Resecting the great saphenous stump with endothelial inversion decreases neither neovascularization nor thigh varicosity recurrence

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Background: **Neovascularization at the saphenofemoral junction is one of the principal causes of recurrent varicose veins after great saphenous vein surgery. Because angiogenic stimulation from the exposed endothelium of the great saphenous vein stump is considered an important trigger for this process, we hypothesized that complete resection of the stump with endothelial inversion might lessen grade 2 groin neovascularization and thereby decrease recurrence of thigh varicosities.**
Methods: **Two groups of consecutive patients with primary varicose veins of the great saphenous vein were studied. Group A was a historical control group of 70 limbs (48 patients) in which conventional flush ligation was performed at the level of the saphenofemoral junction. Group B was a prospectively studied clinical trial cohort of 65 limbs (45 patients), wherein the great saphenous vein stump was completely resected using a side-biting clamp to isolate the saphenofemoral junction, and the resulting common femoral vein venotomy was closed with a running inverting suture. Early postoperative follow-up was performed at 6 weeks. Clinical examinations and duplex ultrasound scans were performed after 2 years of follow-up. Grade 2 groin neovascularization was defined by the presence of >3 mm tortuous new refluxing veins, typically communicating with recurrent varicosities in the thigh.**
Results: **After 2 years, recurrent varicose veins were present in the thighs of 13 of 65 limbs (20%) in group A and in 22 of 61 limbs (36%) of group B ($P = .049$). Grade 2 neovascularization was present at the saphenofemoral junction in six of 65 limbs (9%) of group A and in 12 of 61 limbs (20%) of group B ($P = .127$).**
Conclusion: **Complete resection of the great saphenous vein stump and inversion suturing of the common femoral vein venotomy, instead of simple flush ligation at the level of the saphenofemoral junction, do not appear to decrease grade 2 neovascularization and related thigh varicosity recurrence after great saphenous vein stripping for primary varicose veins.**
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Recurrence of varicose veins after surgery is a common problem that occurs in 20% to 50% of cases, with increasing prevalence attending additional years of follow-up.[1-3] For a long time, recurrence was attributed to incomplete surgery in the groin or popliteal fossa and progressive development of incompetence in residual collaterals. The common use of duplex Doppler scanning in the 1990s, led to gradual acceptance of the conviction that recurrence after surgery is mainly caused by a phenomenon called neovascularization.[1,4-8] One effective way of addressing this problem has been the development of endovenous treatment methods that do not have the same proclivity as open surgical procedures to invoke groin neovascularization.[9-13]

Several alternative surgical techniques have also been proposed to reduce the likelihood of postoperative neovascularization. The construction of an anatomic or prosthetic barrier, using a patch to cover the ligated saphenofemoral junction (SFJ), has been tested in primary varicose vein surgery with promising results.[14-17] Alternatively, technical modifications in the management of the SFJ itself have been proposed to reduce a putative stimulus from the exposed stump endothelium.

The principle of "no stump, no stump-related neovascularization" suggests moving beyond flush ligation to actual resection of the SFJ and an inverting closure of the resultant common femoral venotomy.[6] This completely eliminates the proximal remnant of the great saphenous vein (GSV) and all exposed stump endothelium. Jaeschok et al[18] reported promising 3-month results with this technique, without any further follow-up. This study examines the same hypothesis with 2-year clinical evaluations and duplex ultrasound (DUS) scanning.

METHODS

Patients. A prospective study of 65 limbs (45 patients) with primary varicose veins was conducted between October 2002 and December 2003, wherein the GSV stump was completely resected using a side-biting clamp to isolate the SFJ. The resulting common femoral vein (CFV) venotomy was closed with an inverting suture. The 6-week follow-up and 2-year clinical and DUS findings in the groin and thigh in these limbs were then compared with those of a historical control group of 70 limbs in 48 patients who had attended routine follow-up at the District Hospital (Frutigen, Switzerland) after having undergone GSV stripping with flush SFJ ligation between January 2001 and May 2002.

