ONCOLOGY/RECONSTRUCTION
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# Looking beyond oral mucosa: Initial results of everted saphenous vein graft urethroplasty (eSVGU) in long anterior urethral strictures

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**Abstract** *Objective:* To prospectively evaluate the feasibility and initial results of an everted saphenous vein graft (eSVG) as a dorsolateral onlay, in patients with long anterior urethral strictures and/or chronic tobacco users.

*Patients and methods:* In all, 20 patients with long anterior urethral strictures (>7 cm) and/or chronic tobacco exposed oral mucosa were included in the study. The harvested SVG was hydro-distended, detubularised, and everted. Substitution urethroplasty using an eSVG was performed using a dorsolateral onlay technique. Symptoms were assessed using the International Prostate Symptom Score (IPSS) and uroflowmetry at 1, 3 and 6 months; and voiding and retrograde urethrograms, and urethroscopy were done at 3 months. Failure was defined as failure to void, need for interventions in form of direct-vision internal urethrotomy or endodilatation.

*Results:* Three patients were excluded because they underwent a staged urethroplasty. In all, 17 patients underwent eSVG substitution urethroplasty. The mean (SD, range) follow-up of our patients was 17.64 (5.23, 10–26) months. The mean (SD, range) length of the strictured segment was 14 (2.5, 10–18) cm and the length of the harvested SVG was 16.3 (2.7, 12–20) cm. The mean (SD) IPSS at 1, 3 and

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6 months after catheter removal was 10 (2.8), 10 (3.4) and 10 (1.4) and the quality-of-life score was 1.76 (0.5), 2.05 (1.0) and 2.05 (1.0), respectively. Postoperatively, endodilatation was required in two patients. Complete failure occurred in one patient.

*Conclusions:* An eSVG, as a dorsolateral onlay graft, is a promising and prudent option for long anterior urethral strictures, especially in patients with poor oral hygiene and chronic tobacco use.

## Introduction

Urethral stricture disease has always been a reconstructive dilemma. Bringing oral mucosal grafts (OMGs), the present 'gold standard' for most urethral reconstructive needs, to the forefront is credited to El-Kasaby et al. [1]. OMGs have continued to give reliable and reproducible results in past two decades and have virtually become the 'one-stop shop' for all urethral reconstructive needs. However, recent literature has highlighted some concerns in the use of OMG in certain subsets of patients, namely those with tobacco-exposed oral mucosa [2] and those with pan-anterior strictures [3] that necessitate looking beyond the oral mucosa.

Patients with poor oral hygiene, diseased oral mucosa, and those chronically exposed to tobacco products have less than satisfactory results with OMG and have overall increased donor-site morbidity and low oral recovery as reported by Sinha et al. [2] from northern India. About 58% of the study population in that study had a history of tobacco usage. Another report by the same group found the results of buccal mucosal graft (BMG) urethroplasty was significantly inferior in tobacco users as compared to non-users (58.3% vs 73.8%) [4]. A similar study found almost double the success rate for patients who were not tobacco chewers compared with those who chewed tobacco (85% vs 42%) [5]. Southeast Asia is home to nearly 400 million tobacco users. About 47% of Indian men aged >15 years are tobacco users (use of smokeless tobacco up to five times that of smoked tobacco) [6]. Moreover, two recent studies reported the development of squamous cell carcinoma in OMG-grafted urethra, one from India (after 6 months) [7] and another from the USA (after 16 months) [8], which has precipitated concern about introducing malignancy for the treatment of a benign disease.

OMGs have poorer overall success rates and inconsistent results in long anterior urethral strictures. Success rates of OMG urethroplasty in strictures of >7 cm is almost half that of those <7 cm (40% vs 88%) [3]. Chauhan et al. [5] compared the success of BMG with a lingual mucosal graft in long urethral stricture patients (range 3.2–13.4 cm) and found the stricture length was the significant predictor of success and success was higher in shorter strictures on univariate analysis. Hence, there is a need to look beyond oral mucosa in these subsets of patients. Various other autologous grafts have been used for augmentation namely ureter, appendix, bladder mucosa, and colon, but all with dismal results or poor applicability [9]. Tissue-engineered grafts have also been suggested but this technology is still in its infancy and they are not readily available.

