Guideline versus clinician recommended duration of dual anti-platelet therapy following acute coronary syndrome (ANZACS-QI 78)

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ABSTRACT

AIM: The recommended duration of dual anti-platelet therapy (DAPT) following acute coronary syndrome (ACS) for patients without atrial fibrillation varies from 1 month to 1 year depending on the balance of risks of ischaemia and major bleeding. Patients on DAPT with a high risk of gastrointestinal bleeding are also recommended to receive a proton pump inhibitor (PPI). Our aim was to audit current practice against the 2020 European Society of Cardiology (ESC) guideline recommendations.

METHODS: One hundred consecutive ACS patients treated with percutaneous coronary intervention discharged from Middlemore Hospital and without atrial fibrillation in the first quarter of 2023 were studied. ANZACS-QI ischaemic (I) and bleeding (B) risk scores were calculated, with patients categorised in four groups based on ESC recommendations—low I/low B risk, low I/high B, high I/low B and high I/high B. Guideline and clinician recommended duration of DAPT and prescription of PPI were compared.

RESULTS: All patients were planned for DAPT at discharge and 91% a PPI. Up to four out of five ACS patients could have been planned for shorter DAPT durations based on the ESC guideline recommendations. Over half of included patients (53%) had a high bleeding risk, yet 85% of these patients received 12 months of DAPT despite ESC recommendations of 1–3 months.

CONCLUSIONS: There was a divergence between clinical practice and the recommendations of the 2020 ESC guidelines. We discuss these results in relation to the updated August 2023 ESC guidelines, which have reaffirmed a 12-month duration of DAPT as the default position.

The recommended duration of dual anti-platelet therapy (DAPT—aspirin and a $P2Y_{12}$ inhibitor) following acute coronary syndrome (ACS) for patients without atrial fibrillation varies from 1 month to 1 year depending on the balance of risks of ischaemia and major bleeding. In addition, patients on DAPT who have a high risk of gastrointestinal bleeding are recommended to receive a proton pump inhibitor (PPI).[1]

Over the last 10 years, national and international guidelines have progressively revised recommendations regarding DAPT duration according to estimated ischaemic and bleeding risk. The 2012 European Society of Cardiology (ESC) guidelines recommended 12 months of DAPT unless there was an excessive risk of bleeding.[2] The New Zealand guidelines at the time had a similar 12 months of DAPT default recommendation.[3] By 2018 the ESC, in response to new clinical trial data, recommended reducing the DAPT duration to 6 months in those with high bleeding risk, defined by a Precise-DAPT score ≥25, which is equivalent to a 1-year risk of major bleeding of more than 2%.[4] Following this, the 2020 ESC guidelines for the management of ACS in patients presenting without persistent ST-segment elevation, in force at the time of this study, took an even more nuanced approach.[5] Patients with high bleeding risk were recommended to have up to 3 months of DAPT regardless of ischaemic risk. Those with low ischaemic risk were also recommended to have only 3 months of DAPT, whereas those with high ischaemic but low bleeding risk were recommended 12 months of DAPT. For some patients with high bleeding risk, the use of clopidogrel, a less potent $P2Y_{12}$ inhibitor, may be preferred over the more potent ticagrelor as the second anti-platelet agent. However, these recommendations have been difficult to implement in practice because there have been no risk scores available that accurately estimate bleeding and recurrent ischaemic risks over the relevant 28-day to 1-year post-ACS period. The recently published Aotearoa New Zealand All Cardiology Services Quality Improvement (ANZACS-QI) ischaemic and bleeding risk scores were specifically designed for

this purpose.[6] There is now an opportunity to audit current practice against the 2020 ESC guideline recommendations using these risk scores and to identify opportunities for improvement.

