ShOckwave ballooN or Atherectomy with Rotablation in calcified coronary artery lesions,
the SONAR Trial. ;A randomized controlled trial comparing rates of peri-procedural myocardial infarction after intravascular ultrasound and rotational atherectomy in patients with calcified coronary artery lesions.

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

Summary

ID

NL-OMON53616

Source
ToetsingOnline

Brief title
the SONAR Trial

Condition

- Coronary artery disorders

Synonym
severely calcified coronary arteries

Research involving
Human

Sponsors and support

Primary sponsor: UZ Leuven
Source(s) of monetary or material Support: grant provided by Shockwave Medical;Santa Clara;USA.,Shockwave Medical, Santa Clara, USA

Intervention

Keyword: Atherectomy, Calcified coronary artery lesions, Rotablation, Shockwave balloon

Outcome measures

Primary outcome

Primary outcome: difference in the rate of peri-procedural myocardial infarction (Type 4a of the universal Definition of Myocardial Infarction) in patients allocated to Shockwave IVL group versus RA group.

Secondary outcome

Secondary outcomes: in centres where the index of microcirculatory resistance (IMR) can be measured before and after PCI, a rate of peri-procedural microvascular dysfunction will be measured. Other secondary outcomes: peri-procedural myocardial injury (defined as a peak high sensitivity troponin T of >=0.014ng/mL); descriptive study of IMR measurements in calcified lesions; technical success (defined as a residual stenosis <30% in the presence of TIMI III flow); procedural success (defined as technical success with no in-hospital MACE); in cases where intra-coronary imaging such as OCT is performed:

interaction between calcium score and primary endpoint; comparison of stent expansion between the two groups; procedure cost; procedure duration; radiation dose; cross-over to alternative strategy; 30-day and 1-year MACE.

Study description

Background summary

Percutaneous coronary intervention (PCI) is intended to relieve myocardial ischemia by improving blood flow in the epicardial coronary arteries, thereby relieving angina pectoris and improving outcomes in patients with coronary artery disease (CAD).1 However, the efficacy of PCI may be compromised by incidental microvascular obstruction and peri-procedural myocardial infarction (PPMI), which occurs in about 10-15% of cases and is associated with an increase in the rate of major adverse cardiovascular events (MACE).2 One meta-analysis, including 20 studies and 15*581 patients with stable angina undergoing elective PCI, demonstrated that overall troponin was raised in more than 30% of patients after an elective PCI. Any troponin elevation was associated with a significantly increased mortality risk (4.4% vs 3.3%, p=0.001; OR=1.35, 95% CI 1.13 to 1.60).3 Another meta-analysis used an earlier universal definition of PPMI (Type 4a)4 with a troponin elevation of 3 times the URL as the cut-off point.5 It included 7578 patients from 15 studies of patients undergoing non-emergency PCI with normal baseline troponin levels. Troponin elevation occurred in 28.7% of the procedures and the incidence of Type 4a MI was 14.5%. In keeping with previous data, Type 4a MI increased the risk of MACE compared with those patients without troponin elevation at an average follow-up of about 17.7 months (OR=2.25, 95% CI 1.26 to 4.00, p=0.006). Patients with elevation of troponin less than 3 times the URL did not have a worse prognosis during follow-up (OR=1.85, 95% CI 0.80 to 4.28, p=0.15).5

The mechanism of PPMI is thought to be related to side branch occlusion, coronary artery dissection and acute microvascular damage caused by embolization of plaque debris during the PCI (Figure 2).6,7 Recent data demonstrates a close relationship between peri-procedural myocardial injury or Type 4a PPMI and microvascular dysfunction.8 Microvascular dysfunction, measured with the index of microcirculatory resistance (IMR) significantly increased after elective PCI in patients with stable coronary artery disease, and was significantly associated with myocardial injury and Type 4a PPMI.

The expanding aged population has led to an increase in the frequency of calcified CAD. Moderate and severe calcified coronary lesions are particularly challenging for the interventional cardiologist since these lesions impede the

delivery of intra-coronary devices and increase the risk of stent under-expansion with consequent adverse procedural and clinical outcomes.9 Coronary artery calcification is associated with more frequent peri-procedural myocardial infarction.2,10 To overcome these challenges several devices including non-compliant balloons (including very high-pressure balloons), scoring devices, cutting devices, rotational and orbital atherectomy and excimer laser coronary angioplasty are available to the interventional cardiologist.11 The Shockwave coronary intravascular lithotripsy (IVL) catheter balloon catheter (Shockwave Medical, Santa Clara, CA) is a single-use sterile disposable catheter that contains multiple lithotripsy emitters enclosed in an integrated balloon.12 It emits sonic pressure waves in a circumferential field causing the selective fracture of calcium, altering vessel compliance and permitting further expansion of the vessel wall. This provides a potentially safer alternative to other calcium-modifying devices since there is a low risk of dissection and perforation.13 Furthermore, it is proposed,12 but not yet tested, that this IVL device reduces the risk of atheromatous embolization, which would reduce the risk of peri-procedural myocardial infarction and microvascular dysfunction. Theoretically, the use of IVL, instead of other devices such as rotational atherectomy (RA), could reduce peri-procedural complications, periprocedural myocardial infarction and microvascular dysfunction, and thus, improve the prognosis for patients with moderately and severely calcified lesions.14

Study objective

Since published rates of PPMI are limited in patients treated with RA and IVL, this study is designed as a pilot study in order to measure PPMI in patients treated with RA and IVL. At the same time a comparison will be carried out between the two treatment options.

