**EDITORIAL COMMENT**

**Should We Routinely Use Drug-Eluting Stents for Acute Myocardial Infarction?**

Let’s Wait and See*

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How quickly time flies! It has now been a decade since reporting the first randomized trial of coronary stenting for acute myocardial infarction (AMI). At that time, it was shocking to think that one could place a metal foreign body into a thrombogenic milieu and expect the artery to remain patent. Hence, we and others conducted several randomized trials comparing primary angioplasty and stenting, and carefully excluded lesions at high risk of thrombosis (large thrombus, no reflow), utilized stents with heparin coatings (1), and optimized the antithrombotic strategy (2). These 13 randomized AMI trials showed that compared with percutaneous transluminal coronary angioplasty for AMI, bare-metal stents (BMS) reduced restenosis and target vessel revascularization (TVR) but did not improve mortality (3) or ventricular function (1,2). Based on improved angiographic results and reductions in acute and long-term ischemia, BMS quickly became the standard of care for AMI patients.

When drug-eluting stents (DES) became available, they were widely applied in a variety of off-label indications, including AMI. Although clinical outcomes after off-label use of BMS and DES were generally less favorable than for on-label indications (4,5), 60% of stents were placed for off-label indications. Nevertheless, compared with BMS, DES were associated with less TVR and rates of death and myocardial infarction that were similar to or better than BMS (6–11).

So why are we concerned about DES in the setting of AMI? First, there may be less benefit in AMI patients. Acute lesions may have more thrombus and less fibrous atheroma and may be less prone to restenosis (compared with stable plaques). Second, recurrent angina is infrequent in post-myocardial infarction patients and ischemia-driven TVR is low (5% to 8%) after BMS (1,2). Third, DES may be potentially harmful. After reperfusion, the coronary artery may remain underperfused or compressed from myocardial edema or abnormal vasomotor tone. Difficulty in determining the correct vessel size may result in late stent malapposition, an important contributor to late stent thrombosis. Moreover, clinical presentation with acute coronary syndrome, intracoronary thrombus, low cardiac output, hypotension, and hypercoagulable states—all common during acute myocardial infarction—are strong predictors of DES thrombosis (12–15). The underlying unstable plaque substrate of thin fibrous cap and necrotic atherosclerotic core may further contribute to delays in stent endothelialization and subsequent thrombosis. Finally, premature discontinuation of antiplatelet therapy is of particular concern (16) because medication compliance may be poor after AMI. In fact, one prospective AMI registry (17) found that 14% of patients treated with DES had stopped clopidogrel within the first month. Clearly these issues are concerning to the interventional cardiologist.

Theoretical concerns aside, how well are DES performing in AMI? In this issue of *JACC: Cardiovascular Interventions*, Hannann et al. (18) reported their observations from the New York State PCI Registry. Over a 15-month interval between October 2003 and December 2004, the registry enrolled 1,926 patients who were treated with stents within 12 h of symptom onset of ST-segment elevation myocardial infarction (STEMI). Surprisingly, patients treated with DES had lower mortality and need for subsequent bypass surgery even after adjusting for baseline differences. As in all registries, important anatomical and clinical variables may have resulted in physician selection bias. For example, DES may have been avoided in patients considered for subsequent coronary artery bypass graft, given the surgeon’s reluctance to operate on patients taking clopidogrel. Such selection bias may account for the observed reduction in coronary artery bypass graft after DES, whereas overall TVR was similar between DES and BMS. Likewise, differences in mortality may be caused by selection bias or chance, because randomized trials have not shown a mortality advantage of DES over BMS (19). Finally, stent thrombosis and reinfarction rates were not measured, events were not monitored or adjudicated, and antiplatelet use is unknown. Despite these deficiencies, the topic is very relevant to clinical practice and the suggested safety of DES in STEMI patients is reassuring.

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In contrast, other registries have not shown improvement in major adverse cardiac events when DES is used in STEMI patients (20). In fact, a large European registry suggested that DES are harmful (21). Given the high cost of DES, the GRACE (Global Registry of Acute Coronary Events) investigators speculated that operators may be unlikely to use DES in STEMI patients with a high risk of mortality, and this may account for the low death rate observed in some registries. Accordingly, they performed an analysis excluding STEMI patients who died during the initial hospitalization. Survival after DES and BMS began to diverge at 6 months, and by 2 years patients who received DES had a 4-fold increase in the risk of death compared with BMS (21). Some have speculated that a late increase in mortality may be caused by withdrawal of dual antiplatelet therapy when DES are not fully endothelialized. However, mortality differences between DES and BMS have not been observed in other large stent registries, so interpretation of these conflicting results remains difficult.

Randomized controlled trials are the most precise method of determining the risk and benefit of different treatments. Accordingly, Kastrati et al. (22) published a meta-analysis of 8 randomized trials comparing DES with BMS in 2,786 STEMI patients. The DES significantly reduced the need for re-intervention compared with BMS (5.0% to 13.3%, hazard ratio 0.38, 95% confidence interval 0.29 to 0.50, p < 0.001). During follow-up ranging from 1 to 2 years, death occurred in 4.6% and reinfarction occurred in 3.5%, but there were no differences in stent thrombosis, myocardial infarction, or death between DES or BMS. As better outcomes are often observed in randomized trials compared with registries because of careful patient and lesion selection and improved medication compliance, it is uncertain whether these findings are applicable to a broad STEMI population of higher-risk patients and complex lesions.

One disturbing phenomenon is an apparent increase in subacute stent thrombosis in STEMI patients compared with several years ago. The 30-day risk of BMS thrombosis was 0 to 1% in Stent PAMI (Primary Angioplasty in Myocardial Infarction) (1) and CADILLAC (Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications) (2). In contrast, the current rate of 30-day BMS and DES thrombosis is 1.5% to 2.0% (22,23). The higher contemporary rates of stent thrombosis may be attributable to slight differences in definitions, use of stents in lesions with a high risk of stent thrombosis, or failure to adhere to established recommendations for antithrombotic therapies (2,24).

Clearly, additional data are required before making firm recommendations regarding indications and contraindications for DES in AMI. The HORIZONS (Harmonizing Outcomes with Revascularization and Stents) trial has randomized 2,500 STEMI patients to Taxus DES versus BMS, with 1-year follow-up anticipated by the fall of 2008. However, even these results may be questioned because of potential differences in restenosis and stent thrombosis rates with paclitaxel-eluting stents and sirolimus-eluting stents (19). Moreover, the low adverse event rate within 12 months of primary PCI may limit our ability to detect differences in subacute stent thrombosis and mortality. Therefore, until longer-term follow-up is available for all types of DES, we believe that the appropriateness of DES for STEMI will be hotly debated for years to come.

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