



Deferral of percutaneous coronary intervention in patients undergoing transcatheter aortic valve implantation (PRO-TAVI): an investigator-initiated, multicentre, open-label, non-inferiority, randomised controlled trial

Ronak Delewi*, Hugo M Aarts*, Gijs M Broeze, Kimberley I Hemelrijk, Dirk Jan van Ginkel, Geert A A Versteeg, Maik J Grundeken, Bimmer E P M Claessen, Pim A L Tonino, Carl E Schotborgh, Martijn Meuwissen, Gert K van Houwelingen, Joanna J Wykrzykowska, Giovanni Amoroso, Tessel N Vossenbergh, Pieter A Vriesendorp, Niels van Royen, Jurriën M ten Berg, Jan G P Tijssen, Michiel Voskuil, on behalf of the PRO-TAVI trial investigators†

Summary

Background Coronary artery disease is common in patients undergoing transcatheter aortic valve implantation (TAVI). We aimed to assess whether deferral of percutaneous coronary intervention (PCI) is non-inferior to routine PCI before TAVI in patients with coronary artery disease.

Methods In this investigator-initiated, open-label, randomised controlled trial, done at 12 hospitals in the Netherlands, TAVI patients with coronary artery disease were randomly assigned in a 1:1 ratio to deferral of PCI or PCI before TAVI. Randomisation was done by use of a web-based system with random block sizes of 2 and 4, and stratification by presence of coronary artery disease involving proximal left anterior descending artery. The primary endpoint was a composite of all-cause mortality, myocardial infarction, stroke, and major bleeding at 1 year. Non-inferiority testing was done in the intention-to-treat population against the prespecified margin of 11 percentage points. The study is registered with ClinicalTrials.gov (NCT05078619) and long-term follow-up is ongoing.

Findings Between Oct 7, 2021, and Nov 19, 2024, 466 patients were enrolled: 233 were assigned to deferral of PCI and 233 to PCI before TAVI. Median age was 81 years (IQR 78–84), and 166 (36%) of 466 patients were female. The primary endpoint occurred in 56 (24%) of 233 patients in the deferral group as compared with 60 (26%) of 233 patients in the PCI group (rate difference -1.7% [95% CI -9.5 to 6.2]; hazard ratio 0.89 [95% CI 0.62 – 1.28]; $p=0.0008$ for non-inferiority; $p=0.68$ for superiority).

Interpretation In patients with coronary artery disease undergoing TAVI, deferral of PCI was non-inferior to PCI before TAVI for the 1-year composite of all-cause mortality, myocardial infarction, stroke, and major bleeding. These findings suggest that an initial conservative strategy can be appropriate in selected patients, although patient-tailored treatment decisions remain essential.

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Introduction

Coronary artery disease is a common comorbidity in patients with severe aortic stenosis, affecting around half of patients undergoing transcatheter aortic valve implantation (TAVI).¹ In patients undergoing surgical aortic valve replacement, concomitant coronary artery bypass grafting is recommended.² However, the role of routine percutaneous coronary intervention (PCI) in patients undergoing TAVI remains uncertain, and data to guide practice are scarce.^{2,3} European² and US³ guidelines recommend that PCI should be considered in selected patients with substantial coronary artery disease undergoing TAVI. However, two randomised trials have evaluated PCI strategies in patients undergoing TAVI, with differing results for composite

clinical endpoints, and neither showed a reduction in mortality with PCI.^{5,6} PCI in patients with severe aortic stenosis has historically been considered higher risk because of potential haemodynamic instability.⁷ Furthermore, the use of dual antiplatelet therapy after PCI is associated with increased risk of bleeding in patients undergoing TAVI.^{3,8,9} Therefore, we initiated the Percutaneous Coronary Intervention before Transcatheter Aortic Valve Implantation (PRO-TAVI) trial to evaluate whether a strategy of deferral of PCI in patients with substantial coronary artery disease undergoing TAVI is non-inferior to routine PCI before TAVI with respect to the 1-year composite of all-cause mortality, myocardial infarction, stroke, and major bleeding.

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*Contributed equally

†A complete list of PRO-TAVI trial investigators appears at the end of the Article

Department of Cardiology,
Amsterdam University Medical
Centres, Amsterdam,
Netherlands

(Prof R Delewi MD PhD,
H M Aarts MD, G M Broeze MSc,
K I Hemelrijk MD,
M J Grundeken MD PhD,
B E P M Claessen MD PhD,
Prof J G P Tijssen PhD);

Department of Cardiology,
University Medical Centre
Utrecht, Utrecht, Netherlands

(H M Aarts,
Prof M Voskuil MD PhD);
Department of Cardiology,
St Antonius Hospital,
Nieuwegein, Netherlands

(D J van Ginkel MD,
Prof J M ten Berg MD PhD);
Cardiovascular Research
Institute Maastricht,
Maastricht, Netherlands

(Prof J M ten Berg); Department
of Cardiology, Radboud
University Medical Centre,
Nijmegen, Netherlands

(G A A Versteeg MD,
Prof N van Royen MD PhD);
Department of Cardiology,
Catharina Hospital Eindhoven,
Eindhoven, Netherlands

(Prof P A L Tonino); Department
of Biomedical
Engineering, Technical
University Eindhoven,
Eindhoven, Netherlands

(Prof P A L Tonino); Department
of Cardiology, Haga Hospital,
The Hague, Netherlands
(C E Schotborgh MD);

Department of Cardiology,
Amphia Hospital, Breda,
Netherlands

(M Meuwissen MD PhD);

Department of Cardiology,
Thoraxcentrum Twente,
Medisch Spectrum Twente,
Enschede, Netherlands

(G K van Houwelingen MD PhD);

Department of Cardiology,
Groningen UMC, Groningen,
Netherlands

(J J Wykrzykowska MD PhD);

Department of Cardiology,
OLVG, Amsterdam,
Netherlands

(G Amoroso MD PhD);

Department of Cardiology,
Medical Centre Leeuwarden,
Leeuwarden, Netherlands

(T N Vossen MD PhD);

Department of Cardiology,
Maastricht University Medical
Centre, Maastricht,
Netherlands

(P A Vriesendorp MD PhD)

Correspondence to:

Prof Ronak Delewi, Department
of Cardiology, Amsterdam
University Medical Centres,
1105AZ Amsterdam,
Netherlands
r.delewi@amsterdamumc.nl

Research in context

Evidence before this study

The initiation of the PRO-TAVI trial was accompanied by a systematic review of the literature. We searched PubMed and Embase on July 20, 2022 using terms related to transcatheter aortic valve implantation (TAVI) and percutaneous coronary intervention (PCI) using the search terms: tavi*[Title/Abstract] OR tavr*[Title/Abstract] OR Percutaneous aortic valve*[Title/Abstract] OR Transcatheter Aortic Valve implant*[Title/Abstract] OR transcatheter aortic valve replacement*[Title/Abstract] OR "Transcatheter Aortic Valve Replacement"[MeSH] AND PCI[Title/Abstract] OR percutaneous coronary*[Title/Abstract] OR coronary stenting[Title/Abstract] OR coronary revascularization[Title/Abstract] OR coronary revascularisation[Title/Abstract] OR coronary angioplasty[Title/Abstract] OR PTCA[Title/Abstract] OR percutaneous transluminal coronary angioplasty[Title/Abstract] OR percutaneous coronary intervention[MeSH] and repeated the search on Jan 11, 2026. The only eligible randomised controlled trial initially identified, ACTIVATION, did not show a benefit of PCI in patients with concomitant coronary artery disease undergoing TAVI, but its findings should be interpreted with caution because the trial was prematurely terminated. More recently, a second randomised controlled trial, NOTION-3, showed superiority of PCI in patients with concomitant coronary artery disease undergoing TAVI, primarily driven by a reduction in myocardial infarction and urgent revascularisation. Deferral of PCI has not been investigated by other randomised trials.

