



Treatments of 1242 bulbar urethral strictures: multivariable statistical analysis of results

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Abstract

Purpose We investigated the success rate of different surgical techniques for bulbar stricture repair.

Methods Retrospective study of patients with bulbar urethral strictures treated using different techniques. The primary outcome of the study was to evaluate the overall results of treatment (success vs. failure); the secondary outcome was to evaluate the outcome according to any surgical technique. Cysto-urethrography was performed 1 month following surgery. Patients underwent clinical evaluation, uroflowmetry and residual urine measurement every 6 months for 2 years after surgery and later once on year. When patient showed obstructive symptoms, $Q_{\max} < 12$ ml/s, the urethrography was repeated. Patients who underwent further treatment for recurrent stricture were classified as failures. A bivariable and multivariable statistical analysis was performed.

Results Overall, 1242 patients were included in the study with mean age 40 years (range 12–84). Median stricture length was 4 cm (range 1–8). The median follow-up was 103 months (range 12–362). Over 1242 patients, 916 (73.8%) were success and 326 (26.2%) failures. Fourteen different surgical techniques showed a success rate ranging from 87.5 to 14.3%. The multivariable analysis showed that stricture length was an independent predictor factors for failure: $p < 0.0001$ CI 1146–1509. End–end anastomosis and oral mucosa graft urethroplasty are independent predictor factor of success after internal urethrotomy failure.

Conclusions Our results showed that treatment of bulbar urethral stricture is satisfactory on 73.8% of patients, but with a wide range of success rate (from 14.3 to 87.5%) using different techniques. Oral mucosa is greatly superior to the skin as substitute material.

Keywords Urethra · Urethroplasty · Urethrotomy · Surgical technique · Oral mucosa · Skin graft · Long-term results

Introduction

The true incidence of male urethral stricture diseases remains unknown, with an estimated incidence of up to 627 per 100,000 patients and an annual expenditure of up to \$191 million [1].

Urethral strictures are a frequent source of lower urinary tract symptoms in men [2]. Untreated urethral stricture diseases can result in UTI, acute urinary retention, scrotal–perineal abscess, high-pressure voiding leading to secondary bladder thickening and irritability [2]. Trauma, catheter, urological instrumentation, urethral infection, lichen sclerosus (LS), failed hypospadias repair (FHR), radiotherapy, are common causes of strictures; most cases, however, are idiopathic, probably arising as results of remote unrecognized minor bicycle or motorcycle injury during childhood [2].

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Male urethral strictures are most frequently located in the bulbar tract [3]. Surgical treatment of bulbar urethral strictures includes various surgical techniques ranging from urethrotomy to anastomotic urethroplasty, to skin or oral graft urethroplasty [4, 5]. Patient selection and proper choice of surgical procedure are paramount to maximize the chance of successful outcome in the treatment of any urethral stricture [5]. The main factors to consider in decision-making include stricture site, etiology, length, previous failed treatments, the presence of LS, history of FHR, patient's comorbidity and BMI [5]. Previous papers about urethroplasty outcomes mixed non homogeneous groups (site, etiology) and include relatively short-term (<5 years) data, and long-term results, including a large series of patients, are rarely reported in the literature [6, 7].

The aim of this study is to retrospectively review a large series of patients with bulbar urethral strictures, who underwent treatments using a wide range of different techniques, to evaluate the success rate of all the techniques suggested for repair of bulbar structures and the independent predictor factors for failure.

Methods

We performed a retrospective study of prospectively collected data from a cohort of patients who underwent treatment of bulbar urethral strictures between 1987 and 2016 in our centre by a single surgeon. Inclusion criteria were patients with bulbar urethral strictures. Exclusion criteria were patients with LS, FHR, penile and posterior strictures. Patients who have not met the follow-up criteria were excluded. The primary outcome of the study was to evaluate the overall results of treatment (success vs. failure) using 14 different techniques; the secondary outcome was to evaluate the outcome according to any surgical technique.

