Benefits from invasive treatment in intermittent claudication: It is definitely not IRONIC!

Evidence for an invasive therapy in patients with peripheral artery disease at the stage of intermittent claudication (IC) is limited although frequently performed. Not least questioned by the results of the CLEVER trial [1], showing highest increase in peak walking time upon structured supervised exercise, the benefit of revascularization as compared to a conservative treatment strategy remains a matter of debate. Current guidelines therefore keep it open: „Endovascular revascularization is also indicated in patients with lifestyle-limiting claudication when clinical features suggest a reasonable likelihood of symptomatic improvement and there has been an inadequate response to conservative therapy“ [2]. The recently published IRONIC trial [3] now provides new data in this field.

**Invasive revascularization or not in IC**

IRONIC was a randomized controlled trial, aiming to investigate the benefit from an invasive therapy compared to „real-life” available best conservative treatment in patients with IC [3]. The study population (n = 158) comprised patients with stable IC at a moderate level without activity limiting co-morbidities. All patients received optimal medical care (ASS or clopidogrel, statin, cilostazol 200 mg / d in about ¾ of patients) and were repeatedly advised to structured, non-supervised exercise (> 30 min / day; > 3 × / week). Patients were randomly assigned to either the conservative (n = 79) or the invasive (n = 79) arm of the trial. Invasive therapy was conducted according to the TASC criteria (73 % endovascular, 27 % surgery or hybrid).

The primary endpoint was the health-related quality of life (QoL) at 12 months. As secondary endpoints served initial claudication distance (ICD) and maximal walking distance (MWD) in the treadmill test, ABI measurement, and the composite of an event-free survival.

The results were assessed on intention-to-treat: in the invasive arm 9/79 patients did not receive revascularization while in the non-invasive arm 6/79 patients underwent revascularization due to deterioration of their status. At 12 months, patients who received an additional invasive therapy improved significantly regarding nearly all QoL parameters compared to a conservative management. A significantly higher improvement was achieved in the invasive arm regarding ICD (+ 124 m vs. + 50 meters, p = 0.003), ABI (p < 0.001) and toe pressure (p = 0.03) but not MWD (+ 59 vs. + 30 meters, p = 0.17). Event-free survival at 12 months was similar with 77 % in the invasive and 88 % in the conservative arm, with very few cardiovascular events.

**Discussion**

In the CLEVER trial, supervised exercise training had shown best results in peak walking time which led the authors to the conclusion that supervised exercise is superior to stenting. However, they took only little notice of ICD to be halved after stenting compared to supervised exercise, likewise nearly all parameters of QoL improved significantly upon stenting as outlined in a subsequent letter [4].

The recent IRONIC trial now confirmed these positive results after revascularization and demonstrated a significant benefit in ICD and nearly all of the QoL parameters. The design of IRONIC was closer to daily routine in several aspects: whereas CLEVER solely included patients with aortoiliac disease, these were only 31 in IRONIC while 91 suffered from femoropopliteal and 36 from combined (including infrapopliteal) lesions. Patients in IRONIC were advised to structured – but not supervised exercise, which has limited availability due to its high logistic effort. Of note, in both trials patients with immobilizing co-morbidities, such as reduced cardiac resilience, obesity, or orthopedic conditions were excluded, although we all know these are frequent conditions in IC patients. However, a placebo effect of an invasive therapy cannot be excluded.

In summary, although design and endpoints of both trials differed, they showed concordantly better results regarding QoL but also some objective endpoints for patients with IC after revascularization, which could be offered to all patients even those with immobilizing comorbidities.

**References**


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