

Original Article

Evolution of Antithrombotic Management of Atrial Fibrillation After Percutaneous Coronary Intervention Over 10 Years and Guidelines Uptake

Marie-Claude Beaulieu, MD, Laurie-Anne Boivin-Proulx, MD, Alexis Matteau, MD, SM, Samer Mansour, MD, Jean-François Gobeil, MD, and Brian J. Potter, MDCM, SM

Montreal University Hospital Centre (CHUM) Research Centre and Cardiovascular Centre, Montreal, Quebec, Canada

ABSTRACT

Background: The management of atrial fibrillation and/or flutter (AF) patients requiring percutaneous coronary intervention (PCI) has evolved significantly. The Canadian Cardiovascular Society AF guidelines, last updated in 2020, seek to aid physicians in balancing both bleeding and thrombotic risks.

Methods: A tertiary academic centre registry of patients with AF who had PCI was examined for the antithrombotic therapy at discharge in 4 time periods (cohort 2010–2011; cohort 2014–2015; cohort 2017; cohort 2019). Discharge prescription patterns were compared among the cohorts, using the χ^2 test. In addition, antithrombotic management in cohorts 2017 and 2019 were compared to guideline-expected therapy, using the χ^2 test.

Results: A total of 576 AF patients undergoing PCI were included. Clinical and procedural characteristics were similar among cohorts, except for an increase in drug-eluting stent use in the most recent cohort (94% vs 99%; $P = 0.04$). The rate of oral anticoagulation increased over time (75% vs 89%; $P < 0.01$), driven primarily by an increase in direct oral anticoagulants prescription (63% vs 84%; $P < 0.01$). In contrast to previous cohorts, there was no significant difference between

RÉSUMÉ

Introduction : La prise en charge des patients atteints de fibrillation auriculaire et/ou de flutter (FA) qui ont besoin d'une intervention coronarienne percutanée (ICP) a considérablement évolué. La dernière révision, en 2020, des lignes directrices sur la FA de la Société canadienne de cardiologie vise à aider les médecins à établir l'équilibre entre les risques d'hémorragie et de thrombose.

Méthodes : Nous avons fouillé le registre d'un centre universitaire en soins tertiaires portant sur des patients atteints de FA qui avaient subi une ICP pour nous pencher sur le traitement antithrombotique offert à la sortie de l'hôpital de quatre périodes (cohorte 2010–2011; cohorte 2014–2015; cohorte 2017; cohorte 2019). Nous avons comparé les pratiques en matière d'ordonnances à la sortie de l'hôpital entre les cohortes à l'aide du test du χ^2 . De plus, nous avons comparé la prise en charge des cohortes de 2017 et de 2019 qui avaient reçu le traitement antithrombotique à celles qui avaient reçu le traitement prévu dans les lignes directrices à l'aide du test du χ^2 .

Résultats : Nous avons sélectionné un total de 576 patients atteints de FA qui avaient subi une ICP. Les caractéristiques cliniques et interventionnelles étaient similaires entre les cohortes, à l'exception d'une

Atrial fibrillation and/or flutter (AF) affects more than 30 million people worldwide.^{1,2} To reduce the risk of ischemic stroke and mortality,³ standard of care includes oral anticoagulation (OAC) for patients with additional risk factors.^{4–6} However, up to 30% of patients with AF will have concomitant coronary artery disease, many of whom will require percutaneous coronary intervention (PCI) at some point.^{4,7}

Although the antithrombotic management of patients with either AF or coronary artery disease is well established,^{4,5,8,10} dual antiplatelet therapy (DAPT; acetylsalicylic acid + P2Y12 [platelet adenosine diphosphate receptor]-inhibitor)^{11,12} has been shown to be inferior to OAC for stroke prevention in patients with AF.¹³ Moreover, simply adding OAC to DAPT (so-called triple antithrombotic therapy [TATT]) significantly increases the likelihood of bleeding complications.^{14–16}

In a previous international multicentre study, we demonstrated that the availability of the newer antiplatelet and anticoagulant agents significantly increased practice variability in the management of AF post-PCI.¹⁷ Since then, landmark trials have provided evidence that dual-pathway (OAC + P2Y12-inhibitor) antithrombotic regimens using direct oral anticoagulants (DOACs) could minimize the bleeding risk in AF patients having benefited from PCI,^{18–21} and the Canadian Cardiovascular Society (CCS) AF guidelines were regularly updated as new evidence became available.^{5,9,11,22–25}

Received for publication March 22, 2021. Accepted April 5, 2021.

Ethics Statement: The study protocol was consistent with the ethical guidelines of the 1975 Declaration of Helsinki and was conducted in accordance to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. The CHUM Research Centre (CRCHUM) institutional ethics board approved the study and provided a waiver for informed consent.

Corresponding author: Dr Brian J. Potter, Health Innovation and Evaluation Hub, Research Centre of CHUM, Cardiology & Interventional Cardiology, CHUM, Pavillon S, S03-334, 850, Rue St-Denis, Montréal, Quebec H2 × 0A9, Canada. Tel.: +1-514-890-8000 ext.15473; fax: +1-514-412-7212.

E-mail: brian.potter@umontreal.ca

See page 1031 for disclosure information.

the observed and the guideline-expected anticoagulation rate in cohort 2019 (89% vs 94%; $P = 0.23$).

Conclusions: A combination of expert guidance and educational initiatives in the past decade contributed to dramatic changes in the management of patients with AF undergoing PCI.