Pre-operative patient's investigations

Before urethroplasty, information on demographic and medical history was gathered. All patients underwent a complete pre-operative urological examination including: uroflowmetry, post-void residual (PVR), retrograde urethrogram (RUG), voiding cystourethrogram (VCUG), and urethroscopy.

Surgical techniques and criteria for patient's selection

The complete list of surgical techniques is reported in Table 1. The choice of surgical technique for repair bulbar urethral strictures was selected according to the patient (age, comorbidity, QoL) and stricture features (etiology, length,

previous treatment, associated negative factors). Moreover, some techniques were used at the beginning of our learning curve and later were abandoned due to poor results at long-term follow-up (techniques 4, 8, 11, 14 as reported in Table 1), or to improvement in our background. Other techniques were abandoned due to the preferred use of the oral graft instead of skin grafts (techniques 3, 7 in Table 1). Basically, the use of cold knife internal urethrotomy was limited in patients with idiopathic strictures <3 cm length, and the end–end anastomosis was the preferred technique for traumatic or non-traumatic strictures with complete obliteration of the urethral lumen. Some techniques (technique 10 in Table 1) were used only in anecdotic cases with no extension in a larger series of patients. Other techniques (techniques 5, 12, 13 in Table 1) become our preferred choice due to satisfactory long-term outcome and evolution of our surgical background. Finally, the use of two-stage urethroplasty was limited to patients presenting complex stricture diseases.

Follow-up criteria

After any surgical procedure, the Foley 16 F catheter is left in place for 1 month and a post-operative VCUG is performed. After DVIU urethrotomy, the catheter is left in place for 7 days and post-operative VCUG is not performed. Patients underwent clinical evaluation, uroflowmetry and residual urine measurement every 6 months for 2 years after surgery and later once on year. When patient showed obstructive symptoms, $Q_{max} < 12$ ml/s, the urethrography was repeated. Patients who underwent further treatment for recurrent stricture were classified as failures.

Statistical analysis

Statistical descriptive analysis was performed. Failure was set as reference outcome. A bivariable and multivariable logistic regression analyses were applied considering the following variables: age, etiology, length and type of surgery.

Results

From 1987 to 2016, 3.334 patients were included in our repository database. A total of 2.092 were excluded from our present study according to inclusion/exclusion criteria. Overall, 1242 patients were included in the study. Median patients age was 40 years (range 12–84). Stricture etiology was idiopathic in 783 (63%) patients, catheter in 167 (13.4%), instrumentation in 145 (11.8%), trauma in 121 (9.7%), infection in 15 (1.2%), congenital in 7 (0.6%), radiotherapy in 4 (0.3%). Median stricture length was 4 cm (range 1–8 cm). Out of 1242 patients, 872 (70.2%) underwent previous failed treatments (Table 2). Fourteen

Table 1 Success rate according to the surgical technique

No	Surgical technique (references)	No patients %	Success % follow-up months
1	Cold knife internal urethrotomy	348 (28%)	230 (66.1%) 62 months
2	End–end anastomosis [8]	213 (17.1%)	183 (85.9%) 181 months
3	Augmented anastomotic repair with dorsal skin graft [9]	10 (0.8%)	2 (20%) 234 months
4	Augmented anastomotic repair with dorsal oral mucosal graft [9]	25 (2%)	18 (72%) 162 months
5	Dorsal oral mucosal inlay graft urethroplasty [10–12]	37 (3%)	29 (78.4%) 56 months
6	Dorsal oral mucosal onlay graft urethroplasty [13–15]	25 (2%)	17 (68%) 134 months
7	Dorsal skin onlay graft urethroplasty [13, 14]	33 (2.6%)	19 (57.6%) 241 months
8	One-side oral mucosal graft urethroplasty [16]	15 (1.2%)	7 (46.7%) 103 months
9	Two-stage urethroplasty [17]	73 (5.9%)	39 (53.4%) 152 months
10	Lateral oral mucosal onlay graft urethroplasty [18]	6 (0.5%)	5 (83.3%) 211 months
11	Circumferential substitution oral mucosal graft urethroplasty [19]	12 (1%)	7 (58.3%) 182 months
12	Ventral oral mucosal onlay graft urethroplasty [20–22]	422 (34%)	345 (81.7%) 91 months
13	Ventral only + dorsal inlay oral mucosal grafts urethroplasty	16 (1.3%)	14 (87.5%) 33 months
14	Augmented anastomotic repair with ventral oral mucosal graft [23]	7 (0.6%)	1 (14.3%) 158 months
	Total	1242	916 (73.8%)

