A Randomized Trial of Early Endovenous Ablation in Venous Ulceration

Clinical Paper Review
Prepared by APV Scientific Communications *for Health Care Professionals*

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Purpose:

To assess the clinical outcomes of early endovenous treatment of superficial venous reflux in addition to standard care (multilayer compression/stockings) in contrast to standard care alone in patients with chronic venous ulceration.

Methods:

- Multicenter, randomized, controlled study conducted at 20 centers in the United Kingdom
- Randomization was conducted at 1:1 ratio for the 2 arms consisting of compression therapy and early endovenous ablation or compression therapy alone with possible deferred intervention
- After randomization, endovenous ablation was completed within 2 weeks for the early intervention; after ulcer healing or after at least 6 months in the deferred intervention arm
- Treating team decided on method of ablation: endovenous laser or radiofrequency ablation, ultrasound-guided foam sclerotherapy, or nonthermal, nontumescent methods of treatment (such as cyanoacrylate glue or mechanochemical ablation)
- **Primary endpoints:**
  - Time to ulcer healing from date of randomization at 12 months
- **Secondary endpoints:**
  - Rate of ulcer healing at 24 weeks
  - Rate of ulcer recurrence/ulcer free time during the first year after randomization
  - Patient reported health-related quality of life

Results:

- Screening of 6555 patients resulted in randomization of 450 patients; 226 in the deferred intervention arm and 224 in the early-intervention arm
- Participants baseline characteristics were similar in both groups
- **Primary endpoint:**
  - Time to ulcer healing was shorter in the early-intervention group than in the deferred intervention group
  - Median time to ulcer healing in the early intervention group was 56 days (95% CI, 49 to 66) and 82 days (95% CI, 69 to 92) in the deferred-intervention group
  - More patients had healed ulcers with early intervention (hazard ratio for ulcer healing, 1.38; 95% CI, 1.13 to 1.68; P = 0.001)

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Results (continued):

- **Secondary outcome:**
  - Rate of ulcer healing reported at 24 weeks was higher in the early-intervention group
  - The early-intervention group reported shorter time to ulcer healing than the deferred-intervention group at 12 weeks
  - Ulcer recurrence was lower in the early-intervention group in patients who had ulcers healed within 1 year after randomization
  - Median ulcer free time was greater in the early-intervention group during 1-year follow-up

Table 1: Rate of ulcer healing

	Early Endovenous Treatment Group	Delayed Endovenous Treatment Group
Rate of ulcer healing at 24 weeks	85.6%	76.3%
Rate of ulcer healing at 1 year	93.8% (210/224)	85.8% (194/226)
Rate of ulcer recurrence at 1 year	11.4% (24/210)	16.5% (32/194)
Median ulcer free time (days) at 1 year	306 (IQR 240-328) (N=204)	278 (IQR 175-324) N=203

IQR = Interquartile Range

Table 2: AVVQ outcomes

AVVQ	Baseline	6 weeks	6 months	12 months
Delayed Endovenous Treatment Group (SD)	44.3 (8.7) N=192	41.2 (9.3) N=170	39.5 (10.3) N=140	34.3 (10.4) N=130
Early Endovenous Treatment Group (SD)	44.1 (9.0) N=200	39.4 (10.2) N=176	34.6 (9.4) N=139	32.4 (8.3) N=127
Difference (95% CI)	-0.2 (-2.0, 1.6) P=.84	-2.1 (-4.0, -0.2) P=.03	-4.8 (-6.9, -2.7) P=<0.01	-1.8 (-4.0, 0.3) P=0.1

SD = Standard Deviation, CI = Confidence Interval

- Comparison of quality of life scores (AVVQ, EQ5D and SF36) showed similar results in both arms.

Table 3: EQ5D health index outcomes

EQ5D Health Index	Baseline	6 weeks	6 months	12 months
Delayed Endovenous Treatment Group (SD)	0.73 (0.2) N=226	0.75 (0.2) N=208	0.76 (0.2) N=192	0.80 (0.2) N=182
Early Endovenous Treatment Group (SD)	0.73 (0.2) N=222	0.79 (0.2) N=211	0.81 (0.2) N=186	0.83 (0.2) N=184
Difference (95% CI)	-0.01 (-0.04, 0.03) P=0.76	0.04 (0.00, 0.08) P=0.04	0.04 (0.00, 0.08) P=0.03	0.03 (-0.01, 0.07) P=0.19

SD = Standard Deviation, CI = Confidence Interval

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Results (continued):

Table 4: SF-36 outcomes

SF-36	Baseline	6 weeks	6 months	12 months
Delayed Endovenous Treatment Group (SD)	41.6 (11.9) N=224	44.3 (12.3) N=207	45.9 (12.2) N=193	47.8 (11.2) N=180
Early Endovenous Treatment Group (SD)	41.3 (11.1) N=223	46.6 (10.6) N=212	48.2 (11.0) N=187	49.3 (11.0) N=182
Difference (95% CI)	-0.5 (-2.6, 1.6) P=0.67	2.2 (0.01, 4.4) P=0.04	2.1 (-0.2, 4.3) P=0.07	1.1 (-1.1, 3.3) P=0.34

SD = Standard Deviation, CI = Confidence Interval

Table 5: Type of endovenous intervention

Type of endovenous intervention	Early Intervention	Deferred Intervention
Endothermal ablation only	71 (31.7)	54 (23.9)
Foam sclerotherapy only	111 (49.6)	100 (44.2)
Mechanochemical ablation only	5 (2.2)	1 (0.4)
Endothermal ablation and foam sclerotherapy	27 (12.1)	16 (7.1)
Mechanochemical ablation and foam sclerotherapy	3 (1.3)	0
Abandoned treatment	1 (0.4)	0
No treatment	6 (2.7)	55 (24.3)

Authors' Conclusion:

- EVRA is the first randomized trial to show that early endovenous ablation in addition to compression therapy was associated with a significantly shorter time to healing of venous leg ulcers than delayed endovenous treatment compression therapy.
- The authors discuss that the benefit of early endovenous ablation is likely to be even greater in clinical practice because the trial had high quality, effective compression therapy that is uncommon outside of randomized trials, and ablation is less dependent on patient compliance.
- Early endovenous treatment in addition to compression therapy leads to faster ulcer healing, more time free from ulcers and is more cost effective compared to delayed endovenous treatment in addition to compression therapy.

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