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Original Article

Choice of Oral Anticoagulant: Outcomes in Atrial Fibrillation Patients Post-Stroke Despite Direct Oral Anticoagulant Use

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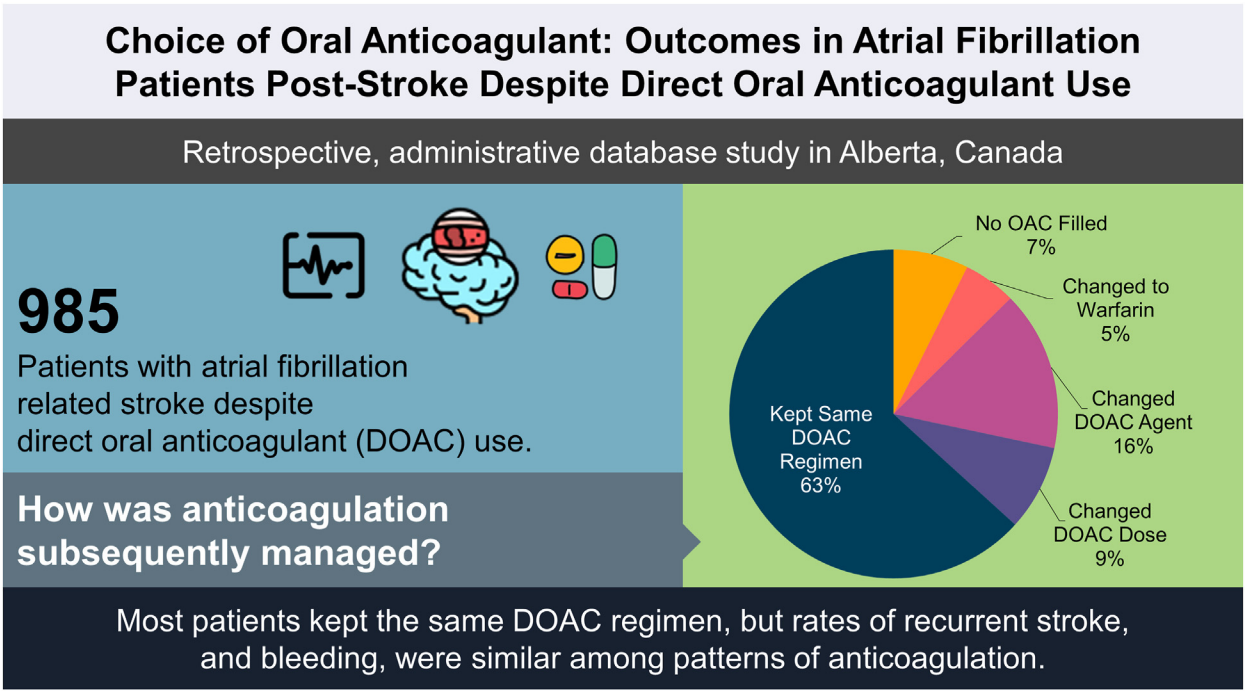

ABSTRACT

Background: For patients with atrial fibrillation who have an ischemic stroke or transient ischemic attack (TIA) despite taking direct oral anticoagulants (DOACs), the optimal strategy for ongoing anticoagulation is unknown.

Methods: Using provincial administrative databases in Alberta, Canada, we compared anticoagulant use before/after the breakthrough

RÉSUMÉ

Contexte: Chez les patients atteints de fibrillation auriculaire qui subissent un accident vasculaire cérébral (AVC) ischémique ou un accident ischémique transitoire (AIT) malgré la prise d'anticoagulants oraux directe (AOD), la stratégie optimale pour la poursuite de l'anticoagulation est inconnue.

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stroke/TIA and assessed recurrence of stroke/TIA or bleeding, with consideration of medication adherence. Adherence was defined as the proportion of days covered (PDC) being $\geq$ 80%.

Results: Among 985 patients, the median age was 80 years (interquartile range 13), with a mean $CHADS_2$ score of 1.7$\pm$ 1 prior to the index event. Patients were followed for a median of 643 days (interquartile range 836). Following the index stroke/TIA event, 623 patients (63%) filled a prescription for the same DOAC regimen, 83 (8%) filled a prescription for a different dose, 155 (16%) switched DOAC agents, 51 (5%) switched to warfarin, and 73 (7%) filled no oral anticoagulant prescription. Patients who kept the same regimen more commonly had TIA index events (59%); patients who changed dose or drug more often had stroke index events (55%-78%). During follow-up, 135 (14%) had stroke/TIA recurrence, and 46 (5%) had bleeding; rates of each did not differ between prescribing patterns. Post-index event, the proportion of patients with a proportion of days covered $\geq$ 80% improved from 55% to 80%.

