BLED bleeding score (**H**ypertension-1, **A**bnormal Renal Function-1, **A**bnormal Liver Function-1, **S**troke History-1, **B**leeding History or Predisposition-1, **L**abile INR-1, **E**lderly $>$ 65 Years-1, **D**rugs or Alcohol-1 each) respectively.[31,32] For regression analyses, the stroke and bleeding risk scores were categorized as "high" and "low" using a score of ≥ 2 as a threshold.[31,32] AF severity was measured using the Canadian Cardiovascular Society Severity in Atrial Fibrillation (CCS-SAF) scale.[33] Support available to patients was measured using relevant components of the Canadian Community Health Survey.[34] Patient demographics were time-independent variables measured at baseline interview. Satisfaction and occurrence of bleeding were time-dependent variables.

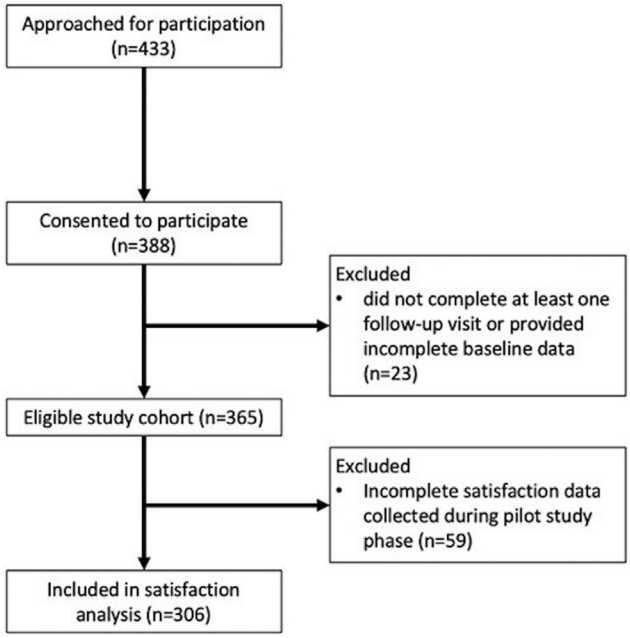

Figure 1. Study flow diagram.

For continuous variables, regression coefficients indicate the mean change in outcome (eg, satisfaction score) for a one-unit change in the explanatory variable, adjusted for all the other variables in the model. For categorical variables, the coefficient indicates the mean change in the outcome for one category vs the other. For variables with multiple levels, one level was chosen as the reference for comparison.

The sample size was one of convenience. We originally specified a larger sample for a comparison of adherence with warfarin vs DOACs, an objective unrelated to the present satisfaction analyses.

Results

The study flow is shown in Figure 1. Characteristics of the participants (N = 306; 58.8% males, average age 69 (SD 10) years] included in the analysis are summarized in Table 1. Pilot study participants (N = 59) were excluded because the study procedures were being iteratively refined during that period (Fig. 1). Participants were followed-up for up to 2 years, with a median follow-up time of 14.1 months (interquartile range 10.5 months), and an average of 3.2 (SD 1.4) study visits per patient.

Satisfaction with therapy

Distributions of the TSQM and ACTS scores are shown in Figures 2 and 3, respectively. Average unadjusted TSQM

Table 1. Participants' baseline characteristics (N = 306)

Characteristic	n (%)
AF type	
Paroxysmal	177 (66.3)
Persistent	38 (14.2)
Long-term persistent	15 (5.6)
Permanent	37 (13.9)
Index OAC	
Warfarin	83 (27.1)
Dabigatran	32 (10.5)
Apixaban	80 (26.1)
Rivaroxaban	111(36.3)
Sex	
Female	126 (41.2)
Male	180 (58.8)
Education	
No college education (high school diploma or lower)	183 (60.4)
College education (undergraduate or higher)	120 (39.6)
CCS−SAF scale	
0	78 (25.9)
1	79 (26.2)
2	58 (19.3)
3	75 (24.9)
4	11 (3.7)
Race	
Caucasian/White	279 (91.2)
Other	27 (8.8)
Marital status	
Single/never married	93 (30.4)
Common-law/married	213 (69.6)
Income (CD)	
Low (< 40,000)	66 (27.0)
Medium (40,000−79,000)	93 (38.1)
High > 80,000)	85 (34.8)
Continuous variables	Mean (SD)
CHA_2DS_2-VASc *	2.8 (1.5)
HAS-BLED†	1.3 (1.1)
Age, y	68.8 (10)

AF, atrial fibrillation; CCS−SAF scale, Canadian Cardiovascular Society Severity of Atrial Fibrillation Scale; CD, Canadian dollars; CHA_2DS_2-VASc, Congestive Heart Failure History, Hypertension History, Age ≥ 75 Years, Age 65 to 74 Years, Diabetes Mellitus, Stroke History, Vascular Disease History, female sex; HAS-BLED, Hypertension, Abnormal Renal Function, Abnormal Liver Function, Stroke History, Bleeding History or Predisposition, Labile INR, Elderly > 65 Years, Drugs or Alcohol; Index OAC, OAC therapy at enrollment; OAC, oral anticoagulants; SD, standard deviation; VKA, Vitamin-K antagonist.

