The TAVI PCI (optimal timing of Transcatheter Aortic Valve Implantation and Percutaneous Coronary Intervention) Trial

Published: 08-10-2021
Last updated: 04-04-2024

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON51090

Source
ToetsingOnline

Brief title
TAVI PCI

Condition

- Other condition
- Cardiac valve disorders

Synonym
"Transcatheter Aortic Valve Implantation and Percutaneous Coronary Intervention" "heart disease: valve disease and coronary vessels"

Health condition

cardiac disorders --> coronary artery disorders

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: University Zurich,University Zurich (Switzerland); research grant of Edwards Lifesciences SA

Intervention

Keyword: cardiology, optimal timing, PCI, TAVI

Outcome measures

Primary outcome

Major adverse cardiovascular events (MACE) at 1 year, defined as a composite

of:

• All-cause death

• Non-fatal myocardial infarction (MI)

• Ischemia-driven revascularization

• Rehospitalization (valve- or procedure-related including heart failure)

• Life-threatening/disabling or major bleeding (according to VARC-2 (5))

Secondary outcome

Secondary endpoints will be assessed at hospital discharge (first and second

hospitalization), 3 months, 1 year, 2 years, and 5 years, and comprise:

• Primary composite endpoint at hospital discharge (first and second

hospitalization), at 3 months, 2 years, and 5 years

• Single components of the primary endpoint

• All-cause death and MI

• All-cause death, MI, and ischemia driven revascularization

• All-cause death, MI, ischemia driven revascularization, and rehospitalization

• Cardiovascular death

• Cardiovascular death and MI

• Stroke

• Peri-procedural MI (PCI)

• Peri-procedural MI (TAVI)

• Major vascular complications (according to VARC-2 (5))

• Bleeding events (Bleeding Academic Research Consortium [BARC] definition)

• Symptom status and change from baseline in symptom status (Canadian Cardiovascular Society [CCS] and New York Heart Association [NYHA] classification)

The following secondary endpoint will be assessed at hospital admission for the second procedure, 3 months, 1 year, 2 years, and 5 years:

• Quality of Life (QoL) as assessed by the Kansas City Cardiomyopathy questionnaire (KCCQ) and the Toronto Aortic Stenosis Quality of Life questionnaire (TASQ)

• Change from baseline in QoL as assessed by the KCCQ and the TASQ

Study description

Background summary

Optimal timing of coronary revascularization in patients with severe aortic stenosis and concomitant coronary artery disease undergoing transcatheter

aortic valve implantation (TAVI) is unknown.
Recent studies have provided a large body of evidence supporting complete coronary revascularization in hemodynamically stable patients presenting with acute coronary syndromes and multivessel disease in comparison to culprit lesion only percutaneous coronary intervention (PCI) and optimal medical therapy for non-culprit lesions. (1-4) Accordingly, it can be assumed that coronary revascularization for coronary artery lesions in patients undergoing TAVI is superior to optimal medical therapy alone. In clinical routine, PCI performed before TAVI represents the standard approach which is supported by observational evidence. Optimal timing of PCI in patients undergoing TAVI has not been investigated, yet. Percutaneous coronary intervention after TAVI may entail the advantage of a lower risk of vascular and bleeding complications and avoid aortic stenosis-related alterations of coronary physiology.

Study objective

The primary objective of this study is to compare in a non-inferiority design the safety and efficacy of iwFR (or comparable resting diastolic indices)-guided complete revascularization after (within 1-45 days) with iwFR (or comparable resting diastolic indices)-guided complete revascularization before (within 1-45 days) TAVI using the Edwards SAPIEN Transcatheter Heart Valve* in patients with severe aortic stenosis and concomitant coronary artery disease accepted for TAVI and PCI by the multidisciplinary Heart Team.
We hypothesize that iwFR (or comparable resting diastolic indices)-guided complete revascularization after TAVI is non-inferior to iwFR (or comparable resting diastolic indices)-guided complete revascularization before TAVI, when using the Edwards SAPIEN Transcatheter Heart Valve*. Non-inferiority of iwFR (or comparable resting diastolic indices)-guided complete revascularization performed after TAVI would provide flexibility in procedural planning, allow for early symptom relief of patients with severe aortic stenosis, and define the transcatheter heart valve design suited best for patients with severe aortic stenosis and concomitant coronary artery disease. Further, coronary revascularization after TAVI may contain a lower risk of vascular and bleeding complications, given the need for dual antiplatelet therapy after PCI, and potentially avoid aortic stenosis-related alterations in coronary physiology.

