Efficacy of dual antiplatelet therapy for three months versus 12 months after coronary artery bypass grafting: multicentre, double blinded, randomised controlled trial

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ABSTRACT

OBJECTIVES
To evaluate the efficacy of dual antiplatelet therapy (DAPT) for three months versus 12 months in saphenous vein graft occlusion while reducing bleeding risk.

DESIGN
Multicentre, non-inferiority, double blind, randomised controlled trial.

SETTING
13 cardiac surgery centres in China, with enrolment between February 2023 and July 2024.

PARTICIPANTS
2300 participants aged 18 to 80 years who underwent elective primary coronary artery bypass grafting with ≥1 saphenous vein graft.

INTERVENTIONS
Participants were randomly assigned (1:1) to receive DAPT (ticagrelor 90 mg twice daily plus aspirin 100 mg once daily) for 12 months or the same dual antiplatelet regimen for the first three months, followed by placebo plus aspirin for nine months.

MAIN OUTCOME MEASURES
The primary outcomes were saphenous vein graft occlusion at one year (non-inferiority) and Bleeding Academic Research Consortium (BARC) type 2, 3, or 5 bleeding (superiority). Secondary outcomes were major adverse cardiovascular events (MACCE), saphenous vein graft failure, venous or arterial graft stenosis, and venous or arterial graft occlusion.

RESULTS
2290 patients (mean age 61.5 (standard deviation (SD) 8.4) years, 20.6% (n=472) women) were included in the modified intention-to-treat set. The mean number of saphenous vein graft segments was 2.5 (SD 0.8). 2070 patients (90.4%) with a total of 5125 saphenous vein graft segments were assessed at one year. Saphenous vein graft occlusion occurred in 280 of 2596 (10.8%) in the three month DAPT group and 283 of 2529 (11.2%) in the 12 month DAPT group (absolute difference −0.31%, 95% confidence interval (CI) −3.13% to 2.52%; P=0.008 for non-inferiority). During a median follow-up of 368 (interquartile range 358-382) days, BARC type 2, 3, or 5 bleeding occurred in 95 patients (8.3%) in the three month DAPT group and 149 patients (13.2%) in the 12 month DAPT group (absolute difference −4.67%, 95% CI −7.18% to −2.16%; P<0.001). The number needed to treat to prevent one bleeding event was 21 (95% CI 13 to 46). MACCE occurred in 26 (2.3%) patients in the three month DAPT group and 27 (2.7%) in the 12 month DAPT group (absolute difference −0.11%, 95% CI −1.48% to 1.26%). The findings for other secondary outcomes were also similar between the two groups.

CONCLUSIONS
A three month DAPT strategy was non-inferior to the 12 month DAPT strategy in saphenous vein graft occlusion and was superior in reducing bleeding risk.

TRIAL REGISTRATION
ClinicalTrials.gov NCT05380063.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Randomised trials have shown that ticagrelor based dual antiplatelet therapy (DAPT) reduces saphenous vein graft (SVG) occlusion compared with aspirin alone but increases bleeding risk

Meta-analysis confirmed that ticagrelor based DAPT reduces failure of SVGs, but the optimal duration of DAPT after coronary artery bypass grafting (CABG) remains unclear

Early post-CABG is recognised as a high thrombotic risk period, and evidence for DAPT use for three months versus 12 months in SVG occlusion and bleeding risk is limited

WHAT THIS STUDY ADDS

This study found that a three month DAPT strategy was non-inferior to a 12 month DAPT strategy in SVG occlusion and was superior in reducing clinically relevant bleeding risk at one year

For patients requiring CABG who tolerated early DAPT, limiting treatment to the first three months postoperatively optimises the benefit-risk balance

Introduction

Despite the use of aspirin, up to 20% of patients requiring saphenous vein grafts (SVGs) experience occlusion within the first year after coronary artery bypass grafting (CABG), which is associated with poor outcomes.[1 2] Studies have shown a statistically significant reduction in SVG failure with ticagrelor based dual antiplatelet therapy (DAPT) for 12 months,[3-5] but at the expense of increased bleeding risk.[6 7]

SVG occlusion is more likely to occur in the first few months after surgery as a result of acute endothelial trauma during the procedure and subsequent platelet activation.[8-10] The pathophysiology of SVG occlusion provides a biological rationale for short term DAPT after CABG, and data show that the thrombotic risk is highest in the early phase after surgery and decreases thereafter.[11 12]

Recent trials support the efficacy and safety of short term DAPT after percutaneous coronary intervention,[13 14] but such an approach has not been tested in patients with CABG.

In this trial, the Timing of Platelet Inhibition after Coronary Artery Bypass Grafting (TOP-CABG), we tested the hypothesis that three months of DAPT with ticagrelor plus aspirin would be non-inferior to 12 months of treatment in SVG occlusion in patients undergoing CABG, while reducing the bleeding risk associated with prolonged treatment.

Methods

Trial design and oversight

We conducted a multicentre, non-inferiority, double blinded, placebo controlled, randomised trial with blinded outcome assessment. Thirteen hospitals participated (see supplementary file, section S1). The trial design is described in detail elsewhere.[15] The trial protocol and the statistical analysis plan are available in the supplementary file. All patients provided written informed consent. Our trial was conducted in strict accordance with the data privacy and security framework of China, which is functionally aligned with the EU's General Data Protection Regulation (see supplementary file, section S2).

Patients

Eligible patients were adults aged 18-80 years who had undergone elective primary CABG surgery with at least one SVG. Major exclusion criteria included concomitant valve or aortic surgery, single vessel coronary artery disease, a requirement for antiplatelet agents other than aspirin post-CABG, and contraindications to ticagrelor or aspirin. Section S3 of the supplementary file provides details of the trial inclusion and exclusion criteria.

Randomisation and trial intervention

After surgery, antiplatelet therapy was initiated within 24 hours to evaluate DAPT intolerance. We excluded patients who were unable to tolerate DAPT (see supplementary section S4). Eligible patients were randomly assigned through a centrally interactive web response system to DAPT for either three months or 12 months in a 1:1 ratio using a site stratified block randomisation with a block size of 10 on postoperative day 5. The 12 month group received 90 mg ticagrelor twice daily plus 100 mg aspirin once daily for one year after CABG. Patients in the three month group received the same regimen for the first three months and then were switched to receive placebo, matching 90 mg ticagrelor twice daily plus 100 mg aspirin once daily for the next nine months. Patients, investigators, outcome assessors, adjudicators, and statisticians were blinded to treatment assignments. All study drugs, including placebo, were manufactured and supplied under good manufacturing practice standards with strict lot control and quality assurance to ensure consistency and blinding. Active and placebo tablets of identical appearance ensured blinding was maintained throughout the trial. Study drugs were labelled with unique, blinded codes and dispensed to sites by the central pharmacy. The online system instructed the local doctor to dispense the drugs based on the drug code, ensuring allocation concealment. No breaches of blinding were reported during the study.

Procedures and outcomes

Follow-up assessments at one, three, six, and nine months were either by telephone or through visits to outpatient clinics. At 12 months, all surviving patients were asked to attend an in-person visit. The proportion of telephone visits was similar between the groups (supplementary figure S1). During each follow-up visit, adherence to the study drug was monitored through pharmacy refill data, pill counts, and structured interviews, including detailed inquiries about missed doses and reasons for non-adherence. During these calls and interviews, patients were reminded of the importance of adherence. Adverse events and clinical outcomes were also collected. Additionally, we provided a 24/7 hotline number in the informed consent documents for patients to report any urgent events. Independent trained research coordinators recorded these events and reported them to the clinicians.

The trial had two primary outcomes: one for non-inferiority and one for superiority. The primary non-inferiority outcome was the graft segment level rate of 100% SVG occlusion at one year after CABG. As more than 99.5% of participants underwent coronary computed tomography angiography for graft assessment, supplementary file, section S5, presents the standardised protocol for this procedure. Section S6 in the supplementary files lists details of graft assessment. The primary superiority outcome was the occurrence of Bleeding Academic Research Consortium (BARC) type 2, 3, or 5 bleeding within one year after CABG.

The secondary outcomes were SVG failure, venous or arterial graft stenosis ≥70%, 100% venous or arterial graft occlusion, and major adverse cardiovascular events (MACCE). SVG failure was defined as a composite of SVG occlusion, SVG revascularisation, myocardial infarction in the territory supplied by a SVG, or sudden death. MACCE was defined as a composite of cardiac death, myocardial infarction, stroke, or revascularisation. Section S7 in the supplementary file lists detailed outcome definitions. Safety outcomes included serious adverse events and non-adherence to the study drug due to bleeding, allergic reaction, or dyspnoea. Members of the clinical events committee centrally adjudicated all events.

