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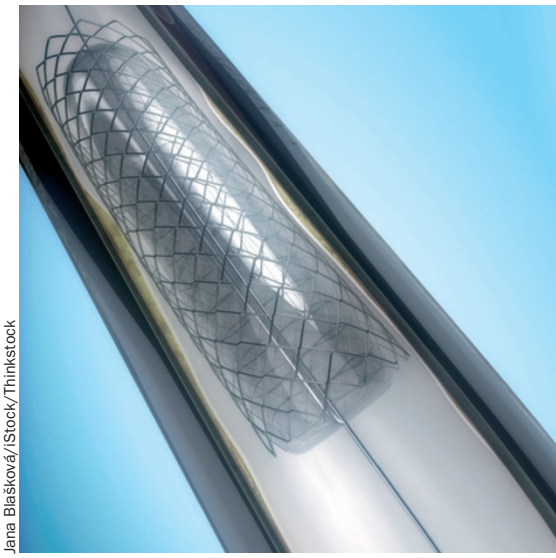
INTERVENTIONAL CARDIOLOGY

SORTing OUT stents—everolimus limits very late stent thrombosis



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Drug-eluting stents (DESs) are safe and effective, and can limit the need for repeat revascularization, but what are the long-term outcomes for patients after antiplatelet therapy has ceased? In a new study, published in *JACC Cardiovascular Interventions,* the team who conducted the SORT OUT IV trial report that, at 3-year follow-up, patients who receive everolimus-eluting stents (EES) have a significant reduction in very-late stent thrombosis formation, compared with individuals who received a sirolimus-eluting stent (SES).

First-generation DESs were approved by the FDA in the USA in 2003, when an SES was demonstrated to be superior to bare-metal stents at preventing major adverse cardiovascular outcomes. The SORT OUT IV trial is a multicentre study originally designed to assess the noninferiority of a second-generation EES (Xience™ V, Abbott Vascular, USA; or PROMUS™, manufactured by Abbott Vascular, USA, and distributed by Boston Scientific, USA) compared with a first-generation SES (Cypher Select™+, Cordis Corporation, USA) at 9-month follow-up. The team enrolled 2,774 patients who were randomly assigned to receive either an SES ($n = 1,384$) or an EES ($n = 1,390$) to treat coronary artery atherosclerotic lesions. Patients in both study arms received an average of 1.6 stents each to treat a total of 3,584 lesions (1,805 and 1,779 in the EES and SES groups, respectively). After the procedure, all patients were recommended a dual antiplatelet regimen of aspirin and clopidogrel (both 75 mg per day); clopidodrel was then stopped after 1 year.

The primary composite end point was any major adverse cardiovascular event (defined as death, myocardial infarction [MI], definite stent thrombosis, and target-vessel revascularization), with an additional patient-centred outcome (any death, MI, or revascularization), and a stent-related end point (cardiac death, target-vessel MI, or ischaemia-driven target-lesion revascularization). In the data presented for this 3-year follow-up, the investigators performed two-sided statistical tests for 95% confidence intervals and *P* value to determine superiority at all end points.

Of the original 2,774 participants, four were lost to follow-up, meaning that final data were available for 99.9% ($n = 2,770$) of patients in the trial. The primary end point occurred in 142 individuals who received an EES and 163 who received an SES (10.2% and 11.8%, respectively), but this numerical difference was not significant (95% CI 0.69–1.08, $P = 0.20$). No significant difference was observed between study arms for either the patient-centred or stent-related outcomes. Patient-centred outcomes occurred in 18.1% and 19.4% (95% CI 0.78–1.10, $P = 0.37$) of participants with an EES or an SES, respectively, and the stent-related outcome in 6.7% (EES) and 7.6% (SES) of patients (95% CI 0.67–1.17, $P = 0.38$). All-cause mortality also did not significantly differ between the two groups of patients (7.2% versus 6.7%; 95% CI 0.81–1.42, $P = 0.62$).

However, the incidence of definite stent thrombosis was significantly lower in patients who received an EES ($n = 3$) compared with those with an SES ($n = 20$; 95% CI 0.04–0.50, $P = 0.002$). Specifically, this difference was seen for very-late stent thrombosis (defined as >12 months after stenting). Only one patient in the EES group had a thrombus >12 months after stent placement, compared with 11 patients in the SES group ($P = 0.021$).

Why should the reduction in stent-thrombosis not affect mortality in patients receiving an EES? The investigators recognize that, "a general lack of statistical power due to an overall low number of definite stent thromboses may be an explanation for stent thrombosis not influencing mortality". They conclude, "as this event occurs in a small number of patients, it may not influence the other end-point components unless longer follow-up is performed".

"Although it is an important study, it has limited clinical impact on the practice in the USA, as SES is no longer being used," explains Ik-Kyung Jang from Harvard Medical School, MA, USA, who was not involved in the study. "However, those patients [who] already received SES are at slightly higher risk of stent thrombosis and, therefore, need to be aware of this late complication," clarifies Jang.

For outcomes like stent thrombosis, second-generation DESs, such as the Xience™ V and PROMUS™ EESs, are undoubtedly superior to first-generation stents. However, as the investigators demonstrate, long-term follow-up is needed to understand their benefits fully. With the promising development of new DESs with biodegradeable polymers, will the incidence of adverse outcomes be reduced even further in the future? Only time will tell.

Tim Geach

Original article Okkels Jensen, L. *et al.* Three-year outcomes after revascularization with everolimus- and sirolimus-eluting stents from the SORT OUT IV trials. *JACC Cardiovasc. Interv.* doi:10.1016/j.jcin.2014.02.014