Analysis of the factors involved in the failure of urethroplasty in men

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Urethral stricture; Urethroplasty; Recurrence; Multivariate statistical analysis

Abstract
Introduction: Outcome of urethroplasty techniques in our environment and risk factors for recurrence of stenosis in these patients are studied in this paper.
Materials and methods: Retrospective study on men with urethral strictures treated with urethroplasty in the period 2000–2012. Maximum flow (Qmax), post-void residual (PVR) urine and patient perception of voiding were obtained pre- and postoperatively. Complications were recorded according to the Clavien-Dindo scale. Recurrent stricture was defined according to clinical criteria and endoscopic or imaging confirmation (failure of urethroplasty). Univariate analysis (log-rank) and multivariate (Cox regression) analysis were performed to define the variables implied in the recurrence.
Results: 82 patients with mean age 55.6 ± 17.4 (19–84 years) underwent surgery for urethroplasty. 28% of patients showed multiple stricture, 73.2% bulbar stricture, 41.5% penile stricture and 14.6% membranous stricture. End-to-end anastomosis was performed in 26 cases (31.7%), flap urethroplasty in 21 (25.6%), urethroplasty with free graft in 31 (37.8%) and two-time urethroplasty in 4 (4.9%). Graft urethroplasty showed a longer operative time (p = 0.02) and shorter hospital stay (P = 0.0035). The results were: mean ΔQmax (mean on baseline) 9.1 ± 7.5 and mean ΔPVR = 65.8 ± 136 (both P < 0.0001). Minor early complications occurred in 8 (9.8%) and major in 3 (3.6%). Recurrence occurred at a mean time of 39.8 ± 39.2 months in 18 patients (21.9%). The percentage of recurrence-free patients was: 91.4% (1-year), 82.1% (5-year) and 78.1% (10-year). Univariate analysis assessed technique used (log-rank, P = 0.13), age (P = 0.2), length stricture (P = 0.003), previous Sachse (P = 0.18), associated lichen (P = 0.18), multiplicity (P = 0.36), year of surgery (P = 0.2), Qmax (P = 0.3) and RPM (P = 0.07) preoperative. End to end anastomosis (HR 4.98, P = 0.04) and length > 3 cm (HR 4.6, P = 0.01) were identified by regression analysis as independent variables associated with poor prognosis.
Conclusion: Length stricture is both prognostic factor and criterion on choosing the type of urethroplasty, and it makes more complicated to compare the success rates of each surgical
procedure. Whatever the stricture size is, the results of anastomotic urethroplasty are worse than those of urethroplasty with buccal mucosal-free grafts.

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PALABRAS CLAVE
Estenosis de uretra; Urethroplastia; Recurrencia; Análisis estadístico multivariante

Análisis de los factores implicados en el fracaso de la urethroplastia en el varón

Resumen
Introducción: Se estudia el resultado de las técnicas de urethroplastia en nuestro entorno y los factores de riesgo de recidiva de la estenosis en estos pacientes.

Material y métodos: Estudio retrospectivo sobre varones con estenosis de uretra tratada mediante urethroplastia en el periodo 2000–2012. Se obtuvieron flujo máximo (Qmáx), residuo postmiccional (RPM) y la percepción del paciente de la situación miccional, pre y post-operatoriamente. Se registraron complicaciones según la escala Clavien-Dindo. La recidiva de la estenosis (fracaso de urethroplastia) se definió mediante criterios clínicos y confirmación endoscópica o de imagen. Se llevó a cabo análisis univariante (log-rank) y multivariante (regresión de Cox) para definir las variables implicadas en la recidiva.

