Et Tu, Bare Metal Stent?

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When performing percutaneous coronary revascularization, physicians nearly always supplement balloon angioplasty with a stent. This decision is based on evidence that stent implantation enhances the procedural success and durability of angioplasty. Benefits of stenting, compared with balloon angioplasty, include a reduction in the incidence of lesion recurrence, manifested as reduced need for repeat revascularization and lower rates of periprocedural myocardial infarction (MI). The major shortcoming of bare metal stents (BMS) is that 20% of native vessel and 30% of saphenous vein graft patients develop angiographic restenosis from neointimal hyperplasia. About half of these patients will have clinical restenosis and require repeat revascularization. In contrast to the favorable results of stents in de novo lesions, stenting of in-stent restenotic lesions with BMS results in more restenosis. Before the drug-eluting stent (DES) era, of multiple therapies investigated, only intracoronary brachytherapy was effective in preventing recurrent in-stent restenosis.

As clinical restenosis became infrequent, another potential and untoward event related to stents became more exposed—namely, stent thrombosis. This disorder can cause abrupt coronary occlusion and frequently clinically manifests as acute MI or death. Although stent thrombosis was common during the early years of BMS use, improvements in the technique of stent implantation and the administration of both aspirin and a thienopyridine (dual antiplatelet therapy) reduced the incidence of acute stent thrombosis to clinically acceptable levels. More recently, however, some investigators have suggested that the incidence of stent thrombosis in patients treated with DES was excessive and greater than that of patients treated with BMS. The initial randomized trials comparing DES with BMS in patients with noncomplex coronary disease do not support this contention. What does appear to be a valid concern, however, is that DES patients must take dual antiplatelet therapy for an extended period of time to achieve outcomes equivalent to BMS patients, and that when stent thrombosis is observed in DES patients, it may occur late (ie, >1 year after implantation). Moreover, there has been a general perception that the risk of stent thrombosis in BMS is limited to the first few weeks and that there is no need for dual antiplatelet therapy beyond 1 month. Accordingly, clinicians now favor BMS for patients who cannot take uninterrupted dual antiplatelet therapy for at least a year and accept the increased risk that such patients will experience restenosis.

Doyle et al suggest in this issue of Circulation that some of our perceptions about the safety of BMS may be incorrect. In a retrospective analysis of a percutaneous coronary revascularization database, these investigators analyzed the frequency and outcomes of stent thrombosis and restenosis during extended follow-up in 4503 patients treated with at least 1 BMS. The primary findings, which have been reported but are underappreciated, are that late (>30 days) and very late (>1 year) stent thrombosis do occur with BMS and are associated with MI and death, and that restenosis can occur late (>1 year) and uncommonly presents as MI (2.1%), but in these patients the death rate is increased. With regard to the occurrence of late BMS thrombosis, the majority of events occurred within the first year, and there was a steady incidence of stent thrombosis out to 10 years, albeit at a very low rate. Many similarities between BMS and DES are highlighted in the study by Doyle et al, including the common use of stents for off-label indications, risk factors for late stent thrombosis (such as acute MI as procedural indication), and the clinical presentation of stent thrombosis. As recently reported with DES, stent thrombosis was more common among patients with an off-label indication, however, in the study by Doyle et al the findings were driven by saphenous vein graft interventions. The authors concluded that BMS may not be as safe as initially considered and share some of the risks for untoward events noted among DES-treated patients.

Strengths of this report include the size and consecutive enrollment of the study cohort; the duration of follow-up; the use of standardized definitions, including the most contemporary definition of stent thrombosis; and the methodologies used for data collection and analysis. On the other hand, the reported cohort reflects the practice patterns of only 1 medical center, and follow-up was available for only 93% of patients, some of whom may not have been contacted in ≤2 years. Accordingly, the ability to generalize these findings broadly may be limited, and the rates of death and MI may be underestimated.
What are the clinical implications of this report? First, as noted by the authors, in-stent restenosis must be considered more than just a nuisance disorder because it can present as MI. Although infrequent (87 cases), these events accounted for more absolute MI events than did stent thrombosis (74 cases) in the report by Doyle et al. Accordingly, one might postulate that in-stent restenosis-related MI would be observed less commonly among DES-treated patients than BMS-treated patients. Such a finding may offset any increase in MI associated with late DES thrombosis and help explain the lack of difference in rates of death and MI observed during extended follow-up of the original BMS versus DES randomized trials and large prospective observational studies.

Second, use of a BMS does not protect against the occurrence of late or very late stent thrombosis. Therefore, this mechanism of coronary occlusion should be considered in BMS-treated patients, even if it occurs years after the BMS procedure, in addition to progression of coronary disease. Also, one might wonder about the possible impact of extended dual antiplatelet therapy on the stent thrombosis and MI event rates in this population. The findings of Doyle et al suggest that dual antiplatelet therapy might be of special value for patients who receive a BMS for lesions located in coronary saphenous bypass grafts, but this remains untested.

Third, not mentioned by the authors is the prominent disparity between the overall rates of death and MI in their study and those attributable to either stent thrombosis or restenosis. At 10 years, the overall rate of death or MI was 39.9%. The rate of MI attributable to restenosis was 2.1%, and the total rate of stent thrombosis was 2.0%. At worst, the combined rate of death/MI attributable to either event was <5%. Thus, the contribution of the stented lesion to major adverse cardiac events is comparatively small. This observation highlights the need to investigate further other mechanisms of death and MI among patients who undergo percutaneous coronary revascularization and to initiate more aggressive therapies to reduce the occurrence of these events.

Not limited to the present report from Doyle et al is a general concern about our ability to accurately identify the incidence of stent thrombosis during extended patient follow-up. For example, in this report, all cases of late stent thrombosis presented with MI, and a subset of MI events were attributed to restenosis. Can we be certain of the mechanism of these events given the limitation of angiography and intravascular ultrasound for determining the pathophysiology of an event? Ideally, stent thrombosis should be counted only when the criteria of definite stent thrombosis are satisfied. Including patients with probable stent thrombosis tends to overestimate its frequency because mechanisms other than stent thrombosis, such as disease progression, can cause MI in the distribution of the stented artery. On the other hand, this definition also fails to capture patients who experience sudden death as a result of stent thrombosis. We wish to emphasize the importance of using the end points of death and MI when comparing different types of stents. Definitions for MI are standardized and well accepted, and data to determine this end point are ascertainable. Furthermore, all-cause death can be determined without ambiguity.

Clinical investigations should emphasize the importance of obtaining complete follow-up, especially for vital status, to permit a more valid comparison of interventional devices.

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References


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