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EDITORIAL COMMENT

Stent Selection in the Iliac Arteries

Don't Fall Through the ICE!*

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In this issue of *JACC: Cardiovascular Interventions*, Krankenberg et al. (1) publish the results of the anticipated randomized, prospective, multicenter (18 German and Swiss sites) ICE (Iliac Artery Stents for Common or External Iliac Artery Occlusive Disease) trial. This well-executed randomized trial addresses an important and clinically relevant question of which stent performs better in the iliac arterial vasculature, self-expanding (SE) or balloon-expandable (BE). Six hundred sixty patients with common or external iliac lesions were randomized to either SE or BE stents in a 1:1 fashion and then followed for the primary endpoint of binary restenosis as assessed by duplex ultrasound at 12 months. The authors report that SE stents were superior to BE stents with a 12-month binary restenosis rate of 6.1% versus 14.9% ($p = 0.006$), respectively, without significant differences in walking impairment, hemodynamic success, amputation rate, and all-cause death or periprocedural complications. The authors should be congratulated for performing a much-needed and long-awaited trial. Should operators use SE stents now in most iliac cases on the basis of these data, or will they "fall through the ice" into unclear waters that need to be better defined despite this first randomized trial?

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Endovascular revascularization of the iliac vessels has become first-line therapy for patients with lifestyle-limiting claudication and hemodynamically significant aortoiliac occlusive disease (2). Although stenting of the iliac arteries has become routine, we should recognize the results of the Dutch Iliac Stent Trial (3). This trial demonstrated that in short lesions (many of which would be included in this study), percutaneous transluminal angioplasty alone with provisional stenting (for residual mean pressure gradient of >10 mm Hg or dissection) is still a viable option, supported by 5-year data demonstrating no difference in the number of reinterventions in the treated iliac arteries (4). When stenting is required, however, it is unknown which type of stent would be best. This led to the design of the ICE trial, the first randomized trial of SE versus BE stents in the iliac arterial occlusive disease.

Results from prior studies regarding primary patency and efficacy of BE versus SE stents have been inconsistent. A large multicenter retrospective study of 2,147 patients (one-third BE and two-thirds SE stents) demonstrated similar primary patency rates at 5 years between BE (79%) and SE (75%) stents (5). Other studies suggest a superiority of SE stents; the power calculation in the ICE trial was based on assumptions of 12-month binary restenosis of 11% after BE and of 2% to 5% after SE stents (6,7). These numbers were derived from a European multicenter trial of 126 patients, which used a flexible BE stent after suboptimal percutaneous transluminal angioplasty result (post-dilation gradient of >10 mm Hg), with primary stent patency at 12 months of 89% (6). The SE numbers were derived from the CRISP-US (Cordis Randomized Iliac Stent Project-US) trial (7), which compared the stainless steel SE Wallstent and the shape memory alloy recoverable technology (SMART) nitinol SE stent, with 9-month restenosis rates of 2.7% to 3.5%. These results should be interpreted with caution given differences in baseline characteristics (e.g., frequency of presentation with restenosis), definition of endpoints (binary restenosis, target lesion revascularization, primary

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patency), duration and completeness of follow-up as well as anatomic location (common iliac artery [CIA] vs. external iliac artery [EIA] disease). The 24-month results of the prospective, nonrandomized, multicenter BRAVISSIMO (Efficacy Study of Iliac Stents to Treat TASC A-B-C-D Iliac Artery Lesions) study (8) demonstrated a primary patency rate of 92.1% for SE stents and 85.2% patency for BE stents, with the only predictors of restenosis being obesity and placement of kissing stents (where BE stents were used). Interestingly, in the BRAVISSIMO study, SE stents were used in more complex lesions (Trans-Atlantic Inter-Society Consensus [TASC] C and D), whereas BE stents were more often used in TASC A and B lesions, perhaps hinting at an advantage of SE over BE stents. In both the ICE as well as BRAVISSIMO studies, the anatomic location of common versus external iliac disease did not affect the type of stent selection, which would be common in clinical practice.

To better understand the results of the ICE trial, one must carefully examine the differences between SE and BE stents. BE stents provide high radial outward force, the ability for precise stent placement and are used more often in ostial common iliac lesions and during the placement of kissing stents (9). On an anatomic basis, the CIA is larger, frequently calcified, and prone to recoil and dissection, whereas the EIA is smaller in diameter, more tortuous, and commonly has diffuse disease. The enhanced radial strength of BE stents may make BE stents better suited for heavily calcified lesions or lesions with greater recoil (10). BE stents, however, may create artificial vessel straightening due to enhanced sheer force, perhaps promoting more neointimal hyperplasia, especially when used in the EIA. These stents are also generally available in shorter lengths, such as BE stents (17-, 27-, 37-, and 57-mm Visi-Pro, Medtronic, Dublin, Ireland) used in the ICE trial. By contrast, SE nitinol stents are flexible, easily adapt to arterial wall pulsatility, conform to varying vessel diameters (11), and are available in longer lengths. This trial, however, randomized BE and SE regardless of lesion location, which makes the results challenging to interpret with respect to anatomic location of disease.

The ICE trial shows a higher restenosis rate than previous trials, with 6.1% for SE stents and an alarming 14.9% for BE stents. A post hoc exploratory subgroup analysis suggests similar restenosis rates between BE and SE stents in heavily calcified lesions ($p_{interaction} = 0.04$), and less pronounced difference in CIA lesions (~60% stents were in CIA). This could be due to the tortuous nature of EIA and high radial force of BE stents leading to increased sheer stress, vessel straightening, and enhanced neointimal proliferation. Furthermore, higher frequency of predilation (38% vs. 26%) and post-dilation (93% vs. 22%) in the SE group may have contributed to better outcomes with SE stents. Regardless of stent selection, we as operators must recognize the risk factors predictive of restenosis/occlusion of iliac artery stents, which include: occlusion versus stenosis, longer lesions, in-stent restenosis lesions, external iliac over common iliac lesion location, and smaller arterial diameter (12), particularly those with circumferential calcification. Early studies have suggested female sex to be a prognostic indicator of poor iliac stent patency rates, though this may be due to smaller caliber iliac arteries (13). Recent data have confirmed that long-term patency of iliac stents may differ by sex with lower patency rates in women (14).

The ICE trial reaffirms excellent 12-month target lesion revascularization rates (97.2% for SE and 93.6% for BE) for iliac artery occlusive disease regardless of stent selection. Though demonstrating a statistically significant difference between the groups, these excellent outcomes highlight that endovascular revascularization with its low morbidity and mortality should be considered the preferred approach for most aortoiliac lesions. Further data are needed regarding the use of drug-coated balloons, particularly for in-stent restenosis (15), as well as drug-eluting and covered stents in iliac vessels. The findings of the ICE trial that SE stents may be superior to BE stents in the treatment of iliac arterial disease are intriguing. We should be careful in the widespread adoption of SE stents given the limitations of this relatively small randomized controlled trial, including a low duplex ultrasound completion rate and a lack of adjudication by an independent core laboratory. Further robust, randomized, prospective, protocol-driven trials are needed with independent core laboratory adjudication of device-related acute adverse events, 12-month and long-term target lesion patency, as well as clinically relevant endpoints. Let us continue investigations to identify subsets of patients (e.g., by CIA vs. EIA location, degree of calcification, lesion length) who benefit from a particular type of stent and not “fall through the ice” by fully adopting a SE stent-first strategy for all iliac endovascular revascularization procedures.

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