Atrial fibrillation in acute coronary syndrome: patient characteristics and appropriate utilisation of anti-thrombotic therapy in New Zealand (ANZACS-QI 39)

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ABSTRACT

BACKGROUND: Concomitant atrial fibrillation (AF) and acute coronary syndrome (ACS) present the difficult therapeutic dilemma of balancing bleeding, cardio-embolic and coronary thrombotic risks with appropriate combinations of antithrombotic medications. We aim to evaluate current New Zealand practice by identifying the incidence of AF in ACS; describe the population characteristics; and assess our antithrombotic management.

METHODS: Consecutive patients ≥18y presenting with ACS who had coronary angiography (2017–2018) were identified from the All New Zealand ACS Quality Improvement (ANZACS-QI) registry. The cohort was divided into three groups: 1) patients with pre-existing AF; 2) new-onset AF; and 3) no AF. Antithrombotic regimens included dual antiplatelet therapy (DAPT), dual antithrombotic therapy (DAT—single antiplatelet plus an oral anticoagulant (OAC)) and triple antithrombotic therapy (TAT).

RESULTS: There were 9,489 patients, 9.6% with pre-existing AF, 4.4% new AF and 86% without AF. Both AF groups were older (median 74 vs 71 vs 65y, p=0.001), had poorer renal function, were more likely to present with heart failure (16% vs 19% vs 8%, p=0.001) and have left ventricular ejection fraction <40% (22% vs 28% vs 13%, p<0.001). They received less percutaneous coronary intervention (PCI) (53% vs 59% vs 70%, p=0.001). In the cohort, 25 different combinations of antithrombotic agents were utilised. Ninety-six percent of patients with any AF had a CHA_2DS_2VASC stroke risk score of ≥2, of whom 48% did not receive OAC. Twenty-four percent received TAT and 19% DAT. OAC use increased slightly with increasing stroke risk but were independent of CRUSADE bleeding risk. Of patients with AF treated with PCI, 53% received DAPT, 11% DAT and 35% TAT. 51% of those at high stroke risk were discharged on DAPT only. In contrast, 19% at low stroke risk received TAT.

CONCLUSION: In New Zealand, one in seven patients presenting with ACS have AF, a third being new-onset AF. Antithrombotic management is inconsistent, with underutilisation of anticoagulants, particularly the DAT regimen, and is inadequately informed by stroke and bleeding risk scores.

Atrial fibrillation (AF), the most commonly encountered clinical arrhythmia, often coexists with acute coronary syndrome (ACS). Its prevalence is increasing with the aging population and complicates the course of acute myocardial infarction (MI) in 2.3–21% of hospitalised patients.[1–3] In the setting of ACS, AF is an independent predictor of worse prognosis with doubling of composite risks for mortality, congestive heart failure and stroke.[3–6] Oral anticoagulation (OAC) is the mainstay

of therapy to prevent stroke and systemic embolism in patients with AF, but has not been shown to prevent stent thrombosis nor is it the treatment of choice for secondary prevention after ACS. In contrast, dual antiplatelet therapy (DAPT) with a $P2Y_{12}$ inhibitor plus aspirin has been proven to reduce the incidence of recurrent ischaemic events and stent thrombosis but less effective in reducing cardio-embolic events in AF.[7–9] Unfortunately, co-prescribing OAC with DAPT, ie, triple antithrombotic therapy (TAT), substantially increases the absolute risk of major haemorrhage by two- to three-fold.[10–12] Hence, in a patient with concomitant ACS and AF, the clinician is faced with the therapeutic dilemma of bleeding, cardio-embolic and coronary thrombotic risks.

The 2013 landmark WOEST trial first tested a dual antithrombotic therapy (DAT) regimen which dropped aspirin and used a single $P2Y_{12}$ inhibitor anti-platelet, namely clopidogrel, in combination with warfarin alone. This approach was associated with a marked reduction in bleeding events with no significant increase in thrombotic events compared to TAT.[13] The result was reflected by international guidelines in the ensuing years suggesting DAT with either aspirin or clopidogrel plus an OAC as a possible regimen for patients with significant bleeding risk.[2,8,14] However, the paucity of larger prospective trials limited its utility. Subsequently, several randomised controlled trials assessing the viability of DAT have followed. The PIONEER AF-PCI trial published in 2016, RE-DUAL trial in 2017 and the recent AUGUSTUS trial together demonstrated that patients with AF undergoing percutaneous coronary intervention (PCI) treated with a novel OAC (NOAC), ie, rivaroxaban, dabigatran and apixaban respectively, in conjunction with a $P2Y_{12}$ inhibitor, had a lower incidence of bleeding without differences in ischaemic events compared to TAT with either a NOAC or warfarin.[15–17]In view of the rapid evolution of evidence for antithrombotic therapy in concurrent AF and ACS, international guidelines have recently been updated.[7–9] There is a risk that clinical implementation may lag behind. This study aims to evaluate current New Zealand practice by identifying the incidence of AF in patients presenting with ACS; describe the population characteristics; and assess the antithrombotic management.

Methods

Data source

Consecutive patients ≥18 years of age presenting with their first ACS who underwent coronary angiography between July 2017 and November 2018 were identified from the All New Zealand Acute Coronary Syndrome Quality Improvement registry (ANZACS-QI).

