Percutaneous Complete Revascularization Strategies Using Sirolimus Eluting Biodegradable Polymer Coated Stents in Patients Presenting With Acute Coronary Syndromes and Multivessel Disease

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To test whether immediate complete revascularization is non-inferior to staged (but within six weeks after index procedure) complete revascularization in ACS patients with multivessel disease

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON54743

Source
ToetsingOnline

Brief title
BioVasc Trial

Condition

- Coronary artery disorders

Synonym
acute coronary syndrome, heart attack

Research involving

Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,Biotronik

Intervention

Keyword: Acute coronary syndrome, Direct Complete Revascularization, Multivessel Disease, Staged Complete Revascularization

Outcome measures

Primary outcome

The main study endpoint is defined as the composite of all-cause mortality, nonfatal type 1 myocardial infarction, any unplanned revascularization, and cerebrovascular events (MACCE) at 1-year post intervention.

Secondary outcome

• Composite clinical outcome of all-cause mortality, nonfatal type 1 myocardial infarction, any unplanned revascularization, and cerebrovascular events (MACCE) at 30 days, 2 and 5 years post intervention.

• All-cause mortality at 30 days, 1, 2 and 5 years

• Myocardial Infarction (Q-wave and non Q-wave MI) at 30 days, 1, 2 and 5 years

• Any revascularization procedure, target lesion revascularization (TLR), Target Vessel Revascularization (TVR) and non-TVR at 30 days, 1, 2 and 5 years

• Major bleeding (not related to coronary-artery bypass grafting, BARC 3-5) at 30 days and 1 year

• Safety and efficacy of immediate complete revascularization in patient subgroups with specific demographics, clinical indications and/or vessel- or lesion characteristic

• Net adverse clinical events at 30 days and one year, a composite of:

• Major bleeding (not related to coronary-artery bypass grafting, BARC 3-5)

• All-cause mortality, myocardial infarction or stroke

• Need for renal replacement therapy at 30 days

• Quality of Life at 30 days and 1 year

Health status will be compared between the 2 groups using the Seattle Angina Questionnaire (SAQ) and the EQ 5D (EuroQol) assessment at 1 and 12 months post procedure.

Study description

Background summary

Invasive coronary angiography followed by primary percutaneous coronary intervention is the treatment of choice in patient presenting with STEMI-ACS1 and NSTEMI-ACS2. Up to 60 percent of these patients have multivessel disease on angiography3-5. Patients with multivessel disease have a worse prognosis than in those with culprit vessel disease only5. It has been debated whether a complete or culprit artery only revascularization strategy is better. Retrospective data in STEMI patients suggested a lower mortality in patients that were treated with culprit artery only compared with multivessel PCI during index procedure6. Since then, four randomized controlled trials have addressed this question in STEMI population; Randomized Trial of Preventive Angioplasty in Acute Myocardial Infarction (PRAMI) trial (n = 465, 23 months follow-up)7, the Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multivessel disease (CvLPRIT) (n = 296, 12months follow-up)8, the Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease (DANAMI-3-PRIMULTI) trial (n = 627, 27months follow-up)9, and the Fractional Flow Reserve-Guided Multivessel Angioplasty in Myocardial Infarction (Compare-Acute) trial (n = 885, 12 months follow-up)10. PCI of the non-infarct related artery was performed at the index procedure ((PRAMI and Compare-Acute), staged before discharge (DANAMI-3-PRIMULTI) or at any time during hospitalization (CvLPRIT). Indication for PCI was significant stenosis as assessed by angiography (PRAMI

and CvLPRIT) or FFR (DANAMI-3-PRIMULTI and COMPARE-ACUTE). There was a significant reduction in primary outcome in all four trials in favor of complete revascularization. However, this was mainly driven by *soft* endpoints. There was no significant reduction in total mortality or myocardial infarction. Based on the results for these four trials, the 2017 ESC STEMI-ACS guidelines give a class II, LOE A, indication for routine revascularization in STEMI patients with multivessel disease, including those presenting with cardiogenic shock1. However, an important shortcoming of the abovementioned studies is the absence of a staged complete revascularization arm. As there is no data that compare immediate and staged complete revascularization, the guidelines don*t advise on when to perform non infarct related artery revascularization.
Data regarding optimal treatment in NSTEMI-ACS is more scarce and a RCT is lacking. In an observational study by Shishesbor and coworkers, they showed that nonculprit multivessel stenting reduced future revascularization rate but this was not associated with lower death rate or myocardial infarction rate11. Recently, a substudy from the Bleeding complications in a Multicenter registry of patients discharged with diagnosis of acute coronary syndrome (BleeMACS) registry (N=4520 patients, 1459 NSTEMI) was published12. They showed that in NSTEMI patients, complete revascularization was associated with a significant lower rate of death (4.5% vs. 8.5%; p=0.002), re-AMI (3.7% vs. 6.6%; p=0.016) and MACE (8.1% vs. 13.9%; p=0.001) at one year follow up. The 2015 ESC NSTEMI-ACS guidelines not specifically advise a culprit only or multivessel PCI strategy. Moreover, they advise to base revascularization strategy on patients clinical status and co-morbidities, as well as disease severity, Class II, LEO B. Interestingly, in contrast to the STEMI population, in NSTEMI population there is a RCT addressing whether staged or direct complete revascularization is better, the Single-Staged Compared With Multi-Staged PCI in Multivessel NSTEMI Patients: The SMILE Trial (N=584 patients)13. There was a significant reduction in primary endpoint 1S-PCI: n = 36 [13.63%] vs. MS-PCI: n = 61 [23.19%]; hazard ratio [HR]: 0.549 [95% confidence interval (CI): 0.363 to 0.828]; p = 0.004) at one year follow up. This was mainly driven by a reduction in target vessel revascularization. There was no significant difference in cardiac death or myocardial infarction between the both groups. This finding deserves further investigation, because the TVR rate (15.4% at 1 year) in the multistage group was unprecedentedly high in the era of current-generation drug-eluting stents.
There is no publication specifically addressing the patients with unstable angina regarding the subject of complete or incomplete revascularization or timing of revascularization.
Taken together, complete revascularization in ACS patients seems reasonable, but timing of revascularization is unknown.