We therefore sought to determine the impact of the publication of the 2018 CCS AF guidelines^{5,9,22,23}—in conjunction with landmark clinical trials and ongoing continuing medical education initiatives—on clinical practice, and to assess whether treatment gaps between observed and guideline-expected antithrombotic therapy still existed at our institution.

Methods

The CHUM AF-STENT registry consists of a prospective cohort of consecutive patients aged ≥ 18 years with documented AF and undergoing PCI with coronary stenting at the Montreal University Hospital Centre (Centre Hospitalier de l'Université de Montréal [CHUM]). This registry built on an original retrospective cohort analysis conducted at the same institution. The CHUM is a tertiary academic centre and interventional cardiology referral centre where 14 operators perform an average of 2000 diagnostic procedures and 1400 angioplasties per year. The study protocol was consistent with the ethical guidelines of the 1975 Declaration of Helsinki and was conducted in accordance to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.²⁶ The CHUM Research Centre (CRCHUM) institutional ethics board approved the study and provided a waiver for informed consent. Patients with an indication for OAC other than AF, those with a contraindication for OAC and/or antiplatelet therapy, and those who were previously included in the data set were excluded from the analysis. Additionally, 4 patients in cohort 2017, who participated in a clinical trial and for whom the type of antithrombotic therapy was unknown, were excluded.

Patients were enrolled during one of 4 time periods. Cohort 2010–2011 represents a “historic” period, before the commercial availability of DOAC (January 2010 to December 2011). Cohort 2014–2015 corresponds to a “pre-guidelines” period (January 2014 to December 2015), from the point at which DOACs and newer P2Y12 inhibitors were commercially available, but prior to publication of the 2016 CCS AF guidelines.⁵ Cohort 2017 represents an “inter-guidelines” period (January to December 2017) immediately after the publication of the 2016 CCS guidelines and early landmark studies,^{5,18,19} but prior to later studies and the publication of the 2018 CCS guidelines update.^{9,20–22}

augmentation de l'utilisation d'une endoprothèse médicamenteuse dans la plus récente cohorte (94 % vs 99 %; $P = 0,04$). Le taux d'anticoagulation par voie orale qui avait augmenté au fil du temps (75 % vs 89 %; $P < 0,01$) était principalement attribuable à l'augmentation des ordonnances d'anticoagulants d'action directe par voie orale (63 % vs 84 %; $P < 0,01$). Contrairement aux cohortes précédentes, il n'y avait aucune différence significative entre le taux d'anticoagulation observé et le taux d'anticoagulation prévu dans les lignes directrices dans la cohorte de 2019 (89 % vs 94 %; $P = 0,23$).

Conclusions : La combinaison des conseils d'experts et des initiatives éducationnelles de la dernière décennie a contribué à des changements radicaux dans la prise en charge des patients atteints de FA qui subissaient une ICP.

Finally, cohort 2019 (January to December 2019) corresponds to a “post-guidelines” period after the publication of the 2018 CCS AF guidelines and landmark trials.^{9,18–22}

The primary outcome of interest was antithrombotic therapy at hospital discharge. Data regarding baseline patient characteristics, clinical presentation, procedural data, and in-hospital outcomes were also abstracted from hospital medical records. Baseline characteristics of patients and procedural data are presented both in aggregate and separately for the 4 cohorts. Continuous data are reported as means and standard deviations, or medians and interquartile ranges, as appropriate, and categorical/binary data are reported as counts and proportions of total.

As significant differences between prescription patterns in the first 3 cohorts have been reported previously,^{17,27} the primary objective of this analysis was to determine whether there were additional changes in prescription patterns following the publication of the 2018 CCS guidelines. Baseline comparisons between cohort 2017 and cohort 2019 were made using a t test for continuous data, the median test for ordinal data, and the Fisher exact test or the χ^2 test for categorical data, as appropriate. Discharge prescription patterns between cohort 2017 and cohort 2019 were compared using the χ^2 test.

Secondarily, we compared the observed prescription patterns in cohort 2017 and cohort 2019 to the expected patterns according to the 2016 AF CCS guidelines and the 2018 AF and antiplatelet CCS guidelines, respectively,^{5,9,22} using the χ^2 test. The expected treatment with perfect guideline adherence was determined by first assessing the indication for anticoagulation for each patient by calculating the Congestive Heart Failure, Hypertension, Age ≥ 75 , Diabetes Mellitus, and Prior Stroke/Transient Ischemic Attack (doubled) (CHADS₂) score, and then combining it with consideration of the patient's age (≥ 65 years), as recommended in both the 2016 and 2018 AF guidelines. Patients who had a guideline indication for OAC with creatinine clearance (calculated by the Cockcroft-Gault method²⁸) ≤ 30 mL/min were expected to be treated with a vitamin K antagonist, whereas those with creatinine clearance > 30 mL/min were expected to receive a DOAC, in accordance with monograph recommendations for most DOACs in Canada at the time. A creatinine clearance cut-off of 30 mL/min was deemed most appropriate for this analysis, as it could be reasonably applied across cohorts.

Flow chart of the population derivation for all Cohorts.