El-Morsi et al. [10] first used a saphenous vein graft (SVG) in 1972 in 10 patients with promising results and suggested it as an alternative to Johanson staged urethroplasty, which was widely used at that time. However, the use of the SVG did not become popular. Later it returned as an option in hypospadias [11] and severe complicated hypospadias cripple [12], with promising results. Kim et al. [13] demonstrated the feasibility of using an autologous SVG in a landmark study in rabbits, with good results at 3 months. Kim and Kwon [14] reviewed and discussed the potential of autologous vein graft use in humans and need for such studies. As per previous experiences in animal studies [15,16] results of everted vs non-everted vein grafts showed better results with the everted graft. Also, valves can be avoided in the everted graft. In our present study, we prospectively evaluated early results of everted SVG urethroplasty (eSVGU) in patients with long anterior urethral strictures and/or chronic tobacco exposure of the oral cavity.

## Patients and methods

All patients with urethral stricture admitted for substitution urethroplasty were evaluated. Patients with either long segment anterior urethral involvement (>7 cm) and/or poor oral hygiene because of chronic tobacco exposure were included for eSVGU. Patients with a urethral calibre of ≤6 F, history of peripheral vascular disease/lower limb ischaemia, venous insufficiency in both the lower limbs with or without ulcers, deep vein thrombosis, age >75 years, previous history of urethroplasty, and presence of two separate strictures requiring two grafts, were excluded.

In all patients a physical examination of genitalia and lower limbs was carried out and symptoms were assessed using the IPSS. Uroflowmetry and post-void residual urine volume (PVR) estimation was carried out. Oral hygiene was assessed by history of chronic tobacco use and oral examination. In addition to a voiding cystourethrogram (VCUG) and retrograde urethrogram (RUG), colour Doppler ultrasonography of both lower limbs to assess the superficial and deep venous system was conducted to determine superficial and deep venous patency or incompetence.

The eSVGU was performed under spinal anaesthesia with a midline perineal incision (Fig. 1a). The urethra was mobilised from the ventral midline to beyond the midline on the dorsal aspect, leaving the fascia and vascular attachment on the other side intact (Fig. 2a; single side urethral mobilisation technique) [17], and opened dorsolaterally. The length of the strictured segment, including the calibre of the urethra, was measured. A suitable sized SVG was retrieved in the upper thigh (Fig. 1b and c) using multiple small incisions (Fig. 1) along the course of the vein, which had been pre-marked during colour Doppler, starting from the sapheno-femoral junction by a second team of urologist with the patient in the same lithotomy position. A 'no touch technique' [18] was used while retrieving the SVG. The vein was ligated proximally and distally including all tributaries to the selected segment, then sectioned and harvested. As soon as the vein was retrieved it was submerged in papaverine solution (30 mg in 100 mL) for 5 min. The vein was adequately hydrodistended to achieve a workable calibre (Fig. 1d and e) by occluding one end and then injecting saline from the other. The SVG was then detubularised (Fig. 1e) and everted (endothelium facing outside the lumen; Fig. 2b) and used as a dorsolateral-onlay patch (Fig. 2b and c) using 4/0 polyglactin 910. The SVG was quilted to the corporal bed using a single running suture along the entire length. A 16-F Foley catheter was placed. In patients with coexisting meatal stenosis/lichen sclerosis (LS) involvement, a generous dorsal meatotomy was given and the graft was fixed using interrupted sutures dorsally and fed into the meatus to be retrieved from below and was continued as a dorsolateral-onlay patch.

Postoperative complications, along with donor-site complications were noted using the Clavien–Dindo grading system. The catheter remained *in situ* for 3 weeks. Symptom assessment including the IPSS and uroflowmetry with PVR was done at 1, 3 and 6 months after catheter removal, and with 3-monthly symptom assessment thereafter. A urethrogram was done at 3 months. The presence of any diverticuli/pouching, area of narrowing, if any and need of direct-vision internal urethrotomy (DVIU)/or any auxiliary procedure were noted. In addition, all patients were evaluated by urethroscopy at 3 months after catheter removal to endoscopically assess the site of the SVG and endoscopic appearance of the SVG. Failure was defined as failure to void or need for interventions in form of DVIU or endodilatation. Data were analysed using the Statistical Package for the Social Sciences (SPSS® version 22, SPSS Inc., IBM Corp., Armonk, NY, USA) and expressed as mean and standard deviation (SD) wherever feasible.