Resultados: Fueron intervenidos 82 pacientes con edad media 55,6 ± 17,4 (19–84) años. La estenosis fue múltiple en 28%. Afectó uretra bulbar en 73,2%, peneana en 41,54% y membranosa en 14,6% de los pacientes. Se practicó anastomosis termino-terminal en 26 casos (31,7%), urethroplastia con colgajo en 21 (25,6%), con injerto libre en 31 (37,8%) y en 2 tiempos en 4 (4,9%). La urethroplastia con injerto conllevó mayor tiempo de quirófano (p = 0,02) y menor estancia hospitalaria (p = 0,0035). En cuanto a resultados, Qmáx medio sobre basal fue 9,1 ± 7,5 e ΔRPM medio −65,8 ± 136 (ambos p < 0,0001). Se presentaron complicaciones precoces menores en 8 (9,8%) y mayores en 3 (3,6%). Sucedió recidiva en 18 pacientes (21,9%), a un tiempo medio de 39,8 ± 39,2 meses. El porcentaje de pacientes libre de recidiva fue 91,4% al año, 82,1% a 5 años y 78,1% a 10 años. El análisis univariante analizó técnica empleada (log-rank; p = 0,13), edad (p = 0,2), longitud de la estenosis (p = 0,0033), Sachse previo (p = 0,18), lenquen asociado (p = 0,18), multiplicidad (p = 0,36), año de cirugía (p = 0,2), Qmáx (p = 0,3) y RPM (p = 0,07) preoperatorio. El análisis de regresión identificó anastomosis termino-terminal (HR 4,9; p = 0,04) y longitud >3 cm (HR 4,6; p = 0,01) como variables independientes asociadas a peor pronóstico.

Conclusión: La longitud de la estenosis es tanto un factor pronóstico como un criterio empleado para decidir el tipo de urethroplastia, lo que supone un elemento de confusión a la hora de comparar el éxito de cada técnica. Independientemente del tamaño de la estenosis, la urethroplastia anastomótica tiene peores resultados que la urethroplastia con injerto libre de mucosa oral.

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Introduction

Although the incidence of urethral stricture in Spain is unknown, we do know whether it affects men under 50 in over half of the cases. It has a significant impact on quality of life and health care expenditures, which in the USA have been estimated around 6000 dollars/year per treated patient. In the past, minimally invasive techniques such as regular dilatation or endoscopic urethrotomy were overused. These techniques do not offer a definitive solution to the problem and, sometimes, they even worsen the outcomes of patients who subsequently undergo an urethroplasty.

Urethroplasty is chosen depending on the location and length of stricture, its etiology, and the degree of spongiosis associated with it, so that decision is frequently based on the operative findings. Traditionally, in the case of short bulbar urethral strictures, end-to-end anastomosis, which shows a high percentage of success, is the preferred option. However, when the stricture is longer than 2 cm or when it is in the pendulous urethra, penile enlargement during erection should be taken into consideration, so grafting and flap techniques are preferred in order to increase the diameter of the urethral plate. These kind of techniques avoid the tension of anastomosis and ensure a lesser degree of shortening and a reduced risk of problems associated with erection.

In order to treat strictures of the penile urethra, different enlargement techniques have been generally used (Orandi penile skin flap, the penile circular fasciocutaneous flap procedure of McAninch, a dorsal buccal mucosal graft using Asopa's ventral urethrotomy). Bulbar urethral strictures are treated with anastomotic techniques, either directly (end-to-end anastomosis), with a dorsal free graft placed on the corpora cavernosa (the augmented anastomotic urethroplasty as described by Webster), or with a biaxial epilated scrotal flap (Gil Vernet); or with techniques based on an enlargement of the urethral plate with preputial skin free grafts or buccal mucosa grafting; or ventral (urethroplasty as proposed by McAninch) or dorsal positioning techniques (Barbagli's urethroplasty). Membranous urethral strictures are generally treated with replacement techniques (progressive perineal urethroplasty), although more recently enlargement techniques using buccal mucosa have been proposed for proximal strictures. A two-stage urethroplasty is a good choice for the treatment of strictures >6 cm or panurethral strictures.
Despite the changes in surgical techniques over the years, we aim to analyze the operative results of the urethroplasty techniques used in our field, and the factors that determine the long-term success or failure of surgery depending on the generic type of the technique used (end-to-end anastomosis, skin flaps, or mucosal grafting), the individual features of the stenosis (length, multiplicity, and location) and of the patient (age, prior surgery, associated lichen, Qmax, PVR).