Added value of this study

The PRO-TAVI trial provides robust data on the treatment of patients with concomitant coronary artery disease undergoing TAVI, showing non-inferiority of deferral of PCI in patients with concomitant coronary artery disease undergoing TAVI compared with routine PCI before TAVI with respect to the primary composite endpoint of all-cause mortality, myocardial infarction, stroke, and major bleeding. We observed a substantial reduction in major bleeding with deferral of PCI. A small proportion of patients assigned to deferral of PCI ultimately underwent PCI after TAVI, all without major periprocedural complications. This trial adds an important dimension to the results of previous studies.

Implications of all the available evidence

The results of the PRO-TAVI trial indicate that an initial strategy of deferring PCI is a viable option for patients with concomitant coronary artery disease undergoing TAVI. These findings support a more selective, patient-centred approach to revascularisation, enabling heart teams to tailor decisions to individual anatomy, comorbidities, and clinical priorities rather than defaulting to routine PCI before TAVI. Contemporary TAVI practice—including advances in valve design and implantation techniques that facilitate commissural alignment and preserve coronary access—further supports the feasibility and safety of revascularisation after TAVI when clinically indicated. Together, the available evidence broadens the therapeutic options for this population and provides a clearer framework for balancing ischaemic and bleeding risks in routine care.

Methods

Study design and participants

The PRO-TAVI trial was an investigator-initiated, open-label, randomised controlled trial, done at 12 hospitals across the Netherlands. Details about the trial design have been published previously.¹⁰ Patients were eligible if they had an indication for TAVI and clinically significant coronary artery disease (defined as at least one stenosis of 70–99% by visual estimation in a native coronary artery with a minimal diameter of 2.5 mm or in a bypass graft) as confirmed by coronary angiography and the local multidisciplinary heart team. A stenosis between 40% and 70% by visual estimation met the definition of significant coronary artery disease if invasive physiological assessment indicated haemodynamic significance, assessed with fractional flow reserve, instantaneous wave-free ratio, or resting full-cycle ratio. Key exclusion criteria were unprotected left-main coronary artery disease or left-main equivalent, and solitary chronic total occlusion. An overview of eligibility criteria is shown in the appendix (p 8). All coronary angiograms of enrolled patients were assessed by a core laboratory of interventional cardiologists masked to treatment allocation.

Participating patients provided written informed consent. The steering committee was solely responsible for the conduct of the trial, the integrity of the data analysis, and the reporting of results. The trial protocol was approved by the national authorities and the ethics committee of the University Medical Centre Utrecht (21/464), as well as by the institutional review board of each participating centre. The trial protocol is available in the appendix. A detailed overview of sites and their principal investigators, and committee members is presented in the appendix (pp 2–3).

Randomisation and masking

Patients were randomly assigned in a 1:1 ratio to deferral of PCI or to PCI before TAVI. Randomisation was done via a web-based system (Castor Electronic Data Capture, Amsterdam, the Netherlands) using random block sizes of 2 and 4. Allocation was stratified according to the presence of coronary artery disease involving the proximal left anterior descending artery, defined as segment 6 in the Synergy between PCI with TAXUS and Cardiac Surgery (SYNTAX) score. Participating centres were unaware of randomisation allocation at other sites.

See Online for appendix

Procedures

In the PCI group, patients underwent PCI before TAVI, preferably within 2 weeks of randomisation. In the deferral group, patients were not scheduled to undergo routine PCI after TAVI unless clinically indicated (eg, persisting anginal symptoms or signs of ischaemia). The strategy and execution of the PCI procedure were left to operator's discretion.

The TAVI procedure, including the primary access route and the type of transcatheter heart valve, was left to the discretion of local multidisciplinary heart teams and was advised to be done within 8 weeks of randomisation.

After TAVI, all patients received low-dose aspirin or oral anticoagulation if indicated. After PCI, patients received dual antiplatelet therapy or single antiplatelet therapy on top of oral anticoagulation if indicated, in accordance with international guidelines.¹¹ Oral anticoagulation was routinely interrupted during TAVI, whereas dual antiplatelet therapy was continued.

Follow-up was done in person or by telephone at 4 and 12 months after randomisation.

Outcomes

The primary endpoint was a composite of all-cause mortality, myocardial infarction, stroke, or major bleeding at 1 year after randomisation. Endpoint definitions followed the Valve Academic Research Consortium 3 (VARC-3), and major bleeding consisted of VARC-3 type 2, 3, or 4 bleeding.¹² Secondary endpoints included the individual components of the primary endpoint and a composite of all-cause mortality, myocardial infarction, and stroke. A complete list of endpoints and definitions is shown in the appendix (pp 9–16). All clinical endpoints were prespecified, and no exploratory outcomes were analysed.

Statistical analysis

The primary endpoint was analysed according to the intention-to-treat principle, including all randomly assigned patients. The 1-year cumulative incidence of the primary endpoint was estimated using Kaplan–Meier methods. For non-inferiority testing, the 1-year rate difference and its 95% CI between the deferral group and PCI group were compared with the prespecified non-inferiority margin of 11 percentage points. Non-inferiority of deferral of PCI was concluded if the upper boundary of the 95% CI for the rate difference was below 11 percentage points, corresponding to a one-sided α level of 2.5%. If non-inferiority was shown, we planned to test for superiority. Sensitivity analyses of the primary endpoint were done in the per-protocol population (defined as all patients who adhered to their assigned treatment), and with the win ratio method.¹³

The sample size calculation assumed a 1-year primary outcome event rate of 15% in both groups.^{8,14} A total of 444 patients would provide 90% power to show

non-inferiority under these assumptions. A sample size of 466 patients was chosen to allow for an anticipated loss to follow-up of 5%.

For time-to-event secondary outcomes, hazard ratios (HRs) and 95% CIs were estimated by use of Cox proportional hazard regression. The proportional hazard assumption was tested with Schoenfeld residuals. CIs were not adjusted for multiplicity and should not be for formal hypothesis testing. Statistical analyses were done with IBM SPSS Statistics version 31.0.0.0 and RStudio, version 2023.12.1.

