

Crossotomy vs crossectomy for saphenous vein sparing surgery in patients with varicose veins due to ostial incontinence: protocol for double blind, multicenter, randomized trial

Eugenio Martelli,^{†,1,2,3} Laura Capoccia,^{†4} Giovanni Sotgiu,⁵ Laura Saderi,⁵ Mariangela Valentina Puci,⁵ Piero Modugno,⁶ Sergio Furgiuele,⁷ Vincenzo Aversano,⁸ Salvatore De Vivo,⁹ Luca Iorio,¹⁰ Allegra Rosa Martelli,¹¹ Stefano Ricci¹²

¹Department of General and Specialist Surgery, Faculty of Pharmacy and Medicine, Sapienza University of Rome; ²Saint Camillus International University of Health Sciences, Rome; ³Division of Vascular & Endovascular Surgery, Department of Surgery, S. Maria Goretti Hospital, Latina; ⁴Division of Vascular & Endovascular Surgery, Department of Cardiovascular Sciences, S. Anna and S. Sebastiano Hospital, Caserta; ⁵Clinical Epidemiology and Medical Statistics Unit, Department of Medicine, Surgery and Pharmacy, University of Sassari; ⁶Division of Vascular Surgery, I.D.I. Hospital, Rome; ⁷Division of Vascular Surgery, Struttura Ospedaliera Mediterranea, Naples; ⁸Division of Angiology, Villa Fiorita Clinic, Capua (CE); ⁹Division of Vascular Surgery, Pellegrini Hospital, Naples; ¹⁰Division of Vascular Surgery, Campobasso Hospital; ¹¹Medicine and Surgery School of Medicine, Campus Bio-Medico University of Rome; ¹²Private practice in Phlebology, Rome, Italy.

†EM and LC have contributed equally

Correspondence: Eugenio Martelli, S. Maria Goretti Hospital, via Lucia Scaravelli, 04100 Latina, Italy.
Tel. (+39)3294003220. E-mail: eugenio.martelli@uniroma1.it

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Abstract

Double-blind/multicenter/randomized trial protocol. Eligibility criteria: age 18-70 years; C2-C5 leg varices secondary to the Great Saphenous Vein (GSV) incontinence; GSV size 6-10mm, at 10cm from the Saphenous-Femoral Junction (SFJ); ostial reflux lasting >0.5 sec at Duplex ultrasound; negative reflux elimination test; acceptance of the GSV sparing treatment plus partial/total varicose veins removal. Exclusion criteria: non-isolated GSV reflux; district already treated; pregnancy/lactation; impaired walking ability; deep vein thrombosis/insufficiency; severe comorbidities. Participants were recruited from 7 Italian tertiary referral centres. Interventions: crossotomy (no SFJ's tributaries ligation) vs crossectomy. The study aimed to verify if GSV drainage through the SFJ's tributaries reduces groin/peripheral recurrences. Primary endpoint: 1-year GSV reflux recurrence, positive to the Valsalva maneuver, originating from the SF. Participants were equally randomized. Participants, caregivers, and those assessing the outcomes blinded to group assignment.

Introduction

Scientific background and explanation of the rationale

One possible cause of inguinal recurrence after traditional surgery for Great Saphenous Vein (GSV) incompetence is the abolition of the physiological drainage of the Saphenous-Femoral Junction (SFJ) Descending Tributaries (DT), when interrupted.¹ GSV stripping, preceded by its section and flush ligation with the femoral vein, impairs the drainage of the superficial tissues of the lower limb, while the ligation of the DT of the SFJ impairs the drainage of the superficial tissues of the lower abdominal wall.

Allowing drainage to the DT during GSV ablation could reduce the number of recurrences. This has been suggested by several studies, where a GSV long stump was left, allowing the physiologic DT drainage through the SFJ.^{2,3}

A different approach is saving the SFJ DT maintaining their drainage in the preserved GSV trunk, as suggested by the CHIVA (Conservatrice Hémodynamique de l'Insuffisance Veineuse en Ambulatoire) treatment, in the hypothesis to limit recurrences.^{4,5}

Hypotheses

In a perspective of GSV conservative surgery, this study protocol aims to investigate if the flush SFJ interruption maintaining the DT drainage in the saphenous stem (crossotomy) is advantageous compared to the traditional flush SFJ interruption with DT ligation (crossectomy), to avoid groin neo-vascularization formation and limit anarchic recurrences by leaving the draining GSV.⁶ Both surgical arms are regularly accepted as correct procedures in the current literature.