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Both groups included only limbs with primary GSV varicosities, in which DUS scan revealed an at least above the knee refluxing main trunk and DUS-demonstrable incompetence of the terminal valve. Limbs with substantive, concomitant small saphenous vein varicosities, congenital vascular malformations, and recurrent varicose veins were excluded. Informed consent was obtained during the preoperative interview at the surgeon's clinic.

All operations were performed by the same experienced vascular surgeon (D. H.). If both limbs were to be operated on, a bilateral procedure was done at the same intervention, and both limbs were entered into the study. Patients stayed overnight and were discharged the next day. Low-molecular-weight heparin was administered once during the evening after surgery. The protocol of the study was approved by the local ethics committee (District Hospital, Frutigen, Switzerland), including use of the historical data as well as the prospective trial.

Surgical procedures. The groin incision was made ≤2 cm above the skin crease and parallel to it. All tributaries of the proximal GSV were carefully dissected and ligated. Dissection was continued to the ventral surface of the CFV to expose the complete circumference of the SFJ and to ligate additional tributaries entering directly into the CFV 1 cm above and below the junction. Stripping of the GSV was performed without invagination to just below the knee. Incompetent perforators and varicosities were treated with mini-phlebectomies by means of Varady phlebectomy hooks.

In the historical group A controls, a conventional flush SFJ ligation was performed with a double tie using resorbable polyglactin. The length of the stump was approximately 0.5 cm. In the group B trial limbs, the CFV was partially excluded using a pediatric Satinsky clamp (Fig 1, *A*), without heparin coverage. The SFJ was divided flush with the CFV surface using a Potts scissors. The venotomy was closed with a single-layer, running monofilament 5-0 polypropylene suture, while taking care to invert the intima into the vein lumen (Fig 1, *B*).

Clinical and duplex ultrasound evaluation. Clinical examination mainly consisted of the evaluation of the presence or absence of recurrent varicose veins, defined as palpable dilated subcutaneous veins with a diameter larger >3 mm.[19] After 2 years, DUS scans were performed by the same physician (M. N.) for both the historical control and the clinical trial limbs. An Acuson Sequoia (Siemens, Malvern, Pa) DUS machine (8-5-MHz linear transducer) was used to study the limb or limbs with the patient supine and then standing. The deep vein system was assessed for patency and pathologic reflux, defined by a >1 second duration.

The site of the previous SFJ was identified, and then, with the color DUS scan preset at low-scale with high persistence, a combination of augmentation and Valsalva maneuvers were used to detect groin tributaries. Each groin was accorded a neovascularization grade from grade 0 to grades 1 and 2, as previously described.[3,5,20] If no new vessel was seen connecting with the ventral aspect of the CFV, the groin was grade 0. If a new connecting venous vessel was found at this site, its diameter and duration of reflux were measured. A tiny ≤3-mm, tortuous vein without reflux received a grade 1. Grade 2 was reserved for refluxing veins >3 mm in diameter that had traceable communications with a superficial varicosity in the thigh. In limbs with clinically obvious recurrent varicose veins, the sonographer not only examined the groin but also looked carefully for other escape points, such as incompetent perforating veins or veins descending from the pelvic region.

