Immediate versus staged complete revascularisation during index admission in patients with ST-segment elevation myocardial infarction and multivessel disease (OPTION–STEMI): a multicentre, non-inferiority, open-label, randomised trial

*Min Chul Kim, Joon Ho Ahn, Dae Young Hyun, Yongwhan Lim, Kyung Hoon Cho, Seung Hun Lee, Seongho Park, Seok Oh, Doo Sun Sim, Young Joon Hong, Ju Han Kim, Myung Ho Jeong, Jang Hyun Cho, Sang-Rok Lee, Dong Oh Kang, Jin-Yong Hwang, Young Jin Youn, Jung-Hee Lee, Young-Hoon Jeong, Jong-Hwa Ahn, Dong-Bin Kim, Eun Ho Choo, Chan Joon Kim, Weon Kim, Jay Young Rhew, Jong-Il Park, Sang-Yong Yoo, Youngkeun Ahn, on behalf of the OPTION–STEMI Investigators**

Lancet 2025; 406: 1032–43

Published Online August 31, 2025 https://doi.org/10.1016/S0140-6736(25)01529-6

See Comment page 984

*Members are listed in the appendix (pp 4–5)

Division of Cardiology, Department of Internal Medicine, Chonnam National University Hospital, Chonnam National University Medical School, Chonnam National University, Gwangju, South Korea (Prof M C Kim MD, Prof J H Ahn MD, Prof D Y Hyun MD, Prof Y Lim MD, Prof K H Cho MD, Prof S H Lee MD, S Park MD, Prof S Oh MD, Prof D S Sim MD, Prof Y J Hong MD, Prof J H Kim MD, Prof M H Jeong MD, Prof Y Ahn MD); **Division of Cardiology, Department of Internal Medicine, Gwangju Veterans Hospital, Gwangju, South Korea** (Prof M H Jeong); **St Carollo General Hospital, Suncheon, South Korea** (J H Cho MD); **Division of Cardiology, Department of Internal Medicine, Jeonbuk National University Hospital, Jeonbuk National University Medical School, Jeonju, South Korea** (Prof S-R Lee MD); **Cardiovascular Center, Department of Internal Medicine, Korea University Guro Hospital, Korea University College of Medicine, Seoul, South Korea** (Prof D O Kang MD); **Division of Cardiology, Department of Internal Medicine, Gyeongsang National University Hospital, Gyeongsang National University College of Medicine,**

Summary

Background The optimal timing of complete revascularisation for patients with ST-segment elevation myocardial infarction (STEMI) and multivessel coronary artery disease remains unclear. We aimed to assess whether immediate complete revascularisation was non-inferior to staged complete revascularisation during the index admission.

Methods We conducted an open-label, randomised, non-inferiority trial at 14 hospitals in South Korea. Patients aged 19 years or older with STEMI and multivessel disease who had undergone percutaneous coronary intervention (PCI) for a culprit lesion were randomly assigned 1:1 to immediate complete revascularisation (PCI for non-culprit lesions during the index procedure) or staged complete revascularisation (non-culprit PCI on another day during the index admission). Web-based, permuted-block randomisation (using mixed block sizes of two or four) was implemented at each participating centre to allocate patients. Non-culprit lesions with 50–69% stenosis were evaluated by fractional flow reserve. Study participants and study investigators were aware of treatment allocation, but members of the independent clinical committee reviewing primary and secondary endpoints were masked to treatment allocation. The primary endpoint was a composite of death from any cause, non-fatal myocardial infarction, or any unplanned revascularisation at 1 year in the intention-to-treat population, and the non-inferiority margin was set at a hazard ratio (HR) of 1·42; if the upper boundary of the one-sided 97·5% CI of the HR was less than 1·42, immediate complete revascularisation would be considered non-inferior to staged complete revascularisation. Reported adverse events consisted of procedural complications, other complications during admission, and in-hospital clinical events occurring during the index admission. This trial is registered with the Clinical Research Information Service (KCT0004457) and ClinicalTrials.gov (NCT04626882). Long-term follow-up is ongoing.

Findings Between Dec 30, 2019, and Jan 15, 2024, 994 patients were enrolled and randomly assigned to immediate revascularisation (n=498; immediate group) or staged revascularisation (n=496; staged group). The primary endpoint occurred at 1 year in 65 patients (13%) in the immediate group and 53 patients (11%) in the staged group (HR 1·24 [95% CI 0·86–1·79]; $p_{non\text{-}inferiority}$=0·24). Rates of stroke, major bleeding, and contrast-induced nephropathy did not differ significantly between the two groups. Cardiogenic shock during the index hospitalisation occurred in 18 (4%) of 498 patients in the immediate group and nine (2%) of 496 patients in the staged complete revascularisation group.

Interpretation Among patients with STEMI and multivessel disease, immediate complete revascularisation was not shown to be non-inferior to staged complete revascularisation during the index admission in terms of incidence of a composite of death from any cause, non-fatal myocardial infarction, or any unplanned revascularisation at 1 year. This finding might inform future clinical guidelines on the role and optimal use of immediate complete revascularisation during the index admission.

Funding Boston Scientific.

Research in context

Evidence before this study

Complete revascularisation is the standard approach for the treatment of patients with ST-segment elevation myocardial infarction (STEMI) and multivessel coronary artery disease. However, the optimal timing of complete revascularisation for these patients remains unclear. We searched PubMed for articles in English published from database inception to May 4, 2025 using the terms "ST-segment elevation myocardial infarction", "multivessel", "non-culprit", "non-infarct-related artery", "staged", "stage", "timing", "complete revascularisation", and "revascularisation", with the appropriate Boolean operators. We found five randomised clinical trials that evaluated the timing of complete revascularisation in patients with STEMI and multivessel coronary artery disease. Two large randomised trials showed that immediate complete revascularisation was non-inferior to staged complete revascularisation in terms of a composite clinical outcome at 1 year. However, one of the trials (BIOVASC) enrolled exclusively patients with acute coronary syndrome (both STEMI and non-ST-segment elevation acute coronary syndrome); and the other (MULTISTARS AMI) enrolled a relatively low-risk STEMI population. Furthermore, most of the enrolled patients in these trials received staged revascularisation for non-culprit lesions after hospital discharge. Three other small randomised trials showed no difference in incidence of clinical outcomes between immediate and staged complete revascularisation. Two of those trials included fewer than 150 patients; the third trial enrolled 209 patients but was prematurely terminated. In this context, immediate complete revascularisation has a class IIb recommendation (level of evidence B) for haemodynamically stable patients with STEMI and without complex coronary anatomy according to 2025 American College of Cardiology, American Heart Association, and Society for Cardiovascular Angiography and Interventions guidelines. The 2023 European Society of Cardiology guidelines recommend complete revascularisation, either during the index procedure or within 45 days for class IA indications.

Added value of this study

OPTION–STEMI was a large-scale, randomised controlled trial comparing immediate complete revascularisation and staged complete revascularisation during the index admission in patients with STEMI and multivessel coronary artery disease. Immediate complete revascularisation was not shown to be non-inferior to staged complete revascularisation during the index admission for the composite endpoint of death from any cause, non-fatal myocardial infarction, or any unplanned revascularisation at 1 year. More than 30% of patients included in this study had acute heart failure (defined as Killip class II or III), and there was a significant interaction between treatment strategy and Killip class (I *vs* II or III), with an increased risk of harm from immediate complete revascularisation for patients with a higher Killip class than those without clinical signs of heart failure. The findings from OPTION–STEMI provide additional insights into the optimal timing of complete revascularisation, as this procedure was performed during the index admission. Moreover, OPTION–STEMI involved many patients with high-risk features, unlike the BIOVASC and MULTISTARS AMI trials.

Implications of all the available evidence

In OPTION–STEMI, there were more adverse events during the index admission in the group allocated to immediate complete revascularisation than in the group allocated to staged complete revascularisation, particularly in patients with a higher Killip class. These findings indicate that immediate complete revascularisation can be considered for haemodynamically stable patients with STEMI with low clinical risk who do not have acute heart failure or cardiogenic shock. This trial shows that immediate complete revascularisation was not non-inferior to staged complete revascularisation performed during the index admission, in contrast to previous trials in which complete revascularisation in the staged group was achieved after the index admission in most patients. Notably, immediate complete revascularisation might be harmful in patients complicated by heart failure, who were rarely included in previous trials.

Introduction

Multivessel coronary artery disease is a common clinical condition, affecting almost half of all patients with ST-segment elevation myocardial infarction (STEMI).[1,2] In these patients, a strategy of complete revascularisation has shown clinical benefit over culprit-only revascularisation.[3–8] Previous randomised clinical trials showed that immediate complete revascularisation was non-inferior to staged complete revascularisation in patients with acute coronary syndrome or STEMI.[9,10] However, in most trials, staged percutaneous coronary intervention (PCI) for non-culprit lesions was performed after hospital discharge rather than during the index admission. Therefore, it remains unclear whether immediate complete revascularisation and staged complete revascularisation conducted during the index hospitalisation would have differing treatment effects.