Statistical analysis

Hierarchical testing was applied to the first hypothesis of SVG occlusion and then to the second hypothesis of BARC type 2, 3, or 5 bleeding. We adjusted the type II error to half, ensuring that the joint power was at least 80%. With an annual occlusion rate of 10% in the DAPT group, a loss to follow-up of 10%, and an average of 2.1 SVG segments in each patient, we estimated that 2300 participants could provide at least 90% power at a one sided α of 0.025 to show a 3.5% non-inferiority margin in the SVG occlusion rate between the two groups. This assumption for occlusion rate was based on previous evidence, including a meta-analysis and major randomised trials (Different Antiplatelet Therapy Strategy After Coronary Artery Bypass Grafting (DACAB) and The Effect of Ticagrelor on Saphenous Vein Graft Patency in Patients Undergoing Coronary Artery Bypass Grafting Surgery (POPular CABG)), which consistently reported SVG occlusion rates of about 9-11% at one year in patients receiving DAPT.[4 5 16] The non-inferiority margin of 3.5% was conservatively defined as about half of the treatment benefit in SVG patency observed with ticagrelor based DAPT over aspirin in previous studies.[3-5] With an annual bleeding event rate of 9% in the three month DAPT group and 15% in the 12 month DAPT group and a loss to follow-up of 10%, we also estimated that 1367 participants could provide at least 90% power at a two sided α of 0.05. The final sample size was 2300 patients.

The efficacy and safety analyses were conducted following the modified intention-to-treat principle by including all randomised patients but excluding those with informed consent but who withdrew before receiving treatment. For SVG occlusion, modified intention to treat also excluded those without available SVG imaging data. The efficacy analyses of primary outcomes were also performed in the per protocol population and as treated population. The per protocol population included patients who did not have major protocol deviations (ie, did not obtain the primary endpoint, crossover, did not achieve ≥80% adherence to the intervention regimen, or were out of the follow-up time window). The as treated population included patients who were analysed according to the actual strategy.

The analysis of the primary outcome of SVG occlusion was conducted on a per graft segment level. A patient level sensitivity analysis was also conducted. A post hoc analysis on per graft level and of SVG patency and SVG stenosis >50% on a per graft segment level was conducted. The generalised estimating equation model with a binomial distribution and log link function was used to estimate the between group absolute risk differences and risk ratios with 95% confidence intervals (CIs), accounting for within patient correlation of multiple graft segments. An exchangeable working correlation structure with sandwich variance estimation was specified, and we included treatment group and study site as covariates in the model. P values for non-inferiority were also reported. The model with independent covariance structures was conducted to test the robustness. Y grafts and sequential grafts were handled according to the predefined segment level definition (supplementary file, section S6). We did not account for graft type in the main analysis; we conducted a post hoc analysis considering graft type specific nested effects.

Cox proportional hazards regression was used to report absolute differences, hazard ratios, and 95% CIs for the analysis of the primary outcome of BARC type 2, 3, or 5 bleeding, including treatment groups and sites. As the proportional hazards assumption for the bleeding outcome was not met (P=0.0073) (supplementary figure S2), we conducted a prespecified 90 day landmark analysis to estimate the absolute differences and hazard ratios. The proportional hazards assumption was satisfied for both the ≤90 days interval (P=0.16) and the >90 days interval (P=0.11) (supplementary figure S3). We also used the Fine and Gray regression model to account for the competing risk of death as a sensitivity analysis.

Effect estimates of secondary outcomes were obtained with models similar to those used for the primary outcomes. Post hoc analyses of 90 day landmark analysis of MACCE, arterial grafts occlusion, and individual components of SVG failure and MACCE were also conducted. We compared safety outcomes between groups using a χ^2 test or Fisher's exact test. To advocate the sex and gender equity in research (SAGER) guidelines,[17] we did a post hoc sex specific analysis for safety outcomes. Prespecified subgroups included sex, medical history, and other characteristics (see protocol in the supplementary file) and the post hoc subgroups were sequential bypass, SAFINOUS risk score,[18] Academic Research Consortium for high bleeding risk (ARC-HBR) score,[19] and predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) bleeding score.[20] We also conducted a post hoc subgroup analysis for bleeding after 90 days. All subgroups were presented as exploratory, and we report the Bonferroni adjusted P values for subgroup interaction.

We excluded missing data on SVGs from the primary analysis. Firstly, we assumed that the missing data for SVGs in patients who had died of cardiovascular causes were for occlusions. Secondly, we imputed the missing data on SVGs using the multilevel multiple imputation method. In addition, we performed a post hoc tipping point analysis to evaluate the robustness of the non-inferiority conclusion under different assumptions for missing data on SVGs.

Because the prevalence of hypertension was higher in the three month DAPT group, we performed a prespecified adjustment for hypertension as a sensitivity analysis for both primary outcomes. We also conducted a post hoc analysis of complier average causal effect analysis using an instrumental variable method to evaluate the impact of adherence on the treatment effect.[21]

All superiority tests were two sided, and we considered P<0.05 to be statistically significant. Non-inferiority tests were one sided, and we considered P<0.025 to be statistically significant. All analyses were done using SAS (version 9.4) and R (version 4.4.2).

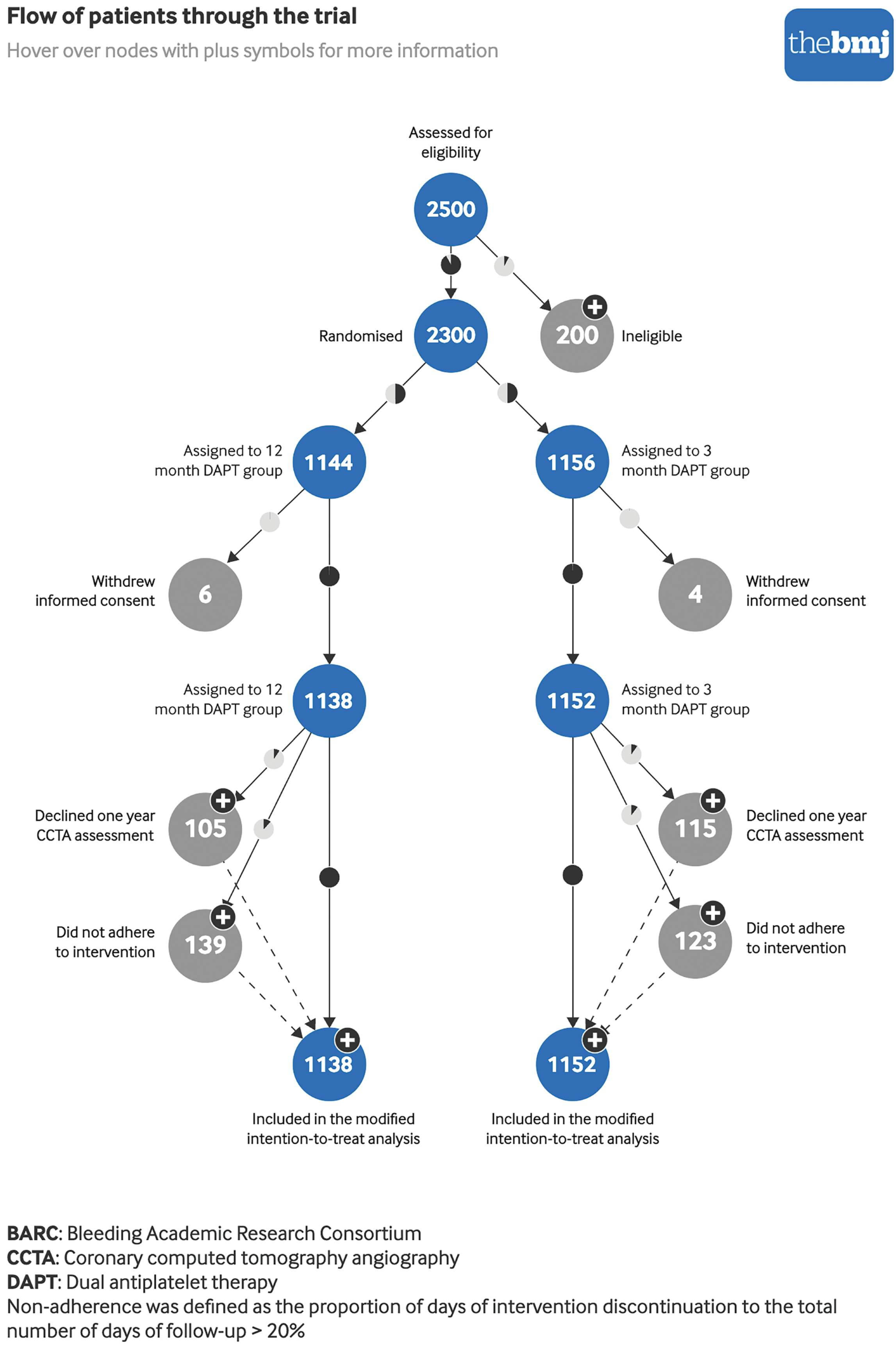


Fig 1 | Flow of participants through the trial. An interactive version of this graphic is available at https://public.flourish.studio/visualisation/27791228/

Table 1 | Baseline characteristics of included patients. Values are number (percentage) unless stated otherwise