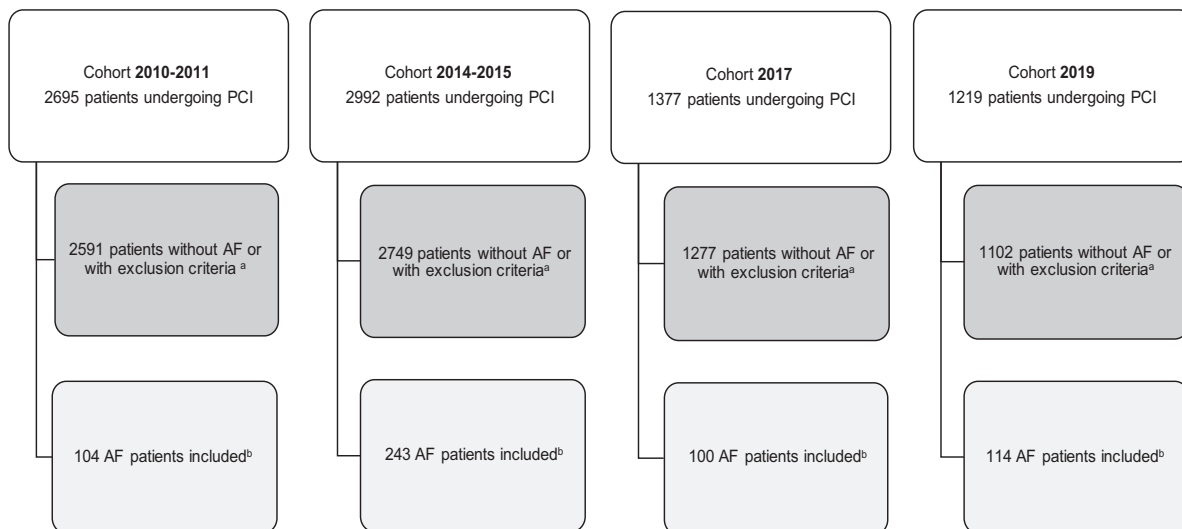


Figure 1. Flowchart of the population derivation for all cohorts. ^aExclusion criteria were indication for oral anticoagulation other than AF, a contraindication for oral anticoagulation or antiplatelet therapy or having been included previously in the data set. ^bPatients also had to be ≥ 18 years of age and had to have had at least one coronary stenting. AF, atrial fibrillation or flutter; OAC, oral anticoagulation; PCI, percutaneous coronary intervention.

(In Canada, apixaban had an indication for creatinine clearance > 25 mL/min, since 2017, but > 30 mL/min remained in effect for other DOACs. The apixaban and rivaroxaban monographs were subsequently modified to > 15 mL/min in late 2019.) If there was no guideline indication for OAC, treatment with DAPT was expected at discharge.

Statistical analyses were performed using SAS 9.3 statistical software (SAS Institute, Cary, NC). A 2-tailed P -value < 0.05 was considered statistically significant, without correction for multiple analyses.

Results

A total of 576 patients with AF were included across all 4 cohorts (Fig. 1). Clinical and procedural characteristics of patients in cohort 2010-2011 ($n = 109$), cohort 2014-2015 ($n = 246$), cohort 2017 ($n = 104$), and cohort 2019 ($n = 117$) are listed in Table 1. Clinical and procedural characteristics were largely similar over time, with the exception of a further increase in the use of drug-eluting stent (DES) (99% vs 94%; $P = 0.04$). The overall in-hospital mortality rate was 3%, and in-hospital major bleeding was 7% (Table 1).

Antithrombotic prescriptions at admission in each cohort are shown in Table 1. There was a significant increase in baseline use of OAC in cohort 2019 ($P = 0.02$) due to a marked rise in DOAC use ($P < 0.01$).

Antithrombotic prescriptions at discharge in each cohort are presented in Table 2. The rate of OAC use at discharge was also significantly higher in cohort 2019 (89% vs 75%; $P < 0.01$), driven by a significant increase in the prescription of DOACs (84% vs 63% of OAC; $P < 0.01$). A concomitant significant decrease in use of acetylsalicylic acid at discharge was also observed ($P < 0.01$). Consequently, dual-pathway regimen prescription increased significantly in cohort 2019 (P

< 0.01), whereas DAPT prescription at discharge was lower ($P = 0.01$). Interestingly, there was no significant change in the TATT prescription at discharge ($P = 0.51$; Fig. 2).

Discharge DOAC doses for cohort 2017 and cohort 2019 are shown in Table 3. Reduced-dose DOACs were prescribed more often than full-dose DOACs at discharge in the latest cohort (cohort 2019), with the exception of apixaban, for which the full dose was most often prescribed ($P = 0.01$). In contrast, patients prescribed TATT more often received reduced-dose rivaroxaban or apixaban, with no significant change between cohort 2017 and cohort 2019. A majority of dual-pathway patients were prescribed reduced-dose rivaroxaban (50%) in cohort 2017, whereas either reduced-dose rivaroxaban (38%) or full-dose apixaban (29%) were the most common prescriptions in cohort 2019 ($P < 0.05$).

Observed and expected (CCS guideline-recommended) OAC rates in cohorts 2017 and 2019 are presented in Table 4. Although there was a significant gap between observed and expected prescriptions in cohort 2017, the overall rates of anticoagulation and DOAC prescription in cohort 2019 were similar to what would be expected with perfect adherence with the 2018 CCS guidelines update (89% vs 94% OAC; $P = 0.23$; and 84% vs 89% DOAC, $P = 0.93$; Fig. 3).