The ANZACS-QI registry is a nation-wide web-based electronic database that captures all patients who present to a New Zealand public hospital with suspected ACS who are investigated with coronary angiography. It records a mandatory dataset including admission and discharge dates, patient demographics, admission ACS risk stratification using the GRACE score, cardiovascular risk factors, investigations, management, in-hospital outcomes and medications at discharge. Details of this registry and data collection have previously been reported.[18] It is audited monthly to ensure >99% of patients have complete data entry throughout all New Zealand hospitals. From 2017, additional data fields for recording pre-existing and new-onset AF were added which we utilised in this study. Patients with atrial flutter were considered to have AF.

Study cohort

From the ANZACS-QI registry, patients with a confirmed diagnosis of non-ST-segment elevation ACS (NSTEACS, comprising both unstable angina and non-ST elevation myocardial infarction [NSTEMI]) or ST-segment elevation myocardial infarction (STEMI), who underwent invasive coronary angiography between July 2017 and November 2018 were included. Only patients who were discharged alive were analysed for medications and antithrombotic management. Patients who were referred for coronary artery bypass grafting (CABG) surgery were excluded. The ANZACS-QI registry does not collect discharge prescriptions after CABG. Moreover, the aetiology and management of post-CABG AF differ, therefore is more appropriately considered separately.

The cohort was divided into three groups for comparison: 1) patients with pre-existing AF, defined as having documented clinical history of paroxysmal, persistent or

permanent AF; 2) patients with new-onset AF, defined as new AF lasting ≥30 minutes confirmed on ECG during index hospital admission without prior documented history of AF; 3) patients without AF. The term "any AF" refers to patients with either pre-existing or new AF.

Definitions

MI was defined according to the contemporary universal definition.[19] Unstable angina is diagnosed if one of the following occurred in the absence of biochemical evidence of myocardial necrosis: 1) >20 minutes angina pain at rest; 2) de novo Canadian Cardiovascular Society class II or III angina or 3) recent destabilisation of stable angina with at least CCS class III angina.[20] The Global Registry ACS (GRACE) score was calculated using variables: age, admission heart rate, systolic blood pressure, serum creatinine level, presentation with cardiac arrest, presence of ST-segment deviation on ECG, elevation of cardiac Troponins and initial Killip Class.[21] Stroke risk for patients with AF was stratified using the CHA_2DS_2VASC score variables: a history of congestive heart failure or presenting Killip Class II or higher, hypertension or admitting systolic BP of ≥140, age, diabetes and gender.[22] All patients had one point for vascular disease considering their ACS presentation. Prior history of stroke was excluded from the calculation as this was not a data field recorded in the ANZACS-QI registry. Bleeding risk for patients was assessed using the CRUSADE score with variables: hematocrit derived from the admission serum haemoglobin, creatinine clearance, admission heart rate, gender, admission Killip Class, history of diabetes mellitus and admission systolic blood pressure.[23] The HAS BLED bleeding score for AF was not utilised as not all the parameters were captured in the registry. Bleeding complications were defined according to the Bleeding Academic Research Consortium (BARC) score.[24]Medications prescribed at discharge including antiplatelets, anticoagulants, beta-blockers, angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB) and statins were identified from the ANZACS-QI registry. Three antithrombotic regimens were specifically assessed: 1) DAPT with aspirin plus a $P2Y_{12}$ inhibitor; 2) DAT with a single antiplatelet, either aspirin or a $P2Y_{12}$ Inhibitor, plus an OAC; 3) TAT with aspirin, a $P2Y_{12}$ inhibitor and an OAC.

Statistical analysis

Descriptive statistics for categorical data are presented as frequencies and column percentages and continuous variables as median with interquartile ranges and/or mean ± standard deviation. Chi-squared test or Fisher exact test was used for comparison between two groups while Wilcoxon-Mann Whitney U test or Student's T-test was used for continuous variables where appropriate. All P-values reported were two-tailed and a P-value <0.05 was considered significant. Data were analysed using SAS statistical package, version 9.4 (SAS Institute, Cary, NC).

Results

A total of 9,489 consecutive patients ≥18 years of age from July 2017 to November 2018 who presented with their first episode of ACS and underwent coronary angiography were identified from the ANZACS-QI registry. This comprised 908 (9.6%) patients with pre-existing AF, 421 (4.4%) with new-onset AF during the index hospitalisation, and 8,160 (86%) without AF. The overall incidence of any AF was 14%. Only 9,316 patients who were discharged alive were analysed for medications and antithrombotic management.

Patient characteristics and presentation (Table 1 and 2)

The diagnosis of NSTEACS was highest among patients with pre-existing AF (pre-existing AF 81% vs new AF 62% vs no AF 72%, p<0.001). On the other hand, those with new-onset AF had a higher proportion of STEMI (19% vs 38% vs 28%, p<0.001). Patients with pre-existing AF were older than those with new-onset AF, who in turn were older than patients without AF (median 74 vs 71 vs 65y, p=0.001). Both AF groups tended to have poorer renal function with higher serum creatinine (median 97 vs 94 vs 87μmol/L, p=0.02) and were more likely to present with heart failure (16% vs 19% vs 8%, p=0.001), higher heart rates (median 75 vs 88 vs 72 beats per minute, p<0.001) and lower systolic blood pressure (mean 140±28 vs 135±30 vs 143±27 mmHg, p=0.003). Patients with any AF had higher proportions of left ventricular impairment

Table 1: Patient characteristics and clinical presentation.

