Transient increased tumescence of the glans penis during penile erection after endovenous ablation of the great saphenous vein

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ABSTRACT

Objective: The primary objective of our study was to investigate the impact of endovenous ablation of the great saphenous vein (GSV) on the degree of tumescence of the glans penis during penile erection as well as on global erectile function (EF).

Methods: We included patients scheduled for one of three different methods of endoluminal treatment. Our questionnaire was composed of the EF domain of the International Index of Erectile Function, an additional question that has been validated for assessment of swelling (tumescence) of the glans penis, and a question on the use of erectogenic medication.

Results: There were 62 patients enrolled in the study. Seven patients (11%) reported a postoperative enlargement of the glans penis on penile erection compared with the subjectively assessed glans tumescence before surgery. Three patients (5%) reported an increased tumescence of the glans 1 week after surgery, and four (7.4%) different patients reported the effect 3 months after surgery. Of these seven men, three had normal EF (score ≥26) at any time. One patient had mild erectile dysfunction before the operation, with an improvement to normal EF from week 1 throughout the observation in the study (3 months).

Conclusions: This is the first prospective study that confirms an unexpected side effect of endoluminal treatment of the GSV occurring in approximately 10% of men. It might be of interest for insufficient responders to phosphodiesterase type 5 inhibitors with varicosis of the GSV in the future. (J Vasc Surg: Venous and Lym Dis 2019;7:387-91.)

Keywords: Erection; Tumescence of the glans penis; Endovenous ablation; Great saphenous vein

Schuller-Petrovic et al[1] previously described side effects of endovenous ablation of the great saphenous vein (GSV), such as ecchymosis (38.4%-52%), pain (13%-41.3%), hematoma (0.8%-2.2%), phlebitis (3.2%), and hyperpigmentation (4%). In 2014, a patient presented 1 week after endovenous laser ablation of the right GSV with a stronger erection in the glans penis. The penis felt markedly larger and firmer than usual, and the patient reported an unexpected improvement of general erectile function (EF). However, the effect spontaneously vanished after 3 weeks.[2] Penile venous surgery as well as other vascular procedures (eg, revascularization) for treatment of erectile dysfunction (ED) are currently considered historic and no longer included in the current European guidelines on ED.[3,4] Sattar et al[5] provided evidence that the so-called penile venous leak is due to a degeneration of the smooth muscle in the cavernous body of the penis; thus, a therapeutic approach to reduce venous outflow from the corpora cavernosa might not be a viable treatment option. Normal erection with a complete cavernous body results in compression of subtunical venules and tunica compressions, finally resulting in a complete cessation of venous drainage out of the cavernous bodies during penile tumescence.[5]

The primary objective of our study was to prospectively investigate the impact of endoluminal thermal ablation of the GSV on the degree of swelling of the glans penis and global EF measured by a questionnaire. We here report on the primary analyses of the data after inclusion of the prespecified number of consecutive patients.

METHODS

We included male patients with incompetent varicose GSV scheduled for one of three different methods of endoluminal treatment at a single university center. All three treatments of the GSV were performed under standardized conditions using tumescent local anesthesia and ultrasound-guided monitoring. In addition, relevant tributaries were also removed by phlebectomy as

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appropriate. We used tumescent anesthesia. The mean volume was 300 mL (280-380 mL). The fluid was injected strictly perivenously along and around the GSV starting below the knee up to the groin. The volume applied in the groin was <40 mL in all subjects.

The formulation is 500 mL sodium chloride plus 17.5 mL prilocaine 1% with epinephrine 1:200,000 (Xylonest 1% with epinephrine 1:200,000; Aspen Germany GmbH, Munich, Germany). The tumescent anesthetic was injected perivenously around the GSV and around the saphenofemoral junction including the tributaries in the groin. The effect of venospasm or erectile properties caused by epinephrine in the solution is not relevant. The duration of the effect is limited (maximum of 2 hours).