Discussion

The CHUM AF-STENT registry reveals several findings pertinent to clinical practice. First, most clinical characteristics of AF patients undergoing PCI have remained stable over the past 10 years. Despite this, significant changes in baseline medication were seen. Use of acetylsalicylic acid at baseline was less common, and OAC use has increased, with more patients treated with DOACs at baseline than before. Discharge OAC prescription has also significantly increased, due

Table 1. Characteristics and baseline antithrombotic treatment of atrial fibrillation/flutter patients pre-PCI

Patient characteristics	Total cohort	Cohort 2010–2011	Cohort 2014–2015	Cohort 2017	Cohort 2019	<i>P</i> *
Baseline characteristics	N = 576	n = 109	n = 246	n = 104	n = 117	
Age, y	73.3 ± 9.8	72.3 ± 9.3	73.0 ± 9.5	74.4 ± 9.0	74.3 ± 8.3	0.74
Male sex	411 (71)	81 (74)	177 (72)	75 (72)	78 (67)	0.38
Diabetes	260 (45)	41 (38)	104 (42)	53 (51)	62 (53)	0.09
Hypertension	424 (74)	68 (62)	173 (70)	85 (82)	98 (83)	0.69
Stroke	60 (10)	14 (13)	17 (7)	7 (7)	22 (19)	0.01
Heart failure	139 (24)	24 (22)	68 (28)	24 (23)	23 (20)	0.54
Bleeding history	16 (0.2)	1 (1)	8 (3)	7 (7)	0 (0)	< 0.01
Body mass index, kg/m ²	28.1 ± 6.2	27.5 ± 5.7	28.1 ± 6.3	27.7 ± 6.2	29.1 ± 6.6	0.10
Creatinine clearance, mL/min	70.4 ± 35.8	69.1 ± 38.5	70.5 ± 36.6	67.5 ± 30.7	75.1 ± 36.3	0.05
CHADS ₂ , median (IQR)	2 (1-3)	2 (1-3)	2 (1-3)	2 (1-3)	2 (2-3)	0.17
HAS-BLED, median (IQR)	2 (1-2)	2 (2-3)	2 (2-3)	1 (1-2)	1 (1-2)	0.92
DES use	404 (70)	40 (37)	150 (61)	98 (94)	116 (99)	0.04
ACS presentation	426 (74)	98 (90)	211 (86)	60 (58)	57 (49)	0.18
Admission medication						
Antiplatelet therapy						
ASA	342 (59)	83 (76)	169 (69)	55 (53)	35 (30)	< 0.01
P2Y12	63 (11)	5 (5)	29 (12)	14 (13)	15 (13)	0.89
Clopidogrel	54 (9)	4 (4)	23 (9)	12 (12)	15 (13)	0.77
Prasugrel	1 (0)	1 (1)	0 (0)	0 (0)	0 (0)	0.10†
Ticagrelor	9 (2)	0 (0)	6 (2.4)	3 (2.7)	0 (0)	
Anticoagulation						
OAC	372 (65)	50 (46)	155 (63)	71 (68)	96 (82)	0.02
VKA	144 (25)	45 (41)	75 (30)	15 (14)	9 (8)	0.11
DOAC	228 (40)	5 (5)	80 (33)	56 (54)	87 (74)	< 0.01
In-hospital events						
Major bleeding (BARC 3 or 5)	18 (3)	1 (1)	5 (2)	4 (4)	8 (7)	0.25
Death (all cause)	15 (3)	5 (5)	3 (1)	4 (4)	3 (3)	0.59

Values are mean (± SD), or n (%), unless otherwise indicated. Boldface indicates significance.

ACS, acute coronary syndrome; ASA, acetylsalicylic acid; BARC, Bleeding Academic Research Consortium category 3 or 5⁴⁰; CHADS₂, Congestive Heart Failure, Hypertension, Age ≥ 75, Diabetes Mellitus, and Prior Stroke/Transient Ischemic Attack (doubled); DAPT, dual antiplatelet therapy; DES, drug-eluting stent; DOAC, direct oral anticoagulant; HAS-BLED, Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly (> 65 Years), Drugs/Alcohol Concomitantly; PCI, percutaneous coronary intervention; OAC, oral anticoagulation; P2Y12, P2Y12 inhibitor; TATT, triple antithrombotic therapy; VKA, vitamin K antagonist.

*Significance applies to the difference between Cohorts 2017 and 2019 only. Comparisons between other cohorts have been published previously.^{17,27}

†*P* for the distribution. Novel P2Y12 inhibitors prasugrel and ticagrelor were grouped together to avoid cells with a zero count.

Table 2. Antithrombotic treatment of atrial fibrillation/flutter patients post-PCI

	Total cohort	Cohort 2010–2011	Cohort 2014–2015	Cohort 2017	Cohort 2019	<i>P</i> *
Discharge medication	N = 561	n = 104	n = 243	n = 100	n = 114	
Antiplatelet therapy						
ASA	518 (92)	104 (100)	242 (100)	90 (90)	82 (72)	< 0.01
P2Y12	553 (99)	104 (100)	243 (100)	94 (94)	112 (98)	0.10
Clopidogrel	509 (91)	104 (100)	212 (87)	86 (86)	107 (94)	0.05
Prasugrel	3 (1)	0 (0)	2 (1)	1 (1)	0 (0)	0.47
Ticagrelor	41 (7)	0 (0)	29 (12)	7 (7)	5 (4)	0.51
Anticoagulation						
OAC	294 (52)	34 (33)	84 (35)	75 (75)	102 (89)	< 0.01
VKA	113 (20)	34 (33)	61 (25)	12 (12)	6 (5)	0.08
DOAC	180 (32)	0 (0)	23 (9)	63 (63)	96 (84)	< 0.01
Combination therapy						
DAPT	264 (47)	70 (67)	159 (65)	23 (23)	12 (11)	0.01
TATT	249 (44)	34 (33)	83 (34)	64 (64)	68 (60)	0.51
Dual pathway	42 (8)	0 (0)	1 (0)	8 (8)	34 (30)	< 0.01

Boldface indicates significance.

