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Advances in Urogenital Trauma and Reconstruction

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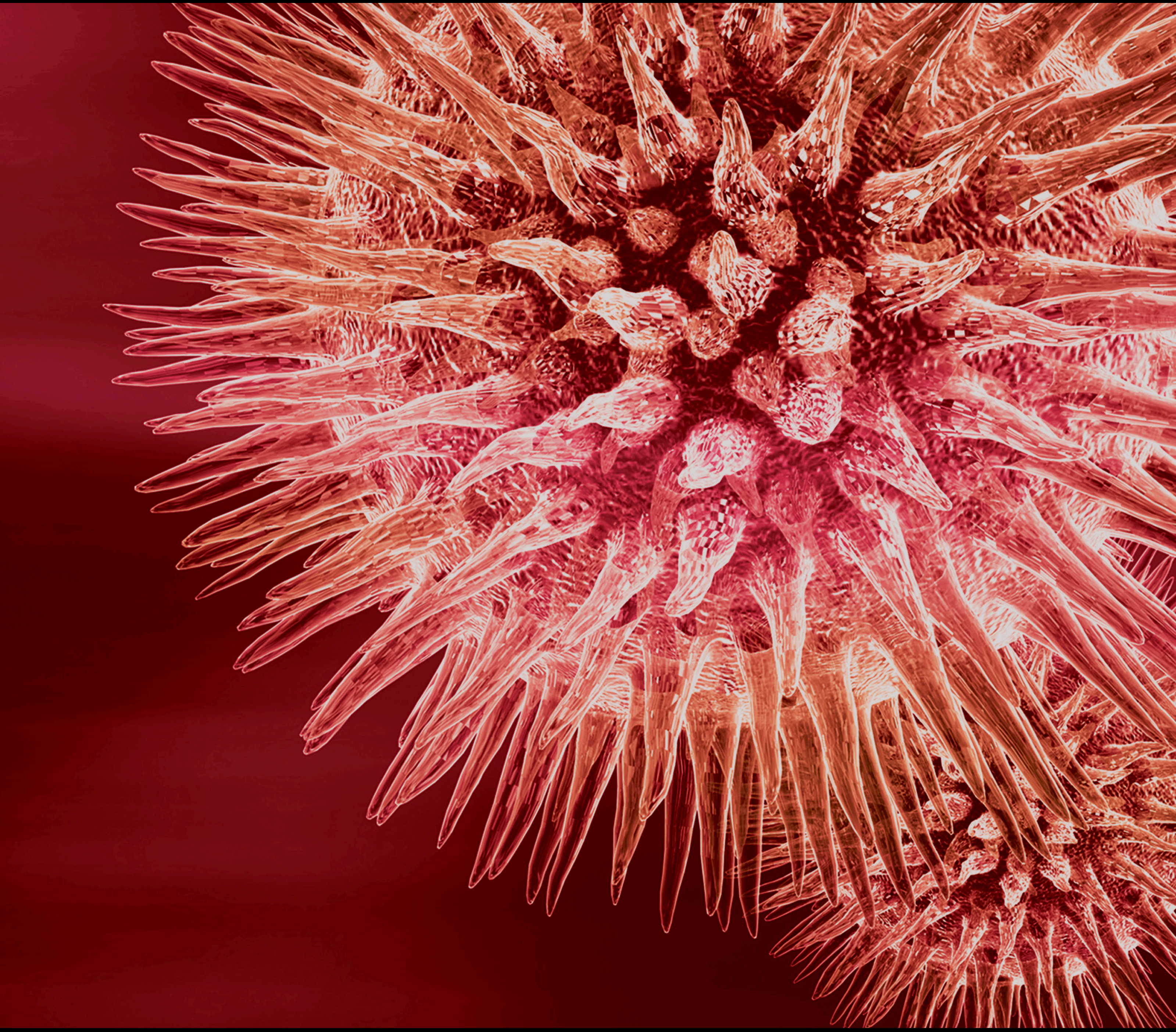