Conclusions: Although most maintained the same DOAC regimen after stroke/TIA, rates of recurrent stroke/TIA and bleeding were similar across prescribing patterns. Stroke/TIA severity may have influenced prescribing practices. DOAC prescription adherence improved poststroke/TIA and signals an opportunity for optimization in patients with atrial fibrillation.

Méthodologie : À partir des bases de données administratives provinciales en Alberta, au Canada, nous avons comparé l'utilisation d'anticoagulants avant/après l'AVC/AIT survenu pendant l'anticoagulothérapie et avons évalué la récurrence d'un AVC/AIT ou d'un saignement, en tenant compte de l'adhésion au traitement médicamenteux. L'adhésion a été définie comme une proportion de jours couverts (PJC) de 80 % ou plus.

Résultats : Chez 985 patients, l'âge médian était de 80 ans (écart interquartile de 13) et le score $CHADS_2$ moyen, de 1,7 $\pm$ 1 avant l'événement de référence. Les patients ont été suivis pendant une médiane de 643 jours (écart interquartile de 836). Après l'AVC/AIT de référence, 623 patients (63 %) ont fait exécuter une ordonnance du même schéma d'AOD, 83 (8 %) ont fait exécuter une ordonnance d'une dose différente, 155 (16 %) sont passés à d'autres AOD, 51 (5 %) sont passés à la warfarine et 73 (7 %) n'ont fait exécuter aucune ordonnance d'anticoagulant oral. Chez les patients qui ont continué à recevoir le même schéma, la plupart (59 %) avaient eu un AIT comme événement de référence; chez les patients qui ont changé de dose ou de médicament, la plupart (55 à 78 %) avaient eu un AVC comme événement de référence. Durant le suivi, 135 (14 %) ont connu un AVC/AIT récurrent et 46 (5 %) ont présenté un saignement; les taux de chaque manifestation ont été similaires pour les différents schémas de prescription. Après l'événement de référence, le pourcentage de patients ayant une PJC $\geq$ 80 % a augmenté, passant de 55 à 80 %.

Conclusions : Malgré le maintien du même schéma d'AOD chez la plupart des patients après l'AVC/AIT, les taux d'AVC/AIT récurrent et de saignement ont été similaires avec tous les schémas de prescription. La gravité d'un AVC/AIT pourrait avoir influencé les pratiques de prescription. L'adhésion aux AOD prescrits s'est améliorée après un AVC/AIT et témoigne d'une possibilité d'optimisation chez les patients atteints de fibrillation auriculaire.

Atrial fibrillation (AF) is the most commonly encountered cardiac arrhythmia and confers significant risk for ischemic stroke and transient ischemic attack (TIA).[1] When the risk of stroke is sufficiently high, based on risk-stratification schemes such as $CHADS_2$ (**C**ongestive Heart Failure, **H**ypertension, **A**ge $\geq$ 75, **D**iabetes, and Prior **S**troke/Transient Ischemic Attack [doubled]), CHA_2DS_2-VASc (**C**ongestive Heart Failure, **H**ypertension, **A**ge [$\geq$ 75 Years] [doubled], **D**iabetes Mellitus, **S**troke [doubled], **V**ascular Disease, **A**ge [65-74] Years, **S**ex **C**ategory [Female]), and CHADS-65 (**C**ongestive Heart Failure, **H**ypertension, **A**ge $\geq$ **65** Years, **D**iabetes, **S**troke/Transient Ischemic Attack), guidelines for AF recommend anticoagulation treatment with direct oral anticoagulants (DOACs) over treatment with warfarin.[2,3] However, despite anticoagulation treatment of AF with DOACs, an approximately 1 per 100 patient-years residual risk of stroke and systemic embolism remains, as reported within the large DOAC clinical trials.[4-6]