*Stroke risk score calculated based on the presence of the following: cardiomyopathy (1 score), hypertension (1 score), age ≥ 75 years (2 scores), age 65-75 years (1 score), diabetes (1 score), stroke (2 scores), vascular disease (1 score), sex category female (1 score).

†Bleeding risk score calculated based on presence of the following: hypertension (1 score), abnormal liver/kidney function (1 score each), stroke (1 score), bleeding (1 score), labile International Normalized Ratio (1 score), elderly- age > 75 years (1 score), drugs or alcohol use (1 score each).

scores were (out of 100; higher scores imply greater satisfaction) as follows: global satisfaction: 71.2 (SD 10.1); convenience: 76.5 (SD 7.12); side effects: 97.4 (SD 6.13); and effectiveness: 68.3 (SD 10.5). Average unadjusted ACTS scores were 11 out of 15 (SD 1.76) on the benefit subscale and 57 out of 60 (SD 2.76) on the burden subscale.

Table 2 shows participants' satisfaction on the TSQM and ACTS subscores, stratified by OAC. The unadjusted ACTS satisfaction with burden score was significantly higher for DOACs than for warfarin (57.28 vs 56.41, $P < 0.05$; SMD 0.33; small effect size). Unadjusted satisfaction regarding convenience with rivaroxaban was greater than that with all other OACs (SMD 0.74; moderate effect size). Overall, patients reported a high satisfaction level with OAC therapy.

Factors associated with satisfaction

Figure 4 summarizes the factors associated with anticoagulation therapy satisfaction in patients with AF based on the repeated-measures regression analyses.

On the TSQM II effectiveness subscale, factors significantly associated with increased patient satisfaction were younger age, female sex, and higher income (Fig. 5). For every year increase in age, the score for satisfaction with the effectiveness of OAC decreased by 0.23 units (2.3 units per 10-year increment of age). Female sex was associated with an approximately 4-unit higher satisfaction-with-effectiveness score than male sex. Patients in the high-income band were about 4 units higher on their satisfaction-with-effectiveness score than those in the low- and medium-income bands.

No factors were found to be significantly associated with satisfaction with side effects or satisfaction with convenience on the TSQM II side effects and convenience subscale in our regression analysis.

Factors significantly associated with higher global satisfaction with OAC on the TSQM II were lower stroke risk, female sex, vitamin K antagonist (VKA) therapy (vs DOAC therapy), and not experiencing bleeding (Fig. 5). Patients with a CHA_2DS_2-VASc score of < 2 had a 3-unit higher global satisfaction score than did patients with higher stroke risk. Being female was associated with an approximately 4-unit higher global satisfaction score, compared with being male. Not experiencing a bleed was associated with an approximately 4-unit higher global satisfaction score than that of patients who bled. Patients on VKA therapy had an approximately 4-unit higher global satisfaction score than did patients on DOACs. Patients' global satisfaction with their therapy also increased significantly over time. On average, the global satisfaction score increased by 0.93 units every 3 months, corresponding to an approximately 4-unit higher level of global satisfaction per year of therapy.

Regression analysis of the ACTS burden subscale results showed younger age and no bleeding experience to be associated with higher satisfaction with medication burden (Fig. 6). For each year increase in age, the satisfaction with burden of OAC score decreased by 0.05 units, corresponding to a 0.5-unit decrease in satisfaction per 10 years of age progression. Not experiencing bleeding was associated with an approximately 0.5-unit higher satisfaction-with-burden score than that for patients who bled. The score for satisfaction with medication burden increased significantly over time. On average, the score for satisfaction with OAC burden increased by 0.29 units every 3 months, corresponding to an approximately 1.2-unit higher score per year of therapy.

On the ACTS benefits subscale, female sex and a lower AF symptom score were significantly associated with higher satisfaction with OAC benefits (Fig. 6). Being female was associated with a 0.69-unit higher score for satisfaction with benefits than being male. The score for satisfaction with