Materials and methods

We performed a retrospective study which analyzed all the male patients treated with urethroplasty techniques at the University Hospital of Getafe over a period from 2000 to 2012. Medical records were reviewed and there was telephone contact to update follow-up information at the end of January 2013, so that all patients had follow-up for more than a year. The demographic characteristics of the patients were analyzed, as well as several features associated with the stricture, including potential causes, the presence of lichen sclerosus, the affected portion of the urethra, stricture length, and multiplicity.

Subjective data about the patient’s voiding status were reviewed and objective data regarding bladder emptying were analyzed. These included both pre- and post-operative Qmax and PVR in all patients. Those cases where dilation procedures had been performed within a period of less than a month before surgery were excluded from the analysis. Operative data regarding the type of technique, duration of the procedure, hospital stay and the complications according to the Clavien-Dindo scale and the recommendations of the EAU1,2,3 were recorded. Given the diversity of the surgical techniques used in such a long period, single-stage urethroplasty was generically classified into 3 categories: end-to-end anastomotic urethroplasty, graft and flap urethroplasty.

We studied the association between stricture length, expressed in centimeters, and the type of technique. Stricture recurrence (urethroplasty failure) was defined through the combination of criteria for clinical worsening and endoscopic or radiologic confirmation (urethrocystography) of re-stricture. Both a univariate analysis (Kaplan–Meier study and log-rank test) and a multivariate analysis (Cox regression) were carried out to recognize the variables involved in the prognosis of this series of patients.

Results

A total of 82 patients with an average age of 55.6 ± 17.4 years (range 19–84) underwent urethroplasty due to urethral strictures at different levels. In 47 (57.3%) patients, the etiology of the stricture was unknown and in 35 (42.7%) patients an etiologic factor was detected: (11%) transurethral resections of the prostate, 2 (2.4%) cases of bladder catheterization, 7 (8.6%) traumas, 9 (11%) inflammatory causes, 6 (7.3%) congenital ones, and 2 (2.4%) ischemic causes.

As for stricture length, in 11 cases (13.4%) it measured <1 cm; in 13 cases (15.8%), 1–2 cm; in 20 cases (24.4%), 2–3 cm; in 15 cases (18.3%), 3–4 cm; in 9 cases (11%), 4–5 cm; in 5 cases (6.1%), 5–6 cm; and in 9 cases (11%), >6 cm. A total of 35 patients (42.7%) had a history of previous urethrotomy, 44 patients (53.7%) had undergone dilation prior to urethroplasty, 12 patients (14.6%) showed genital sclerotic lichen, and 22 patients (26.8%) had recurrent urinary tract infections. Strictures were multiple in 23 (28%) cases. Taking into account such multiplicity, strictures affected the bulbar urethra in 73.2% of the patients (60 cases), the penile urethra in 41.5% of the patients (34 cases), and the membranous urethra in 14.6% of the patients (12 cases). Two-stage urethroplasty was performed in 4 patients (4.9%) and single-stage urethroplasty in 78 patients (95.1%). End-to-end anastomosis was performed in 26 patients (31.7%), flap urethroplasty in 21 (25.6%), and free-graft urethroplasty in 31 patients (37.8%).

There is an association between the type of technique used and the length of the stricture (Cochran-Armitage; p = 0.027), with strictures treated with end-to-end urethroplasty being shorter and those treated with free graft techniques being longer (Table 1). Flap urethroplasty was performed using preputial skin in 12 cases, penile skin in 6, and epilated scrotal skin in 3 cases. Graft urethroplasty was performed with ventrally-placed preputial skin in 3 cases and with buccal mucosa in 28 cases. In the latter group, the free graft was ventrally placed in 6 cases and dorsally placed in 25 cases.