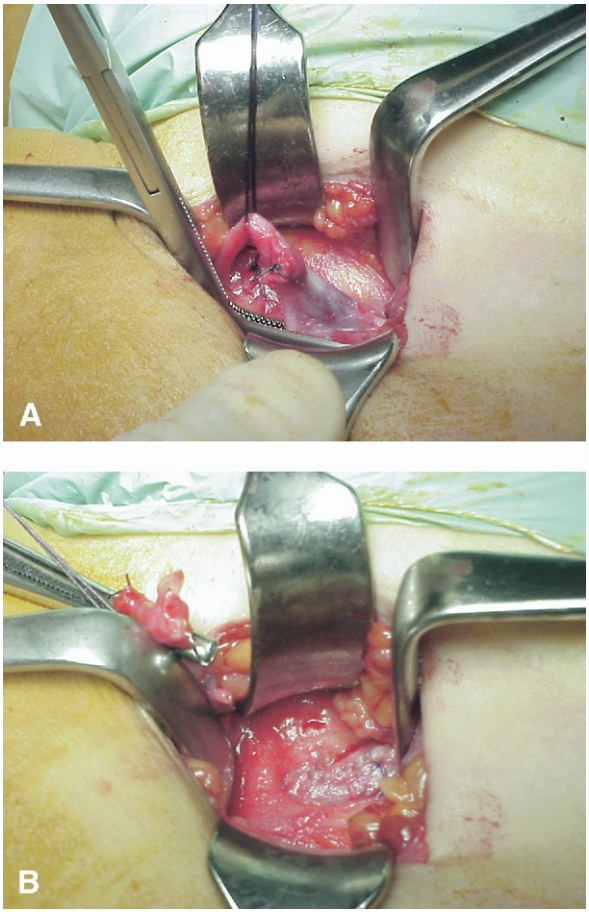

Fig 1. A, After the great saphenous vein is dissected up to the level of the saphenofemoral junction and all its tributaries are divided, a Satinsky clamp is used to exclude the saphenofemoral junction before the great saphenous vein is cut longitudinally exactly at its junction with the common femoral vein. **B,** An inverting running suture of the venotomy of the common femoral vein has been finished.

Statistical analysis. Prevalences of clinically evident thigh varicosities and DUS-defined neovascularization were compared using contingency table analysis. A $P < .05$ indicated statistical significance.

RESULTS

The characteristics of patients and limbs in both groups were similar (Table). No postoperative infection or symp-

Table. Characteristics of patients and limbs

Characteristic	*Group A*	*Group B*
Patients, No.	48	45
Age, mean ± SD years	49 ± 6	50 ± 5
Female patients, No. (%)	39 (81)	39 (87)
Bilateral surgery, No. (%)	22 (46)	20 (44)
Limbs, No.	70	65
Preoperative CEAP, No. (%)		
C2 to C3	54 (77)	47 (72)
C4 to C6	16 (23)	18 (28)

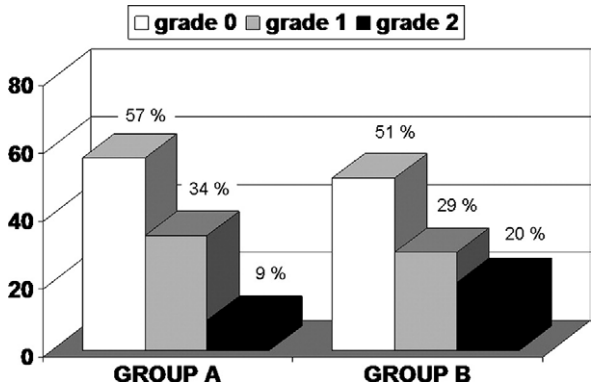

Fig 2. Incidence of the different degrees of neovascularization on duplex ultrasound scan after 2 years in group A (ligation at the saphenofemoral junction) and group B (resection of the stump of the great saphenous vein).

tomatic deep vein thrombosis was noted among the group A control limbs, but one group B trial limb had a superficial wound infection below the knee.

Two-year follow up was available for 65 group A control limbs (92%) and 61 group B trial limbs (93%). Neither the trial nor control group had evidence on DUS scanning of CFV stenosis or deep vein thrombosis at the site of the previous SFJ. DUS-defined neovascularization was present at the site of the previous SFJ in 28 control limbs (43%): 22 were grade 1, and six limbs were grade 2 (Fig 2). The six latter limbs had clinically evident thigh varicosities that communicated with >3-mm SFJ-site neovascular tributaries. Grade 1 neovascularization was not associated with clinically evident thigh varicosities. Seven other control limbs had clinical varicosities, but each had demonstrable reflux sourced from either a perforating vein or pelvic vein incompetence. Saphenofemoral junction neovascularization was visualized in 30 trial limbs (49%): 18 were grade 1 and 12 were grade 2 (Fig 2). The 12 limbs all bore above knee clinical varicosities communicating with newly formed SFJ-site tributaries. Ten other trial limbs had thigh varicosities, and just as was observed in the control limbs, these had feeding sources unrelated to lesser grade groin neovascularization.