Table 2 Success/failure according to the previous treatments

Previous treatment	No patients	Success (%)	Failure (%)
None	370 (29.8%)	286 (77.3%)	84 (22.7%)
Dilation	39 (3.1%)	28 (71.8%)	11 (28.2%)
1 urethrotomy	206 (16.7%)	163 (79.1%)	43 (20.9%)
2 urethrotomies	131 (10.5%)	113 (86.3%)	18 (13.7%)
> 2 urethrotomies	102 (8.2)	69 (67.6%)	33 (32.4%)
Urethroplasty	31 (2.5%)	22 (71%)	9 (29%)
Associated treatments	363 (29.2)	235 (64.7%)	128 (35.3%)

Table 3 Success rate according to the follow-up (in years)

Follow-up years	No patients	Success (%)	Failure (%)
1–5 years	325 (26.2%)	251 (77.2%)	74 (22.8%)
5–10 years	400 (32.2%)	299 (74.8%)	101 (25.2%)
10–15 years	275 (22.1%)	200 (72.7%)	75 (27.3%)
15–20 years	202 (16.3%)	143 (70.8%)	59 (29.2%)
20–25 years	35 (2.8%)	20 (57.1%)	15 (42.9%)
25–30 years	4 (0.3%)	2 (50%)	2 (50%)
> 30 years	1 (0.1%)	1 (100%)	

different surgical techniques were used (Table 1). The oral mucosa was used as substitute material in 565 (45.5%) patients and penile skin in 43 (3.4%). Median follow-up was 103 months (range 12–362). Out of 1242 patients, 916 (73.8%) were classified as success and 326 (26.2%) as failures. Patients who did not underwent any previous treatment showed 77.3% success rate, and patients who underwent any previous treatment showed 72.2% success rate, and only patients who underwent more that 2

urethrotomies (67.6%) or associated treatments (64.7%) showed a success rate < 70% (Table 2). The success rate greatly decreases after more than 20 years' follow-up (Table 3), and the incidence of stricture recurrences is high (42% and 22.6%) the first 2 years after surgery (Table 4). The success rate according to the surgical technique is summarized in Table 1. The end–end anastomosis showed high success rate (85.9%), whereas the success rate of oral mucosa used as onlay or inlay graft showed a

Table 4 Incidence of stricture recurrences according to the follow-up time (in years)

Follow-up time (years)	Stricture recurrences
0–1 year	134 (41.1%)
1–2 years	75 (23%)
2–3 years	28 (8.6%)
3–4 years	27 (8.3%)
4–5 years	11 (3.4%)
5–6 years	35 (10.7%)
10–15 years	12 (3.7%)
15–20 years	4 (1.2%)
Total	326 (26.2%)

greatly difference according to the graft placement: ventral onlay + dorsal inlay 87.5%, lateral onlay 83.3%, ventral onlay 81.7%, dorsal inlay 78.4%, dorsal onlay 68%. The use of oral mucosa associated with anastomotic repair showed lesser success rate: dorsal augmentation 72%, ventral augmentation 14.3%. Oral mucosa urethroplasties showed 78% overall success rate and penile skin 48% with different long-term follow-up: the penile skin median follow-up was 103 months (range 183–281), and the oral mucosa 95 months (range 13–230).

No statistically significant difference was reported between the mean age of patients with success vs. failure: 41.91 ± 16.11 vs. 42.50 ± 16.36 ($p = 0.564$). The mean length was statistically lower in success group respect failure: $2.76 \text{ cm} \pm 1.42$ vs. 3.03 ± 1.52 ($p = 0.009$). The number of previous internal urethrotomy did not impact significantly on success rate (Table 5).

