Optimizing Percutaneous Coronary Intervention Outcomes

The Next Steps

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Death and myocardial infarction rates have been reduced significantly with the enhanced management of cardiovascular risk factors. That’s the good news. Conversely, a significant risk for subsequent adverse ischemic events remains, particularly after acute coronary syndromes (ACS). This risk of recurrent ischemic events appears to be highest early after the ACS event, decreasing over time to that of chronic stable angina by 6 to 12 months. The cause of increased events is a composite of disease progression, especially in the culprit vessel in the absence of intervention, but it also involves nonculprit lesions that appear to have a variable risk of progression.

Much has been learned about the potential risk of late recurrent events. Vulnerable plaques, often in multiple lesions and vessels, have been described in patients with ACS via different imaging modalities, including plaque rupture as seen on intravascular ultrasound, increased plaque temperature, angioscopic descriptions of plaque disruption with intracoronary thrombus, and morphological markers identified by coronary angiography. Associated with these morphological definitions of plaque instability have been the systemic patient markers of inflammation, best described by C-reactive protein, which is a significant predictor of late adverse ischemic events.

Although all of the described markers have been associated with lesion instability, leading to an increased risk of late ischemic outcomes, the impact of therapeutic interventions has been harder to define. Late event rates appear to be related to lesion and clinical markers, suggesting the existence of a definable patient group with increased risk. The benefits of early percutaneous coronary intervention (PCI) for ACS accrue from decreasing early recurrent events attributable to the primary culprit lesion and from reducing the risk of late culprit lesion progression. Late restenosis of the primary lesion as well as disease progression in nonprimary (untreated) lesions, however, all contribute to an increased risk of late events. In this drug-eluting stent era with low restenosis rates, if secondary “at risk” lesions could be identified and treated at the time of the initial PCI, late outcomes should improve. Several questions remain: What is the magnitude of the risk of nonculprit lesion progression leading to late events? How can one easily identify at-risk noncritical lesions? Could prophylactic revascularization of noncritical lesions with drug-eluting stents lead to improved outcomes?

In this issue of Circulation, Glaser et al partially address the above issues. They evaluated the relative risk of nonculprit lesion progression from the National Heart, Lung, and Blood Institute Dynamic Registry. In all, 5.8% of patients had late angiography documenting progressive disease in vessels not initially treated, and in the majority (87%) of cases late progressive lesions were not significantly stenotic on initial angiography. Nearly one third of the progressions occurred in the primary target vessel and were equally distributed proximal or distal to the primary lesion. Furthermore, as the authors point out, because of the elimination of cases without follow-up angiography, the true incidence of progressive disease may have been higher. As opposed to restenosis, which rarely results in death or myocardial infarction, progressive lesion disease appears to possess the characteristics of an unstable plaque with the inherent risk of death or myocardial infarction. More than half of the patients presented with ACS. Thus, the risk of late progression, not surprisingly, is related to the initial clinical presentation, being more common in patients with ACS. A substudy population with available pre- and late angiography showed no clear angiographic predictors of future noncritical lesion instability. More underlying multivessel coronary artery disease was present in the progression group, however, and interestingly, statin use was also higher in the progression group, possibly reflecting greater suspected risk on the part of the practitioners.

Do these data suggest that the concept of “prophylactic stenting” is flawed? No. To the contrary, these data support the principle that now that the restenosis rate is in the single digits, more attention must be aimed at preventing late adverse outcomes related to progressive disease. It appears that what the authors have identified is a high-risk population with more underlying significant disease, perhaps a greater resistance to usual risk management, and a higher rate of rapidly progressive, previously noncritical coronary disease, which increases the risk of late adverse unstable coronary events. Better ways are needed to risk-stratify nonsignificant coronary disease while better defining systemic patient risks such as inflammation. The goal is to define appropriate noncritical lesions for early selected revascularization, further supported by optimum adjunctive medical risk management. The consequence should be improved late outcomes.
Examples of potential strategies include better defining the length of the primary lesion. In the article by Glaser and coworkers, the relatively high incidence of progression in the target vessel suggests that stenting may be too focal, accounting for the relatively high incidence of target vessel progression. Enhanced techniques to define potential vessel plaques also need to be refined. Although coronary angiography was not helpful in their study, historically angiography has been shown to define unstable coronary disease to a reasonable degree. In addition, Goldstein et al, using angiographic criteria, did demonstrate a predictive risk for multiple unstable lesions. Intravascular ultrasound also may specifically detect plaque fractures or other markers of lesion instability. Ocular coherence tomography and plaque temperature measurement have the potential to provide much more detailed definition of the plaque instability. In addition, growing evidence indicates that MRI may provide a noninvasive method to detect unstable plaque. The good news is that solutions should be forthcoming.

In addition to local plaque behavior, another important area of focus is the systemic inflammatory response, which is predictive of late risk. This inflammatory response may be further enhanced by the PCI stent procedure itself. Thus, the primary treatment via producing a systemic inflammatory response may contribute to the later risk of progression. Statins, particularly high dose, appear to block plaque progression and to reduce inflammatory responses. Likewise, a recent report indicates that statins reduce the PCI-related inflammatory response. Therefore, better systemic risk management should further reduce the risk of late progression.

Can all of the risk be mediated by systemic therapy alone? This seems unlikely. Lipid-lowering trials in patients with stable angina in general require 12 to 18 months or longer before a significant reduction in coronary event rates is observed. During this interval, the primary and secondary lesions remain at risk. Thus, the use of stenting for the primary and appropriately selected secondary lesions with selected adjunctive medical therapy should provide the greatest late benefits.

In summary, Glaser et al have significantly contributed to our understanding of the minimal risk of clinically important lesion progression after PCI treatment. Improved diagnostic tools should enhance identification of at-risk noncritical lesions. Coupled with better characterization of the inflammatory risk and the use of intensive statin and antiplatelet therapy, the combination of revascularization should enhance outcomes for all PCI patients, but particularly for those whose initial presentation is ACS. The initial use of one or two more stents could ultimately reduce total cost by preventing late hospitalizations with ACS. Thus, as we evolve in the drug-eluting stent era with low restenosis rates, greater attention needs to be placed on optimizing subacute and late outcomes by focusing on better management of the entire at-risk coronary vasculature. Success in reaching this goal will further improve patient outcomes.

References

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