Current guidelines recommend complete revascularisation for patients with STEMI and multivessel coronary artery disease rather than culprit-only revascularisation, but evidence for routine immediate multivessel PCI remains scarce.[11,12] Furthermore, few randomised clinical trials have evaluated the timing of complete revascularisation during the index admission in patients with STEMI and multivessel coronary artery disease. The timing of complete revascularisation in earlier landmark trials that compared complete and culprit-only revascularisation varied.[3–7] Complete revascularisation was done a median of 2 days after the initial PCI procedure (IQR 2–4) in the Third Danish

Jinju, South Korea (Prof J-Y Hwang MD); **Division of Cardiology, Department of Internal Medicine, Wonju Severance Christian Hospital, Yonsei University Wonju College of Medicine, Wonju, South Korea** (Prof Y J Youn MD, Prof J-H Lee MD); **Chung-Ang University Thrombosis and Biomarker Center, Chung-Ang University Gwangmyeong Hospital, Gwangmyeong, South Korea** (Prof Y-H Jeong MD); **Division of Cardiology, Department of Internal Medicine, Chung-Ang University College of Medicine, Seoul, South Korea** (Prof Y-H Jeong); **Division of Cardiology, Department of Internal Medicine, Gyeongsang National University Changwon Hospital, Gyeongsang National University College of Medicine, Changwon, South Korea** (Prof Y-H Jeong, Prof J-H Ahn); **Division of Cardiology, Department of Internal Medicine, Bucheon St Mary's Hospital, The Catholic University of Korea, Bucheon, South Korea** (Prof D-B Kim MD); **Division of Cardiology, Department of Internal Medicine, Seoul St Mary's Hospital, The Catholic University of Korea, Seoul, South Korea** (Prof E H Choo MD); **Division of Cardiology, Department of Internal Medicine, Uijeongbu St Mary's Hospital, The Catholic University of Korea, Uijeongbu, South Korea** (Prof C J Kim MD); **Division of Cardiology, Department of Internal Medicine, Kyung Hee University Medical Center, Kyung Hee University College of Medicine, Seoul, South Korea** (Prof W Kim MD); **Presbyterian Medical Center, Jeonju, South Korea** (J Y Rhew MD); **Division of Cardiology, Department of Internal Medicine, Yeungnam University Medical Center, Yeungnam University College of Medicine, Daegu, South Korea** (Prof J-H Lee, Prof J-I Park MD); **Division of Cardiology, Department of Internal Medicine, Good Morning Hospital, Pyeongtaek, South Korea** (Prof S-Y Yoo MD); **Division of Cardiology, Department of Internal Medicine, Gangneung Asan Hospital, University of Ulsan College of Medicine,**

Gangneung, South Korea
(Prof S-Y Yoo)

Correspondence to:
Prof Youngkeun Ahn, Division of Cardiology, Department of Internal Medicine, Chonnam National University Hospital, Chonnam National University Medical School, Gwangju 61469, South Korea
cecilyk@jnu.ac.kr

See Online for appendix

Study of Optimal Acute Treatment of Patients with STEMI (DANAMI-3–PRIMULTI) trial,[5] a mean of 2·1 days after the initial PCI procedure (SD 1·0) in a trial comparing fractional flow reserve-guided revascularisation with the conventional strategy in acute STEMI patients with multivessel coronary artery disease (Compare-Acute trial),[6] and a median of 1 day after the initial PCI procedure (IQR 1–3) during the index hospitalisation or 23 days (13–34) after hospital discharge in the Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early PCI for STEMI (COMPLETE) trial.[7] We conducted the Optimal Timing of Fractional Flow Reserve-Guided Complete Revascularization for Non-Infarct-Related Artery in ST-segment Elevation Myocardial Infarction with Multivessel Disease (OPTION–STEMI) trial to evaluate whether immediate complete revascularisation at the time of the primary PCI was non-inferior to staged complete revascularisation at another time during the index admission in patients with STEMI and multivessel coronary artery disease.

Methods

Study design and participants

OPTION–STEMI was an investigator-initiated, multicentre, open-label, non-inferiority, randomised controlled trial conducted at 14 hospitals in South Korea. Details of the participating investigators and trial organisation are provided in the appendix (pp 4–7).

Patients were eligible for the trial if they were aged 19 years or older, presented with STEMI and multivessel coronary artery disease, and underwent successful PCI for a culprit artery. Successful PCI for the culprit artery was defined as achievement of a residual stenosis of less than 20% on angiography and grade 2 or grade 3 flow according to the Thrombolysis in Myocardial Infarction grading system. Patients whose ischaemic symptom onset occurred more than 12 h before the primary PCI were excluded. Multivessel coronary artery disease was defined as at least one non-culprit lesion with a diameter of 2·5 mm or more and 50% stenosis or greater by visual estimation. The main exclusion criteria were cardiogenic shock during the initial treatment or after the culprit treatment, unprotected left main coronary artery disease with more than 50% stenosis by visual estimation, and chronic total occlusion of the non-culprit artery. Full details of the inclusion and exclusion criteria are provided in the appendix (pp 9–10). Data on patient sex were collected from medical records.

All patients provided written informed consent before enrolment. The trial rationale and design have been previously published.[13] The study protocol was approved by the institutional review board of Chonnam National University Hospital (Gwangju, South Korea; approval number CNUH-2019–318; date of approval Nov 12, 2019) and by the institutional review board of each participating site. An independent data and safety monitoring board approved the initial trial protocol and subsequent amendments and monitored patient safety periodically. A clinical event adjudication committee assessed all clinical events (appendix p 6; members of the clinical event adjudication committee were not study investigators). The study protocol and statistical analysis plan are included in the appendix (pp 47–151). This trial was prospectively registered with the Clinical Research Information Service (KCT0004457) and subsequently registered at ClinicalTrials.gov (NCT04626882; appendix p 8). Patient follow-up is ongoing and expected to continue for a maximum of 5 years.

Randomisation and masking

Trial participants were randomly assigned in a 1:1 ratio to either immediate complete revascularisation with simultaneous PCI for the culprit and non-culprit lesions (immediate group), or staged complete revascularisation that included PCI for non-culprit lesions on another day (ie, not on the day on which revascularisation of the culprit lesion was done) during the index admission (staged group). Random assignment was done on the basis of randomly permuted block sizes of two or four with a web-based randomisation system (TnW Software, Seoul, South Korea). A computer-generated randomisation sequence was generated by an independent programmer who was not involved in the trial. Patients were enrolled by participating physicians, and both the physicians and research coordinators were granted access to the web-based randomisation system. Study participants and study investigators were not masked to the group allocation. Members of the independent clinical event adjudication committee reviewing the primary and secondary endpoints were masked to the treatment group allocation.

Procedures

Timing of revascularisation for non-culprit lesions in the staged group was not prespecified and was left to the operators' discretion; however, patients generally underwent staged procedures as soon as possible, unless they experienced complications such as acute kidney injury, acute heart failure, cardiogenic shock or other in-hospital events that could delay the staged procedure. In both groups, fractional flow reserve was measured in non-culprit lesions that had 50–69% stenosis as estimated. In contrast, non-culprit lesions with 70% or greater stenosis by visual estimation were revascularised without fractional flow reserve measurements.[7] PCI was done with a third-generation, biodegradable-polymer, everolimus-eluting stent (Synergy; Boston Scientific, Malborough, MA, USA) as recommended by the protocol; alternatively, other stents, drug-coated balloons, or plain balloon angioplasty at the operators' discretion was permitted by the protocol. All participants received guideline-directed medical treatment, including lifestyle modifications and pharmacological therapies.[11,14] Choice of P2Y12 inhibitor, vascular access site, use of manual thrombus aspiration,

use of a glycoprotein IIb/IIIa inhibitor, and use of intravascular imaging were left to the operators' discretion.

All data on fractional flow reserve and coronary angiograms were analysed at the core laboratory (appendix p 7). Follow-up assessments were conducted with office visits or telephone calls at 1, 6, and 12 months after random assignment. Information regarding any clinical events and cardiovascular medications was collected systematically at each visit. Each event was independently reviewed by three committee members of the clinical event adjudication committee and resolved through discussion and majority vote in case of discrepancy. Survival status was cross-validated with the use of the Korean National Health Insurance database.