Methods

New Zealand patients with ACS investigated with coronary angiography are routinely recorded in the ANZACS-QI registry. Consecutive ACS patients (n=100) treated with percutaneous coronary intervention (PCI) discharged from Middlemore Hospital were selected from the ANZACS-QI registry from 1 January 2023 to 1 May 2023. Patients with atrial fibrillation were excluded, as the risk scores were developed for those without atrial fibrillation. For each patient, the electronic clinical notes were reviewed to confirm the ACS diagnosis and PCI procedure. The clinician-recommended DAPT duration at the time of hospital discharge was taken from the electronic clinical record. The ANZACS-QI 28-day to 1-year ischaemic (I) and bleeding (B) risk scores were calculated for each patient using the published algorithms using the variables shown in Table 1.[6] Patients were initially categorised in four groups based on ESC-recommended risk cut-points (≤2% vs >2%)—low I/low B risk, low I/high B, high I/low B and high I/high B.[5] The guideline recommendations are the same for patients with high bleeding risk irrespective of the ischaemic risk, so for reporting purposes the low I/high B and high I/high B groups were combined. Guideline recommended versus clinician recommended DAPT duration for each of the three groups was compared. The prescription of proton pump inhibitors (PPI), another guideline recommended medication, was also recorded. This audit has received Counties Manukau locality approval (application #1803).

Results

Of the 100 patients included, the mean age at index presentation was 63.4 years (SD 12.3) and 73% were male (Table 1). Thirty-nine percent were European, 7% New Zealand Māori and 25% Pacific peoples. The mean New Zealand Index of Deprivation (NZDep) quintile was 3.5 (SD 1.5).

Table 1: Baseline demographics, clinical features and relevant investigations.

Demographic	Frequency (n=100)
Age (SD), year	63.4 (12.3)
Male	73
Ethnicity	
European	39
New Zealand Māori	7
Pacific peoples	25
Indian	15
Chinese/Other Asian	14
New Zealand Index of Deprivation (SD), (quintile)	3.5 (1.5)
Quintile 1	16
Quintile 2	18
Quintile 3	15
Quintile 4	17
Quintile 5	34

Table 1 (continued): Baseline demographics, clinical features and relevant investigations.

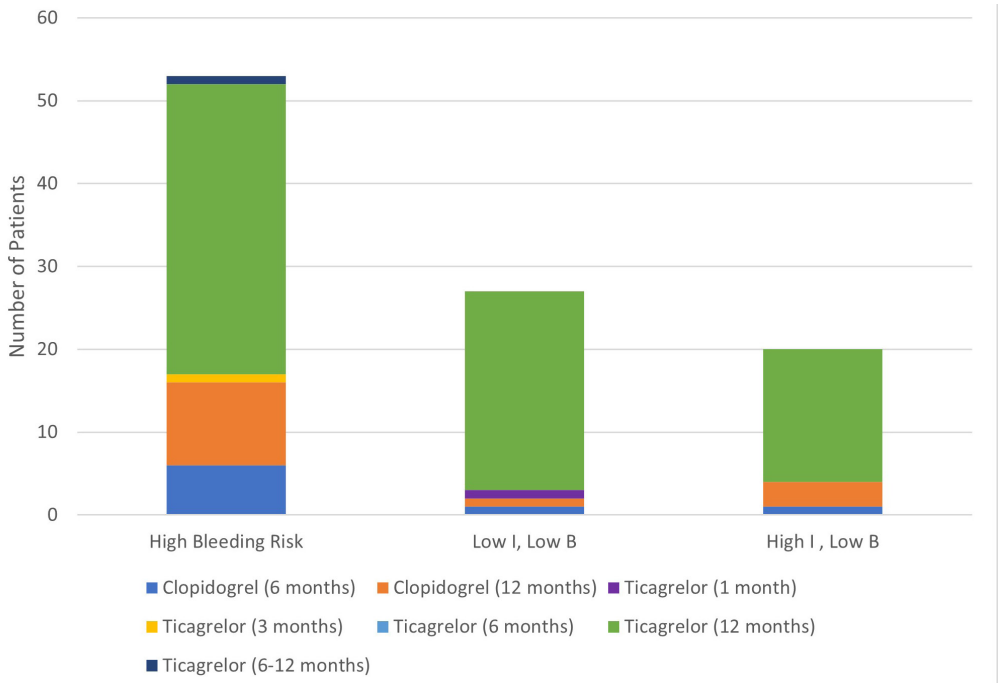
Heart rate (bpm)	91 (15)
Estimated GFR[1] (SD), (mL/min/1.73m2)	69.4 (24.4)
Haemoglobin level (SD), units	157 (15.3)
Low Hb[2]	17
Coronary artery disease severity	
Single vessel disease	74
Double vessel disease	23
Triple vessel disease or LMS	3
History of CVD[3]	
No prior CVD	73
Prior MI	26
Other prior CVD	1
Diabetes mellitus	33
With insulin	13
Current smoker	18
Type of ACS[4]	
NSTEMI[5]	57
STEMI[6]	29
Unstable angina	14
Worst Killip class in hospital	1 (0.5)
I	92
II–IV	8
Left ventricular ejection fraction	
Normal (≥50%)	61
Mid-range (40–49%)	18
Reduced (<40%)	17
Prior hospitalisation for bleeding	2
Index admission bleeding	1
Total: HDL cholesterol ratio	4.5 (1.8)