An independent data and safety monitoring board provided oversight of patient safety. A clinical event committee, unaware of treatment allocation, adjudicated all events potentially related to the primary and secondary endpoints, using source documentation incorporating clinical examinations and imaging studies. The trial was registered at Clinicaltrials.gov (NCT05078619), and long-term follow-up is ongoing.

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

From Oct 7, 2021, to Nov 19, 2024, 466 patients were enrolled in the trial; 233 were randomly assigned to the deferral group and 233 to the PCI group (figure 1). Four patients did not adhere to their treatment allocation (one patient in the deferral group and three patients in the PCI group).

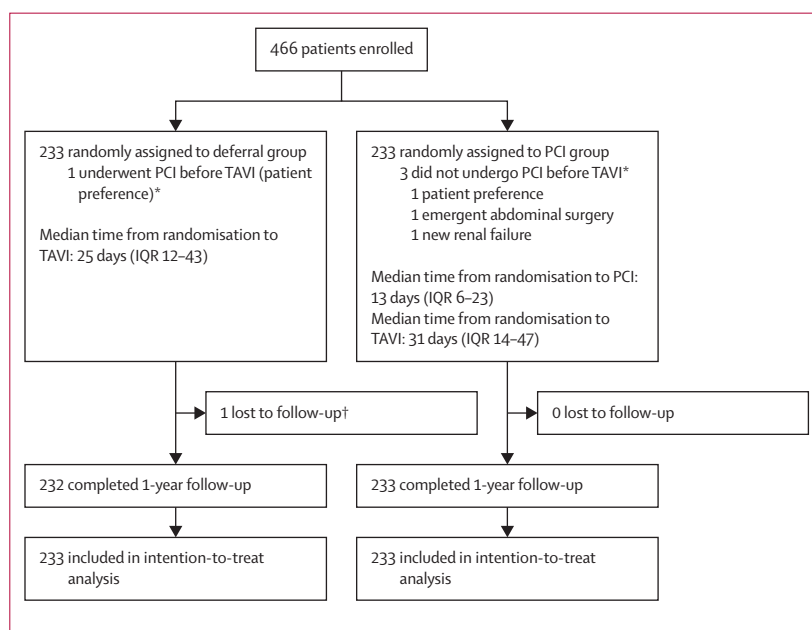


Figure 1: Trial profile

PCI=percutaneous coronary intervention. TAVI=transcatheter aortic valve implantation. *Not included in the per-protocol analysis. †Patient lost to follow-up at day 150.

	Deferral group (n=233)	PCI group (n=233)
Patient characteristics		
Age, years	81 (77–84)	81 (78–84)
Sex		
Female	84 (36%)	82 (35%)
Male	149 (64%)	151 (65%)
BMI, kg/m ²	25.9 (23.6–29.0)	26.0 (23.8–29.3)
New York Heart Association functional class		
I or II	110 (47%)	117 (50%)
III or IV	123 (53%)	116 (50%)
Angina	85 (36%)	103 (44%)
Frailty*	34 (15%)	45 (19%)
Medical history		
Previous myocardial infarction	46 (20%)	57 (24%)
Previous PCI	47 (20%)	51 (22%)
Previous coronary artery bypass graft	13 (6%)	19 (8%)
Previous surgical aortic valve replacement	5 (2%)	8 (3%)
Previous stroke	19 (8%)	22 (9%)
Atrial fibrillation	80 (34%)	82 (35%)
Peripheral vascular disease	41 (18%)	40 (17%)
Diabetes	75 (32%)	75 (32%)
Hypertension	154 (66%)	157 (67%)
Hypercholesterolaemia	148 (64%)	151 (65%)
Oral anticoagulants	83 (36%)	86 (37%)
Risk scores		
STS-PROM score	3.1 (1.9–4.9)	3.1 (2.0–5.2)
EuroSCORE II	2.9 (1.9–4.3)	2.9 (2.1–4.9)
Echocardiographic characteristics		
Aortic valve area, cm ²	0.8 (0.7–0.9)	0.8 (0.7–0.9)
Peak pressure gradient, mm Hg	68 (55–84)	66 (52–78)
Mean pressure gradient, mm Hg	41 (33–49)	39 (31–46)
Left ventricular ejection fraction		
Preserved ejection fraction, ≥50%	175 (75%)	166 (71%)
Mildly reduced ejection fraction, 41–49%	28 (12%)	25 (11%)
Reduced ejection fraction, ≤40%	30 (13%)	42 (18%)
Bicuspid aortic valve†	7/232 (3%)	5 (2%)
Moderate or severe aortic regurgitation‡	38/231 (16%)	44 (19%)
Angiographic characteristics		
SYNTAX score	10 (6–17)	10 (5–17)
Invasive physiological assessment	32 (14%)	33 (14%)
Triple-vessel disease	30 (13%)	29 (12%)
Proximal left anterior descending artery	50 (21%)	50 (21%)
Proximal lesion	133 (57%)	136 (58%)
Coronary stenosis severity		
Coronary lesion with stenosis >90%	139 (60%)	139 (60%)
Coronary lesion with stenosis 70–90%	77 (33%)	80 (34%)
Coronary lesion with stenosis 40–70%	17 (7%)	14 (6%)

Data are median (IQR), n (%), or n/N (%). EuroSCORE=European System for Cardiac Operative Risk Evaluation. PCI=percutaneous coronary intervention. STS-PROM=Society of Thoracic Surgeons Predicted Risk of Mortality. SYNTAX=Synergy between PCI with TAXUS and Cardiac Surgery. TAVI=transcatheter aortic valve implantation. *Frailty was assessed using the Edmonton frailty scale, ranging from 0 to 18 and frailty defined as a score above 5. †Denominators vary due to missing echocardiography data at baseline.

Table 1: Baseline characteristics

	Deferral group (n=233)	PCI group (n=233)
PCI*		
Time from randomisation to PCI procedure, days	..	13 (6–23)
Timing of PCI procedure†		
Before TAVI procedure	..	213/229 (93%)
Concomitantly with TAVI procedure	..	15/229 (7%)
Multivessel PCI	..	63/229 (28%)
Median total length of stents, mm	..	28 (18–44)
Drug-eluting stent	..	209/229 (91%)
Calcium modification	..	16/229 (7%)
Residual SYNTAX score	..	0 (0–6)
TAVI procedure characteristics		
TAVI performed‡	229 (98%)	230 (99%)
Time from randomisation to TAVI procedure, days	25 (12–43)	31 (14–47)
Transfemoral access route	214/229 (93%)	214/230 (93%)
Local anaesthesia without conscious sedation	198/229 (86%)	191/230 (83%)
Balloon-expandable transcatheter heart valve§	125/228 (55%)	117/229 (51%)
Cerebral protection	6/229 (3%)	3/230 (1%)
Predilatation	125/229 (55%)	130/230 (57%)
Postdilatation	38/229 (17%)	38/230 (17%)

Data are median (IQR), n/N (%), or n (%). PCI=percutaneous coronary intervention. SYNTAX=Synergy between PCI with TAXUS and Cardiac Surgery. TAVI=transcatheter aortic valve implantation. *Four patients did not undergo PCI (one patient died before PCI; one patient chose not to undergo PCI; one patient underwent emergent abdominal surgery; and one patient due to new renal failure). †One patient underwent elective PCI after urgent non-transfemoral TAVI. ‡Seven patients did not undergo TAVI (six died before TAVI, whereas one patient in the deferral group chose not to undergo TAVI). §Two TAVI procedures were not accompanied by the implantation of a transcatheter heart valve due to procedural difficulties.

