BEST-CLI: Best Surgery vs Less-Than-OK-Endo

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Hello and welcome to the November 2022 edition of *Vascular Disease Management*. This month we discuss the results of the long-awaited Best Surgical Therapy in Patients With Critical Limb Ischemia (BEST-CLI) randomized control trial (RCT), which was presented at the American Heart Association's 2022 Scientific Sessions.[1]

The BEST-CLI trial was touted as the modern update to the RCT Bypass vs Angioplasty in Severe Ischemia of the Leg (BASIL),[2] which was published in 2005. BASIL demonstrated no significant difference in the rate of amputation-free survival in patients presenting with chronic limb-threatening ischemia (CLTI) who were suitable candidates for surgical bypass or endovascular therapy. The BEST-CLI trial was conducted in a similar framework as BASIL: a comparison between surgical bypass first vs endovascular treatment first in patients with CLTI. BEST-CLI deviated from BASIL with 2 important exceptions: first, the surgical group was divided into 2 cohorts (cohort 1: bypass surgery first with adequate saphenous vein conduit vs endovascular therapy; cohort 2: bypass surgery first with no adequate saphenous vein conduit vs endovascular therapy); second, the primary outcome of BEST CLI was broader than BASIL, with BEST-CLI using the now commonly accepted composite of major adverse limb events (MALE, including major amputation or major limb reintervention) in combination with all-cause death.

Utilizing an intent-to-treat analysis, the BEST-CLI trial showed that the primary outcome occurred in 42.6% of the surgical group vs 57.4% of the endovascular group ($P<.001$). This was driven by a much higher rate of major reintervention in the endovascular therapy arm (surgery 9.2% vs endovascular 23.5%). There was also a significantly lower rate of above-the-knee amputation with surgery compared with endovascular treatment in cohort 1 (10.4% vs 14.9%). There were no major differences in the primary safety endpoints between groups. Surgery was technically successful in 98.3% and endovascular in 84.7% of subjects. Patients treated surgically required 6 days in the hospital compared with 3 days in the endovascular arm. In cohort 2, there was no important difference in the rate of the primary outcome or important safety endpoints.

Unfortunately, despite the long wait for an updated RCT in this disease state, BEST-CLI does little to alter the status quo. Here are 3 reasons why:

First, the exceedingly high rate of technical failure in the endovascular therapy arm (15.3%) vs the surgical arm (1.7%) in cohort 1 accounts for more than the entirety of the difference between groups. The absence of an analysis or explanation of these technical failures, which in contemporary endovascular-based studies has been less than 5% and should be expected to be closer to that seen in the surgical arm,[3-5] is a major flaw of this study. This is particularly important given the use of MALE as the study primary endpoint since technical failures inevitably lead to repeat revascularization attempts. Furthermore, there were no objective competency requirements for endovascular or surgical operators, which would be expected in a study of the magnitude of BEST-CLI.

Second, modern endovascular techniques were underutilized in the study. For example, in the superficial femoral artery lesions enrolled, only 7% of patients underwent atherectomy and less than half of patients received drug-eluting therapies (drug-coated balloons or stents). The provided procedural characteristics also do not provide granular detail regarding alternative access, lesion-crossing techniques, or anatomic complexity, which may have explained the high endovascular technical failure rates.

Third, there were significant problems with the running of the trial including protocol deviations, data missingness, and loss to follow-up within BEST-CLI. The flaws exceed the acceptable level for modern, large RCTs. For example, in the surgical arm of cohort 1, 25 of the 718 patients assigned to surgery underwent endovascular-first treatment instead of their assigned surgical treatment, 94 patients withdrew, 68 were lost to follow-up, 37 did not consent to follow-up at 48 months, and 27 were followed until their sites were terminated early. Across all 4 study arms, a total of 363 patients withdrew, were lost to follow-up, or were excluded due to data missingness/integrity issues, accounting for 19.8% of the overall analysis cohort.

In conclusion, the interpretation of the BEST-CLI resulting in surgical superiority (with adequate venous conduit) over endovascular-first treatment of CLTI should be tempered in the setting of an extremely high rate of endovascular therapy failure, driving revascularization and tipping the results toward surgery on a backdrop of nearly 20% of the enrolled patients being lost to follow-up. Simply stated, BEST-CLI was an analysis documenting surgical bypass vs substandard endovascular practice, and therefore, does not substantially add to the original BASIL trial. Furthermore, BEST-CLI fails to consider patients without adequate outflow for bypass, which is frequently seen in this cohort. In the coming weeks, we plan to evaluate our own data at Cardiovascular Institute of the South to examine the rates of technical success with endovascular techniques, and we predict this will be a better indicator of modern endovascular results. ■

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