Original Article

Does aetiology of urethral stricture influence the survival of the buccal mucosa graft?—comparative study in patients with penile urethral stricture due to lichen sclerosus *vs.* idiopathic group

Manuel Hevia, Agustín Fraile, Enrique Sanz, Alberto Artiles, Marta Santiago, Silvia García-Barreras, Guillermo Fernández-Conejo, Rafael Rodríguez-Patrón, Javier Burgos-Revilla

Urology unit of Hospital Universitario Ramón y Cajal, IRYCYS (Ramon y Cajal Hospital Biosanitary Research Institute), University of Alcala, Madrid, Spain

Contributions: (I) Conception and design: M Hevia, A Fraile; (II) Administrative support: R Rodríguez-Patrón, J Burgos-Revilla; (III) Provision of study materials or patients: R Rodríguez-Patrón, J Burgos-Revilla, G Fernández-Conejo, S García-Barreras; (IV) Collection and assembly of data: M Hevia, A Fraile, A Artiles, M Santiago; (V) Data analysis and interpretation: M Hevia, A Fraile; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Manuel Hevia. Urology unit of Hospital Universitario Ramón y Cajal, University of Alcala, M-607, km. 9, 100, 28034, Madrid, Spain. Email: manuel.hevia.palacios@gmail.com or mhevia@salud.madrid.org.

Background: Lichen sclerosus (LS) is one of causes of male urethral stricture, mainly penile or anterior urethra, and frequently associated with phimosis. This disease involves penile skin and surrounding tissues, which might affect long-term graft survival after a substitution urethroplasty. The aim of this study is to assess LS impact on urethral grafts, comparing outcomes in the LS group versus idiopathic urethral stricture.

Methods: Retrospective descriptive analysis of male patients who underwent urethroplasty with buccal mucosa graft (BMG) at our academic institution during the last decade [2008–2021]. Patients were allocated to LS group or idiopathic group depending on the aetiology of urethral stricture. The LS was confirmed by histology. Data collected included patient baseline characteristics, stricture description, perioperative parameters, surgical technique and outcomes. Kaplan-Meier survival analysis was performed to assess graft survival in both groups, as univariate and multivariate analysis were performed trying to identify independent risk factors for graft survival. Primary outcome was treatment success, defined as the no need for further treatments.

Results: Forty-eight male patients underwent substitution urethroplasty, 11 in LS group and 37 in idiopathic group. Baseline characteristics between both groups were different mainly in terms of age and stricture features (length), with larger strictures in LS group (6.8 *vs.* 3.5 cm). All grafts were procured from buccal mucosa, while no differences in grafts survival were observed between both groups (40.3 *vs.* 38.4 months). Mean of patient global impression of improvement (PGI-I) score was 2.1 in LS group *vs.* 2.4 in idiopathic group. Age, aetiology and smoking habit seems to be independent risk factors for graft survival, but not in multivariate analysis.

Conclusions: Patients with LS have longer strictures than idiopathic group. No differences were found in graft survival between both groups and independent risk factor for graft survival were not identified.

Keywords: Lichen sclerosus (LS); urethral stricture; buccal mucosa graft urethroplasty (BMG urethroplasty); reconstructive urethral surgery

Submitted Dec 12, 2021. Accepted for publication Sep 22, 2022.
doi: 10.21037/tau-21-1149
View this article at: https://dx.doi.org/10.21037/tau-21-1149

Introduction

Lichen sclerosus (LS) is a chronic inflammatory disease, hypomelanotic and lymphocyte-mediated skin disorder associated with important morbidity (1). This disease was first described by Weir in 1875 (2), and later in 1928 Sthümer coined the term balanitis xerotica obliterans (BXO) and proposed a traumatic etiology for it (3). Currently, the term BXO is in disuse since in 1995 the American Academy of Dermatology recommended the use of the term LS for future reports (4).

The estimated prevalence of LS varies between 1 in 300 to 1 in 100 with a peak incidence between 21–30 years (5); 14–29% of all urethral strictures are due to LS (6), while 30% of patients with genital LS will develop urethral stricture disease (7).

The etiology of LS is still the subject of debate, although it has been related to autoimmune processes, infectious pathology, trauma, and genetic alterations (8-10).

In a study carried out by Oyama *et al.*, in patients with LS antibodies against extracellular matrix protein 1 (ECM-1) were detected in 67%, while in the control group this antibody was detected only in 7% of the patients, which could partly explain the autoimmune etiology of this disease (11). In a recent publication, it was demonstrated that in the urethral biopsy of patients undergoing urethroplasty in patients with LS there was increased inflammation compared to patients without LS as well as overexpression of marker T cells such as CD8 and CCL-4. Positive staining for various viruses such as human papillomavirus, varicella zoster virus, or Epstein Bar virus could suggest an infectious etiology (9).

There is also an association between LS and systemic factors such as high body mass index (BMI), concomitant coronary artery disease, diabetes mellitus, and smoking patients (12).

Patients with LS present an involvement of the foreskin and glans in between 57–100% and the meatus in 4–37% with involvement of the urethra in approximately 20% of patients (13,14). The whitish appearance of the skin is secondary to the loss of melanocytes and the low production of melanin (15).