Characteristics	Overall n=2290	3 month DAPT (n=1152)	12 month DAPT (n=1138)
Mean (SD) age (years)	61.5 (8.4)	61.3 (8.3)	61.6 (8.5)
Women	472 (20.6)	236 (20.5)	236 (20.7)
Current smoker	418 (18.3)	218 (18.9)	200 (17.6)
Mean (SD) height (cm)	167.1 (7.5)	167.2 (7.4)	167.0 (7.5)
Mean (SD) weight (kg)	71.9 (11.4)	72.2 (11.5)	71.5 (11.3)
Mean (SD) BMI	25.7 (3.2)	25.8 (3.2)	25.6 (3.2)
Diabetes	988 (43.1)	509 (44.2)	479 (42.1)
Hypertension	1615 (70.5)	838 (72.7)	777 (68.3)
Hyperlipidaemia	1511 (66.0)	772 (67.0)	739 (64.9)
Chronic obstructive pulmonary disease	25 (1.1)	14 (1.2)	11 (1.0)
Peripheral vascular disease	336 (14.7)	178 (15.5)	158 (13.9)
Cerebrovascular disease	336 (14.7)	182 (15.8)	154 (13.5)
Heart failure	43 (1.9)	18 (1.6)	25 (2.2)
Use of CIED	5 (0.2)	4 (0.3)	1 (0.1)
Acute coronary syndrome*	208 (9.1)	95 (8.2)	113 (9.9)
Previous myocardial infarction	527 (23.0)	282 (24.5)	245 (21.5)
Previous percutaneous coronary intervention	381 (16.6)	191 (16.6)	190 (16.7)
Previous cardiac surgery	11 (0.5)	3 (0.3)	8 (0.7)
Angina severity (CCS class):			
I	287 (12.5)	137 (11.9)	150 (13.2)
II	1361 (59.4)	676 (58.7)	685 (60.2)
III	612 (26.7)	323 (28.0)	289 (25.4)
IV	30 (1.3)	16 (1.4)	14 (1.2)
Heart function severity (NYHA class):			
I	251 (11.0)	120 (10.4)	131 (11.5)
II	1349 (58.9)	674 (58.5)	675 (59.3)
III	673 (29.4)	351 (30.5)	322 (28.3)
IV	17 (0.7)	7 (0.6)	10 (0.9)
Mean (SD) creatinine (μmol/L)	74 (20)	74 (21)	74 (19)
Mean (SD) eGFR (mL/min/1.73m^2)	94 (15)	94 (15)	95 (15)
Mean (SD) LDL-C (mmol/L)	2 (1)	2 (1)	2 (1)
Missing	22 (1.0)	12 (1.0)	10 (0.9)
Mean (SD) left ventricular ejection fraction	60 (8)	60 (8)	60 (8)
Preoperative drugs†:			
Beta blocker	1839 (80.3)	918 (79.7)	921 (80.9)
ACE inhibitor or ARB	684 (29.9)	333 (28.9)	351 (30.8)
Statin	1773 (77.4)	875 (76.0)	898 (78.9)
Aspirin	25 (1.1)	15 (1.3)	10 (0.9)
Clopidogrel	25 (1.1)	14 (1.2)	11 (1.0)
Ticagrelor	4 (0.2)	2 (0.2)	2 (0.2)
Sternotomy	2287 (99.9)	1150 (99.8)	1137 (99.9)
Cardiopulmonary bypass	1382 (60.3)	716 (62.2)	666 (58.5)
Mean (SD) cardiopulmonary bypass duration (mins)	114 (36)	114 (38)	113 (34)
On-pump surgery	1369 (59.8)	711 (61.7)	658 (57.8)
No touch technique for SVGs	51 (2.2)	30 (2.6)	21 (1.8)
Sequential bypass configuration for SVGs	1209 (52.8)	612 (53.1)	597 (52.5)
Missing	25 (1.1)	13 (1.1)	12 (1.1)
Left internal mammary artery	2167 (94.6)	1089 (94.5)	1078 (94.7)
Right internal mammary artery	20 (0.9)	15 (1.3)	5 (0.4)
Radial	46 (2.0)	22 (1.9)	24 (2.1)
Mean (SD) No of graft segments/patient	3.5 (0.7)	3.5 (0.7)	3.4 (0.7)
Mean (SD) No of artery graft segments/patient	1.0 (0.3)	1.0 (0.3)	1.0 (0.3)
Mean (SD) No of SVG segments/patient	2.5 (0.8)	2.5 (0.8)	2.5 (0.8)
Mean (SD) SYNTAX score	30.5 (11.7)	31.2 (11.7)	29.8 (11.7)
Missing	168 (7.3)	85 (7.4)	83 (7.3)

ACE=angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blocker; CABG=coronary artery bypass grafting; CCS=Canadian Cardiovascular Society; CIED=cardiac implantable electronic device; DAPT=dual antiplatelet therapy; eGFR=estimated glomerular filtration rate; LDL-C=low density lipoprotein cholesterol; NYHA=New York Heart Association; SD: standard deviation; SVG=saphenous vein graft; SYNTAX=synergy between percutaneous coronary intervention with Taxus and cardiac surgery.
*Occurred within two weeks before elective primary CABG.
†Preoperative drugs within 24 hours before surgery.

Patient and public involvement

As patient and public involvement were not common in the China when the study was initiated, no patients or members of the public were involved in setting the research question or the outcome measures nor in developing plans for recruitment, design, and implementation of the study. Also, no patients were asked to advise on data interpretation or writing of the manuscript.

Table 2 | Primary outcomes and secondary outcomes by modified intention-to-treat analyses

Outcomes	No/Total No		Kaplan-Meier rate (%)		Difference (% (95% CI))	Risk ratio (95% CI)	Hazard ratio (95% CI)	P value
	3 month DAPT	12 month DAPT	3 month DAPT	12 month DAPT				
Primary								
SVG occlusion (per graft segment)	280/2596	283/2529			−0.31 (−3.13 to 2.52)	0.96 (0.79 to 1.17)		0.69*
BARC type 2, 3, or 5 bleeding	95/1152	149/1138	8.3	13.2	−4.67 (−7.18 to −2.16)		0.62 (0.48 to 0.81)	‹0.001
Secondary								
SVG failure†	201/1152	207/1138			−0.46 (−4.59 to 3.67)	0.96 (0.81 to 1.15)		0.67
Any graft stenosis ≥70% (per graft segment)‡	99/3633	89/3552			0.13 (−0.96 to 1.22)	1.09 (0.81 to 1.47)		0.56
Any graft occlusion ≥70% (per graft segment)	319/3633	317/3552			−0.06 (−2.26 to 2.14)	0.99 (0.83 to 1.19)		0.92
MACCEs§	26/1152	27/1138	2.3	2.7	−0.11 (−1.48 to 1.26)		0.95 (0.56 to 1.64)	0.86
Post hoc								
SVG patency (per graft segment)¶	2196/2596	2130/2529			0.53 (−2.70 to 3.76)	1.01 (0.98 to 1.03)		0.67
SVG stenosis ›50% (per graft segment)**	120/2596	116/2529			0.04 (−1.62 to 1.71)	1.01 (0.77 to 1.33)		0.92
Arterial grafts occlusion (per graft segment)	39/1037	34/1023			0.33 (−1.92 to 2.57)	1.13 (0.72 to 1.78)		0.58
Death	5/1152	7/1138	0.4	0.6	−0.18 (−0.77 to 0.41)		0.70 (0.22 to 2.22)	0.55
Components of SVG failure:								
SVG revascularisation	1/1152	0/1138			NA	NA		NA
SVG territory myocardial infarction††	2/1152	2/1138			−0.00 (−0.34 to 0.34)	0.99 (0.14 to 7.00)		›0.99
Components of MACCEs:								
Cardiovascular death	1/1152	2/1138	0.1	0.2	−0.09 (−0.38 to 0.21)		0.50 (0.05 to 5.50)	0.57
Non-fatal myocardial infarction	2/1152	2/1138	0.2	0.2	−0.00 (−0.35 to 0.34)		1.00 (0.14 to 7.07)	›0.99
Non-fatal stroke	18/1152	20/1138	1.6	1.8	−0.19 (−1.24 to 0.86)		0.89 (0.47 to 1.68)	0.72
Revascularisation	6/1152	3/1138	0.5	0.5‡‡	0.38 (−0.48 to 1.23)		2.03 (0.51 to 8.10)	0.32

BARC=Bleeding Academic Research Consortium; CI=confidence interval; DAPT=dual antiplatelet therapy; MACCE=major adverse cardiovascular event; NA=not available; SVG=saphenous vein graft.
*P=0.008 for non-inferiority.
†A composite endpoint of SVG occlusion, SVG revascularisation, myocardial infarction in myocardial territory supplied by an SVG, or sudden death
‡Stenosis ≥70% defined as venous or arterial graft with stenosis ≥70% but not occluded.
§A composite endpoint of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke or revascularisation.
¶SVG patency defined as SVG with stenosis ≤50%.
**SVG stenosis ›50% defined as SVG with stenosis ›50% but not occluded.
††Site was not adjusted in the model due to non-convergent results.
‡‡The third revascularisation event occurred when only 269 patients remained at risk, so the corresponding decrement in the Kaplan-Meier survival curve was proportionally larger, leading to a higher cumulative incidence compared with the crude rate of 0.26%.