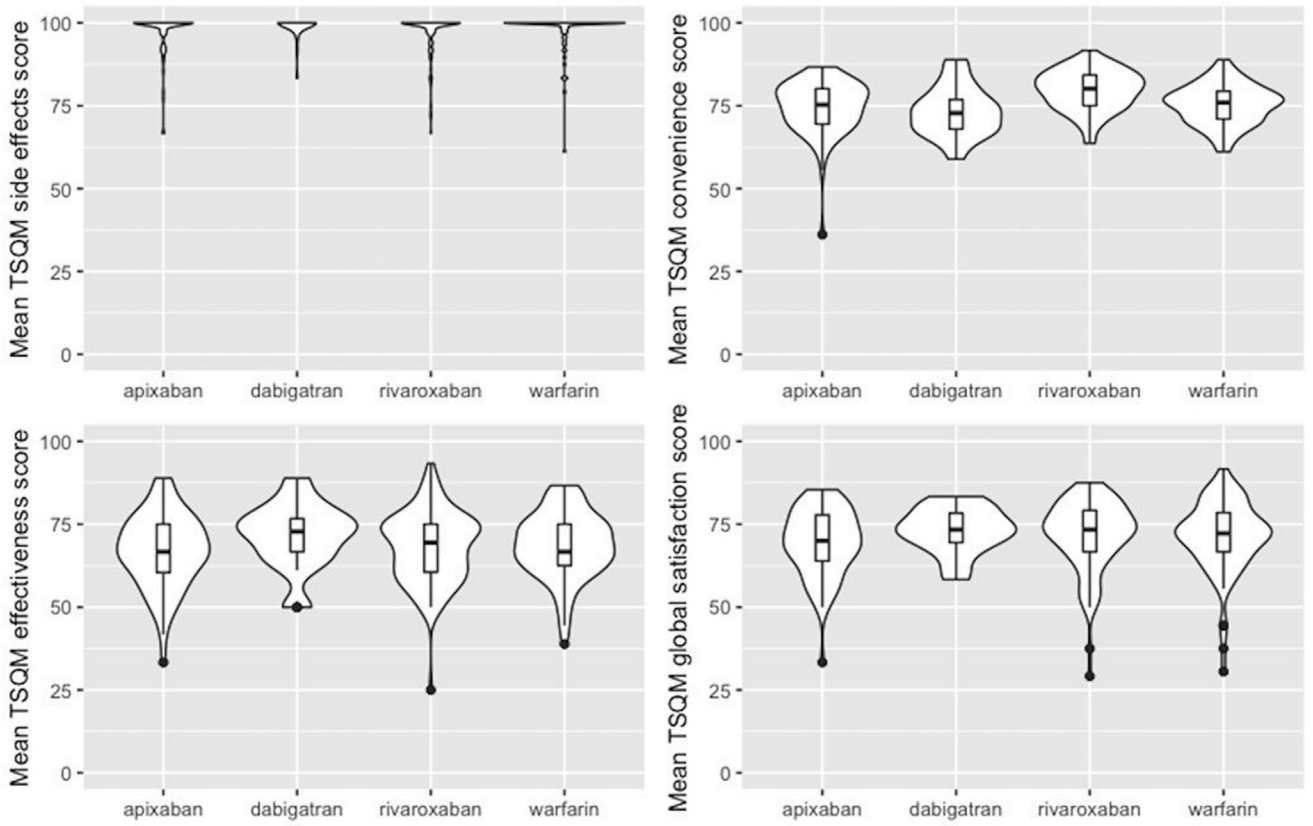

Figure 2. Violin plots of the distributions of the Treatment Satisfaction Questionnaire for Medication (TSQM) satisfaction scores. Higher scores mean greater satisfaction.

benefits was approximately 0.23 units higher per unit decrease in the AF symptom severity score. Satisfaction with benefits increased significantly over time. On average, the score for satisfaction with OAC benefits increased by 0.10 units every 3 months, corresponding to 0.4-unit increase per year of therapy.

Discussion

In this study of patients with AF taking OACs, patient-reported satisfaction levels on the TSQM II and ACTS were high. Unadjusted analyses showed significantly greater satisfaction with the burden of therapy with DOACs, compared with that with warfarin (a small-magnitude effect) and greater satisfaction with the convenience of rivaroxaban, the only once-daily DOAC in the study, compared with all other OACs (a moderate-magnitude effect). After adjustment for all other variables, VKA therapy was associated with a higher level of global satisfaction than DOAC treatment. No other significant differences among OAC classes or individual OACs were found. Our exploration of patient factors associated with satisfaction revealed a few patterns. Satisfaction with the benefits and burden of oral anticoagulants on the ACTS scale, and global satisfaction on the TSQM II scale, tended to increase over time. The patient factors somewhat consistently associated with higher satisfaction on multiple scales were female sex and younger age; experiencing no bleeding was associated with a higher satisfaction level on some scales.

