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EDITORIAL COMMENT

Intrastent Tissue Prolapse and Late Cardiac Events

Innocent Bystander or Culprit?*

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Intrastent tissue protrusion is not an infrequent finding in patients undergoing coronary intervention, especially if used in conjunction with intravascular imaging. Tissue protrusion has been detected by intravascular ultrasound (IVUS) imaging in at least one-third of all percutaneous coronary interventions, and its incidence is even higher when optical coherence tomography is used (1). Despite this, our understanding of its clinical significance remains uncertain. Smaller studies have found differing results regarding its significance, with some reporting high risk for clinical events and others finding no such association. Thus, it seems only natural to wonder whether tissue protrusion increases the risk for adverse cardiac events such as distal embolization and/or stent thrombosis. Moreover, if such associations do exist, would stent post-dilation alone be an effective treatment?

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In this issue *of JACC: Cardiovascular Interventions*, Qiu et al. (2) bring some clarity to this question by presenting the most systematic analysis of the occurrence (as detected by IVUS) and clinical significance of intrastent tissue prolapse in a subset of 2,072 patients who were enrolled in the ADAPT-DES (Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents) study. Their findings were as follows: 1) tissue protrusion in their cohort was seen in 34% of lesions by IVUS; 2) tissue protrusion was more commonly seen in patients with myocardial infarction (i.e., ST-segment elevation myocardial infarction [STEMI] or non-STEMI) compared with those with unstable angina or stable disease); 3) intrastent plaque prolapse was not associated with increased cardiac death, myocardial infarction, or stent thrombosis at 2 years; and 4) the presence of intrastent plaque prolapse was associated with reduced risk for target lesion revascularization (TLR) at 2 years.

Several findings deserve further comment. First, the increased incidence of tissue prolapse in patients presenting with myocardial infarction has been reported previously (3). This is not surprising given what we know of the types of plaques underlying STEMI and non-STEMI. The majority of these lesions are ruptured plaques filled with thrombogenic particles and associated with heavy clot burden. Stenting these lesions results in this material (thrombus in particular) protruding through the stent struts. The relationship of tissue prolapse with larger myocardial infarction as measured by creatine kinase, creatine kinase–MB, and troponins should not be thought of as causal but rather only associative. Larger thrombus burden would be expected in larger myocardial infarctions, and these cases would have greater incidence of tissue prolapse.

Second, why was tissue prolapse not associated with increased risk for late cardiac events? There are a few possibilities. One is that material that prolapses through struts is mainly thrombus, and once flow is restored, thrombus resolution will take place via endogenous thrombolytic mechanisms. A previous IVUS study in patients undergoing stenting for acute myocardial infarction demonstrated an initially high incidence (70%) of tissue prolapse, which had completely resolved at the time of 13-month reimaging

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(4). Another possibility might be that this was not a natural history study. Treatment was left to the discretion of the operator, and it seems likely that most patients with plaque prolapse underwent aggressive stent post-dilation, as indicated by larger device diameters and higher balloon pressures. Thus, the effect of plaque prolapse on late events would be confounded by the post-imaging operator intervention.

Third, is plaque prolapse associated with reduced risk for TLR? Again, the effects of operator intervention in the tissue protrusion group could heavily affect study outcomes. If, as we surmise, aggressive post-dilation was performed after "thrombus/tissue" was seen in the stent, this represents a significant confounder that could alter the relationship between tissue prolapse and TLR. A larger final luminal area in the tissue prolapse group might have prevented some cases of restenosis, as minimal stent area and follow-up minimal luminal area are significantly and positively correlated (5). Thus, it remains entirely possible that operator intervention is responsible for the association of tissue prolapse with reduced risk for TLR.

In addition to these issues, there are additional limitations to the study of Qiu et al. (2) that deserve comment. Different types of tissue may prolapse through struts and perhaps have differential effects on late cardiac events. Strut penetration into the necrotic core with prolapse of its contents into the lumen might have greater long-term deleterious effects than thrombus which would be expected to resolved. We have previously shown prolapse of struts into necrotic core regions was more frequent in thrombosed stents than in patent ones (6). Soeda et al. (1) used optical coherence tomography, a technology with much higher resolution than IVUS, to show that it was only the irregular disrupted plaque protrusions that were associated with an increased incidence of adverse events, not the smooth protrusions (1). An additional proof that some forms of tissue protrusion are not totally benign is the experience with tissue prolapse after stenting of degenerate saphenous venous graft lesions, which often contain extensive foam cells and large necrotic cores (7,8).

What should we conclude from the study of Qiu et al. (2)? Intrastent tissue protrusions are not infrequently encountered post-coronary stenting, especially in patients presenting with myocardial infarction. It remains unclear whether tissue prolapse really has little clinical significance as suggested by the results of the present study, because operator intervention with aggressive stent post-dilation prevented a clear understanding of its natural history. What we can say is that optimizing post-procedural stent expansion in cases in which tissue prolapse is seen may minimize any potential adverse effect it might have on cardiac events. Given its frequent occurrence, routine imaging and post-dilation in cases in which it is present should become standard, especially in patients presenting with STEMI or non-STEMI. Better characterization of the type and extent of the prolapsed tissue with a technique such as optical coherence tomography is needed to determine whether some types of tissue prolapse carry clinical significance while others do not. The findings of this study may also be important for researchers developing stents with a closed-cell design to minimize thrombus or tissue prolapse and embolization. With tissue protrusion being such a common finding and with the clinical event rate in patients with protrusion being so low, it will be extremely difficult to design a study adequately powered to detect a statistically and clinically meaningful difference between stents with new design and the currently used ones.

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