Outcomes

The primary endpoint was a composite of death from any cause, non-fatal myocardial infarction (including both spontaneous and procedure-related myocardial infarction), or any unplanned revascularisation at 1 year after random assignment. Secondary endpoints were the same composite endpoint reported at 1 month and 6 months after random assignment, as well as the following endpoints reported at 1, 6, 12, 24, 36, 48, and 60 months after random assignment: individual components of the primary endpoint; death from cardiac cause; death from non-cardiac cause; target lesion revascularisation; target vessel revascularisation; non-target vessel revascularisation; hospitalisation for unstable angina; hospitalisation for heart failure; stroke; definite or probable stent thrombosis; major bleeding (defined as Bleeding Academic Research Consortium type 3 or 5); and contrast-induced nephropathy during the index admission (appendix p 11). Outcomes up to 12 months after random assignment are reported here; longer-term outcomes will continue to be collected and will be reported at subsequent timepoints, up to 5 years after random assignment.

Myocardial infarction was defined according to the fourth universal definition of myocardial infarction,[15] and unplanned repeat revascularisation was defined according to the Academic Research Consortium-2 consensus.[16] Detailed definitions of all trial endpoints are provided in the appendix (pp 12–16). Collected adverse events comprised procedural complications, other complications during admission, and in-hospital clinical events that occurred during the index admission.

Statistical analysis

This study was designed to test the hypothesis that immediate complete revascularisation would be non-inferior to staged complete revascularisation during the index admission with regard to the primary endpoint. We assumed that the event rate of the primary endpoint at 1 year would be 10·5% in the staged group.[5,6] With a non-inferiority margin set at a hazard ratio (HR) of 1·42, we estimated that 994 patients would provide the trial with a power of 80% to show non-inferiority with

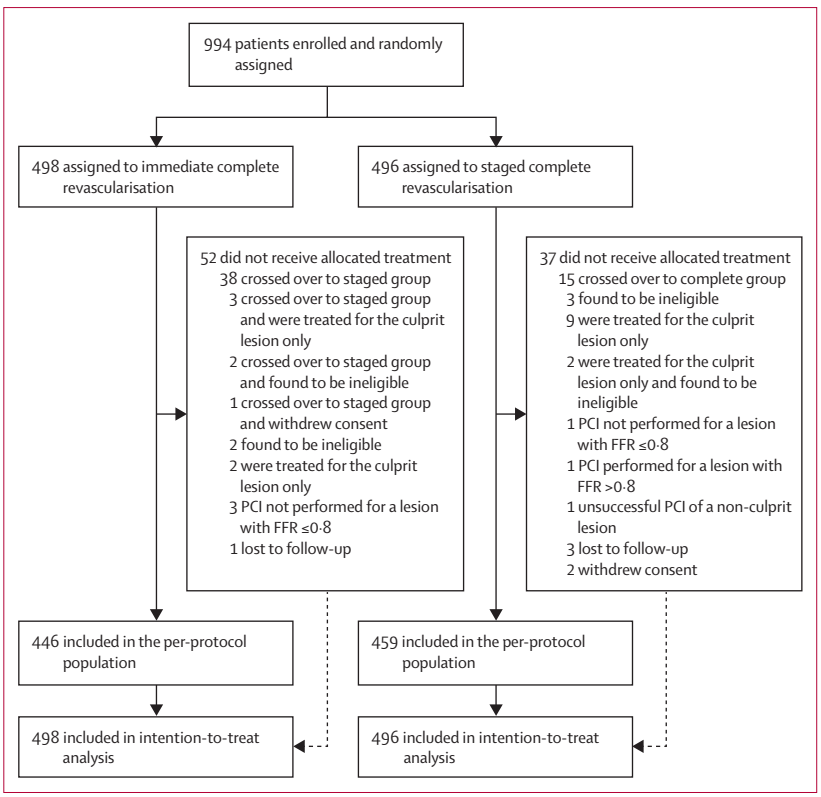

Figure 1: **Trial profile**
FFR=fractional flow reserve. PCI=percutaneous coronary intervention.

a one-sided 2·5% significance level and 4% dropout rate. A protocol amendment was implemented 30 months after enrolment began, changing the one-sided type I error rate from 5% to 2·5% and increasing the sample size from 784 to 994 patients. Details of the sample size calculation, including this amendment, are provided in the appendix (p 17, 112–124, 147–151).

All analyses were done according to the intention-to-treat principle. A post-hoc sensitivity analysis excluding patients who withdrew consent after random assignment and those subsequently found to be ineligible was also done. No imputation methods were applied to address missing data for these patients. The cumulative event rate of the study endpoints was estimated with the Kaplan–Meier method. Treatment effects were assessed using Cox proportional hazards regression, and results are reported as HRs with 95% CIs. Odds ratio was calculated for contrast-induced nephropathy because it was a binary outcome assessed during hospitalisation rather than a time-to-event outcome. The proportional hazards assumption was verified using Schoenfeld residuals. If the upper boundary of the one-sided 97·5% CI of the HR for the primary endpoint was less than the prespecified non-inferiority margin of 1·42, immediate complete revascularisation was considered non-inferior to staged complete revascularisation. A sensitivity analysis was conducted in the per-protocol

	Immediate complete revascularisation group (n=498)	Staged complete revascularisation group (n=496)
Patient characteristics		
Age, years	66·0 (57·0–76·0)	65·0 (58·0–76·0)
Sex		
Male	396 (80%)	393 (79%)
Female	102 (20%)	103 (21%)
BMI, kg/m²	24·0 (22·1–26·0)	24·2 (22·0–26·3)
Missing data	3 (<1%)	1 (<1%)
Current smoker	205 (41%)	202 (41%)
Former smoker	97 (19%)	85 (17%)
Baseline clinical characteristics		
Hypertension	245 (49%)	253 (51%)
Diabetes	211 (42%)	205 (41%)
Use of insulin	8 (2%)	9 (2%)
Dyslipidaemia	295 (59%)	280 (56%)
Family history of premature coronary artery disease*	34 (7%)	27 (5%)
Previous percutaneous coronary intervention	49 (10%)	50 (10%)
Previous myocardial infarction	40 (8%)	36 (7%)
Previous heart failure	22 (4%)	20 (4%)
Previous cerebrovascular disease	40 (8%)	38 (8%)
Previous peripheral artery disease	9 (2%)	8 (2%)
Previous chronic kidney disease†	37 (7%)	34 (7%)
Receiving dialysis	6 (1%)	4 (<1%)
Location of infarct		
Anterior	215 (43%)	230 (46%)
Inferior	250 (50%)	233 (47%)
Lateral	109 (22%)	124 (25%)
Posterior	54 (11%)	48 (10%)
Isolated posterior	15 (3%)	19 (4%)
Left bundle-branch block	6 (1%)	3 (<1%)
Systolic blood pressure, mm Hg	120 (110–140)	120 (110–140)
Diastolic blood pressure, mm Hg	80 (64–80)	80 (61–80)
Heart rate, beats per minute	77 (65–90)	80 (67–90)
Killip class ≥2	171 (34%)	158 (32%)
Left ventricular ejection fraction	50·3% (11)	49·7% (11)
Missing data	10 (2%)	3 (<1%)
Symptom to balloon time, min	133 (72–261)	137 (72–240)
Door to balloon time, min	69 (55–89)	69 (56–90)
Radial access	371 (74%)	379 (76%)
Arteries with stenosis		
2	392 (79%)	397 (80%)
3	106 (21%)	99 (20%)
Location of culprit lesion		
Left anterior descending artery	221 (44%)	234 (47%)
Left circumflex artery	62 (12%)	67 (14%)
Right coronary artery	215 (43%)	195 (39%)
Location of non-culprit lesions		
Left anterior descending artery	222 (45%)	212 (43%)
Left circumflex artery	218 (44%)	215 (43%)
Right coronary artery	162 (33%)	167 (34%)

(Table 1 continued on next page)

population, which included patients whose treatment had no protocol deviations (appendix p 139). The interaction term between the randomised groups and the key subgroups was assessed for the primary endpoint of the prespecified subgroup analyses. No imputation methods were used to infer missing values for the baseline variables.

No interim analyses were done. There was no adjustment for multiple testing or multiplicity of study outcomes for the number of comparisons. To prevent overinterpretation of statistical significance, p values for secondary endpoints are not reported. Analyses were done by an independent statistician with SPSS software (version 27) and R software (version 4.4). Further details on the statistical methods are provided in the appendix (pp 18–19).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between Dec 30, 2019, and Jan 15, 2024, 994 patients were enrolled and randomly assigned to receive either immediate complete revascularisation (n=498; immediate group) or staged complete revascularisation (n=496; staged group; figure 1). We were unable to maintain a screening log for the trial. Screening data for the largest recruiting centre (where prospective screening was conducted) are provided in the appendix (pp 24–25). 52 (10%) of 498 patients assigned to the immediate group and 37 (7%) of 496 patients assigned to the staged group did not receive the allocated treatment (figure 1). Median age was 66·0 years (IQR 57·0–76·0). 789 (79%) patients were men, and 205 (21%) were women (table 1). Data on race or ethnicity were not collected. 329 (33%) patients presented with heart failure (Killip class II or III). Mean left ventricular ejection fraction for all participants was 50·0% (SD 10·5). The median length of hospital stay was 4 days (IQR 3–6) in the immediate group and 5 days (IQR 4–8) in the staged group.