Our results can be interpreted in the context of 2 recent systematic reviews examining patient satisfaction with OACs. Katerenchuk et al. meta-analyzed 20 studies of various designs in which satisfaction with OACs for AF or venous thromboembolism were measured.[35] The ACTS burden score was significantly higher with DOACs than VKAs, and the ACTS benefit score was marginally higher with DOACs than VKAs, both with high heterogeneity. The TSQM results favored DOACs over VKAs on all the subscales, also with high heterogeneity.[35] All results were graded as having "very low" or "low" certainty, except for the TSQM effectiveness score, which was deemed to have "moderate" certainty.[35] Patient factors associated with satisfaction were not reported.[35]

Afzal et al. performed a narrative systematic review including 7 studies of patients with AF, measuring OAC satisfaction using both the TSQM and ACTS scales.[36] The results were mixed, with most showing satisfaction scores favoring DOACs or no difference, and a small number showing higher satisfaction with VKAs.[36] A small number of studies showed that patients on rivaroxaban, compared to those on other ACs, were more satisfied in one or more domains of the scales.[36] Patient factors associated with satisfaction were not reported.[36]

As in our study, others have also found greater patient satisfaction with the convenience of rivaroxaban compared to that of VKAs.[37,38] The SAKURA AF registry substudy, however, showed a higher convenience score for rivaroxaban vs other DOACs, but no significant difference compared to

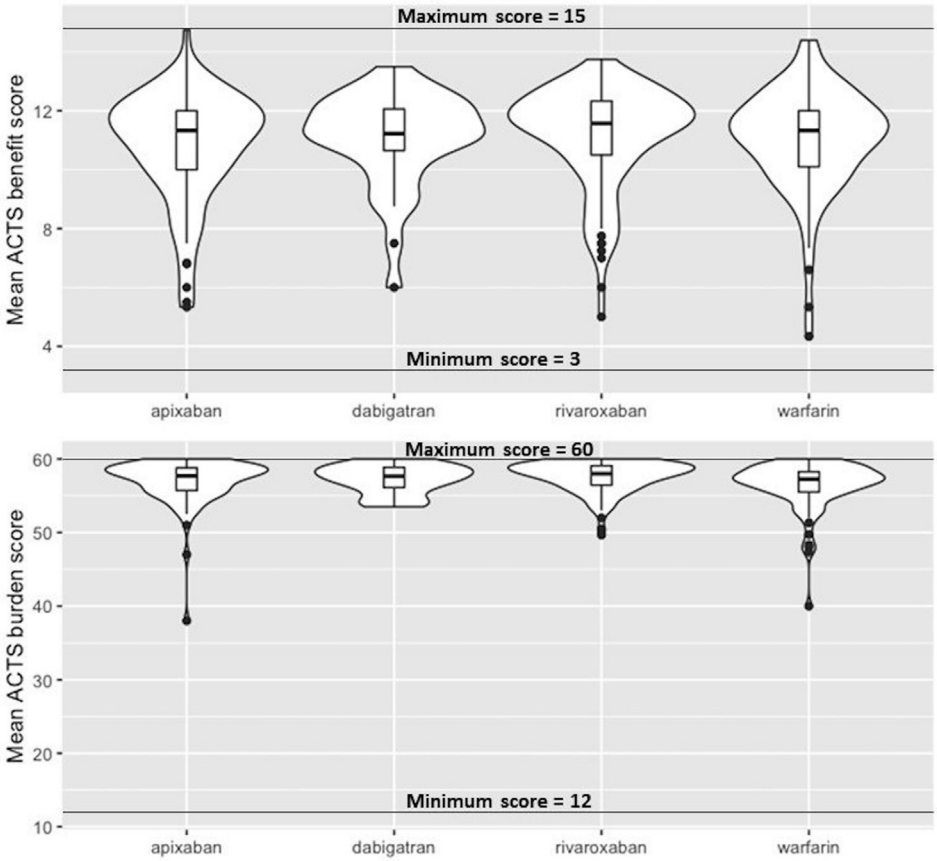

Figure 3. Violin plots of the distributions of the Anti-Clot Treatment Scale (ACTS) satisfaction scores. Higher scores mean greater satisfaction.

warfarin.[17] Non-AF-specific literature has identified a complex medication dosing regimen as being negatively associated with satisfaction, and a qualitative study in patients with AF identified that more patients were satisfied with the reduced complexity of their therapy when they switched from VKA to DOAC therapy.[8,16] The SAKURA AF registry substudy also showed greater satisfaction with DOACs on the ACTS burden subscale, and no difference on the ACTS benefits subscale, as we also observed.[17] The same investigators showed that lower satisfaction with DOAC benefit was independently associated with increased risk of stroke or systemic embolism, further pointing to the relationship between OAC satisfaction and patient outcomes.[11]

Few studies have examined factors associated with patient satisfaction with OACs, and a couple of these studies have found an association of being female with higher satisfaction with OAC therapy, as in our study. One study, albeit small, found that being female was associated with higher satisfaction with OAC convenience, and the SAKURA AF registry found an association of being female with greater satisfaction with OAC side effects.[17,19] An association of younger age with a higher satisfaction level was found in our study; others have

Table 2. Average satisfaction scores over follow-up, stratified by index oral anticoagulant; higher scores mean greater satisfaction

Satisfaction measure	All DOACs	Warfarin	Dabigatran	Apixaban	Rivaroxaban
TSQM II					
Effectiveness	68.10	68.72	71.45	67.00	68.03
Side effects	97.27	97.65	98.98	97.08	96.93
Convenience	76.87	75.38	73.29	74.54	79.62[†]
Global	71.09	71.35	73.11	69.45	71.77
ACTS					
Burden (of 60)	57.28[*]	56.41	57.22	56.91	57.58
Benefit (of 15)	11.01	11.03	10.98	10.81	11.15

DOACs, direct oral anticoagulants; TSQM II, Treatment Satisfaction Questionnaire for Medication version 2; ACTS, Anti-Clot Treatment Scale.

