The EVRA Trial: Early Intervention in Venous Reflux

Original Article: A Randomized Trial of Early Endovenous Ablation in Venous Ulceration
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**A complete list of the Early Venous Reflux Ablation (EVRA) trial investigators is provided in the Supplementary Appendix, available at NEJM.org.*

OBJECTIVE

Venous disease is the most common cause of leg ulceration. Although compression therapy improves venous ulcer healing, it does not treat the underlying causes of venous hypertension. Treatment of superficial venous reflux has been shown to reduce the rate of ulcer recurrence, but the effect of early endovenous ablation of superficial venous reflux on ulcer healing remains unclear. In the Effect of Surgery and Compression on Healing and Recurrence (ESCHAR) study, superficial venous surgery in combination with compression therapy resulted in lower rates of recurrence of venous leg ulcers than compression therapy alone[12,13] but was not associated with higher rates of ulcer healing. Therefore, the Early Venous Reflux Ablation (EVRA) trial was conducted to evaluate the role of early endovenous treatment of superficial venous reflux as an adjunct to compression therapy in patients with venous leg ulcers.

METHODS

In a prospective trial conducted at 20 centers in the United Kingdom, investigators randomly assigned 450 patients with venous leg ulcers to receive compression therapy and undergo early endovenous ablation of superficial venous reflux within 2 weeks after randomization (early intervention group) or to receive compression therapy alone, with consideration of endovenous ablation deferred until after the ulcer was healed or until 6 months after randomization if the ulcer was unhealed (deferred-intervention group). The primary outcome was the time to ulcer healing. Secondary outcomes were the rate of ulcer healing at 24 weeks, the rate of ulcer recurrence, the length of time free from ulcers (ulcer-free time) during the first year after randomization, and patient-reported health-related quality of life.

RESULTS

Patient and clinical characteristics at baseline were similar in the two treatment groups. The time to ulcer healing was shorter in the early-intervention group than in the deferred-intervention group; more patients had healed ulcers with early intervention. The median time to ulcer healing was 56 days (95% CI, 49 to 66) in the early-intervention group and 82 days (95% CI, 69 to 92) in the deferred-intervention group. The rate of ulcer healing at 24 weeks was 85.6% in the early-intervention group and 76.3% in the deferred-intervention group. The median ulcer-free time during the first year after trial enrollment was 306 days in the early-intervention group and 278 days in the deferred intervention group ($P = 0.002$). The most common procedural complications of endovenous ablation were pain and deep-vein thrombosis.

DISCUSSION

In the EVRA trial, investigators found that faster ulcer healing can be attained if an endovenous intervention is performed promptly. The difference between treatment groups was statistically significant despite the provision of high-quality compression therapy in both groups, which might explain the good healing rates observed overall. Such effective compression therapy is probably not commonplace outside randomized trials, which may help explain the much slower healing times seen in the "real world."[14,15] Accordingly, the improvement in ulcer healing with early endovenous intervention is likely to be greater in clinical practice than was observed in this trial.

KEY POINTS

Significant findings of this clinical trial:

- Early endovenous ablation of superficial reflux was shown to be effective for speeding venous-ulcer healing and improving ulcer-free time

Broader clinical implications considering the interdependent relationship between the veins and lymphatics:

- Chronic venous insufficiency overloads the lymphatic system and can lead to permanent lymphatic damage[16]
- Compromised lymphatic function can lead to cellulitis that further damages the lymphatics, setting in motion a spiral of more frequent infections and worsening symptoms[17]

CONCLUSION

Early endovenous ablation of superficial venous reflux resulted in faster healing of venous leg ulcers and more time free from ulcers than deferred endovenous ablation.

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