ASA, acetylsalicylic acid; DAPT, dual antiplatelet therapy; DOAC, direct oral anticoagulant; OAC, oral anticoagulation PCI, percutaneous coronary intervention; P2Y12, P2Y12 inhibitor; TATT, triple antithrombotic therapy; VKA, vitamin K antagonist.

*Significance applies to the difference between cohorts 2017 and 2019 only.

to substantial uptake of DOAC therapy. Furthermore, this guideline-appropriate intensification of antithrombotic management of AF patients was observed in spite of a dramatic shift to nearly exclusive DES use (99%) in this population. These findings highlight the significant impact that landmark

clinical trials, CCS guidelines, and educational initiatives have had on clinical practice.

Increased DOAC prescription is in line with the CCS AF guidelines and landmark studies published in the past 5 years.^{9,18-22,23} The higher TATT prescription rate since

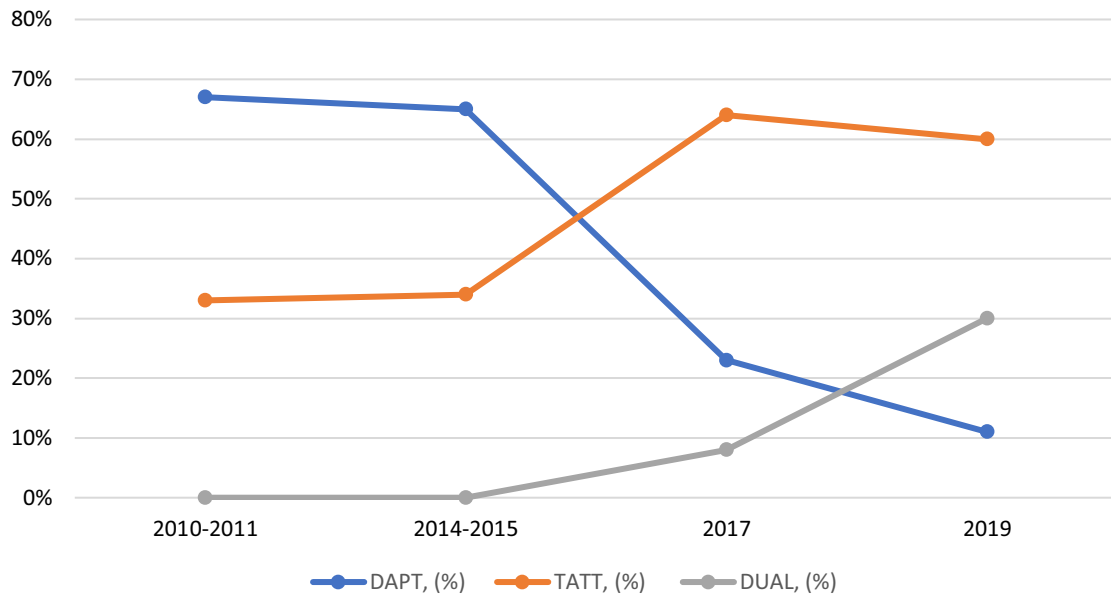


Figure 2. Time trends in combination therapy prescriptions at discharge. DAPT, dual antiplatelet therapy; DUAL, dual pathway; TATT, triple antithrombotic therapy.

Table 3. Discharge DOAC dosage for cohort 2017 and cohort 2019

DOAC at discharge*	Cohort 2017	Cohort 2019	P
All patients	N = 100	N = 114	
Dabigatran†	9 (9)	3 (3)	0.04
Rivaroxaban 15 mg q.d.	25 (25)	42 (37)	0.06
Rivaroxaban 20 mg q.d.	5 (5)	3 (3)	0.36
Apixaban 2.5 mg b.i.d.	17 (17)	20 (18)	0.91
Apixaban 5 mg b.i.d.	7 (7)	22 (19)	0.01
Patients on TATT	n = 64	n = 68	
Rivaroxaban 15 mg q.d.	20 (31)	29 (43)	0.17
Rivaroxaban 20 mg q.d.	4 (6)	1 (1)	0.15
Apixaban 2.5 mg b.i.d.	16 (25)	15 (22)	0.69
Apixaban 5 mg b.i.d.	5 (8)	12 (18)	0.09
Patients on dual pathway	n = 8	n = 34	
Rivaroxaban 15 mg q.d.	4 (50)	13 (38)	0.54
Rivaroxaban 20 mg q.d.	1 (13)	2 (6)	0.37
Apixaban 2.5 mg b.i.d.	1 (13)	5 (15)	0.87
Apixaban 5 mg b.i.d.	0 (0)	10 (29)	0.06

Values are n (%), unless otherwise indicated. Boldface indicates significance.

b.i.d., twice daily; DOAC, direct oral anticoagulant; q.d., once daily; TATT, triple antithrombotic therapy.

†Edoxaban not shown, as it was not prescribed.

‡Dabigatran full dose and reduced-dose were combined because it was rarely prescribed.