[*] $P = 0.029$ all DOACs vs warfarin, assessed by t test.

[†] Analysis of variance test: $P < 0.05$; post hoc pairwise t test with Bonferroni's correction: rivaroxaban vs warfarin $P = 0.0007$; rivaroxaban vs dabigatran $P = 0.0058$; rivaroxaban vs apixaban $P = 0.0003$.

Subscales	Patient variables									
	Female sex	Younger age	Severity of AF	No bleed	VKA as index OAC	High income	White race	Low bleeding risk*	Low stroke risk†	AF type
Satisfaction with burden		■	□	■	□					
Satisfaction with benefit	■		■							
Satisfaction with effectiveness	■	■			□	■	□			
Satisfaction with side effects		□	□	□				□		
Satisfaction with convenience										□
Global satisfaction	■	□	□	■	■		□	□	■	

■ Statistically significant ($P < 0.05$)
□ Marginally significant ($0.05 \leq P < 0.1$)

Figure 4. Factors associated with anticoagulation satisfaction at a glance. AF, atrial fibrillation; OAC, oral anticoagulant; VKA, vitamin K antagonist.

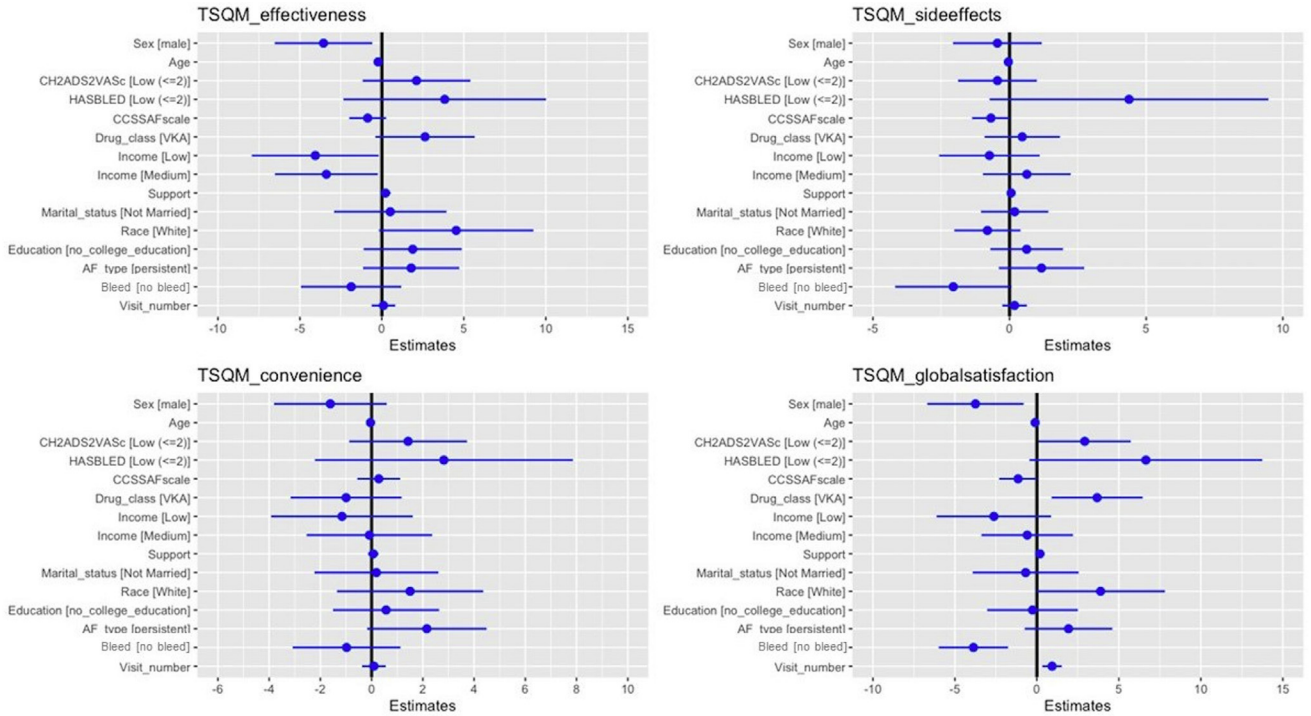

Figure 5. Forest plots of the estimates of the effects of factors associated with satisfaction on the Treatment Satisfaction Questionnaire for Medication (TSQM II; see Supplemental Table S1 for more details). Age, Canadian Cardiovascular Society Severity of Atrial Fibrillation Scale (CCSSAF) scale, support, and visit number were continuous variables. AF, atrial fibrillation; CHA_2DS_2-VASc, Congestive Heart Failure, Hypertension, Age $\geq$ 75 Years, Age 65 to 74 Years, Diabetes Mellitus, Stroke, Vascular Disease, Sex Category; HASBLED, Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly ($>$ 65 Years), Drugs or Alcohol; VKA, vitamin K antagonist.