Table 2: Characteristics of the PCI and TAVI procedures

Baseline characteristics of the enrolled patients are shown in table 1. Median age was 81 years (IQR 78–84), and 166 (36%) of 466 patients were female. The median Society of Thoracic Surgeons Predicted Risk of Mortality score was 3.1% (IQR 1.9–5.0%). Coronary artery disease complexity was characterised by a median SYNTAX score of 10 (IQR 5–17). An overview of bleeding risk factors and medical therapy details are shown in the appendix

Figure 2: Time-to-event Kaplan–Meier curves for the primary composite endpoint and its individual components

Kaplan–Meier curves show the primary composite endpoint of all-cause mortality, myocardial infarction, stroke, or major bleeding (A), and the individual components of all-cause mortality (B), myocardial infarction (C), stroke (D), and major bleeding (E), in patients with significant coronary artery disease undergoing TAVI with deferral of PCI or PCI before TAVI. Event rates were based on Kaplan–Meier estimates in time-to-first-event analyses. HR=hazard ratio. PCI=percutaneous coronary intervention. TAVI=transcatheter aortic valve implantation.

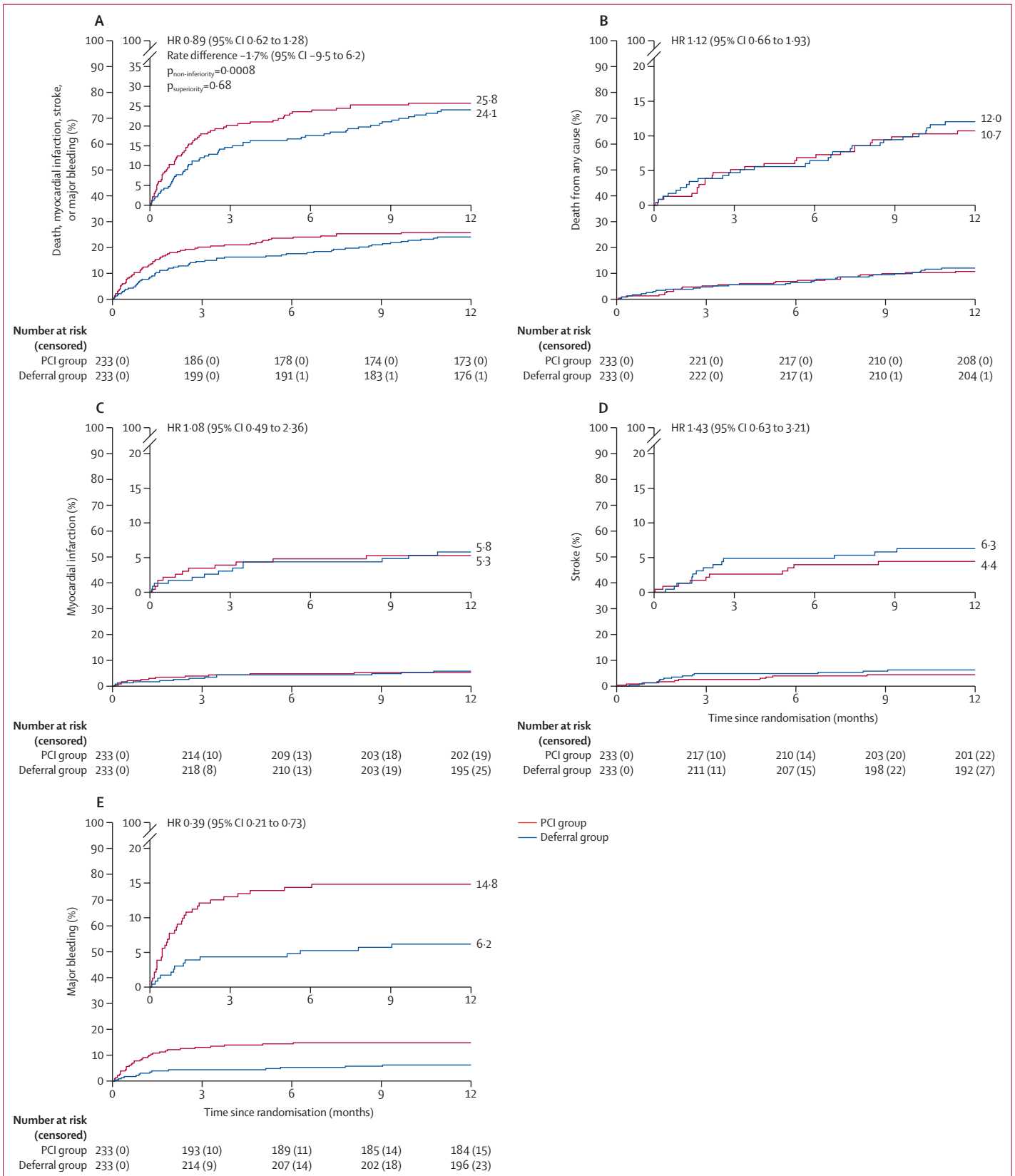
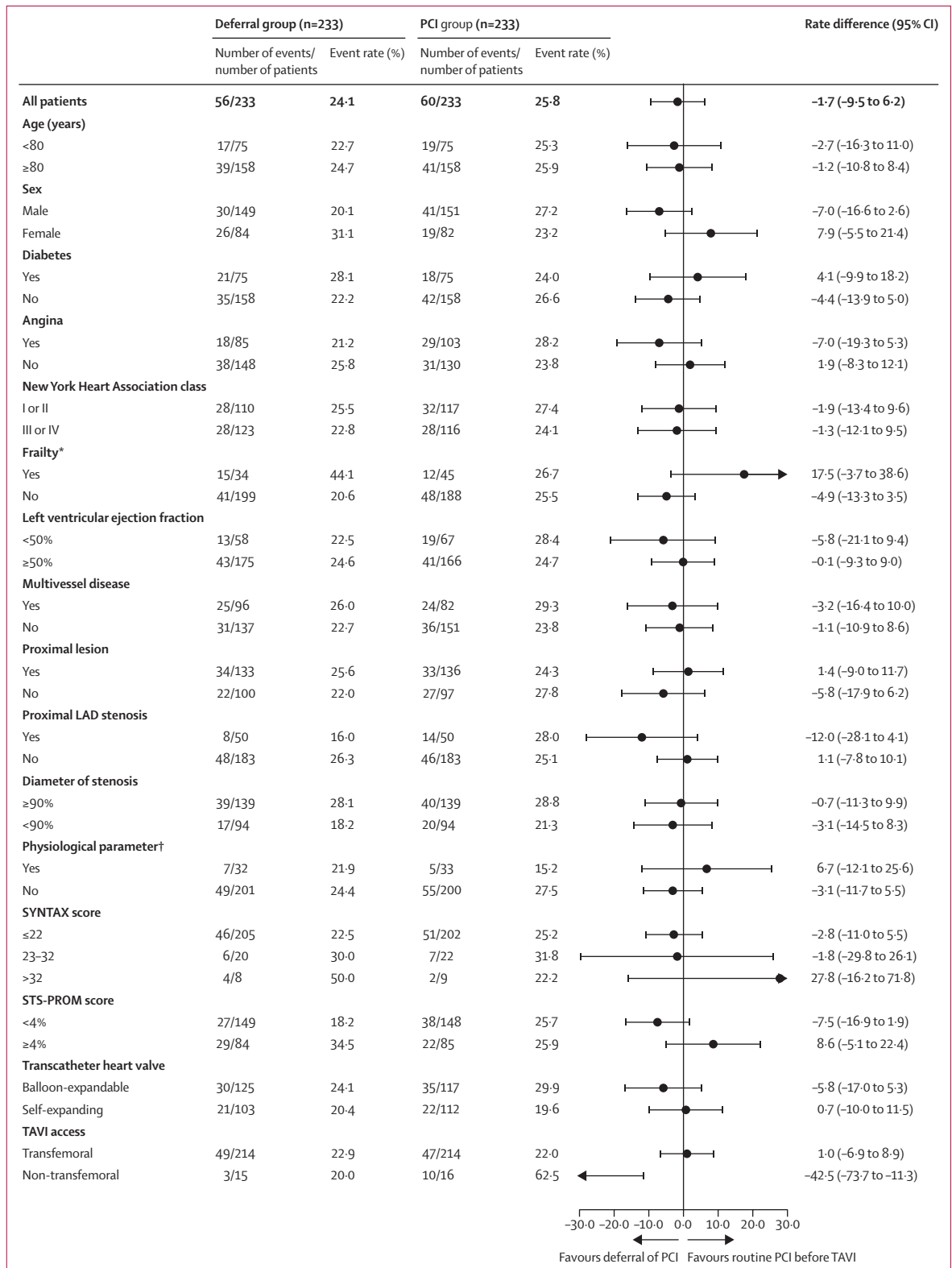


