context of overall plaque burden in CV risk prediction.

2. Intravascular ultrasound (IVUS) has been the predominant invasive imaging modality used to ascertain plaque features. The spatial resolution of IVUS (~150 µm) is insufficient for the diagnosis of pathological thin-cap fibroatheroma (TCFA; fibrous cap of 65 to 80 µm). Therefore, the limited predictive ability of IVUS to identify TFCA may have contributed to imprecision in the characterization of lesion morphological changes over time. Virtual histology and integrated backscatter IVUS techniques have been developed to provide additional insight into individual plaque risk stratification by providing information about the spatial distribution of various plaque tissue types (i.e., lipid, fibrous, calcific, etc.). Unfortunately, the spatial resolution of backscatter-based IVUS techniques remains limited, and the ability to accurately distinguish various plaque tissues when compared with real histology is questionable.

3. Most plaque ruptures are subclinical but these events may be a principal mechanism underlying plaque progression and, ultimately, the development of plaque burden. Disregarding rupture-prone plaque risks ignoring the pathophysiological substrate for plaque progression, and ultimately increases in plaque burden.

In conclusion, with the existing, although imperfect, evidence on vulnerable plaque from various clinical studies, there is ample space for debating the predictive value of vulnerable plaque identification. However, promoting the concept of the vulnerable plaque as a myth may hinder further research capable of obtaining novel insights into the transformation of subclinical plaque rupture into manifest atherosclerosis, and limiting the accumulation of knowledge that may shed light on mechanisms of plaque progression. In the absence of evidence, we should not assume evidence of absence in the role of high-risk plaque in the genesis of atherothrombotic events.

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REPLY: Vulnerable Plaque

Absence of Evidence or Evidence of Absence

We thank Drs. Albaghdadi and Muse for extending our discussion on the merit of detecting “vulnerable plaques” by imaging. We agree with Albaghdadi and Muse that we should not neglect a potential role of individual plaque imaging in our risk assessment of patients. As we discussed in our article, identifying certain plaque characteristics may improve our accuracy of risk prediction. Our intent was to emphasize, however, that there is overwhelming evidence—using various tools of assessment—in regard to the strong relationship between the burden of atherosclerotic disease and risk of myocardial infarction and death (1) compared with the much weaker data on “vulnerable plaques” in this context. Indeed, none of the papers listed by Albaghdadi and Muse in support of “vulnerable plaque” risk prediction adjusted for plaque burden: Puchner et al. (2) merely adjusted for stenosis severity. Furthermore, major adverse cardiovascular events in the study by Stone et al. (3)—as discussed in our paper—are composed almost exclusively of “soft” events, which should not be compared with predicting death as is the case with most of the studies listed for plaque burden. Current evidence suggests the atherosclerotic plaque volume is the predominant factor for determining risk of myocardial infarction and death, whereas specific plaque characteristics may have a modifying effect. It is unclear at present which individual plaque features are most useful for this purpose and whether such assessment is of clinical value. Furthermore, the “vulnerable” characteristics of a given plaque should not be seen out of context of the patient’s specific milieu. The fate of a plaque rupture largely depends...
on the patient’s vulnerability—which is often neglected in our considerations of patients’ risk of adverse events. The “protecting” effect of dense calcium found by Criqui et al. (4) indeed may be interpreted as a marker for individuals who are resistant to vascular thrombosis in response to plaque ruptures and thus exhibit more features of plaque healing/organization, which is often neglected in our considerations of patients’ risk of adverse events. The “protecting” effect of dense calcium found by Criqui et al. (4) indeed may be interpreted as a marker for individuals who are resistant to vascular thrombosis in response to plaque ruptures and thus exhibit more features of plaque healing/organization in the absence of events. The PESA (Progression of Early Subclinical Atherosclerosis) study found subclinical atherosclerotic disease in 63% of participants within a middle-aged cohort (5). The discussion on risk assessment in patients warrants a broader, comprehensive view rather than focusing on individual plaque components.

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Musculoskeletal Pain and Cancer Risk of Staff Working With Fluoroscopically Guided Procedures

We took great interest in the paper by Orme et al. (1) recently published in the Journal; however, we have some concerns regarding the statistical analysis. As the authors noted, it has already been indicated that the incidence of musculoskeletal pain is associated with higher case volumes and more years in practice for interventional cardiologists. In other words, the total time exposed to a radiation-bearing lead apron might lead to increased risk of musculoskeletal pain. Therefore, it is essential to investigate the association between the total radiation exposure time (self-reported exposure time per week × years in the current profession) and the proportion of work-related pain. Similarly, the association between the total time of wearing a lead apron (time per week × years in the current profession) and the proportion of work-related pain also should be analyzed. Unfortunately, years in current profession was not integrated into the analysis when the authors investigated the factors associated with increase of work-related pain. As a result, this led to some cumbersome and feeble explanations, such as constant and different physical stress to argue why nonphysician employees in the interventional lab reported a higher prevalence of work-related musculoskeletal pain, even if they were younger with fewer working years. If the authors investigated the association between musculoskeletal pain and the total time the catheterization lab operators and staff wore a radiation-bearing lead apron, they might have been to obtain evidence to clarify the issue. Moreover, it might have been more interesting to investigate whether there is any correlation between the pain score and the total time of wearing a lead apron in participants exposed to radiation without taking a pain medication.

In this cross-sectional case-control study, the authors identified no difference in cancer prevalence between groups (9% vs. 9%; p = 0.96). We suspect a significant bias within this analysis because many staff involved in procedures with radiation exposure had fewer working years and less cancer risk, exhibiting a linear/linear-quadratic, no-threshold radiation relationship with stochastic effects (2). Thus, the comparison of cancer prevalence between groups should be stratified by the working years.

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