

Proposed RCT using a Multiplate algorithm to expedite urgent cardiac surgery and determine safety and cost effectiveness

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Dual antiplatelet therapy (DAPT) significantly reduces mortality and recurrent events in patients with acute coronary syndromes. However, patients requiring coronary artery bypass grafting (CABG) face an increased bleeding risk due to DAPT, leading to a conventional “washout” period of up to seven days before surgery. This waiting period extends hospital stay and contributes to higher healthcare costs. Importantly, up to 50% of patients exhibit no significant platelet inhibition during this time. Platelet function testing using the Multiplate analyser may allow for earlier surgery in patients whose platelet function has recovered, potentially reducing hospital stay and associated costs. We propose a prospective randomized controlled trial to evaluate the safety, efficacy, and cost-effectiveness of this approach.

Aims and hypotheses

We aim to determine whether early CABG, guided by Multiplate platelet function testing, is non-inferior to conventional delayed surgery in terms of postoperative bleeding and transfusion requirements. We hypothesise that Multiplate-guided surgery does not increase bleeding risk and results in comparable or improved healthcare outcomes.

Study design

Two parallel studies are proposed.

1. Randomised Controlled Trial (RCT): Eligible patients will be randomized to either early surgery (treatment group) or standard care (control group) after meeting predefined Multiplate criteria.
2. Prospective Observational Study: Patients who do not qualify for the RCT but undergo either early or delayed surgery will be followed for data collection to support broader health economic analysis.

Eligibility criteria

Participants must:

- Require CABG following recent use of clopidogrel, ticagrelor, or prasugrel.
- Be within the traditional antiplatelet washout window.
- Meet Multiplate criteria indicating sufficient platelet recovery for surgery.

Measurements and outcome definitions

- *Primary outcome*: Chest drain output at 24 hours postoperatively, indexed to blood volume (Nadler equation).
- *Secondary outcomes*: Red cell and platelet transfusion requirements, quality of life (EQ5DL) at baseline and 6 months, surgery and discharge dates, readmission, and mortality.
- *Multiplate testing*: ADP and TRAP pathway results compared to an established algorithm. Aspirin response documented but not used for eligibility.
- *Additional data*: Patient weight and height (for blood volume), and timepoint relative to last antiplatelet dose.

Sample size calculation

Based on retrospective data for the control group, the coefficients of variation of both groups are assumed to be 0.500. Group sample sizes of 107 in the first group and 107 in the second group achieve 80% power to detect non-inferiority using a one-sided, two-sample t-test. The margin of non-inferiority is 0.200. The true ratio of the means at which the power is evaluated is 1.000. The significance level (alpha) of the test is 0.025.

Feasibility

Given that approximately 50% of CABG patients are on DAPT and half meet the Multiplate eligibility threshold, we estimate each site could recruit 25 patients annually. A multicentre effort involving 6 hospitals performing 200–400 CABG

procedures annually could achieve recruitment targets within three years (Assuming a quarter of potential patients make it from initial assessment to study completion).

Collaborators / research partners

We are in discussions with Prof. Jason Abbott (UNSW) a colleague with a good track record for academic collaboration. Engagement with the Multiplate supplier (Haemoview) and ANZSCTS is underway. Ethics approvals at institutional and national levels are being pursued, with planned registration through ANZCTR.

Specific issues for discussion

1. Is a single 6-month quality-of-life follow-up sufficient?
2. What is the most effective pathway for multi-centre approval, funding, and recruitment?
3. What local and central resources are required, including budgeting for personnel and data management?