AF guidelines recommend that patients who experience a stroke while on oral anticoagulant (OAC) therapy be managed with an emphasis on addressing medication adherence, ensuring guideline-concordant dosing, and avoiding drug interactions.[2] In the absence of such contributory factors, a switch to another OAC may be considered[2,7]; however, robust clinical evidence to describe and support such a strategy is lacking. Although no randomized trials directly compare the efficacy of DOACs, a strategy of changing the original DOAC to one with an alternative mechanism of action has been utilized by prescribers.[8] A recent retrospective cohort study suggested that a change in OAC type is not associated with reduced rates of stroke recurrence, compared to no change in OAC, although this study focused on patients anticoagulated with vitamin K antagonists.[9]

Given the uncertainty of clinical outcomes with these varying treatment options, we sought to describe OAC prescribing in patients with AF, following an ischemic stroke/TIA, who are already taking a DOAC, and assess recurrent stroke/TIA and bleeding outcomes poststroke, with consideration of medication adherence.

Methods

Study design

This was a retrospective review of patients with AF who were on a DOAC and were discharged from hospitals with a

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See page 609 for disclosure information.

diagnosis of ischemic stroke/TIA, from January 2011 to October 2019. The Alberta Strategy for Patient-Oriented Research Unit linked administrative databases that capture all interactions within the single-payer, universal-access healthcare system in Alberta, Canada; including the following: the Discharge Abstract Database, for hospitalizations; the National Ambulatory Care System, for emergency department encounters; the Physician Claims Database, for outpatient physician visits; the Pharmaceutical Information Network, for outpatient medication dispensation data; the Provincial Laboratory Database, for laboratory values; and the Provincial Registration and Vital Statistics Database, to ascertain death.

Patient population

Patients aged $\geq$ 18 years who were discharged alive from an acute care setting, emergency department, or rehabilitation facility in Alberta with a diagnosis of ischemic stroke or TIA, based on the International Classification of Diseases, 10th revision (ICD-10) codes H34.1, I63, and G45.9 (referred to as the index event) were included. Next, AF or atrial flutter in the previous 10 years was confirmed, based on the patient having at least 1 diagnosis in a hospital setting or at least 2 diagnoses at least 30 days apart in an outpatient setting, using the ICD-10 and ICD, 9th revision, Clinical Modification (ICD-9-CM) codes. The accuracy of ICD-9 and ICD-10 codes for stroke and TIA has been validated previously against chart audit data in Alberta.[10] Patients had to have community pharmacy prescription fills for dabigatran, apixaban, or rivaroxaban within 120 days prior to the index event. Patients were excluded if they had any of the following: moderate-severe mitral stenosis; mechanical heart valve; stroke/TIA within 90 days before the index event; stroke/TIA while originally admitted for another diagnosis or procedure; lack of database entries, suggesting a lack of healthcare-system contact within 120 days following discharge from the index event; or primary residence outside of Alberta, based on postal code. Edoxaban was not investigated in our study, owing to its very limited use (n = 2) during the study period.

Outcomes

The primary outcome was the proportion of patients within each anticoagulant prescribing strategy pre- vs post-index event, based on OAC prescription pharmacy fills. Strategies were predefined as follows: those that kept the same DOAC regimen; those that kept the same DOAC agent but changed dose; and those that changed to an alternative DOAC, changed to warfarin, or did not fill an OAC prescription. Secondarily, we sought to determine the proportion of patients who had a recurrent stroke/TIA, or an occurrence of a bleeding event requiring medical attention. A recurrent stroke/TIA was identified via ICD-10 codes for ischemic stroke or TIA within inpatient, emergency, and outpatient settings (Supplemental Table S1). Bleeding events were defined as either of the following: (i) fatal, intracerebral, subarachnoid, in other critical area, gastrointestinal, genitourinary, or other bleeding based on ICD-10 codes within a hospital inpatient setting (Supplemental Table S1); or (ii) bleeding based on the ICD-10 codes in an emergency department requiring a transfusion of whole blood or packed red blood cells. Patient follow-up ceased with a clinical event, including recurrent stroke/TIA, bleeding, or death. In the absence of these outcomes, patients were followed to the end of the study period, which encompassed a minimum of 6 months for all patients.