The mean surgical time of the entire series was 164.5 ± 65.6 (40–370 min) and the length of hospital stay was 4.3 ± 4 (1–30) days. On discharge date, 13 patients (15.8%) had a cystostomy catheter. The mean time of removal of the bladder catheter was 30 ± 46.3 (1–97) days. Graft urethroplasty required a longer surgical time (Kruskal–Wallis; p = 0.02) and a shorter hospital stay (Kruskal–Wallis, p = 0.0035) than the other techniques (Table 2).

Data on preoperative Qmax and PVR were available in 79 cases (96.3%), but values were considered reliable only in 62 patients (75.6%), either because they did not undergo dilation or because they underwent that procedure within a period of over a month. In such cases the Qmax value was 5.8 ± 3.5 (1.1–15.7) ml/min and PVR was 92.9 ± 124.9 (0–500) ml, prior to surgery, respectively. Qmax and PVR were assessed in all patients 3 months after surgery, with respective values of 15.6 ± 7.9 (4–40) ml/min and 30 ± 66.7 (0–318) ml. The mean ΔQmax on basal was 91.1 ± 7.5 (Student’s t-test; p < 0.0001) and the mean ΔPVR was 65.8 ± 136 (Student’s t-test; p < 0.0001).

Complications occurred in 20 patients (24%). Eleven of those (13.4%) were early complications seen within the first month of surgery: 8 (9.75%) were minor complications, and 3 (3.6%) were major ones. Major complications included reoperation for fistula (2 cases) and hemorrhagic shock which required a blood transfusion and ICU stay (1 case). Minor complications comprised fistulas treated with bladder catheterization (5 cases), perineal bruising (2 cases), and urinary tract infection (1 case). Late complications occurred between the first month and the first year of surgery, in 9 patients (11%): 7 (8.6%) showed relapse with clinical worsening and endoscopic data of persistent strictures in the first year of surgery, and 2 (2.4%) were patients who showed erectile dysfunction, and who claimed to have been potent prior to surgery. Other 15 patients (18.3%) were impotent before surgery.
On the other hand, 4 patients (4.9%) showed urinary incontinence before the surgical procedure, which was resolved with surgery in 3 of them. An improvement of the bladder function was confirmed in 64 patients (78%) throughout treatment, although endoscopic or radiological data indicating stricture relapse to some degree were detected in 4 of them (4.9%). On the other hand, throughout follow-up, in 18 cases (22%) the surgical procedure was considered a failure since symptoms accompanied by data indicating stricture relapse reappeared. The mean time to relapse in these patients was 39.8 ± 39.2 (6–120) months. A year later, 91.4% (CI 95% 82.8–95.8) of patients were free of disease; 5 years later, that percentage was 82.1% (CI 95% 71.5–89), and 10 years later, 74.9% (CI 95% 61.7–84.2) (Fig. 1). Recurrence was resolved in 7 cases with new urethroplasty techniques (38.9%), in 1 case (5.6%) with perineal urethrotomy, in 4 cases (22.2%) with internal urethrotomy, and in 6 cases (33.3%) in a conservative way with dilation therapy. The univariate analysis assessed a series of variables, including the generic type of the technique used (log-rank; \(p = 0.13\)), the age of patients (log-rank; \(p = 0.2\)), stricture length (log-rank; \(p = 0.003\)) (Fig. 3), the fact of having previously undergone Sachse’s urethrotomy (log-rank; \(p = 0.18\)) (Fig. 4), associated lichen (log-rank; \(p = 0.18\)), multiplicity (log-rank; \(p = 0.36\)), year of surgery (log-rank; \(p = 0.2\)), Qmax (log-rank; \(p = 0.3\)) (Fig. 5), and preoperative PVR (log-rank; \(p = 0.07\)). With regard to the type of technique, in the year following surgery, 19.2% (CI 95% 8.5–40.2) of end-to-end urethroplasties failed, 4.8% (CI 95% 0.7–29.3) of those which used flaps and 3.3% (CI 95% 0.5–21.4) of those based on grafts also failed. 5 years later, 27.3% (CI 95% 14–49%), 14.3% (CI 95% 4.8–38%), and 6.7% (CI 95% 1.7–24.1%) of each technique, respectively, failed (Fig. 2). With regard to stricture length, 4.5% (CI 95% 1.1–17%) of the patients with strictures <3 cm failed therapy after a year, and 5 years later, 6.9% (CI 95% 2.3–20%) of those patients showed failure; whereas in the case of those with strictures >3 cm, 13.4% (CI 95% 5.8–29.3%) of them failed therapy after a year, and 31% (CI 95% 18.4–49.1%) of patients showed failure 5 years later (Fig. 3). The regression analysis identified the practice of end-to-end anastomosis (HR 4.98; \(p = 0.04\)) and stricture