The three treatments were endovenous laser ablation (1470-nm radial laser; biolitec AG, Wien, Austria), radiofrequency ablation (ClosureFast; Medtronic, Dublin, Ireland), and ultrasound-guided foam sclerotherapy (2% 1:4 double syringe system polidocanol foam [Aethoxysklerol; Chemische Fabrik Kreussler GmbH & Co, Wiesbaden, Germany]; maximal amount, 10 mL).

The indication can be classified by two different aspects. The first is a general indication, such as cosmetic concerns or symptomatic patients (aching, throbbing, feeling of a heavy leg, fatigue, cramps, pruritus, restless leg, ankle swelling and tenderness, or pain along bulging varicose veins). The second aspect includes anatomic or pathophysiologic symptoms, such as vein diameter, reflux time, and shallow saphenous veins.[6] All patients enrolled in the study suffered from hemodynamically relevant insufficiency of the GSV and clinical symptoms of chronic venous insufficiency like heaviness of the lower limbs, edema (C3), or eczema (C4). The clinical findings and relevant refluxes during Valsalva maneuver lasting >0.5 second in the GSV documented in all subjects led to the indication for venous surgery or endovenous thermal ablation of the GSV. Immediately after the procedure, all patients received eccentric compression up to the thigh for 24 hours in addition to a compression stocking (class 2, 23-32 mm Hg) for 4 weeks. Thrombosis prophylaxis with low-molecular-weight heparin (Tinzaparin; Leo Pharma, Neu-Isenburg, Germany) was administered for 10 days postoperatively. According to the German guidelines for treatment of varicose veins, postoperative thrombosis prophylaxis with low-molecular-weight is facultative. In our clinical protocol, this setting is routinely used.

To confirm and to quantify any improvement in erection or increased swelling of the glans, we carried out a prospective longitudinal survey in which patients were asked to complete a questionnaire. This eight-item questionnaire was composed of the EF domain of the International Index of Erectile Function (IIEF), a validated tool for evaluating EF (questions 1-6),[7,8] and an additional newly created seventh question assessing glans penis tumescence during erection (Appendix, online only). This seventh question had established face validity through expert review and was tested and validated for reliability by asking 16 healthy male volunteers to complete the questionnaire twice at an interval of 4 weeks (reliability, 100%). In the main study, patients were asked directly about potency-enhancing medication in an eighth question. In addition, data on prognostic variables for ED were collected. Prognostic factors that we have taken into consideration include arteriosclerosis,[9,10] diabetes mellitus,[11] previous pelvic surgery (eg, history of prostate surgery),[12] use of any medication for ED, and polyneuropathy.[13] ED was defined as IIEF score of <26.[14] Participation in the trial was offered to consecutive eligible male patients scheduled for elective unilateral, endoluminal treatment of the GSV at the Department of Dermatology at the Lübeck Campus of Schleswig-Holstein University Medical Center. Patients were asked to complete the EF domain of the IIEF questionnaire with two supplementary questions at three visits during the course of the study. The patient had to complete the questionnaire for the first time on the day of surgery (U1), before the procedure was carried out. All patients were followed up for 3 months after surgery and re-evaluated at week 1 (U2) and week 12 (U3). This schedule was a result of the normal postoperative visits of this surgery and the initial case that presented 1 week after surgery.[2] In September 2014, we received ethics committee approval for our study.

The study has a prospective longitudinal design. The level of significance was set at 5%, with a statistical power of 80%. Study planning was based on the *t*-test, and the sample size was increased by 5% to 10%. For health-related quality of life, a change of half a standard deviation[15] (4 points) was assumed to be the minimal clinically important difference. As no data on the variance of the difference between repeated IIEF self-assessments were available, the pilot study was powered to detect a correlation coefficient of 0.5. When the pilot study resulted in a correlation coefficient of 0.72, the final

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center prospective, observational cohort study
- **Key Findings:** Using a validated questionnaire of erectile function, 11 of 62 patients (11%) reported postoperative subjective enlargement of the glans penis on penile erection compared with glans tumescence preoperatively, without a sustained positive impact on general erectile function.
- **Take Home Message:** We recommend, as part of the consent process, that male patients undergoing great saphenous vein ablation be informed about this potential off-target effect.

analysis sample size of 56 was calculated using PowerShell 3.0.43 (Microsoft, Redmond, Wash) and augmented to 62 to offset loss to follow-up.[16] Percentages use the full sample size of 62 as the denominator unless indicated otherwise. R 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria) was used for analyses. Patients were enrolled in the study once they had given informed consent in writing.