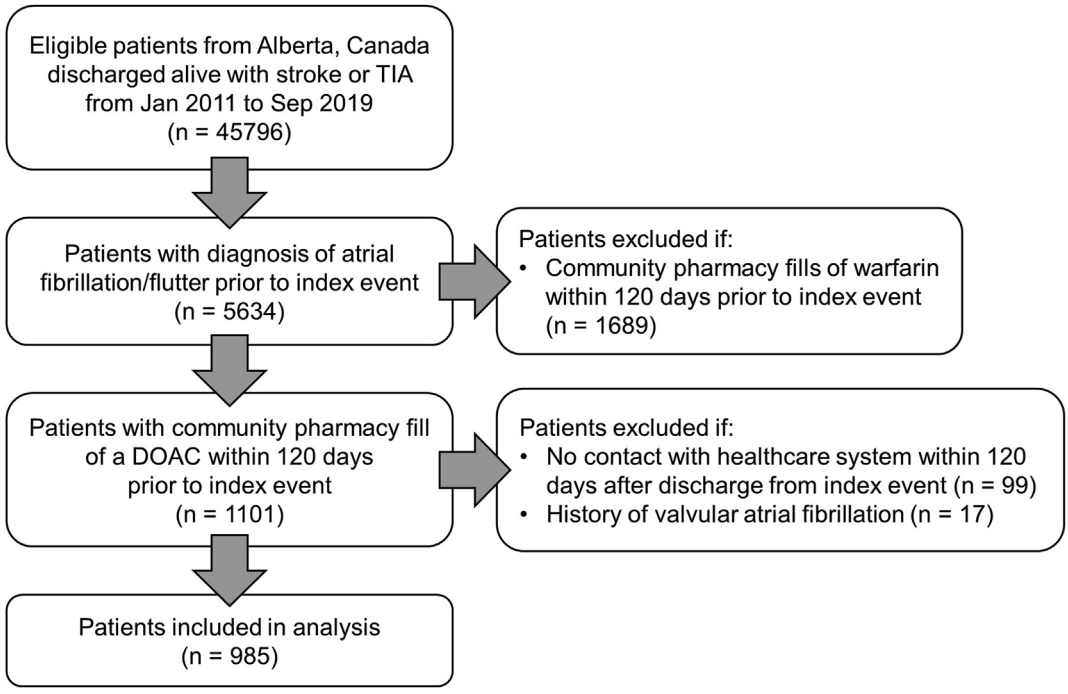

Figure 1. Study flow diagram. A total of 45,796 patients in Alberta, Canada were initially identified within administrative databases. A total of 985 were analyzed within this study who had a history of atrial fibrillation (AF) and filled a direct oral anticoagulant (DOAC) prescription prior to a stroke or transient ischemic attack (TIA), and met the additional inclusion/exclusion criteria listed. Jan, January; Sep, September.

Table 1. Patient baseline characteristics

Characteristic	All study patients (N = 985)
Female sex	457 (46)
Age, y	
Median (IQR)	80 (13)
≥ 85	290 (29)
75–84	394 (40)
65–74	195 (20)
< 65	106 (11)
$CHADS_2$ prior to index event	
Mean (SD)	1.7 (1)
5–6	4 (0.4)
3–4	113 (11)
1–2	697 (71)
0	171 (17)
Medical history	
Prior stroke or TIA	112 (11)
Prior bleeding event	29 (3)
Index event type	
Stroke	497 (50)
TIA	488 (50)
Length of stay, d, median (IQR)	2 (7)
Follow-up, d, median (IQR)	643 (836)
Deaths during follow-up	316 (32)
Creatinine clearance, mL/min	
≥ 90	78 (8)
50–89	578 (59)
30–49	264 (27)
15–29	26 (3)
≤ 14	1 (< 1)
Not documented	38 (4)

Values are n (%), unless otherwise indicated.

$CHADS_2$, **C**ongestive Heart Failure, **H**ypertension, **A**ge ≥ 75, **D**iabetes, and Prior **S**troke/TIA [doubled] score; IQR, interquartile range; SD, standard deviation; TIA, transient ischemic attack.

Medication adherence was investigated using the proportion of days covered (PDC) method. The PDC is a measure of the ratio of total days covered by refills within a period to the total number of days from the first prescription fill to the end of the period.[11] The period was 1 year, unless follow-up ended due to a clinical event. Patients with a PDC ratio ≥ 80% were considered adherent, as a PDC < 80% is a known risk factor for AF-related stroke.[11,12]

Data analysis

Descriptive results are presented as proportions, mean ± standard deviation, or median with interquartile range (IQR). Creatinine clearance (CrCl) was based on the modified Cockcroft-Gault equation standardized to a weight of 72 kg, using the last recorded creatinine value prior to discharge from the index event. A Cox regression model was used to generate hazard ratios for recurrent stroke/TIA risk factors. Statistical tests were performed with level of significance of $P < 0.05$, and 95% confidence intervals were calculated. Ethics approval was obtained from the University of Alberta Health Research Ethics Board (Pro00104912).