Results

Overall, 2300 patients were randomised between 14 February 2023 and 8 July 2024. Of these, 2290 patients comprised the modified intention-to-treat population (fig 1). Supplementary table S1 shows the number of patients enrolled in each study site. Overall, 465 and 279 patients were excluded from the per protocol population for SVG occlusion and bleeding, respectively (supplementary table S2).

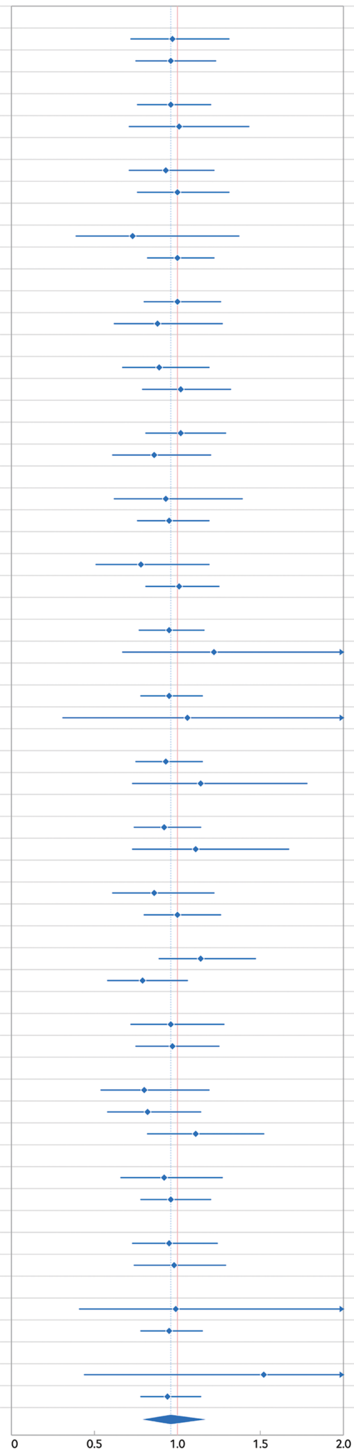
The mean number of SVG segments was 2.5 (standard deviation (SD) 0.8). The mean age was 61.5 years (SD 8.4), and 472 (20.6%) patients were women. Acute coronary syndrome occurred in 208 (9.1%) patients within two weeks before CABG (table 1). Supplementary table S3 provides detailed information on graft segments. Supplementary table S4 shows the drugs used during follow-up. The median duration of DAPT was 90 days (interquartile range (IQR) 81-95 days) in the three month DAPT group and 364 (348-379) days in the 12 month DAPT group. Eleven (1.0%) patients in the three month DAPT group received active ticagrelor after the three month visit. Supplementary figure S4 provides the rates for non-adherence to study drugs during follow-up.

Information on outcome assessment was available for 2070 patients (90.4%) with a total of 5125 SVG segments (including four patients assessed using coronary angiography). The primary non-inferiority outcome of SVG occlusion occurred in 280 of 2596 SVG segments (10.8%) in the three month DAPT group and 283 of 2529 SVG segments (11.2%) in the 12 month DAPT group (absolute difference −0.31%, 95% CI −3.13% to 2.52%; P=0.008 for non-inferiority) (table 2). Similar results were observed in the per protocol population (supplementary table S5), as treated population (supplementary table S6), sensitivity analysis of imputing patients who died of cardiovascular causes as occluded (supplementary table S7), multiple imputation (supplementary table S8), using model with independent covariance structure (supplementary table S7), considering graft type specific nested effect (supplementary table S7), adjusting for history of hypertension (supplementary table S7), and complier average causal effect analysis (supplementary table S7). The post hoc analysis of the tipping point showed that the loss of non-inferiority required 0% of missing data on SVGs in patients in the 12 month DAPT group assumed to have occlusions, and higher than 18% of missing data on SVGs in patients in the three month DAPT group assumed to have occlusions (supplementary table S7). The sensitivity analysis at the per patient level (three month group: 200/1037 (19.3%); 12 month group: 207/1033 (20.0%); absolute difference −0.41%, 95%

Saphenous vein graft occlusion in prespecified and post hoc subgroups

Analyses were performed at per graft segment level. Sequential bypass, SAFINOUS risk score (categorised by median, with higher score indicated higher graft failure risk), ARC-HBR bleeding risk, and PRECISE-DAPT bleeding risk are post hoc subgroups. For each subgroup, risk ratios and 95% CIs are not adjusted for multiple comparisons. P for interaction adjusted for multiple testing are presented. The following subgroups were not adjusted for site due to non-convergence of results: history of myocardial infarction, active smokers, eGFR, beta blocker use, SYNTAX score, sequential bypass, ARC-HBR bleeding risk, and PRECISE-DAPT bleeding risk

Subgroups	3 month DAPT	12 month DAPT	Risk ratio (95% CI)	Risk ratio (95% CI)	Risk ratio for interaction (95% CI)	P for interaction	Adjusted P for interaction
Age (years)							
≥65	106/948 (11.18)	122/1035 (11.79)	0.97 (0.72 to 1.31)		1.01 (0.68 to 1.49)	0.96	>0.99
<65	174/1648 (10.56)	161/1494 (10.78)	0.96 (0.75 to 1.23)				
Sex							
Men	200/2077 (9.63)	201/2014 (9.98)	0.96 (0.76 to 1.20)		0.96 (0.63 to 1.45)	0.84	>0.99
Women	80/519 (15.41)	82/515 (15.92)	1.01 (0.71 to 1.43)				
Body mass index							
≥ 25	145/1468 (9.88)	145/1399 (10.36)	0.93 (0.71 to 1.22)		0.94 (0.64 to 1.38)	0.74	>0.99
< 25	135/1128 (11.97)	138/1130 (12.21)	1.00 (0.76 to 1.31)				
Acute coronary syndrome							
Yes	21/210 (10.00)	40/264 (15.15)	0.73 (0.39 to 1.37)		0.72 (0.37 to 1.40)	0.31	>0.99
No	259/2386 (10.85)	243/2265 (10.73)	1.00 (0.82 to 1.22)				
Hypertension							
Yes	208/1904 (10.92)	191/1770 (10.79)	1.00 (0.80 to 1.26)		1.13 (0.74 to 1.72)	0.58	>0.99
No	72/692 (10.40)	92/759 (12.12)	0.88 (0.62 to 1.27)				
Diabetes							
Yes	123/1138 (10.81)	130/1058 (12.29)	0.89 (0.67 to 1.19)		0.87 (0.59 to 1.28)	0.49	>0.99
No	157/1458 (10.77)	153/1471 (10.40)	1.02 (0.79 to 1.32)				
Hyperlipidaemia							
Yes	199/1722 (11.56)	185/1665 (11.11)	1.02 (0.81 to 1.29)		1.20 (0.79 to 1.81)	0.39	>0.99
No	81/874 (9.27)	98/864 (11.34)	0.86 (0.61 to 1.20)				
Myocardial infarction							
Yes	74/642 (11.53)	57/526 (10.84)	0.93 (0.62 to 1.39)		0.99 (0.63 to 1.57)	0.97	>0.99
No	206/1954 (10.54)	226/2003 (11.28)	0.95 (0.76 to 1.19)				
Current smoker							
Yes	55/485 (11.34)	68/473 (14.38)	0.78 (0.51 to 1.19)		0.78 (0.48 to 1.25)	0.29	>0.99
No	225/2111 (10.66)	215/2056 (10.46)	1.01 (0.81 to 1.25)				
Left ventricular ejection fraction							
≥50%	247/2248 (10.99)	259/2217 (11.68)	0.95 (0.77 to 1.16)		0.80 (0.43 to 1.51)	0.5	>0.99
<50%	33/348 (9.48)	24/312 (7.69)	1.22 (0.67 to 2.22)				
eGFR (mL/min/1.73m²)							
≥60	268/2519 (10.64)	277/2462 (11.25)	0.95 (0.78 to 1.15)		0.76 (0.22 to 2.64)	0.67	>0.99
<60	12/77 (15.58)	6/67 (8.96)	1.06 (0.31 to 3.62)				
Statin							
Yes	216/2012 (10.74)	235/2055 (11.44)	0.93 (0.75 to 1.15)		0.82 (0.50 to 1.34)	0.42	>0.99
No	64/584 (10.96)	48/474 (10.13)	1.14 (0.73 to 1.78)				
Beta blocker							
Yes	220/2096 (10.50)	230/2040 (11.27)	0.92 (0.74 to 1.14)		0.83 (0.52 to 1.33)	0.44	>0.99
No	60/500 (12.00)	53/489 (10.84)	1.11 (0.73 to 1.67)				
ACE inhibitor or ARB							
Yes	75/765 (9.80)	89/809 (11.00)	0.86 (0.61 to 1.22)		0.86 (0.57 to 1.30)	0.48	>0.99
No	205/1831 (11.20)	194/1720 (11.28)	1.00 (0.80 to 1.26)				
Pump use							
On-pump	177/1621 (10.92)	144/1528 (9.42)	1.14 (0.89 to 1.47)		1.45 (0.98 to 2.15)	0.062	>0.99
Off-pump	103/975 (10.56)	139/1001 (13.89)	0.79 (0.58 to 1.06)				
No of SVG segments							
≥3	153/1571 (9.74)	150/1487 (10.09)	0.96 (0.72 to 1.28)		0.99 (0.67 to 1.45)	0.95	>0.99
<3	127/1025 (12.39)	133/1042 (12.76)	0.97 (0.75 to 1.25)				
SYNTAX score							
<23	54/446 (12.11)	84/567 (14.81)	0.80 (0.54 to 1.19)		0.72 (0.43 to 1.19)	0.3	>0.99
23-32	78/837 (9.32)	95/823 (11.54)	0.82 (0.58 to 1.14)		0.73 (0.46 to 1.16)		
>32	128/1141 (11.22)	97/974 (9.96)	1.11 (0.82 to 1.52)				
Sequential bypass							
Yes	117/1224 (9.56)	123/1211 (10.16)	0.92 (0.66 to 1.27)		1.04 (0.72 to 1.51)	0.83	>0.99
No	163/1372 (11.88)	160/1318 (12.14)	0.96 (0.78 to 1.20)				
SAFINOUS risk score							
≥11 points	159/1512 (10.52)	161/1432 (11.24)	0.95 (0.73 to 1.24)		0.97 (0.66 to 1.42)	0.88	>0.99
<11 points	121/1071 (11.30)	122/1081 (11.29)	0.98 (0.74 to 1.29)				
ARC-HBR bleeding risk							
High	18/112 (16.07)	14/111 (12.61)	0.99 (0.41 to 2.38)		1.14 (0.46 to 2.82)	0.77	>0.99
Low	262/2484 (10.55)	269/2418 (11.12)	0.95 (0.78 to 1.15)				
PRECISE-DAPT bleeding risk							
High	9/58 (15.52)	6/60 (10.00)	1.52 (0.44 to 5.22)		1.61 (0.46 to 5.62)	0.48	>0.99
Low	271/2538 (10.68)	277/2469 (11.22)	0.94 (0.78 to 1.14)				
Overall	280/2596 (10.79)	283/2529 (11.19)	0.96 (0.79 to 1.17)				