LS causes destructive scars that can lead to urinary and sexual problems, and decreased quality of life. Symptoms are itching, pain, difficulty in retraction of the foreskin and poor urination flow (16). Examination shows typical ivory to white papules that fuse into plates of different sizes, commonly with a non-retractable foreskin and frequent meatal stenosis (16,17).

The progression of the disease can lead to phimosis and urethral stricture as a consequence urination at high pressures that finally causes reflux towards the Littré glands causing inflammation and fibrosis at that level (1). The diagnosis of LS remains eminently clinical and histological. The presence of circulating antibodies against ECM-1 could indicate the severity of the disease (1,11). Patients with LS present potential malignancy of penile lesions in carcinoma *in situ* (CIS) or squamous cell carcinoma (SCC) (18).

When LS involves the urethra, treatment is more difficult and there is no gold standard treatment for patients with urethral strictures caused by LS. Surgical treatment depends on various factors such as the location, the extent of the stenotic segment, its caliber, the progression of the disease and the factors specific to each patient (19).

The purpose of this study is to analyze the survival of the oral mucosa graft in patients undergoing urethroplasty based on their etiology, comparing patients with LS *vs.* patients with idiopathic etiology. This study is based on the hypothesis that patients with LS, having greater local inflammation and poorer tissue quality, could have a higher rate of graft failure. We present the following article in accordance with the STROBE reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-21-1149/rc).

Methods

Patient population and study design

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ramón y Cajal institutional ethics committee (Reference No. 50/21) and individual consent for this retrospective analysis was waived. We performed an observational, descriptive and retrospective study on a cohort of patients with penile urethral stricture of idiopathic etiology and patients with LS who underwent urethroplasty with buccal mucosa graft (BMG) between January 2008–January 2021 in a tertiary academic institution. Patients were requested to read and sign the informed consent explaining the surgical procedure and the complications.

The inclusion criteria were patients with idiopathic etiology penile urethral stricture or LS who underwent urethroplasty with oral mucosa graft, who had not undergone previous urethroplasties. Patients with concomitant urethral strictures in another location were excluded. The diagnosis of LS was made according to

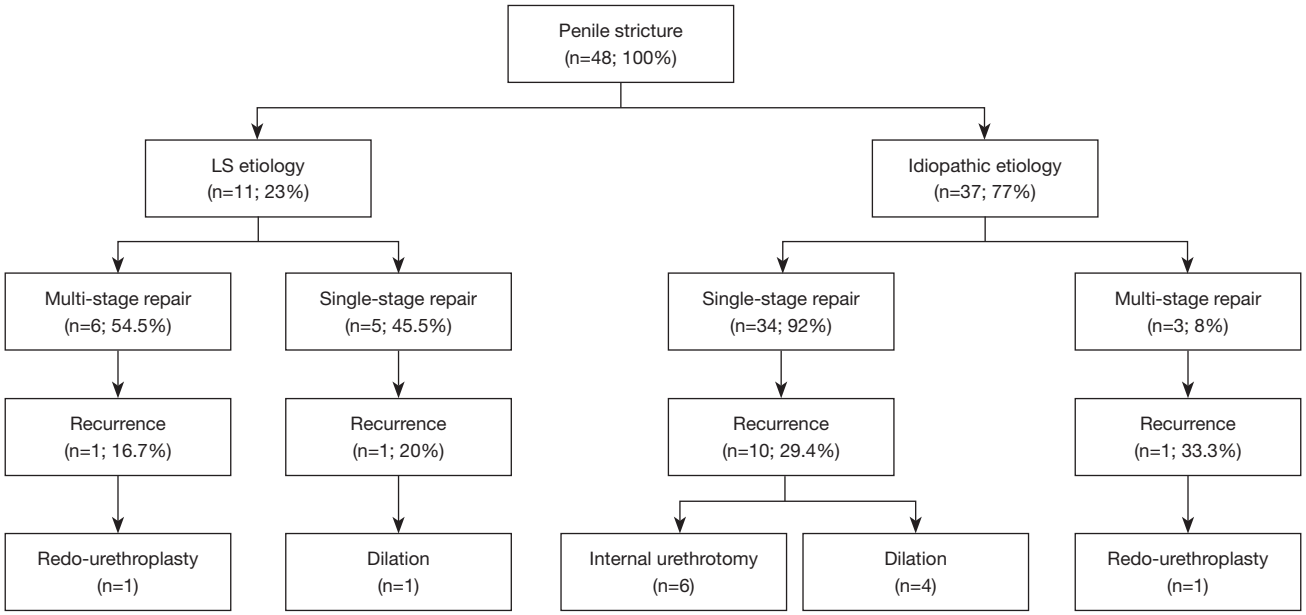

Figure 1 Management of penile stricture in our cohort. LS, lichen sclerosus.

the clinical appearance and confirmed by histology. No malignant histological features were identified. Primary outcome was treatment success, defined as the no need for further treatments with absence of stricture in endoscopy or urethrography, as well as non-obstructive flow study and graft survival was defined as the stricture recurrence-free time in previous grafted area. We included only patients with complete clinical data.

Patients with less than 12 months of follow-up were excluded from the study.

A detailed clinical history and physical examination were performed to evaluate the etiology of the stricture. Retrograde urethroscopy and fluoroscopic retrograde urethrogram were performed in all patients to demarcate the location and length of the stricture. Urine culture was routinely obtained. Data collected included patient baseline characteristics, stricture description, perioperative parameters, surgical technique and outcomes. Kaplan-Meier survival analysis was performed to assess graft survival in both groups, as univariate and multivariate analysis were performed trying to identify independent risk factors for graft survival.