Procedural characteristics are shown in table 1 and in the appendix (pp 26–28). 205 (21%) patients had three arteries with stenosis on baseline angiogram, 750 (75%) patients received PCI via radial access, and 257 (26%) patients received PCI with the guidance of intravascular imaging. In the staged group, the median time to the staged procedure was 3 days (IQR 2–4). Crossover from one treatment group to the other occurred in 44 (9%) patients in the immediate group and 15 (3%) patients in the staged group (figure 1). Fractional flow reserve was 0·85 (SD 0·08) as measured in 629 (48%) of 1303 non-culprit lesions, and 518 (82%) of these lesions had a fractional flow reserve value of 0·81 or higher. Revascularisation was done in 410 (63%) of 654 non-culprit lesions in the immediate

group and 359 (55%) of 649 non-culprit lesions in the staged group. Intravascular imaging was used more frequently for treatment of the culprit artery in the immediate group than in the staged group. However, for treatment of the non-culprit artery, the use of intravascular imaging was higher in the staged group than in the immediate group (appendix pp 26–27).

Follow-up at 1 year was completed in 987 (99%) patients. Medication use at discharge and follow-up and blood pressure and laboratory findings at baseline and follow-up are shown in the appendix (pp 29–32). Dual-antiplatelet therapy was used in 691 (70%) patients at 1 year (appendix p 30). Mean LDL cholesterol at 1 year was 56·6 mg/dL (SD 21·9) in the immediate complete revascularisation group and 59·8 mg/dL (23·1) in the staged complete revascularisation group (appendix p 32).

At 1 year, the primary endpoint occurred in 65 (13%) of 498 patients in the immediate complete revascularisation group and 53 (11%) of 496 patients in the staged complete revascularisation group (HR 1·24 [95% CI 0·86–1·79]; $p_{non\text{-}inferiority}$=0·24; table 2; figure 2). There were no significant differences in the rates of individual components of the primary endpoint (death from any cause [table 2; appendix pp 20, 33], non-fatal myocardial infarction [table 2; appendix pp 21, 34], or any unplanned repeat revascularisation [table 2; appendix p 22]). The composite rate of non-fatal and fatal myocardial infarction events was 5% in both groups (appendix p 34). A post-hoc analysis excluding procedure-related myocardial infarction (table 2; appendix p 34) did not change the primary outcome (HR 1·29 [95% CI 0·88–1·87]; appendix p 35). As the usage rate of intravascular imaging differed between the two groups, a post-hoc analysis was conducted adjusting for intravascular imaging use, and the primary outcome between the two groups remained unchanged (HR 1·23 [95% CI 0·86–1·77]; data not shown). The cumulative incidences of other secondary endpoints were similar in the two groups (table 2). Rates of safety endpoints such as stroke, stent thrombosis (appendix p 36), major bleeding, and contrast-induced nephropathy did not differ significantly between the two groups (table 2). Adverse events during hospitalisation are shown in table 3. One patient in the staged complete revascularisation group underwent unplanned revascularisation for a non-culprit lesion before the staged procedure.

In the prespecified analysis of study endpoints at 1 month and 6 months, event rates for the primary endpoint and all secondary endpoints were similar in the two groups (appendix pp 37–38). By the 6-month timepoint, there were more deaths from any cause in the immediate revascularisation group than in the staged revascularisation group (HR 1·89 [95% CI 1·03–3·47]; appendix p 38); however, deaths from any cause was a secondary endpoint, and CIs were not adjusted for multiplicity.

In the per-protocol population (figure 1), a primary endpoint event occurred in 56 (13%) of 446 patients in

	Immediate complete revascularisation group (n=498)	Staged complete revascularisation group (n=496)
(Continued from previous page)		
Baseline SYNTAX score‡	19·5 (6·3)	19·6 (5·9)
Missing data	1 (<1%)	10 (2%)
Residual SYNTAX score‡	5·4 (3·6)	5·4 (3·4)
Missing data	3 (<1%)	11 (2%)
Procedural characteristics		
Thrombus aspiration	109 (22%)	105 (21%)
Use of glycoprotein IIb/IIIa inhibitor	42 (8%)	45 (9%)
Guidance of intravascular imaging	118 (24%)	139 (28%)
Intravascular ultrasonography	55 (11%)	43 (9%)
Optical coherence tomography	63 (13%)	96 (19%)
Time to staged procedure, days	NA	3 (2–4)
Missing data	NA	26 (5%)
Fractional flow reserve in non-culprit lesions‡§	278/654 (43%)	351/649 (54%)
Missing data	2 (<1%)	4 (<1%)
Mean value of fractional flow reserve	0·86 (0·08)	0·85 (0·08)
Fractional flow reserve >0·80	238/278 (86%)	280/351 (80%)
Fractional flow reserve ≤0·80	40/278 (14%)	71/351 (20%)
Revascularisation for non-culprit lesions	410/654 (63%)	359/649 (55%)
Stents used per patient in index procedure	2 (1–2)	1 (1–1)
Stents used per patient in index plus staged procedures	NA	2 (1–2)
Mean diameter of stents in index procedure, mm	3·08 (0·38)	3·09 (0·42)
Missing data	17 (3%)	17 (3%)
Mean diameter of stents in index plus staged procedures, mm	NA	3·07 (0·38)
Missing data	NA	17 (3%)
Total length of stents in index procedure, mm	48 (29–68)	32 (24–48)
Missing data	6 (1%)	17 (3%)
Total length of stents in index plus staged procedures, mm	NA	48 (31–76)
Missing data	NA	16 (3%)
Contrast use in index procedure, mL	180 (140–225)	130 (100–180)
Contrast use in index plus staged procedures, mL	NA	220 (170–298)
Fluoroscopy time for index procedure, min	16·4 (11·3–23·1)	9·5 (6·5–14·6)
Missing data	47 (9%)	43 (9%)
Fluoroscopy time for index plus staged procedures, min	NA	18·5 (13·3–27·6)
Missing data	NA	41 (8%)
Total radiation area dose in index procedure, cGycm²	8140 (5416–11 980)	5388 (3693–8388)
Missing data	51 (10%)	46 (9%)
Total radiation area dose in index plus staged procedures, cGycm²	NA	8985 (6151–13 601)
Missing data	NA	43 (9%)
Total length of hospital stay, days	4 (3–6)	5 (4–8)

Data are mean (SD), median (IQR), n (%), or n/N (%). NA=not applicable. SYNTAX=synergy between percutaneous coronary intervention with taxus and cardiac surgery. Percentages for location of non-culprit lesion sum to more than 100% because some patients had lesions in more than one artery. *Defined as diagnosis of the disease in a male first-degree relative before age 55 years or in a female first-degree relative before age 65 years. †Defined as either a history of chronic kidney disease or receipt of dialysis. ‡Data were obtained at the angiographic core laboratory. §Fractional flow reserve not done in specified patients despite diameter stenosis between 50% and 69% by visual assessment; no patients with diameter stenosis ≥70% by visual assessment received fractional flow reserve.