Materials and Methods

This study protocol follows the checklist reported in the CONSORT guidelines.⁷

Trial design

This is a multicenter, equally randomized (1:1 for two groups allocation ratio), double-blind trial protocol involving seven Italian divisions of vascular surgery. Each centre must first obtain permission from its ethical committee to join the study. No changes to methods are expected after trial commencement.

Participants

The eligibility criteria were: i) age between 18 and 70 years; ii) clinical class C2-C5 leg varices, according to Clinical Etiologic Anatomic Pathophysiologic classification, suitable for phlebectomies, secondary to the GSV incontinence; iii) GSV size between 6 and 10 mm, at 10 cm from the SFJ; iv) reflux of ostial origin lasting more than 0.5 sec at Duplex Ultrasound (DUS); the terminal valve of the common femoral vein is considered incompetent on DUS when Valsalva and/or calf squeeze maneuvers produce GSV reflux;⁸ v) acceptance of the GSV sparing treatment -plus partial/total varicose veins removal- by signing a written informed consent; and vi) negative Reflux Elimination Test (RET).⁹

RET is negative when GSV reflux doesn't disappear after dig-

ital compression of the varicose vein, eventually at the passage point of the reflux from the GSV to the supra-fascial tributary. This is due to the presence of at least one distal re-entry perforator on the GSV (Figure 1).

RET is positive when the reflux disappears after digital compression of the varicose vein (Figure 2).

In the case of RET positivity, the reflux is drained by a re-entry positioned on the varix. The GSV axis does not have its own drainage of blood refluxing. So, after phlebectomy of the varix the GSV can be emptied only towards the SFJ: in fact, the GSV no longer has reflux. In this case, the eventual interruption of the SFJ without saphenectomy would favour GSV thrombosis. Therefore, this case does not allow GSV saving except through a two-stage tactic (CHIVA II crossotomy), after waiting for the creation of a new distal perforator on the GSV axis.⁶

These cases aren't included in our study.

We consider only negative RET cases, *i.e.* those in which the GSV drains the reflux through a distal perforator placed on its axis: so, even after interrupting the SFJ, a retrograde flow remains in the saphenous axis. The inclusion of the RET-negative patients only, generally representing 30% of all the GSV refluxing cases, makes reaching the required numbers more complex.

The exclusion criteria were: i) pelvic reflux, or not-isolated GSV reflux; ii) district already treated; iii) pregnancy and lactation; iv) a defective calf muscular pump, or impaired walking ability; v) (history of) deep vein thrombosis/insufficiency; vi) diabetes; severe renal, hepatic, cardiorespiratory, autoimmune diseases; malignancy. Participants will be recruited from 7 tertiary referral centres in 3 contiguous Italian regions, namely: Lazio (the Divisions of Vascular Surgery of S. Maria Goretti Hospital in Latina, and I.D.I. Hospital in Rome), Campania (the Divisions of Vascular Surgery of S. Anna and S. Sebastiano Hospital in Caserta, Pellegrini Hospital and Struttura Ospedaliera Mediterranea in Naples, and the Division of Angiology of Villa Fiorita Clinic in Capua, CE), and Molise (the Division of Vascular Surgery of Campobasso Hospital).

