REvascularization versus optimal medical therapy on left Ventricular ISchemia reduction: Exploring the associations between ischemia, functional outcome and collaterals in the treatment of Chronic Total Occlusion patients

Published: 15-04-2019
Last updated: 12-04-2024

1- To determine whether PCI of the CTO will yield a higher reduction of ischemia assessed by exercise myocardial perfusion SPECT from baseline to follow-up compared to a control group.
2- To evaluate the effect of PCI of the CTO on improvement in...

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

Summary

ID

NL-OMON49007

Source
ToetsingOnline

Brief title
REVISE-CTO

Condition

- Coronary artery disorders

Synonym
chronic total coronary occlusion

Research involving

Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Abbott

Intervention

Keyword: Coronary occlusion, Myocardial ischemia, Percutaneous Coronary Intervention

Outcome measures

Primary outcome

The primary objective of the REVISE-CTO study is to determine whether in CTO patients, selected with a ischemic threshold, PCI of the CTO results in a greater reduction of the ischemic burden assessed with exercise myocardial perfusion SPECT from baseline to 6 months follow-up compared to a control group (OMT only).

Secondary outcome

Secondary objectives are:

To assess the effect of PCI of the CTO compared to the control group on:

1) Functional outcome: (angina) symptoms, quality of life, cardio-pulmonary exercise capacity.

2) Left ventricular function: global function, segmental wall thickening and infarct size.

3) Ventricular repolarization ECG markers on rest and exercise ECG.

Objectives from the collateral study performed in patients undergoing PCI of the CTO (n=41).

To assess the influence of collaterals on:

4) Myocardial ischemia at baseline and follow-up assessed with exercise myocardial perfusion SPECT and compare the parameters in the CTO with the remote area.

5) Functional outcome, global and regional left ventricular function and infarct size

Clinical objectives from the registry and randomized trial:

7) All outcomes will be stratified for gender and the prospective registry data will be used to evaluate the different CTO treatment strategies and outcomes in women compared to men

8) Safety endpoints and major clinical cardiac events will be registered and compared between treatment strategies

Study description

Background summary

A chronic total occlusion (CTO) is a 100% (complete) chronic coronary artery blockage and present in about 20% of patients with coronary artery disease (CAD). Patients with a CTO have a worse clinical outcome compared to non-CTO patients, irrespective of age or other co-morbidities. Currently CTO lesions are more often treated by percutaneous coronary intervention (PCI) in routine clinical practice, leading to expensive dedicated CTO programs and improvements in procedural techniques and devices. However whether PCI is the optimal treatment of CTO patients remains controversial, as there are increased complication risks with thus far no clear clinical benefit. Also the blood flow from collateral arteries is believed to be sufficient to prevent ischemia and preserve function of the CTO territory. However, while in resting conditions this may be adequate, during exercise the collaterals fail to supply the myocardium and patients will experience ischemia reducing their exercise-capacity and quality of life. Although observational data showed

benefit of successful PCI of the CTO, none of the randomized CTO trials found clinical benefit compared to optimal medical therapy (OMT) only, though a beneficial effect on angina reduction was found. This has energized the theory that a pre-treatment ischemic substrate (threshold) is required to justify CTO revascularization. In post-hoc analysis PCI led to a greater ischemia reduction compared to OMT and ischemia reduction was associated with improved outcome. Currently only limited data is available on the effect of PCI of the CTO on ischemia reduction and subsequent functional outcome, and no comparison exist with a control group. Furthermore there is insufficient insight on the association between the extent of the collateral perfusion network and the ischemic burden in patients. Patients with a CTO constitute an unique population to not only study the clinical effects of (PCI) treatment but also the physiological effects on the ischemic burden reduction. These data are highly warranted to more definitely determine the guidelines for optimal CTO treatment.

Study objective

1- To determine whether PCI of the CTO will yield a higher reduction of ischemia assessed by exercise myocardial perfusion SPECT from baseline to follow-up compared to a control group.
2- To evaluate the effect of PCI of the CTO on improvement in functional status, infarct size and left ventricular function from baseline to follow-up compared to the control group.
3- To study the association between ischemia reduction and functional outcome and left ventricular function.
4- To assess the influence of the collateral flow index on the ischemic burden (reduction), functional status, infarct size and left ventricular (contractile) function (hibernation).