	Pre-existing AF (n=908)	New AF (n=421)	No AF (n=8,160)	**P-values**		
				Pre-existing AF vs New AF	Pre-existing AF vs No AF	New AF vs No AF
Demographics						
Age (years) Median (IQR)	74 (67–80)	71 (64–79)	65 (56–73)	0.001	<.001	<.001
Male, n (%)	618 (68)	278 (66)	5,643 (69)	0.463	0.499	0.177
Ethnicity (%) European/Other NZ Māori Pacific Indian Other Asians	 726 (80) 123 (14) 32 (4) 11 (1) 16 (2)	 311 (74) 62 (15) 24 (6) 10 (2) 14 (3)	 6,137 (75) 863 (11) 427 (5) 399 (5) 334 (4)	0.033	<.001	0.014
Past medical history and risk factors						
History of CVD, n (%)	509 (56)	144 (34)	2,738 (34)	<.001	<.001	0.783
Prior MI, n (%)	329 (36)	95 (23)	1,822 (22)	<.001	<.001	0.909
Prior CHF, n (%)	126 (14)	22 (5)	241 (3)	<.001	<.001	0.008
Diabetes mellitus, n (%)	244 (27)	90 (21)	1,863 (23)	0.032	0.006	0.488
Smoking history Never Ex smoker Current smoker	 411 (45) 382 (42) 115 (13)	 192 (46) 143 (34) 86 (20)	 3,502 (43) 2,723 (33) 1,935 (24)	<.001	<.001	0.279
BMI Mean ± SD	29.8±6.13	29.0±7.0	29.2±5.9	0.003	0.003	0.104
Clinical presentation						
Type of ACS, n (%) Unstable angina NSTEMI STEMI	 161 (18) 576 (63) 171 (19)	 27 (6) 232 (55) 162 (38)	 1,185 (15) 4,684 (57) 2,291 (28)	<.001	<.001	<.001
Admission HR Median (IQR)	75 (65–91)	88 (69–110)	72 (63–84)	<.001	<.001	<.001
Admission systolic BP Mean ± SD Median (IQR)	 140±28 139 (120–156)	 135±30 133 (114–152)	 143±27 140 (125–160)	0.005	0.001	<.001
Admission Killip Class I II, III, IV	 759 (84) 149 (16)	 343 (81) 78 (19)	 7,467 (92) 693 (8)	0.340	<.001	<.001
Cardiac arrest at admission, n (%)	37 (4)	27 (6)	266 (3)	0.064	0.195	0.001
Hospital length of stay Median days (IQR)	4 (3–7)	5 (3–8)	4 (3–5)	0.012	<.001	<.001

Table 2: Investigations and risk scores.

	Pre-existing AF (n=908)	New AF (n=421)	No AF (n=8,160)	**P-values**		
				Pre-existing AF vs new AF	Pre-existing AF vs no AF	New AF vs no AF
Investigations						
Hemoglobin n Median (IQR)	 137 (125–149)	 140 (127–152)	 142 (131–153)	0.059	<.001	0.007
Renal function Serum creatinine Median (IQR) eGFR 60+ 45–<60 30–<45 <30	 97 (82–116) 479 (53) 245 (27) 143 (16) 41 (5)	 94 (78–113) 245 (58) 107 (25) 47 (11) 22 (5)	 87 (75–102) 6,158 (75) 1,241 (15) 485 (6) 276 (3)	0.021 0.095	<.001 <.001	<.001 <.001
Lipid profile LDL Median (IQR)	 2.0 (1.2–2.9)	 2.1 (1.3–3.0)	 2.5 (1.5–3.4)	0.038	<.001	<.001
LVEF assessed, n (%) Normal ≥50% Mild 40-49% Moderate/severe <40% Not quantified further*	 324 (36) 133 (15) 196 (22) 255 (28)	 164 (39) 71 (17) 116 (28) 70 (17)	 3,888 (48) 1,354 (17) 1,033 (13) 1,885 (23)	<.001	<.001	<.001
Risk scores						
GRACE score (prob. in-hospital death) Low <1% Intermediate 1-3% High ≥3%	 81 (9) 338 (37) 489 (54)	 20 (5) 133 (32) 268 (64)	 2,309 (28) 3,351 (41) 2,500 (31)	0.001	<.001	<.001
CHA_2DS_2VASC score <2 2–3 4+	 33 (4) 329 (36) 546 (60)	 20 (5) 182 (43) 219 (52)	 1,041 (13) 4,318 (53) 2,801 (34)	0.020	0.015	0.023
CHA_2DS_2VASC score Mean ± SD	3.7±1.3	3.5±1.3	3.0±1.3	0.020	0.001	<.001
CRUSADE score <30 31–40 >40	 644 (71) 174 (19) 90 (10)	 267 (63) 97 (23) 57 (14)	 6,022 (74) 1,482 (18) 656 (8)	0.019	0.089	<.001
CRUSADE score Mean ± SD	 26 ± 11	 27 ± 11	 24 ± 11	0.005	0.004	<.001

*LVEF not documented or not assessed during index admission.

with an ejection fraction <40% (22% vs 28% vs 13%, p<0.001), a high GRACE score with a predicted in-hospital mortality of ≥3% (54% vs 64% vs 31%, p<0.001), higher mean CHA_2DS_2VASC score (3.7±1.3 vs 3.5±1.3 vs 3.0±1.3, p<0.05) and mean CRUSADE score (26±11 vs 27±11 vs 24±11, p<0.001). In contrast, only patients with pre-existing AF, but not new AF, were more likely to have a prior history of cardiovascular disease (56% vs 34% vs 34%, p<0.001), MI (36% vs 23% vs 22%, p<0.001) and congestive heart failure (14% vs 5% vs 3%, p<0.001) compared to those without AF. Gender, ethnicity, history of diabetes mellitus and smoking were similar across all three groups.