![Figure 1](image1.png)  
**Figure 1** Recurrence-free survival for the total series (\(n = 82\)).

![Figure 2](image2.png)  
**Figure 2** Recurrence-free survival depending on the generic type of technique (urethroplasty in 2 stages is excluded due to small number of patients).
length >3 cm (HR 4.6; p=0.01) as independent variables associated with a worse prognosis (Table 3).

### Discussion

It seems advisable that each center should know the long-term success rate achieved with its surgical technique so that they can provide realistic data to patients and this fact is particularly important in reconstructive techniques such as urethroplasty. Despite the fact that in most cases the etiology of urethral stricture disease remains unknown, understanding the cause leading to it is essential when considering the most appropriate surgical technique for its resolution.5, 6 On the other hand, stricture length, its location, and the possible previous treatment received by the patient are those factors which determine the choice of procedure.6-8,14

In most series, despite its high failure rate, urethrotomy is still the preferred approach for the initial management of urethral strictures. For each centimeter of stricture length, it has been estimated that the relative risk of failure increases by 22%.15 According to the records in our institution, 43% of the total number of patients had undergone previous endoscopic management, which may have complicated the correct interpretation of Qmax and VPR as predictive factors of prognosis in this series. Urethrotomy only makes sense in the case of short bulb urethral strictures, since it shows high failure rates when strictures are long, when they are located in the pendulous urethra, or when they show dense spongiosis.16 Besides, multiple previous endoscopic procedures may lead to a more complex open approach and, according to some authors, with lower success rates.17 These kind of treatments were possibly overused at our center at certain times in the past. Nevertheless, we cannot say that this had a negative impact on the success of urethroplasty techniques.

We do know that stricture length is a prognostic factor and, at the same time, a factor used when choosing the type of urethroplasty1-3. Thus, it may be a source of confusion

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**Table 3** Cox regression model for predicting recurrence showing the effect of the type of urethroplasty corrected by the length of the stenosis.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Coefficient</th>
<th>SE</th>
<th>Chi-square</th>
<th>p</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastomotic technique</td>
<td>1.605</td>
<td>0.81</td>
<td>3.92</td>
<td>0.04</td>
<td>4.98 (1.02–24.36)</td>
</tr>
<tr>
<td>Technique with flap</td>
<td>1.114</td>
<td>0.81</td>
<td>1.88</td>
<td>0.17</td>
<td>3.05 (0.62–14.98)</td>
</tr>
<tr>
<td>Length &gt;3 cm</td>
<td>1.526</td>
<td>0.60</td>
<td>6.37</td>
<td>0.01</td>
<td>4.60 (1.41–15.04)</td>
</tr>
</tbody>
</table>

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**Figure 3** Recurrence-free survival according to the length of the stricture.