[1]Glomerular filtration rate
[2]Low haemoglobin: Hb <115g/L for women, <130g/L for men
[3]Cardiovascular disease
[4]Acute Coronary Syndrome
[5]Non-ST Elevation Myocardial Infarction
[6]ST Elevation Myocardial Infarction

Table 2: Duration of planned dual anti-platelet therapy by risk group.

Second anti-platelet	Duration (months)	Low I, low B	Low I, high B	High I, low B	High I, high B
Clopidogrel	6	1	3	1	3
	12	1	0	3	10
Ticagrelor	1	1	0	0	0
	3	0	0	0	1
	6	0	0	0	0
	6–12	0	0	0	1
	12	24	6	16	29
Total		27	9	20	44

Figure 1: Clinician decision on duration and type of dual anti-platelet therapy by risk group.



All patients were planned for DAPT at discharge and 91% a PPI. All patients received aspirin. For the second anti-platelet agent, 78 were planned for ticagrelor and 22 clopidogrel (Table 2). The majority of patients (89%) received a recommendation for 12 months of DAPT.

High ischaemic/low bleeding risk (20% of patients): The 2020 ESC guidelines recommend 12 months of DAPT. Of the 20 patients in this category, 19 were consistent with the guidelines and were planned for 12 months of DAPT (Table 1). Sixteen of these patients were planned for ticagrelor and three for clopidogrel alongside aspirin. The one patient who did not receive 12 months of DAPT was planned for 6 months of aspirin and clopidogrel.

Low ischaemic/low bleeding risk (27% of patients): The 2020 ESC guidelines recommend 3 months of DAPT. Of the 27 patients in this category, 24 (89%) were planned for 12 months of DAPT

Figure 2: Percentage of patients planned for guideline recommended duration of dual anti-platelet therapy according to ischaemic and bleeding risk categories.

