Near-infrared spectroscopy for cardiovascular risk assessment? Not ready for prime time

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This editorial refers to ‘Determinants of high cardiovascular risk in relation to plaque composition of a non-culprit coronary segment visualized by near-infrared spectroscopy in patients undergoing percutaneous coronary intervention’3, by S.P.M. de Boer et al., on page 282

The rupture of an unstable atherosclerotic plaque precedes the majority of acute coronary syndromes, and considerable effort has been devoted to identifying patients at increased risk of future coronary ischaemic events. Atherosclerosis imaging is a potentially attractive strategy to detect vulnerable coronary plaques, with each modality having its own advantages and limitations. Different characteristics of the atherosclerotic plaque can be targeted with imaging, such as the number and severity of luminal narrowings with angiography, atheroma burden and remodelling with intravascular ultrasoundography (IVUS), elastic properties with elastography, radiofrequency-determined plaque types with virtual histology, fibrous cap thickness and necrotic core with optical coherence tomography, extent of calcifications with computed tomography, and inflammation with positron emission tomography.1 Near-infrared spectroscopy (NIRS) provides chemical assessment of tissues, and catheter-based NIRS can generate spectra that may distinguish cholesterol from collagen, which could be explained by the fact that 90% of patients were treated with statins.

The relatively weak correlation between NIRS and IVUS means that < 10% of the variance in plaque burden is explained by LCBI. Whether this observation means that NIRS can provide relevant complementary information to IVUS cannot be determined with the results of the current study. Alternatively, the low correlation could potentially be explained by methodological issues pertaining to IVUS and NIRS imaging and analysis in this study. IVUS imaging was performed at a frequency of 20 MHz, which results in lower image resolution compared with higher frequency (40–45 MHz) catheters. Also, IVUS and NIRS imaging were performed using different catheters, not with a catheter combining both modalities; given the limited spatial registration of NIRS, the matching of the arterial segment to be evaluated by both techniques may have been suboptimal. Thirdly, it appears that a single cross-section was measured on IVUS as only area measurements are reported. The selection process for the two-dimensional cross-section of interest to be analysed should have been described. On the other hand, if a longer arterial segment was traced, it would have been interesting to know the method of selection for the segment of interest and its length. Indeed, distance from the ostium has been reported to be an independent predictor of LCBI.5 In the present study, however, the authors have not reported this parameter and do not seem to have included it in the multivariable models. Finally, the reproducibility of repeated NIRS pullbacks and measurements are not presented.

The authors argue that the weak or non-significant associations between LCBI and both clinical characteristics and plasma biomarkers suggest that NIRS could provide additional independent information about cardiovascular risk. An alternative explanation could be that technical or conceptual issues related to NIRS may be responsible for these results, as discussed below. Indeed, it is surprising that diabetes did not affect the findings on NIRS, especially given that the severity and progression of coronary atherosclerosis as evaluated by IVUS have been shown to be associated with the presence of diabetes.4 Plasma total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides did not correlate with NIRS-determined LCBI, which could be explained by the fact that 90% of patients were treated with statins.

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The important question of the clinical value of NIRS will need to be addressed by attempting to link LCBI with future cardiovascular events. The current study could not address this crucial issue because of its cross-sectional design. Nevertheless, there were no differences in LCBI between patients presenting with ACS (47% of the study population) and those with stable angina (53%). This result contrasts with that of a previous NIRS study which reported significant differences in the frequency of lipid-rich plaques, in both the culprit and non-culprit lesions, between patients with unstable and stable angina.6 Plaque burden determined with IVUS has been shown to be predictive of future cardiac events;7 if NIRS reliably identified lipid-rich plaques in patients, it could theoretically provide prognostic information. The relationship of NIRS and clinical findings could, however, be obscured by the fact that not all plaque ruptures result in a cardiovascular event (some ruptures are clinically silent) and not all such events are the result of plaque rupture (some coronary events are related to plaque erosion).8 A small study of 87 patients has recently suggested that differences in plaque lipid content could be detected after 7 weeks of intensive statin therapy, while no differences were seen on IVUS.9 Thus, NIRS might be a sensitive tool to detect early changes in plaque content. Indeed, NIRS has been shown to detect accumulation of lipids within the arterial wall at an early stage of experimental atherosclerosis in pigs, thereby predicting the subsequent development of fibroatheromas.10 Interestingly, LCBI detected by NIRS seemed to correlate well with the presence of coronary endothelial dysfunction, a characteristic of early atherosclerosis, in a study of 32 patients.11 Further, recent data suggest that axial redistribution of LCBI is an acute prognostic marker for post-procedural myocardial infarction12 and that stenting of lesions with large LCBI may be associated with greater risk of intra-stent thrombus formation.13

Catheter-based isolated NIRS imaging provides very limited spatial registration and no structural information on the arterial wall. Combining the strengths of IVUS for arterial wall imaging and the potential strengths of NIRS could provide benefits for more refined assessment of vascular disease. A combined NIRS and IVUS catheter was approved by the US Food and Drug Administration for coronary use in patients, and its potential has recently been highlighted in a case series.14 Studies evaluating this combined NIRS–IVUS catheter are ongoing, and the future will tell whether this tool will be of additional value. Other combinations in multimodality imaging catheters are also possible.15

de Boer et al. conclude the discussion of their study by wondering about the potential of NIRS to provide additional information.
about the patients’ cardiovascular risk. So, where does this leave NIRS for risk assessment? While the study adds to the body of data collected with catheter-based NIRS, it could not address the prognostic value of this imaging modality. The presence or absence of links between LCBI on NIRS at baseline and future cardiovascular outcomes will need to be evaluated. Future work should also aim at determining whether NIRS can detect changes over time in LCBI in patients treated with antiatherosclerotic therapies, and whether such changes are clinically relevant and correlate with changes in clinical outcomes. Until the association between NIRS findings and future cardiovascular events is established, it will not be possible to know if there is a role for NIRS in the assessment of cardiovascular risk. Whether three-vessel NIRS would be required and whether such an evaluation could influence the intensity of medical therapy or the revascularization strategy is not known. Thus, it is not clear at this stage how NIRS would be used in clinical practice for this indication. The search therefore continues for improved strategies for the identification of the vulnerable plaque, the vulnerable artery, and, most importantly, the vulnerable patient.

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