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ACE=angiotensin converting enzyme; ARB=angiotensin receptor blocker; ARC-HBR=Academic Research Consortium for high bleeding risk; DAPT=dual antiplatelet therapy; eGFR=estimated glomerular filtration rate; PRECISE-DAPT=predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy; SAFINOUS=saphenous vein graft failure; SVG=saphenous vein graft; SYNTAX=synergy between percutaneous coronary intervention with Taxus and cardiac surgery

Fig 2 | Saphenous vein graft occlusion in prespecified and post hoc subgroups. An interactive version of this graphic is available at https://public.flourish.studio/visualisation/28443980/

CI −5.44% to 4.62%) and the post hoc analysis at the per graft level (three month group: 237/1935 (12.2%); 12 month group: 234/1875 (12.5%); absolute difference −0.18%, 95% CI −3.34% to 2.99%) showed that the SVG occlusion rate was similar between groups (supplementary table S7). The post hoc analysis of SVG patency and SVG stenosis >50% also showed that the rate was similar between groups (table 2). The effect of three month DAPT on SVG occlusion was consistent among prespecified subgroups and post hoc subgroups (fig 2). Notably, across different baseline ischaemic risk measured by synergy between percutaneous coronary intervention with Taxus and cardiac surgery (SYNTAX) score, and graft failure risk measured by the saphenous vein graft failure (SAFINOUS) risk score, the effect also remained homogeneous.

Overall, 2288 (99.9%) patients completed one year follow-up. Among the median follow-up of 368 (IQR 358-382) days, BARC type 2, 3, or 5 bleeding occurred in 95 patients (Kaplan-Meier rate 8.3%) in the three month DAPT group and 149 patients (Kaplan-Meier rate 13.2%) in the 12 month DAPT group (hazard ratio 0.62, 95% CI 0.48 to 0.81; P<0.001) (fig 3 and table 2). The number needed to treat to prevent one bleeding event was 21 (95% CI 13 to 46). Similar results were observed in the per protocol population (supplementary table S5), as treated population (supplementary table S6), and sensitivity analyses (supplementary table S9). In the landmark analysis, the risk difference was not observed within 90 days (hazard ratio 0.76, 95% CI 0.55 to 1.06; P=0.10) but was observed after 90 days (0.45, 0.30 to 0.69; P<0.001) (supplementary figure S5 and table S9). The results of a post hoc analysis of events occurring after 90 days were similar in all patients (supplementary table S9). The effect of three month DAPT on BARC type 2, 3, or 5 bleeding was consistent among prespecified and post hoc subgroups (supplementary figure S6). In different baseline bleeding risk measured by ARC-HBR criteria and PRECISE-DAPT score, the effect also remained consistent. The post hoc subgroup analyses for bleeding after 90 days also showed no statistically significant interactions across subgroups (supplementary figure S7). Supplementary table S10 shows the rates of different types of bleeding episodes and locations.

The secondary outcomes of SVG failure occurred in 201/1152 patients (17.4%) in the three month DAPT group and 207/1138 patients (18.2%) in the 12 month DAPT group (absolute difference −0.46%, 95% CI −4.59% to 3.67%) (table 2). The rate of SVG revascularisation and SVG territory myocardial infarction were similar between the two groups (table 2 and supplementary figure S8). Rates of stenosis ≥70% in all graft segments were low and were similar between groups (2.7% in the three month DAPT group and 2.5% in the 12 month DAPT group; absolute difference 0.13%, 95% CI −0.96% to 1.22%) (table 2). Occlusion rates in all graft segments and arterial graft segments were also similar between groups (table 2). MACCE occurred in 26/1152 (Kaplan-Meier rate 2.3%) patients in the three month DAPT group and 27/1138 (Kaplan-Meier rate 2.7%) patients in the 12 month DAPT group (hazard ratio 0.95, 95% CI 0.56 to 1.64) (supplementary figure S9 and table 2). Incidences of each component of MACCE were similar between the two groups (table 2). In the post hoc landmark analysis of MACCEs, the risk difference was not observed within 90 days or after 90 days (supplementary table S11). In the post hoc analyses of in-hospital outcomes, the risk differences were also not observed (supplementary table S12).

There were no statistically significant differences in the frequency of serious adverse events overall and adverse events of interest. Serious adverse events were reported in 378 (32.8%) patients in the three month DAPT group and 401 (35.2%) patients in the 12 month DAPT group. Because of bleeding events, 39 (3.4%) patients in the three month DAPT group and 40 (3.5%) patients in the 12 month DAPT group did not adhere to the allocated intervention (supplementary table S13). Supplementary table S14 shows the sex specific adverse events.

Discussion

In this trial, three months of DAPT with ticagrelor plus aspirin was associated with a lower risk of bleeding without a loss of efficacy in patients with SVG occlusion compared with 12 months of treatment. These results were consistent across prespecified subgroups. These findings, together with other evidence, should help inform the antiplatelet strategy for patients requiring CABG surgery.

Comparison with other studies

The Study of Platelet Inhibition and Patient Outcomes (PLATO) trial was the first large scale randomised study to establish the efficacy of ticagrelor in patients with acute coronary syndrome.[22] Its CABG sub-study emphasised the statistically significant cardiovascular death benefits and comparable bleeding safety of ticagrelor based DAPT for 6-12-months compared with clopidogrel based DAPT.[23] This sub-study laid the foundation for further research of similar interests, although it was a subgroup analysis with limited statistical power to draw a definitive conclusion. In this context, the TOP-CABG trial complements and extends these findings by addressing the question of optimal DAPT duration.

A meta-analysis of three randomised trials found that ticagrelor based DAPT, compared with aspirin alone, was associated with a 44% lower risk of SVG failure (ie, occlusion or stenosis ≥50%) but a 154% higher risk of BARC type 2, 3, or 5 bleeding.[3] The Different Antiplatelet Therapy Strategy After Coronary Artery Bypass Grafting—Follow-up Extension (DACAB-FE) study showed a lower risk of MACCE with DAPT treatment for one year after CABG compared with aspirin or ticagrelor monotherapy, underscoring the long term ischaemic benefit.[24] Current European and American guidelines recommend DAPT for patients with acute coronary syndrome.[25 26] The recent

European Society of Cardiology consensus statement on antithrombotic therapy after CABG explicitly states that for patients undergoing CABG, DAPT with aspirin and clopidogrel or ticagrelor for 12 months is recommended to reduce graft failure.[27] Our trial is consistent with the population highlighted by this recommendation. Of note, about 10% of patients experienced acute coronary syndrome events within the preceding two weeks, whereas a substantial proportion underwent elective CABG in the context of recently worsened ischaemic events. Although bleeding risk was not used as a criterion at trial enrolment, a systematic monitoring process, together with post hoc bleeding risk assessment, suggested that patients enrolled in the TOP-CABG trial were predominantly at low risk of bleeding. This cohort with low bleeding risk, comprising patients with varying degrees of recent ischaemic symptoms, mirrors the real world clinical population undergoing elective CABG.[4] The patients' profile also helps to explain the rationale for selecting DAPT rather than aspirin monotherapy as the reference strategy and mitigates concerns that our comparator does not reflect guideline recommended therapy for stable coronary syndrome. Furthermore, DAPT has been applied beyond the scope of recommendations to some extent in clinical practice. A national survey of surgeons from the UK showed that 91% of cardiac surgeons used DAPT in selective patients with CABG and 38% of them routinely initiated DAPT treatment for all such patients.[28] This variation in practice underscores the lack of robust evidence to guide optimal antithrombotic therapy