Table 1: **Baseline and procedural characteristics**

	Immediate complete revascularisation group (n=498)	Staged complete revascularisation group (n=496)	Hazard ratio (95% CI)*
Primary endpoint			
Death from any cause, non-fatal myocardial infarction, or any unplanned repeat revascularisation	65 (13%)	53 (11%)	1·24 (0·86–1·79); $p_{non\text{-}inferiority}$=0·24
Secondary endpoints			
Death from any cause	37 (7%)	26 (5%)	1·44 (0·87–2·38)
Any non-fatal myocardial infarction	19 (4%)	25 (5%)	0·77 (0·42–1·39)
Spontaneous (not procedure-related) myocardial infarction	16 (3%)	17 (3%)	0·95 (0·48–1·89)
Procedure-related myocardial infarction	3 (<1%)	8 (2%)	0·38 (0·10–1·42)
Any unplanned repeat revascularisation	28 (6%)	24 (5%)	1·19 (0·69–2·05)
Death from cardiac cause	28 (6%)	21 (4%)	1·35 (0·77–2·37)
Death from non-cardiac cause	9 (2%)	5 (1%)	1·83 (0·63–5·13)
Target lesion revascularisation	10 (2%)	9 (2%)	1·12 (0·46–2·76)
Target vessel revascularisation	17 (4%)	10 (2%)	1·73 (0·79–3·77)
Non-target vessel revascularisation	17 (4%)	16 (3%)	1·08 (0·55–2·14)
Hospitalisation for unstable angina	27 (6%)	36 (8%)	0·75 (0·46–1·24)
Hospitalisation for heart failure	21 (4%)	25 (5%)	0·85 (0·48–1·52)
Stroke†	18 (4%)	14 (3%)	1·31 (0·65–2·64)
Definite or probable stent thrombosis	10 (2%)	8 (2%)	1·26 (0·50–3·20)
Acute stent thrombosis	8 (2%)	1 (<1%)	8·00 (1·00–63·97)
Major bleeding‡	14 (3%)	21 (4%)	0·66 (0·34–1·31)
Contrast-induced nephropathy§	25/492 (5%)	32/492 (7%)	0·77 (0·45–1·32)¶||

Data are n (Kaplan–Meier estimated % at 1 year), hazard ratio (95% CI), or n/N (%), unless otherwise stated. *Hazard ratios are for immediate complete revascularisation compared with staged complete revascularisation at 1 year; 95% CIs for secondary endpoints have not been adjusted for multiplicity and should not be used to infer treatment effects. †Ischaemic stroke occurred in 14 patients in the immediate group and 12 patients in the staged group; haemorrhagic stroke occurred in four patients in the immediate group and two in the staged group. ‡Bleeding Academic Research Consortium type 3 or 5 indicates major bleeding. §Defined as an increase in serum creatinine level by at least 0·5 mg/dL (≥44·2 µmol/L) or an increase in serum creatinine level to at least 1·25 times the baseline level within 72 h of contrast agent exposure. ¶Odds ratio (with 95% CIs calculated using unadjusted logistic regression) is shown instead of hazard ratio. ||Ten patients (six in the immediate group and four in the staged group) with end-stage renal disease were excluded from the analysis.

Table 2: **Primary and secondary endpoints in the intention-to-treat population**

the immediate group and 46 (10%) of 459 in the staged group (HR 1·28 [95% CI 0·87–1·89]; $p_{non\text{-}inferiority}$=0·31; appendix pp 23, 39). Figure 3 shows the results of the primary endpoint according to the prespecified subgroups. Treatment effect varied according to Killip class, with an increased risk of harm from immediate complete revascularisation for patients with a higher Killip class (II or III) than for those without clinical signs of heart failure (Killip I; $p_{interaction}$=0·04). Among 329 patients with Killip class II or higher, the primary endpoint occurred in 39 (23%) of 171 patients in the immediate group and in 21 (13%) of 158 in the staged group (figure 3). In addition, 23 of 27 cardiogenic shock events (table 3) and nine of 14 early stent thrombosis events (appendix p 36) occurred in patients with Killip class II or III (with all instances occurring during or after PCI for a non-culprit artery).

We also conducted a post-hoc stratified analysis to compare patients who had fractional flow reserve-guided revascularisation with those who had angiography-guided revascularisation (appendix p 41). Among patients who received in-hospital staged complete revascularisation, the incidence of the primary endpoint was significantly lower in the fractional flow reserve group than in the non-fractional flow reserve group.

Three patients (one in the immediate group and two in the staged group) withdrew consent after random assignment, and nine (four in the immediate group and five in the staged group) were subsequently found to be ineligible (figure 1). In a post-hoc sensitivity analysis excluding these patients, the results remained unchanged (appendix p 42).

Discussion

In the OPTION–STEMI trial, immediate complete revascularisation in patients with STEMI and multivessel coronary artery disease was not shown to be non-inferior to staged complete revascularisation during the index admission (with a median time to staged procedure of 3 days [IQR 2–4]) for a primary composite endpoint of death from any cause, non-fatal myocardial infarction, or any unplanned revascularisation at 1 year.

Although complete revascularisation for patients with STEMI and multivessel coronary artery disease has become a standard treatment strategy since around 2019, following the results of several landmark trials such as the PRAMI, CvLPRIT, DANAMI-3–PRIMULTI, Compare-Acute and COMPLETE trials,[3–7] the optimal timing of complete revascularisation remains uncertain. Two large randomised trials comparing immediate and staged complete revascularisation in patients with myocardial infarction showed favourable results for immediate complete revascularisation compared with staged complete revascularisation.[9,10] The Percutaneous Complete Revascularization Strategies Using Sirolimus-Eluting Biodegradable Polymer-Coated Stents in Patients Presenting With Acute Coronary Syndrome and Multivessel Disease (BIOVASC) trial[9] found that immediate complete revascularisation in patients with acute coronary syndrome (approximately 40% of whom had STEMI) was non-inferior to staged complete revascularisation for the primary composite outcome of all-cause death, myocardial infarction, unplanned ischaemia-driven revascularisation, or cerebrovascular events at 1 year. In the Multi-vessel Immediate versus Staged Revascularization in Acute Myocardial Infarction (MULTISTARS AMI) trial,[10] which enrolled only patients with STEMI and multivessel disease, immediate complete revascularisation was also non-inferior to staged complete revascularisation for a similar composite endpoint. The incidence of death from any cause was numerically (but not statistically significantly) higher in the immediate group than in the staged group in our trial as well as in both of these previous trials.[9,10] These findings support the current guideline recommendation that immediate complete revascularisation might be considered for haemodynamically stable

patients with STEMI with multivessel disease.[12] In the STEMI subgroup analysis of the BIOVASC trial, the incidence of the primary endpoint did not differ between the two groups, and death from any cause was also numerically higher in the immediate group than in the staged group (2·3% *vs* 1·3%).[17] The main differences between OPTION–STEMI and previous randomised clinical trials evaluating the timing of complete revascularisation in patients with STEMI and multivessel disease were the timing of the staged procedure and the Killip class distribution of the patients. In OPTION–STEMI, the median time to staged revascularisation was 3 days (IQR 2–4), compared with 15 days (IQR 4–28) in BIOVASC[9] and 37 days (IQR 30–43) in MULTISTARS AMI,[10] and most clinical events in the staged groups in both trials (mainly due to unplanned revascularisation and myocardial infarction) occurred during the early phase after the index procedure, allowing the possibility of a non-culprit lesion progressing before the staged procedure. Higher levels of systemic inflammation (which can promote plaque instability, microvascular dysfunction, and prothrombotic activity) during the acute phase of myocardial infarction might have contributed to these findings.[18] In OPTION–STEMI, in which the staged procedure was completed during the index admission, only one patient in the staged complete revascularisation group underwent unplanned PCI for a non-culprit lesion before the staged procedure. These results suggest that staged revascularisation during the index admission can mitigate the risk of progression of non-culprit lesions.

In this study, more than 30% of patients had acute decompensated heart failure (Killip class II or III). Subgroup analysis suggested heterogeneity in treatment effects by Killip class: immediate complete revascularisation appeared to be associated with worse outcomes in patients with Killip class II or higher, but not in those with Killip class I. Furthermore, our findings of higher numbers of cardiogenic shock events and early stent thrombosis events in patients with Killip class II or III than in patients with Killip class I are partly consistent with the results of the Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock (CULPRIT-SHOCK) trial.[19] CULPRIT-SHOCK showed that immediate multivessel PCI resulted in a greater risk of harm compared with culprit-only PCI in patients with myocardial infarction and multivessel coronary artery disease. Although cardiogenic shock is a more severe haemodynamic state than most cases of acute decompensated heart failure, conducting immediate multivessel PCI in any patient with acutely impaired cardiac function might cause further harm. During the acute phase of myocardial infarction, the myocardium is particularly vulnerable and can be further damaged by a higher contrast volume or by procedural complications during PCI.[18] In this trial, death from any cause was numerically higher in the immediate revascularisation group, which might also be primarily attributable to the high proportion of patients with Killip class II or III. However, there was no difference in clinical outcomes between the two treatment groups in patients with Killip class I; these results are line with the those of previous randomised trials[9,10] that involved more haemodynamically stable patients.

