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## Population-Based Analysis of Venous Thrombotic Events Following Saphenous Ablation

Benarroch-Gampel, K.M. Sheffield, C.A. Boyd, T.S. Riall, L.A. Killewich, University of Texas Medical Branch, Galveston, Tex

Background: Venous thrombotic events following great and small saphenous vein ablation procedures for varicose veins have been reported. Current knowledge of these events is based on single institution studies with small sample sizes

Methods: The National Surgical Quality Improvement Program (NSQIP) database (2005-2009) was used to identify a total of 3,874 patients who underwent radiofrequency ablation (RFA) or endovenous laser ablation (EVLA) of the great and small saphenous veins with or without stab phlebectomy. Outcome variables included clinically documented postoperative deep vein thrombosis (DVT) or pulmonary embolism (PE). Bivariate and multivariate logistic regression analyses were performed to identify factors

associated with venous thrombotic events after ablation procedures.

Results: A total of 2,897 (74.8%) patients underwent RFA and 977 (25.2%) underwent EVLA for lower extremity varicose veins. Patients who underwent RFA were more likely to be older (53.8 y vs 51.8 y, P<.0001), obese (42.8% vs 38%, P=.009), diabetic (8.5% vs 6.4%, P=.01) hypertensive  $(31.9\% \times 36.8\%, P=.002)$  and to have undergone procedures involving both veins  $(24\% \times 34\%, P<.0001)$ . Patients who underwent EVLA were more likely to have received general anesthesia (56.9% vs 40.8%, P<.0001), to have undergone concomitant stab phlebectomy (44.9% vs 31.7%, to have integrate concommant state pine ectoring (44.7% ss 51.7%, P<.0001), and had longer operative times (63.6 min ss 57.3 min, P<.0001). The incidence of DVT (1.74% vs 1.52%, P=.63) and pulmonary embolus (0.07% vs 0%, P=1) were similar between EVLA and RFA. No significant predictors of DVT in the postoperative period were identified on bivariate or multivariate analyses. In the subgroup of patients who underwent ablation procedures only (no stab phlebectomy, N=2514), there was a trend toward higher incidence of DVT in patients undergoing EVLA (2.6% vs 1.4%, P=.057). After adjusting for patient demographics, patients presenting with lower extremity ulcers were 2.4 times more likely to develop DVT compared to those without ulcers (OR=2.4, 95% CI=1.01-6.11, P=.04). In the multivariate model when only ablation procedures were performed, EVLA was associated with an 83% increase in odds of DVT compare to RFA, although not statistically significant (OR=1.83, 95% CI= 0.95 - 3.52, P = .06)

Conclusions: The incidence of venous thrombotic events after saphenous ablation is low. However, given that patients with lower extremity ulcers experienced an increased risk of DVT, care should be taken to ensure that the ablation catheter is positioned an appropriate distance from the sapheno-femoral or sapheno-popliteal junction, and postprocedural preventative measures such as early ambulation and lower extremity compression should be emphasized. The finding of a trend toward increased venous thrombotic events in patients undergoing EVLA warrants further investigation in a large patient population.

## Increased Estrogen Receptor-Mediated Venous Relaxation in Human Varicose Veins

J.D. Raffetto<sup>1</sup>, O.M. Reslan<sup>2</sup>, R.A. Khalil<sup>2</sup>, <sup>1</sup>VA Boston HCS, West Roxbury, Mass, <sup>2</sup>Brigham and Women's Hospital, Boston, Mass

Background: The incidence of varicose veins is similar among older male and female subjects. Given that estrogen receptors (ERs) have a significant vasodilator effect in various arterial preparations, we hypothesized that ERs may mediate venous dilation in the setting of varicose veins. We have recently shown that estrogenic compounds induce relaxation of rat inferior vena cava in an ER subtype-specific fashion. This study was designed to test whether specific ERs mediate relaxation in human veins, and whether ER-mediated activity and vein relaxation are enhanced in varicose veins.

Methods: Specimens of greater saphenous vein from male patients (average 69 years old) undergoing lower extremity bypass (n=5) were used as control veins. Varix segments were obtained from male patients (average 56 years old) undergoing varicose vein stripping (n=6). Circular vein segments were equilibrated under 2 g of tension in a tissue bath containing Krebs solution, bubbled with 95% O<sub>2</sub> 5% CO<sub>2</sub>, at 37°C, and the changes in isometric contraction were recorded. Vein segments were precontracted with 96 mM KCl depolarizing solution or the  $\alpha$ -adrenergic receptor agonist phenylephrine (Phe  $10^{-5}$  M). To test for the specific ER, vein segments were treated with increasing concentrations ( $10^{-12}$  to  $10^{-5}$  M) of  $17\beta$ estradiol (E2, activator of most ERs), PPT (ERα agonist), DPN (ERβ agonist), and G1 (GPR30 agonist), and the % venous relaxation was re-