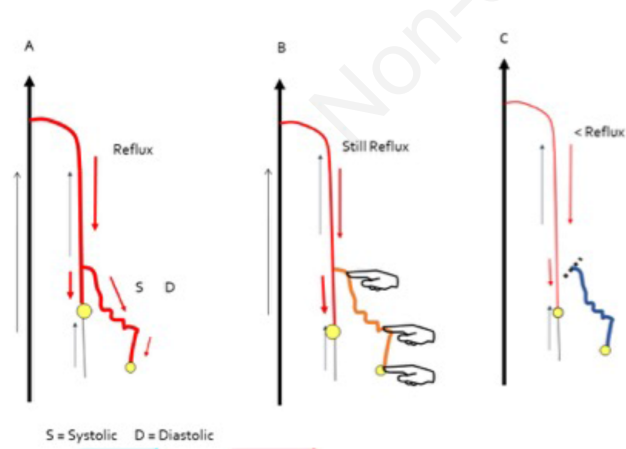


Figure 1. Negative RET: (A) when reflux re-entry is centred on the great saphenous vein (GSV) stem (even if not exclusively), (B) finger compression on the varix will not eliminate the reflux; (C) the same after a phlebectomy. In this case, interruption of the sapheno-femoral junction is indicated, since the GSV stem has a drainage based on a distal perforator.

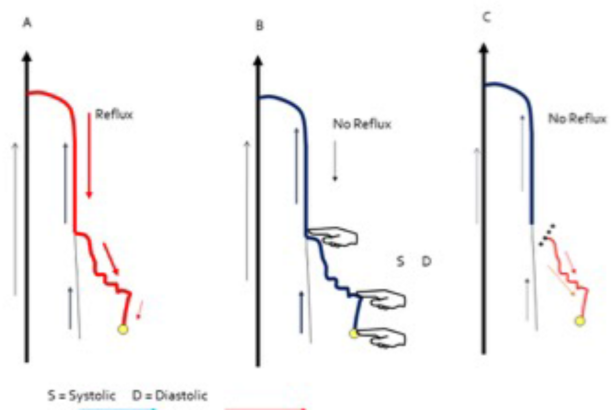


Figure 2. Positive RET: (A) the reflux re-entry is centred on a tributary varice; (B) the occluding digital compression on the varix makes the reflux disappear in the entire venous system; (C) tributary phlebectomy eliminates the reflux in the Great Saphenous Vein (GSV). In this case, the interruption of the sapheno-femoral junction is not necessary, and might cause thrombosis of the GSV.

Interventions

Grading of the varicosity extension accomplished according to Pittaluga *et al.*¹⁰ Each of the 4 faces of the limb (posterior, medial, anterior, lateral) divided into 8 parts (total =32 zones) in the pre-operative map: 3 zones for the thigh, 3 zones for the calf, 1 for the knee, and 1 for the foot. Extension of varicosity classified in: A=1-2 zones (limited phlebectomy); B=3-7 zones (medium-extension phlebectomy); C>7 zones (extensive phlebectomy).

Body Mass Index (BMI), gender, age, and DUS examination in standing position (evaluation of GSV reflux, incontinence of ostial origin, positive Valsalva and compression/release maneuvers, caliber at 10 cm from the SFJ, RET, and supra-GSV femoral valve continence) will be recorded as well.

All patients must answer the Chronic Venous Insufficiency Questionnaire (CIVIQ-20) and Venous Clinical Severity Score (VCSS) before surgery and at follow-up.^{11,12}

After varicosities mapping by DUS, local anaesthesia adopted for all the patients enrolled and stab phlebectomies of prevalent varicosities performed, with isolation of the GSV stem.

The SFJ interruption will be randomized at this time between the following two techniques, without stripping: i) crossotomy, flush SFJ ligation, preserving the DT for the maintenance of the GSV flow to keep it open and functioning (group A, Figure 3); blood flow is discharged through the distal GSV perforators, necessarily preserved and functioning;⁴⁻⁶ ii) crossotomy: flush SFJ ligation with accurate interruption of all the DT, but with the preservation of the GSV (group B, Figure 4), the rationale is that the ablation of the distal saphenous axis is not essential to varicose treatment, and unnecessarily aggressive.

SFJ will be ligated with a 3/0 non-absorbable suture, with a clip placed longitudinally under the ligature to avoid any residual stump on the femoral vein. The clip will be positioned using a 90-degree clip-positioner, to avoid angled positioning. It will pinch the femoral wall, and the free extremities of the clip will be strictly joined to each other, without any interposition of biological material. Then, the divided GSV stump will be sutured by non-

absorbable 3/0 suture.⁶ Operating times will be calculated.