Results

Baseline characteristics

Among 985 patients included (Fig. 1; Table 1), the median age was 80 years (IQR 13); 46% were female; and the majority (97%) had a CrCl ≥ 30 mL/min. The mean $CHADS_2$ score was 1.7 ± 1 prior to the index event, with 11% having a prior history of stroke/TIA. A similar proportion of index events were identified as stroke (50%) vs TIA (50%), and the median length of admissions was 2 days (IQR 7). Patients were followed up for a median of 643 days (IQR 836), during which 316 deaths occurred.

OAC prescription fills pre- and post-index event

Following the index event, 623 of 985 patients (63%) filled the same DOAC regimen; 83 (8%) filled a prescription for a different dose of the same DOAC; 155 (16%) switched DOAC agents; 51 (5%) switched to warfarin; and 73 (7%) filled no OAC prescription (Fig. 2). Of those who filled a prescription for a different dose, 62 (75%) filled an increased dose prescription, and 21 (25%) filled a decreased dose prescription.

Prior to the index event, the levels of use of dabigatran (n = 323; 33%), apixaban (n = 317; 32%), and rivaroxaban (n = 343; 35%) were similar (Fig. 3). Patients who switched DOACs most commonly filled apixaban prescriptions post-index event (72%). Among the patients who remained on a DOAC, the distribution of DOAC agent prescriptions filled was significantly different pre- vs post-index event ($P < 0.05$), as follows: dabigatran (33% vs 27%); apixaban (32% vs 43%); and rivaroxaban (35% vs 30%). Dabigatran was the single DOAC prescription being filled from 2011 to 2012, with fills of prescriptions for apixaban and rivaroxaban emerging in 2013, and proportional use increasing thereafter (Supplemental Fig. S1).

Differences in prescribing were seen based on the type of index event. Of patients kept on the same DOAC regimen, a lower proportion had experienced stroke (41%) than TIA. Patients that changed to a different DOAC dose, a different DOAC agent, warfarin, or no OAC more commonly had stroke (55%, 72%, 78%, and 60%, respectively) than TIA. Compared to the overall cohort, patients that changed to warfarin had longer admissions (11 days), longer durations of follow-up (915 days), a higher proportion of deaths (10%), and a higher proportion of either a CrCl < 30 mL/min or no documented creatinine value (12%). Patients that did not fill an OAC prescription post-index event had shorter durations of follow-up (40 days), with a higher proportion experiencing death (63%).

Recurrent stroke or TIA, and bleeding outcomes

During follow-up, 135 of 985 patients (14%) experienced a recurrence of stroke (49%) or TIA (51%), occurring a median of 244 days (IQR 439) from the index event (Table 2). The proportion of patients with recurrent stroke/TIA was similar across prescribing categories; however, the group that did not fill an OAC prescription had more recurrent stroke/TIAs (32%), with most of these events being strokes (65%) occurring at a shorter time to event (17 days [IQR 32]).

A total of 46 of 985 (5%) experienced a bleeding event during follow-up, of which the majority were either gastrointestinal (63%) or intracranial/subarachnoid (23%) in nature (Table 2). The proportion of patients with bleeding events