**Figure 4** Recurrence-free survival according to prior history of Sachse.

**Figure 5** Recurrence-free survival according to preoperative Qmax (n = 62).
when analyzing the healing power of each technique. End-to-end urethroplasty is considered to have higher success rates than augmentation urethroplasty for the treatment of bulbar urethral strictures, although this assessment might be biased due to the own definition of this indicator. In fact, when strictures are $<$2 cm end-to-end anastomosis is the preferred choice, with excision of the diseased urethra, spatulation, and anastomosis of the edges. Many surgeons consider that when strictures are $>$2 cm, the urethral light is well preserved and the area of spongiosfibrosis around that light is limited, augmentation urethroplasty with dorsal or ventral graft positioning, preferably from the oral mucosa, is the ideal technique with successful long-term results in about 90% of patients, who even do better with a judicious use of internal urethrotomy and achieve success rates of 97%. Experience with the use of free grafts is positive even in elderly patients.

In some cases where an end-to-end anastomosis was chosen, despite getting elastic ends, there is some tension when approximating the edges, which leads to risk of ischemia and relapse. In such cases, it is recommended to perform an augmented anastomotic urethroplasty where the 2 remaining ends are dorsally spatulated and the graft is sutured around the spatulated margins, whereas the 2 urethral ends are sutured to the ventral hemicircumference. Augmented nontransected anastomotic urethroplasty is a modification of augmented anastomotic urethroplasty which implies complete excision of strictures but without transecting the spongy tissue.

According to Andrich et al., anastomotic urethroplasty is considered the approach of choice for short defects since it showed a lower re-strictuire rate (13% after 10 years) when compared with a heterogeneous group of replacement urethroplasties with flaps or grafts performed in the 1980s (31% after 10 years), and because it showed a lower complication rate (7 vs. 31%). The retrospective analysis carried out by Barbagli et al. on 375 patients revealed that the success rate for bulbar stricture repair at a single stage was 83.5%. The anastomotic repair also showed better results with respect to techniques of free grafting and augmented anastomotic repair 28. On the other hand, buccal mucosa grafts did better than preputial skin grafts (82.2 vs. 59.6% success rates). These data allowed a better stratification of the classical results of replacement urethroplasty at the Institute of Urology (London, United Kingdom).

With regard to the factors potentially influencing the success or failure of surgery, Barbagli et al., in a recent observational retrospective descriptive study on patients with bulbar urethral strictures, pointed out that the preoperative peak flow rate (7 ml/s) is an independent predictor of success in urethroplasties with buccal mucosa grafts. In this research experience, age, the length and type of stricture, and the previous treatment received by the patient were not determining factors in the results of the procedure. In another retrospective study which analyzed 495 patients with associated comorbidity who had undergone different types of urethroplasty in the state of California, stricture length ($>$4 cm), the fact of having previously undergone failed urethroplasty or urethrotomy, smoking habits, and diabetes mellitus were unfavorable prognostic factors. Our experience with strictures in any urethral segment identified stricture length and the use of urethroplasty techniques with free grafts as independent prognostic factors, whereas age, time of surgery, previous urethrotomy, preoperative postvoid residual volume, and multiplicity did not affect the results of the procedure. As we pointed out above, preoperative Qmax values were not predictive factors of success either, although this was possible due to the fact that the sample under analysis was reduced since there were a lot of patients who had undergone dilation prior to surgery.

**Conclusion**

Stricture length is, on the one hand, a major prognostic factor, and, on the other hand, a major criterion for choosing the type of urethroplasty, so it acts as a source of confusion in the analysis of a particular type of urethroplasty, giving apparently better results to anastomotic urethroplasty than to any other kind of surgery. On the other hand, in our overall experience, augmented urethroplasty objectively showed better outcomes than anastomotic urethroplasty. Even different types of flap urethroplasty performed in the past showed worse evolution than free graft urethroplasty, although this difference did not reach statistical significance in our series. A higher number of case reports would be desirable to confirm whether this observation that augmented urethroplasty with free grafts is the technique which shows better long-term results remains the same when stratifying the analysis according to the topography of strictures.

**Conflict of interest**

The authors declare that they have no conflict of interest.

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