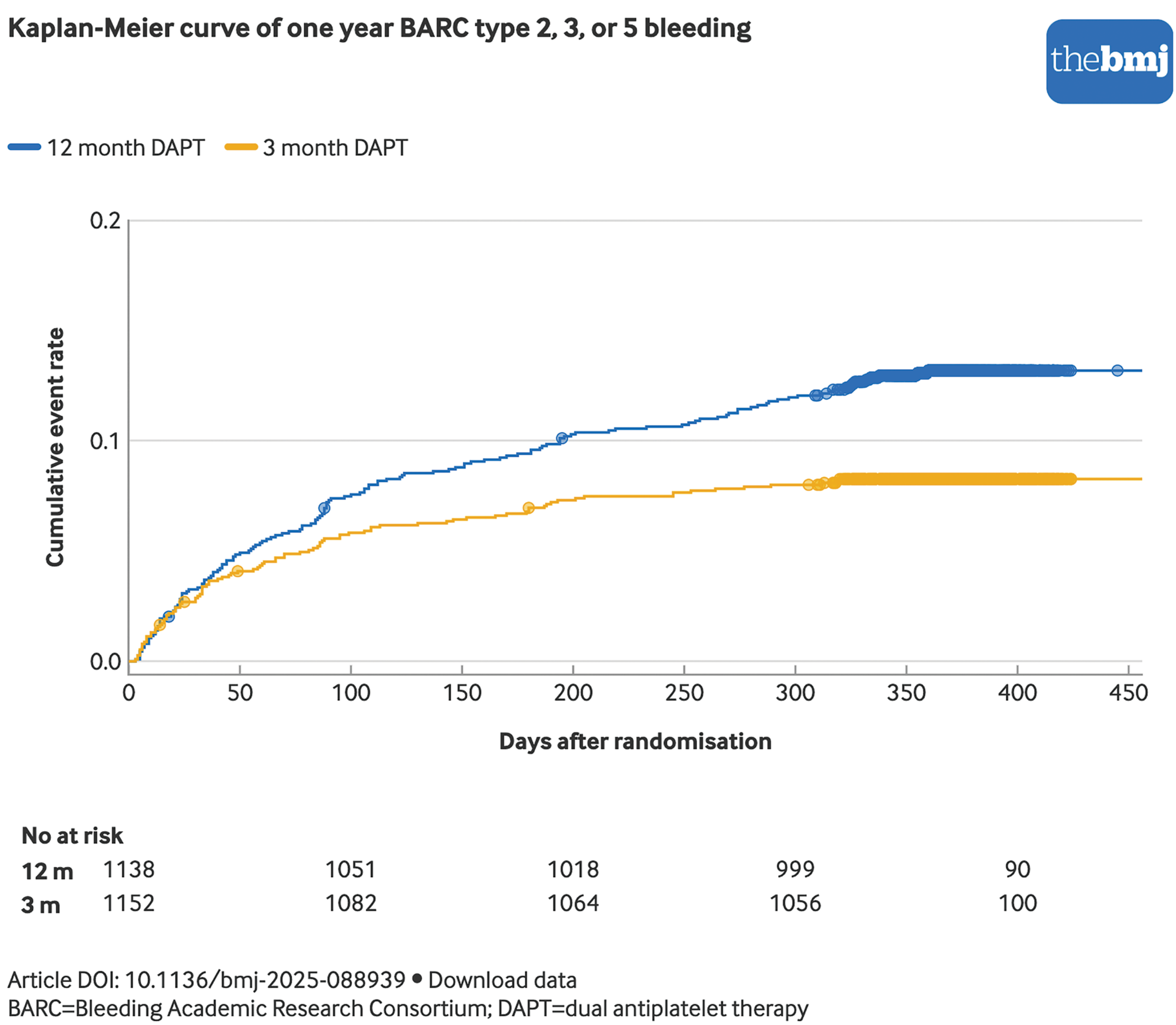

Fig 3 | Kaplan-Meier curve of one year BARC type 2, 3 or 5 bleeding. An interactive version of this graphic is available at https://public.flourish.studio/visualisation/28444446/

after CABG. A three month DAPT strategy was tested in a small trial,[5] but evidence has remained limited until now. Our study provides a balanced strategy by limiting DAPT intervention to the highest risk period for thrombosis[9 29 30] and then shifting to aspirin monotherapy.

The rationale for shorter duration DAPT is supported by the temporal dynamics of platelet activation and graft healing: postoperative platelet hyperactivity peaks in the first few months after CABG, and re-endothelialisation is largely completed by this time[8-10] Data from the Graft Patency Between the No-touch Vein Harvesting Technique and Conventional Approach in Coronary Artery Bypass Graft Surgery (PATENCY) trial showed that the SVG occlusion rate was 3.8% at three months after surgery and remained stable at 12 months.[11] The Ticagrelor Antiplatelet Therapy to Reduce Graft Events and Thrombosis (TARGET) trial showed a comparable SVG occlusion rate at one year (15.4%) and two years after surgery (14.6%).[31 32] Thus, continued potent antiplatelet therapy beyond the early postoperative period may be unnecessary to reduce SVG occlusion and increase haemorrhagic risk.[33 34] Building on this concept, the ongoing One Month Dual Antiplatelet Therapy With Ticagrelor in Coronary Artery Bypass Graft Patients (ODIN) trial will test whether one month of DAPT with ticagrelor plus aspirin improves graft patency compared with aspirin alone in patients with chronic coronary disease, without increasing bleeding risk.[35 36]

The observed reduction in bleeding from DAPT use for three months aligns with the directionality of previous studies,[4 16 37 38] although absolute rates varied due to differences in populations and important distinctions in trial design and intervention timing. For example, in our trial the bleeding rate of 13.2% in the 12 month DAPT group was lower than that in the POPular CABG trial (BARC 2-5: 17.7%) and the DACAB trial (non-CABG related bleeding: 30.4%), and the rate of major bleeding (BARC 3-5: 1.7%) was also lower than that in the Dual Antiplatelet Therapy with Ticagrelor and Acetylsalicylic Acid (ASA) vs. ASA Only after Isolated Coronary Artery Bypass Grafting in Patients with Acute Coronary Syndrome (TACSI) trial (major bleeding defined as bleeding warranting admission to hospital: 4.9%).[4 16 39] These discrepancies are likely attributable to several key factors. Firstly, the timing of randomisation and intervention initiation differed substantially. In our trial, randomisation was conducted on postoperative day 5, allowing for the exclusion of patients with early perioperative bleeding intolerance and capturing a stabilised cohort, whereas in the POPular and DACAB trials, treatment was initiated immediately post-CABG,[4 16] a period of increased inherent bleeding risk. Secondly, the patient populations varied. Our trial exclusively enrolled patients undergoing elective, isolated CABG surgery, potentially representing a lower risk profile compared with trials that included patients needing more urgent care or different surgical contexts. Finally, the definition of bleeding events (eg, DACAB's focus on non-CABG related bleeding)[4] also contributed to variations across trials. Therefore, although direct numerical comparisons are challenging, the consistent directional benefit remains robust and clinically significant. More broadly, our observed rates of BARC type 3 bleeding (1.6% *v* 1.3%) mirror the pattern seen in The Effect of Ticagrelor on Health Outcomes in Diabetes Mellitus Patients Intervention Study (THEMIS) and the Prevention of Cardiovascular Events in Patients with Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin-Thrombolysis in Myocardial Infarction 54 (PEGASUS-TIMI 54) trials (ticagrelor TIMI major bleeding: 2.2-2.6% *v* placebo 1.0-1.1%),[37 38] reinforcing that bleeding risk is modifiable through both patient selection and regimen intensity and duration. Although the participants in the TOP-CABG trial were predominantly at low risk of bleeding, the post hoc subgroup results showed a similar effect in the high bleeding risk subpopulation. However, these results should be interpreted with caution due to limited statistical power to detect subgroup differences.

Our findings contribute to the existing evidence base of antiplatelet therapy optimisation after CABG. Contemporary efforts to balance ischaemic protection with bleeding risk have primarily focused on two strategies: lowering treatment intensity or shortening treatment duration. The recently published TACSI trial,[39] conducted in patients with acute coronary syndrome, explored the former strategy and showed that aspirin monotherapy for 12 months was associated with a similar risk of MACCEs compared with DAPT while significantly reducing bleeding. The TACSI and TOP-CABG trials differed notably in trial design and study population. TACSI was a registry based, open label trial that evaluated the effect of lowering treatment intensity on MACCEs, whereas TOP-CABG was a prospective, double blind trial that evaluated the effect of shortening treatment duration on SVG occlusion. Despite these differences, both studies converge on a consistent clinical insight that in appropriately selected patients, reducing exposure to antiplatelets may preserve ischaemic protection while meaningfully improving net clinical benefit.