Figure 3: Subgroup analyses of the primary composite endpoint of all-cause mortality, myocardial infarction, stroke, and major bleeding

Subgroup analyses are shown for prespecified baseline and procedural characteristics. All percentages are Kaplan–Meier estimates. Patients were included in subgroup analyses if they had at least one lesion that fulfilled subgroup criteria. LAD=left anterior descending artery. PCI=percutaneous coronary intervention. STS-PROM=Society of Thoracic Surgeon Predicted Risk of Mortality. SYNTAX=Synergy between PCI with TAXUS and Cardiac Surgery. TAVI=transcatheter aortic valve implantation. *Frailty was assessed using the Edmonton frailty scale, ranging from 0 to 18 and frailty defined as a score above 5. †Physiological parameters included fractional flow reserve, and instantaneous wave-free ratio.



(pp 17–18). Data on race and ethnicity were not collected because such information is not routinely recorded in Dutch heart centres as it warrants additional approval by national authorities and ethics committees.

Median time between randomisation and allocated PCI was 13 days (IQR 6–23). PCI was done before TAVI in 213 (93%) of 229 patients. Median time between randomisation and TAVI was 25 days (IQR 12–43) in the deferral group, and 31 days (14–47) in the PCI group. A total of 242 (53%) of 457 patients underwent TAVI with a balloon-expandable transcatheter heart valve. The procedural characteristics of PCI and TAVI are given in table 2. Antithrombotic regimens used during TAVI admission are shown in the appendix (p 18).

Data regarding the occurrence of the primary endpoint at 1 year were available for 465 (>99%) of 466 patients. In the intention-to-treat analysis (n=466), the composite of all-cause mortality, myocardial infarction, stroke, or major bleeding occurred in 56 (24%) of 233 patients in the deferral group as compared with 60 (26%) of 233 patients in the PCI group. The rate difference between the deferral group and the PCI group was –1.7%

(95% CI –9.5 to 6.2; HR 0.89 [95% CI 0.62 to 1.28]; figure 2A), which met the requirement for non-inferiority (p=0.0008) but not for superiority (p=0.68). No clear heterogeneity was observed across prespecified subgroups (figure 3). The only subgroup with a rate difference 95% CI not crossing 0 was the small non-transfemoral access subgroup, and this estimate should be interpreted cautiously.

The per-protocol analysis (n=462) showed consistent effect estimates, with a rate difference of –1.5% (95% CI –9.4 to 6.4; HR 0.89 [95% CI 0.62–1.29]). Details are presented in the appendix (pp 5, 19). The hierarchical win ratio was consistent with the results of the intention-to-treat and per-protocol analysis (HR 1.04 [95% CI 0.72–1.49]; appendix p 6).

The individual components of the primary endpoint are displayed in figures 2B–E and table 3. Major bleeding occurred in 14 (6%) of 233 patients in the deferral group and 34 (15%) of 233 patients in the PCI group (HR 0.39 [95% CI 0.21–0.73]; table 3; figure 2E). In the deferral group, seven (3%) of 233 patients had major access-site related bleeding, whereas 20 (9%) of 233 patients in the