Results: In control veins, ER agonists caused a small concentrationdependent relaxation of KCl contraction that reached a maximum at  $10^{-5}$  M [E2  $(15.93\pm6.44)\approx DPN~(15.28\pm6.23)>PPT~(13.93\pm4.20)>G1~(7.97\pm3.73)$ ]. ER agonists-induced relaxation of KCl contraction was not different or only slightly greater in varicose veins [E2 (19.69 $\pm$ 4.75)  $\approx$  PPT

 $(19.76\pm3.02) > G1 (17.73\pm2.07) > DPN (15.24\pm4.36)$ ]. Compared to the relaxation of KCl contraction, ER agonists caused greater relaxation of Phe contraction in control veins [ $E2(25.00\pm5.66) \approx PPT(25.09\pm5.90) >$ DPN  $(19.56\pm 8.90) > G1 (13.68\pm 8.26)$ ]. In comparison, the ER agonists caused significantly greater relaxation of Phe contraction in varicose veins  $[E2\ (50.76\pm 8.16)\approx DPN\ (51.11\pm 8.69)> PPT\ (46.68\pm 10.69)> G1$  $(42.30\pm6.98)$ ].

Conclusion: In control veins, ER agonists cause small relaxation of KCl-induced contraction, suggesting some inhibition of Ca2+ through voltage-gated channels; and greater relaxation of Phe contraction, suggesting inhibition of additional receptor-operated Ca<sup>2+</sup> channels or -sensitization mechanisms. In varicose veins, ER agonists cause markedly greater relaxation of Phe, but not KCl, contraction, suggesting greater expression/activity of ER and enhanced post-ER inhibitory effects on receptor-operated Ca<sup>2+</sup> channels or Ca<sup>2+</sup>-sensitization mechanisms, leading to less contractile and more distensible veins, and thereby possibly account for the increased venous dilation associated with varicose veins.

## Which is More Important for Postoperative Recovery: Laser Wavelength or Fibers?

L.S.K. Kabnick, New York University, New York, NY

Background: Rapid progression in technique and technology has characterized the growth of endovenous laser ablation since its inception. Moreover, the treatment parameters that have demonstrated significance in altering patient outcomes including: power, wavelength, linear endovenous energy density (LEED), and type of fiber-tip. Postoperative outcomes concerning pain and bruising have been attributed to vein wall perforation. This study presents an in-vitro method to quantify the potential for pain and bruising by comparing the degree of perforation of vessels with regard to wavelength and fibers

Table I. Results 1.

Group	Laser	Power	Leeds	Fiber	N	Mean	SD
C1	810nm	14W	80J/cm	BT	12	19.0%	12.5%
C2	810nm	14W	80J/cm	JT	12	2.09%	7.25%
C3	1470nm	6W	42J/cm	BT	12	16.6%	14.6%
C4	1470nm	6W	42J/cm	JT	12	1.94%	3.39%

Table II. Results 2.

Comparison	Mean difference	95% CI for difference	P value
Groups			
Gl vs G2	16.9%	8.11, 25.69	.001
Gl vs G3	2.40%	-9.12, 13.92	.669
Gl vs G4	17.05%	8.91, 25.81	.001
G2 vs G3	-14.50%	-24.45, -4.54	.007
G2 vs G4	0.15%	-4.77, 5.07	.95
G3 vs G4	14.65%	5.23, 24.06	.005

Methods: A direct comparison was performed using 810nm and 1470nm diode lasers at clinically relevant treatment parameters in combination with Bare Tip (BT) vs. Jacketed Tip (JT) fibers. Cohorts of 12 samples each were tested encompassing 810 nm/BT Fiber, 810 nm/JT Fiber, 1470 nm/BT Fiber, and 1470nm/JT Fiber. Simulated veins with a thickness of 0.5 mm were staked on a gelatin base. The fibers were attached to a motorized slide and oriented so the fiber tip was in contact and parallel to the vein throughout each test run. The assembly was covered with sheep blood to a depth of 2 - 3 mm. The pullback slide and laser were started simultaneously, pulling fibers over the vein at set rates to achieve the desired LEEDs. The lengths of all perforations within a vein segment were measured, added together and divided by the vein length to obtain the percent length of perforation.

**Results:** The results show the degree of perforation for each test group along with the t-test statistical analysis between groups. (See Tables I and II) The actual treatment lengths had a mean of 61.6mm  $\pm$  5.4mm. There was no significant difference between the groups of vessel lengths.

Conclusions: Surprisingly, neither wavelength was superior when comparing like fibers in degree of perforations. However, jacketed tip fibers demonstrated a significantly lower degree of perforation compared to bare tip fibers with either the 810 or 1470 nm lasers at standard clinical parameters. This in vitro study suggests that jacketed tip fibers are superior in terms of postoperative recovery limiting pain and bruising.