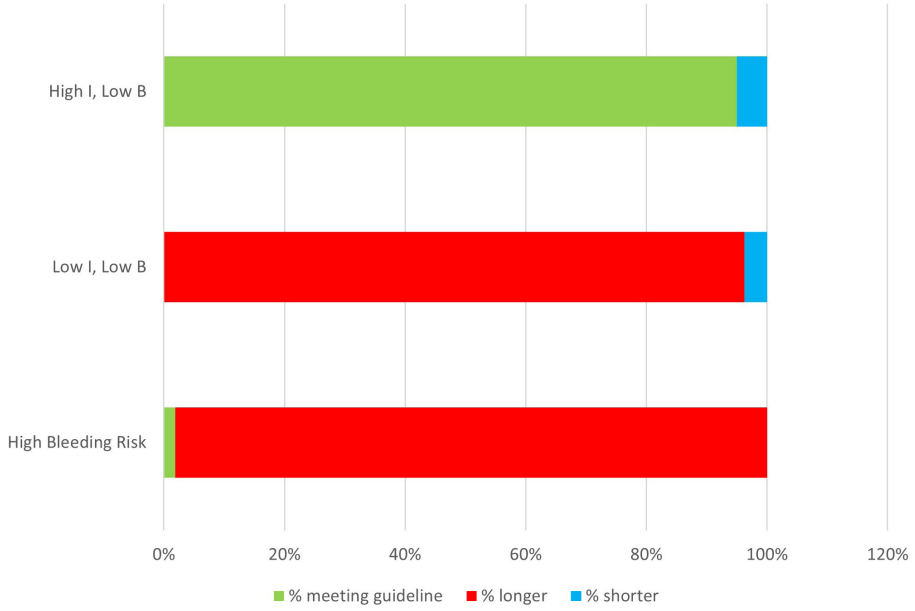
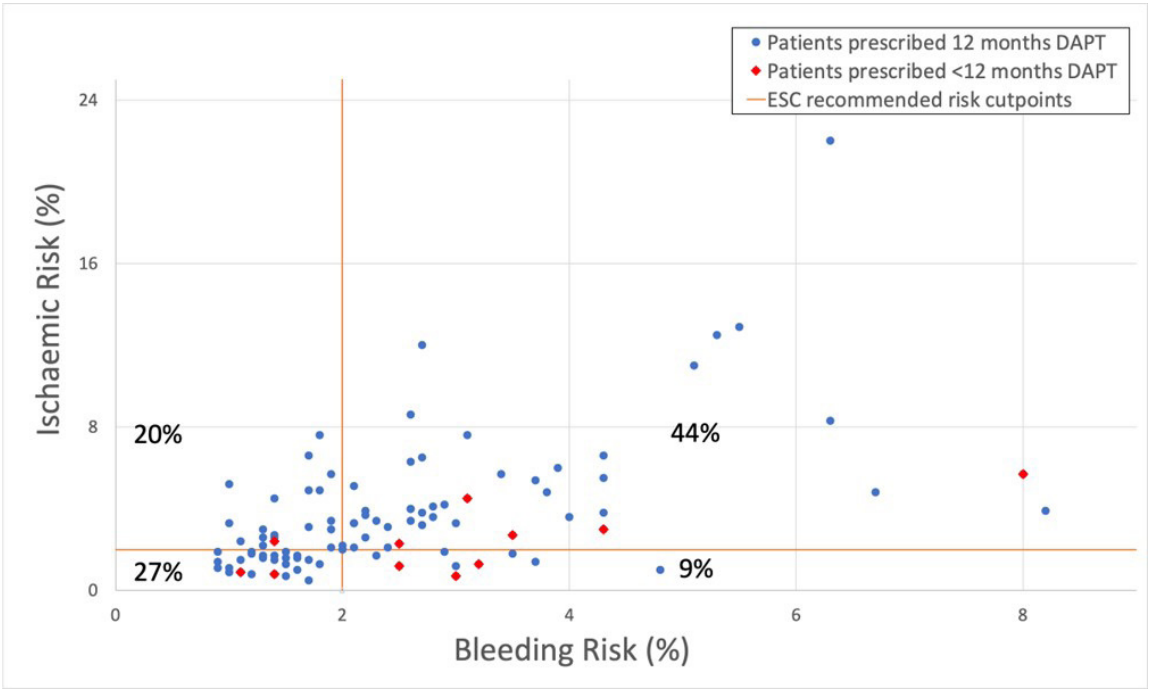


Figure 3: Bleeding versus ischaemic risk.



with aspirin and ticagrelor. The three other patients were planned for DAPT with clopidogrel for 6 months, clopidogrel for 12 months and ticagrelor for 1 month, respectively.