2017 is also in agreement with the CCS 2018 AF guidelines recommendation of TATT for 1 day to 6 months for patients with a CHADS₂ score ≥ 1 in the setting of acute coronary syndrome or elective PCI with high thrombotic features^{9,22}—a recommendation that places greater weight on reduction of thrombotic events and less weight on the risk of major bleeding during the period of TATT. The significant uptake of dual-pathway antithrombotic therapy with reduced-dose DOACs since 2017 also reflects the impact of randomized trial data from the An **O**pen-label, Randomized, Controlled, Multicenter Study Exploring **T**wo Treatment Strategies of **R**ivaroxaban and **O**ne of Oral Vitamin K Antagonist in Patients With **A**trial Fibrillation Who Undergo **P**ercutaneous

Coronary Intervention (PIONEER AF-PCI¹⁹; rivaroxaban, 2016) and **R**andomized Evaluation of **D**ual Antithrombotic Therapy with Dabigatran vs Triple Therapy With Warfarin in Patients With Nonvalvular Atrial Fibrillation Undergoing **P**ercutaneous **C**oronary **I**ntervention (RE-DUAL PCI¹⁸; dabigatran, 2017) studies that demonstrated that such regimens could minimize bleeding risk without a signal for an increase in ischemic events. The recent shift to full-dose dual-pathway antithrombotic management with apixaban is also advocated in the 2018 updates of the CCS antiplatelet and AF guidelines^{9,22} and likely also reflects the impact of the publication of the AUGUSTUS (An Open-Label, 2 × 2 Factorial, Randomized, Controlled Clinical Trial to Evaluate the Safety of Apixaban vs. Vitamin K Antagonist and Aspirin vs. Placebo in Patients With Atrial Fibrillation and Acute Coronary Syndrome and/or Percutaneous Coronary Intervention) trial in early 2019 that reinforced the safety advantage of dual-pathway over triple therapy.²⁰ The **E**doxaban **T**reatment **V**ersus **V**itamin K Antagonist in Patients With **A**trial **F**ibrillation Undergoing **P**ercutaneous **C**oronary **I**ntervention (ENTRUST-AF-PCI) trial further supported the safety and anti-ischemic efficacy of dual-pathway therapy over TATT, with no significant difference in ischemic events between the 2 groups,²¹ but its impact on clinical practice in our latest cohort appears to have been modest. These findings align with the results of recent retrospective studies of AF patients undergoing PCI in Korea and Europe.^{29,30}

Interestingly, the observed drop in DAPT prescription occurred concomitantly with the rise in DES use over that of bare-metal stents, which had been historically preferred for these patients because of the possibility of shorter DAPT duration following bare-metal stent implantation.³¹⁻³³ However, recent evidence has supported the safety of shorter courses of DAPT (3-6 months) with second-generation DES.^{9,34,35} Indeed, recent studies among patients at high risk of bleeding, including those requiring OACs, have shown the

Table 4. Observed and guideline-expected rates and type of oral anticoagulation post-2016 and post-2018 CCS guidelines

Inter-guidelines period	2017 observed (N = 100)	2016 CCS AF guidelines "expected" (N = 100)	P
Anticoagulation			
No	25 (25)	6 (6)	< 0.01
Yes	75 (75)	94 (94)	
Type of anticoagulation			
DOACn (%)	63 (84)	86 (91)	< 0.01
VKA	12 (16)	8 (9)	
Post-guidelines period	2019 observed (N = 114)	2018 CCS AF guidelines "expected" (N = 114)	P
Anticoagulation			
No	12 (11)	7 (6)	0.23
Yes	102 (89)	107 (94)	
Type of anticoagulation			
DOAC	96 (84)	101 (89)	0.93
VKA	6 (5)	6 (5)	

Values are n (%), unless otherwise indicated.

AF, atrial fibrillation/flutter; CCS, Canadian Cardiovascular Society; DOAC, direct oral anticoagulant; VKA, vitamin K antagonist.

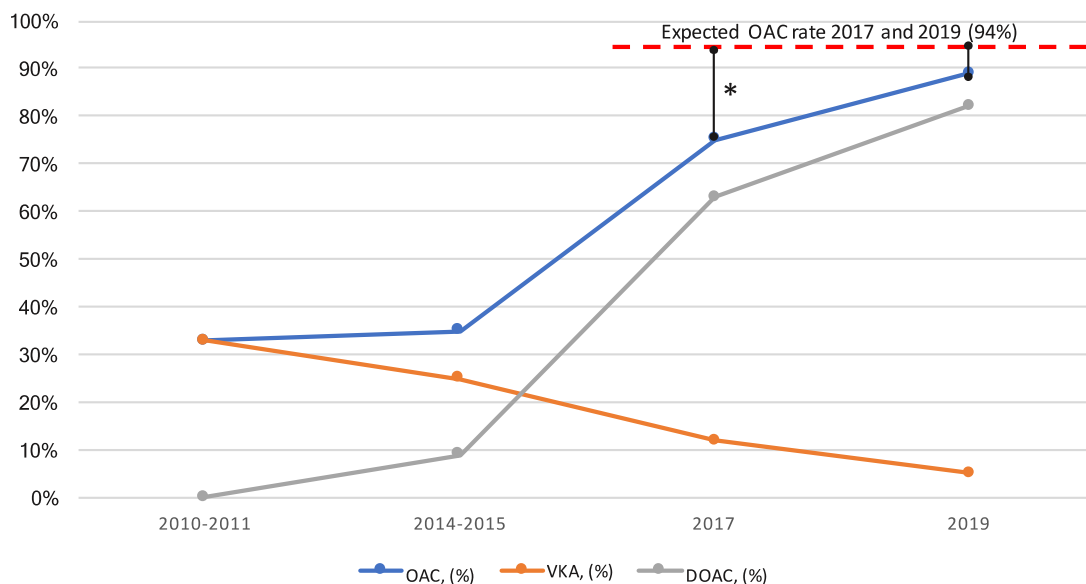


Figure 3. Time trends in anticoagulation prescription at discharge. *Significant difference between expected and observed OAC rate in 2017 ($P < 0.01$). DOAC, direct oral anticoagulant; OAC, oral anticoagulation; VKA, vitamin K antagonist.