Clinical implications

Taken together, our findings support a shift in future guidelines from a uniform approach towards more individualised management. In this context, the TOP-CABG strategy of ticagrelor based DAPT for three months was a reasonable consideration for patients who were considered suitable for DAPT and tolerated early postoperative therapy. Our exploratory subgroup analyses may also provide insights into individualised post-CABG antiplatelet strategies. Overall, the treatment effects were broadly consistent across subgroups defined by bleeding risk (ARC-HBR and PRECISE-DAPT), ischaemic complexity (SYNTAX score), and risk of graft failure (SAFINOUS score), although the trial was not powered to detect subgroup differences. Notably, among patients with higher ischaemic complexity (SYNTAX score >32), the three month DAPT strategy was not associated with a statistically significant increased risk of SVG occlusion compared with the 12 month strategy, despite a numerically higher event rate. This finding suggests that the three month DAPT strategy does not appear to confer an excess risk of graft occlusion in patients with a higher ischaemic burden. Importantly, our study population predominantly consisted of patients with low to moderate bleeding risk, which is consistent with contemporary real world practice. However, the generalisability of these findings to patients at high bleeding risk remains uncertain, and further studies are warranted to better define the optimal antiplatelet strategy in this population.

In addition, the timing of DAPT initiation is another key aspect of post-surgical care. Although our study did not compare initiation windows, further study is needed to investigate the optimal timing. Beyond antithrombotic therapy, optimisation of surgical techniques, intensive lipid lowering therapy, and standardised perioperative management remain essential to further reduce ischaemic and bleeding events.[40 41] The extended follow-up of the TOP-CABG, along with other ongoing large scale trials such as ODIN[35 36] will also be essential to confirm these short duration strategies in contemporary CABG care.

Strengths and limitations of this study

Our large trial evaluated short term DAPT after CABG, providing robust statistical power. However, several limitations should be considered. Firstly, a small proportion of patients did not complete the assessment of SVG occlusion and were excluded from the main analysis, which may potentially bias the results towards non-inferiority. The results of different imputation methods, however, suggested the robustness of the effects. Secondly, 11.4% of patients did not adhere to the study drug, which may have attenuated the observed treatment effect. However, the non-adherence rate was similar between groups and consistent findings across per protocol, as treated, and complier average causal effect analyses support the robustness of the conclusions. Thirdly, our findings may not be generalised to patients with coexisting atrial fibrillation requiring anticoagulation or those with severe renal dysfunction. Furthermore, pre-randomisation screening for DAPT intolerance excluded patients who are prone to bleeding during the early postoperative phase, which may introduce survivor bias and limit the generalisability of our findings to patients at higher bleeding risk. Although the baseline characteristics were similar between patients who were excluded due to DAPT intolerance and those who were included, baseline data were not collected for most excluded patients. Therefore, the potential selection bias may be underestimated. Fourthly, although ticagrelor has shown slightly superior protection against SVG compared with clopidogrel,[42] the conclusions of our trial are specific to ticagrelor based regimens. Extrapolation to other P2Y12 inhibitors should be made cautiously. Fifthly, about 80% of participants were enrolled from a single centre. Although international recommendations largely guide CABG surgical techniques, perioperative management, and postoperative antiplatelet strategies, the predominance of enrolment from one centre may still limit the generalisability to other healthcare settings with differing patient characteristics, surgical practices, and perioperative management patterns. Sixthly, the trial was powered for the primary endpoint of SVG patency and may have been underpowered to detect differences in secondary clinical endpoints, particularly MACCE. These findings should therefore be interpreted as exploratory. Seventhly, our trial was not designed to identify patients for whom aspirin monotherapy was preferable; comparing a shortened DAPT strategy with aspirin alone represented a logical next step. Eighthly, although the non-inferiority margin was determined based on statistical preservation of effect considerations and expert consensus, it was not informed by empirical data on patient preference or established thresholds for minimal clinically important differences. Therefore, the selected margin may not represent a validated clinical threshold. Ninthly, the data and safety monitoring board review was conducted every six months. While no major safety concerns were identified during the trial, we acknowledge that a more frequent monitoring schedule would have aligned better with evolving standards for high risk surgical interventions, and a more geographically diverse and multi-institutional committee structure would further enhance independence. Tenthly, our security protocol relied on two stage authentication involving a mandatory virtual private network gateway followed by application level credentials. Although this security measure provides robust network isolation, we acknowledge that it does not constitute formal two factor authentication as defined by modern cybersecurity standards, representing a technical limitation. Eleventhly, a higher rate of infection events was observed in the 12 month DAPT group. However, our trial did not systematically collect data on baseline infection risk factors, duration of antibiotic treatment, or details of prophylactic antibiotic use, which limited our ability to adjust for these factors.

Conclusions

Among patients undergoing elective CABG with SVG, a three month DAPT strategy had similar one year rates of SVG occlusion while statistically significantly reducing bleeding risk compared with a 12 month DAPT strategy. Future studies should focus on long term outcomes and their comparison with alternative P2Y12 based regimens.

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Contributors: XY, JL, LL, and LZ contributed equally to this work as joint first authors. XY, JL, LL, and LZ conceived and designed the study and drafted the initial manuscript. JL managed data. YW and LL conducted analyses. JL and LL interpreted the data. SH supervised the study, obtained funding, and is guarantor. XY, JL, LL, LZ, KC, QC, WF, XianqiangW, XinW, FX, SL, YY, XW, HW, AD, ZC, HG, TZ, XC, JG, LZ, SL, ZS, JW, YW, WL, and SH critically revised the manuscript for important intellectual content. YW, JL, LL, and SH had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. The corresponding authors attest that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Ethical approval: This study was approved by the central ethics committee at Fuwai Hospital (approval No 2022-1774) and the collaborating centres; all participants gave informed consent before taking part in the study.

Data sharing: Deidentified data and codes underlying the results reported in this manuscript are openly and publicly available at Dryad Digital Repository with a persistent identifier: https://doi.org/10.5061/dryad.jsxksn0qs. If you encounter problems accessing the data, please contact the corresponding author.

Transparency: The lead author (SH) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned and registered have been explained.

Dissemination to participants and related patient and public communities: This study was presented as a featured hot line session at the European Society of Cardiology Congress 2025 on 1 September 2025 and will be disseminated through scientific publications in peer reviewed journals and presentations at national meetings in China. The results will also be shared with the clinicians at participating sites through investigator meetings.

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1 Fitzgibbon GM, Kafka HP, Leach AJ, Keon WJ, Hooper GD, Burton JR. Coronary bypass graft fate and patient outcome: angiographic follow-up of 5,065 grafts related to survival and reoperation in 1,388 patients during 25 years. *J Am Coll Cardiol* 1996;28:616-26. doi:10.1016/0735-1097(96)00206-9
2 Goldman S, Sethi GK, Holman W, et al. Radial artery grafts vs saphenous vein grafts in coronary artery bypass surgery: a randomized trial. *JAMA* 2011;305:167-74. doi:10.1001/jama.2010.1976
3 Sandner S, Redfors B, Angiolillo DJ, et al. Association of Dual Antiplatelet Therapy With Ticagrelor With Vein Graft Failure After Coronary Artery Bypass Graft Surgery: A Systematic Review and Meta-analysis. *JAMA* 2022;328:554-62. doi:10.1001/jama.2022.11966
4 Zhao Q, Zhu Y, Xu Z, et al. Effect of Ticagrelor Plus Aspirin, Ticagrelor Alone, or Aspirin Alone on Saphenous Vein Graft Patency 1 Year After Coronary Artery Bypass Grafting: A Randomized Clinical Trial. *JAMA* 2018;319:1677-86. doi:10.1001/jama.2018.3197
5 Saw J, Wong GC, Mayo J, et al. Ticagrelor and aspirin for the prevention of cardiovascular events after coronary artery bypass graft surgery. *Heart* 2016;102:763-9. doi:10.1136/heartjnl-2015-308691
6 Cardoso R, Knijnik L, Whelton SP, et al. Dual versus single antiplatelet therapy after coronary artery bypass graft surgery: An updated meta-analysis. *Int J Cardiol* 2018;269:80-8. doi:10.1016/j.ijcard.2018.07.083
7 Bonaca MP, Storey RF, Theroux P, et al. Efficacy and Safety of Ticagrelor Over Time in Patients With Prior MI in PEGASUS-TIMI 54. *J Am Coll Cardiol* 2017;70:1368-75. doi:10.1016/j.jacc.2017.07.768
8 de Vries MR, Simons KH, Jukema JW, Braun J, Quax PH. Vein graft failure: from pathophysiology to clinical outcomes. *Nat Rev Cardiol* 2016;13:451-70. doi:10.1038/nrcardio.2016.76
9 Ivert T, Dalén M, Ander C, Stålesen R, Lordkipanidzé M, Hjemdahl P. Increased platelet reactivity and platelet-leukocyte aggregation after elective coronary bypass surgery. *Platelets* 2019;30:975-81. doi:10.1080/09537104.2018.1542122
10 Gaudino M, Antoniades C, Benedetto U, et al, ATLANTIC (Arterial Grafting International Consortium) Alliance. Mechanisms, Consequences, and Prevention of Coronary Graft Failure. *Circulation* 2017;136:1749-64. doi:10.1161/CIRCULATIONAHA.117.027597
11 Tian M, Wang X, Feng W, et al. No-touch versus conventional vein in coronary artery bypass grafting: three year follow-up of multicentre randomised PATENCY trial. *BMJ* 2025;389:e082883. doi:10.1136/bmj-2024-082883
12 Lamy A, Devereaux PJ, Prabhakaran D, et al, CORONARY Investigators. Effects of off-pump and on-pump coronary-artery bypass grafting at 1 year. *N Engl J Med* 2013;368:1179-88. doi:10.1056/NEJMoa1301228
13 Mehran R, Baber U, Sharma SK, et al. Ticagrelor with or without Aspirin in High-Risk Patients after PCI. *N Engl J Med* 2019;381:2032-42. doi:10.1056/NEJMoa1908419
14 Ge Z, Kan J, Gao X, et al, ULTIMATE-DAPT investigators. Ticagrelor alone versus ticagrelor plus aspirin from month 1 to month 12 after percutaneous coronary intervention in patients with acute coronary syndromes (ULTIMATE-DAPT): a randomised, placebo-controlled, double-blind clinical trial. *Lancet* 2024;403:1866-78. doi:10.1016/S0140-6736(24)00473-2
15 Yuan X, Chu Q, Chen K, et al. Multicentre, randomised, double-blind, parallel controlled trial to investigate timing of platelet inhibition after coronary artery bypass grafting: TOP-CABG trial study. *BMJ Open* 2023;13:e070823. doi:10.1136/bmjopen-2022-070823
16 Willemsen LM, Janssen PWA, Peper J, et al. Effect of Adding Ticagrelor to Standard Aspirin on Saphenous Vein Graft Patency in Patients Undergoing Coronary Artery Bypass Grafting (POPular CABG): A Randomized, Double-Blind, Placebo-Controlled Trial. *Circulation* 2020;142:1799-807. doi:10.1161/CIRCULATIONAHA.120.050749