High bleeding risk (53% of patients): The 2020 ESC recommendation for high bleeding risk is 1–3 months of DAPT. Fifty-three patients had a high bleeding risk. Of these, 44 (83%) had a high ischaemic risk. Forty-five patients (85%) were planned for DAPT for 12 months—35 with ticagrelor (78%) and 10 with clopidogrel (22%). Alongside aspirin, one patient was planned for ticagrelor for 3 months, six for clopidogrel for 6 months and one for ticagrelor for 6–12 months. Fourteen patients had a bleeding risk greater than 4% and 12 of these patients received a recommendation for 12 months of DAPT.

Ninety-one of the 100 patients received a concurrent PPI (Table 3). Of the 53 with a high bleeding risk, 48 (91%) received a PPI. Of the 48, 31 (65%) were planned for omeprazole, 16 (33%) pantoprazole and one patient received lansoprazole.

Discussion

At discharge, post-ACS patients were appropriately planned for both DAPT and PPIs. There was, however, a divergence between clinical practice and the recommendations of the 2020 ESC guidelines that prevailed during the time course of this study regarding the duration of DAPT. Clinicians appear to have been adhering more to the older guidelines,[2,4] which recommended 12 months of DAPT as the default position. Since this study was performed, the ESC, after further consideration of the evidence, have modified their recommendations in the 2023 guidelines for the management of ACS.[1] Twelve months of DAPT is again recommended as the default approach, although alternative approaches of reducing DAPT duration or de-escalation of therapy intensity can be considered, particularly with the aim of reducing bleeding events in high bleeding risk patients.

In our real-world cohort, over 50% of patients were at high bleeding risk, for which the 2020 ESC guideline recommended ≤3 months of DAPT, and the current 2023 guideline suggests a reduced duration can be considered. Although 85% of the high bleeding risk patients in this study were planned for 12 months of DAPT, there are indications that clinicians are modifying DAPT therapy in response to bleeding risk. In particular, a higher proportion of high bleeding risk patients were planned for clopidogrel than those at lower risk. There were also more high bleeding risk patients planned for a reduced, 6-month course of DAPT.

A meta-analysis of coronary stenting trials assessing short versus longer duration DAPT found that ischaemic events were reduced by longer DAPT for patients at low bleeding risk, but in those at high bleeding risk, defined using the Precise-DAPT score, longer DAPT duration was associated with similar ischaemic event rates but higher bleeding rates.[7] In the subgroup with acute

Table 3: Choice of proton pump inhibitor.

	Choice of PPI	Number of patients
Clopidogrel	Lansoprazole	1
	Omeprazole	3
	Pantoprazole	15
	No PPI	3
	Total	22
Ticagrelor	Lansoprazole	0
	Omeprazole	60
	Pantoprazole	12
	No PPI	6
	Total	78

coronary syndromes they reported a similar result, albeit with relatively small numbers of events. Two subsequent clinical trials in patients at high bleeding risk treated with third generation stents have reported similar findings.[8,9] Despite these studies supporting a shortened period of DAPT, concern has been expressed that the clinical trials for reducing DAPT intensity have excluded the highest risk ACS patients, and that the trials were non-inferiority trials and were therefore not powered to detect differences in ischaemic outcomes.[1]

Most patients in the high ischaemic, low bleeding risk group (95%) received treatment consistent with the guidelines (Figure 2). However, no patients in the low ischaemic, low bleeding risk group were planned for a shorter course of DAPT. Although the 2020 ESC guideline recommended a shorter duration of DAPT in this low ischaemic/low bleeding risk group, the updated guideline does not make this recommendation. We are unaware of specific clinical trial data to guide clinicians for these patients. The availability of the ANZACS-QI risk scores would theoretically make it possible to investigate the benefits of 12-month versus 3-month DAPT in this sub-group, but the low event rates in these patients may make this challenging to do.