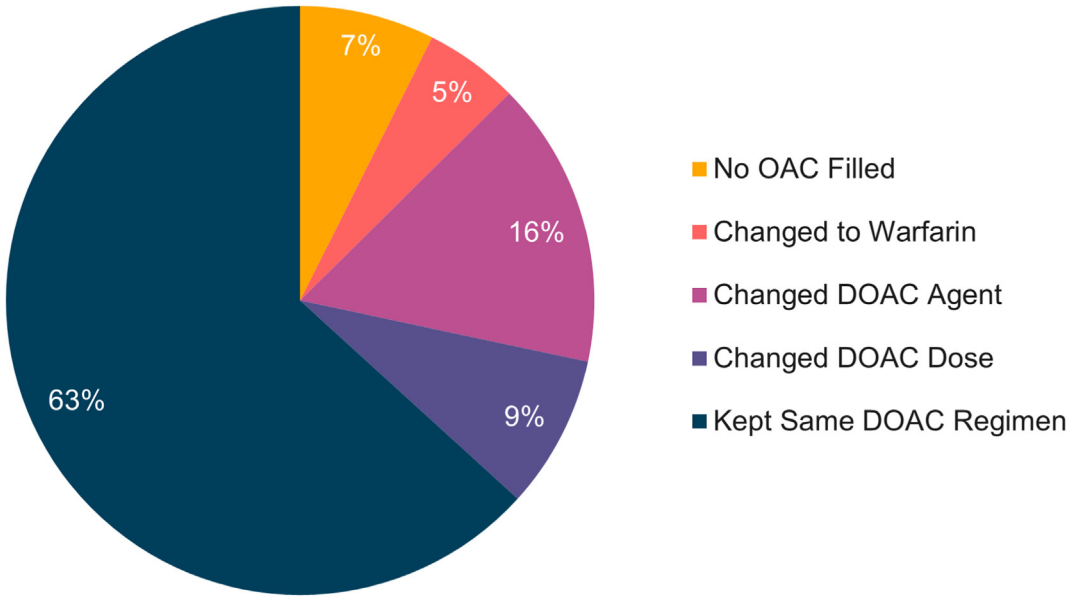

Figure 2. Oral anticoagulant (OAC) prescribing post-index event. For patients with atrial fibrillation who have a stroke or transient ischemic attack despite direct OAC (DOAC) therapy, the prescribing practices for oral anticoagulation are depicted as proportions of the total cohort. A total of 623 of 985 patients (63%) filled the same DOAC regimen; 83 (8%) filled a prescription for a different dose of the same DOAC; 155 (16%) switched DOAC agents; 51 (5%) switched to warfarin; and 73 (7%) filled no OAC prescription.

was similar across prescribing categories. The median time to event was 536 days (IQR 773), although patients that did not fill an OAC prescription had a shorter time to event, at 60 days (IQR 53).

Adherence

Prior to the index stroke/TIA event, 540 patients (55%) were considered adherent, with a PDC $\geq$ 80% for DOACs, and this improved to 85% over the first year following the index event (Table 3). Adherence rates post-index event among those having recurrent stroke/TIA (87 of 104; 84%) and bleeding (30 of 38; 79%) were comparable to those in the entire cohort.

Risk factors for recurrence of stroke or TIA

DOAC prescription fill properties, including prescribing strategy, DOAC agent, and adherence $\geq$ 80% were not found to be predictive of stroke/TIA recurrence based on our Cox regression model (Supplemental Table S2). Of the patient factors assessed, only age at time of index event was a significant predictor of recurrence (hazard ratio 1.032, 95% confidence interval 1.005-1.06).

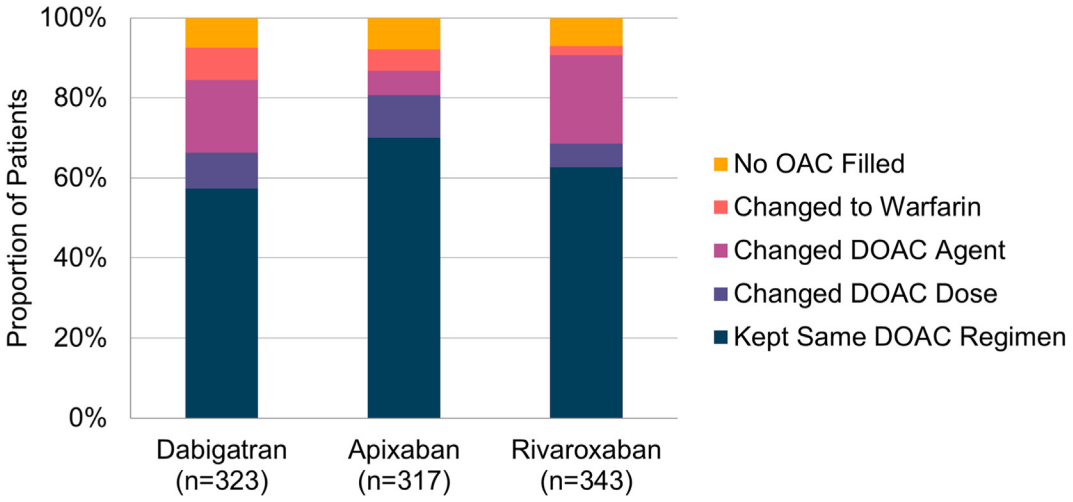

Figure 3. Oral anticoagulant (OAC) prescribing based on pre-index event direct OAC (DOAC) therapy. Following a breakthrough stroke despite the use of dabigatran (n = 323), apixaban (n = 317), or rivaroxaban (n = 343), the prescribing pattern for subsequent OAC use was analyzed. The proportion of patients (%) per prescribng pattern for each DOAC used pre-index event is illustrated.

