Distal Embolization After Percutaneous Coronary Interventions

Prediction, Prevention, and Relevance*

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Atherosclerotic plaques responsible for coronary heart disease are heterogeneous in their composition, containing a variable amount of lipid, scar tissue, calcium, neovessels, inflammatory cells, and thrombotic material (1). In comparison with lesions found in stable coronary heart disease, coronary lesions responsible for acute coronary syndromes (ACS) consist of disrupted plaques with superimposed thrombus, and disrupted plaques in turn tend to have larger necrotic lipid cores and greater plaque inflammation (1).

Spontaneous distal embolization of thrombus or atheromatous gruel from the epicardial culprit lesion is common in ACS and might be further triggered by percutaneous coronary interventions (PCIs) (2,3). Factors that increase the risk of distal embolization include PCI of vein grafts containing large amounts of friable atheroma, PCI on culprit lesions containing thrombus responsible for ACS, and the use of atherectomy. Distal embolization leads to microvascular obstruction, sluggish flow, or no-reflow and has been postulated to result in myocardial necrosis; however, not all forms of sluggish or no-reflow are due to distal embolization. Slow flow or no-reflow in ACS might also be the consequence of microvascular vasoconstriction and microvascular damage resulting from extensive myocardial necrosis, in which case it might be a marker rather than direct contributor to myocardial damage (4–6). The clinical and prognostic impact of post-PCI distal embolization is not unambiguously established, although it is plausible that distal embolization could obstruct nutritive flow to viable myocardium, thereby inducing necrosis with an adverse effect on clinical outcome; however, no-reflow occurring as a consequence of necrosis would not have any direct effect on outcome independent of the extent and severity of underlying necrosis (4–6). Regardless of the mechanism, slow flow or no-reflow after PCI is generally associated with an adverse clinical outcome in ACS (7).

In this issue of the Journal, 2 papers report on the relationship between measures of plaque composition and the frequency of post-PCI distal embolization in patients with ST-segment elevation myocardial infarction (STEMI) (8) or angina (9). The plaque composition was assessed by Virtual Histology intravascular ultrasound (VH-IVUS) (Volcano Therapeutics, Inc., Rancho Cordova, California) in which spectral analysis of radiofrequency ultrasound backscatter signals from the IVUS images are evaluated to define fibrous area, fibro-fatty area, dense calcific area, and necrotic core area within the plaque (10). In the first study, 71 patients with STEMI undergoing primary PCI were evaluated for evidence of distal embolization after stenting, with ST segment re-elevation (corroborated by increased corrected Thrombolysis In Myocardial Infarction [TIMI]-frame count) as a marker of distal embolization. Before stenting, the culprit lesion was subjected to mechanical thrombectomy followed by IVUS examination, and VH-IVUS was used to characterize plaque constituents. The necrotic core volume in the culprit lesion was the major direct correlate of distal embolization, which occurred in 15.5% of patients: a necrotic core volume of $\geq 33.4 \text{ mm}^3$ predicted distal embolization with 82% sensitivity and 64% specificity (8). Pre-stent thrombectomy alone also induced distal embolization in 13 (18%) patients. In another study, 44 patients with angina undergoing PCI were evaluated for signs of distal embolization (9). Distal embolization was detected by the number of high-intensity transient signals (HITS) with a Doppler guidewire (11,12). Once again, the necrotic core size by VH-IVUS before PCI was an independent predictor of distal embolization, and patients in the highest tertile of HITS count had a significantly larger necrotic core area compared with patients in lower tertiles (9). Although both studies come to similar conclusions, several issues must be considered to place these interesting observations into perspective. First of all, both studies had a small sample size and the findings were not prospectively validated in an independent additional cohort of patients; thus the observations must be considered preliminary. Second, the patterns observed on VH-IVUS do not consistently correlate with histology, raising concerns that inferences from VH-IVUS as to identity of plaque components must be taken with a grain of salt (10,13,14). Third, even if one were to assume that identifying the risk of distal embolization by VH-IVUS will lead to selective use of adjunctive distal protection techniques and improved clinical outcome, to perform VH-IVUS of the culprit lesion in STEMI, the authors had to perform thrombectomy first.

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which added time and in itself triggered distal embolization in 18% of cases—hardly a desirable outcome (8). Fourth, even if we could accurately predict lesions most likely to cause distal embolization, can distal embolization be prevented and, if so, does that translate into better ventricularographic or clinical outcome? Several studies have shown that adjunctive use of distal protection devices with PCI in ACS reduces distal embolization; however, despite such success, a majority of the randomized controlled clinical trials have failed to demonstrate any beneficial impact of distal protection devices on infarct size, left ventricular function and remodeling, or clinical outcome (15–21). These discouraging outcomes data have once again raised the question of whether distal protection devices are effective in eliminating all distal emboli or whether distal embolization leading to slow flow or no-reflow after PCI is more a marker or correlate of myocardial damage rather than an important contributor to myocardial damage. Not withstanding these limitations, the 2 reports in this issue of the Journal provide potentially interesting information that needs to be validated prospectively in larger cohorts of patients. The clinical significance of post-PCI distal embolization, the effectiveness of distal protection devices in preventing embolization, and the ultimate impact of reducing distal embolization on robust markers of clinical outcome remain uncertain and warrant further investigation.

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