Angiographic findings, management and complications (Table 3)

Despite having a greater burden of cardiovascular comorbidities, both AF groups were less likely to undergo PCI during the index admission (53% vs 59% vs 70%, p=0.001). When presenting with STEMI, patients with pre-existing AF were less likely to receive acute reperfusion compared to those without AF (primary PCI 50% vs 59%, p<0.001 and acute thrombolysis 21% vs 26%, p<0.001), whereas new-onset AF was similar (primary PCI 55% vs 59%, p=0.235 and acute thrombolysis 25% vs 26%, p=0.235). A finding of no significant obstructive coronary artery disease was more frequent in patients with any AF (17.5% vs 14%, p<0.02). Overall in-hospital mortality was low in the study population but was marginally higher in patients with any AF (3% vs 5% vs 2%, p<0.03).

Discharge medications and antithrombotic management (Table 4)

Among the 9,316 patients discharged alive, beta-blocker dispensing rates were higher in patients with any AF than those without AF (82% vs 85% vs 78%). Statins were less likely to be prescribed to patients with pre-existing AF (86% vs 91% vs 93%). ACEI/ARB was similar among the three groups (70% vs 73% vs 73%).

In this study, 25 different combinations of antiplatelets (aspirin, clopidogrel, ticagrelor and prasugrel) and anticoagulants (warfarin, dabigatran and rivaroxaban) were utilised. Patients with pre-existing AF were least likely to receive aspirin followed by patients with new AF, while those without AF had the highest proportion (76% vs 85% vs 97%, p<0.001). A similar trend was

Table 3: Angiographic findings, management and complications.

	Pre-existing AF (n=908)	New AF (n=421)	No AF (n=8,160)	**P-values**		
				Pre-existing AF vs new AF	Pre-existing AF vs no AF	New AF vs no AF
CAD >50% on angiogram, n (%)				0.127	<.001	0.017
No obstructive CAD	172 (19)	66 (16)	1,138 (14)			
Single/ double VD	461 (51)	238 (57)	5,164 (63)			
Three VD and/or LMS >50%	275 (30)	117 (28)	1,858 (23)			
Acute Reperfusion for STEMI, n (%)				0.157	<.001	0.235
Primary PCI	86 (50)	89 (55)	1,363 (59)			
Thrombolysis	36 (21)	41 (25)	587 (26)			
None	49 (29)	32 (20)	341 (15)			
PCI during index admission	485 (53)	250 (59)	5,679 (70)	0.001	<0.001	<0.001
In-hospital complications						
Death	23 (3)	23 (5)	127 (2)	0.007	0.029	<.001
Stroke	5 (1)	7 (2)	32 (0.4)	0.061	0.413	0.003
Overt bleeding (BARC) after angiography/PCI	41 (5)	16 (4)	291 (4)	0.550	0.149	0.801
BARC 2, 3a, 3b, 3c and 5	26 (3)	15 (3.5)	217 (3)	0.024	0.131	0.131

Table 4: Medications prescribed at discharge.

	Pre-existing AF n=885	New AF n=398	No AF n=8,033	**P-value**		
				Pre-existing AF vs new AF	Pre-existing AF vs no AF	New AF vs no AF
Statin	764 (86)	363 (91)	7,469 (93)	0.013	<.001	0.179
Beta-blocker	724 (82)	337 (85)	6,289 (78)	0.209	0.015	0.002
ACEI/ARB	620 (70)	290 (73)	5,856 (73)	0.306	0.072	0.988
Aspirin	671 (76)	338 (85)	7,757 (97)	<.001	<.001	<.001
Other anti-platelets Clopidogrel Ticagrelor Prasugrel	666 (75) 420 (47) 242 (27) 4 (0.04)	320 (80) 145 (36) 174 (44) 0 (0)	7,246 (90) 1,899 (24) 5,343 (67) 4 (0.001)	0.043	<.001	<.001
Any anticoagulants	529 (60)	141 (35)	283 (4)	<.001	<.001	<.001
Warfarin	147 (16)	16 (4)	147 (2)	<.001	<.001	0.002
Dabigatran	379 (43)	122 (31)	154 (2)	<.001	<.001	<.001
Rivaroxaban	8 (1)	4 (1)	13 (0.2)	0.743	<.001	0.004
Anti-thrombotic regimens						
Dual anti-platelet therapy (DAPT)	307 (35)	228 (57)	6,943 (86)	<.001	<.001	<.001
Single anticoagulant plus single antiplatelet (DAT)	188 (21)	54 (14)	95 (1)	0.001	<.001	<.001
Triple antithrombotic therapy (TAT)	246 (28)	62 (16)	164 (2)	<.001	<.001	<.001
Single antiplatelet only	43 (5)	24 (6)	694 (9)	0.383	<.001	0.069
Single anticoagulant only	93 (11)	25 (6)	24 (0.3)	0.015	<.001	<.001

seen in $P2Y_{12}$ inhibitors (75% vs 80% vs 90%, p<0.05); however, clopidogrel was more commonly dispensed to patients with any AF than those without AF (47% vs 36% vs 24%, p<0.05) and vice versa for ticagrelor (27% vs 44% vs 67%, p<0.05). Prasugrel was rarely used in our population.