There are likely to be a number of reasons for the divergence between clinical practice and guideline recommendations. The ESC guidelines do not provide a clear risk stratification implementation process. In particular, they do not recommend a specific ischaemic risk score to guide the decision regarding DAPT duration, and while the Precise-DAPT score is discussed as a bleeding score developed to guide DAPT duration decision, its use is not strongly endorsed. This leaves clinicians uncertain regarding how to implement the guideline in practice. During the period when these patients were admitted, clinicians did not routinely use multivariable risk scores to assess bleeding or ischaemic risk. Translation of the guideline into clinical practice requires relevant, readily accessible and easy to calculate risk scores. A further reason is likely to be that there is no randomised clinical trial evidence that applying a risk stratification guided DAPT duration decision making improves outcomes. In the absence of accessible multivariable risk stratification tools and clinical trial guidance, clinicians are more likely to follow a one-size-fits-all approach for all but those with very obvious single risk factors for bleeding, such as the very elderly and those with chronic renal disease. There may also be a time lag for clinical practice to catch up with changes in guideline recommendations. Cardiology clinicians may give greater weight to ischaemic complications than bleeding complications and perceive using a longer DAPT duration as "veering on the side of caution", despite the clinical trial evidence that a shorter course of DAPT may be of greater overall benefit for many patients. In clinical practice there are also other factors not accounted for by the risk scores that might also influence the decision regarding DAPT duration. These include procedural variables such as stent type, lesion location and length, and vessel size, and specific clinical situations such as the need for non-cardiac surgery. Other factors include clinicians being slow to adapt to changes in guidelines and risk scores not used or available to implement the guideline recommendations. During the period when these patients were admitted, clinicians did not routinely use multivariable risk scores to assess bleeding or ischaemic risk. There is an opportunity to improve care by making these scores a part of routine practice. Integration of these risk scores into routine clinical practice will require clear guideline guidance together with making the risk scores readily available. The risk scores are currently available via a web-based calculator (https://www.vareanz.auckland.ac.nz/anzacs-qi-calculator/). They will shortly be available within the ANZACS-QI registry, and the risk scores will be automatically generated at the time the registry forms are completed and made available to clinicians for use at discharge and at the first post-discharge visit.

The evidence around DAPT duration post-ACS continues to evolve. Key limitations have been difficulties in standardising ischaemic and bleeding risk assessment and concerns around selective clinical trial enrolment. The use of the ANZACS-QI equations embedded in the real-world comprehensive ANZACS-QI cohort is an opportunity to design clinical trials to help answer important questions in post-ACS management.

Limitations

This study is retrospective and from a single centre, and thus is subject to the usual limitations of this design. However, it is likely that practice in most other cardiology units in New Zealand would be broadly similar. This study focussed on clinician decision for DAPT duration and is not powered to assess the impact on ischaemic or bleeding events, and is based on the duration

planned at discharge, not on how long DAPT was actually continued. This study also did not consider interventional factors that may require a longer duration of DAPT. The study did not audit practice in ACS patients who did not receive PCI.

Conclusion

During the period when these patients were admitted, clinicians did not routinely use multivariable risk scores to assess bleeding or ischaemic risk. However, by applying the new ANZACS-QI risk scores to the cohort, we have found that up to four out of five ACS patients could have been planned for shorter DAPT durations based on the 2020 ESC guideline recommendations. Although the more recent 2023 ESC guideline has swung back towards a default 12-month DAPT approach, it still endorses shorter durations in high bleeding risk patients. There may therefore be an opportunity to improve care by making the ANZACS-QI scores a part of routine practice. The ANZACS-QI registry is a real-world clinical trial platform. It could be utilised to study whether treating the nearly half of patients with high bleeding risk for shorter DAPT courses can reduce bleeding complications without increasing ischemic complications, and whether in the one third of low I and B risk patients shorter courses can minimise use of expensive anti-platelet agents without increasing risk.

COMPETING INTERESTS
No relevant disclosures.

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