The 2-year between-group differences all had a nonsignificant α level, although the prevalence of thigh varicosities of varying extent—22% in the historical controls and 36% for the trial limbs—was indeed a narrow miss at $P = .049$ and $P = .592$ for the 43% prevalence of SFJ neovascularization, irrespective of grade, in the control limbs vs 49% for the trial limbs. The prevalence of varicosity-linked, grade 2 neovascularization—9% in the control limbs and 20% for trial limbs—had a key value of $P = .127$.

DISCUSSION

The results of the present study suggest that modifying the technique of managing the SFJ by resecting the GSV stump completely, instead of simpler flush ligation, does not decrease postoperative neovascularization or improve 2-year clinical results. After 2 years, in fact, the prevalence of clinically evident recurrent varicose veins was almost significantly higher among the trial limbs. Yet, the prevalence of recurrent varicose veins above the knee in communication with >3 mm, grade 2, neovascular SFJ tributaries was not statistically different between the two groups. Hence, the promising 3-month results reported by Jaeschok et al[18] could not be confirmed in this study.

Interpretation of our results needs to be conditioned by its several limitations. Prospectively studied trial limbs were compared with a recent historical control group, precluding randomization. Although one senior surgeon performed all operations and one experienced physician conducted all DUS scans at identical time periods, with >90% follow-up on demographically similar groups, different ligature and suture materials were used and selective and unintentional bias cannot be excluded. The sample size is constraining for a negative result. No power determination was made before the study, which might have been based on a contemplated 50% differential in the 2-year prevalence of grade 2 neovascularization. As they are, the results must be regarded as observational and suggestive that the trial technique will not best patching or emulate the neovascularization avoidance that characterizes endovenous elimination of a refluxing GSV.[9-17]

The pathophysiology of SFJ recurrent reflux remains poorly understood. Postoperative DUS scans show a remarkable proclivity of the former SFJ site to re-establish venous connections after an apparently correct surgical ligation.[4,5,7] Several explanations about how, when, and why new veins develop at the former SFJ have been proposed, including angiogenic stimulation by the exposed GSV stump endothelium or the wound healing process, transnodal lymphovenous connections, dilation of CFV vasa vasorum, and disturbed venous drainage of ligated suprainguinal tributaries.[6] In particular, hypoxic intima beyond the GSV ligature has been postulated as an important neovascularization initiator.

It is known that the responses of endothelial cells to hypoxia initiate a signalling cascade of intracellular and molecular events that may explain several vascular pathologic situations.[21,22] A recent immunohistochemical study demonstrated that the expression of vascular endothelial growth factor (VEGF) and VEGF-receptors were up-regulated in neovascular veins compared with both varicose and normal

veins.[23] In view of the crucial role of the endothelium, some authors have attempted to mitigate neovascularization by inverting the free endothelial border of the ligated GSV stump with a running suture. Frings et al[24] reported a reduction of DUS-diagnosed recurrence after 2 years, from 11% to 3% in 152 limbs. Haas et al,[25] however, could not reproduce these results. They observed 9% neovascularization between 4 and 54 months after inverting suture of the GSV and no difference between the group with the inversion of the stump and two other groups without it among 490 groins.