The null hypothesis is that there is no difference in peri-procedural myocardial infarction (Type 4a of the universal Definition of Myocardial Infarction) or microvascular dysfunction in patients treated with IVL or RA.

Primary outcome: difference in the rate of peri-procedural myocardial infarction (Type 4a of the universal Definition of Myocardial Infarction) in patients allocated to Shockwave IVL group versus RA group.

Secondary outcomes: in centres where the index of microcirculatory resistance (IMR) can be measured before and after PCI, a rate of peri-procedural microvascular dysfunction will be measured. Other secondary outcomes: peri-procedural myocardial injury (defined as a peak high sensitivity troponin T of >=0.014ng/mL); descriptive study of IMR measurements in calcified lesions; technical success (defined as a residual stenosis <30% in the presence of TIMI III flow); procedural success (defined as technical success with no in-hospital MACE); in cases where intra-coronary imaging such as OCT is performed: interaction between calcium score and primary endpoint; comparison of stent

expansion between the two groups; procedure cost; procedure duration; radiation dose; cross-over to alternative strategy; 30-day and 1-year MACE.

Study design

In this multicentre, prospective, randomized-controlled open label study we will measure rates of peri-procedural myocardial infarction and changes in microvascular function after PCI in 170 patients (85 per arm) treated with Shockwave intravascular lithotripsy (IVL) versus RA. Patients with moderately and/or severely calcified coronary lesions, with the expected need of plaque modification, which are equally suitable for IVL and RA and on the condition that with or without low profile balloon (<= 1.5 mm) preparation, a >= 2.5 non-compliant balloon can cross the lesion, will be recruited according to the scheme in Figure 1. The calcified lesion must be suitable for both IVL and RA as defined in Figure 1 and the operator believes that either IVL or RA could be used. The primary outcome will be difference in the rate of peri-procedural myocardial infarction (Type 4a of the universal Definition of Myocardial Infarction). Peri-procedural myocardial injury and infarction will be defined by an increase in high-sensitivity Troponin T according to the Fourth Universal Definition of Myocardial Infarction,15 while microvascular dysfunction will be defined by an Index of Microcirculatory Resistance (IMR) of >=25.16 Patients will undergo study-related clinical follow up at 30 days and 12 months.

Intervention

- Shockwave ballon
- Rotablatie

Study burden and risks

Minor complaints due to extra blood samples at 8 and 16hr post PCI.

Contacts

Public
UZ Leuven

Herestraat 49
Leuven 3000
BE
Scientific
UZ Leuven

Herestraat 49

Leuven 3000
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patient older than 18 years.
The subject has stable or unstable angina pectoris, or a positive functional study for ischemia.
The subject is eligible for PCI.
The subject gives consent prior to study inclusion.
The subject has a moderate to severe calcified lesion with the expected need of plaque modification, on the condition that with or without low profile balloon (<= 1.5 mm) preparation, a >= 2.5 non-compliant balloon can cross the lesion.
The calcified lesion has a 50-90% diameter stenosis by angiographic assessment.

Exclusion criteria

Previous and/or planned brachytherapy of target vessel.
Pregnant and/or breast-feeding females or females who intend to become pregnant.
Patients who intend to have a major surgical intervention within 6 months of enrolment in the study.
Patients who previously participated in this study.
Subject has experienced an acute myocardial infarction 72 hours prior to the index procedure, as defined either by the presence of a new Q-wave in 2 or more contiguous leads, or by a CK greater than two times site upper reference limit (URL) with presence of CK-MB greater than the site URL.
The subject has suffered a stroke or transient ischemic neurological attack or cerebrovascular accident within the past six months, or has any known intracranial mass, arteriovenous malformation, aneurysm or other intracranial

pathology.
The subject has experienced a significant gastrointestinal or genitourinary bleed within the past six months, or has had any active bleeding within two months.
Planned revascularization of target vessel within 1 year after index procedure.
Lesions not ideal for Shockwave treatment:
Longer than 40mm.
The target vessel contains intraluminal thrombus.
The subject has had a prior stent in the target lesion, including a 5mm zone proximal and distal to the lesion.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	31-10-2022
Enrollment:	65
Type:	Anticipated

Ethics review

Approved WMO

Date:	03-04-2023
Application type:	First submission
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	NCT05208749
CCMO	NL81701.078.22