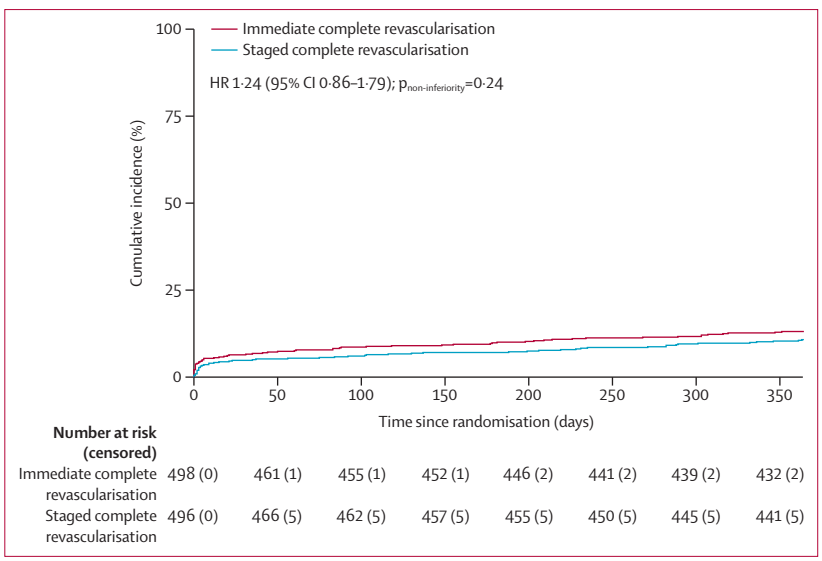

Figure 2: **Kaplan–Meier curves for cumulative incidence of the primary endpoint at 1 year**
The primary endpoint was a composite of death from any cause, non-fatal myocardial infarction (both spontaneous and procedure-related), or any unplanned revascularisation. HR=hazard ratio.

Fractional flow reserve was evaluated for non-culprit lesions with 50–69% diameter stenosis by visual assessment in this trial. However, other trials of fractional flow reserve-guided revascularisation for patients with STEMI assessed fractional flow reserve for non-culprit lesions with a diameter stenosis of 50% or greater.[5,6,20–22] As a result, the mean fractional flow reserve value was higher in OPTION–STEMI than in these other trials, and 82% of the non-culprit lesions that underwent evaluation had a fractional flow reserve value of 0·81 or higher in this trial. In the FFR-Guidance for Complete Nonculprit Revascularization (FULL REVASC) trial,[23] the proportion of fractional flow reserve-evaluated non-culprit lesions with 50–69% diameter stenosis that had a fractional flow reserve value of 0·81 or higher was 66%. One of the reasons for this difference between OPTION–STEMI and FULL REVASC[22] is that FULL REVASC included a higher proportion of patients with non-culprit lesions in the left anterior descending coronary artery compared with OPTION–STEMI. The left anterior descending coronary artery supplies a larger area of the myocardium than the other coronary arteries; therefore, it tends to have lower fractional flow reserve values. Other potential reasons for these findings include possible overestimation of the severity of stenosis and underestimation of the fractional flow reserve value during the index procedure in

	Immediate complete revascularisation group (n=498)	Staged complete revascularisation group (n=496)
Procedural complications		
No-reflow phenomenon	22 (4%)	23 (5%)
Coronary artery perforation	3 (<1%)	3 (<1%)
Coronary artery perforation requiring pericardiocentesis	2 (<1%)	1 (<1%)
Fractional flow reserve-related complications	0/278	3/351 (<1%)*
Need for cardiopulmonary resuscitation	6 (1%)	8 (2%)
Need for mechanical circulatory support†	3 (<1%)	3 (<1%)
Complications during hospitalisation		
Cardiogenic shock	18 (4%)	9 (2%)
Cardiogenic shock in patients with Killip II or III	15/171 (9%)	8/158 (5%)
Need for mechanical circulatory support†	10 (2%)	5 (1%)
New or worsening of heart failure	16 (3%)	15 (3%)
Pulmonary complications‡	9 (2%)	12 (2%)
Anaphylactic reaction to contrast agent	1 (<1%)	0
Critical limb ischaemia	1 (<1%)	1 (<1%)
Mechanical complications of myocardial infarction	2 (<1%)	1 (<1%)
Need for mechanical ventilation	18 (4%)	10 (2%)
Vascular access site-related complications	7 (1%)	7 (1%)
In-hospital clinical events		
Death from any cause	13 (3%)	6 (1%)
Non-fatal myocardial infarction	13 (3%)	13 (3%)
Any unplanned repeat revascularisation	12 (2%)	9 (2%)
Unplanned revascularisation for non-culprit lesions before planned staged procedure	NA	1 (<1%)
Death from cardiac cause	13 (3%)	6 (1%)
Death from non-cardiac cause	0	0
Target lesion revascularisation	9 (2%)	6 (1%)
Target vessel revascularisation	10 (2%)	6 (1%)
Non-target vessel revascularisation	5 (1%)	4 (<1%)
Stroke	7 (1%)	4 (<1%)
Definite or probable stent thrombosis	9 (2%)	5 (1%)
Major bleeding	7 (1%)	14 (3%)

Data are n (%), or n/N (%). NA=not applicable. *Ventricular tachycardia in one patient, coronary dissection in one patient, and significant bradycardia requiring transient pacing in one patient. †All mechanical circulatory supports were venoarterial extracorporeal membrane oxygenation. ‡Pulmonary complications included pneumonia, pulmonary thromboembolism, and pulmonary haemorrhage.

Table 3: **Adverse events during the index hospitalisation**

OPTION–STEMI.[24] The rate of PCI for non-culprit lesions in the current trial was 59%, similar to the rates in other trials of fractional flow reserve-guided revascularisation.[5,6,20–23] Nonetheless, approximately 40% of patients in both groups did not undergo PCI for non-culprit lesions, resulting in both groups receiving culprit-only PCI in these cases. This similarity in treatment might have diluted any true difference between the groups, and therefore the results should be interpreted with caution. A stratified analysis comparing fractional flow reserve-guided revascularisation with angiography-guided revascularisation showed that the incidence of the primary endpoint was lower in the fractional flow reserve group than in the non-fractional flow reserve group in patients who received in-hospital staged complete revascularisation. Although the baseline severity of stenosis in non-culprit lesions could affect outcomes (all non-culprit lesions in the non-fractional flow reserve group had at least a 70% diameter stenosis), these findings suggest that fractional flow reserve might not be reliable in the acute stage of STEMI. Because fractional flow reserve might be underestimated in the acute setting of STEMI due to factors such as alterations in hyperaemic coronary flow, microvascular resistance, and infarct location, current guidelines do not recommend assessment of fractional flow reserve for non-culprit lesions in patients with STEMI.[11,24]

In our trial, there were more unplanned repeat revascularisation events in the immediate group than in the staged group, which appears inconsistent with the numerically lower rate of non-fatal myocardial infarction in the immediate group. This discrepancy was primarily driven by a higher rate of target vessel revascularisation in the immediate group. In patients who underwent target vessel revascularisation (appendix p 44), most events in both groups arose from myocardial infarction, and a high incidence of acute stent thrombosis caused a higher incidence of target vessel revascularisation in the immediate group than in the staged group. Although the number of non-fatal myocardial infarction events was higher in the staged group, this difference was attenuated when fatal events were included, with a composite event rate of 5% in both groups. Furthermore, more procedure-related myocardial infarctions, which are not considered repeat revascularisation events, occurred in the staged group than in the immediate group. The low rate of fractional flow reserve in the immediate group (due to a high rate of non-culprit lesions with ≥70% diameter stenosis) could have been another cause of the higher rate of target vessel revascularisation in this group.

In keeping with the intention-to-treat principle, we retained all randomly assigned participants in the primary analysis, including nine later deemed ineligible and three who withdrew consent after random assignment. We considered that excluding these individuals from the analyses could have reintroduced selection bias and compromised the prognostic balance established by random assignement.[25,26] All eligibility adjudications and consent withdrawals were handled according to the rules set out in the statistical analysis plan before the database lock. A post-hoc sensitivity analysis excluding these subgroups yielded results consistent with the primary analysis.