Complete resection of the stump, as used in our trial group, is a more radical approach than just hiding or destroying the stump endothelium, because the CFV venotomy eliminates all GSV endothelium, and its inverting closure insolates the cut edge of the CFV from other groin contents. Our negative result may just reflect sample-size vitiation or be an indication that eliminating one factor among several is insufficient to make a meaningful difference. Angiogenesis is not limited to the exposed endothelium of the stump or to the site on the CFV and may begin in surrounding supporting tissue, neighboring lymph nodes, and in tissue reaction to surgical sutures.[7,26] Neovascular veins have even been recognized around a prosthetic patch implanted to function as a barrier against neovascularization.[27] Endovascular approaches may hold the best promise. Wound healing is minimized, and normal prograde venous flow from the pudendum and lower abdomen is generally preserved, but 5-year follow-up is the longest available, and recurrent SFJ reflux can occur considerably later.[1,9-13]

CONCLUSION

Complete resection of the proximal GSV stump in the groin and inverting suture of the resulting CFV venotomy, instead of simple flush ligation at the level of the SFJ, does not appear to decrease grade 2 neovascularization and its associated recurrent thigh varicosities at 2 years after surgical stripping of the GSV for primary varicose veins.

AUTHOR CONTRIBUTIONS

Conception and design: DH, MN
Analysis and interpretation: DH, MM
Data collection: DH, MN
Writing the article: DH, MM
Critical revision of the article: MM
Final approval of the article: DH, MM, MN, US
Statistical analysis: US, MM
Obtained funding: Not applicable
Overall responsibility: DH