## Results

Of the 20 selected patients, 17 underwent eSVGU (patient characteristics Table 1). Three patients were
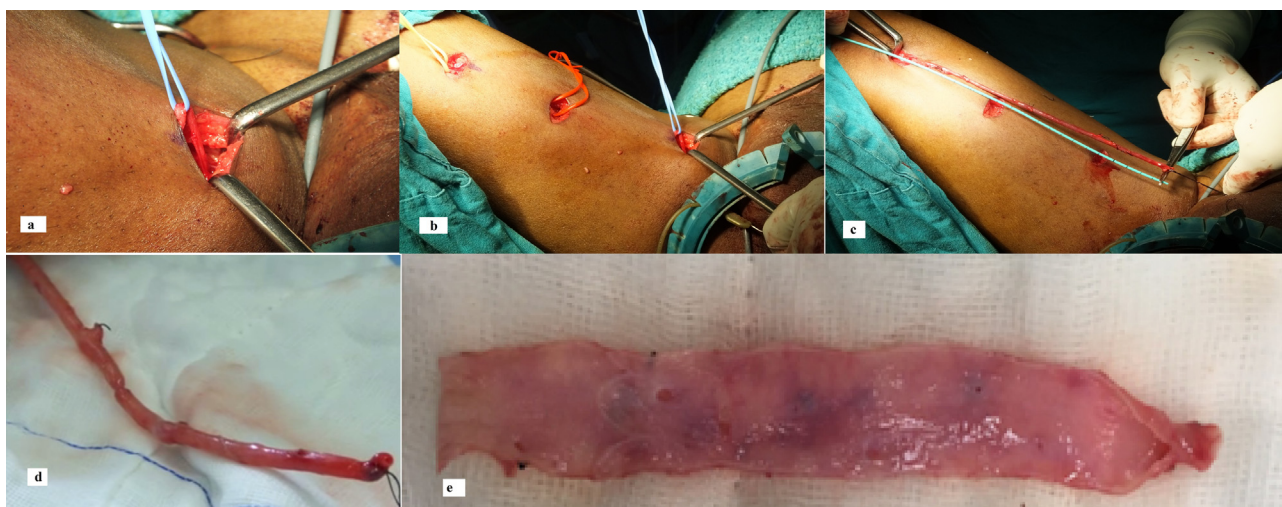


**Fig. 1**    (a) Lithotomy position with simultaneous exposure of thigh for saphenous vein harvesting. (b) Harvesting of saphenous vein from thigh using multiple small incisions. (c) Length of harvested saphenous vein. (d) Hydro-distension of saphenous vein. (e) De-tubularised SVG.
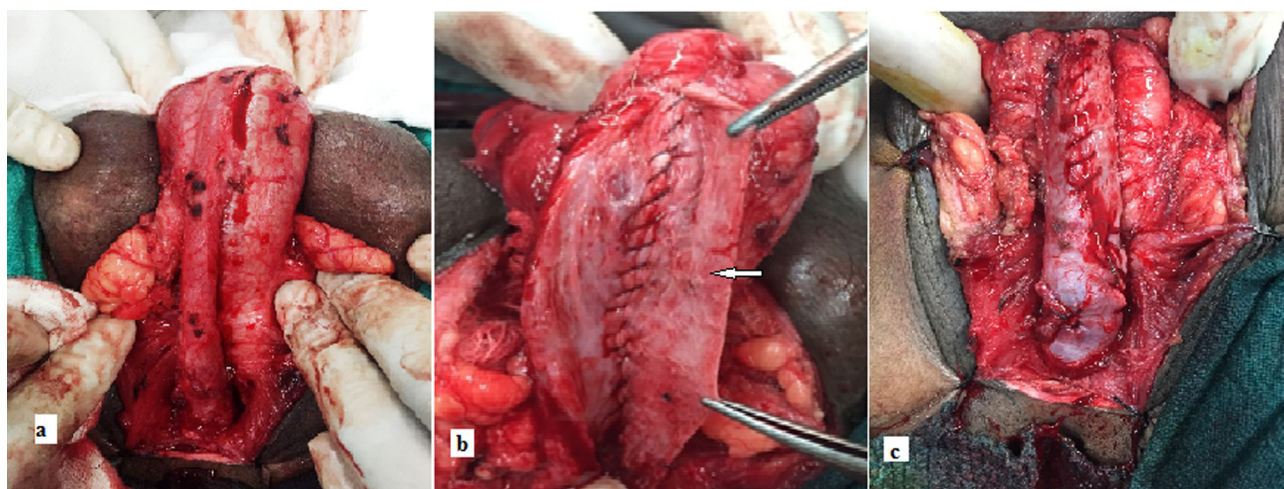
**Fig. 2** Intraoperative photographs. (a) Urethral mobilisation with eversion of penis into the perineum. (b) SVG as dorsolateral onlay (white arrow). (c) Complete tubularisation of urethra.