17 Van Epps H, Astudillo O, Del Pozo Martin Y, Marsh J. The Sex and Gender Equity in Research (SAGER) guidelines: Implementation and checklist development. *Eur Sci Ed* 2022;48:e86910doi:10.3897/ese.2022.e86910.
18 Antonopoulos AS, Odutayo A, Oikonomou EK, et al, SAFINOUS-CABG (Saphenous Vein Graft Failure—An Outcomes Study in Coronary Artery Bypass Grafting) group. Development of a risk score for early saphenous vein graft failure: An individual patient data meta-analysis. *J Thorac Cardiovasc Surg* 2020;160:116-127.e4. doi:10.1016/j.jtcvs.2019.07.086
19 Urban P, Mehran R, Colleran R, et al. Defining High Bleeding Risk in Patients Undergoing Percutaneous Coronary Intervention. *Circulation* 2019;140:240-61. doi:10.1161/CIRCULATIONAHA.119.040167
20 Costa F, van Klaveren D, James S, et al, PRECISE-DAPT Study Investigators. Derivation and validation of the predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score: a pooled analysis of individual-patient datasets from clinical trials. *Lancet* 2017;389:1025-34. doi:10.1016/S0140-6736(17)30397-5
21 Peugh JL, Strotman D, McGrady M, Rausch J, Kashikar-Zuck S. Beyond intent to treat (ITT): A complier average causal effect (CACE) estimation primer. *J Sch Psychol* 2017;60:7-24. doi:10.1016/j.jsp.2015.12.006
22 Wallentin L, Becker RC, Budaj A, et al, PLATO Investigators. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med* 2009;361:1045-57. doi:10.1056/NEJMoa0904327
23 Held C, Asenblad N, Bassand JP, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes undergoing coronary artery bypass surgery: results from the PLATO (Platelet Inhibition and Patient Outcomes) trial. *J Am Coll Cardiol* 2011;57:672-84. doi:10.1016/j.jacc.2010.10.029
24 Zhu Y, Zhang W, Dimagli A, et al. Antiplatelet therapy after coronary artery bypass surgery: five year follow-up of randomised DACAB trial. *BMJ* 2024;385:e075707. doi:10.1136/bmj-2023-075707
25 Vrints C, Andreotti F, Koskinas KC, et al, ESC Scientific Document Group. 2024 ESC Guidelines for the management of chronic coronary syndromes. *Eur Heart J* 2024;45:3415-537. doi:10.1093/eurheartj/ehae177
26 Virani SS, Newby LK, Arnold SV, et al, Peer Review Committee Members. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation* 2023;148:e9-119. doi:10.1161/CIR.0000000000001168
27 Sandner S, Gaudino M, Agewall S, et al. Antithrombotic therapy after coronary artery bypass graft surgery: a Clinical Consensus Statement of the ESC Working Group on Cardiovascular Surgery, the ESC Working Group on Cardiovascular Pharmacotherapy, and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2025;ehaf423. doi:10.1093/eurheartj/ehaf423
28 Comanici M, Raja SG. Dual-Antiplatelet Therapy After Coronary Artery Bypass Grafting: A Survey of UK Cardiac Surgeons. *J Cardiothorac Vasc Anesth* 2023;37:2517-23. doi:10.1053/j.jvca.2023.08.146
29 Dunning J, Versteegh M, Fabbri A, et al, EACTS Audit and Guidelines Committee. Guideline on antiplatelet and anticoagulation management in cardiac surgery. *Eur J Cardiothorac Surg* 2008;34:73-92. doi:10.1016/j.ejcts.2008.02.024
30 Wang Z, Qian Z, Ren J, Men J, Wen J, Wei M. Long period and high level of D-dimer after coronary artery bypass grafting surgery. *Int Heart J* 2018;59:51-7. doi:10.1536/ihj.16-595
31 Kulik A, Abreu AM, Boronat V, Kouchoukos NT, Ruel M. Ticagrelor versus aspirin and vein graft patency after coronary bypass: A randomized trial. *J Card Surg* 2022;37:563-70. doi:10.1111/jocs.16189
32 Kulik A, Abreu AM, Boronat V, Kouchoukos NT, Ruel M. Ticagrelor versus aspirin 2 years after coronary bypass: Observational analysis from the TARGET trial. *J Card Surg* 2022;37:1969-77. doi:10.1111/jocs.16492
33 Landi A, Valgimigli M. Antithrombotic therapy in patients with established atherosclerotic coronary disease. *Heart* 2023;109:1034-43. doi:10.1136/heartjnl-2022-321603
34 Sandner S, Redfors B. Ticagrelor monotherapy after CABG-Probably not at all and definitely not forever. *J Card Surg* 2022;37:1978-9. doi:10.1111/jocs.16503
35 Sandner S, Gaudino M, Redfors B, et al. One-month DAPT with ticagrelor and aspirin for patients undergoing coronary artery bypass grafting: rationale and design of the randomised, multicentre, double-blind, placebo-controlled ODIN trial. *EuroIntervention* 2024;20:e322-8. doi:10.4244/EIJ-D-23-00699
36 Sandner S, Redfors B, Ruel M, Gaudino M. LETTER: An update on changes to the design of the ODIN trial. *EuroIntervention* 2025;21:e332-3. doi:10.4244/EIJ-D-24-00974
37 Steg PG, Bhatt DL, Simon T, et al, THEMIS Steering Committee and Investigators. Ticagrelor in Patients with Stable Coronary Disease and Diabetes. *N Engl J Med* 2019;381:1309-20. doi:10.1056/NEJMoa1908077
38 Bonaca MP, Bhatt DL, Cohen M, et al, PEGASUS-TIMI 54 Steering Committee and Investigators. Long-term use of ticagrelor in patients with prior myocardial infarction. *N Engl J Med* 2015;372:1791-800. doi:10.1056/NEJMoa1500857
39 Jeppsson A, James S, Moller CH, et al, TACSI Trial Group.TACSI Trial Group. Ticagrelor and Aspirin or Aspirin Alone after Coronary Surgery for Acute Coronary Syndrome. *N Engl J Med* 2025;393:2313-23. doi:10.1056/NEJMoa2508026
40 Verma S, Leiter LA, Teoh H, et al. Effect of evolocumab on saphenous vein graft patency after coronary artery bypass surgery (NEWTON-CABG CardioLink-5): an international, randomised, double-blind, placebo-controlled trial. *Lancet* 2025;406:1223-34. doi:10.1016/S0140-6736(25)01633-2
41 Kulik A, Ruel M, Jneid H, et al, American Heart Association Council on Cardiovascular Surgery and Anesthesia. Secondary prevention after coronary artery bypass graft surgery: a scientific statement from the American Heart Association. *Circulation* 2015;131:927-64. doi:10.1161/CIR.0000000000000182
42 Solo K, Lavi S, Kabali C, et al. Antithrombotic treatment after coronary artery bypass graft surgery: systematic review and network meta-analysis. *BMJ* 2019;367:l5476. doi:10.1136/bmj.l5476

Supplementary information: Section S1-S7, figures S1-S9, tables S1-S14, and references