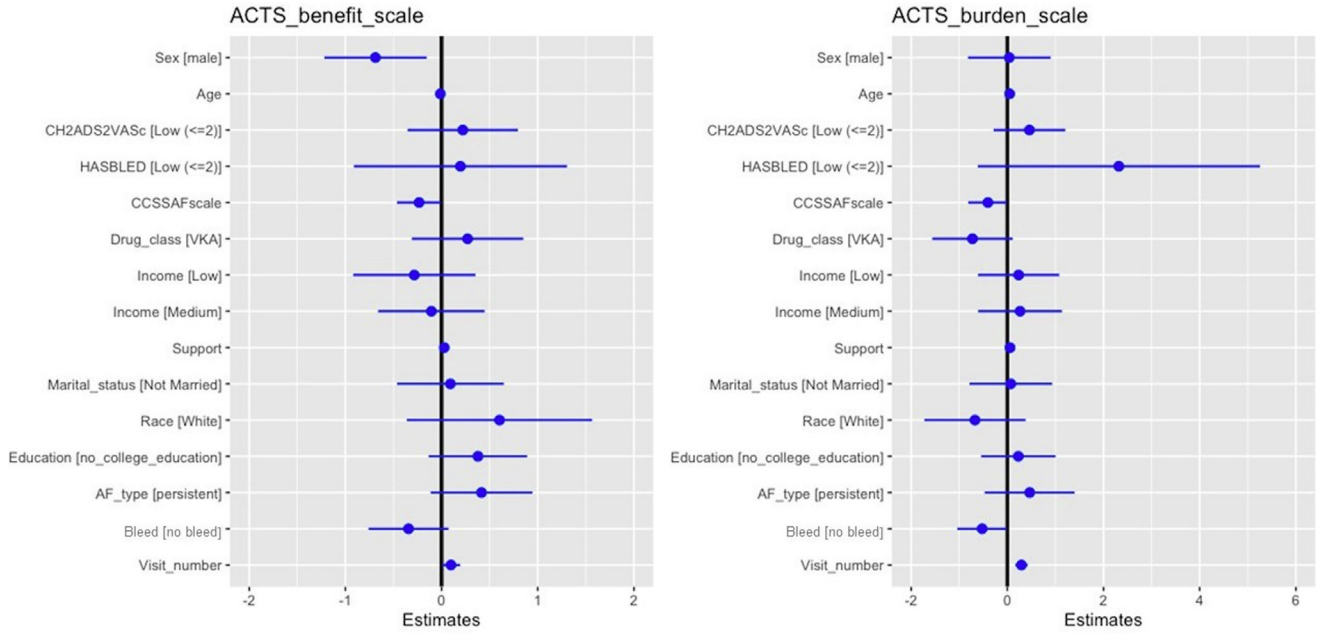

Figure 6. Forest plots of the estimates of the effects of factors associated with satisfaction on the Anti-Clot Treatment Scale (ACTS; see Supplementary Table S2 for more details). Age, Canadian Cardiovascular Society Severity of Atrial Fibrillation Scale (CCS-SAF) scale, support, and visit number were continuous variables. Refer to Table 1 for abbreviations and definitions. AF, atrial fibrillation; CHA_2DS_2-VASc, Congestive Heart Failure, Hypertension, Age $\geq$ 75 Years, Diabetes Mellitus, Stroke, Vascular Disease, Age 65 to 74 Years, Sex Category; HASBLED, Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly ($>$ 65 Years), Drugs/Alcohol Concomitantly; VKA, vitamin K antagonist.

found varying directions of association for these factors.[17,18,24]

Ours is the first long-term study to use repeated-measures regression analysis and to show increasing overall satisfaction with OAC therapy over time, increasing satisfaction with its benefits over time, and an increase in patients finding therapy less burdensome over time. Using a different regression technique, the SAKURA AF registry found an association between longer duration of therapy and higher satisfaction level.[17]

Clinical significance

Our results have some potentially clinically applicable implications. Patients with AF can take OACs and be highly satisfied with them, which might lower clinicians' reluctance to prescribe OACs in some cases where there is concern about the burdens exceeding the potential benefits. If patients can be supported to continue with therapy, they may be reassured to know that their overall satisfaction may get better with time. Patients may be moderately more satisfied with rivaroxaban than with other OACs from a convenience viewpoint, possibly because of its single—daily dose regimen and lack of International Normalized Ratio testing (notably, edoxaban, another single—daily dose OAC, which was not included in our study). Female patients and younger patients may be more likely to be satisfied with therapy, and hence may be particularly ideal OAC therapy candidates when it is otherwise indicated, whereas older and male patients may require additional education and support to sustain their satisfaction so they remain adherent and persist with therapy.

