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EDITORIAL COMMENT

Illuminating Culprit Plaque Histology by Optical Coherence Tomography

Shedding New Light on Old Insights*

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Coronary atherosclerosis continues to be major cause of death in the developed world (1). Although we have known for at least a century that fissures and ruptures of coronary arteries are the cause of coronary thrombosis and, in the last 2 decades, that plaque erosion and calcified nodule are additional causes of thrombosis, our ability to use this knowledge in a real-time fashion to affect the treatment of patients with acute coronary syndromes (ACS) has been limited (2). Although angiography-guided percutaneous coronary intervention (PCI) has become the standard of care for treatment of ACS, it provides little understanding of culprit plaque phenotypes and relies instead on recanalization of obstructed arteries by mechanical means. This has led to decades of improvements in devices and in pharmacological agents aimed at relieving luminal obstruction. Although iteration in currently used techniques continues to evolve, it seems unlikely that further major advancement in the care of patients with ACS will come through this type of inquiry. The recent introduction of intracoronary optical coherence tomography (OCT) to the armamentarium of the interventional cardiologist offers us a chance to observe in living patients for the first time the morphologies underlying luminal thrombus formation and perhaps in the future to tailor therapies based on information gained in a prospective fashion.

In this issue of *JACC: Cardiovascular Interventions*, Higuma et al. (3) offer the first glimpses into what such a world would look like by describing the incidence, morphological characteristics, and PCI outcomes of culprit plaques in 112 patients presenting with ST-segment elevation myocardial infarction (STEMI). The authors report that plaque rupture was the dominant morphology underlying cases of STEMI but that plaque erosion and calcified nodule accounted for up to one-third of cases. These data suggest that although these cases are linked by the common clinical endpoint of ST-segment elevation, the underlying features and causes of STEMI are considerably more complex.

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Before the recent introduction of OCT in the coronary imaging arena, knowledge about the etiology of luminal thrombosis was generated through careful autopsy analysis of cases of sudden coronary death. Plaque rupture refers to a lesion consisting of a necrotic core with an overlying thin, ruptured fibrous cap that leads to luminal thrombosis because of contact of flowing blood with a highly thrombogenic necrotic core (4). Conversely, plaque erosion shows a luminal thrombus with an underlying base rich in smooth muscle cells and proteoglycans with mild inflammation (5). More than one-half of erosions are devoid of a necrotic core, but when present, the core does not communicate with the lumen because of the thickened fibrous cap. The least common of all lesions giving rise to acute coronary thrombosis is the calcified nodule, recognized by calcified plates with calcified bony nodules that protrude into the lumen resulting in discontinuity of the fibrous cap with an overlying thrombus (6).

Pathological examination of 200 cases of sudden coronary death with thrombosis demonstrated that the majority of subjects (65%) had evidence of underlying plaque rupture as the etiology, whereas 30%

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of cases showed evidence of plaque erosion (2). Only 5% of cases showed calcified nodule as the underlying cause. Moreover, significant differences in patient demographics existed, with erosion being the predominant morphology underlying thrombi in younger women, whereas plaque rupture was dominant in men regardless of age and in older (i.e., >50 years of age) women (5). Calcified nodule remains a poorly understood entity that is mainly seen in older individuals.

Autopsy data have their limitations. They are subject to referral bias (i.e., representing mostly young, sudden coronary death victims and excluding nonfatal myocardial infarction cases). These limitations raise the important question of whether the incidence of different plaque morphologies at autopsy are truly representative of what is seen during the care of living patients.

Intracoronary OCT is a technique that measures backscattered light, or optical echoes, derived from an infrared light source directed at the arterial wall. The favorable resolution capabilities (10 to 15 μm), validated ex vivo, allow superior definition on the order necessary to resolve thin fibrous caps and other defining features of plaque morphology. Although previous work has defined plaque morphologies of patients presenting in ACS by OCT (7), the study of Higuma et al. (3) is the first to define the incidence of the 3 lesion morphologies (i.e., rupture, erosion, and calcified nodule) in patients presenting with acute STEMI. Their findings are similar to the autopsy findings reported in the preceding text with important caveats as mentioned in the following text. In their study, Higuma et al. (3) report that although patients with erosion were younger than those with rupture, male versus female differences were not as easily discernable. This is likely because of the small sample size and the predominantly male makeup of the study subjects. Rupture was by far the dominant lesion morphology. As expected, erosion and calcified nodule had a higher prevalence of fibrous plaque and lower incidence of lipid burden. Interestingly, diameter stenosis after thrombectomy was not different among the 3 plaque types, contrasting sharply with some autopsy reports in which plaque erosions had less luminal stenosis compared with rupture cases (5). This might be due partly to limitations of OCT wherein residual thrombus burden after thrombectomy might make it difficult to define where plaque begins and thrombus ends. Moreover, the limited axial penetration of OCT makes it hard to detect tissues that reside behind thrombus.

What, then, to make of these data and their implications for the management of cases of STEMI? There is good reason to believe that the data presented by Higuma et al. (3) are probably correct in terms of their identification of plaque phenotypes. However, in order to begin to translate this knowledge to the care of patients, we need a better understanding of the differing pathophysiology of these lesions. One immediate and important example is in the analysis of thrombi in these cases. Although autopsy data have suggested that in plaque erosions, thrombi are later stage compared with ruptures, the details of cellular and molecular makeup of thrombi in erosion cases remain largely understudied in living patients (8). Such data could have tremendous importance for how these lesions are treated. It is likely that thrombus initiation in cases of erosion occurs well before the beginning of symptoms. Older organized thrombi, as seen in cases of erosion, may be more difficult to resolve by mechanical means or strategies using antiplatelet agents alone. Autopsy cases show that intramyocardial emboli are more common in eroded plaques (70% of cases) compared with ruptures (40%) (9). Although Higuma et al. (3) reported no differences in Thrombolysis In Myocardial Infarction flow grade ≤2 among the 3 lesion morphologies, this seems likely the result of the small samples size and limited clinical indices for detecting microvascular perfusion. From clinical experience with cases like those studied by Higuma et al. (3), overwhelming and residual thrombus may be seen in cases of OCT-defined erosions that might be more amenable to triple anticoagulant therapy with aspirin, clopidogrel, and warfarin/oral anti-Xa inhibitors. Further study of this issue is clearly warranted.

In summary, the data of Higuma et al. (3) raise perhaps more questions than they answer. The clear demonstration of differences in plaque morphology in cases of STEMI reinforces decades-long autopsy data demonstrating similar findings. For OCT to fully meet its potential, it needs to become an imaging modality with important clinical relevance. Before this is possible, a more clear link between differing lesion morphology/pathophysiology in STEMI cases and its treatment needs to be made in an experimental clinical setting. Precision medicine requires that we begin to move beyond the limits of angiography. In the future, we need to customize the care of the STEMI patient tailored to the specifics of his or her disease.

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