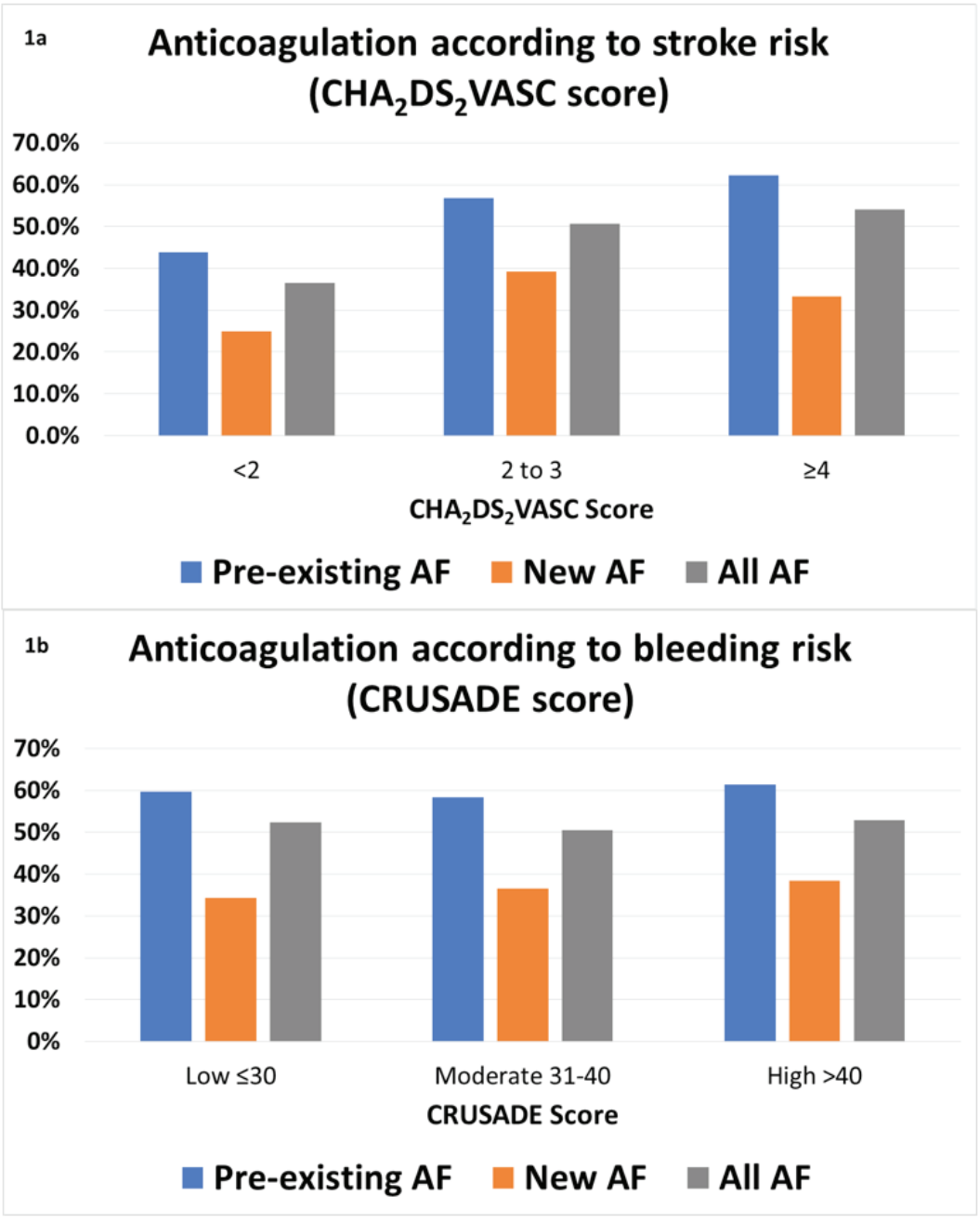
As for OACs, patients with any AF were dispensed more than those without AF, albeit only half of them (52% vs 4%, p<0.001). This proportion of OACs on discharge was low considering many had a CHA_2DS_2VASC score of ≥2 (pre-existing AF 96% and new AF 95%). Majority of these OACs prescribed were dabigatran as opposed to warfarin (75% dabigatran vs 24% warfarin). Apixaban, although heavily favoured internationally for stroke prevention in AF due to its lower bleeding risk profile, is not available in New Zealand during the study period.

Patients with new-onset AF were less likely to be discharged with an OAC than those with pre-existing AF (35% vs 60%, p<0.001) and more likely to be on DAPT (57% vs 35%, p<0.001). A relatively small percentage were treated with TAT (28% pre-existing AF vs 16% vs new AF, p<0.001) and even less with DAT (21% vs 14%, p<0.001).

Risk stratification (Figure 1)

When stratified by the CHA_2DS_2VASC score, there is higher OAC use with increasing stroke risk for both AF groups. Those with new AF were less likely to receive OAC than pre-existing AF. When both groups were combined, OACs were prescribed to 36.5% of patients with low stroke risk (CHA_2DS_2VASC <2) but only half of those with moderate (CHA_2DS_2VASC 2-3, 50.7%) and high stroke risk (CHA_2DS_2VASC ≥4, 54.1%) (p=0.034 across stroke risk bands). In contrast, when

Figure 1: Oral anticoagulation on discharge post-ACS according to stroke (CHA_2DS_2VASC) risk (1a) and bleeding (CRUSADE) risk (1b).