Operative technique

Of the 48 patients, 9 of them underwent a multistage repair (6 of LS group and 3 of idiopathic group). Patients with mild spongiofibrosis and urethral caliber >6 Ch were chosen for one-stage reconstruction. Patients with urethral plate <6 Ch o severe spongiofibrosis were selected for multistage repair (1). Only in cases of extensive spongiofibrosis, removal of the urethra was performed. LS was present in 11 patients. Of the 11 patients, 6 of them underwent multiple stage urethroplasty. Thirty-nine patients (81.3%) were operated using a standard dorsal urethroplasty technique described by Barbagli *et al.* (20). In nine patients (18.8%) with adverse local conditions, two-stage repair was done (*Figure 1*).

Single-stage BMG urethroplasty

A urethroscopy is performed to delimit the length and location of the stricture and a guide wire is passed through the stricture. Circumcoronal incision was made. Urethra was approached after degloving. Corpus spongiosum was dissected off the corpora cavernosa and rotated. A dorsal urethrotomy was made throughout the stricture with extension into the normal urethral lumen, 1–1.5 cm both proximally and distally. Urethrotomy length was measured. All BMG were harvested from the inner cheek as described by Morey and McAninch (21). Donor site was closed with running 3-zero absorbable suture. Graft was quilted to the corpora cavernosa with 4-zero absorbable interrupted suture. Two running sutures were made on each side of the defect over 18 Ch silicone catheter. Retrograde

urethrogram was performed 21 days postoperatively to ensure no extravasation before urethral catheter was removed.

Multistage BMG urethroplasty

Two-stage penile urethroplasty was described by Johanson, as an evolution of the Denis-Browne technique used for hypospadias repair (22). Of the 9 patients who underwent multi-stage repair in 6 of them there were absence of urethral plate or severe spongiofibrosis. The fibrotic tissue was excised and the BMG was harvested, prepared and quilted with interrupted 4-zero absorbable suture. The transverse diameter of the neourethra should be at least 2.5 cm. We apply Aquacel Ag® directly to the graft, followed by a large piece of sterile cotton. The dressing was fixed by the 2-zero silk skin edges suture. The dressing and urethral catheter were removed 5 days postoperatively. One of the patients presented a partial retraction of the graft that did not warrant additional surgery (*Figure 2*). At 6 months, the neourethra was closed according to the Tiersch-Duplay principle (23,24) (*Figure 3*). Dartos flap was made to avoid urethra-cutaneous fistula. The other 3 patients with preserved urethral plate without severe spongiofibrosis, the urethra was fully longitudinally opened along its ventral surface and the spongiosum tissue was sutured. The penile skin margins were sutured to the margins of the urethral plate, and the new urinary meatus was located in the healthy urethral mucosa (25). Six months later, the urethra was grafted and tubulized. Initially, the lateral margins of the urethral plate were dissected from the penile skin. Then an incision is made in the midline of the urethral plate and its edges are separated. BMG was harvested and applied as dorsal inlay (26) (*Figure 4*). Urethra was tubularized with 4-zero absorbable running suture. Dartos flap was created to avoid urethra-cutaneous fistula. Retrograde urethrogram was performed 21 days postoperatively before catheter removal.

Figure 2 Patient with penile urethral stricture due to LS that undergoing two-stage BMG urethroplasty. Partial graft retraction is seen (red arrow). LS, lichen sclerosus; BMG, buccal mucosa graft.

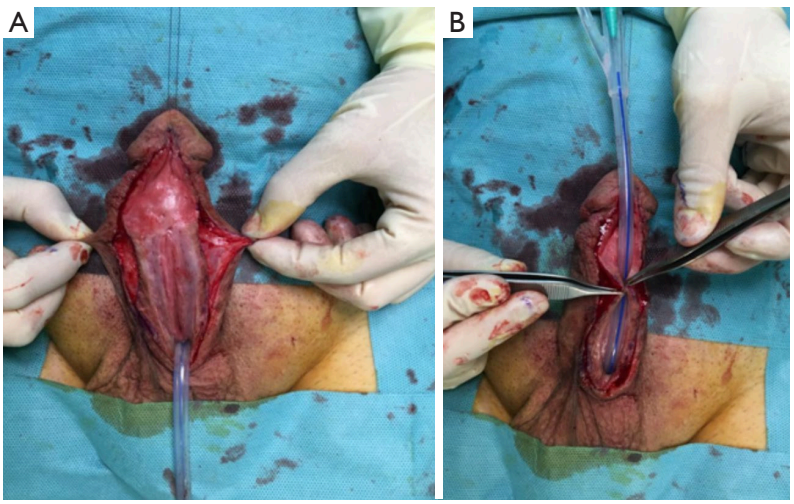

Figure 3 Patient with distal penile idiopathic stricture undergoing two-stage BMG urethroplasty. (A) Note the difference between the grafted area corresponding to the urethra and proximally the native urethra. (B) Urethra was closed according to the Thiersch-Duplay principle. BMG, buccal mucosa graft.

Figure 4 Second stage in patient with preserved urethral plate. BMG was applied as dorsal inlay. BMG, buccal mucosa graft.