Post-operative treatment was standardized: immediate walking, 7 days strong analgesic hemostatic compression, 7-15 days additional local compression if necessary, and elastic stockings hereinafter. Physicians involved in the postoperative and follow-up controls will be blinded to the treatment performed. Analysis of the satisfaction degree by visual-analog pain rating scale from 0 to 10. Patients' hospitalization will be calculated.

Outcomes

At 7 days, possible post-operative pain, number of analgesics assumed, minimal/complete wound dehiscence, serosity, irritation, hematoma, or infection will be reported.

At 3 months, possible keloid or recurrent varicose veins will be assessed.

At 1 year, CIVIQ-20, VCSS, clinical examination for recurrence of varicosity (A, B, C), DUS for possible GSV reflux (positive to the Valsalva maneuver and originating from the SFJ), caliber, and patency will be performed.

Total costs will be calculated, and all data will be collected in an *ad hoc* database.

Primary outcome measure: 1-year GSV reflux positive to the Valsalva maneuver and originating from the SFJ.

Secondary outcome measures: GSV patency and caliber; 1-year peripheral recurrence (varicosity A, B, C); preoperative and 1-year quality of life; surgical complications; surgical time; PRS analysis of postoperative pain.

No change to trial outcomes after the trial commenced.

Sample size

Based on the 5-year recurrence rate of 1.1% and 7.4% after flush SFJ ligation with or without sparing of the DT,² respectively (ref), a significance level (alpha) of 0.05 and a statistical power of 0.80, a total sample size of 320 estimated to be recruited (n=160 per single group). Recruitment completed in one year.

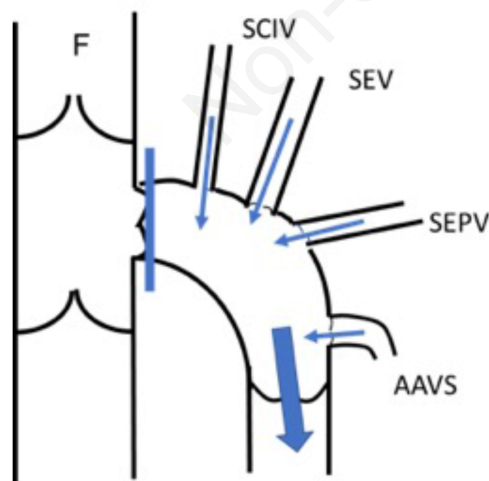


Figure 3. Crossotomy: only flush ligation of the sapheno-femoral junction. F, Common Femoral Vein; SCIV, Superficial Circumflex Iliac Vein; SEV, Superficial Epigastric Vein; SEPV, Superficial External Pudendal Vein; AASV, Anterior Accessory Saphenous Vein.

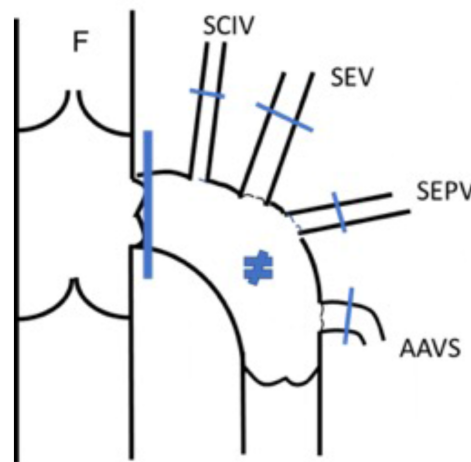


Figure 4. Crossotomy: flush ligation of the sapheno-femoral junction and of all its tributaries. F, Common Femoral Vein; SCIV, Superficial Circumflex Iliac Vein; SEV, Superficial Epigastric Vein; SEPV, Superficial External Pudendal Vein; AASV, Anterior Accessory Saphenous Vein.