Our results and those of other studies indicate that individual patients may or may not be more satisfied with DOAC than VKA therapy. Regardless of the OAC prescribed, patients require significant support (eg, tailored education, shared decision-making, frequent follow-up, behavioural strategies, clarifying misconceptions) to maintain adherence and persistence with therapy.[39,40]

Limitations

Our results should be interpreted in light of the study's limitations. Like all observational studies, ours is susceptible to selection biases (eg, nonresponse bias, survival bias, and incidence—prevalence bias). For example, those who discontinued their participation may have been more or less satisfied with their therapy than those who continued. Hence, our results should not be extrapolated beyond patients who are continuing to take OACs. Also, our study, like most in this area, is hindered by the fact that patients had limited experience on which to base their satisfaction perceptions. Ideally, patients would experience taking both a VKA and a DOAC to inform their satisfaction responses. Lastly, we may not have included some variables that could be associated with satisfaction in our analyses, such as insurance coverage status or a measure of comorbidity.

Conclusions

Overall, patients with AF were highly satisfied with their anticoagulation therapy, with a few differences of small magnitude among OAC classes and individual OACs. Participants' overall satisfaction with benefit, and global satisfaction, increased with time, and they found OAC therapy to be less burdensome over time. DOACs were found to be slightly less burdensome than warfarin, and rivaroxaban was

perceived as being modestly more convenient than all other OACs. Significant and consistent predictors of greater satisfaction were female sex and younger age.

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Disclosures

The authors have no conflicts of interest to disclose.

References

1. Pistoia F, Sacco S, Tiseo C, et al. The epidemiology of atrial fibrillation and stroke. Cardiol Clin 2016;34:255-68.
2. You JJ, Singer DE, Howard PA, et al. Antithrombotic therapy for atrial fibrillation: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2012;141(2 suppl):e531S-75S.
3. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society in collaboration with the Society of Thoracic Surgeons. Circulation 2019;140:e125-51.
4. Andrade JG, Verma A, Mitchell LB, et al. 2018 focused update of the Canadian Cardiovascular Society guidelines for the management of atrial fibrillation. Can J Cardiol 2018;34:1371-92.
5. Lip GY, Lane DA. Stroke prevention in atrial fibrillation: a systematic review. JAMA 2015;313:1950-62.
6. Salmasi S, Loewen PS, Tandun R, et al. Adherence to oral anticoagulants among patients with atrial fibrillation: a systematic review and meta-analysis of observational studies. BMJ Open 2020;10:e034778.
7. Wang W, Saczynski J, Lessard D, et al. Physical, cognitive, and psychosocial conditions in relation to anticoagulation satisfaction among elderly adults with atrial fibrillation: The SAGE-AF study. J Cardiovasc Electrophysiol 2019;30:2508-15.
8. Dias-Barbosa C, Balp Kulich K, et al. A literature review to explore the link between treatment satisfaction and adherence, compliance, and persistence. Patient Prefer Adherence 2012;6:39-48.
9. Morisky DE, Ang A, Krousel-Wood M, et al. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens 2008;10:348-54.
10. Geng YP, Lan DH, Liu N, et al. Patient-reported treatment satisfaction with dabigatran versus warfarin in patients with non-valvular atrial fibrillation in China. Thromb Haemost 2018;118:1815-22.
11. Hori K, Okumura Y, Koichi N, et al. Association of patient satisfaction with direct oral anticoagulants and the clinical outcomes: Findings from the SAKURA AF registry. J Cardiol 2020;76:80-6.
12. Wang Y, Kong MC, Lee LH, et al. Knowledge, satisfaction, and concerns regarding warfarin therapy and their association with warfarin adherence and anticoagulation control. Thromb Res 2014;133:550-4.
13. Smet L, Heggermont WA, Goossens E, et al. Adherence, knowledge, and perception about oral anticoagulants in patients with atrial fibrillation at high risk for thromboembolic events after radiofrequency ablation. J Adv Nurs 2018;74:2577-87.
14. Bauer KA. Pros and cons of new oral anticoagulants. Hematology Am Soc Hematol Educ Program 2013;2013:464-70.
15. Fawzy AM, Lip GYH. Pharmacokinetics and pharmacodynamics of oral anticoagulants used in atrial fibrillation. Expert Opin Drug Metab Toxicol 2019;15:381-98.
16. Salmasi S, Kapanen AI, Kwan L, et al. Atrial fibrillation patients' experiences and perspectives of anticoagulation therapy changes. Res Social Adm Pharm 2020;16:1409-15.
17. Okumura Y, Yokoyama K, Matsumoto N, et al. Patient satisfaction with direct oral anticoagulants and warfarin findings from the SAKURA AF Registry. Int Heart J 2018;59:1266-74.
18. Hanon O, Chaussade E, Gueranger P, et al. Patient-reported treatment satisfaction with rivaroxaban for stroke prevention in atrial fibrillation. A French Observational Study, the SAFARI Study. PLoS One 2016;11:e0166218.
19. Gospos J, Bernaitis N. Treatment expectations, convenience, and satisfaction with anticoagulant treatment: perceptions of patients in South-East Queensland, Australia. J Clin Med 2019;8:863.
20. Ng DL, Gan GG, Chai CS, et al. Comparing quality of life and treatment satisfaction between patients on warfarin and direct oral anticoagulants: a cross-sectional study. Patient Prefer Adherence 2019;13:1363-73.
21. Oh S, Kim JS, Oh YS, et al. Quality of anticoagulation and treatment satisfaction in patients with non-valvular atrial fibrillation treated with vitamin K antagonist: result from the KORean Atrial Fibrillation Investigation II. J Korean Med Sci 2018;33:e323.
22. Coleman CI, Coleman SM, Vanderpoel J, et al. Patient satisfaction with warfarin- and non—warfarin-containing thromboprophylaxis regimens for atrial fibrillation. J Investig Med 2013;61:878-81.
23. Koretsune Y, Kumagai K, Uchiyama S, et al. Patient-reported treatment satisfaction with rivaroxaban in Japanese non-valvular atrial fibrillation patients: an observational study. Curr Med Res Opin 2018;34:2157-64.
24. Suárez Fernández C, Castilla-Guerra L, Cantero Hinojosa J, et al. Satisfaction with oral anticoagulants in patients with atrial fibrillation. Patient Prefer Adherence 2018;12:267-74.
25. Fumagalli S, Cardini F, Roberts AT, et al. Psychological effects of treatment with new oral anticoagulants in elderly patients with atrial fibrillation: a preliminary report. Aging Clin Exp Res 2015;27:99-102.
26. Atkinson MJ, Kumar R, Cappelleri JC, et al. Hierarchical construct validity of the treatment satisfaction questionnaire for medication (TSQM version II) among outpatient pharmacy consumers. Value Health 2005;8(suppl 1):S9-24.
27. Cano SJ, Lamping DL, Bamber L, et al. The Anti-Clot Treatment Scale (ACTS) in clinical trials: cross-cultural validation in venous thromboembolism patients. Health Qual Life Outcomes 2012;10:120.