Postoperative course and follow up criteria

Patients received prophylactic antibiotic treatment with amoxicillin/clavulanic acid 875/125 mg prior to the intervention and subsequently continued with amoxicillin at prophylactic doses until removal of the bladder catheter. Patients who underwent first stage urethroplasty remained hospitalized for 5 days until the removal of the dressing and urethral catheter. The patients who underwent single stage or second-stage of multi-stage repair remained hospitalized for 2 days.

At 3 weeks of a single stage repair or second-stage of multi-stage repair, a retrograde and voiding cystourethrography was performed to verify the integrity of the urethra and the absence of a fistula. The follow-up assessment included uroflow at 6 months and one year after surgery. Urethrography and urethroscopy were performed in patients with obstructive symptoms, Q max <14 mL/s or decrease in Q max of more than 10 mL/s. Treatment success was defined as the no need for further treatments, including dilatation with absence of stricture in endoscopy or urethrography (27,28). For patient satisfaction patient global impression of improvement (PGI-I) was measured, being 1 very much better post-operative condition, and 7 very much worse post-operative condition. Follow-up period was defined as the time from urethroplasty to the last clinical control or failure event. In cases of multistage surgery, the follow-up for the success of the urethroplasty begins from the second stage.

Statistical analysis

Evaluation of data distribution showed a normal distribution of the study data set.

The paired *t*-test was performed on preoperative and postoperative peak-flow and the Fisher exact test was used to assess success between groups. The Chi-square test was used to compare categorical data. A P value <0.05 was considered statistically significant. Using multiple logistic regression, the variables that were closest to statistical significance in the univariate analysis were entered and investigated to predict the graft survival. Age, BMI, smoking habit, stricture length and stricture etiology were used as predictors of graft survival. Time to failure was analyzed using the Kaplan-Meier estimates and cox regression. Survival times were measured in months and were censored at the date of the event or at the date of last follow-up. An alpha value of 5% was considered as threshold for significance. Hazard ratio and 95% confidence intervals (CIs) were calculated for each variable.

Results

Descriptive data of patients are summarized in *Table 1*. Overall of 48 patients with penile stricture were treated with BMG urethroplasty from January 2008 to January 2021. In 11 (23%) patients, the etiology of stricture was due to LS and in the other 37 (77%) patients the etiology was idiopathic. Four patients (8.3%) have undergone endoscopic urethrotomy. Median patient's age was 37 [interquartile range (IQR) 30–46] years in LS group and 54 (IQR 20–84) years in idiopathic group. Stricture length was 8 (IQR 5–8) cm in LS group and 3 (IQR 2.5–4) cm in idiopathic group. Thirty-nine patients (81.3%) were operated using a standard dorsal and in nine patients (18.8%) multi-stage repair was done. Of these nine patients, 6 of them had LS. Four patients (8.3%) presented mild complications in immediate postoperative (<30 days). Three patients presented penoscrotal hematoma (grade I Clavien-Dindo classification) and another patient presented partial retraction of the oral mucosa graft (grade I Clavien-Dindo classification), although no additional surgeries were required. Mean follow-up was 40 (IQR 12–80) months in LS group and 40 (IQR 12–85) months in idiopathic group. Success of urethroplasty was 81.8% (9/11) in LS group and 70.3% (26/37) in idiopathic group. The 13 failures (27.1%) were treated with urethrotomy in 6 patients (46.1%) with stenotic rings (located at the distal graft anastomosis in 2 cases and at the proximal graft anastomosis in 4). Two patients underwent a redo-urethroplasty and the rest of the patients underwent a periodic urethral dilation program.

Table 1 Baseline demographics and patients' characteristics

Variables	Group A (BXO/LS) (N=11)	Group B (idiopathic) (N=37)	Total (N=48)	P value
Age, (years, median)	37 (IQR 30–46)	54 (IQR 20–84)	46 (IQR 20–84)	0.001
ASA, n (%)				0.31
1	7 (63.6)	14 (37.8)	21 (43.8)	
2	3 (27.3)	16 (43.3)	19 (39.6)	
3	1 (9.1)	7 (18.9)	8 (16.7)	
BMI, kg/m^2	28 (IQR 24–30)	27 (IQR 23–33)	27.5 (IQR 23–33)	0.77
Smoking, n (%)	2 (18.1)	11 (29.7)	13 (27.1)	0.06
Endoscopic urethrotomy, n (%)	1 (9.1)	3 (8.1)	4 (8.3)	0.83
Qmax pre (mL/s, median)	6 (IQR 4–9)	7 (IQR 3–9)	6.5 (IQR 3–9)	0.24
Qmax post (mL/s, median)	16 (IQR 14–19)	18 (IQR 11–44)	17 (IQR 11–44)	0.48
Nº strictures (median)	1 (IQR 1–2)	1 (IQR 1–2)	1 (IQR 1–2)	0.40
Stricture length (cm, median)	8 (IQR 5–8)	3 (IQR 2.5–4)	5.5 (IQR 2.5–8)	0.005
Graft length (cm median)	5 (IQR 2–7)	4 (IQR 3–5)	4.5 (IQR 2–7)	0.31
Graft width (cm, median)	2 (IQR 1–2)	2 (IQR 1–2)	2 (IQR 1–2)	0.68
Single stage repair, n (%)	5 (45.5)	34 (91.9)	39 (81.3)	–
Multi-stage repair, n (%)	6 (54.5)	3 (8.1)	9 (18.8)	–
Nº grafts (median)	1 (IQR 1–2)	1 (IQR 1–2)	1 (IQR 1–2)	0.11
Bladder catheter (days, median)*	22 (IQR 15–35)	21 (IQR 14–30)	21.5 (IQR 14–35)	0.84
Success, n (%)	9 (81.8)	26 (70.3)	35 (77.1)	0.42
Graft survival (months, median)	40 (IQR 7–80)	38 (IQR 10–85)	39 (IQR 7–85)	0.87
PGI-I score (median)	2 (IQR 1–3)	2 (IQR 1–4)	2 (IQR 1–4)	0.14
Follow-up (months, median)	40 (IQR 12–80)	40 (IQR 12–85)	40 (IQR 12–85)	0.67