Study design

TAVI PCI is an investigator-initiated, randomized, multi-center, two-arm, open-label, non-inferiority trial. Patients with severe aortic stenosis and concomitant coronary artery disease will be randomized in a 1:1 ratio to instantaneous wave-free ratio (iwFR)-guided complete coronary revascularization
1) before (within 1-45 days) TAVI (Group 1), or
2) after (within 1-45 days) TAVI (Group 2)

Intervention

TAVI & PCI are the same for patients participating in the trial as for all other patients not participating, as only the sequence of procedures is investigated in the study.

TRANSCATHETER AORTIC VALVE IMPLANTATION (TAVI)
Interventional cardiologists selected to participate as Investigators in this study are qualified and board certified. All clinicians have broad experience with the procedures. Transcatheter aortic valve implantation is performed according to current guidelines and recommendations using the he commercially available balloon-expandable Edwards SAPIEN Transcatheter Heart Valve* (see 8.1.1).(6) The choice of prosthesis size is left at the discretion of the operator. The Edwards SAPIEN Transcatheter Heart Valve*, the associated delivery system, and all components will be used according to the respective Instructions for Use (IFU). During the procedure, at least 5000 IU or 70 - 100 IU/kg unfractionated heparin to maintain an ACT >250 seconds is required. After TAVI, antiplatelet therapy with aspirin is given. Patients with any indication for oral anticoagulation are treated with oral anticoagulation alone.

Edwards SAPIEN Transcatheter Heart Valve*
The Edwards SAPIEN Transcatheter Heart Valve* respective Instructions for Use (IFU) have to be followed and filed in the investigator site file.
The manufacturer is Edwards Lifesciences LLC, One Edwards Way, lrvine, CA 92614, United States Of America.

PERCUTANEOUS CORONARY INTERVENTION (PCI)
Interventional cardiologists selected to participate as Investigators in this study are qualified and board certified and have broad experience with the procedures. Coronary revascularization is performed according to current guidelines and recommendations using CE certified devices.(30) Coronary revascularization should be attempted in all coronary artery lesions with 40-90% diameter stenosis and iwFR (or a comparable resting diastolic index) <=0.89 or with >90% diameter stenosis on coronary angiogram (by visual estimation) in a coronary artery >=2.5 mm in diameter. While measurement of iwFR (or resting full-cycle ratio [RFR], diastolic hyperemia-free ratio [DFR], or a comparable resting diastolic index) is mandatory for the assessment of coronary artery lesions with 40-90% diameter stenosis, investigators are asked to also perform other resting and hyperemic indices such as resting distal to aortic coronary pressure ratio (Pd/Pa), fractional flow reserve (FFR), quantitative flow ratio (QFR), coronary flow reserve (CFR), or index of microcirculatory resistance (IMR). Quantiative flow ratio analysis will be performed offline at the Andreas Grüntzig Coronary Angiography and Physiology Core Lab for all patients. Complete revascularisation is desirable, but the extent of revascularisation is left to the discretion of the operator performing PCI. All lesions identified as amenable to PCI at randomisation should undergo coronary revascularization. The access site (radial or femoral), the use of intravascular imaging modalities (optical coherence tomography, intravascular ultrasound), and the use of PCI equipment (drug-eluting stent, drug-coated