The findings from OPTION–STEMI should be assessed in the light of its limitations. First, this trial used an open-label design. To help overcome potential bias, members of the clinical events committee were masked to the group assignments, and outcome analyses were conducted using predefined endpoint criteria. Nonetheless, events such as repeat revascularisation were not adjudicated in a blinded manner, as both

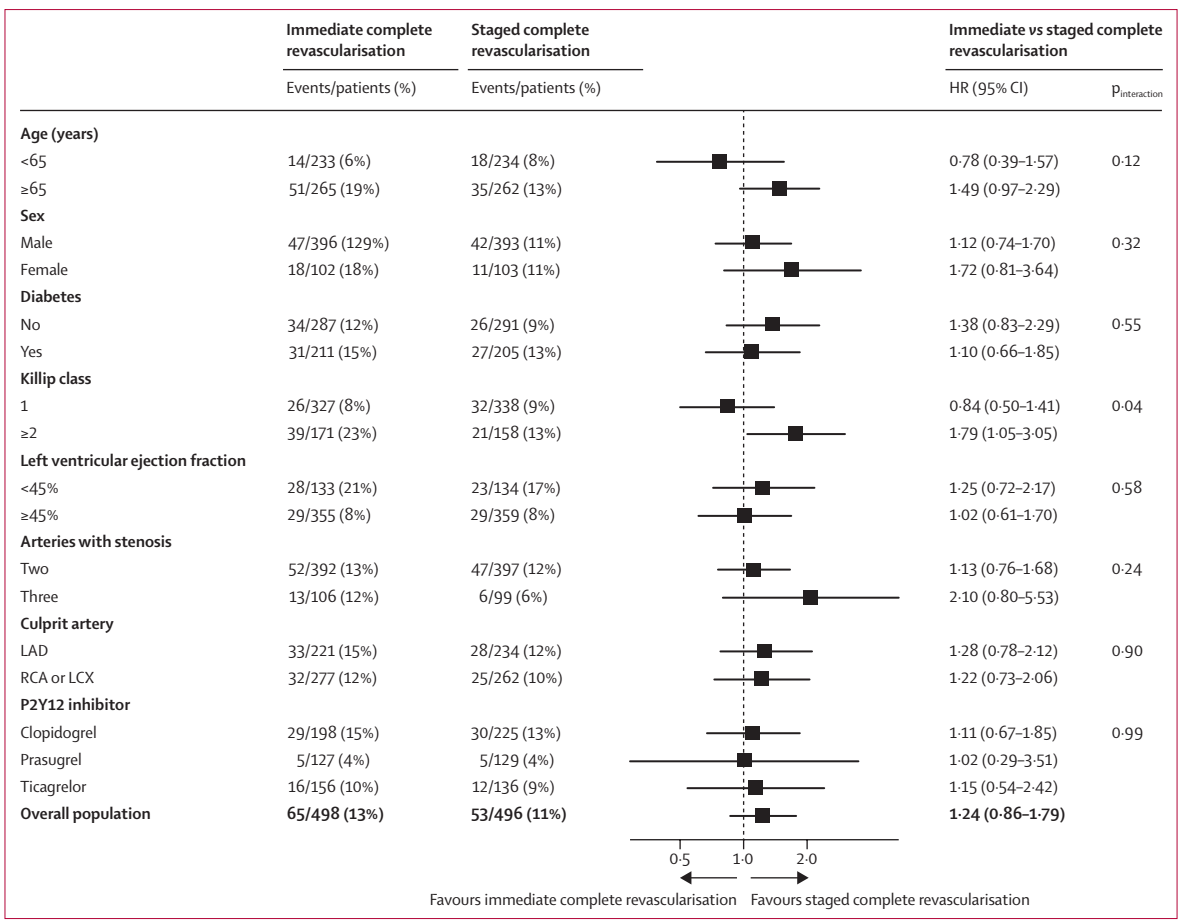

Figure 3: **Subgroup analysis of the primary endpoint**
The forest plot shows numbers of patients with events in the treatment groups overall and in prespecified subgroups at 1 year. The widths of the CIs have not been adjusted for multiplicity and should not be used to infer definitive treatment effects. HR=hazard ratio. LAD=left anterior descending artery. LCX=left circumflex artery. RCA=right coronary artery.

patients and treating physicians were aware of treatment allocation. Therefore, the possibility of bias cannot be fully excluded. Second, more than 80% of the patients were enrolled from a single institution, and the trial included only east Asian patients, which might limit the generalisability of the findings. In the screening log for the largest recruiting centre, only 3% of patients with STEMI were excluded at the operators' discretion, which suggests minimal subjective selection. However, 42% of patients met at least one protocol-defined exclusion criterion, and only 55% of all patients with STEMI presenting during the study period were enrolled. This high rate of exclusion might limit the generalisability of the trial findings to the broader STEMI population. Third, the rate of protocol violation, including crossover to other groups, was high in both groups, exceeding the projected dropout rate of 4%. Thus, the results should be interpreted cautiously. Nonetheless, the results of the per-protocol analyses were similar to those of the intention-to-treat analyses, and the per-protocol population (446 in the immediate group and 459 in the staged group) was larger than the intention-to-treat population in other timing-related trials.[9,10] Fourth, the usage rate of intravascular imaging differed between the two groups. Acute stent thrombosis occurred more frequently in the immediate group than in the staged group despite the higher use of intravascular imaging for culprit lesions in the former. Furthermore, there was no change in the primary outcome between the two groups after adjustment for intravascular imaging use. Fifth, fractional flow reserve for non-culprit lesions was used in the immediate group as well as in the staged group, which is not recommended in current guidelines,[11,24] as already discussed. Furthermore, routine use of fractional flow reserve had no benefit compared with angiographic assessment of non-culprit lesions in several randomised trials.[21,22] Therefore, routine use of fractional flow reserve for lesions with 50–69% diameter stenosis and differences in the timing of fractional flow reserve between the immediate and stage groups could have influenced the results of this study. In addition, a known limitation of fractional flow reserve assessment for

non-culprit lesions is its inability to evaluate plaque characteristics, such as lipid-rich cores or thin fibrous caps, which are associated with future adverse events despite non-flow-limiting physiology.[27] Plaque vulnerability for non-culprit lesions is a well-established predictor of future cardiovascular events. Ongoing randomised controlled trials investigating intravascular imaging evaluation for non-culprit lesions (eg, NCT05812963 and NCT05701358) are expected to provide further insight into this issue. Sixth, higher-than-expected event rates in the immediate group and high early mortality in both groups might have contributed to the wide CIs for the HR of the primary endpoint in this trial, thereby reducing statistical power. Additionally, the 95% CI for the primary endpoint crossed both the line of identity and the prespecified non-inferiority margin. Thus, the most accurate interpretation of our trial is that it did not demonstrate non-inferiority of immediate complete revascularisation compared with staged complete revascularisation during the index admission, and this result should be considered inconclusive.[28] Seventh, the non-inferiority margin in our trial was an HR of 1·42, which is relatively large; however, margins of 1·40 or higher are commonly used in cardiovascular device and pharmacological non-inferiority trials[29] (for example, the non-inferiority margins of the BIOVASC[9] and MULTISTARS AMI[10] trials were 1·39 and 1·46, respectively). Eighth, we conducted multiple testing with 15 study endpoints. Because the statistical analysis plan did not adjust for multiplicity in testing secondary outcomes, these results should be interpreted as exploratory because of the potential for type I error. Ninth, as in many cardiovascular trials, women constituted only about 20% of the study population. Interpretation of the study findings should include the consideration that the guideline recommendations, which generally apply equally to men and women, are frequently based on trials with female under-representation. Tenth, there was an inverse relationship between the number of deaths from any cause and non-fatal myocardial infarctions in this trial, which is an uncommon finding in cardiovascular trials. We believe that this finding is primarily attributable to procedure-related myocardial infarction. Although the difference between the number of deaths from any cause and non-fatal myocardial infarction appeared more pronounced in our study than in previous timing-related trials,[9,10] possibly due to a higher proportion of patients with a higher Killip class, a similar trend has been observed across previous timing-related trials.[9,10] Finally, procedure-related myocardial infarction was included in non-fatal myocardial infarctions as an endpoint. In line with previous trials,[9,10] we acknowledge that the inclusion of procedural-related myocardial infarction might have skewed the findings of this trial.

In conclusion, the findings from OPTION–STEMI are that, for patients with STEMI and multivessel coronary artery disease, immediate complete revascularisation was not shown to be non-inferior to staged complete revascularisation during the index hospitalisation with respect to a composite endpoint of death from any cause, non-fatal myocardial infarction, or any unplanned revascularisation at 1 year. Moreover, the risk of harm from immediate complete revascularisation was greater in patients with Killip class II or higher (ie, those with clinical signs of heart failure) than in those without such signs. Therefore, immediate complete revascularisation might be better limited to haemodynamically stable patients with STEMI at low clinical risk of adverse events who do not have acute heart failure or cardiogenic shock.

Contributors

MCK and YA designed the trial and contributed to final analyses and data interpretation. MCK wrote the first draft and YA revised the manuscript. MCK and JHA analysed the data collected at the core laboratory. MCK and YA accessed and verified all the underlying data. All other authors participated in the enrolment of patients, contributed to clinical follow-up, and revised the manuscript for important intellectual content. All authors had full access to all the data in the study, verified the data, and vouch for the fidelity of the trial to the protocol. All authors approved the final version of the manuscript and had final responsibility for the decision to submit for publication.