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Editorial Board

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Editorial

Advances in Urogenital Trauma and Reconstruction

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Trauma is a major health burden and accounts for approximately 10% of all deaths worldwide [1]. It is the major cause of death in people aged 15–45 years [2]. Interpersonal violence and traffic road accidents are well-known and major sources of trauma, although iatrogenic injuries cannot be neglected. The urogenital tract and organs are at risk during abdomino-pelvic and perineal trauma [3, 4]. With the exception of high-grade renal trauma, urogenital trauma is rarely fatal [3]. Nevertheless, adequate initial treatment of urogenital trauma is important to reduce life-long incapacity related to renal insufficiency, lower urinary tract symptoms, urinary incontinence, or impotence [3, 4]. A specific entity of trauma is the iatrogenic injury provoked during medical procedures. Especially, the urethra is at risk for iatrogenic trauma [5]. Any trauma (iatrogenic or noniatrogenic) to the urethral mucosa can cause a subsequent urethral stricture [6]. Treatment of urethral strictures is a major challenge to the reconstructive urologist. Thorough knowledge of the anatomy of the male and female urethra, diagnostics tools, and all reconstructive options are required to obtain optimal results when treating male and female strictures. This special issue wants to provide this knowledge to the reader. In general, urethroplasty offers the best results with respect to urethral patency in the long term [7]. Nevertheless, all types of urethroplasty have an inherent risk of failure. In this case, redo-urethroplasty is an option [8]. Redo-urethroplasty might differ from primary urethroplasty and these differences need to be explored in order to provide adequate counselling to the patient with respect to outcome. Excision and primary anastomosis is one of the options to treat short bulbar and posterior strictures and provides excellent long-term results [9, 10]. This technique included mobilization of the bulbar urethra and transection at the site of the stricture and might be associated with sexual disturbances [11]. Therefore, functional outcomes and quality of life must be taken into account when performing excision and primary anastomosis. In order to reduce the surgical trauma of spongiosal transection during excision and primary anastomosis, the vessel-sparing (nontransecting) modification has been proposed [12]. Before switching to this new technique, one must be certain that this technique at least equals the results of the "older" technique. Only if there is improvement, one can proceed with a new technique.

The primary goal of cancer treatment is cure and improvement of overall survival. Penile cancer is a relatively rare cancer but with a tremendous psychological impact because the treatment will affect the genital appearance of the patient. Any attempt to maintain and/or restore the initial genital appearance as much as possible should be encouraged [13]. Glans resurfacing has been described and is currently incorporated in clinical practice guidelines for superficial penile cancer (stage $\leq$ T1a) [13]. Only small case series have been reported. A step-by-step description of this technique and review of the literature is needed to encourage urologists to perform this technique.

Reconstructive urologists are sometimes faced with the congenital urogenital anomalies. Reconstruction is a challenge, and the functional outcome is of utmost importance. In this issue, the laparoscopic Vecchietti operation to increase the size of the vagina in Mayer-Rokitansky-Küster-Hauser syndrome will be evaluated for functional and sexual outcomes.

Conflicts of Interest

The editors have no conflicts of interest.

Nicolaas Lumen
Francisco Martins
Enzo Palminteri
Achilles Ploumidis

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Research Article

Primary versus Redo Urethroplasty: Results from a Single-Center Comparative Analysis

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Objectives. To explore the differences between primary and redo urethroplasty and to directly compare according stricture-free survival (SFS). *Materials and Methods*. Data of all male patients who underwent urethroplasty at Ghent University Hospital were collected between 2000 and 2018. Exclusion criteria for this analysis were age <18 years and follow-up <1 year. Two patient groups were created for further comparison: the primary urethroplasty (PU) group (no previous urethroplasty) and redo urethroplasty (RU) group (≥1 previous urethroplasty), irrespective of prior endoscopic treatments. A comparison between groups was performed using the Mann–Whitney *U* test and Fisher's Exact test. SFS was calculated using Kaplan–Meier statistics. A functional definition of failure, being the need for further urethral manipulation, was used. Uni- and multivariate Cox regression analyses were performed on the entire patient cohort. *Results*. 805 patients were included. Median (IQR) follow-up of the PU ($n = 556$) and RU ($n = 249$) groups was 87 (50–136) and 76 (40–133) months, respectively ($p = 0.1$). The RU group involved more penile strictures ($p < 0.001$), Lichen Sclerosus ($p = 0.016$), failed hypospadias repair ($p = 0.004$), multistage procedures ($p < 0.001$), and definitive perineostomies ($p = 0.001$). The 5- and estimated 10-year SFS was, respectively, 86% and 79% for the PU group and, respectively, 75% and 63% for the RU group ($p < 0.001$). Prior urethroplasty (HR: 1.52; $p = 0.01$) and diabetes (HR: 1.83; $p = 0.03$) remained statistically significant in the multivariate Cox regression analysis. *Conclusions*. Several differences between primary and redo urethroplasties exist. Redo urethroplasty entails a distinct patient population to treat and is, in general, associated with lower stricture-free survival than primary urethroplasty, although more homogeneous series are required to corroborate these results. Prior urethroplasty and diabetes are independent risk factors for urethroplasty failure.