Informed consent was obtained from each patient. The study was carried out in compliance with national legislation and the latest version of the Declaration of Helsinki. Ethical approval for the study was obtained from the Ethics Commission of the University of Lübeck (Az14-199).

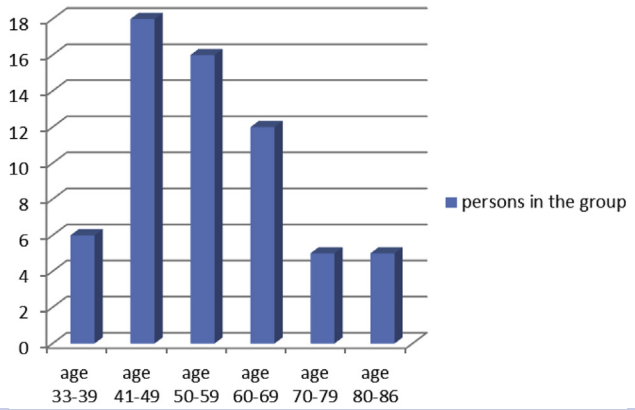

Fig 1. Ages of the responders.

RESULTS

Patients were recruited during a period of 18 months from September 2015 to February 2017. We recruited 62 patients (Table I). The patients' age ranged from 33 to 89 years (median, 54 years; Fig 1). Of 186 questionnaires, 11 were not returned or were incomplete: 1 before surgery, 3 at 1 week, and 7 at 3 months after surgery. A responder analysis was not possible.

The procedures were carried out on the right leg in 35 (56.5%) patients and on the left leg in 27 (43.5%) patients. The majority of the patients (n = 45 [73%]) underwent endovenous laser therapy, followed by 12 (19%) foam sclerotherapies and 5 (8%) radiofrequency ablations (Fig 2).

In the assessment of EF, 25 patients reported normal EF across all visits, as defined by an IIEF score of ≥26. The remaining 37 patients reported mild ED, mild to moderate ED, moderate ED, and severe ED (Table II). The distribution of severity groups did not change much during the course of the study (Fig 3).

Table I. Baseline characteristics of patients (N = 62)

Patient's history	No.
Endovenous laser ablation	46
Radiofrequency ablation	4
Foam sclerotherapy	12
Left leg	27
Right leg	35
Hypertension	14
Radical prostatectomy	4
Transurethral resection of the prostate	2
Heart attack	8
Urogenital trauma	1
Coronary sclerosis	1
Diabetic	2
Stroke syndrome	1
Peripheral arterial obstructive disease	1

On question 7, seven (11%) patients reported an increased glans tumescence during erection compared with the preoperative status, with three reports (5%; paired *t*-test, $P = .0832$) already at visit U2 (1 week after intervention), which appeared to be reversible until U3. However, there was no significant difference between U2 and U3 (paired *t*-test, $P = .709$). Four patients (7.4%) reported an increased swelling of the glans penis at visit U3 (3 months after intervention). Increased swelling of the glans penis was found significantly more often at visit U3 compared with baseline U1 (paired *t*-test, $P = .0446$). None of these seven patients with increased swelling of the glans penis took any medication for ED or had any poor prognostic factor. Five had an endovenous laser ablation and two had foam sclerotherapy. Of these seven men, three reported normal EF (IIEF score ≥26) during the course of the study. One patient had mild ED at baseline (visit U1) and reported an improvement of EF after the intervention at 1 week and 3 months, with IIEF scores of 25 (U1), >28 (U2), and 27 (U3), respectively. The remaining three men who reported postoperative increased tumescence of the glans penis at erection reported ED throughout the time of observation with IIEF scores as follows: 23 (U1), 17 (U2), and 18 (U3); 8 (U1),