excluded because they underwent staged urethroplasty (calibre ≤6 F). Four patients had a history of chronic smoking, while 13 had a history of chronic chewing of tobacco/pan masala (Table 1). The mean (SD, range) follow-up of our patients was 17.64 (5.23, 10–26) months. In all, 16 patients were symptomatically improved and voiding, with satisfactory flow at the time of submission of study with improved quality of life. The postoperative outcomes are summarised in Table 2. At the 3-month follow-up urethrogram, the anterior urethra calibre was good in 14 patients (Fig. 3a and b). Two patients had an area of narrowing in the bulbar urethra on RUG. Both had flimsy adhesions and underwent endodilatation (Clavien–Dindo Grade IIIa). None of these patients required any further procedure thereafter. One patient had complete failure at 3 months (was unable to void with a significant PVR, Clavien–Dindo Grade IIIb; preoperatively he had had a pan-anterior stricture with LS) and he later underwent staged urethroplasty. Additionally, perineal wound infection with pus discharge occurred in one patient and one had partial wound dehiscence at the donor site (both Clavien–Dindo Grade I). No wound dehiscence was noted at the recipient sites. None of our patients had postoperative penile curvature or chordee. Of the 10 patients who required a simultaneous meatoplasty, four patients are currently on regular self-meatal dilatation (all had LS preoperatively). As per protocol, all patients underwent urethroscopy at 3 months. The grafted site could be delineated in all, but the appearance was indistinguishable from the rest of urothelium (Fig. 4a). Mucosal ingrowth without any area of narrowing was seen in two patients (Fig. 4b). There was no evidence of any urethral diverticuli or pouching in any of our patients. Among seven patients who had LS-related stricture, one patient had complete failure at 3 months and one patient required

endodilatation, while among those with non-LS-related stricture, only one patient required endodilatation. The resultant final donor site scar was well concealed and cosmetically acceptable (Fig. 5).

**Discussion**

In the last 25 years, several experimental and clinical studies have established the supremacy of OMG as an ideal urethral substitute but recently some authors have started questioning its widespread applicability [19]. Kero et al. [20] suggested oral mucosa to be a reservoir for human papilloma virus, especially type 16, in normal healthy males reporting for regular dental health checkups. This has raised the need for regular oral scrapings before blindly using oral mucosa as a substitution graft for the urethra and putting the urethra of the patient and their sexual partners at an increased risk of future malignancy, as has been reported in a few cases [7,8]. This has led to a renewal in the search for other available alternatives to oral mucosa. Tissue-engineered grafts have emerged as possible options but with the initial limitations [21] of graft contracture, costliness, most studies having been conducted in animal models and not yet been extrapolated to humans except in a few instances, the technology itself is in its developmental infancy and further research is needed for its endorsement in urethroplasty.