28. Durlak JA. How to select, calculate, and interpret effect sizes. J Pediatr Psychol 2009;34:917-28.

29. Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2nd ed. Hillsdale, N.J: L. Erlbaum Associates, 1988.

30. Schober P, Vetter TR. Repeated measures designs and analysis of longitudinal data: if at first you do not succeed-try, try again. Anesth Analg 2018;127:569-75.

31. Lip GY, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on Atrial Fibrillation. Chest 2010;137:263-72.

32. Pisters R, Lane DA, Nieuwlaat R, et al. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. Chest 2010;138:1093-100.

33. Dorian P, Cvitkovic SS, Kerr CR, et al. A novel, simple scale for assessing the symptom severity of atrial fibrillation at the bedside: the CCS-SAF scale. Can J Cardiol 2006;22:383-6.

34. Statistics Canada. Canadian Community Health Survey: Public use microdata file. Ottawa: Special Surveys Division, Statistics Canada, 2020.

35. Katerenchuk V, Duarte GS, Martins e Pereira G, et al. Satisfaction of patients with nonvitamin K anticoagulants compared to vitamin K antagonists: a systematic review and meta-analysis. Thromb Haemost 2021;121:366-82.

36. Afzal SK, Hasan SS, Babar ZU. A systematic review of patient-reported outcomes associated with the use of direct-acting oral anticoagulants. Br J Clin Pharmacol 2019;85:2652-67.

37. Hohnloser SH, Cappato R, Ezekowitz MD, et al. Patient-reported treatment satisfaction and budget impact with rivaroxaban vs. standard therapy in elective cardioversion of atrial fibrillation: a post hoc analysis of the X-VeRT trial. Europace 2016;18:184-90.

38. Stephenson JJ, Shinde MU, Kwong WJ, et al. Comparison of claims vs patient-reported adherence measures and associated outcomes among patients with nonvalvular atrial fibrillation using oral anticoagulant therapy. Patient Prefer Adherence 2018;12:105-17.

39. Salmasi S, Kwan L, MacGillivray J, et al. Assessment of atrial fibrillation patients' education needs from patient and clinician perspectives: A qualitative descriptive study. Thromb Res 2019;173:109-16.

40. Andrade JG, Aguilar M, Atzema C, et al. The 2020 Canadian Cardiovascular Society/Canadian Heart Rhythm Society comprehensive guidelines for the management of atrial fibrillation. Can J Cardiol 2020;36:1847-948.

Supplementary Material

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