Distal Evaluation of Functional performance with Intravascular sensors to assess the Narrowing Effect - Combined pressure and Doppler FLOW velocity measurements

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2.1 Primary ObjectiveTo determine the prognostic value of combined FFR and CFR measurements to predict the 24-month rate of MACE.2.2 Secondary ObjectivesTo describe the test/retest repeatability of combined FFR and CFR measurements.To explore...

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

Summary

ID

NL-OMON50216

Source
ToetsingOnline

Brief title
DEFINE FLOW

Condition

- Coronary artery disorders

Synonym
atherosclerosis, coronary artery disease

Research involving
Human

Sponsors and support

Primary sponsor: University of Texas Medical School at Houston
Source(s) of monetary or material Support: University of Texas Medical School,Volcano Corp.

Intervention

Keyword: Coronary artery disease, Coronary Flow Velocity Reserve, Fractional Flow Reserve, Functional stenoses severity

Outcome measures

Primary outcome

Primary endpoint

• 24-month rate of major adverse cardiac events:

o all-cause death

o documented myocardial infarction

o unplanned, urgent revascularization (not cross-over revascularization)

o elective revascularization (both non-urgent and repeat procedures)

Secondary outcome

Secondary endpoints

• Canadian Cardiovascular Society (CCS) anginal class (or freedom from angina)

at 6, 12, 18, and 24 months (then 5 and potentially also 10 years depending on

resources)

• Number of anti-anginal medications at the same time points as CCS angina class

• Cerebrovascular events at any time

• Bland-Altman bias, limits of agreement, and reproducibility coefficient for

repeated physiology measurements

• Procedure time from anticoagulation to completion of physiologic measurements

• Number of tracings excluded by core physiology lab due to noise, artifact, or

loss of signal

Study description

Background summary

Optimal selection of lesions for percutaneous coronary intervention (PCI) remains an important challenge, given both the cost and invasive nature of the procedure. Prior randomized trials [17531660] [19144937] [22924638] have demonstrated that mainly stable patients with atherosclerotic coronary artery disease (CAD) experience superior outcomes when fractional flow reserve (FFR) guides PCI instead of anatomic appearance. However, FAME 2 indicates that approximately 80% of patients experience no adverse events over 1 year despite a reduced FFR [22924638]. Therefore, a clear opportunity exists for further refinement of lesion selection for PCI.

Conceptually, pressure-based FFR alone cannot fully describe the clinical physiology of the coronary arteries [16940193]. Instead, the three variables of pressure, flow, and resistance together are required, of which only two are simultaneously independent. Hence, it remains unproven if physiologic measures of stenosis severity in addition to FFR can refine selection of lesions for PCI or offer independent prognostic value.

Study objective

2.1 Primary Objective

To determine the prognostic value of combined FFR and CFR measurements to predict the 24-month rate of MACE.

2.2 Secondary Objectives

To describe the test/retest repeatability of combined FFR and CFR measurements.

To explore individual components of MACE, alternative MACE groupings, and angina burden.

To determine the rate of MACE and angina burden during extended follow-up (up to 5 years depending on study resources).

To document the procedural effort and success rate for combined pressure and Doppler flow measurements.

2.3 Exploratory Objectives

For each alternative physiologic variable, the prognostic value, test/retest repeatability, and angina burden will be computed in an analogous manner to CFR above.

Study design

Prospective, observational, non-randomized, multicenter study

Intervention

Based on the average FFR and CFR measurements, PCI will be performed immediately or deferred as follows:
• FFR >0.8 = defer

• FFR <=0.8
o CFR <2.0 = immediate PCI
o CFR >=2.0 = defer

Study burden and risks

The risks associated with participation in the study are equivalent of those associated with standard FFR-guidance of
treatment. De patien burden consists of telephone contact at 6, 12, 18, 24 months and 5 years, and if funding allows at 10 years.

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

3.1 Inclusion Criteria, 3.1.1 Age >= 18 years., 3.1.2 Eligible for PCI based on local practice standards during the current procedure (PCI cannot be staged)., 3.1.3 At least one epicardial stenosis of >=50% diameter (by visual or quantitative assessment) and meeting the following criteria as determined by the operator based on either a prior or the current diagnostic angiogram:
• <100% diameter (not a chronic, total occlusion);
• in a native coronary artery (including side branches but excludes bypass grafts);
• of >=2.5mm reference diameter (near the level of the stenosis);
• and supplies sufficiently viable myocardium (exclude regions of known, prior, transmural myocardial infarction)., 3.1.4 Ability to understand and the willingness to sign a written informed consent.

Exclusion criteria

Anatomic exclusions:, 3.2.1 Prior CABG., 3.2.2 Preferred treatment strategy for revascularization would be CABG based on local practice standards., 3.2.3 Left main coronary artery disease requiring revascularization., 3.2.4 Extremely tortuous or calcified coronary arteries precluding intracoronary physiologic measurements. Operators may also exclude subtotal or similar high-grade lesions, which in their judgment may be threatened by ComboWire placement., 3.2.5 Known severe LV hypertrophy (septal wall thickness at echocardiography of >13 mm)., Clinical exclusions:
3.2.6 Inability to receive intravenous adenosine (for example, severe reactive airway disease, marked hypotension, or high-grade AV block without pacemaker)., 3.2.7 Recent (within 3 weeks prior to cardiac catheterization) ST-segment elevation myocardial infarction (STEMI) in any arterial distribution (not

specifically target lesion)., 3.2.8 Culprit lesions (based on clinical judgment of the operator) for either STEMI or non-STEMI cannot be included., 3.2.9 Severe cardiomyopathy (LV ejection fraction <30%)., 3.2.10 Planned need for cardiac surgery (for example, valve surgery, treatment of aortic aneurysm, or septal myomectomy)., General exclusions:
3.2.11 A life expectancy of less than 2 years., 3.2.12 Inability to sign an informed consent, due to any mental condition that renders the subject unable to understand the nature, scope, and possible consequences of the trial or due to mental retardation or language barrier., 3.2.13 Potential for non-compliance towards the requirements for follow-up visits., 3.2.14 Participation or planned participation in another cardiovascular clinical trial before completing the 24 month follow-up.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-10-2014
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	07-10-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-01-2015

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-08-2020
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	NL48375.018.14