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Near-Infrared Spectroscopy Predicts Cardiovascular Outcome in Patients With Coronary Artery Disease

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ABSTRACT

BACKGROUND Near-infrared spectroscopy (NIRS) is capable of identifying lipid core-containing plaques, which can subsequently be quantified as a lipid core burden index (LCBI). Currently, no data are available on the long-term prognostic value of NIRS in patients with coronary artery disease (CAD).

OBJECTIVES This study sought to determine the long-term prognostic value of intracoronary NIRS as assessed in a nonculprit vessel in patients with CAD.

METHODS In this prospective, observational study, NIRS imaging was performed in a nonculprit coronary artery in 203 patients referred for angiography due to stable angina pectoris (SAP) or acute coronary syndrome (ACS). The primary endpoint was the composite of all-cause mortality, nonfatal ACS, stroke, and unplanned coronary revascularization.

RESULTS The 1-year cumulative incidence of the primary endpoint was 10.4%. Cumulative 1-year rates in patients with an LCBI equal to and above the median (43.0) versus those with LCBI values below the median were 16.7% versus 4.0% (adjusted hazard ratio: 4.04; 95% confidence interval: 1.33 to 12.29; $p = 0.01$). The relation between LCBI and the primary endpoint was similar in SAP and ACS patients (p value for heterogeneity = 0.14). Similar differences between high and low LCBI were observed in pre-specified secondary endpoints.

CONCLUSION CAD patients with an LCBI equal to or above the median of 43.0, as assessed by NIRS in a nonculprit coronary artery, had a 4-fold risk of adverse cardiovascular events during 1-year follow-up. This observation warrants confirmation by larger studies with extended follow-up. (The European Collaborative Project on Inflammation and Vascular Wall Remodeling in Atherosclerosis – Intravascular Ultrasound Study [AtheroRemoIVUS]; NCT01789411)
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Near-infrared spectroscopy (NIRS) is a novel, catheter-based technique capable of identifying lipid core-containing plaques within the coronary artery wall (1). Currently, no data are available on the long-term prognostic value of NIRS in patients with coronary artery disease.

We therefore performed a prospective study to assess the prognostic value of coronary plaque

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detection, as evaluated with NIRS, on the occurrence of major adverse cardiac and cerebrovascular events (MACCE) in the real-world setting of everyday clinical practice, in which patients with both stable angina and acute coronary syndrome (ACS) present for coronary angiography. Parallel to this objective, it was our aim to investigate whether imaging of a single segment without significant luminal narrowing of a nonculprit coronary artery could be used for risk stratification.

METHODS

STUDY POPULATION AND DESIGN. The ATHEROREMO-NIRS (The European Collaborative Project on Inflammation and Vascular Wall Remodeling in Atherosclerosis-Near-Infrared Spectroscopy) substudy (2) was a prospective, single-center, observational study assessing the prognostic value of coronary NIRS, performed at the Thoraxcenter, Erasmus Medical Center, Rotterdam, the Netherlands. All patients had an indication, as determined by their treating physician (as part of routine clinical care), for diagnostic coronary angiography and/or percutaneous coronary intervention (PCI) due to either stable angina pectoris or an ACS. Detailed inclusion and exclusion criteria are listed in the Online Table 1.

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Subsequent to the standard angiography and PCI (when applicable), NIRS of a nonculprit coronary artery was performed. The NIRS target segment of the nonculprit coronary artery was required to be at least 40 mm in length and without significant luminal narrowing (<50% stenosis) as assessed by online angiography. The order of preference for selection of the nonculprit vessels was predefined in the study protocol: 1) left anterior descending artery; 2) right coronary artery; and 3) left circumflex artery.

This study was approved by the Medical Ethics Committee of the Erasmus Medical Center, and performed in accordance to the Declaration of Helsinki (2008, 6th revision). Written informed consent was obtained from all participants.

SAMPLE SIZE. The ATHEROREMO-IVUS (The European Collaborative Project on Inflammation and Vascular Wall Remodeling in Atherosclerosis-Intravascular Ultrasound) study had a pre-specified sample size of 800 patients, and was designed to explore multiple relations between genetic and serum biomarkers and coronary plaque characteristics (2). It was during the course of the ATHEROREMO-IVUS study that intracoronary NIRS became commercially available and accessible for our cardiac catheterization lab. The ultimate sample size of the ATHEROREMO-NIRS substudy (203 consecutively consenting patients) was not based on prior effect estimates but rather on the time point of availability and local institutional review board approval (April 2009) of the NIRS technique as ATHEROREMO evolved.

NEAR-INFRARED SPECTROSCOPY. The U.S. Food and Drug Administration-approved NIRS system, as used in this study, consists of a 3.2-F rapid exchange catheter, a pullback and rotation device, and a console (InfraReDx, Burlington, Massachusetts). Image acquisition was performed by a motorized catheter pullback at a speed of 0.5 mm/s and 240 rpm in a proximal segment of a nonculprit artery, starting distal to a side branch. The system performed 1,000 chemical measurements per 12.5 mm, in which each measurement interrogated 1 to 2 mm^2 of vessel wall from a depth of approximately 1 mm in the direction from the luminal surface toward the adventitia (1). Areas of the artery with spectral characteristics of a lipid core were displayed in yellow within the image map, called a chemogram. NIRS images were analyzed offline by an independent core laboratory (Cardialysis, Rotterdam, the Netherlands). Core laboratory personnel were blinded to all other patient and outcome data.

STUDY ENDPOINTS. The pre-specified primary endpoint was the incidence of MACCE, defined as the composite of all-cause mortality, nonfatal ACS, stroke, and unplanned coronary revascularization during 1-year follow-up, exclusive of events related to the culprit lesion at the index angiography. Secondary endpoints included: 1) the composite of all-cause mortality and nonfatal ACS; 2) the composite of all-cause mortality, nonfatal ACS, and stroke; and 3) the composite of all-cause mortality, nonfatal ACS, and unplanned coronary revascularization during follow-up. Endpoints were adjudicated by a clinical events committee on the basis of original source data. Members of the clinical events committee were blinded to other patient data and NIRS imaging characteristics. Post-discharge survival status was obtained from municipal civil registries. Nonfatal ACS included ST-segment elevation myocardial infarction (STEMI), non-STEMI, or unstable angina pectoris as defined in accordance with the guidelines of the European Society of Cardiology (3,4). Stroke was defined according to the guidelines of the European Stroke Organization (5). Unplanned coronary revascularization was defined as PCI or coronary artery bypass grafting, which initially was not planned after the index angiography and enrollment in the study.

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome
CI = confidence interval
CLR = culprit lesion related
HR = hazard ratio
IQR = interquartile range
IVUS = intravascular ultrasonography
LCBI = lipid core burden index
MACCE = major adverse cardiac and cerebrovascular events
NIRS = near-infrared spectroscopy
PAD = peripheral artery disease
STEMI = ST-segment elevation myocardial infarction