	Deferral group (n=233)*		PCI group (n=233)		Rate difference (95% CI)	Hazard ratio (95% CI)
	Events, n	Event rate, † %	Events, n	Event rate, † %		
Primary endpoint‡						
Composite of all-cause mortality, myocardial infarction, stroke, or major bleeding	56	24%	60	26%	–1.7 (–9.5 to 6.2)	0.89 (0.62 to 1.28)
Secondary endpoints						
Composite of all-cause mortality, myocardial infarction, or stroke	48	21%	38	16%	4.3 (–2.7 to 11.4)	1.28 (0.84 to 1.96)
Death from any cause	28	12%	25	11%	1.3 (–4.5 to 7.1)	1.12 (0.66 to 1.93)
Cardiovascular death	17	7%	16	7%	0.4 (–4.3 to 5.2)	1.07 (0.54 to 2.11)
Myocardial infarction§	13	6%	12	5%	0.5 (–3.7 to 4.8)	1.08 (0.49 to 2.36)
Stroke	14	6%	10	4%	1.8 (–2.3 to 6.0)	1.43 (0.63 to 3.21)
Any bleeding, VARC-3 types I–IV	40	18%	98	43%	–25.1 (–33.2 to –17.0)	0.34 (0.24 to 0.50)
I	26	11%	73	32%
II	4	2%	15	7%
III	8	4%	18	8%
IV	2	1%	3	1%
Major bleeding, VARC-3 types II, III, IV	14	6%	34	15%	–8.6 (–14.2 to –3.1)	0.39 (0.21 to 0.73)
Any revascularisation¶	24	11%	11	5%	6.0 (1.0 to 10.9)	2.20 (1.08 to 4.50)
Urgent revascularisation	13	6%	7	3%	2.7 (–1.1 to 6.5)	1.86 (0.74 to 4.66)
Study lesion revascularisation**	18	8%	7	3%	5.0 (0.8 to 9.3)	2.59 (1.08 to 6.21)
Acute kidney injury stage 3 and 4	1	<1%	3	1%	–0.9 (–2.6 to 0.8)	0.33 (0.03 to 3.18)
Hospitalisation	72	32%	79	35%	–2.4 (–11.2 to 6.3)	0.88 (0.64 to 1.21)

PCI=percutaneous coronary intervention. TAVI=transcatheter aortic valve implantation. VARC-3=third Valve Academic Research Consortium. *One patient was lost to follow-up (day 150) without any event prior to this date. †Event rates based on 1-year Kaplan–Meier estimates in time-to-first-event analyses. ‡p=0.0008 for non-inferiority; hazard ratio should be interpreted as exploratory given that the proportional hazard assumption was violated. §Type 4 and 5 myocardial infarction in three patients (1.3%) in the deferral group, and in two patients (0.9%) in the PCI group. ¶Excluding index PCI procedures (one procedure due to protocol violation in the deferral group, 229 procedures in the PCI group). ||Urgent revascularisation included all procedures that were done in an urgent, emergent, or salvage setting, adjudicated in accordance with the American College of Cardiology's and American Heart Association's Key Data Elements and Definitions for Cardiovascular Endpoint Events in Clinical Trials. **Study lesion was defined as the study segment including the 5 mm margin proximal and distal to stent. In the deferral group, study lesion revascularisation was defined as a PCI of the study lesion. In the PCI group, study lesion revascularisation was defined as (recurrent) PCI of the study lesion.

Table 3: Primary and secondary endpoints

PCI group had major access-site related bleeding. The composite of all-cause mortality, myocardial infarction, and stroke occurred in 48 (21%) patients in the deferral group and in 38 (16%) of 233 patients in the PCI group (rate difference 4.3% [95% CI -2.7 to 11.4]; HR 1.28 [95% CI 0.84 to 1.96]; table 3; appendix p 7).

The results for the secondary endpoints are shown in table 3. Severe acute kidney injury was observed in one (<1%) of 233 patients in the deferral group as compared with three (1%) of 233 patients in the PCI group. In the deferral group, 24 (11%) of 233 patients underwent PCI after random assignment, with a median time of 87 days between randomisation and the procedure (IQR 51–218 days). Of these, 13 (6%) of 233 patients required urgent revascularisation and 11 (5%) underwent elective revascularisation (nine patients due to cardiac symptoms and two asymptomatic patients due to treating physician's preference). All procedures were done without major periprocedural complications. Anginal status and heart failure symptoms at 1 year are shown in the appendix (p 20).

Discussion

In patients with significant coronary artery disease undergoing TAVI, deferral was found to be non-inferior to the TAVI with preceding PCI strategy with respect to the composite of all-cause mortality, myocardial infarction, stroke, and major bleeding at 1 year.

Significant coronary artery disease is common in patients undergoing TAVI and is often identified during routine preprocedural evaluation with computed tomography or coronary angiography.^{1,15} The optimal management of significant coronary artery disease in patients undergoing TAVI remains uncertain. Observational studies have not shown a clear benefit of PCI in this setting.^{3,16} In 2021, ACTIVATION was the first randomised trial to evaluate routine PCI before TAVI in patients with significant coronary artery disease and did not show non-inferiority of PCI with respect to the composite primary endpoint of all-cause mortality and rehospitalisation.⁶ PCI before TAVI was also associated with a higher risk of bleeding. However, the trial enrolled fewer patients than originally planned and recruitment extended over 7 years. Moreover, the trial reflects a different era in TAVI practice. In the recent NOTION-3 trial, 455 patients with significant coronary artery disease undergoing TAVI were randomly assigned to either PCI or conservative management.⁷ Significant coronary artery disease was defined as a fractional flow reserve of 0.80 or less or a coronary lesion with a stenosis of at least 90% by visual estimation. PCI was associated with a lower incidence of the composite of all-cause mortality, myocardial infarction, and urgent revascularisation at a median follow-up of 2 years. This difference was mainly driven by lower rates of myocardial infarction and urgent revascularisation in the PCI group. Patients undergoing PCI also had a higher risk of bleeding, consistent with observations from the ACTIVATION trial.

The PRO-TAVI trial showed non-inferiority of a strategy of deferral of routine PCI compared with PCI before TAVI. The composite endpoint included both ischaemic and bleeding events, capturing potential trade-offs associated with PCI deferral. Non-inferiority was largely driven by a lower incidence of major bleeding in the deferral group, likely attributable to the omission of dual antiplatelet therapy; other bleeding risk factors were similar between groups. Major bleeding after TAVI has been associated with worse long-term clinical outcomes and quality of life.^{9,17,18} Deferral of PCI was associated with a numerically higher incidence of the ischaemic composite endpoint of all-cause mortality, myocardial infarction, and stroke. The non-inferiority finding of the current trial should therefore not be interpreted as ischaemic equivalence. These findings also differ from those of the NOTION-3 trial, which reported a reduction in myocardial infarction and urgent revascularisation with PCI.⁷ However, our observations are broadly consistent with evidence from trials in patients with stable coronary artery disease without concomitant valvular disease, in which routine revascularisation did not reduce the risk of death or myocardial infarction.^{19–21} In the PRO-TAVI trial, only 24 of 233 patients assigned to the conservative strategy ultimately underwent PCI during follow-up. Revascularisation after TAVI was feasible and few procedural complications were reported. Coronary access after TAVI has improved with newer valve designs, although it can still be challenging in some cases.^{22,23} These findings suggest that a strategy of deferring PCI until clinically indicated after TAVI can be feasible for many patients undergoing TAVI.

