JACC: CARDIOVASCULAR IMAGING VOL. 11, NO. 6, 2018
© 2018 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER

iVIEW

EDITOR'S PAGE

Ruptures and Thickening

Optical Coherence Tomography as the Arbiter of the Fibrous Cap

Farouc A. Jaffer, MD, PhD,[a] Y. Chandrashekhar, MD[b]

Coronary artery disease remains a leading cause of mortality worldwide, primarily through acute events mediated by progression and disruption of thrombosis-provoking atheroma. The necrotic core of advanced atheroma harbors highly prothrombotic material, including components of tissue factor, von Willebrand factor, and plasminogen activator inhibitor-1. Exposure of these contents to flowing blood can spur thrombosis and is a critical feature of many acute coronary syndromes (ACS). It is therefore vital that the fibrous cap, a collagen-rich structure overlying advanced atheroma, resist disruption and maintain separation of blood from thrombogenic necrotic cores.

Intravascular imaging using intravascular ultrasound (IVUS) and optical coherence tomography (OCT) is becoming increasingly important for improving outcomes of percutaneous coronary intervention (PCI) and helps reduce "geographic miss" or inadequately covering residual diseased segments when deploying stents (1). OCT, a high-resolution imaging modality based on the backscatter of light, also provides valuable insights into the architecture of the fibrous cap. In this issue of *iJACC*, 2 studies using OCT provide new understanding of the importance of the fibrous cap. In the first study, Hougaard et al. (2) investigated plaque ruptures that remained uncovered, as seen with OCT, in patients with ST-segment elevation myocardial infarction undergoing primary PCI with coronary stenting. The key insight motivating this study was the recognition that the most stenotic zone of the angiographic culprit lesion might not always match the site of the culprit plaque (3). The investigators recognized therefore that a subset of stented lesions might not actually cover the actual culprit plaque rupture site driving the ACS.

What might be the frequency of such uncovered plaque ruptures following PCI with stenting? To address this query, the investigators imaged 77 patients with ACS using intravascular OCT as well as IVUS with plaque composition assessment. Patients underwent OCT and IVUS within 48 h of PCI, but not prior to PCI, a potential weakness of the study. In 10 of 77 patients with suitable image quality, the investigators found evidence on OCT of 11 uncovered or partially covered plaque rupture sites in 10 patients. These sites demonstrated a cavity appearance on OCT. All such sites were located proximal to the stent, with the majority located very near to the proximal stent edge (average distance 0.15 mm). Overall, uncovered plaque ruptures were uncommonly found. Intriguingly, uncovered lesions had greater positive remodeling, necrotic cores, and plaque burden and tended to be of shorter length compared with covered lesions. However, as astutely noted by the editorialists Mori et al. (4), cavities have not been observed in patients with coronary artery disease with sudden cardiac death, raising the possibility that the residual cavity may have been caused by PCI itself. Without baseline imaging prior to PCI, it

From the [a]Cardiovascular Research Center and Cardiology Division, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; and the [b]University of Minnesota and VA Medical Center, Minneapolis, Minnesota. Dr. Jaffer has received sponsored research grants from Merck Sharp & Dohme, Canon, and Siemens; and is a consultant for Boston Scientific, Abbott Vascular, and Siemens. Dr. Chandrashekhar has reported that he has no relationships relevant to the contents of this paper to disclose.

ISSN 1936-878X/$36.00 https://doi.org/10.1016/j.jcmg.2018.05.009

is not possible to know if a coronary artery cavity can occur naturally.

What is the natural history of such uncovered plaque ruptures (cavities)? To answer this next important question, the investigators performed follow-up intravascular OCT and IVUS with plaque composition assessment at the 12-month mark in the same patients, a strength of this study. They found that 3 of 8 upstream uncovered culprit plaque ruptures did not sufficiently heal and remained with residual cavities. Notably, uncovered plaque rupture sites experienced a reduction of about 50% in luminal area, and 2 of 3 patients with persistent cavities developed recurrent symptoms. Perhaps persistent ruptures could provide a highly accessible route for inflammatory leukocytes to enter the uncovered plaque site and drive plaque progression. Overall, this intriguing paper reinforces that OCT could help avoid harmful geographic miss (5) by identifying accurately the culprit rupture site. However, optical coherence tomographic studies prior to primary PCI are needed to test this hypothesis.