1. Introduction

Urethroplasty is considered the standard treatment option for urethral stricture disease (USD) as it offers substantially higher long-term success rates than direct vision internal urethrotomy (DVIU) or urethral dilatation [1, 2]. However, despite its satisfying outcome, there is a subgroup of patients in which failure is encountered. Several risk factors for failure after urethroplasty have been described, among which prior therapy for USD [3–6]. Against this background, the question whether redo urethroplasty provides the same satisfying outcome as primary urethroplasty should be considered.

So far, scarce data are available on the management of recurrent USD and only little is known about the differences between primary and redo urethroplasty. A redo urethroplasty is often more challenging as recurrent urethral strictures usually have denser and more extensive scar tissue.

Moreover, since potential grafts or flaps may have already been used in previous urethroplasties, the armamentarium of the surgeon becomes smaller in a redo setting [7].

Be that as it may, the prognostic significance of prior urethroplasty remains highly controversial since several authors have published their experience with redo urethroplasty and reported success rates equivalent to primary urethroplasty [5, 7–14]. However, these reports contain several limitations and the different definitions of failure and different follow-up protocols make it hard to draw adequate conclusions [15]. To date, the largest comparative series was published by Levine et al., but included only 49 redo procedures and despite the differences in stricture length, stricture location, and applied surgical technique between groups, a Cox regression analysis to confirm the prognostic value of these characteristics was not performed [11]. Undoubtedly, additional evidence upon this subject is required and should be based on a comparative analysis with a higher volume of redo urethroplasties.

Considering the above, the aim of this study is to explore the differences between primary and redo urethroplasty and to directly compare the according stricture-free survival (SFS), with more power than the existing reports.

2. Patients and Methods

2.1. Patients. A database of all male patients who underwent urethroplasty at Ghent University Hospital was enrolled between 2000 and 2018. This database contains extensive information about patient and stricture characteristics, previous interventions, and other relevant information (suprapubic catheter, urinary tract infection (UTI)). Exclusion criteria for this analysis were age <18 years and duration of follow-up <1 year. Within the included patients, two patient groups were created for further comparison: the primary urethroplasty (PU) group, defined as patients without previous urethroplasty, and the redo urethroplasty (RU) group, defined as patients who underwent ≥1 urethroplasty, both irrespective of prior DVIU/dilatation. The study was approved by the local Ethics Committee (EC/2014/0438) and all included patients provided written informed consent.

2.2. Perioperative Management. Preoperatively, patients were evaluated through history taking, physical examination, and technical investigations (uroflowmetry, ultrasonic residue measurement and retrograde urethrography (RUG) and/or voiding cystourethrography (VCUG) and/or cystoscopy). A urine culture was performed one week before urethroplasty and appropriate antibiotics were started 24 hours before surgery in case of infection. All operations were performed by two surgeons (W. O. and N. L.).

Generally, a VCUG was performed fourteen days postoperatively and in case of no extravasation of contrast, the transurethral catheter was removed. In cases with contrast extravasation, the transurethral catheter was replaced and a VCUG was again performed one week later.

Follow-up visits included history taking, physical examination, and uroflowmetry and were performed after three months, after one year, and annually thereafter. Additional technical investigations were only administered in case of arguments for urethroplasty failure such as symptoms or an obstructive voiding curve (<15 ml/s). A subgroup of patients was followed by the referring urologist due to practical considerations.