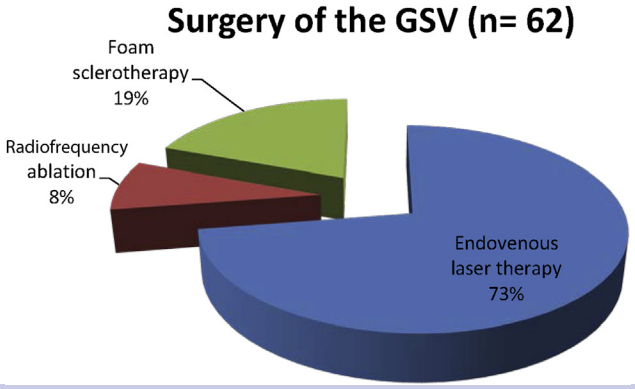

Fig 2. Distribution of the different procedures. *GSV*, Great saphenous vein.

Table II. International Index of Erectile Function (IIEF) scores during the course of the study

	Before surgery	1 Week after surgery	3 Months after surgery
No ED (score 26-30)	25	25	25
Mild ED (score 22-25)	17	15	9
Mild-moderate ED (score 17-21)	9	5	7
Moderate ED (score 11-16)	6	10	6
Severe ED (score 1-10)	5	5	7
No.	62	60	54

ED, Erectile dysfunction.

8 (U2), and 10 (U3); and 18 (U1), 16 (U2), and 17 (U3). Overall, postoperative increased glans tumescence and use of erectogenic medication did not correlate with ED. The age of these seven men ranged from 46 to 83 years.

DISCUSSION

There are several treatment options for the management of varicosis of the GSV. The endovenous thermal methods of laser and radiofrequency ablation used in this study ensure that patients experience relatively little pain for a limited time and can rapidly resume their normal activities.[17] Endovenous laser ablation and radiofrequency ablation are as effective as conventional surgery in treating saphenous venous insufficiency.[18] Ultrasound-guided foam sclerotherapy has a significantly higher recurrent reflux rate at the saphenofemoral junction.[19] The methods differ in the mode of venous ablation, but they all induced comparable hemodynamic effects caused by occlusion of the GSV or abolishment of venous reflux. Tumescent anesthetic was injected perivenously around the saphenofemoral junction including the tributaries in the groin. The effect of venospasm caused by epinephrine in the solution is not as relevant as the reduction of venous diameter due to the volume of the perivenous fluid. The duration of venospasm in the tributaries in the groin potentially following application of tumescent anesthesia is limited and cannot last longer than the anesthetic effect. Arterial inflow is not affected by perivenous tumescent anesthesia.

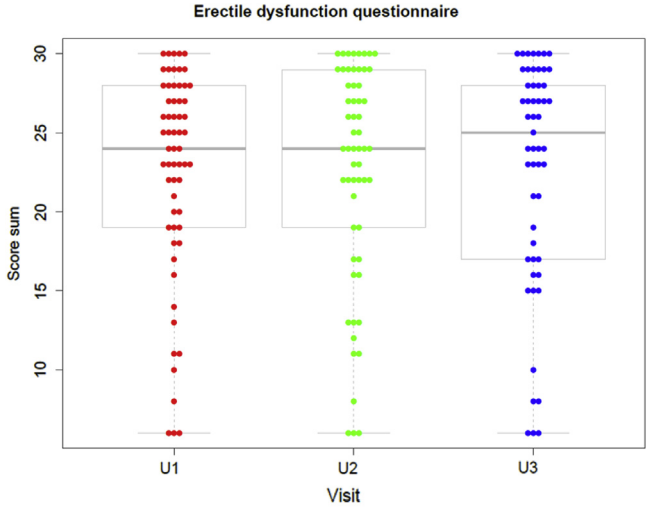

Fig 3. Overall erectile dysfunction (ED) questionnaire score did not change significantly between visits: mixed scatter and box plots. Each *dot* represents an individual International Index of Erectile Function (IIEF) score (EF domain, questions 1-6 of the questionnaire) of 62 individual patients at the three time points (*U1*, day of surgery; *U2*, week 1; *U3*, week 12). No significant difference was found by Kruskal-Wallis or analysis of variance testing.