Study design

In this multicentre prospective study 82 CTO patients will be randomly assigned to the invasive arm (PCI+OMT) or to the control arm (OMT only). All patients with a documented CTO in a native coronary artery, considered to be older than 3 months, will be prospectively screened. As part of routine clinical practice an SPECT (ischemia) and CMR (viability) scan will be performed to determine the clinical need for CTO revascularization. Patients are deemed eligible when they meet the ischemic threshold in the CTO territory (defined as >12.5% of ischemia with <50% transmural extent of infarction).

All consecutive CTO patients will be asked to be included into the prospective registry. The registry will give a description of the current CTO management strategies and an estimation on the risks and benefits of the different strategies. Registry data will be analysed separately for women and men to detect possible gender differences. All patients will be evaluated for safety

and adverse cardiac events.

Intervention

All patients will receive OMT, which focus on antianginal therapy, aiming for at least two antianginal medications, adequate lipid-lowering therapy, antiplatelet therapy and blood pressure lowering medication. In the control group revascularization is only reserved in case of OMT failure (e.g., progressive or refractory symptoms or the development of acute coronary syndrome). PCI will be performed according to standard clinical practice, including antegrade and retrograde approaches at the discretion of the operator. After successful PCI assessment of intracoronary collateral indices pressure (CFIp) and flow (CFIv) will be performed using a pressure and flow wire. The wire will be placed distal to the treated CTO lesion and measurements will be performed before and during low-pressure balloon occlusion. During low-pressure balloon occlusion the wire distal of the CTO lesion will solely measure the pressure and flow indices from the collaterals. Measurements will be performed during rest and maximal hyperaemia, induced by adenosine. Collateral indices are calculated as: CFIp = (Poccl*CVP) / (Pao*CVP) and CFIv = (CFIbaseline)/ (CFIpost*PCI)

Study burden and risks

1 visit at baseline, for inclusion (about 1 hour)
1 telephone contact for the standardized questionnaires for angina, dyspnoea and quality of life (approx. 15 min)
1 visit after 6 months for repeat SPECT, repeat MRI, resting ECG and standardized questionnaires (about 10 hours)
Telephone contact at 1 year and every consecutive year until 10 years follow-up (approx. 15 min)

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. A chronic total occlusion is present and target lesion. A CTO is required to meet the following characteristics:
• A 100% luminal narrowing of the coronary artery without antegrade flow, i.e. Thrombolysis in Myocardial Infarction flow grade 0 or 1;
• Older than 3 months, established with previous PCI or with angiographic characteristics;
• Amenable to percutaneous revascularization.
2. Patient has a clinical indication to perform CTO PCI.
3. A SPECT is performed at baseline to assess ischemia and a cardiac magnetic resonance imaging (CMR) scan to assess viability, as part of routine patient care. Patients are deemed eligible for the randomized trial when they meet the ischemic threshold in the CTO territory.
The ischemic threshold is defined as:
• >12.5% of ischemia;
• With <50% transmural extent of infarction.
4. Subject agrees to undergo follow-up SPECT at 6 months after initial inclusion
5. Subject is able to verbally confirm understanding and he/she provides written informed consent prior to any Clinical Investigation related procedure, as approved by the appropriate Ethics Committee.

Exclusion criteria

• Subject is younger than 18 years of age;
• Persistent or permanent atrial fibrillation;
• Presence of a non-MRI compatible cardiac device, i.e. pacemaker or

implantable cardioverter defibrillator;
• Body weight > 250 kg;
• Unable to exert, i.e. due to physical disability;
• Any contraindication for SPECT or CMR, i.e. cerebrovascular clips, claustrophobia;
• Known renal insufficiency (estimated Glomerular Filtration Rate [eGFR] <60 mL/min/1.73m2 or serum creatinine level of >2.5 mg/dL or subject on dialysis);
• Hypersensitivity or allergy to contrast with inability to properly pre-hydrate;
• Presence of a comorbid condition with a life expectancy of less than one year;
• Participation in another trial;
• Subject is belonging to a vulnerable population (per investigator*s judgment, e.g., subordinate hospital staff) or is unable to read or write.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	19-07-2019
Enrollment:	82
Type:	Actual

Ethics review

Approved WMO

Date:	15-04-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	30-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL67186.018.18