superior efficacy and safety of certain DESs compared to bare-metal stenting when shorter courses of DAPT are necessary.^{36,37} It would appear that DOAC-based dual-pathway antithrombotic regimens are acceptable to clinicians who might otherwise have opted for shortened courses of DAPT in higher bleeding-risk patients receiving a DES. Moreover, preferring DES at the index procedure may avoid repeat procedures due to restenosis and thereby help reduce the risk of bleeding complications overall.³⁸

We observed a marked decrease in overall antithrombotic practice variability over time, and discharge prescriptions in cohort 2019 were highly aligned with the 2018 CCS AF guidelines.^{9,22} Despite this, one notable area of practice divergence remains. When prescribing TATT, the 2018

guidelines recommended either vitamin K antagonist or rivaroxaban at 2.5 mg twice daily. However, as this dose of rivaroxaban was not until recently available in Canada, practitioners who might eschew warfarin TATT were forced to select a higher-dose DOAC. Now recently approved for vascular protection³⁹ in Canada, it remains nevertheless unclear whether clinicians will prefer off-label (albeit evidence-based) usage of this dosage of rivaroxaban in the context of TATT to the higher doses of DOACs now recommended in the 2020 edition of the AF guidelines.²³ By way of a parallel, prior to the publication of AUGUSTUS,²⁰ we found that a majority of patients (70%) who received apixaban-TATT received an inappropriately reduced dose according to approved dosing criteria.

Limitations

Certain limitations of the present analysis must be acknowledged. Although the CHUM AF-STENT is a prospective registry, it relies on abstracting data from patients' medical records, which is subject to possible ascertainment bias. Second, the defined creatinine clearance cutoff of > 30 mL/min for expected DOAC prescription might have falsely lowered the rate of expected DOAC use. Although DOACs are now approved for use with filtration rates as low as 15 mL/min, that approval occurred late in the study period, and its effect on prescriptions is therefore likely to be minimal. Also, the total number of patients who received DOACs at each dose was small, thereby limiting the interpretation of these results. In addition, this study was conducted in a single tertiary academic centre and might not be representative of clinical practice in other community or academic centres in Canada. Overall adherence to national guidelines may be better ascertained through larger, multicentre studies. Finally, as many patients referred to our centre for PCI are followed at outside clinics, we cannot provide robust clinical outcome data beyond hospital discharge.

Conclusions

The management of patients with AF undergoing PCI has undergone a significant evolution over the past 10 years. Although clinical practice variability initially increased with the introduction of newer anticoagulants and antiplatelet agents prior to clear CSS guidance, the combination of the CCS AF and antiplatelet guidelines, landmark clinical trials, and continuing professional education initiatives appears to have contributed to substantial increases in DOAC prescriptions, with the majority of patients being discharged on dual-pathway and TATT antithrombotic regimens in the 2019 cohort. Current practice appears now to be highly aligned with guideline recommendations.

Funding Sources

Dr Brian J. Potter is supported by a Fonds de recherche du Québec-Santé career award (267436).

Disclosures

Dr Alexis Matteau has received speaker fees from Bristol-Myers-Squibb and AstraZeneca. Dr Brian J. Potter has received honoraria or speaker fees from Bayer Canada, the BMS/Pfizer Alliance, and Servier and has received research funding from Bayer Canada. The other authors have no conflicts of interest to disclose.

References

1. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a global burden of disease 2010 study. *Circulation* 2014;129:837–47.
2. Rahman F, Kwan GF, Benjamin EJ. Global epidemiology of atrial fibrillation. *Nat Rev Cardiol* 2016;13:501.
3. Wolf PA, Dawber TR, Thomas Jr. HE, Kannel WB. Epidemiologic assessment of chronic atrial fibrillation and risk of stroke: the Framingham study. *Neurology* 1978;28:973–7.
4. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J* 2016;37:2893–962.
5. Macle L, Cairns J, Leblanc K, et al. 2016 focused update of the Canadian Cardiovascular Society guidelines for the management of atrial fibrillation. *Can J Cardiol* 2016;32:1170–85.
6. Sterne JA, Bodalia PN, Bryden PA, et al. Oral anticoagulants for primary prevention, treatment and secondary prevention of venous thromboembolic disease, and for prevention of stroke in atrial fibrillation: systematic review, network meta-analysis and cost-effectiveness analysis. *Health Technol Assess* 2017;21:1–386.
7. Kravev S, Schneider K, Lang S, Suselbeck T, Borggrefe M. Incidence and severity of coronary artery disease in patients with atrial fibrillation undergoing first-time coronary angiography. *PLoS One* 2011;6:e24964.
8. Mancini GB, Gosselin G, Chow B, et al. Canadian Cardiovascular Society guidelines for the diagnosis and management of stable ischemic heart disease. *Can J Cardiol* 2014;30:837–49.
9. Mehta SR, Bainey KR, Cantor WJ, et al. 2018 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology focused update of the guidelines for the use of antiplatelet therapy. *Can J Cardiol* 2018;34:214–33.
10. Members Task Force, G Montalescot, Sechtem U, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the task force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J* 2013;34:2949–3003.
11. Tanguay JF, Bell AD, Ackman ML, et al. Focused 2012 update of the Canadian Cardiovascular Society guidelines for the use of antiplatelet therapy. *Can J Cardiol* 2013;29:1334–45.
12. Valgimigli M, Bueno H, Byrne RA, et al. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: the task force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2018;39:213–60.
13. ACTIVE Writing Group of the ACTIVE Investigators Connolly S, Pogue J, et al. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the atrial fibrillation clopidogrel trial with irbesartan for prevention of vascular events (ACTIVE W): a randomised controlled trial. *Lancet* 2006;367:1903–12.
14. Apostolakis S, Sullivan RM, Olshansky B, Lip GY. Hormone replacement therapy and adverse outcomes in women with atrial fibrillation: an analysis from the atrial fibrillation follow-up investigation of rhythm management trial. *Stroke* 2014;45:3076–9.
15. Hansen ML, Sorensen R, Clausen MT, et al. Risk of bleeding with single, dual, or triple therapy with warfarin, aspirin, and clopidogrel in patients with atrial fibrillation. *Arch Intern Med* 2010;170:1433–41.
16. Lamberts M, Olesen JB, Ruwald MH, et al. Bleeding after initiation of multiple antithrombotic drugs, including triple therapy, in atrial fibrillation patients following myocardial infarction and coronary intervention: a nationwide cohort study. *Circulation* 2012;126:1185–93.
17. Potter BJ, Ando G, Cimmino G, et al. Time trends in antithrombotic management of patients with atrial fibrillation treated with coronary stents: results from TALENT-AF (The international Atrial STENT–Atrial Fibrillation study) multicenter registry. *Clin Cardiol* 2018;41:470–5.