REFERENCES

1. Fischer R, Linde N, Duff C, Jeanneret C, Chandler JG, Seeber P. Late recurrent saphenofemoral junction reflux after ligation and stripping of the greater saphenous vein. J Vasc Surg 2001;34:236-40.
2. van Rij AM, Jiang P, Solomon C, Christie RA, Hill GB. Recurrence after varicose vein surgery: A prospective long-term clinical study with duplex ultrasound scanning and air plethysmography. J Vasc Surg 2003;38: 935-43.
3. De Maeseneer MG, Vandenbroeck CP, Hendriks JM, Lauwers PR, Van Schil PE. Accuracy of duplex evaluation one year after varicose vein surgery to predict recurrence at the sapheno-femoral junction after five years. Eur J Vasc Endovasc Surg 2005;29:308-12.
4. Jones L, Braithwaite BD, Selwyn D, Cooke S, Earnshaw JJ. Neovascularisation is the principal cause of varicose vein recurrence: results of a randomised trial of stripping the long saphenous vein. Eur J Vasc Endovasc Surg 1996;12:442-5.
5. De Maeseneer MG, Ongena KP, Van den Brande F, Van Schil PE, De Hert SG, Eyskens EJ. Duplex ultrasound assessment of neovascularisation after saphenofemoral or sapheno-politeal junction ligation. Phlebology 1997;12:64-8.
6. Fischer R, Chandler JG, De Maeseneer MG, Frings N, Lefebvre-Vilardebo M, Earnshaw JJ, et al. The unresolved problem of recurrent saphenofemoral reflux. J Am Coll Surg 2002;195:80-94.
7. van Rij AM, Jones GT, Hill GB, Jiang P. Neovascularization and recurrent varicose veins: more histologic and ultrasound evidence. J Vasc Surg 2004;40:296-302.
8. De Maeseneer MG. Neovascularization: an adverse response to proper groin dissection. In: Bergan JJ, ed. The vein book. Burlington, San Diego, London: Elsevier Academic Press, 2007. p. 239-47.
9. Min RJ, Khilnani N, Zimmet SE. Endovenous laser treatment of saphenous vein reflux: long-term results. J Vasc Interv Radiol 2003;14: 991-6.
10. Merchant RF, Pichot O, Closure Study Group. Long-term outcomes of radiofrequency obliteration of saphenous reflux as a treatment for superficial venous insufficiency. J Vasc Surg 2005;42:502-9.
11. Agus GB, Mancini S, Magi G and the IEWG. The first 1000 cases of Italian Endovenous-laser Working Group (IEWG). Rationale and long-term outcomes for the 1999-2003 period. Int Angiol 2006;25:209-15.
12. Pichot O, Kabnick L, Creton D, Merchant RF, Schuller-Petrovic S, Chandler JG. Duplex ultrasound scan findings two years after great saphenous vein radiofrequency endovenous obliteration. J Vasc Surg 2004;39:189-95.
13. Klanifard B, Holdstock JM, Whiteley MS. Radiofrequency ablation (VNUS closure) does not cause neo-vascularisation at the groin at one year: results of a case controlled study. Surgeon 2006;4:71-4.
14. Glass GM. Prevention of sapheno-femoral and sapheno-popliteal recurrence of varicose veins by forming a partition to contain neovascularisation. Phlebology 1998;13:3-9.
15. Earnshaw JJ, Davies B, Harradine K, Heather BP. Preliminary results of PTFE patch saphenoplasty to prevent neovascularisation leading to recurrent varicose veins. Phlebology 1998;13:10-3.
16. De Maeseneer MG, Giuliani DR, Van Schil PE, De Hert SG. Can interposition of a silicone implant after sapheno-femoral ligation prevent recurrent varicose veins? Eur J Vasc Endovasc Surg 2002;24: 445-9.
17. De Maeseneer GM, Philipsen TE, Vandenbroeck CP, Lauwers PR, Hendriks JM, De Hert SG, et al. Closure of the cribriform fascia: an efficient anatomical barrier against postoperative neovascularisation at the saphenofemoral junction? A prospective study. Eur J Vasc Endovasc Surg 2007;34:361-6.
18. Jaeschok RR, Bahrami F. Die "sichere" Crossektomie der vena saphena magna–eine technische Alternative. In Abstractband 38. Jahrestagung der Deutschen Gesellschaft für Phlebologie, Schultz-Ehrenburg U (ed), Berlin 1996;16:7.
19. Eklöf B, Rutherford RB, Bergan JJ, Carpentier PH, Gloviczki P, Kistner RL, et al. Revision of the CEAP classification for chronic venous disorders: consensus statement. J Vasc Surg 2004;40:1248-52.
20. De Maeseneer MG, Tielliu IF, Van Schil PE, De Hert SG, Eyskens EJ. Clinical relevance of neovascularisation on duplex ultrasound in the long-term follow-up after varicose vein operation. Phlebology 1999;14: 118-22.
21. Michiels C, Arnould T, Thibaut-Vercruyssen R, Bouaziz N, Janssens D, Remacle J. Perfused human saphenous veins for the study of the origin of varicose veins: role of the endothelium and of hypoxia. Int Angiol 1997;16:134-41.
22. Michiels C, Arnould T, Remacle J. Endothelial cell responses to hypoxia: initiation of a cascade of cellular interactions. Biochim Biophys Acta, 2000;1497:1-10.

23. Rewerk S, Noppeney T, Winkler M, Willeke F, Duczek C, Meyer AJ. Pathogenese der Primär- und Rezidiv-varikosis an der Magna-Krosse. Die Rolle von VEGF und VEGF-Rezeptor. Phlebologie 2007;36: 137-42.
24. Frings N, Nelle A, Tran P, Fischer R, Krug W. Reduction of neoreflux after correctly performed ligation of the saphenofemoral junction. A randomized trial. Eur J Vasc Endovasc Surg 2004;28:246-52.
25. Haas E, Burkhardt T, Maile N. Rezidivhäufigkeit durch Neoangiogenese nach modifizierter Krossektomie. Phlebologie 2005;2:101-4.
26. Stücker M, Netz K, Breuckmann F, Altmeyer P, Mumme A. Histomorphologic classification of recurrent saphenofemoral reflux. J Vasc Surg 2004;39:816-21.
27. Bhatti TS, Whitman B, Harradine K, Cooke SG, Heather BP, Earnshaw JJ. Causes of re-recurrence after polytetrafluoroethylene patch saphenoplasty for recurrent varicose veins. Br J Surg 2000;87:1356-60.

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