At bivariable analysis, age and etiology did not correlate with failure. The multivariable analysis showed that stricture length is an independent predictor factor for failure: $p < 0.0001$ CI 1146–1509. End–end anastomosis, dorsal oral mucosal inlay graft urethroplasty, dorsal oral mucosal onlay graft urethroplasty and ventral oral mucosal

onlay graft urethroplasty are independent predictor factors of success after internal urethrotomy failure. Data are summarized in Table 6.

Discussion

Our survey represents one of the largest series of patients with bulbar urethral strictures reported in the literature. Some data emerging from our study are already occasionally reported in the literature, but our large number of patients strongly validate and strengthen even better the data here reported: the oral mucosa showed to be greatly superior to penile skin in any bulbar urethroplasty (78% success rate vs 48%), the previous treatments of strictures by dilation, urethrotomy, urethroplasty or associated treatment showed minimal influence in the outcome of repair (Table 2), the multivariable analysis showed that stricture length was an independent predictor factors for failure.

The successful management of urethral strictures demands attention not only to surgical detail, but also to procedure selection. No single technique is appropriate for all situations and the successful surgeon will have a repertoire of operations to choose from. Stricture location, length, complicating features, multiplicity and proximity to or involvement of the sphincter mechanism all have impact on the choice of appropriate operation. We here present our experience using 14 different techniques to repair any different types of bulbar urethral strictures from simple to complex, from primary to redo repair. Of course, over time the choice of the technique was also greatly influenced by the evolution of our background (oral mucosa vs skin, non-transection techniques vs transection techniques). One of the main profitable experiences for a surgeon is to learn experience by himself/herself and translate it into the courage to abandon surgical strategy with poor outcome. Although powered statistical analysis could provide objective information, personal surgical experience combined with

Table 5 Previous internal urethrotomy

	N previous treatment					Total
	1	2	3	4	5	
Outcome						
Success						
Count	286	28	345	22	235	916
% within outcome	31.2%	3.1%	37.7%	2.4%	25.7%	100.0%
Failure						
Count	84	11	94	9	128	326
% within outcome	25.8%	3.4%	28.8%	2.8%	39.3%	100.0%
Total						
Count	370	39	439	31	363	1242
% within outcome	29.8%	3.1%	35.3%	2.5%	29.2%	100.0%

Table 6 Multivariable analysis

Multivariable logistic regression	<i>p</i> value	OR	95% CI for OR	
			Lower	Upper
Technique				
Urethrotomy	Reference	1	–	–
End–end anastomosis	<0.0001	0.335	0.210	0.532
Augmented anastomotic repair with dorsal skin graft	0.040	5.405	1.082	27.013
Augmented anastomotic repair with dorsal oral mucosal graft	0.071	0.416	0.160	1.078
Dorsal oral mucosal inlay graft urethroplasty	<0.0001	0.183	0.073	0.460
Dorsal oral mucosal onlay graft urethroplasty	0.024	0.326	0.123	0.863
Dorsal skin onlay graft urethroplasty	0.644	0.826	0.367	1.859
One-side oral mucosal graft urethroplasty	0.896	0.926	0.294	2.917
Two-stage urethroplasty	0.243	0.683	0.360	1.295
Lateral oral mucosal onlay graft urethroplasty	0.155	0.202	0.022	1.829
Circumferential substitution oral mucosal graft urethroplasty	0.641	0.745	0.217	2.559
Ventral oral mucosal onlay graft urethroplasty	<0.0001	0.198	0.123	0.317
Ventral only + dorsal inlay oral mucosal grafts urethroplasty	0.002	0.084	0.017	0.409
Augmented anastomotic repair with ventral oral mucosal graft	0.117	5.686	0.646	50.027
Etiology				
Unknown	Reference	1	–	–
Catheter	0.371	1.199	0.806	1.783
Instrumentation	0.223	1.295	0.855	1.964
Trauma	0.122	0.659	0.388	1.118
Congenital	0.342	2.219	0.429	11.493
Infection	0.433	0.579	0.148	2.265
Radiotherapy	0.814	1.331	0.123	14.356
Length	<0.0001	1.315	1.146	1.509
Previous treatments				
None	Reference	1	–	–
Dilatation	0.887	1.059	0.480	2.339
Urethrotomy	0.246	1.243	0.861	1.796
Urethroplasty	0.493	1.362	0.564	3.290

personalized patient approach, including patient's expectation, might be a powerful tool to improve the success rate in urethral reconstruction. In the current study, we tried to combine the descriptive result analysis with a multivariable analysis to combine the two information.