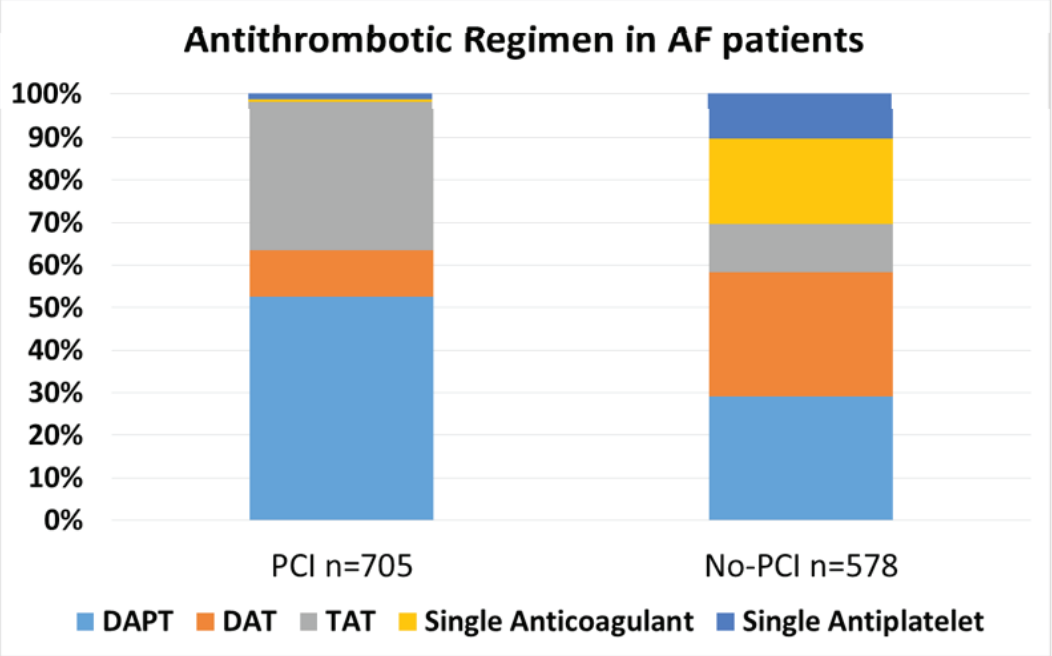


stratified by the CRUSADE bleeding risk score, the use of OAC was similar across the risk bands (p=0.86).

Percutaneous intervention and anti-thrombotic management in AF (Figures 2 and 3)

Figure 2 shows the proportions of each antithrombotic regimen for those with and without PCI. Of the 1,283 patients with any AF, 705 (55%) were treated with PCI, of whom 53% received DAPT, 11% DAT, 35% TAT and 0.7% single anticoagulant. When stratified by the CHA_2DS_2VASC score, as stroke risk increased, there was a trend towards decreased utilisation of DAPT (p=0.062) but no significant change in TAT (p=0.197), while DAT remained low irrespective of stroke risk (p=0.48). However, 51% of those with high stroke risk (CHA_2DS_2VASC ≥4) were still discharged on DAPT only, whereas 19% of patients with low stroke risk (CHA_2DS_2VASC <2) were treated with TAT and 7% with DAT. On

Figure 2: Antithrombotic regimen on discharge post-ACS for those with and without PCI.



the other hand, choice of antithrombotic regimen appears to have no interaction with bleeding risk across the spectrum according to CRUSADE score (DAPT p=0.99, DAT p=0.48, TAT p=0.85).

Discussion

This study examines the current New Zealand practice in managing patients with concomitant AF and ACS after recent updates to evidence and international guidelines. The main results of the study are—1) one in seven patients in New Zealand presenting with ACS have either pre-existing AF or new-onset AF; 2) patients with AF are associated with more cardiovascular comorbidities and less likely to receive PCI; and 3) antithrombotic management was inconsistent, with evidence of underutilisation of OAC in those with significant stroke risk and overutilisation in those with low stroke risk. The DAT antithrombotic regimen supported by recent prospective trials are underutilised compared to TAT.

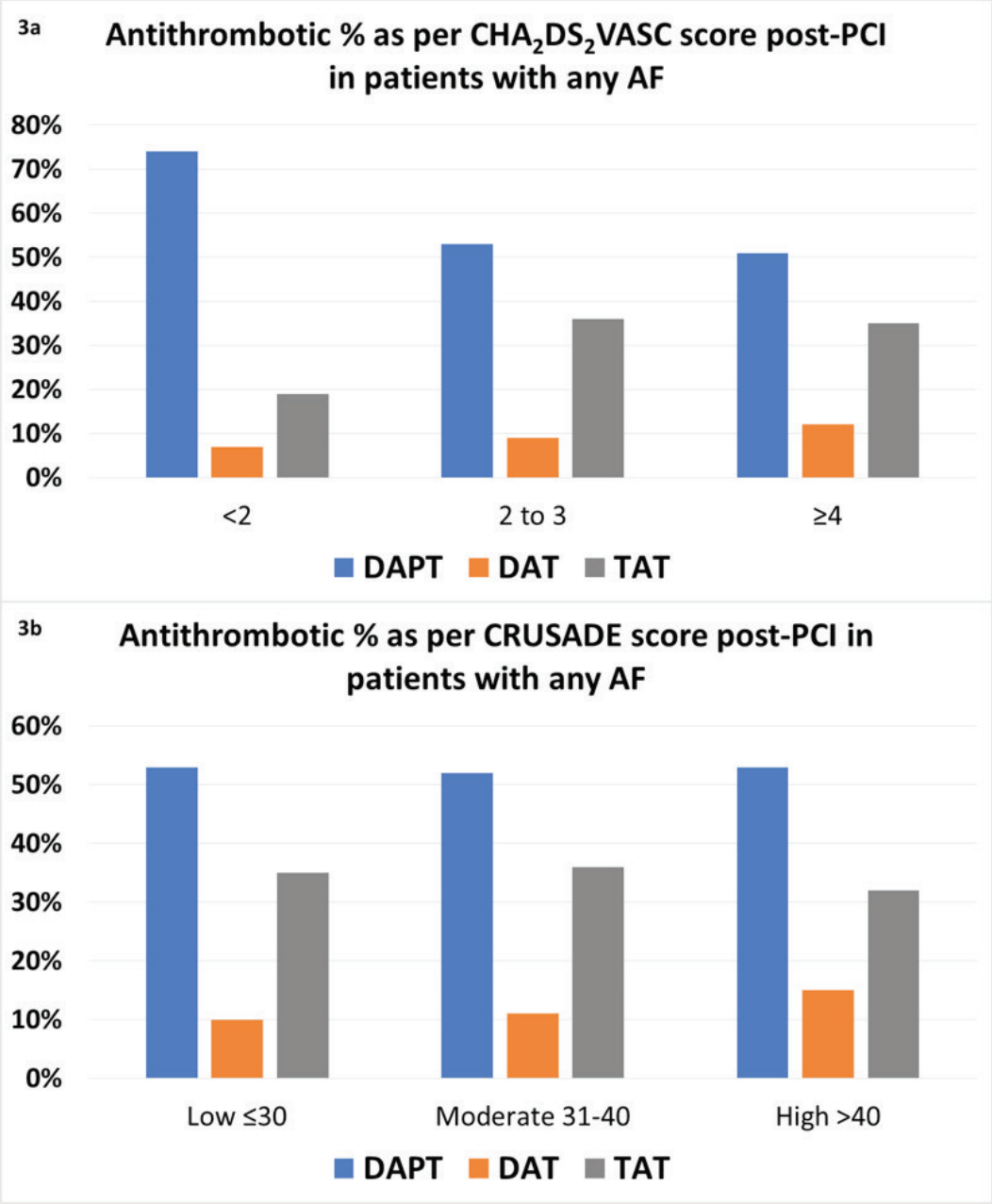
Incidence and patient characteristics of AF in ACS