Study objective

To test whether immediate complete revascularization is non-inferior to staged (but within six weeks after index procedure) complete revascularization in ACS

patients with multivessel disease

Study design

This study is a prospective, multicenter, randomized, two-arm, international, open-label, non-inferiority study. Due to the design characteristics of the study, the study investigators and operators cannot be blinded. However, the clinical event adjudication committee, consisting of cardiologists who are not participating in the study, will be blinded for the treatment arm of the patients to avoid a potential bias in the adjudication process of events

Intervention

At the index procedure, the culprit lesion (cause of complaints/acute coronary syndrome) will be treated according to standard of care with a Biotronik Orsiro DES (Sirolimus-Eluting stent). If there are additional significant lesions besides the culprit lesion, patients will be randomized to direct complete revascularization or staged complete revascularization. In the direct complete revascularization group all lesions will be treated during the index procedure. In the staged complete revascularization group, only the culprit lesion will be treated during the index procedure. The remaining significant lesions will be treated later but within six weeks after the index procedure. In both arms the additional lesions will also be treated with Biotronik Orsiro DES (Sirolimus-Eluting stent).

Study burden and risks

Participation contributes to expansion of the knowledge base with respect to best treatment of patients presenting with an acute coronary syndrome and more than one narrowed artery, which may assist physicians in their choice of treating any future patients. When participating in this study, you will have more medical check-ups than when you would not be participating in the study. In addition, you will be treated with a stent that was developed with the latest technology.

Patients will be implanted with two or more Biotronik Orsiro DES, Sirolimus-Eluting stent systems. This stent model is approved to be used. Therefore there is no higher risk associated with implantation of these systems in this study. The risk associated with stent implantation in general is among others dependent on the severity of the narrowing(s) in your coronary arteries, your symptoms but also other factors.
For this study data from patients medical files will be gathered. There will be no additional tests as compared to normal procedures.

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

1. Age >= 18 years or minimum age as required by local regulations
2. The patient is an acceptable candidate for treatment with a drug eluting stent in accordance with the applicable guidelines on percutaneous coronary interventions, manufacturer*s Instructions for Use and the Declaration of Helsinki
3. Patient indication, lesion length and vessel diameter of the target lesion(s) are according to the *Instructions for Use* that comes with every Biotronik Orsiro (Sirolimus-Eluting stent) system. Patients should qualify for both systems before randomization
4. The patient is willing and able to cooperate with study procedures and required follow up
visits

5. The subject or legal representative has been informed of the nature of the study and agrees to its provisions and has provided an EC approved written informed consent, including data privacy authorization
6. diagnosed Acute coronary syndrome according to ESC guidelines/criteria
7. Multivessel disease

Exclusion criteria

• Age <18 years and > 85 years
• Single coronary vessel disease
• Patients in cardiogenic shock
• Patients who cannot give informed consent or have a life expectancy of less than 1year
• Absolute contraindications or allergy that cannot be pre-medicated, to iodinated contrast or to any of the study medications, including both aspirin and P2Y12 inhibitors.
• Enrollment in another study with another investigational device or drug trial that has not reached the primary endpoint The patient may only be enrolled once in the BioVAsc study
• PCI in the previous 30 days.
• Presence of a chronic total occlusion
• Women of childbearing potential who do not have a negative pregnancy test within 7 days before the procedure and women who are breastfeeding.
• Planned surgery within 6 months of PCI unless dual antiplatelet therapy is maintained throughout the peri-surgical period

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-06-2018
Enrollment:	794
Type:	Actual

Medical products/devices used

Generic name:	Orsiro en Orsiro Mission Sirolimus eluting stent
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	21-06-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-07-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-05-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-08-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	16-03-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-08-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-05-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-11-2023
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
CCMO	NL64686.078.18