Bulbar urethral strictures represent a very wide range of diseases that it is very difficult to standardize the surgical treatment. In our survey, 14 different surgical techniques showed a success rate ranging from 87.5 to 14.3% at long-term follow-up, and some “well-known” surgical techniques (end–end anastomosis, ventral oral mucosa graft) herewith confirm the high success rate at long-term follow-up. Some surgical techniques (two-stage repair) are used in complex recurrent strictures with high pathological involvement of tissues and this may explain the low success rate of these techniques (53.4%). Some techniques (urethroplasty with one-side oral graft) have been used to repair long strictures involving both distal and proximal bulbar tracts and this may explain the low success rate of these techniques (46.7%).

In our survey, only 4 techniques showed a success rate > to 80%, 2 techniques showed a success rate > 70%, 2 techniques showed a success rate > 60%, 3 techniques showed success rate > 50%, and 3 technique showed a success rate < 50%. According to the results of our current study, at present, in our daily clinical practice, we mainly select the surgical techniques showing a success rate > 80%. Some techniques showing a poor success rate were used at the beginning of our learning curve, but over time, we have abandoned these techniques favoring other techniques offering better success rate. This represents an important message for the reader: the continuous evaluation and update of the results of your surgeries may greatly help you in improving the quality of your surgery, better selecting the more efficient techniques.

Finally, we would like to place emphasis on the high success of cold knife urethrotomy (66.1%) with 61-month follow-up.

The evaluation of short- or long-term results of DVIU, as reported in the literature, is a challenging topic because

patient selection, follow-up criteria, success vs failure criteria are not homogenous and sometimes would be difficult to take a home message from these reports. The failure rate after initial DVIU is reported to be at least 50% and this procedure should be considered; in the majority of patients, a temporizing measure until definitive reconstruction can be planned. However, such negative conclusions often originate from a non-homogeneous series, including strictures with remarkable difference in site, etiology, pathology, previous treatments, or with relative small cohorts with poor follow-up. Moreover, some articles never reported the site, etiology, and pathology of the strictures treated by DVIU. There is a lack of information in a highly homogeneous subset of patients, treated in high volume centers, which could offer a new insight about the DVIU destiny.

Our study also suggest that patient should be under strict follow-up control for 5 years after surgery, when the stricture recurrence is higher, and should be classified as cured only after a 6 years' follow-up.

We would like to emphasize the many limits of our study. The sample size of some series of patients remains small and, thus, the results may not be fully sufficient to draw definitive conclusions. Only 5 patients showed follow-up > 25 years. This retrospectively evaluated study is without a control group. Furthermore, the absence of quality-of-life questionnaires or patient-reported outcome measures is another limitation of our study. Indeed, the recurrence rate could be higher when one considers patients reported outcome or only subjective data. This is particularly true when we investigate the outcome of anterior urethra reconstruction with oral mucosa graft, which involves not only functional, but also esthetic and sexual domains.

Conclusions

In our study, only few techniques have stood the test of time at long-term follow-up. The oral mucosa is greatly superior to the penile skin as substitute material. Patients who underwent treatment of bulbar urethral stricture should be classified as cured only after 6 years' follow-up.

Author contributions Authors whose names appear on the submission have contributed sufficiently to the scientific work and therefore share collective responsibility and accountability for the results. GB: project development, manuscript writing. FM: project development. SB: data analysis. SS: data analysis. CL: data analysis. DB and VB: data analysis and statistical analysis. ML: project development, manuscript editing.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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