AF is common in patients with acute MI, due to some extent to their shared co-morbidities. The incidence of any AF in this study was 14%, of which 9.6% were pre-existing AF and 4.4% were new AF. This is comparable to contemporary trials and registries over the past two decades with reported incidences varying between 2.3 to 21%.[1,2,25] Two retrospective studies utilising the GRACE registry identified pre-existing AF incidences of 7.9% and 8.5%, and new AF at 6.2% and 9.2%, respectively.[26,27] More recently, the EPICOR Registry reported that, out of 10,568 patients with ACS, 4.7% had pre-existing AF and 3.6% developed new onset AF.[5] A recent large meta-analysis with 43 studies demonstrated the incidence of any AF at 13%, pre-existing AF 7% and new-onset AF 10%.[28]Consistent with other international studies, we found patients with pre-existing AF tend to be older with established cardiovascular comorbidities, particularly congestive heart failure and MI. On the other hand, patients with new-onset AF were younger, with cardiovascular background similar to those without AF. Nonetheless, both AF groups were more likely to present to hospital with a lower systolic blood pressure and higher heart rate in the context of ACS, possibly reflecting underlying LV dysfunction and impaired haemodynamics.

PCI in AF

Patients with AF underwent less PCI, most likely due to greater age, poorer renal function and a higher proportion of either multi-vessel disease (29% vs 23%, any AF vs no AF) or no significant coronary artery disease (CAD) on angiography (17.5% vs

Figure 3: Antithrombotic regimen on discharge post-PCI for ACS according to stroke risk (CHA_2DS_2VASC) (3a) and bleeding risk (CRUSADE) (3b).



13%). In similar studies, patients with AF were more likely to undergo CABG.[5,26,27,29] We excluded this group of patients as recent trials in antithrombotic management of AF in ACS do not include those managed with CABG.

Antithrombotic management of concomitant AF and ACS

The management approach to concomitant AF and ACS relies on the assessment of ischaemic, thromboembolic and bleeding risks. Guidelines have suggested DAPT without OAC in those with low stroke risk whose CHA_2DS_2VASC <2. In patients with CHA_2DS_2VASC ≥2, the recommendation had been to treat with TAT for a duration of one to six months followed by DAT.[8,14,25] If bleeding concern prevails, TAT duration can be minimised, but this still doubles the risk of major haemorrhage.[10–12] If bleeding risk is high then treatment with DAT may be considered according to the 2013 WOEST trial.[13] This regimen has been limited in clinical practice partly due to the lack of more prospective data. However, several

randomised controlled trials have since been published demonstrating safety and efficacy of DAT against TAT. In PIONEER AF-PCI, patients with non-valvular AF undergoing PCI with stent placement that received lower dose rivaroxaban 15mg daily plus a $P2Y_{12}$ inhibitor had less bleeding than those on TAT with warfarin at one year (18.0% vs 26.7%, HR 0.63; 95% CI 0.50 to 0.80; P<0.001).[15] The RE-DUAL trial demonstrated less bleeding with either 110mg (15.4% vs 26.9%, HR 0.52; 95% CI 0.42 to 0.63; p<0.001) or 150mg twice daily Dabigatran plus a $P2Y_{12}$ inhibitor immediately post-PCI (20.2% vs 25.7%, HR 0.72; 95% CI 0.58 to 0.88; p<0.001).[16] Most recently, the AUGUSTUS trial included both patients after PCI and medically managed ACS. Standard dose Apixaban 5mg twice daily plus a $P2Y_{12}$ inhibitor resulted in less bleeding and fewer hospitalisations.[17] All three trials showed no differences in thromboembolic events compared to warfarin TAT.