Saphenous vein is readily obtainable, its calibre and the length that can be harvested matches that of the urethra, even for the most extensive urethral reconstruction. Kahveci et al. [22] have suggested that the vein graft mainly acts as a scaffold, the endothelium sloughing off after 3 days, with transitional epithelium ingrowth resulting in uroepithelisation of the neourethra by 3 weeks. Studies in a rabbit model [13] have suggested that the SVG is associated with urethral mucosa sur-

**Table 1** Demographic, preoperative and intraoperative characteristics of the patient population.

| Variable | Number of patients | Mean (SD, range) |
| --- | --- | --- |
| Age, years | 17 | 41.06 (13.43, 21–60) |
| Duration of symptoms, years | 17 | 5.73 (7.0, 0.25–30) |
| Chronic tobacco exposure, years | | |
|   Smoked | 4 | 9.5 (3.0, 5–12) |
|   Non-smoked (tobacco /pan masala) | 13 | 8.6 (3.0, 5–15) |
| Previous repeated dilatations, $n$ | 10 | 2.2 (1.2, 1–5) |
| Previous DVIU, $n$ | 10 | 2 (1.3, 1–4) |
| Patients with supra-pubic catheter drainage, $n$ | 4 | NA |
| History of catheterisation, $n$ | 12 | NA |
| IPSS | 13 | 21.15 (3.1, 16–28) |
| Preoperative quality-of-life assessment score | 17 | 4.9 (0.69, 4–6) |
| Narrow external meatus, $n$ | 10 | NA |
| Haemoglobin, g/dL | 17 | 12.39 (2.35, 8.5–15.8) |
| Creatinine, mg/dL | 17 | 0.87 (0.17, 0.6–1.2) |
| $Q_{max}$, mL/s | 13 | 8.07 (4.03, 2.7–15.3) |
| PVR, mL | 13 | 99.46 (53.25, 30–230) |
| Aetiology, $n$ | 17 | |
|   Idiopathic | 7 | |
|   Inflammatory (LS) | 7 | |
|   Post-infectious | 2 | |
|   Post-traumatic/iatrogenic | 1 | |
| Site of stricture, $n$ | 17 | |
|   Peno-bulbar[*] | 11 | |
|   Pan-anterior[**] | 6 | |
| Intraoperative | | |
| Calibre of urethra in strictured segment, F | 17 | 7.53 (0.51, 7–8) |
| Length of strictured segment, cm | 17 | 14 (2.5, 10–18) |
| Length of harvested SVG, cm | 17 | 16.3 (2.7, 12–20) |
| Need of intraoperative meatoplasty, $n$ | 10 | |
| Total operative time including SVG harvesting, min | 17 | 186.58 (23.28, 150–240) |
| Time for harvesting only, min | 17 | 18.41 (2.57, 15–22) |

$Q_{max}$, maximum urinary flow rate.
[*] Peno-bulbar urethral stricture: stricture involving part of penile and bulbar urethra but not the entire segment of it.
[**] Pan-anterior urethral stricture: stricture involvement from external urethral meatus to whole of anterior urethra (penile and bulbar).

**Table 2** Postoperative characteristics of patients.

| Variable | | Number of patients | Mean (SD, range) |
| --- | --- | --- | --- |
| Uroflowmetry at 1 month | $Q_{max}$, mL/s | 17 | 22.06 (7.86, 6.30–32.9) |
| | PVR, mL | 17 | 24.17 (34.14, 0–150) |
| Uroflowmetry at 3 month | $Q_{max}$, mL/s | 16 | 22.22 (8.34, 9.2–38.4) |
| | PVR, mL | 16 | 41.94 (69.27, 0–300) |
| Uroflowmetry at 6 month | $Q_{max}$, mL/s | 16 | 21.90 (6.27, 10.9–31.2) |
| | PVR, mL | 16 | 22.20 (12.40, 8–56) |
| IPSS at 1 month | | 17 | 10 (2.8, 7–18) |
| Quality-of-life score at 1 month | | 17 | 1.76 (0.5, 1–3) |
| IPSS at 3 months | | 16 | 10 (3.4, 7–22) |
| Quality-of-life score at 3 months | | 17 | 2.05 (1.0, 1–6) |
| IPSS at 6 months | | 16 | 10 (1.14, 8–12) |
| Quality-of-life score at 6 months | | 17 | 2.05 (1.0, 1–6) |