*, except for patients undergoing first stage urethroplasty. BXO, balanitis xerotica obliterans; LS, lichen sclerosus; ASA, American Society of Anesthesiologists; PGI-I, patient global impression of improvement; IQR, interquartile range.

In one of the patients with LS with recurrence of urethral stricture, a biopsy of the stenotic area was performed, obtaining a pathological diagnosis of scar tissue with chronic inflammation without evidence of LS recurrence. Graft survival was 40 (IQR 7–80) months in LS group and 38 (IQR 10–85) months in idiopathic group. Median of PGI was 2 (IQR 1–3) in LS group and 2 (IQR 1–4) in idiopathic group.

Age, aetiology and smoking habit were not independent risk factors for graft survival in univariate and multivariate analysis (*Table 2*). There was no difference in graft survival between LS group and idiopathic group (HR: 0.58; 95% CI: 0.12–2.75) (*Figure 5*). We did not observe any complications in relation with oral harvesting.

Discussion

Lichen sclerosis is a chronic inflammatory skin disease first described by Weir in 1875 (2). Males with LS are affected by urethral stricture disease, present in nearly 30% of cases (29,30). Microscopic findings that characterize LS are the presence of hyperkeratosis, collagen deposition and thinning of the epidermis (31).

LS related strictures show a characteristic inflammatory infiltrate with presence of lymphocytes, which is believed to play an important role in the pathophysiology of the disease (32). It has been hypothesized that immune-mediated dysregulation may be a cause of LS. This theory is supported by the presence of abnormal T lymphocyte clones in the

Table 2 Hazard ratio and 95% confidence interval for predicting graft survival

Variables	Univariate analysis graft survival			Multivariate analysis graft survival		
	HR	95% CI	P value	HR	95% CI	P value
Age	1.03	0.9–1.1	0.09	1.05	0.9–1.1	0.23
Smoking	3.22	0.9–11.2	0.06	2.39	0.6–8.3	0.19
BMI	0.99	0.7–1.2	0.95			
Stricture length	0.92	0.6–1.3	0.63			
Aetiology	0.99	0.0–18.7	0.09	1.47	0.7–2.3	0.31

BMI, body mass index.

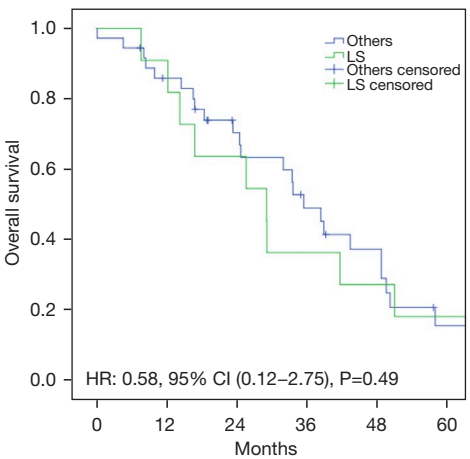

Figure 5 Graft long-term survival according to etiology. LS, lichen sclerosus.

histopathological study of LS-affected tissue (33).

The Koebner phenomenon suggests the relationship between a cutaneous traumatic antecedent and the appearance of LS, although the causal relationship has not yet been established (8,34,35). Approximately 2.3–8.4% of patients with LS develop penile cancer, with a mean time to onset of about 12 years, suggesting a need for long-term disease control (13,36). The goal of treatment in patients with LS is first to control symptoms and then to prevent the development of urethral stricture and SCC (1). LS-related strictures pose a challenge to the urologist and conservative treatments, such as dilations or repeated urethrotomies, have not yielded good results (37). There is no one surgical gold standard for treatment of LS urethral strictures (19). The selection of surgical treatment depends on the location, extension and progression of the disease, as well as the patient's own factors. The recurrence rate is high and patients should be informed about it (18).

LS is a scar forming disease which in men can cause debilitating and progressive urethral stricture disease (38). LS patients have a higher risk of recurrence after urethroplasty (25–71%) compared to patients undergoing urethroplasty for another cause (10–15%) (31,39-41). A recently published systematic review demonstrated no significant difference between the pooled recurrence rate in patients with LS compared to patients without LS (P=0.36). However, across only long-term studies, recurrence risk was significantly higher for patients with LS (OR 1.83, P=0.05) (42).

