Primary Percutaneous Coronary Intervention With Drug-Eluting Stents
Another Chapter in the Stent Controversy

Eric R. Bates, MD

Primary percutaneous coronary intervention (P-PCI) is the preferred reperfusion strategy for patients with ST-segment elevation myocardial infarction if it can be performed rapidly by an experienced team. Compared with balloon angioplasty, routine bare-metal stent (BMS) implantation decreases risk for target vessel revascularization (TVR) and possibly reduces myocardial infarction rates but does not reduce mortality rates. Therefore, BMS has become the dominant P-PCI strategy, despite initial concern about increased stent thrombosis rates from delayed healing or inadequate late stent apposition due to initial thrombus trapping. Less established is the role of drug-eluting stents (DES) in P-PCI. DES have the potential to further decrease TVR rates but may increase risk for stent thrombosis. In fact, the risk of stent thrombosis might even be higher in P-PCI than in electively treated patients because of the combination of increased platelet activation, delayed healing, lack of endothelialization, and the proinflammatory and prothrombotic environment in the infarct artery.

Several relatively small randomized clinical trials have shown inconsistent efficacy for DES over BMS for P-PCI. Three meta-analyses of these trials have concluded that there is no difference in death or myocardial infarction rates, but TVR rates are decreased. Variably included were 12 studies that differed in trial design, inclusion criteria, endpoint definitions, stent types, duration of clopidogrel treatment, and type of follow-up (angiographic versus clinical). They were limited by sample size and duration of follow-up and usually required angiographic documentation of stent thrombosis, which may have underestimated its true incidence.

In this issue of Circulation: Cardiovascular Interventions, Kukreja et al report a single-center registry study that is an expanded version of a previous publication. Again including the 185 ST-segment elevation myocardial infarction patients treated with Sirolimus-eluting stents (SES) from April 2002 to February 2003, they compare the results with 531 patients treated with BMS from January 2000 to April 2002 and 1022 patients treated with paclitaxel-eluting stents (PES) from February 2003 to December 2005. In the initial publication, the SES patients were compared with 183 patients previously treated with BMS and 136 patients subsequently treated with PES. As before, there were no differences between BMS and DES in the 3-year rates of mortality, reinfarction, TVR, or stent thrombosis.

This report has several limitations, including previous publication of the results from 584 of the 1738 patients, sequential recruiting periods, unbalanced cohort sizes with differential recruitment rates and follow-up duration, differences in baseline characteristics between cohorts, and temporal differences in procedural and adjunctive treatments over the 6-year study period. In fact, the use of clopidogrel, β-blockers, angiotensin-converting enzyme inhibitors, and statins during the study period fell far short of current guideline recommendations. Moreover, the statements suggesting superiority of SES over PES seem misplaced, given the statistical insignificance of the analyses, the small number of patients in the SES cohort, and the many differences between the SES and PES cohorts. It should be noted that a prior meta-analysis of 3 randomized clinical trials comparing PES and BMS in 925 patients found similar rates of death and reinfarction and a significant reduction in TVR (4.7% versus 8.3%) with PES; the same conclusion was reached with larger numbers of SES patients in the randomized trials. Nevertheless, repeating the challenging conclusion that DES offers no advantage over BMS in P-PCI is an important statement to consider, given the need for prolonged dual antiplatelet therapy with DES to decrease the risk of stent thrombosis, the extra cost of DES, and the fact that DES implantation in ST-segment elevation myocardial infarction is off-label use.

In contrast to the registry report by Kukreja et al, the 2-year data from the Massachusetts registry1 of 1221 propensity score–matched pairs of DES and BMS patients demonstrated a reduction in mortality and TVR rates with DES, and an analysis from the New York State registry found a reduction in mortality rates, but not TVR rates, with DES. These reports were limited to patients treated before 2005, so they represent the earliest experience with DES, in which selection bias may have influenced stent choice and off-label use may have been more cautiously pursued. Additionally, duration of clopidogrel therapy differed between groups.

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From the Division of Cardiovascular Diseases, Department of Internal Medicine, University of Michigan, Ann Arbor, Mich.

Correspondence to Eric R. Bates, MD, CVC Cardiovascular Medicine, 1500 E Medical Center Drive SPC 5869, Ann Arbor, MI 48109-5869, E-mail ebates@umich.edu

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Kukreja et al. suggest that the lack of benefit in their report was a result of the large number of patients with PES with slightly worse results than BMS and the small number of patients with SES with better results than BMS. They note that the PES Versus Conventional Stent in Myocardial Infarction with ST-Segment Elevation (PASSION) trial,13 the largest trial of PES versus BMS, demonstrated no benefit (although nonsignificant trends were favorable for each of the components of the composite primary end point, which showed a 31% relative risk reduction with PES), whereas the Trial to Assess the Use of the Cypher Stent in Acute Myocardial Infarction Treated With Balloon Angioplasty (TYPHOON),14 the largest trial of SES versus BMS, favored SES. However, it is important to note that the TVR rates with DES in both trials were similar (5.6% for SES and 5.3% for PES). The difference was in revascularization rates for BMS (13.4% in TYPHOON versus 7.8% in PASSION). TYPHOON included an angiographic subset, and noninvasive stress testing was performed on a routine basis at 6 months, which may have increased BMS revascularization rates. PASSION did not screen for restenosis and enrolled fewer patients with diabetes and more patients with larger target vessels, which may have decreased BMS revascularization rates. Also, the use of different BMS in the trials may have influenced TVR rates.

So, what can we conclude from the evidence base about DES in P-PCI? The only consistent message is that there is no increased risk for stent thrombosis with 1- to 2-year follow-up. Otherwise, the reports offer conflicting conclusions about mortality, reinfarction, and TVR benefits with DES. Do DES decrease mortality rates? Because there was no benefit in the mortality, reinfarction, and TVR benefits with DES. Do DES up. Otherwise, the reports offer conflicting conclusions about mortality rates. Also, the use of different BMS in the trials may have influenced TVR rates.

References


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