2.3. Statistical Analysis. Baseline and per- and postoperative characteristics were analyzed using descriptive statistics. The comparison between groups was performed using the Mann–Whitney *U* test and Fisher's Exact test for continuous and categorical variables, respectively. Complications within 90 days postoperatively were categorized according to the Clavien–Dindo classification system [16]. For SFS, the time-to-event was measured as the interval between the operation date and the date of the diagnosis of the failure. A functional definition of failure, being the need for further urethral manipulation (including simple dilatation), was used [17]. Patients were censored at the time of the latest follow-up or death. SFS was calculated using Kaplan–Meier statistics and groups were compared using the Log-Rank test. Uni- and multivariate Cox regression analyses with the calculation of the Hazard Ratio (HR) to predict failure were performed on the entire patient cohort for the following variables: age, stricture length, location, etiology, previous interventions, urethroplasty technique, comorbidities, presence of suprapubic catheter, and UTI. Only the statistically significant variables from the univariate analysis were entered in the multivariate analysis. All statistical tests were 2-sided and a p value <0.05 was considered statistically significant. The analysis was performed using SPSS® 25.0.

3. Results

In total, 805 patients were included in this study. The median follow-up of the PU group ($n = 556$) and RU group ($n = 249$) was 87 and 76 months, respectively ($p = 0.1$). Baseline characteristics are displayed in Table 1. Age, follow-up, stricture length, and comorbidities were comparable between groups. Penile strictures ($p < 0.001$), strictures due to Lichen Sclerosus ($p = 0.016$), and strictures due to failed hypospadias repair ($p = 0.004$) were significantly more frequent in the RU group. RU techniques comprised significantly more multistage procedures ($p < 0.001$) and definitive perineal urethrostomies ($p = 0.001$) and significantly less anastomotic repairs ($p < 0.001$) and free graft urethroplasties ($p = 0.028$). In both groups, "other urethroplasty techniques" mainly consisted of meatoplasties (>95%), which were proportionally more frequently performed in the RU group ($p = 0.004$).

Per- and postoperative characteristics are displayed in Table 2. The hospital stay was significantly longer in the PU group ($p = 0.01$), in contrast to the comparable operation time, catheter stay and extravasation ratio. The complication rate was 25% and 24% for the PU and RU groups, respectively. In both groups, complications were predominantly low-grade (Clavien–Dindo grade 1-2: 175/805; 22%) [16]. Grade 3 complications involved urinary

Table 1: Baseline characteristics.