This study is based on the hypothesis that patients with LS, having greater local inflammation and poorer tissue quality, could have a higher rate of graft failure although our results do not go in that direction. The comparison between both groups shows a higher success rate in the LS *vs.* idiopathic group (82% *vs.* 70%) unlike the results published to date in the literature, although these differences are not statistically significant as shown in *Table 1*. We do not believe that these differences are due to the fact that the strictures in the idiopathic group were more complex, given that all the cases involved patients who underwent the first urethroplasty and the LS group had longer strictures. Although the patients with LS were younger, we do not think that this is the reason why there is a higher success rate in this group, as shown by the univariate and multivariate analysis. One of the factors that could influence these results in addition to the small sample size, although it has not been the subject of study on our part, would be the learning curve of the surgeons involved, since in the beginning they would have started with simpler cases and with the acquisition of experience and the skill would have treated more complex cases such as patients with urethral strictures due to LS.

Urethral strictures due to LS frequently require

urethroplasty for successful long-term treatment. Different varieties of tissue have been used in the past, however, in recent years the use of oral mucosal grafts has been gaining preponderance in urethral reconstruction (37). Single-stage and multiple-stage procedures using oral mucosa have been reported to give acceptable results. The use of skin in patients with LS should be avoided due to the risk of recurrence (1,8,43). Single-stage urethroplasty with BMG is a feasible treatment for panurethral stricture due to LS and has been suggested to be preferable over a two-stage urethroplasty (18). In this sense, Kulkarni *et al.* described, for panurethral strictures, urethroplasty with oral mucosa graft, one-sided dissection in a single stage, in a cohort of patients in whom LS is the most frequent cause of panurethral stricture (44). Angulo *et al.* concluded that in patients with long anterior urethral strictures due to LS, Kulkarni urethroplasty provides more efficient and better patient reported outcome than Johanson-Bracka urethroplasty. On the other hand, it prevents the cosmetic and functional deterioration inherent in two-stage surgery (45). A recent systematic review showed that stricture free-rate in patients with LS underwent urethroplasty was 88% *vs.* 60% for single-stage and staged urethroplasty respectively (46). The recently published EAU-Guidelines on urethral stricture concluded that single-stage BMG urethroplasty provides patency rates between 65 and 100% and is not inferior to staged BMG urethroplasty (47). Xu *et al.* reported a series of one-stage urethroplasty in patients with LS with a success rate of 88.9% at a mean follow-up of 38.7 months (range, 12–110 months) (48). Warner *et al.* published that penile inversion technique is a feasible option for the management of urethral strictures (including LS) with several advantages over the other techniques like no penile skin incision or a single-stage surgery (49). Complex penile strictures can be classified into two types according to etiology. The first type is those produced by LS and the second by other causes such as failed hypospadias, iatrogenesis and infection. In patients with complex anterior urethral strictures the role of 2-stage oral mucosa graft urethroplasty is well known (25).

Horiguchi *et al.* recommended stage-urethroplasty in patients with complex strictures, including strictures associated with LS or failed hypospadias (50). Figler *et al.* concluded that staged penile urethroplasty is a safe and effective treatment in patients with LS and failed hypospadias repair (51).

In these patient's population Selim et al reported a 79.1% overall success rate with mean follow-up 34.1 months, using two-stage BMG urethroplasty in long anterior urethral stricture. During the first stage, the graft is performed and the urethra is tubularized in a second stage after 6–9 months (52). On the other hand, Joshi *et al.* suggest that a two-stage urethroplasty in patients with LS has a risk of recurrence of the disease if the entire diseased urethra is not removed, thus increasing the risk of failure. Therefore, in case of staged repair, the entire diseased urethral plate should be removed with subsequent application of BMG and closure of the second stage after 6 months (25).

Traditionally the two-stage urethroplasty consisted of a first stage with the application of the graft and a second stage 6 months later for tubularization of the urethra (53), but according to the reported series, the graft retraction rates is between 20% and 38% with the additional surgeries that this entails (54,55). For this reason, Joshi et al propose a two-stage urethroplasty, the first stage consisting of marsupialization of the urethra without using grafts and a second stage applying BMG as dorsal inlay (25,26). Of the 38 patients included in the study, 34 (89.5%) were successful with a median follow-up of 44 months (12–158 months). No patient required revision surgery prior to the second stage (25). Several groups concur that LS is associated with a higher rate of stricture recurrence (13,56), although this difference was not found in our study which is limited at first by a retrospective analysis of the data with all the limitations applicable to this kind of studies. Second, the small sample size. Another weakness is the follow-up, since for patients undergoing urethroplasty with graft it seems reasonable to carry out a mean follow-up of 5 years since most recurrences occur in this period of time (57).

Further prospective, randomized studies are necessary to evaluate long-term graft survival in these patients.

Conclusions

We conclude that no differences were found in graft survival between both groups and independent risk factor for graft survival were not identified. No differences were found in the need for post-urethroplasty treatment between both groups.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the

STROBE reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-21-1149/rc

Data Sharing Statement: Available at https://tau.amegroups.com/article/view/10.21037/tau-21-1149/dss

Peer Review File: Available at https://tau.amegroups.com/article/view/10.21037/tau-21-1149/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-21-1149/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ramón y Cajal institutional ethics committee (Reference No. 50/21) and individual consent for this retrospective analysis was waived.

