Early vs deferred endovenous ablation reduced time to ulcer healing in venous leg ulcers with varicose veins

Gohel MS, Heatley F, Liu X, et al; EVRA Trial Investigators. ***A randomized trial of early endovenous ablation in venous ulceration.*** *N Engl J Med. 2018;378:2105-14.*

Clinical impact ratings: GM ★★★★★★☆ D ★★★★★★☆

Question

In patients with venous leg ulcers and superficial venous reflux (varicose veins), what is the relative effectiveness of early vs deferred endovenous ablation added to compression therapy?

Methods

Design: Randomized controlled trial (Early Venous Reflux Ablation [EVRA] trial). ISRCTN 02335796.

Allocation: Concealed.*

Blinding: Blinded* (assessors of ulcer healing).

Follow-up period: 12 months.

Setting: 20 clinical centers in the UK.

Patients: 450 patients > 18 years of age (mean age 68 y, 55% men) who had an open venous leg ulcer for 6 weeks to 6 months, an ankle–brachial index ≥ 0.8, and clinically important primary or recurrent superficial venous reflux. Exclusion criteria included deep venous occlusive disease or other condition that precluded superficial venous ablation, leg ulcers with a non-venous cause, need for skin grafting, inability to adhere to compression therapy, or pregnancy.

Intervention: Early (n = 224) or deferred (n = 226) endovenous ablation added to compression therapy. The early group received superficial venous reflux ablation within 2 weeks and duplex ultrasonography 6 weeks after ablation. In the deferred group, ablation was considered after the ulcer had healed or ≥ 6 months after randomization if the ulcer had not healed. The method for ablation was at the discretion of the clinical team; the main refluxing truncal vein was ablated first, beginning at the lowest point of reflux when possible.

Outcomes: Primary outcome was time to ulcer healing. Secondary outcomes included ulcer healing and ulcer recurrence at 1 year, ulcer-free time at 1 year, and disease-specific quality of life (QoL) (Aberdeen Varicose Vein Questionnaire) and overall QoL (EuroQol Group 5-Dimension 5-Level questionnaire and Medical Outcomes Study 36-Item Short-Form Health Survey) at 6 weeks and 6 and 12 months.

Patient follow-up: 90% (intention-to-treat analysis).

Main results

Ulcer healing and recurrence results are in the Table. Median ulcer-free time at 1 year was increased in the early group vs the deferred group (306 vs 278 d, P = 0.002). Groups did not differ for QoL at any follow-up time.

Early vs deferred endovenous ablation added to compression therapy in patients with venous leg ulcers and superficial venous reflux†

Outcomes	*Early ablation*	*Deferred ablation*	*aHR‡ (95% CI)*	
Median time to ulcer healing (d)	56	82	1.4 (1.2 to 1.7)	
	Event rates		*RBI (CI)*	*NNT (CI)*
Ulcer healed at 1 y	94%	86%	9% (3 to 17)	13 (8 to 42)
			RRR (CI)	
Ulcer recurrence at 1 y	11%	16%	31% (−13 to 57)	Not significant

†aHR = adjusted hazard ratio; other abbreviations defined in Glossary. RBI, RRR, NNT, and CI calculated from data in article.

‡Adjusted for age, ulcer size, ulcer duration, and recruitment center.

Conclusion

In patients with venous leg ulcers and superficial venous reflux, early endovenous ablation reduced time to ulcer healing and increased healing at 1 year compared with deferred ablation.

**See Glossary.*

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Commentary

Population surveys find leg ulcers in 0.5% to 1% of older adults (1, 2). In 50% to 70% of cases, it is a venous ulcer due to primary (varicose) or secondary (postthrombotic) venous insufficiency (1, 2). Such ulcers can be painful, are unsightly, may be malodorous, are often slow to heal and likely to recur despite intense specialized care, frustrate patients and clinicians, and carry social and economic burdens (1, 2, 3).

The bedrock of management to heal venous ulcers remains graded leg compression therapy (30 to 40 mm Hg). Recurrence can be reduced by vein ligation or stripping and by less traumatic endovenous outpatient procedures that occlude or ablate the relevant incompetent superficial veins (2, 4).

All patients in the EVRA trial had compression therapy and half also had an endovenous procedure (mostly foam sclerotherapy or endothermal ablation) about 3 months after ulcer onset. The results were clinically important: Median times to ulcer healing and recurrence rates were lower with the endovascular intervention than with conservative therapy alone. But endovascular intervention was followed by a small numerical excess (9 vs 3) of deep venous thrombosis (DVT) (mostly calf and subclinical).

The trial of 450 patients excluded 1772 patients who had an ulcer for > 6 months. Applying these results to clinical practice will require early referral to vascular units. Another 199 patients were excluded because of "deep venous occlusive disease precluding superficial venous intervention," and < 7% of enrolled patients had a history of DVT. So, is this trial relevant for patients with postthrombotic leg ulcers? Perhaps. 32% of included patients had evidence of deep venous reflux in common femoral, femoral, or popliteal veins, presumably due to earlier subclinical DVT.

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