Subsequently, the American and European guidelines were updated recommending DAT with NOACs and minimising TAT duration.[9] The 2019 American College of Cardiology in particular supports DAT after PCI in ACS unless their ischaemic risk outweighs bleeding risk in which case a period of TAT for up to six weeks may be considered.[7]Our study highlights current New Zealand practice. There appears to be suboptimal use of OACs compared with what might be beneficial according to current guidelines and recent clinical trials. Only half (52%) of the patients were discharged on a regimen containing OAC despite 96% having a significant CHA_2DS_2VASC score ≥2, which would justify stroke prevention. Conversely, there is some evidence of over-utilisation of TAT which was used in a third (36.5%) of the group of patients with low stroke risk, CHA_2DS_2VASC <2, potentially exposing them to unnecessary bleeding risks. In the PCI population, 51% of patients with any AF were discharged on DAPT despite having significantly high stroke risk (CHA_2DS_2VASC ≥4) and 19% of those with low stroke risk (CHADVASC <2) were treated with TAT. Meanwhile, the DAT regimen was significantly underutilised at 7%.

In regards to objective risk assessment, there is a small increase in OAC dispensing with increasing stroke risk, predominantly driven by patients with pre-existing AF. In contrast, bleeding risk stratified by the CRUSADE score had only marginal impact on anticoagulation and antithrombotic regimen decisions. It would appear that risk stratification was underused. However, this assumption has limitations. Stroke risk in our cohort is underestimated considering we excluded history of stroke from the CHA_2DS_2VASC calculation as it was not a data parameter in the ANZACS-QI registry. Similarly, CRUSADE score was used to estimate bleeding risk as opposed to the recommended HAS BLED score considering that history of liver disease, stroke, major bleeding, alcohol use and patient INR were not captured in the registry. The CRUSADE score was originally developed to assess the bleeding risk specifically for ACS patients and validated for those on antiplatelet therapy.[23] Nevertheless, the HAS BLED score was developed for those with AF to guide anticoagulation therapy, which has limited validation in patients with ACS. The development of a risk score specific for concomitant AF and ACS is necessary.

New-onset AF and antithrombotic management

Of the patients who presented with new AF during the index hospitalisation, only one third were dispensed an OAC. They were more likely to be discharged on DAPT compared to those with pre-existing AF (57% vs 35%). This partly reflects uncertainty regarding the long-term thromboembolic implications of new-onset AF in the context of ACS. Yet, patients with new AF in our study had comparably higher CHA_2DS_2VASC, CRUSADE and GRACE scores to those with pre-existing AF, which predicts greater short- and long-term mortality and bleeding risks. Studies which assessed the prognostic impact of any AF in ACS have observed its adverse effect with some proposing that new-onset AF may confer even higher risk of mortality than those with pre-existing AF, and in those that reverted to sinus rhythm, up to half had future AF recurrence.[1,5,27,28] Hence, current international consensus for management of new-onset AF in ACS is to consider anticoagulation if thromboembolic risk is significant, although the long-term outcome of OAC therapy in this group remains an area for further exploration. There is also inconsistency regarding the definition of significant new-onset AF, in particular with its duration. For the

ANZACS-QI registry, by national clinical consensus, new AF was defined as at least one episode of AF lasting ≥30 minutes that was confirmed on ECG or cardiac monitoring without a prior documented history of AF. This definition, however, may underestimate the true burden of AF.

Limitations

This study suffers the same limitations as with analysis of any retrospective registry data. The conclusions may not apply to patients with ACS who were medically managed as we only included those who underwent angiography. Only medications prescribed at discharge were assessed, therefore it does not reflect medium or long-term antithrombotic practices. We acknowledge the study population was extracted from a time the international guidelines were evolving and that clinical practice tends to lag behind guidelines. However, it demonstrates our current practice providing a direction for improving future management.

Conclusion

In New Zealand, one in seven patients presenting with ACS have AF, a third being new-onset AF. There is a lack of consistency in antithrombotic management with evidence that decisions were often not informed by objective stroke and bleeding risk assessment. About half the patients at elevated stroke risk are discharged without anticoagulation. Dual antithrombotic combination therapy, which is supported by recent clinical trials, is underutilised. In contrast, a significant proportion of patients at low stroke risk appear to have been over-treated, potentially exposing them to unnecessary bleeding risk. This prompts action to be taken to implement a national consensus guideline to ensure optimal outcomes for our patients.

Competing interests:
Nil.

Acknowledgements:
Charles Yao-Cheng Ho and Mildred Lee were funded by the Middlemore Cardiac Trust. Andrew Kerr received salary support from the HRC. ANZACS-QI programme implementation, coordination and analysis: The ANZACS-QI software was developed and supported by Enigma Solutions. Programme implementation is coordinated by the National Institute for Health Innovation (NIHI) at the University of Auckland. The ANZACS-QI programme is funded by the New Zealand Ministry of Health. ANZACS-QI Governance group: Andrew Kerr (chair), Chris Nunn, Dean Boddington, Gary Sutcliffe, Gerry Devlin, Harvey White, John Edmond, Jonathon Tisch, Kim Marshall, Mayanna Lund, Michael Williams (deputy chair), Nick Fisher, Seif El Jack, Sue Riddle, Tony Scott. ANZACS-QI Project management: Kristin Sutherland (Project Manager), Charmaine Flynn (Northern coordinator), Maxine Rhodes (Southern coordinator). Data analysis: Mildred Lee. We acknowledge all the New Zealand cardiologists, physicians, nursing staff and radiographers who have supported and contributed to ANZACS-QI.

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www.nzma.org.nz/journal-articles/atrial-fibrillation-in-acute-coronary-syndrome-patient-characteristics-and-appropriate-utilisation-of-anti-thrombotic-therapy-in-new-zealand-anzacs-qi-39

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