At the other end of the spectrum, Nishiguchi et al. (6) harnessed OCT to study the thickness rather than the rupture or absence of the fibrous cap. It is well recognized that the high-resolution capabilities of OCT allow reliable measurement of the fibrous cap thickness, especially when enhanced imaged analysis is performed (7). In an intriguing randomized study of 3-week delayed versus immediate moderate-dose statin therapy in 53 patients with ACS, the investigators performed OCT imaging of nonculprit plaques at 3 time points: baseline, 3 weeks, and 36 weeks. Remarkably, immediate prescription of statins (even just moderate, not high intensity) conferred a benefit on fibrous cap thickening beyond delayed statin prescription. As eloquently articulated by the editorialists Min et al. (8), this observation could provide a new mechanism as to why immediate statin therapy in patients with ACS might acutely stabilize plaques and reduce event rates, far before a reduction in plaque burden might occur.

OCT continues to shed valuable light on mechanisms of ACS and plaque stabilizing pharmacotherapy, and even though there are challenges for precise diagnosis of thin-capped fibroatheroma (9), OCT remains the current gold-standard method to assay the fibrous cap in patients, provided its limitations, artifacts, and mimics are carefully recognized (7). What of the future of fibrous cap assessment? Novel imaging technologies such as micro-OCT (10) and optical coherence tomographic near-infrared fluorescence molecular imaging (11) could provide even greater insights into fibrous cap structure and its prorupture milieu, such as penetrating cholesterol crystals and heightened inflammatory proteolytic activity. More recent advances such as polarization sensitive OCT (12) will possibly reveal even more about the fibrous cap dynamics. The fibrous cap surface-lumen interface is where substantial risk resides for patients with ACS, and OCT is illuminating the path forward.

ADDRESS FOR CORRESPONDENCE: Dr. Y. Chandrashekhar, University of Minnesota/VAMC, Division of Cardiology (Mail Code: 111c), 1 Veterans Drive, Minneapolis, Minnesota 55417. E-mail: shekh003@umn.edu.

REFERENCES

1. Maehara A, Matsumura M, Ali ZA, Mintz GS, Stone GW. IVUS-guided versus OCT-guided coronary stent implantation. J Am Coll Cardiol Img 2017;10:1487–503.

2. Hougaard H, Hansen HS, Thayssen P, Antonsen L, Jensen LO. Uncovered culprit plaque ruptures in patients with ST-segment elevation myocardial infarction assessed by optical coherence tomography and intravascular ultrasound with iMap. J Am Coll Cardiol Img 2018;11:859–67.

3. Legutko J, Jakala J, Mintz GS, et al. Virtual histology-intravascular ultrasound assessment of lesion coverage after angiographically-guided stent implantation in patients with ST Elevation myocardial infarction undergoing primary percutaneous coronary intervention. Am J Cardiol 2012;109:1405–10.

4. Mori H, Narula J, Virmani R. Juxta-lesional cavitary formation in coronary intervention: imaginary, incidental, or iatrogenic? J Am Coll Cardiol Img 2018;11:868–71.

5. Liu J, Maehara A, Mintz GS, et al. An integrated TAXUS IV, V, and VI intravascular ultrasound analysis of the predictors of edge restenosis after bare metal or paclitaxel-eluting stents. Am J Cardiol 2009;103:501–6.

6. Nishiguchi T, Kubo T, Tanimoto T, et al. Effect of early pitavastatin therapy on coronary fibrous-cap thickness assessed by optical coherence tomography in patients with acute coronary syndrome: the ESCORT study. J Am Coll Cardiol Img 2018;11:829–38.

7. Kini AS, Vengrenyuk Y, Yoshimura T, et al. Fibrous cap thickness by optical coherence tomography in vivo. J Am Coll Cardiol 2017;69:644–57.

8. Min JK, Chandrashekhar Y, Narula J. The immediate effects of statins on coronary atherosclerosis: can phenotype explain outcome? J Am Coll Cardiol Img 2018;11:839–41.

9. Nakano M, Yahagi K, Yamamoto H, et al. Additive value of integrated backscatter IVUS for detection of vulnerable plaque by optical frequency domain imaging. J Am Coll Cardiol Img 2016;9:163–72.

10. Liu L, Gardecki JA, Nadkarni SK, et al. Imaging the subcellular structure of human coronary atherosclerosis using micro-optical coherence tomography. Nat Med 2011;17:1010–4.

11. Yoo H, Kim JW, Shishkov M, et al. Intra-arterial catheter for simultaneous microstructural and molecular imaging in vivo. Nat Med 2011;17:1680–4.

12. Villiger M, Otsuka K, Karanasos A, et al. Coronary plaque microstructure and composition modify optical polarization. J Am Coll Cardiol Img 2017 Dec 9 [E-pub ahead of print].