EDITORIAL COMMENT

Vulnerable Plaque Detection: When OCT Is Not Enough*

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Ultimately, the goal of the in vivo, intravascular imaging detection of vulnerable plaque is to provide the clinician with a diagnostic tool that identifies high risk plaques prospectively in order to treat and prevent acute coronary syndrome (ACS) events. In this context there are a number of ways to look at the study by Nakano et al. (1) in this issue of JACC.

The first way to look at this data is pessimistic—that the study by Nakano et al. (1) is one of an increasing number of (admittedly small) studies questioning the accuracy of the optical coherence tomographic (OCT) diagnosis of a thin-cap fibroatheroma (TCFA) (2,3). OCT has been touted as the most promising and robust of several intravascular imaging technologies for vulnerable plaque detection. (Of note, there is no difference between optical frequency domain imaging [OFDI] used in the current study and frequency domain [FD]-OCT manufactured by St. Jude Medical [Minneapolis, Minnesota]; they merely represent different implementations of the same fundamental technology.) For example, in a core-lab study by Kim et al. (4), the intraobserver reproducibility was high for the in vivo assessment of both fibrous cap thickness and lipid arc; but in the interobserver analysis (a more fair representation of what might happen clinically), 4 highly trained individuals had an intraclass correlation coefficient of 0.49 for fibrous cap thickness and 0.77 and 0.71 for the maximum and average lipid arc, respectively (4). Similarly, in the current study the positive predictive value of OCT alone was only 60%; and the negative predictive value was 88% (1). Limitations to the accurate OCT assessment of lipid plaque include, but are not limited to, artifacts caused by shallow or tangential beam angulation and confounders such as the presence of fibrous cap macrophages, both of which can produce dropout and the appearance of lipid (whether or not lipid is actually present) leading to a false-positive diagnosis. In addition, quantification of lipid by OCT is problematic and is restricted to the arc of lipidic plaque (which may or may not be adequate for TCFA diagnosis).

The second way to look at the study by Nakano et al. (1) is more optimistic—that the use of 2 imaging technologies may improve on the diagnostic accuracy of a single technology, including OCT. Using 2 catheters and 2 machines is cumbersome, expensive, and unrealistic. However, and while once a fantasy, combined imaging devices are now a reality. Infraredx (Burlington, Massachusetts) has developed a combined intravascular ultrasound (IVUS) and near-infrared spectroscopic (NIRS) catheter that is available commercially (5). Prototype combination IVUS and OCT catheters have been developed and used in animal models (6,7). If combined imaging technologies are the answer, then the question become which ones. Grayscale IVUS+NIRS? Grayscale IVUS+OCT? Radiofrequency IVUS+OCT? OCT+NIRS (or other similar method to detect lipid)? All are now technically possible, but issues of intellectual property may limit the commercialization of certain combinations. For example, of the 3 distinct and different radiofrequency IVUS technologies that have been developed, only integrated backscatter (IB)-IVUS (the radiofrequency IVUS technology that was used in the study by Nakano et al. [1]) is owned by a company that also makes OCT. Unlike OFDI and FD-OCT, these 3 radiofrequency IVUS technologies are not interchangeable; they use different algorithms;
and each, alone or in combination with OCT, requires histologic and clinical validation. Unfortunately, IB-IVUS is the least available of the 3, being only available in Japan.

Third, while Nakano et al. (1) are to be commended on their study and while histopathologic correlations are important, at some point it is necessary to move away from pathologic correlation to clinical outcomes studies—initially as prospective registries and ultimately as multicenter trials. Imaging findings that reliably predict (or exclude) events are more important than studies showing that one or another technology (or any combination of technologies) correlate with histopathology with a great degree of accuracy—even if the imaging technology is flawed when compared with histopathology. Unlike IVUS-virtual histology that was used in the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) (8), VIVA (VH-IVUS in Vulnerable Atherosclerosis) (9), and AHEROREMO-IVUS (European Collaborative Project on Inflammation and Vascular Wall Remodeling in Atherosclerosis-Intravascular Ultrasound) (10) studies, prospective clinical data associated with patient outcomes are not available for IB-IVUS or OCT or the combination. In addition, pathology studies do not indicate which findings are important in vivo. Nakano et al. (1) focused on the % lipidic area by IB-IVUS. The essential message of their study is that combining fibrous cap thickness assessment by OCT (a limitation of IVUS with or without radiofrequency tissue characterization) with lipid quantification by IB-IVUS (a limitation of OCT) improved on either alone. However, the reported positive predictive value of 100% and negative predictive value of 98% are unrealistically optimistic and unlikely to survive greater scrutiny, especially when studied clinically.

Finally, recent clinical, in vivo imaging studies using OCT have suggested that ruptured plaques with thrombus formation may less common, underlying only approximately 50% of ACS cases (11–15), than have been suggested pathologically (16). Thus, while identifying vulnerable plaques that are TCFA and preventing TCFA-rupture-related ACS may be launderable, this approach ignores the issue of other vulnerable morphologies such as erosions, precursors of spontaneous coronary dissection, calcified nodules, and severe stenoses.

Ultimately, we return to the study by Nakano et al. (1) and the other studies noted previously that attempt to provide the clinician with a robust, accurate, easy-to-use, and easy-to-understand and interpret diagnostic tool that has a high positive and negative predictive value in the clinical setting and that does not require specific expertise or a core-lab analysis to determine whether a plaque is a TCFA and whether it should be treated preemptively: a yes/no, “red light”/“green light,” “treat”/“don’t treat” tool. OCT alone does not appear to be this tool. Perhaps combination imaging devices or technologies. Only time and only clinical studies will tell.

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REFERENCES


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