The severity of coronary artery disease in enrolled patients was modest, with a median SYNTAX score of 10, similar to that reported in the NOTION-3 trial (median SYNTAX score of 9).⁷ The proportions of patients with coronary artery lesions exceeding 90% stenosis were also similar between the two trials. These findings are broadly consistent with a previous meta-analysis of patients with coronary artery disease undergoing TAVI, in which the mean baseline SYNTAX score was approximately 14 among 3994 patients.²⁴ Moreover, the PRO-TAVI cohort included patients across a broad spectrum of anginal symptoms, including Canadian Cardiovascular Society classes III and IV angina. In contrast, ACTIVATION primarily enrolled patients with few or no anginal symptoms.⁶ In the PRO-TAVI trial, patients were enrolled predominantly on the basis of angiographic findings, with invasive physiological assessment used in 65 (14%) of 466 patients. Physiological assessment was encouraged for intermediate stenoses but not mandatory because its clinical value in patients with severe aortic stenosis remains uncertain.^{25–27} The FAITAVI trial recently reported that fractional flow reserve-guided PCI was associated with a lower incidence of major adverse cardiac and cerebrovascular events at 12 months in

patients undergoing TAVI, although this finding was primarily driven by non-cardiovascular death.²⁸ Further studies are needed to clarify the optimal role of invasive physiological assessment in patients with aortic stenosis and concomitant coronary artery disease.

Routine revascularisation in patients with significant coronary artery disease undergoing TAVI has not received a class I recommendation in US and European guidelines.²⁴ The 2025 European guidelines state that PCI should be considered in patients with high-grade coronary artery lesions exceeding 90% stenosis (class IIa recommendation).² In this context, the PRO-TAVI trial suggests that a conservative strategy with deferral of routine PCI might be feasible and associated with a lower incidence of major bleeding. Deferral of PCI might help to avoid unnecessary invasive procedures and reduce health-care costs and patient burden—considerations that are especially relevant for older, comorbid patients undergoing TAVI.

Decision making by multidisciplinary heart teams remains central to the management of these patients. Such an approach allows assessment of both ischaemic and bleeding risks, facilitating optimal patient selection and procedural planning. In particular, the heart team plays a central role for patients at high bleeding risk or in those in whom coronary access after TAVI is anticipated to be technically challenging.

This trial has several limitations. First, the open-label design meant that investigators and patients were aware of treatment allocation. To minimise potential bias, we assessed hard clinical endpoints with standardised definitions, and endpoints were adjudicated by an independent clinical event committee that was unaware of treatment allocation. Second, non-inferiority was tested against a relatively wide prespecified margin of 11 percentage points. In addition, the observed bleeding rates (6% in the deferral group and 15% in the PCI group) were substantially higher than those assumed in the study design (1–2%), meaning that a key assumption underlying the sample size calculation was not met. These departures from the original design assumptions should be carefully considered when interpreting the study's findings. Third, our results apply only to patients fulfilling trial eligibility criteria, which excluded those with unprotected left main coronary artery disease and contributed to the relatively low coronary complexity observed in the study population. Similarly, none of the enrolled patients underwent repeat TAVI, and only 3% had previously undergone surgical aortic valve replacement, which can affect future coronary access. Furthermore, the median age of the enrolled patient was 81 years, consistent with the indications for TAVI at the time of enrolment. These findings should therefore be interpreted with caution when extrapolating to future TAVI populations, which might include younger patients. Fourth, bleeding-risk classification could not be fully assessed according to all relevant variables defined

in the VARC high bleeding risk consensus document, which was published after the trial had commenced. Fifth, outcomes are reported at 1-year follow-up, although longer-term follow-up is planned. Longer-term data will provide valuable insights, especially as TAVI is increasingly done in younger patients with longer anticipated survival. Lastly, the results reflect practice across Dutch heart centres, and although the Dutch health-care system's structured heart-team pathways share similarities with many other high-income countries, these findings might not be generalisable to other health-care systems, particularly where close follow-up and timely revascularisation are less common.

In conclusion, deferral in patients with significant coronary artery disease undergoing TAVI was non-inferior to PCI before TAVI for the 1-year composite of all-cause mortality, myocardial infarction, stroke, or major bleeding.

PRO-TAVI trial investigators

Ronak Delewi, Hugo M Aarts, Gijs M Broeze, Kimberley I Hemelrijk, Dirk Jan van Ginkel, Geert A A Versteeg, Daniel C Overduin, Marcel A M Beijk, Jan Baan, Marije M Vis, Jorrit S Lemkes, Robbert J de Winter, Michael G Dickinson, Adriaan O Kraaijeveld, Mostafa M Mokhles, Thomas C Dessing, Pim van der Harst, Geert E H Leenders, Frank van der Kley, Maik J Grundeken, Bimmer E P M Claessen, Pim A L Tonino, Carl E Schotborgh, Martijn Meuwissen, Gert K van Houwelingen, Joanna J Wykrzykowska, Giovanni Amoroso, Tessel N Vossenber, Pieter A Vriesendorp, Niels van Royen, Jurriën M ten Berg, Jan G P Tijssen, and Michiel Voskuil.

Contributors

RD and MV designed the trial and wrote the protocol together with HMA. RD, HMA, GMB, and MV accessed and verified the data. RD, HMA, GMB, JGPT, and MV interpreted the data and wrote the manuscript, which was revised by KIH, DJvG, GAAV, MJG, BEPMC, PALT, CES, MM, GKvH, JJW, GA, TNV, PAV, NvR, and JMtB. All authors had access to all the included data and had final responsibility for the decision to submit for publication.

Declaration of interests

RD reports educational or research grants from Boston Scientific, Abiomed, Edwards Lifesciences, Sanofi, Meril Life, Novartis, and Amgen. MAMB reports speakers fees from Edwards Lifesciences and Abbott Medical Nederland. FvdK reports consulting or speaker fees from Abbott Vascular, Edwards Lifesciences, and Boston Scientific. MJG reports an unrestricted research grant from Abbott Vascular; and speaker fees paid to the institution from Boston Scientific, Philips–Volcano, and Medtronic. BEPMC reports research grants from Philips, Novo Nordisk, Cleerly, B Braun, Nipro, Faraday Therapeutics, Amgen, and Translumina; and consultancy or speaker fees from Abbott Vascular, Medtronic, Boston Scientific, Translumina, Johnson & Johnson, BBraun, MSD, Novo Nordisk, and Philips. PALT reports a research grant from Haemonetics; and lecture fees from Medtronic. JJW reports research grants Medtronic and US2ai; and speaker fees BSC, Meril, Medtronic, Abbott, and Edwards Lifesciences. TNV reports consulting fees from Boston Scientific; speaker fees from Edwards Lifesciences and Boston Scientific; and support for meeting attendance from Abbott and Medtronic. PAV reports educational or research grants from Edwards Lifesciences and Abbott; and consulting or speaker fees from Medtronic and Abbott. NvR reports research grants from Abbott, Philips, Biotronik, and Medtronic; speaker fees from Abbott and Bayer; and support for meeting attendance or travel from Meril. JMtB reports educational grants from ZonMw and Medtronic. HMA, GMB, KIH, DJvG, GAAV, DCO, JB, MMV, JSL, RjdW, MGD, AOK, MMM, TCD, PvdH, GEHL, CES, MM, GKvH, GA, JGPT, and MV declare no competing interests.

