The EMPIRE Study—Review and Comment

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The EMPIRE study arrived art by Kasliwal and associated (*see pages* xxxx) evaluated the safety and efficacy of a slow-release sirolimus-eluting stent (coated with the help of a durable polymer) in an "all-comers" like population. There were virtually no clinical or angiographic exclusion criteria, except prior coronary artery bypass graft (CABG), acute myocardial infarction (AMI), and the use of other drug-eluting stents (DES) in the target vessel. In particular, the study involved patients with multi-vessel stenting, vessels of small diameter (2.5 mm), and long lesions requiring long stents (up to 38 mm). Multiple and overlapping stenting was done in the target vessels. More than two-thirds of the patients had <3 mm long stents, with the mean reference vessel diameter being 2.42 mm; almost 50% of the implanted stents (n = 386 in 300 patients) ranged from 18–38 mm in length, the average length being above 20 mm; and 27% of patients were implanted with multiple stents.

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One-third of the patients were diabetic, while almost half had recent MI. The details of the patients and procedures show the complexity of the cases included in this registry. This is important when it comes to long-term results, clinically and angiographically.[1]

Two-thirds of the patients were followed up clinically at six months. One of the limitations of the study is that only one-third of the patients were available for repeat angiography. However, re-angiography is becoming an increasingly difficult proposition due to greater cost-consciousness and because the results of percutaneous coronary intervention (PCI) are known to be more durable more than in the pre-DES era. These problems hamper long-term clinical studies as well.

The authors reported a 100% success rate in implantation and no in-hospital major adverse cardiac events (MACE). It is encouraging that there were no stent-related MACE, in particular, thrombosis and MI, at 30 days. The technical characteristics of the stent system, such as deliverability, are excellent and superior to some of the other systems available. In fact, this is confirmed by our experience from the German ProNova study.[2]

Two deaths were reported at 6 months. While there is no evidence of acute stent thrombosis, the authors correctly state that they "cannot rule it out." In the worst case, the late stent thrombosis rate can be calculated as 0.6%. It is lower if calculated on the basis of the total number of stents instead of the number of patients in this complex cohort.

The angiographic restenosis rate was reported to be 12.6%, and the total MACE rate (repeat revascularization, MI, death) was less than 5%. The mean late loss in luminal diameter at six months was 0.59 mm.

These results compare very well with those achieved with other polymer-based sirolimus-eluting or paclitaxel-eluting stents, as well as with our experience from the ProNova study in Germany. We had implanted 77 stents in 65 patients of all-comer characteristics and the occurrence of MACE was 10.7%, target lesion revascularization (TLR) being the main culprit (n = 6). There was no MI or stent thrombosis, and only one death (unidentified if related to study device) The in-stent restenosis rate was 12.5% if calculated on the basis of the number of patients who consented to recatheterization, and 8% if calculated on the basis of the total number of target vessels treated. The figures for late loss in luminal diameter were similar to those of the EMPIRE study and within the same range as those of the recent ENDEAVOR study,[3] which used LIMUS-eluting stents.

The EMPIRE results attest to the high safety profile of the stent, considering that the population of patients was more complex than that covered by many other stent studies. The safety of DES has become an increasingly important issue.[4] An aggressive antiproliferative drug may almost completely inhibit the restenotic process and may prevent re-endothelialization of the stent for too long, resulting in late stent thrombosis. One might hypothesize that there is an inverse relationship between the late loss parameter (potential to inhibit proliferation) and the MACE rate, i.e., the acute stent thrombosis and MI or death rate.[5]

The risk factors for stent thrombosis may be the drug, the polymer, the stent design,[6] the trauma of implantation,

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or all of these together. Longer stents, as well as discontinuation of dual antiplatelet therapy, are considered the most important risk factors for acute and late stent thrombosis.[7,8] The EMPIRE study did not report compliance with extended dual antiplatelet therapy and long stents were used in a high percentage of patients—both of which were additional high-risk factors for the patients covered.

The data from the EMPIRE study must be interpreted in the light of the aforementioned challenges and the results of other real-world stent studies. The Reality and Sirtax trials with sirolimus DES reported MACE rates of 8–11% at follow-up of up to nine months, while studies with paclitaxel DES reported MACE rates of up to 13.7% (roughly half consisted of acute ischemic events like MI, stent thrombosis and death).[9] Considering the very low MI, death and stent thrombosis rates reported by the EMPIRE study, ProNova appears to be a safe and efficacious stent. However, as is applicable to all DES currently in use, dual antiplatelet therapy might be mandatory for up to 12 months or even longer to minimize the risk of late stent thrombosis. As we learn more about the safety concerns associated with the use of DES, long-term freedom from stent thrombosis and MI is likely to acquire increasingly greater significance than late loss as a surrogate marker for the efficacy of the stent, measuring the potential to inhibit neo-intimal formation. The final judgment of the clinical value of a stent will be made on the basis of its long-term safety.

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