18. Cannon CP, Bhatt DL, Oldgren J, et al. Dual antithrombotic therapy with dabigatran after PCI in atrial fibrillation. *N Engl J Med* 2017;377:1513–24.
19. Gibson CM, Mehran R, Bode C, et al. Prevention of bleeding in patients with atrial fibrillation undergoing PCI. *N Engl J Med* 2016;375:2423–34.
20. Lopes RD, Heizer G, Aronson R, et al. Antithrombotic therapy after acute coronary syndrome or PCI in atrial fibrillation. *N Engl J Med* 2019;380:1509–24.
21. Vranckx P, Valgimigli M, Eckardt L, et al. Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI): a randomised, open-label, phase 3b trial. *Lancet* 2019;394:1335–43.
22. Andrade JG, Verma A, Mitchell LB, et al. Cusced update of the Canadian Cardiovascular Society guidelines for the management of atrial fibrillation. *Can J Cardiol* 2018;34:1371–92.
23. 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.
24. Andrade JG, Nattel S, Macle L. The Canadian Cardiovascular Society atrial fibrillation guidelines program: a look back over the last 10 years and a look forward. *Can J Cardiol* 2020;36:1839–42.
25. Proietti M, Lane DA, Boriani G, Lip GYH. Stroke prevention, evaluation of bleeding risk, and anticoagulant treatment management in atrial fibrillation contemporary international guidelines. *Can J Cardiol* 2019;35:619–33.
26. von Elm E, Altman DG, Egger M, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Int J Surg* 2014;12:1495–9.
27. Boivin-Proulx LA, Deneault-Marchand A, Matteau A, et al. Time-trends and treatment gaps in the antithrombotic management of patients with atrial fibrillation after percutaneous coronary intervention: Insights from the CHUM AF-STENT Registry. *Clin Cardiol* 2020;43:216–21.
28. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976;16:31–41.
29. Lane DA, Dagues N, Dan GA, et al. Antithrombotic treatment in patients with atrial fibrillation and acute coronary syndromes: results of the European Heart Rhythm Association survey. *Europace* 2019;21:1116–25.
30. Park J, Choi EK, Han KD, et al. Temporal trends in prevalence and antithrombotic treatment among Asians with atrial fibrillation undergoing percutaneous coronary intervention: a nationwide Korean population-based study. *PLoS One* 2019;14:e0209593.
31. Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation: the task force for the management of atrial fibrillation of the European Society of Cardiology (ESC). *Europace* 2010;12:1360–420.
32. January CT, Wann LS, Alpert JS, et al. 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 practice guidelines and the Heart Rhythm Society. *Circulation* 2014;130:e199–267.
33. Lip GY, Windecker S, Huber K, et al. Management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve interventions: a joint consensus document of the European Society of Cardiology Working Group on Thrombosis, European Heart Rhythm Association (EHRA), European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS) and Asia-Pacific Heart Rhythm Society (APHRS). *Eur Heart J* 2014;35:3155–79.
34. Bangalore S, Kumar S, Fusaro M, et al. Short- and long-term outcomes with drug-eluting and bare-metal coronary stents: a mixed-treatment comparison analysis of 117,762 patient-years of follow-up from randomized trials. *Circulation* 2012;125:2873–91.
35. Palmerini T, Biondi-Zoccai G, Della Riva D, et al. Stent thrombosis with drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. *Lancet* 2012;379:1393–402.
36. Ariotti S, Adamo M, Costa F, et al. Is bare-metal stent implantation still justifiable in high bleeding risk patients undergoing percutaneous coronary intervention?: a pre-specified analysis from the ZEUS trial. *JACC: Cardiovasc Interv* 2016;9:426–36.
37. Urban P, Meredith IT, Abizaid A, et al. Polymer-free drug-coated coronary stents in patients at high bleeding risk. *N Engl J Med* 2015;373:2038–47.
38. Holmes DR, Kereiakes DJ, Garg S, et al. Stent thrombosis. *J Am Coll Cardiol* 2010;56:1357–65.
39. Eikelboom JW, Connolly SJ, Bosch J, et al. Rivaroxaban with or without aspirin in stable cardiovascular disease. *N Engl J Med* 2017;377:1319–30.
40. Cao D, Mehran R, Dangas G, et al. Validation of the Academic Research Consortium high bleeding risk definition in contemporary PCI patients. *J Am Coll Cardiol* 2020;75:2711–22.