Data sharing

Data collected for this trial will not be made publicly available. However, the study team will consider reasonable collaboration requests, which can be directed to r.delewi@amsterdamumc.nl. Additional study-related documents (study protocol and statistical analysis plan) are available online.

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References

- Tarantini G, Tang G, Nai Fovino L, et al. Management of coronary artery disease in patients undergoing transcatheter aortic valve implantation. A clinical consensus statement from the European Association of Percutaneous Cardiovascular Interventions in collaboration with the ESC Working Group on Cardiovascular Surgery. *EuroIntervention* 2023; **19**: 37–52.
- Praz F, Borger MA, Lanz J, et al, and the ESC/EACTS Scientific Document Group. 2025 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2025; **46**: 4635–736.
- Aarts HM, van Hemert ND, Meijls TA, et al. Percutaneous coronary intervention in patients undergoing transcatheter aortic valve implantation: a systematic review and meta-analysis. *Neth Heart J* 2023; **31**: 489–99.
- Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA Guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2021; **143**: e72–227.
- Patterson T, Clayton T, Dodd M, et al, and the ACTIVATION Trial Investigators. ACTIVATION (Percutaneous Coronary Intervention prior to transcatheter aortic Valve implantation): a randomized clinical trial. *JACC Cardiovasc Interv* 2021; **14**: 1965–74.
- Lønborg J, Jabbari R, Sabbah M, et al, and the NOTION-3 Study Group. PCI in patients undergoing transcatheter aortic-valve implantation. *N Engl J Med* 2024; **391**: 2189–200.
- Kodali SK, Moses JW. Coronary artery disease and aortic stenosis in the transcatheter aortic valve replacement era: old questions, new paradigms: the evolving role of percutaneous coronary intervention in the treatment of patients with aortic stenosis. *Circulation* 2012; **125**: 975–77.
- Brouwer J, Nijenhuis VJ, Delewi R, et al. Aspirin with or without clopidogrel after transcatheter aortic-valve implantation. *N Engl J Med* 2020; **383**: 1447–57.
- van Nieuwkerk AC, Aarts HM, Hemelrijk KI, et al. Bleeding in patients undergoing transfemoral transcatheter aortic valve replacement: incidence, trends, clinical outcomes, and predictors. *JACC Cardiovasc Interv* 2023; **16**: 2951–62.
- Aarts HM, Hemelrijk KI, Broeze GM, et al. Deferral of routine percutaneous coronary intervention in patients undergoing transcatheter aortic valve implantation: rationale and design of the PRO-TAVI trial. *Am Heart J* 2025; **281**: 133–39.
- Ten Berg J, Sibbing D, Rocca B, et al. Management of antithrombotic therapy in patients undergoing transcatheter aortic valve implantation: a consensus document of the ESC Working Group on Thrombosis and the European Association of Percutaneous Cardiovascular Interventions (EAPCI), in collaboration with the ESC Council on Valvular Heart Disease. *Eur Heart J* 2021; **42**: 2265–69.
- Généreux P, Piazza N, Alu MC, et al, and the VARC-3 Writing committee. Valve Academic Research Consortium 3: updated endpoint definitions for aortic valve clinical research. *J Am Coll Cardiol* 2021; **77**: 2717–46.
- Pocock SJ, Ariti CA, Collier TJ, Wang D. The win ratio: a new approach to the analysis of composite endpoints in clinical trials based on clinical priorities. *Eur Heart J* 2012; **33**: 176–82.
- Nijenhuis VJ, Brouwer J, Delewi R, et al. Anticoagulation with or without clopidogrel after transcatheter aortic-valve implantation. *N Engl J Med* 2020; **382**: 1696–707.
- Faroux L, Guimaraes L, Wintzer-Wehekind J, et al. Coronary artery disease and transcatheter aortic valve replacement: JACC state-of-the-art review. *J Am Coll Cardiol* 2019; **74**: 362–72.
- Minten L, Wissels P, McCutcheon K, et al. The effect of coronary lesion complexity and preprocedural revascularization on 5-year outcomes after TAVR. *JACC Cardiovasc Interv* 2022; **15**: 1611–20.
- Avvedimento M, Nuche J, Farjat-Pasos JI, Rodés-Cabau J. Bleeding events after transcatheter aortic valve replacement: JACC state-of-the-art review. *J Am Coll Cardiol* 2023; **81**: 684–702.
- van Nuland PJA, van Ginkel DJ, Overduin DC, et al. The impact of stroke and bleeding on mortality and quality of life during the first year after TAVI: a POPular TAVI subanalysis. *Catheter Cardiovasc Interv* 2024; **104**: 1107–18.
- Boden WE, O'Rourke RA, Teo KK, et al, and the COURAGE Trial Research Group. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med* 2007; **356**: 1503–16.
- Maron DJ, Hochman JS, Reynolds HR, et al, and the ISCHEMIA Research Group. Initial invasive or conservative strategy for stable coronary disease. *N Engl J Med* 2020; **382**: 1395–407.
- De Bruyne B, Pijls NHJ, Kalesan B, et al, and the FAME 2 Trial Investigators. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. *N Engl J Med* 2012; **367**: 991–1001.
- Aarts HM, Hemelrijk KI, Broeze GM, et al. Nationwide analysis of PCI After TAVR from the Netherlands heart registration. *Catheter Cardiovasc Interv* 2025; **107**: 824–32.
- Costa G, Sammartino S, Strazzieri O, et al. Coronary cannulation following TAVR using self-expanding devices with commissural alignment: the RE-ACCESS 2 Study. *JACC Cardiovasc Interv* 2024; **17**: 727–37.
- D'Ascenzo F, Verardi R, Visconti M, et al. Independent impact of extent of coronary artery disease and percutaneous revascularisation on 30-day and one-year mortality after TAVI: a meta-analysis of adjusted observational results. *EuroIntervention* 2018; **14**: e1169–77.
- Gallinoro E, Paolisso P, Bertolone DT, et al. Absolute coronary flow and microvascular resistance before and after transcatheter aortic valve implantation. *EuroIntervention* 2024; **20**: e1248–528.
- Scarsini R, Pesarini G, Zivelonghi C, et al. Physiologic evaluation of coronary lesions using instantaneous wave-free ratio (iFR) in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation. *EuroIntervention* 2018; **13**: 1512–19.
- Ahmad Y, Göteborg M, Cook C, et al. Coronary hemodynamics in patients with severe aortic stenosis and coronary artery disease undergoing transcatheter aortic valve replacement: implications for clinical indices of coronary stenosis severity. *JACC Cardiovasc Interv* 2018; **11**: 2019–31.
- Ribichini FL, Scarsini R, Pesarini G, et al, and the FAITAVI Trial investigators. Physiology vs angiography-guided percutaneous coronary intervention in transcatheter aortic valve implantation: the FAITAVI trial. *Eur Heart J* 2025; **ehaf974**. <https://doi.org/10.1093/eurheartj/ehaf974>.