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

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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 reinfarction 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 registry 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.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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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, 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), 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 randomized trials of BMS versus balloon angioplasty and BMS versus DES, it is possible that the mortality benefit seen in the Massachusetts and New York registries was due to selection bias and uncorrected confounding variables. Do DES decrease reinfarction rates? The insignificant trend for reduction of reinfarction with DES in the randomized trials may well have been due to different durations of clopidogrel administration. There is no obvious mechanistic reason to support a benefit with DES over BMS now that patients are supposed to receive ≥1 year of dual antiplatelet therapy, regardless of stent type, along with β-blockers, angiotensin-converting enzyme inhibitors, and statins, when possible. Do DES decrease TVR rates? The purported benefit of DES in reducing TVR rates may be an illusion. The BMS 3-year TVR rates in the study by Kukreja et al. was 8%, which was lower than the 1-year rate of 13% seen in the DES randomized trials, where routine angiographic follow-up may have increased rates, and similar to the DES rates in PASSION and TYPHOON. Clinically, revascularization rates for restenosis after P-PCI are lower than with elective PCI, probably due to the absence of ischemic symptoms because of infarcted areas of myocardium. Moreover, improved stent designs and thinner strut diameters appear to have reduced restenosis risk with BMS. Therefore, it can be argued that equipoise exists in the comparison of DES with BMS for P-PCI and that we need larger numbers of patients and longer follow-up to reach definitive conclusions about the efficacy and safety of DES in P-PCI. The fact that the prestigious group of investigators from the Thoraxcenter found no difference in 3-year outcomes between BMS, SES, and PES in an unselected population of ST-segment elevation myocardial infarction patients challenges the recent enthusiasm for DES in P-PCI.

By the time of publication, the results of the Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) study will have been announced. Approximately 3000 patients were randomized in a 1:3 ratio to BMS or PES, more than doubling the number of patients treated with DES previously enrolled in randomized trials and correcting the large imbalance between SES and PES in the trials. The best chance for DES benefit would be in TVR reduction. Even then, because of cost considerations, it could be argued that selective use of DES to prevent restenosis and TVR in high-risk patients (diabetic patients) and in high-risk lesions (longer and smaller diameter stents) could be recommended, as it has been for elective PCI in hospital systems with limited financial resources. The greatest challenge in selecting patients for DES implantation, however, is determining emergently whether the patient is a candidate for prolonged thienopyridine therapy. As with elective procedures, DES should be avoided in the presence of financial barriers to continuing prolonged dual antiplatelet therapy, social barriers that may limit patient compliance, or medical issues involving bleeding risks or the need for invasive or surgical procedures in the following year that would interrupt antiplatelet therapy.

Disclosures

None.

References


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