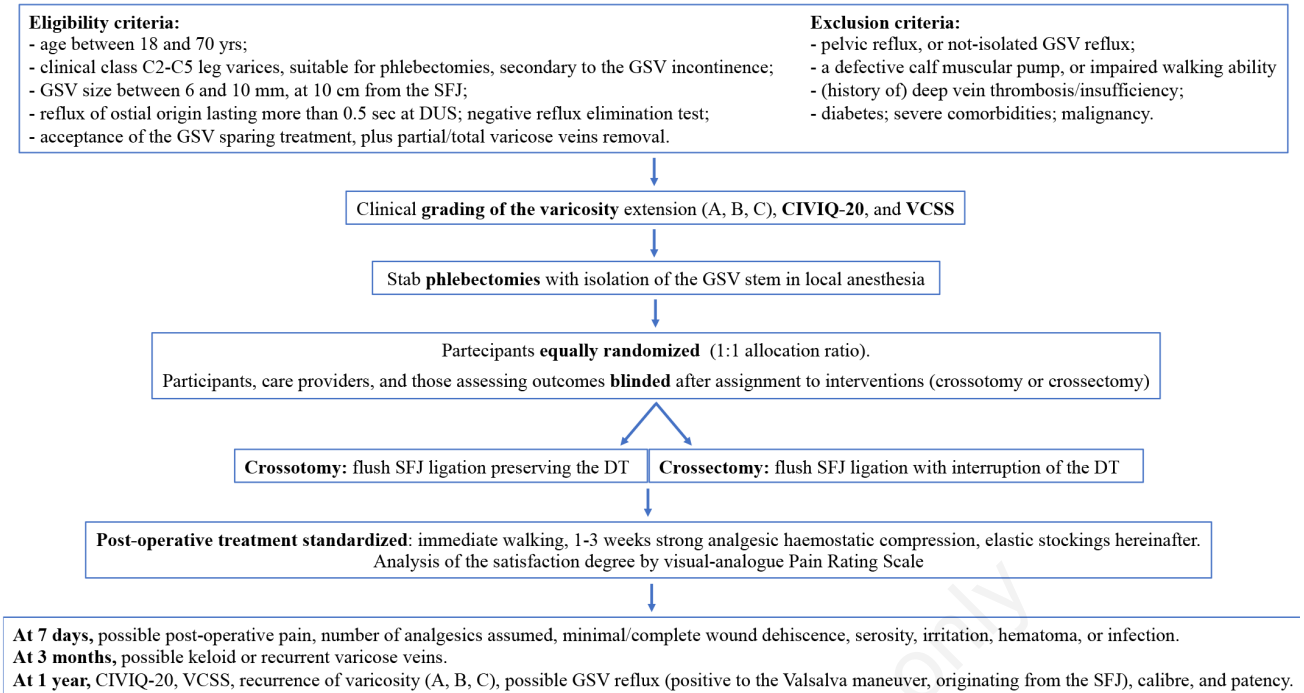


Figure 5. Flow diagram of the progress through the clinical phases of the trial. GSV, Great Saphenous Vein; SFJ, Saphenous-Femoral Junction; DUS, Duplex Ultrasound; CIVIQ-20, Chronic Venous Insufficiency Questionnaire; VCSS, Venous Clinical Severity Score; DT, Descending Tributaries.

Randomization

A computer-generated randomization list utilizing random number generation will be employed. Participants' enrollment will be equally randomized (1:1 allocation ratio).

The generation of the random allocation sequence, enrollment, and assignment of participants to interventions will be performed by different nurses or physicians who will not interact with each other in the various steps of these processes.

Blinding

Participants, care providers, and those assessing outcomes will be blinded after assignment to interventions (crossotomy or crossectomy). Specifically, participants will be given a generic dismissal letter simply reporting "SFJ ligation and phlebectomies" (without specifying if crossotomy or crossectomy), and those assessing outcomes will not be the operators (Figure 5).

Statistical methods

Demographic and baseline disease characteristics will be summarized with the use of descriptive statistics. Categorical variables will be reported as absolute numbers and percentages. Continuous variables will be reported as mean and Standard Deviation (SD), or median and Interquartile Range (IQR). Outcome differences between crossotomy and crossectomy will be evaluated using Student-t or Mann-Whitney tests for quantitative variables, in accordance with the Shapiro-Wilk normality test. Chi-squared or Fisher exact tests will be used for the comparison of qualitative characteristics. A p-value <0.05 will be considered statistically significant. Statistical analyses will be conducted using STATA version 17.

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