$Q_{max}$, maximum urinary flow rate.

rounded with stratified columnar epithelium of several layers and bundles of circular smooth muscles and that the grafted vein could not be discerned from the rest of the urethra on Masson's trichrome staining. The SVG group showed minimal staining, signifying less collagen and hence less fibrosis and the lining of the grafted vein was completely reintegrated with the urothelium (immunohistochemistry analysis) [13]. Likewise, the endoscopic appearance of the grafted sites in our present patients was identical to the rest of the urethra (Fig. 4a). Previous studies [16] suggested the use of an everted graft to overcome the theoretical obstruction from the presence of valves and for better graft imbibition. With its thin wall the SVG rapidly establishes a blood supply,
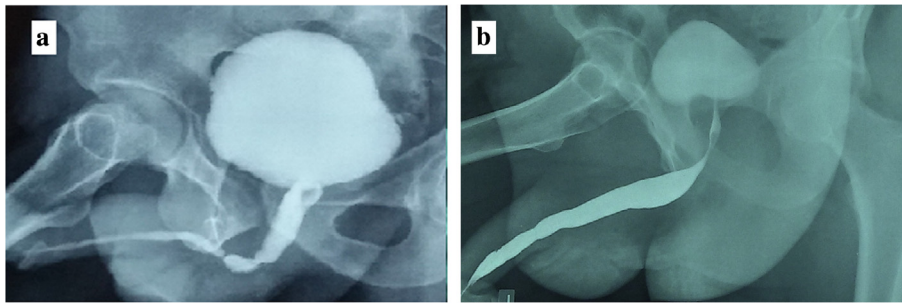
**Fig. 3** (a) Preoperative urethrogram in a patient with LS showing pan-anterior urethral stricture extending up to bulb. (b) Postoperative urethrogram in the same patient showing good calibre of whole anterior urethra.
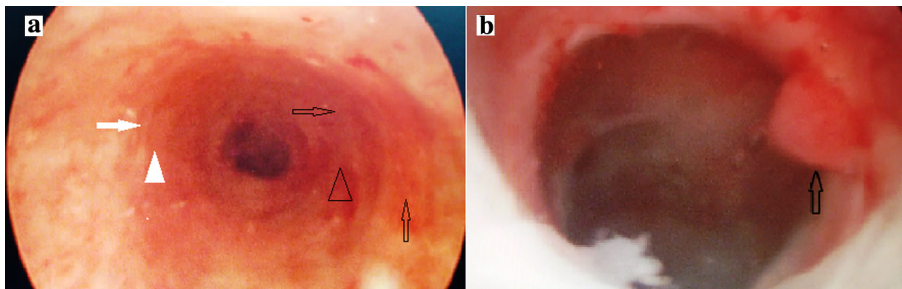


**Fig. 4** (a) Endoscopic appearance of augmented urethra; the black arrow marks the grafted side, which is indistinct from rest of the urethra, while the white arrow shows the normal urethra. (b) Endoscopic appearance of urethral mucosal fold (black arrow) that occurred in two of our patients.



**Fig. 5** Postoperative photograph of donor site in thigh. Incision scar is small, concealed and cosmetically acceptable to patients.

which prevents ischaemia and graft contracture. Also, hair is not a problem and the multilayer structure of the vein provides for a robust graft, less vulnerable to ballooning and fistula formation. Implicit elasticity provided by the muscle coat and elastic fibres can prevent penile curvature and also should not impinge on erectile function.

