

# Drug-eluting stents for ST-elevation myocardial infarction: ready for prime time?

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Primary percutaneous coronary intervention, performed in a timely manner, is currently the standard of care for patients with acute ST-elevation myocardial infarction (STEMI). Numerous clinical trials have shown the superiority of balloon angioplasty over thrombolytic therapy in decreasing the composite endpoint of death, reinfarction, and stroke in patients with STEMI [1]. Nonetheless, the efficacy of balloon angioplasty in the setting of STEMI is limited by the high risk of early reocclusion and late restenosis, providing the initial rationale for the development of coronary stents. Subsequent studies have confirmed that the implantation of bare-metal stents reduced the risk of reinfarction and target vessel revascularization compared with balloon angioplasty [2]. Bare-metal stents soon gave way to drug-eluting stents (DESs), which were first used in lower-risk, non-STEMI patient populations and were then rapidly adopted in STEMI interventions. However, the early enthusiasm for DESs subsided because of reports of very late stent thrombosis following their implantation, and the concern was especially serious for STEMI patients.

The culprit plaques in STEMI patients usually contain a large necrotic core, a thin fibrous cap, and heavy inflammatory cell infiltration, together with extensive thrombus formation. Strut penetration into the necrotic core is apparently related to delayed endothelialization and healing at the site of DES placement [3]. Furthermore, positive arterial remodeling, thrombus resorption, and stent undersizing during the index procedure may all lead to late stent malapposition, with an increased risk of stent thrombosis [4]. Hence, the lesions of STEMI patients are more complex than those of non-STEMI patients, and the risk of stent thrombosis is certainly higher as well. A number of studies have ensued to evaluate the safety and efficacy of DESs in STEMI patients. In this issue of the journal, the DEBATER trial investigators compared the use of sirolimus-eluting versus bare-metal stents in 907 patients with STEMI [5]. They found that the incidence of very late stent thrombosis was very low and similar between the two groups, reassuring clinicians of the long-term safety of DESs in this patient population.

It is now accepted that DESs can markedly reduce the risk of restenosis and, accordingly, DES use has again

been expanded to STEMI patients. Two randomized trials published in 2006 showed the benefits of DESs over bare-metal stents in patients undergoing a primary percutaneous coronary intervention for STEMI [6,7], furthering the support for clinical utilization of the DESs. For example, the TYPHOON trial showed that the placement of sirolimus-eluting stents relative to bare-metal stents significantly reduced the incidence of target vessel failure at the 1-year follow-up (7.3 vs. 14.3%, respectively,  $P = 0.004$ ), with similar rates of stent thrombosis in the two groups (3.4 vs. 3.6%, respectively,  $P = 1.00$ ). Similarly, the PASSION trial showed a more favorable rate of target lesion revascularization for paclitaxel-eluting stents compared with bare-metal stents in STEMI patients (5.3 vs. 7.8%, respectively,  $P = 0.23$ ), with an identical incidence of stent thrombosis in both groups at the 1-year follow-up (1.0%). Subsequent randomized trials also confirmed the greater efficacy yet similar safety of DESs compared with bare-metal stents for patients with STEMI, indicating that DESs can be used safely in the setting of STEMI [8]. However, long-term data are still limited on the safety and efficacy of DESs in STEMI patients and are largely provided by the DEBATER trial. At the 5-year follow-up, as shown in the current issue [5], the cumulative incidence of death plus myocardial infarction was similar in both groups (11.0 vs. 9.7%, respectively,  $P = 0.51$ ), whereas the rate of very late stent thrombosis at 1–5 years of follow-up was quite low (2.0 vs. 0.7%, respectively,  $P = 0.12$ ). These observations strengthened the proposal that DESs are safe for long-term use in STEMI interventions. By contrast, although sirolimus-eluting stents promoted a lower rate of repeat revascularization than bare-metal stents after 1 year, this difference dwindled over time, and was not significant at the 5-year follow-up. Although controversial, this finding highlights the possibility of a late ‘catch-up’ phenomenon after DES implantation.

DES technology has advanced rapidly over the past decade, and late stent thrombosis may be less of a clinical issue with the advent of newer-generation DESs. Indeed, the superiority of newer-generation DESs over early-generation DESs is shown by their relatively low propensity to induce stent thrombosis. For instance, newer-generation everolimus-eluting stents markedly

reduced the risk of very late stent thrombosis compared with early-generation sirolimus-eluting and paclitaxel-eluting stents in a large registry of 12 339 consecutive patients [9]. In addition, recent reports showed that newer-generation DESs were even safer when compared with bare-metal stents [10]. The EXAMINATION trial randomized 1498 patients with STEMI to receive either a newer-generation everolimus-eluting stent or a bare-metal stent [11]. The primary endpoint of all-cause death, any recurrent myocardial infarction, and any revascularization at the 1-year follow-up was similar in both groups (11.9 vs. 14.2%, respectively,  $P = 0.19$ ). However, target lesion revascularization was significantly lower in patients receiving the DES compared with the bare-metal stent (2.1 vs. 5.0%, respectively,  $P = 0.003$ ), as was definite stent thrombosis (0.5 vs. 1.9%, respectively,  $P = 0.019$ ). Finally, the COMFORTABLE AMI trial randomized 1161 patients with STEMI to receive biolimus-eluting or bare-metal stents [12]. At the 1-year follow-up, the composite primary endpoint of cardiac death, target vessel related reinfarction, and ischemia-driven target lesion revascularization was significantly lower in the biolimus-eluting stent group than in the bare-metal stent group (4.3 vs. 8.7%, respectively,  $P = 0.004$ ). A similar but insignificant trend was observed for the rate of definite stent thrombosis (0.9 vs. 2.1%, respectively,  $P = 0.10$ ). Therefore, the EXAMINATION and COMFORTABLE AMI trials together showed a reduction of approximately two-fold to four-fold in the rate of stent thrombosis with newer-generation DESs relative to bare-metal stents, highlighting the safety and efficacy of the new devices in STEMI intervention.

In summary, the DEBATER trial shows that long-term outcomes of STEMI patients treated with early-generation DESs are favorable, with a low risk of very late stent thrombosis. Early-generation DESs are no longer used in routine clinical practice. However, newer-generation DESs show better clinical outcomes by significantly reducing the occurrence of stent thrombosis. Therefore, we believe that DESs should be considered the preferred devices for use in STEMI interventions.

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## Conflicts of interest

There are no conflicts of interest.

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