Declaration of interests

MCK reports research grants from Medtronic, HK inno.N, and DIO Medical and speaker fees from Hanmi Pharmaceutical and Daiichi Sankyo. KHC reports research grants from Biotronik and Medtronic. SHL reports research grants from Boston Scientific, Abbott Vascular, and the Korean Cardiac Research Foundation; consulting fees from Dotter and Abbott Vascular; and speaker fees from Abbott Vascular, Medtronic, MicroPort, and Norvatis. YJH reports research grants from Boston Scientific, Abbott Vascular, and ChongKunDang; and funding from the South Korean Ministry of Health and Welfare and Republic of Korea Development Institute. Y-HJ reports research grants from Sam Jin Pharmaceutical, Hanmi Pharmaceutical, Yuhan, Biotronik, and U and I Corporation and speaker fees from Daiichi Sankyo, Sanofi-Aventis, Hanmi Pharmaceutical, and Daewoong Pharmaceutical. CJK reports research grants from ChongKunDang. YA reports research grants from Boston Scientific, Pharmicell, Shinpoong Pharmaceutical, Abbott Vascular, Eli Lilly and Company, KyungDong Pharmaceutical, and Medtronic; funding from the Basic Research Laboratory for Vascular Remodeling Research Center, National Research Foundation of Korea, Administrative Office of the Korea-US Collaborative Research Fund, and Cardiovascular Research Foundation. All other authors declare no competing interests.

Data sharing

Individual patient data will not be publicly available, but will be made available upon reasonable request to the corresponding author. The protocol and statistical analysis plan of the OPTION–STEMI trial are provided in the appendix (pp 47–124 for the protocol and pp 125–151 for the statistical analysis plan).

Acknowledgments

This trial was investigator-initiated, with grant support from Boston Scientific. We thank the trial staff members and the other members of the cardiac catheterisation laboratories at the participating centres. We especially thank Eunju Park for their effort to collect clinical data and to ensure the accuracy and completeness of the data. At the time of patient enrolment, MHJ, Y-HJ, J-HL, and SY-Y were affiliated with Chonnam National University Hospital (Gwangju, South Korea), Gyeongsang National University Changwon Hospital (Changwon, South Korea), Yeungnam University Medical Center (Daegu, South Korea), and Gangneung Asan Hospital (Gangneung, South Korea), respectively. The current affiliations are Gwangju Veterans Hospital (Gwangju, South Korea) for MHJ, Chung-Ang University Gwangmyeong Hospital (Gwangmyeong, South Korea) for Y-HJ, Wonju Severance Christian

Hospital (Wonju, South Korea) for J-HL, and Good Morning Hospital (Pyeongtaek, South Korea) for S-YY.

References

1 Park DW, Clare RM, Schulte PJ, et al. Extent, location, and clinical significance of non-infarct-related coronary artery disease among patients with ST-elevation myocardial infarction. *JAMA* 2014; **312:** 2019–27.

2 Sorajja P, Gersh BJ, Cox DA, et al. Impact of multivessel disease on reperfusion success and clinical outcomes in patients undergoing primary percutaneous coronary intervention for acute myocardial infarction. *Eur Heart J* 2007; **28:** 1709–16.

3 Wald DS, Morris JK, Wald NJ, et al, and the PRAMI Investigators. Randomized trial of preventive angioplasty in myocardial infarction. *N Engl J Med* 2013; **369:** 1115–23.

4 Gershlick AH, Khan JN, Kelly DJ, et al. Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multivessel disease: the CvLPRIT trial. *J Am Coll Cardiol* 2015; **65:** 963–72.

5 Engstrøm T, Kelbæk H, Helqvist S, et al, and the DANAMI-3—PRIMULTI Investigators. Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease (DANAMI-3—PRIMULTI): an open-label, randomised controlled trial. *Lancet* 2015; **386:** 665–71.

6 Smits PC, Abdel-Wahab M, Neumann FJ, et al, and the Compare-Acute Investigators. Fractional flow reserve-guided multivessel angioplasty in myocardial infarction. *N Engl J Med* 2017; **376:** 1234–44.

7 Mehta SR, Wood DA, Storey RF, et al, and the COMPLETE Trial Steering Committee and Investigators. Complete revascularization with multivessel PCI for myocardial infarction. *N Engl J Med* 2019; **381:** 1411–21.

8 Biscaglia S, Guiducci V, Escaned J, et al, and the FIRE Trial Investigators. Complete or culprit-only PCI in older patients with myocardial infarction. *N Engl J Med* 2023; **389:** 889–98.

9 Diletti R, den Dekker WK, Bennett J, et al, and the BIOVASC Investigators. Immediate versus staged complete revascularisation in patients presenting with acute coronary syndrome and multivessel coronary disease (BIOVASC): a prospective, open-label, non-inferiority, randomised trial. *Lancet* 2023; **401:** 1172–82.

10 Stähli BE, Varbella F, Linke A, et al, and the MULTISTARS AMI Investigators. Timing of complete revascularization with multivessel PCI for myocardial infarction. *N Engl J Med* 2023; **389:** 1368–79.

11 Byrne RA, Rossello X, Coughlan JJ, et al, and the ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur Heart J* 2023; **44:** 3720–826.

12 Rao SV, O'Donoghue ML, Ruel M, et al. 2025 ACC/AHA/ACEP/NAEMSP/SCAI guideline for the management of patients with acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2025; **151:** e771–862.

13 Kim MC, Ahn JH, Hyun DY, et al, and the OPTION–STEMI Investigators. Timing of fractional flow reserve-guided complete revascularization in patients with ST-segment elevation myocardial infarction with multivessel disease: rationale and design of the OPTION–STEMI trial. *Am Heart J* 2024; **273:** 35–43.

14 Neumann FJ, Sousa-Uva M, Ahlsson A, et al, and the ESC Scientific Document Group. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J* 2019; **40:** 87–165.

15 Thygesen K, Alpert JS, Jaffe AS, et al, and the Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. Fourth universal definition of myocardial infarction (2018). *Circulation* 2018; **138:** e618–51.

16 Garcia-Garcia HM, McFadden EP, Farb A, et al, and the Academic Research Consortium. Standardized end point definitions for coronary intervention trials: the Academic Research Consortium-2 consensus document. *Circulation* 2018; **137:** 2635–50.

17 Scarparo P, Elscot JJ, Kakar H, et al. Immediate versus staged complete revascularisation in patients presenting with STEMI and multivessel disease. *EuroIntervention* 2024; **20:** e865–75.

18 Widimsky P, Holmes DR Jr. How to treat patients with ST-elevation acute myocardial infarction and multi-vessel disease? *Eur Heart J* 2011; **32:** 396–403.

19 Thiele H, Akin I, Sandri M, et al, and the CULPRIT-SHOCK Investigators. PCI strategies in patients with acute myocardial infarction and cardiogenic shock. *N Engl J Med* 2017; **377:** 2419–32.

20 Lee JM, Kim HK, Park KH, et al, and the FRAME-AMI Investigators. Fractional flow reserve versus angiography-guided strategy in acute myocardial infarction with multivessel disease: a randomized trial. *Eur Heart J* 2023; **44:** 473–84.

21 Puymirat E, Cayla G, Simon T, et al, and the FLOWER-MI Study Investigators. Multivessel PCI guided by FFR or angiography for myocardial infarction. *N Engl J Med* 2021; **385:** 297–308.

22 Böhm F, Mogensen B, Engstrøm T, et al, and the FULL REVASC Trial Investigators. FFR-guided complete or culprit-only PCI in patients with myocardial infarction. *N Engl J Med* 2024; **390:** 1481–92.

23 Böhm F, Mogensen B, Östlund O, et al. The Full Revasc (Ffr-gUidance for compLete non-cuLprit REVASCularization) registry-based randomized clinical trial. *Am Heart J* 2021; **241:** 92–100.

24 Thim T, van der Hoeven NW, Musto C, et al. Evaluation and management of nonculprit lesions in STEMI. *JACC Cardiovasc Interv* 2020; **13:** 1145–54.

25 Rehman AM, Ferrand R, Allen E, Simms V, McHugh G, Weiss HA. Exclusion of enrolled participants in randomised controlled trials: what to do with ineligible participants? *BMJ Open* 2020; **10:** e039546.

26 Nüesch E, Trelle S, Reichenbach S, et al. The effects of excluding patients from the analysis in randomised controlled trials: meta-epidemiological study. *BMJ* 2009; **339:** b3244.

27 Park SJ, Ahn JM, Kang DY, et al. Preventive percutaneous coronary intervention versus optimal medical therapy alone for the treatment of vulnerable atherosclerotic coronary plaques (PREVENT): a multicentre, open-label, randomised controlled trial. *Lancet* 2024; **403:** 1753–65.

28 Mauri L, D'Agostino RB Sr. Challenges in the design and interpretation of noninferiority trials. *N Engl J Med* 2017; **377:** 1357–67.

29 Head SJ, Kaul S, Bogers AJ, Kappetein AP. Non-inferiority study design: lessons to be learned from cardiovascular trials. *Eur Heart J* 2012; **33:** 1318–24.