The length of the graft is an asset and a luxury considering the long segment strictures in our present patients (Table 1). All of our patients had stricture lengths of ≥10 cm and seven of these had LS-related strictures, still all were repaired with a single graft. The length of stricture is also an important determinant

for defining the operative method and prognosticating results [5]. Chen et al. [23] reported an 82% success rate for strictures of > 4 cm and 76% for those of ≥6 cm. A study by Yalcinkaya et al. [3], using BMG, reported a success rate of 88% for stricture lengths of ≤7 cm and only 40% for those of > 7 cm, with failure for all four patients with pan-urethral strictures.

eSVGU is performed under spinal anaesthesia, which is a perceived advantage as compared to OMG that needs to be done under general anaesthesia and this helps towards faster recovery and better pain control. The anaesthesia time is also less as compared to general anaesthesia. Unlike OMG, all our present patients were

allowed all types of oral feeding within 6 h of surgery. We did not encounter any limb oedema, ecchymosis, or any other donor-site morbidity except in one patient who had partial wound dehiscence at the donor site (Clavien–Dindo Grade I). This was in contrast to limb complications cited in the cardiovascular surgery literature such as limb oedema (52.3%), paresthesia (29.5%), Erysipelas (9.1%), lymphorrhoea (4.5%), and deep venous thrombosis (2.3%) [24]. This may be related to our careful patient selection, use of preoperative colour Doppler mapping of the saphenous vein (which has been related to decreased limb morbidity [25]), and our present patient population being markedly different from patients in need of bypass surgery from which these complications' have been reported. The thigh scar is concealed and cosmetically acceptable, which may result in better patient acceptance.

Previous studies from India [2,4,5] have reported that a subset of patients with poor oral hygiene due to chronic exposure to tobacco products generally have poor outcomes with OMG and therefore, the saphenous vein appears to be a feasible graft material for this subset of patients.

Colour Doppler, as an additional part of patient evaluation, is helpful for precise intraoperative localisation and rapid retrieval, besides giving valuable information about the patency and competence of the superficial and deep venous systems [25]. On colour Doppler evaluation of the lower limbs, one patient had unilateral perforator incompetence at the level of the calf and so the contralateral saphenous vein was harvested. Venospasms during saphenous vein harvesting for cardiac bypass are a known fact and minimal handling with a 'no touch technique' is described as a preventive measure [8]. As a further measure to prevent venospasm, as soon as the vein is retrieved it is submerged in papaverine solution as described in methods section [26].

On one hand a SVG provides a lengthy graft but the width can become an issue sometimes, especially in near obliterative strictures. Although we did not encounter such a situation in the present study, areas of focal narrowing on the native urethral plate can be dealt with using a conjoint parallel graft but for near obliterative pan-urethral strictures even this may not suffice.

On routine endoscopy at 3 months, non-obstructive mucosal ingrowth was found in two patients (Fig. 4b); cold cup biopsy of the ingrowth was taken and histopathological examination revealed chronic non-specific inflammation with small bit of urothelium with hemosiderin-laden macrophages. The examination of the adjacent bulbar urethra showed stratified squamous epithelium with chronic non-specific inflammation. On subsequent endoscopy after 3 months, there was no evidence of any mucosal ingrowth at the previous site. There were no complications after cold cup biopsy of the mucosal ingrowths. These findings confirm previous reports of uroepithelisation over saphenous vein scaffold [22]. The ideal groups of patient for eSVGU are those stricture patients with poor oral hygiene but no history of peripheral vascular disease/lower limb ischaemia, venous insufficiency in both the lower limbs with or without ulcers, and deep vein thrombosis. We excluded patients with varicose veins based on vascular surgery literature. A varicosed vein is not a suitable graft for them because of a mismatch in calibre and possible concerns about the use of a diseased vein wall. However, we think that it may be accessed in future studies, as such a vein would provide more width and the success of eSVGU is not the intima but the scaffold provided by the fibrous framework.

Our present study of this initial experience is not without shortcomings, such as the small number of patients, short-term follow-up, and absence of any comparative arm with the established BMG. Although, the success of the urethroplasty technique is established by its long-term results, the aim of our present study was to evaluate early results, as it could only form the 'initial adopters' stage of the IDEAL (Idea, Development, Exploration, Assessment and Long-term follow-up) recommendations [27] of the development of any new surgical procedure.

## Conclusion

An autologous SVG is a viable option in long-segment urethral strictures, with minimum morbidity, especially in patients who are chronic tobacco users. More studies with larger patient populations and long-term follow-ups are needed.

## Conflict of interest

None.

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