References

1. Stewart L, McCammon K, Metro M, et al. SIU/ICUD Consultation on Urethral Strictures: Anterior urethra-lichen sclerosus. Urology 2014;83:S27-30.
2. Weir RF. Ichthyosis of the tongue and vulva - Digital Collections - National Library of Medicine [Internet]. [citado 17 de abril de 2021]. Available online: https://collections.nlm.nih.gov/catalog/nlm:nlmuid-101522568-bk
3. Stühmer A. Balanitis xerotica obliterans (post operationem) und ihre beziehungen zur kraurosis glandis et preaeputii penis. Arch Dermatol Syphilol. 1928;156:613-23.
4. Meffert JJ, Davis BM, Grimwood RE. Lichen sclerosus. J Am Acad Dermatol 1995;32:393-416; quiz 417-8.
5. Kizer WS, Prarie T, Morey AF. Balanitis xerotica obliterans: epidemiologic distribution in an equal access health care system. South Med J 2003;96:9-11.
6. Patel CK, Buckley JC, Zinman LN, et al. Outcomes for Management of Lichen Sclerosus Urethral Strictures by 3 Different Techniques. Urology 2016;91:215-21.
7. Erickson BA, Elliott SP, Myers JB, et al. Understanding the Relationship between Chronic Systemic Disease and Lichen Sclerosus Urethral Strictures. J Urol 2016;195:363-8.
8. Belsante MJ, Selph JP, Peterson AC. The contemporary management of urethral strictures in men resulting from lichen sclerosus. Transl Androl Urol 2015;4:22-8.
9. Levy A, Browne B, Fredrick A, et al. Insights into the Pathophysiology of Urethral Stricture Disease due to Lichen Sclerosus: Comparison of Pathological Markers in Lichen Sclerosus Induced Strictures vs Nonlichen Sclerosus Induced Strictures. J Urol 2019;201:1158-63.
10. Erickson BA, Tesdahl BA, Voznesensky MA, et al. Urethral lichen sclerosus under the microscope: a survey of academic pathologists. Can J Urol 2018;25:9328-33.
11. Oyama N, Chan I, Neill SM, et al. Autoantibodies to extracellular matrix protein 1 in lichen sclerosus. Lancet 2003;362:118-23.
12. Hofer MD, Meeks JJ, Mehdiratta N, et al. Lichen sclerosus in men is associated with elevated body mass index, diabetes mellitus, coronary artery disease and smoking. World J Urol 2014;32:105-8.
13. Depasquale I, Park AJ, Bracka A. The treatment of balanitis xerotica obliterans. BJU Int 2000;86:459-65.
14. Riddell L, Edwards A, Sherrard J. Clinical features of lichen sclerosus in men attending a department of genitourinary medicine. Sex Transm Infect 2000;76:311-3.
15. Carlson JA, Grabowski R, Mu XC, et al. Possible mechanisms of hypopigmentation in lichen sclerosus. Am J Dermatopathol 2002;24:97-107.
16. Powell JJ, Wojnarowska F. Lichen sclerosus. Lancet 1999;353:1777-83.
17. Chalmers RJ, Burton PA, Bennett RF, et al. Lichen sclerosus et atrophicus. A common and distinctive cause of phimosis in boys. Arch Dermatol 1984;120:1025-7.
18. Chung ASJ, Suarez OA. Current treatment of lichen sclerosus and stricture. World J Urol 2020;38:3061-7.
19. Daneshvar M, Hughes M, Nikolavsky D. Surgical Management of Fossa Navicularis and Distal Urethral Strictures. Curr Urol Rep 2018;19:43.
20. Barbagli G, Selli C, di Cello V, et al. A one-stage dorsal free-graft urethroplasty for bulbar urethral strictures. Br J