balloon, rotablation, etc.) are left at the discretion of the operator. In general, PCI of chronic total occlusions (CTO) that are well collateralized should only be attempted if, in the opinion of an experienced CTO operator, there is a high likelihood of PCI success.
All patients must be pre-treated with aspirin. During the procedure, at least 5*000 IU or 70 - 100 IU/kg unfractionated heparin to maintain an activated clotting time (ACT) >250 seconds is required. Following PCI with stent implantation, dual antiplatelet therapy (DAPT) with aspirin and the P2Y12 inhibitor clopidogrel should be given according to current guidelines and for at least 3 months, preferably 6 months.(31) In patients not already pre-treated with aspirin or clopidogrel, an initial dose of aspirin of 250-500 mg i. v. and a loading dose of clopidogrel of 300-600 mg orally should be given peri-procedurally.
Patients with any indication for oral anticoagulation are treated with triple therapy for 1 to 4 weeks, followed by dual therapy (oral anticoagulation and clopidogrel) for at least 3 months and up to 12 months, based on their individual bleeding and ischemic risks and according to current guideline recommendations.(31, 32)

Study burden and risks

The risks and benefits of the procedures, PCI and TAVI, are the same for patients participating in the trial as for all other patients not participating, as only the sequence of procedures is investigated in the study.

PCI prior to TAVI (Group 1)
Percutaneous coronary intervention before TAVI may be related with a reduced ischemic burden during valve implantation and rapid pacing, but may have an increased bleeding risk when dual antiplatelet therapy is administered after PCI. In two meta-analyses (see 4.1 BACKGROUND AND RATIONALE), revascularization before TAVI conferred no clinical advantage with respect to clinical outcomes,(28, 29) but was related with an increased risk of major vascular complications and mortality.(28) In line with these findings, PCI shortly before TAVI was associated with an increased risk of minor bleeding and vascular injury as compared with remote staged PCI in a retrospective cohort study.(26) These studies, however, are limited by their rather small sample size and their observational, retrospective design.

PCI after TAVI (Group 2)
Percutaneous coronary intervention after TAVI may entail the advantage of a lower risk of vascular and bleeding complications and avoid aortic stenosis-related alterations of coronary physiology, but may be related with an increased ischemic risk during valve implantation and rapid pacing

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Patients >=18 years with severe aortic stenosis and concomitant coronary artery disease accepted for transfemoral TAVI with an Edwards SAPIEN Transcatheter Heart Valve* by transfemoral access and PCI by the multidisciplinary Heart Team
• Severe aortic stenosis defined as aortic valve area (AVA) <=1.0 cm2 and/or mean pressure gradient >=40 mmHg (echocardiography) and at least one of:
1) Dyspnea
2) Angina symptoms
3) Syncope
4) Decline in left ventricular ejection fraction <50%, symptoms or fall in blood pressure on exercise testing, or presence of high-risk criteria (peak transaortic velocity >5.5 m/s, severe valve calcification, peak transaortic

velocity progression >=0.3 m/s per year, or severe pulmonary hypertension with systolic pulmonary artery pressure >60 mmHg) according to current guidelines(6)
• At least one coronary artery lesion with 40-90% diameter stenosis and iwFR <=0.89 or with >90% diameter stenosis on coronary angiogram (by visual estimation) in a coronary artery >=2.5 mm in diameter and Thrombolysis in Myocardial Infarction (TIMI) flow grade III, deemed amenable to PCI within 45 days before or after TAVI
• Written informed consent

Exclusion criteria

• TAVI by transapical, subclavian, or transaortic access
• Admission with acute myocardial infarction within 30 days before randomization
• Elective coronary revascularization within 3 months before randomization
• Previous coronary artery bypass grafting (CABG)
• Syntax Score I >=33
• Any contraindications for dual antiplatelet therapy with aspirin and a P2Y12 inhibitor (clopidogrel, ticagrelor or prasugrel), except for patients on oral anticoagulation
• Planned open heart surgery
• Known pregnancy at the time of inclusion
• Life expectancy <1 year due to other severe non-cardiac disease
• Participation in another clinical study with an investigational product
• Acute COVID-19 infection
• Patient with previously treated aortic stenosis

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-01-2022
Enrollment:	100
Type:	Actual

Medical products/devices used

Generic name:	Edwards SAPIEN Transcatheter Heart ValveTM
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	08-10-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-07-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-11-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT04310046
CCMO	NL76284.078.21