Table 2. Characterization of recurrent strokes/TIAs, and bleeding events post-index event

Events	All patients (N = 985)	Kept same DOAC regimen (n = 623)	Changed DOAC dose (n = 83)	Changed DOAC agent (n = 155)	Changed to warfarin (n = 51)	No OAC prescription filled (n = 73)
Patients with recurrent stroke/TIA	135 (14)	75 (12)	13 (16)	16 (10)	8 (16)	23 (32)
Recurrent event type						
Stroke*	66 (49)	34 (45)	6 (46)	7 (44)	4 (50)	15 (65)
TIA*	69 (51)	41 (55)	7 (54)	9 (56)	4 (50)	8 (35)
Days to recurrent event, median (IQR)	244 (439)	388 (635)	115 (209)	282 (314)	245 (513)	17 (32)
Patients with bleeding event	46 (5)	28 (4)	2 (2)	8 (5)	3 (6)	5 (7)
Bleeding location						
ICH† or SAH†	11 (24)	4 (14)	0 (0)	2 (25)	1 (33)	4 (80)
Gastrointestinal†	29 (63)	20 (72)	2 (100)	4 (50)	2 (67)	1 (20)
Other†,‡	10 (22)	4 (14)	0 (0)	2 (25)	0 (0)	0 (0)
Days to bleeding event, median (IQR)	536 (773)	504 (749)	1104 (2131)	663 (372)	1002 (2434)	60 (53)

Values are n (%), unless otherwise indicated.

DOAC, direct OAC; ICH, intracranial hemorrhage; IQR, interquartile range; OAC, oral anticoagulant; SAH, subarachnoid hemorrhage; TIA, transient ischemic attack.

* Percentages are expressed as a proportion of all patients or patients in each prescribing strategy with a recurrent stroke or TIA.

† Percentages are expressed as a proportion of all patients or patients in each prescribing strategy with a bleeding event.

‡ Other: genitourinary, other critical areas including intraspinal, intraocular, retroperitoneal, intraarticular and pericardial hemorrhage, other areas including epistaxis and hemothorax.

Discussion

In this study, the most common strategy to manage anticoagulation after a stroke/TIA despite DOAC therapy was to keep the same DOAC regimen (63% of patients), followed by changing to another DOAC (16%), changing the dose (8%), changing to warfarin (5%), and no OAC therapy (7%). Over a median follow-up time of 643 days after their initial event, 7% of the cohort had a stroke, 8% had a TIA, and 5% had a bleeding event. The rates of stroke seen in this cohort are comparable to those seen in previous observational studies examining rates of AF-related strokes with prior anticoagulation,[9,13] as were bleeding rates.[14] Overall, proportions of patients with stroke/TIA recurrence and bleeding events were similar between the different prescribing strategies in this study. This result is similar to that in a previous analysis showing that a change in OAC, primarily from vitamin K antagonists, was not associated with decreased risk of recurrent ischemic stroke, compared to no change in OAC.[9]

Although these results do not point to a preferred approach to managing anticoagulation, they may reflect the importance of an individualized decision-making process. For example, the severity of the index event appears to have influenced prescribing patterns, as patients experiencing TIA and shorter hospital stays were more commonly maintained on the same DOAC regimen, whereas patients with stroke and comparatively longer lengths of stay more frequently had dose changes or were switched to an alternative anticoagulant therapy.