Urol 1996;78:929-32.
21. Morey AF, McAninch JW. Technique of harvesting buccal mucosa for urethral reconstruction. J Urol 1996;155:1696-7.
22. Johanson B. The reconstruction in stenosis of the male urethra. Z Urol 1953;46:361-75.
23. Thiersch C. Über die Entstehungweise und operative Behandlung des Epispadie. Arch Heilkd. 1869;10:20.
24. Duplay S. On the surgical treatment of hypospadias and epispadias. Archives General Medicine 1880;145:257.
25. Joshi PM, Barbagli G, Batra V, et al. A novel composite two-stage urethroplasty for complex penile strictures: A multicenter experience. Indian J Urol 2017;33:155-8.
26. Asopa HS, Garg M, Singhal GG, et al. Dorsal free graft urethroplasty for urethral stricture by ventral sagittal urethrotomy approach. Urology 2001;58:657-9.
27. Mangera A, Patterson JM, Chapple CR. A systematic review of graft augmentation urethroplasty techniques for the treatment of anterior urethral strictures. Eur Urol 2011;59:797-814.
28. Barbagli G, Montorsi F, Guazzoni G, et al. Ventral oral mucosal onlay graft urethroplasty in nontraumatic bulbar urethral strictures: surgical technique and multivariable analysis of results in 214 patients. Eur Urol 2013;64:440-7.
29. Kulkarni S, Barbagli G, Kirpekar D, et al. Lichen sclerosus of the male genitalia and urethra: surgical options and results in a multicenter international experience with 215 patients. Eur Urol 2009;55:945-54.
30. Liu JS, Walker K, Stein D, et al. Lichen sclerosus and isolated bulbar urethral stricture disease. J Urol 2014;192:775-9.
31. Granieri MA, Peterson AC, Madden-Fuentes RJ. Effect of Lichen Sclerosis on Success of Urethroplasty. Urol Clin North Am 2017;44:77-86.
32. Grimes MD, Tesdahl BA, Schubbe M, et al. Histopathology of Anterior Urethral Strictures: Toward a Better Understanding of Stricture Pathophysiology. J Urol 2019;202:748-56.
33. Regauer S. Immune dysregulation in lichen sclerosus. Eur J Cell Biol 2005;84:273-7.
34. Miller RA. The Koebner phenomenon. Int J Dermatol 1982;21:192-7.
35. Pock L. Koebner phenomenon in lichen sclerosus et atrophicus. Dermatologica 1990;181:76-7.
36. Barbagli G, Palminteri E, Mirri F, et al. Penile carcinoma in patients with genital lichen sclerosus: a multicenter survey. J Urol 2006;175:1359-63.
37. Acimovic M, Milojevic B, Milosavljevic M, et al. Primary dorsal buccal mucosa graft urethroplasty for anterior urethral strictures in patients with lichen sclerosus. Int Urol Nephrol 2016;48:541-5.
38. Levy AC, Moynihan M, Bennett JA, et al. Protein Expression Profiles among Lichen Sclerosus Urethral Strictures-Can Urethroplasty Success be Predicted? J Urol 2020;203:773-8.
39. Warner JN, Malkawi I, Dhradkeh M, et al. A Multi-institutional Evaluation of the Management and Outcomes of Long-segment Urethral Strictures. Urology 2015;85:1483-7.
40. Meeks JJ, Erickson BA, Granieri MA, et al. Stricture recurrence after urethroplasty: a systematic review. J Urol 2009;182:1266-70.
41. Palmer DA, Marcello PW, Zinman LN, et al. Urethral Reconstruction with Rectal Mucosa Graft Onlay: A Novel, Minimally Invasive Technique. J Urol 2016;196:782-6.
42. Kurtzman JT, Blum R, Brandes SB. One-Stage Buccal Mucosal Graft Urethroplasty for Lichen Sclerosus-Related Urethral Stricture Disease: A Systematic Review and Pooled Proportional Meta-Analysis. J Urol 2021;206:840-53.
43. Singh JP, Priyadarshi V, Goel HK, et al. Penile lichen sclerosus: An urologist's nightmare! - A single center experience. Urol Ann 2015;7:303-8.
44. Kulkarni S, Kulkarni J, Surana S, et al. Management of Panurethral Stricture. Urol Clin North Am 2017;44:67-75.
45. Angulo JC, Arance I, Esquinas C, et al. Treatment of long anterior urethral stricture associated to lichen sclerosus. Actas Urol Esp 2017;41:123-31.
46. Esperto F, Verla W, Ploumidis A, et al. What is the role of single-stage oral mucosa graft urethroplasty in the surgical management of lichen sclerosus-related stricture disease in men? A systematic review. World J Urol 2022;40:393-408.
47. Lumen N, Campos-Juanatey F, Greenwell T, et al. European Association of Urology Guidelines on Urethral Stricture Disease (Part 1): Management of Male Urethral Stricture Disease. Eur Urol 2021;80:190-200.
48. Xu YM, Feng C, Sa YL, et al. Outcome of 1-stage urethroplasty using oral mucosal grafts for the treatment of urethral strictures associated with genital lichen sclerosus. Urology 2014;83:232-6.
49. Warner JN, Tracey JM, Zhumkhawala AA, et al. Penile inversion through a penoscrotal incision for the treatment of penile urethral strictures. Investig Clin Urol 2016;57:135-40.
50. Horiguchi A. Substitution urethroplasty using oral mucosa graft for male anterior urethral stricture disease: Current

topics and reviews. Int J Urol 2017;24:493-503.
51. Figler BD, Gomella A, Hubbard L. Staged Urethroplasty for Penile Urethral Strictures From Lichen Sclerosus and Failed Hypospadias Repair. Urology 2018;112:222-4.
52. Selim M, Salem S, Elsherif E, et al. Outcome of staged buccal mucosal graft for repair of long segment anterior urethral stricture. BMC Urol 2019;19:38.
53. Bracka A. The role of two-stage repair in modern hypospadiology. Indian J Urol 2008;24:210-8.
54. Andrich DE, Mundy AR. Climate - a potential cause of primary graft failure in buccal mucosal graft urethroplasty. J Urol 2009;181:15.
55. Barbagli G, De Angelis M, Palminteri E, et al. Failed hypospadias repair presenting in adults. Eur Urol 2006;49:887-94; discussion 895.
56. Levine LA, Strom KH, Lux MM. Buccal mucosa graft urethroplasty for anterior urethral stricture repair: evaluation of the impact of stricture location and lichen sclerosus on surgical outcome. J Urol 2007;178:2011-5.
57. Palminteri E, Lumen N, Berdondini E, et al. Two-sided dorsal plus ventral oral graft bulbar urethroplasty: long-term results and predictive factors. Urology 2015;85:942-7.

Cite this article as: Hevia M, Fraile A, Sanz E, Artiles A, Santiago M, García-Barreras S, Fernández-Conejo G, Rodríguez-Patrón R, Burgos-Revilla J. Does aetiology of urethral stricture influence the survival of the buccal mucosa graft?—comparative study in patients with penile urethral stricture due to lichen sclerosus *vs.* idiopathic group. Transl Androl Urol 2022;11(11):1512-1522. doi: 10.21037/tau-21-1149

