



Figure 2. Pathological Findings Collected From the Culprit Lesion Showed Fibrin Clots

(A) Hematoxylin and eosin stain. (B) Phosphotungstic acid hematoxylin stain.

stenosis. Two years later, ISR developed that was treated with another SES. Once again, re-ISR developed 19 months later inside the SES that was implanted for ISR of the initial SES. Multimodality imaging (intravascular ultrasound [IVUS], coronary angiography, and optical coherence tomography [OCT]) were used (Fig. 1). IVUS showed the culprit lesion, which was an ISR lesion, to be echolucent tissue. Coronary angiography showed it to be sharply demarcated white tissue. OCT findings of the lesion showed that although the surface of the culprit lesion (which appeared as a white surface by angiography) was a signal-rich structure, underneath it contained a low signal and some microchannels in the deeper layer tissue. Percutaneous coronary intervention was performed with a distal protection device, and the pathological examination of the aspirate demonstrated fibrin clots (Fig. 2). Kume et al. (1) reported earlier that signal-rich structures without backscattering visualized by OCT are fibrin clots. The low-signal images in the deep tissue layer contained microchannels suggestive of organized thrombi. These results indicate that the white neointima-like coverage visualized by angiography after SES implantation could be a fibrin clot covering chronically formed thrombi, and that multimodality imaging could help in understanding the pathogenesis of ISR patterns after drug-eluting stent implantation.

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APPENDIX

For supplementary videos and their legends, please see the online version of this article.

Fat Around the Heart

We are intrigued by the report of Cheng et al. (1) on pericardial fat volume as a predictor of increased death and disability for cardiovascular disease. Although the investigators were not able to distinguish epicardial fat from pericardial fat and consequently omitted a discussion on the prognostic value of epicardial fat in predicting premature death and disability from cardiovascular disease, the data are of great interest. Threshold values of epicardial fat thickness (measured by echocardiography) were established previously, and increased epicardial fat mass was proposed as a predictor of cardiovascular disease by Iacobellis et al. (2). Furthermore, current knowledge of epicardial and pericardial fat suggests that these 2 tissues have different metabolic and physiologic properties (3-5). Given the difference in the metabolic function and anatomical locations of epicardial and pericardial fat, it may be reasonable to ask the following 2 questions. First, does pericardial fat increase the atherosclerotic burden because of the known immunomodulatory function of white adipose tissue (6,7)? Secondly, does epicardial fat increase the chances of heart failure because of its anatomical proximity to the myocardium? We have reasoned previously that epicardial fat delivers substrate directly to the heart and sets the stage for myocardial steatosis, akin to visceral fat setting the stage for hepatic steatosis (8). In short, there remain many unanswered questions regarding the fat around the heart, but with the help of modern technologies, the answers may be just around the corner.

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REPLY

We appreciate the letter from Thomas et al. for emphasizing the emerging value of measuring fat around the heart. However, we respectfully disagree with the primary assertion in the letter, since we in fact did study epicardial fat as defined by the letter authors. On computed tomography (CT), our designation of pericardial fat was "all adipose tissue detected within the pericardium," which matches the definition of epicardial fat specified by Iacobellis et al. (1). A closer look at our work will additionally reveal that we separately studied the volume of adipose tissue inside and outside of the pericardium. In doing so, we showed that only fat inside the pericardium held predictive power for the risk of future cardiovascular events.

Although some investigators performing CT-based research have defined pericardial fat as we did (2-4), others have used pericardial fat to encompass adipose tissue both inside and outside of the pericardium (5,6). Undoubtedly this nonuniform labeling creates confusion. Given the increasing attention paid to fat surrounding the heart and coronary arteries, standardization of terminology may be in order. This notwithstanding, readers of the literature should cautiously examine the methodology to ensure understanding of the exact fatty depot being measured.

The ability to derive additional prognostic information from standard noncontrast calcium scoring CT by quantifying fat volume inside the pericardium is important. We look forward to understanding further the impact of this measure through future investigations.

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Prognostic Significance of Strain Imaging in Amyloidosis

In the interesting article in a recent issue of *JACC* by Koyama et al. (1), tissue Doppler (TD) longitudinal strain measured at the left ventricular (LV) base was reported to be an independent predictor of outcome in patients with cardiac amyloid light-chain (AL) amyloidosis. These findings point out an interesting potential clinical application of strain imaging for risk stratification in these subjects. However, caution is needed in accepting the independent prognostic role of basal strain, as a number of established prognostic factors, such as LV ejection fraction, New York Heart Association functional class, natriuretic peptide plasma concentration, cardiac troponins, indexed left atrial volume, the ratio of mitral peak velocity of early filling to early diastolic mitral annular velocity, right ventricular dysfunction, and renal failure, were not considered in survival analyses. Several evidences confirmed a major impact of these factors on clinical outcome in patients with cardiac AL amyloidosis (2). This may be of particular importance because nearly 70% of cardiovascular events (15 of 22) occurred in group 3 (cardiac amyloidosis with clinical evidence of heart failure), where the relative contribution of these variables to clinical outcome is expected to be relevant. Even if a subgroup analysis showed a borderline significant association of basal strain with outcome among patients with no clinical evidence of heart failure, it should be considered that most of these variables are important determinants of outcome in the pre-clinical stages of heart failure as well (3).

In addition, we believe that the evaluation of strain imaging as a prognosticator in cardiac AL amyloidosis should not be limited to the assessment of baseline deformation values. We recently reported an early improvement in both average longitudinal strain and systolic dyssynchrony after treatment with melphalan and dexamethasone, an aspect that was not detectable by color TD (4). Because response to therapy is an important predictor of survival in these patients, the prognostic meaning of changes in strain pattern after therapy might be an intriguing issue to investigate. The clinical impact of myocardial dyssynchrony—a controversial question in cardiac amyloidosis, for which, to date, 3-dimensional echocardiography and color TD have yielded conflicting results, ranging from increased dyssynchrony to abnormal hypersynchronization—may also represent an interesting application of strain imaging. Lastly, the promising role of speckle tracking imaging should be pointed out. Very recent