**EDITORIAL COMMENT**

**Embolization**

The “Dark Side” of Percutaneous Coronary Interventions*

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Filters placed distal to native coronary lesions have not provided the hoped clinical benefit, but they changed forever our ideas on the frequency and relevance of downstream embolization during angioplasty. The first pilot studies of angioplasty and stenting using the Angioguard guidewire filter (Cordis, Johnson & Johnson, Miami Lakes, Florida) in 15 (1) and 37 (2) native coronary arteries were carried out in patients with acute coronary syndromes and stable angina. Atheromatous particles were retrieved from 100% (1) and 75% (2) of the Angioguard filters, respectively.

Intracoronary Doppler guidewire (DGW) and coronary flow reserve have been replaced by pressure guidewires and fractional flow reserve to assess lesion severity. It is the merit of 2 groups (Iena, Germany and Osaka, Japan) (3–7) to have identified a new application for this technique in the detection of coronary emboli in vivo.

The Iena group showed that Doppler ultrasound could detect high-intensity transient signals (HITS) produced by Sephadex microspheres (Amersham Pharmacia Biotech, Uppsala, Sweden) in an in vitro model (3), identifying and counting particles with a mean diameter of 52 μm. In this issue of *JACC: Cardiovascular Interventions*, Okamura et al. (7) confirm that methylmethacrylate microspheres ≥50 μm in diameter could be detected as HITS, with a close relationship between DGW counts and particle number. In both studies, however, artificial particles were used. The acoustic properties of these particles made of homogeneous polymers with a spherical shape are likely to be different from those of heterogeneous emboli composed of soft atheroma and thrombus in various phases of organization, with very irregular shapes as shown in histology studies of retrieved specimens (2,8).

The associations among the number of HITS, flow impairment, and myocardial necrosis have been varied across several studies. Some studies have observed no significant relationship between HITS and post-procedural coronary flow velocity reserve (CFVR) (3,5) or rise in myocardial necrosis markers (3). In contrast, other studies have shown positive correlation between the number of HITS and coronary resistance index (5), CFVR (6), troponin, and creatine kinase-MB rise after percutaneous coronary intervention (PCI) (5,6). Okamura et al. (4) provided further support that DGW-detected HITS truly identified emboli, showing in 16 ST-segment elevation myocardial infarction (STEMI) patients that HITS were detected in all patients undergoing PCI with no distal filter protection device but in no patient randomized to receive the Percusurge GuardWire (Medtronic AVE, Santa Rosa, California). A common limitation in these studies (3–7) was the inability of DGW to estimate the size of embolic particles in vivo, which might play a role in the functional consequences of the embolization (9,10).

There is consistent evidence that in patients undergoing elective PCI, HITS are detected more often after stent implantation than after balloon dilation (3,5,6). One of these studies showed that balloon and/or stent advancement was associated with a higher number of HITS, compared with that seen during pre-dilation and post-dilation (6). The timing of maximal detection of HITS was immediately after balloon deflation (3,4).

In the clinical part of the present study, Okamura et al. (7) enrolled 37 consecutive patients with acute STEMI. After coronary thrombectomy using an aspiration catheter, patients underwent a PCI-staged procedure requiring a first balloon dilation, second balloon dilation, stenting, and then post-dilation. The number of DGW-detected HITS was reported after each passage. The relationship between number of HITS and no-reflow was assessed using myocardial contrast echocardiography (MCE) and angiographic indexes of microvascular perfusion. High-intensity transient signals were detected in 95% of patients and were more frequent after stenting, in agreement with previous studies (3,5,6). The correlation observed between the number of HITS after first balloon dilation and after stenting is a novel finding and suggests the possibility to detect a higher plaque friability in patients with STEMI at an early stage and potentially plan a treatment to prevent further myocardial damage.

The lack of correlation between number of HITS, presence of no-reflow evaluated by MCE, and left ventricular remodeling may have several explanations. The prevalence of no-reflow assessed by MCE was only 5.4% (2 of 37 patients). This might have been a consequence of the highly

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selected population and of the universal use of coronary thrombectomy. Thrombus aspiration has been shown to reduce microvascular obstruction assessed by MCE in a previous study (11), and it improved myocardial reperfusion in a recent randomized study in acute STEMI (12). Moreover, no-reflow is multifactorial (13), with capillary impairment due to post-ischemic damage of vessel wall integrity, obstruction, and myocardial swelling being the prevailing mechanisms rather than embolization or spasm of arteriolar resistance vessels. The use of nisorandil, nitroprusside with further thrombectomy, was left to the operator's discretion in the present study. These drugs may also offset the detrimental effects of embolized particles. Finally, the variability of interindividual microcirculatory response to embolized particles due to differences in baseline inflammatory state (14) and inflammatory response to the PCI itself might also influence the functional consequences of emboli. As microvascular obstruction assessed by MCE predicts left ventricular remodeling (15), it is not surprising that the number of HITS did not show a correlation with left ventricular remodeling. This could explain the absence of a relationship between number of HITS and left ventricular ejection fraction at 22 days. The higher number of HITS in patients with transient impairment of Thrombolysis In Myocardial Infarction (TIMI) flow grade and the relationship between total number of HITS and corrected TIMI frame count suggests that emboli can exert a detrimental effect on CFVR, as suggested by a previous study (6). However, while in that study the reduction of postprocedural CFVR was due to increase of baseline average peak velocity, an elegant study (16) with quantitative cardiovascular magnetic resonance imaging in 40 patients undergoing elective PCI showed that the myocardial perfusion reserve index was impaired 24 h after PCI in segments with new areas of late gadolinium enhancement distal to the stent, due to a blunted hyperemic response in the presence of normal baseline blood flow, and that this impairment reverted to normal 6 months after the index procedure. These data probably indicate the presence of 2 patterns of impairment of CFVR that can depend on the extent of irreversible myocardial damage, the degree of microvascular dysfunction, and not ultimately the size of emboli, which has been shown to be heterogeneous, varying from 47 to 2,503 μm in vivo (2).

In conclusion, the study by Okamura et al. (7) shows that iatrogenic embolization during PCI, in the setting of acute STEMI, is a common phenomenon that can be detected by intracoronary DGW. Its functional and clinical impact might not be relevant when previous thrombectomy already shielded the microcirculation and the underlying myocardium from the detrimental effect of a greater atherothrombotic burden and in the presence of a complex multifatorial link between microvascular obstruction and ongoing myocyte death.

Further studies combining DGW with new imaging techniques, such as optical coherence tomography, may facilitate the identification of plaques at risk for distal embolization.

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