EDITORIAL COMMENT

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BEST-CLI versus BASIL-2 Trial: Conflicting Results?

Chronic limb-threatening ischemia (CLTI) is defined as ischemic rest pain or tissue loss of the lower limb due to atherosclerotic disease[1]. Severe limb ischemia prevalence is growing given the increased global burden of diabetes, metabolic syndrome, end-stage renal disease and population ageing, with notorious impact in economics and health related quality of life (HRQoL).

Increasing interest has been growing towards an endovascular-first revascularization approach in CLTI in the last few years. This inclination is supported by the last Global Vascular Guidelines on CLTI Management[1] published in 2019, since the anatomic staging of disease GLASS (Global Limb Anatomic Staging System), designed to correlate mainly with endovascular outcomes, is considered essential for revascularization decision-making. Bypass versus Angioplasty for Severe Ischemia of the Leg (BASIL)-1 trial[2] published in 2005, was the only randomized multicentre clinical trial comparing endovascular-first (plain balloon angioplasty) to vein-bypass first revascularization strategy in patients with CLTI due to infra-inguinal disease in nearly two decades (452 patients). No significant difference was noted in the primary outcome amputation-free survival; however, better results were noted in vein-bypass first group after two years.

BASIL-1 subanalysis[3] revealed that only 25% of the patients included in the trial had infra-popliteal disease (104 patients), with or without femoropopliteal disease. Primary technical success was 86% in the vein-bypass group and only 73% in the plain balloon angioplasty group. Given the technological advance and the increment in the immediate technical success using endovascular interventions in recent years, debate continued regarding which treatment approach would be more advantageous for CLTI patients in nowadays reality.

Best Endovascular versus Best Surgical Therapy in Patients with CLTI (BEST-CLI) trial[4] (1830 patients treated in over 150 hospitals from United States, Canada, Italy, Finland and New Zealand, median follow-up 2.7 years) and BASIL-2 trial[5] (345 participants treated in 41 unit in United Kingdom, Sweden and Denmark, median follow-up 3.3 years), recruitment from 2014-2020, are two recently published real-world randomized trials with intention to treat which compared vein-bypass with best endovascular treatment in CLTI patients. Vascular and endovascular surgeons and interventional radiologists were allowed to used their preferred technique and equipment, including drug coated balloons, bare metal/drug eluting stents and atherectomy devices. Both trials encompassed real world patients: 68-75% diabetic, 80-89% with limb tissue loss and 5-13% with previous intervention to the trial leg. While BEST-CLI comprised patients with CLTI due to infrainguinal arterial disease eligible both for open and endovascular surgery without excessive risk for surgery, BASIL-2 contained only patients with infra-popliteal disease eligible for both techniques with life expectancy >6 months. About 44% of BEST-CLI participants were treated for

infra-popliteal disease. High immediate technical success rates were registered in endovascular subgroups in both trials, 85% in BEST-CLI and 95% in BASIL-2. These results are in line with contemporary series from triallists vascular units, which report a 90% technical success rate for infra-popliteal endovascular treatment[6].

BEST-CLI and BASIL-2 design had major differences, which has significant implications in trials' analysis and conclusions. Primary endpoint in BEST-CLI was all cause death or Major Adverse Limb Event (MALE), including above ankle amputation and first major reintervention (new bypass, surgical interposition graft, thrombolysis and surgical thrombectomy). On the other hand, primary endpoint in BASIL-2 was all-cause death or above ankle amputation (MALE was a secondary endpoint). BEST-CLI was designed in two parallel trials according to availability of great saphenous vein suitable for bypass (evaluated by ultrasound). Cohort 1 (1434 patients) was constituted by patients with suitable vein and cohort 2 (396 patients) without suitable vein. Both cohorts were randomly stratified 1:1 to best-endovascular treatment or surgical bypass (using alternative vein or prosthetic conduit in cohort 2). More than half of the index bypasses in cohort 1 were femoral-pedal-tibial or popliteal-pedal-tibial. A significant difference was noted in the primary endpoint (risk reduction rate, RRR, 32%) and in secondary endpoints major reintervention (RRR 65%, with 43% of major re-interventions occurring within 30 days) and major amputation (RRR 27%) in cohort 1 favouring great saphenous vein bypass. No difference was registered in all cause death between endovascular and surgery groups. Prior ipsilateral infra-inguinal revascularization and age >80 years-old were the groups less favoured by surgery. No significant difference was noted in the primary efficacy endpoint in cohort 2 (although this cohort was likely underpowered). A significant 44% RRR was noted in major reintervention favouring endovascular intervention over alternative bypass conduit in patients without suitable great saphenous vein.

In BASIL-2 patients were randomly assigned to bypass group (172 patients, only 84% had vein bypass, suitability of great saphenous vein was not specified) or best endovascular group (173 patients). Primary endpoint favoured endovascular treatment (hazard ratio 1.35) due to fewer deaths in endovascular group. The 30-day post procedural morbidity, MALE and death were similar in both groups.

To resume, BEST-CLI compared best bypass surgery versus best endovascular treatment in infra-inguinal CLTI with acceptable surgical risk, while BASIL-2 compared best endovascular versus possible bypass surgery in infra-popliteal CLTI patients. An infra popliteal subanalysis of BEST-CLI and both trials pooled results analysis are waited. HRQoL and pain scores improved in both surgery and endovascular groups in BASIL-1, BASIL-2 and BEST-CLI, with a predisposition towards fastest pain improvement in surgical groups.

A few practical questions remain. What is considered a suitable great saphenous vein in pre-operative ultrasound? Which patients have excessive surgical risk? Does anatomical complexity influence endovascular primary technical success and MALE? Which treatment is more cost-effective? Trials suggest that bypass surgery could be advantageous for patients with infra-inguinal or infra-popliteal disease with low surgical risk with suitable great saphenous vein, while best endovascular treatment may be better for high-risk patients without suitable autologous conduit. Consequently, despite attractiveness of minimally invasive advanced endovascular techniques, the possibility for treatment outside operative theater (improving surgery waiting lists) and the option for outpatient treatment in some centres (decreasing hospitalization time), an endovascular-first strategy in all CLTI patients is an erroneous concept. Endovascular and open surgery are complementary. This highlights the need for young practitioner formation and expertise in both open and endovascular methods for optimal patient care.

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