In clinical practice, patients presenting with stroke/TIA events despite anticoagulant therapy require assessment to determine if treatment failure occurred or if they were on inadequate therapy due to poor adherence, or whether other factors were in play, such as discordant dosing and drug-drug interactions. Adherence of our cohort improved post-index event, with the proportion with PDC $\geq$ 80% increasing from 55% to 85%. The proportion of patients with PDC $<$ 80% pre-index event is higher than that seen in previous studies,[11,12] suggesting that poor adherence was a factor for breakthrough strokes/TIAs requiring intervention in our cohort. The improvement in adherence across all prescribing categories post-index event is in alignment with a practice of encouraging adherence and implementing strategies such as compliance packaging regardless of therapy prescribed. However, those who have breakthrough stroke/TIA despite good adherence may carry intrinsically strong drivers of thrombogenesis that outweigh normally sufficient levels of anticoagulation, or may exhibit pharmacokinetic variability that causes inadequate anticoagulation despite guideline-concordant dosing, such as poor absorption or excessive metabolism. This risk-enriched population that has already failed stroke prevention once may benefit greatly from DOAC steady-state concentration measurements to rule out pharmacokinetic reasons for failure. Calibrated, DOAC-specific assays are becoming more widely available, such that their integration into initial assessment protocols may help individualize and improve upon overall stroke/TIA treatment.

Table 3. Proportion of adherent patients (PDC > 80%) based on prescribing categories during follow-up

Timing	All study patients (N = 985)	Kept same DOAC regimen (n = 623)	Changed DOAC dose (n = 83)	Changed DOAC agent (n = 155)	Changed to warfarin (n = 51)	No OAC prescription filled (n = 73)
Pre-index event	540 (55)	342 (55)	47 (57)	93 (60)	23 (45)	35 (48)
Post-index event*	732/861 (85)	499 (80)	66 (80)	128 (83)	N/A	N/A

Values are n (%).

DOAC, direct OAC; N/A, not applicable; OAC, oral anticoagulant; PDC, proportion of days covered.

* Percentages are expressed as a proportion of the total number of patients remaining on a DOAC after the index event.

Changing to an alternative anticoagulant in the absence of factors compromising anticoagulation is a recommendation included in guidelines based on expert opinion.[2,8] For patients in our population who changed DOAC agents, switching to apixaban was the predominant strategy. Although apixaban is superior, compared with warfarin, in reducing AF-related stroke or systemic embolism, bleeding, and mortality[5] and is one of the most used DOACs in current practice, no randomized, head-to-head trials to date have compared the efficacy and safety of the available DOACs. Of interest, adherence post-index event improved, despite most patients being switched to apixaban, which is criticized for being more difficult to adhere to than rivaroxaban, owing to the twice-daily dosage.

The year of index event was highly predictive of the strategy to change to warfarin. From 2011 to 2012 in our cohort, dabigatran and warfarin were the only available OACs for stroke prevention in AF. From 2013 onward, the annual proportion of patients switching to warfarin declined due to availability of apixaban and rivaroxaban, and across the last 2 years of follow up, apixaban and rivaroxaban were the most common DOACs and were used at similar rates (Supplemental Fig. S1)

Patients who did not fill any OAC prescriptions following their index event had substantially shorter follow-up times, with a median of 40 days (IQR 191), during which 63% died, 32% had a recurrent stroke/TIA, and 7% had a bleeding event. This category likely was comprised of patients who had a poor prognosis.

This study has a number of limitations associated with design, as it is a retrospective, observational study of administrative data using diagnostic codes. All characteristics of breakthrough stroke/TIA during DOAC treatment could not be accounted for, including stroke severity, alternate stroke etiologies, and suboptimal risk-factor management of alcohol use, tobacco use, sleep apnea, obesity, diabetes, hypertension, and dyslipidemia; such information could better rationalize decisions to continue or change DOAC regimens. Measures of body weight, anti-Xa level, and/or thrombin time on admission would also improve evaluation of DOAC use, and nonprescription medication use would allow thorough investigation of drug-drug interactions.

Conclusion

In our study, only about one-third of patients filled a different OAC regimen prescription after a breakthrough stroke or TIA, including changing the original DOAC dose (8%), changing the DOAC agent (16%), or changing to warfarin (5%). Despite different approaches to managing OAC post-stroke, rates of stroke/TIA recurrence and bleeding events were similar. Patient factors, such as preference, and stroke vs TIA severity may have influenced prescribing decisions. DOAC adherence was improved post-index event and should be optimized in all patients with AF. Further research is required to confirm whether choice of OAC reduces stroke risk in patients who experience DOAC treatment failure in the absence of factors causing inadequate anticoagulation.

Ethics Statement

Ethics approval was obtained from the University of Alberta Health Research Ethics Board (Pro00104912).

Patient Consent

The authors confirm that a waiver of consent was obtained by the University of Alberta Health Research Ethics Board given the retrospective nature and use of de-identified data for this study.

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The authors have no funding sources to declare.

Disclosures

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2023.05.001.