Patient Blood Management for Adult Cardiac Surgery

Randwick Hospital Campus 2023



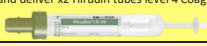
<p>Pre-Op</p> <p>Goals are:</p> <p>1. to optimise timing for semi-urgent surgery and</p> <p>2. to have platelets available for high risk cases</p>	<p>Anaemia: Hb < 130g/L (Male) < 120g/L (Female) Or Ferritin < 100mcg/L Or Transferrin Sat ≤ 20%</p>	→ YES	Follow preoperative Haemoglobin Optimisation pathway, ideally > 2 weeks before surgery, but benefit seen at any time perioperatively														
	<p>Fibrinogen < 2g/L</p>	→ YES	Inform Anaesthetic team as may require cryoprecipitate post CPB														
	<p>Do you have time (1-2 hours for test result) to check platelet function Mon-Fri 9am –4pm? First call COAG LAB Ext. 23482</p> <p>usually if :</p> <p>Ticagrelor < 3 days Clopidogrel < 5 days Prasugrel < 7 days</p> <p>(Not recommended if isolated aspirin use) Hand deliver x2 Hirudin tubes level 4 Coag lab</p>	→ YES	<p>Pathology request form or eMR requesting 'multiplate- platelet function - ROTEM'</p> <p>Please indicate any antiplatelet therapy</p> <p>Aim for green zone at 24h pre-op</p> <table border="1"> <thead> <tr> <th>Multiplate Test</th> <th>Red Zone ABNORMAL</th> <th>Green Zone Normal</th> </tr> </thead> <tbody> <tr> <td>ADP</td> <td>≤40</td> <td>>40</td> </tr> <tr> <td>ASPI (AA)</td> <td>≤20</td> <td>>20</td> </tr> <tr> <td>TRAP</td> <td>≤77</td> <td>>77</td> </tr> </tbody> </table>	Multiplate Test	Red Zone ABNORMAL	Green Zone Normal	ADP	≤40	>40	ASPI (AA)	≤20	>20	TRAP	≤77	>77	<p>LOW RISK</p> <p>→ HIGH RISK</p>	<p>GREEN ZONE: Proceed to OT (no pre-arranged platelets)</p> <p>RED ZONE: If NON-URGENT <u>DELAY 48 hours and re-test</u></p>
	Multiplate Test	Red Zone ABNORMAL	Green Zone Normal														
	ADP	≤40	>40														
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<p>(Not recommended if isolated aspirin use) Hand deliver x2 Hirudin tubes level 4 Coag lab</p> 	→ NO	<p>Must Proceed? No time for Multiplate or the wait period for ceasing DAPT</p>	→ HIGH RISK	<p>Arrange platelet availability (at least one pooled platelets)</p> <p>If recent APT consider Multiplate-platelet function test pre-op in Anaesthetic bay especially second case as likely coming off bypass after 4pm (normal multiplate is reassuring to avoid platelet transfusion)</p>													
<p>Booked high risk cases</p>	→ YES	<p>Re-do surgery Double procedure Aortic surgery Low platelets < 100x10⁹/L</p>	→ HIGH RISK														

Figure 1: Institutional algorithm for pre-operative management of cardiac patients

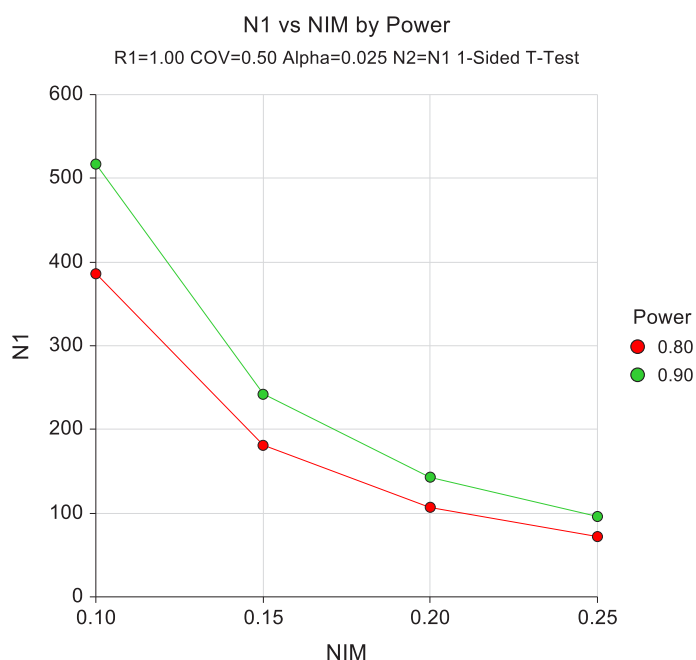


Figure 2: Sample size calculation for non-inferiority margin of 20% with 80% power (107 for each arm of the RCT)