Our study is the first one to show a correlation between the endovenous interventions and a temporal increased tumescence of the glans penis on erection after the intervention and verifies our case report.[2] Anatomically, the superficial dorsal vein of the penis predominantly drains the skin and superficial tissues, although there are multiple emissary veins that link the deeper areas of the penis, including the cavernous body, with the superficial dorsal vein of the penis.[20] Venous drainage of the cavernous bodies of the penis mainly functions through the deep dorsal vein of the penis.[20,21] This vein opens into the periprostatic plexus and subsequently into the internal iliac vein.[22] In addition, blood drains from the cavernous bodies through the internal pudendal vein into the internal iliac vein.[21,22] Of particular interest in these cases is the venous blood flow through the superficial dorsal veins of the penis that drain into the two external pudendal veins, which themselves subsequently open into the GSV.

Ablation of the GSV in the groin, especially in the saphenofemoral junction, could therefore hypothetically reduce the venous drainage of the penis and thus potentially affect the degree of glans penis tumescence and also general EF. Another hypothesis could be that the effect might be caused by heat-induced inflammatory processes in the groin. Varicose changes to the pelvic veins are frequently observed in women with a pelvic vein syndrome.[23] In male patients, spermatic vein incompetence is affected with scrotal varicoceles. Pelvic venography or magnetic resonance imaging could provide information here. However, most pelvic veins open into the internal pudendal vein through various plexuses and therefore do not touch the surgical area through the saphenofemoral junction.[22] Surgery of the veins is not included as a treatment option in the current European Association of Urology guidelines on ED.[3] Until now, no occlusive vein surgery for treatment of ED has proved to be effective.[24] However, it might be of interest to prospectively study men with ED and insufficient response to phosphodiesterase type 5 inhibitors who are diagnosed with a high burden of varicosis of the legs indicated for endovenous treatment.

Limitations of our study are the schedule of the IIEF questionnaire with the short interval of 1 week after surgery because the IIEF is just validated for an interval of 4 weeks.[14] This was because of our first described case,[2] in which the swelling of the glans was reported in the first days postoperatively. There was no randomization of the patients because it was a single-arm observational study. By nature of a single-arm study, we have not included a comparative arm. Even a restriction to one therapy might be construed as a clinical trial so that studies with homogeneous treatments should be conducted as a next step. There was no quantification of the magnification of the glans swelling (only yes/no questionnaire). The wide age range suggests inhomogeneity of tests of EF. In this study, a penile ultrasound examination was not practicable because penile ultrasound is an invasive, vascular test that needs an intracavernal injection. It could be an option in further studies.

CONCLUSIONS

This is the first prospective study that confirms a transient increased tumescence of the glans penis after endovenous treatment of GSV varicosis, as reported in a case by Zimbelmann and Cordes.[2] However, a positive impact on general EF could not be proved. Although it occurs in approximately 10% of men treated, patients should be informed about this potential side effect in consenting to intervention.

AUTHOR CONTRIBUTIONS

Conception and design: JC, MZ, RV, BK
Analysis and interpretation: JC, MZ, AM, MK, RV, HB, AR, BK
Data collection: MZ
Writing the article: JC, AM, MK, RV, HB, AR, BK
Critical revision of the article: JC, MZ, AM, MK, RV, HB, AR, BK
Final approval of the article: JC, MZ, AM, MK, RV, HB, AR, BK
Statistical analysis: Not applicable
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Overall responsibility: JC

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