	Total ($n = 805$)	PU ($n = 556$)	RU ($n = 249$)	p value
Median age (years) (IQR)	51 (36–63)	53 (36–65)	50 (36–62)	0.3
Median follow-up (months) (IQR)	83 (46–135)	87 (50–136)	76 (40–133)	0.1
Median stricture length (cm) (IQR)	3.0 (1.5–6.0)	3.0 (1.5–6.3)	3.0 (2.0–6.0)	0.5
Stricture location n (%)				
Penile	207 (26)	121 (22)	86 (35)	**<0.001**
Bulbar	365 (45)	271 (49)	94 (38)	**0.005**
Posterior	102 (13)	84 (15)	18 (7.2)	**0.002**
Multifocal	63 (7.8)	41 (7.4)	22 (8.8)	0.5
Panurethral	59 (7.3)	39 (7.0)	20 (8.0)	0.7
Meatus of perineostomy	9 (1.1)	0 (0)	9 (3.6)	**<0.001**
Stricture etiology n (%)				
Idiopathic	276 (34)	178 (32)	98 (39)	0.050
Iatrogenic	336 (42)	247 (44)	89 (36)	**0.025**
External trauma	111 (14)	83 (15)	28 (11)	0.2
Inflammatory	73 (9.1)	41 (7.4)	32 (13)	**0.016**
Failed hypospadias repair	75 (9.3)	40 (7.2)	35 (14)	**0.004**
Tumor	9 (1.1)	7 (1.3)	2 (0.80)	0.7
Previous interventions n (%)				
None	170 (21)	170 (31)	0 (0)	**<0.001**
1 DVIU/dilatation	125 (16)	125 (23)	0 (0)	**<0.001**
>1 DVIU/dilatation	259 (32)	258 (46)	1 (0.40)	**<0.001**
Urethroplasty	88 (11)	0 (0)	88 (35)	**<0.001**
Urethroplasty + DVIU/dilatation	159 (20)	0 (0)	159 (64)	**<0.001**
Endoscopic realignment	3 (0.37)	2 (0.36)	1 (0.40)	>0.9
Open realignment	1 (0.12)	1 (0.18)	0 (0)	>0.9
Urethroplasty technique n (%)				
Transecting anastomotic repair	206 (26)	162 (29)	44 (18)	**<0.001**
Nontransecting anastomotic repair	115 (14)	91 (16)	24 (9.6)	**<0.001**
Free graft urethroplasty	264 (33)	196 (35)	68 (27)	**0.028**
Pedicled flap urethroplasty	42 (5.2)	26 (4.7)	16 (6.4)	0.3
Combined	35 (4.3)	19 (3.4)	16 (6.4)	0.1
Multistage urethroplasty	38 (4.7)	13 (2.3)	25 (10)	**<0.001**
Definitive perineostomy	43 (5.3)	17 (3.1)	26 (10)	**<0.001**
Others	62 (7.7)	32 (5.8)	30 (12)	**0.004**
Comorbidity n (%)				
Smoking	110 (14)	77 (15)	33 (14)	0.8
Diabetes	55 (7.1)	34 (6.4)	21 (8.7)	0.3
Cardiovascular comorbidity	138 (18)	97 (18)	41 (17)	0.7
Suprapubic catheter n (%)	192 (24)	147 (26)	45 (18)	**0.01**
UTI n (%)	216 (27)	157 (28)	59 (24)	0.2

PU = primary urethroplasty; RU = redo urethroplasty; IQR = interquartile range; cm = centimeters; DVIU = direct vision internal urethrotomy; UTI = urinary tract infection. p values comparing the PU group and RU group <0.05 are highlighted in bold.

retention with placement of a suprapubic catheter (3/805; 0.37%) and hematomas (5/805; 0.62%), abscesses (5/805; 0.62%), fistulas (13/805; 1.6%), and Fournier gangrene (1/805; 0.12%) requiring surgical intervention.

In the PU and RU groups, respectively, 95 (17%) and 68 (27%) patients suffered a failure. The 5- and estimated 10-year SFS were, respectively, 86% (95% CI: 83–89%) and 79% (95% CI: 75–83%) for the PU group and, respectively, 75% (95% CI: 69–81%) and 63% (95% CI: 55–71%) for the RU group ($p < 0.001$) (Figure 1, Table 2). Respectively, 38 (40%), 33 (35%), and 24 (25%) failures from the PU group and 29 (43%), 25 (36%), and 14 (21%) failures from the RU group occurred within the first postoperative year, between the first and fifth postoperative years and after more than five years postoperatively.

Univariate analysis identified longer strictures (HR: 1.05; $p = 0.003$), multifocal strictures (HR: 2.30; $p < 0.001$), iatrogenic strictures (HR: 1.37; $p = 0.044$), failed hypospadias repair (HR: 2.02; $p = 0.001$), prior urethroplasty (HR: 1.78; $p < 0.001$), and diabetes (HR: 1.83; $p = 0.04$) as risk factors for failure (Table 3). Prior urethroplasty (HR: 1.52; $p = 0.01$) and diabetes (HR: 1.83; $p = 0.03$) were identified as

Table 2: Pre- and postoperative characteristics.

	Total ($n = 805$)	PU ($n = 556$)	RU ($n = 249$)	p value
Median operation time (min) (IQR)	105 (82–131)	105 (83–130)	105 (80–135)	0.8
Median hospital stay (days) (IQR)	3 (2–4)	3 (2–4)	2 (2–4)	**0.01**
Median catheter stay (days) (IQR)	14 (10–15)	14 (11–15)	14 (9–15)	0.5
Significant extravasation at first VCUG n (%)	44 (7.7)	31 (7.2)	13 (8.8)	0.6
Complications (Clavien–Dindo) n (%)				
None	606 (75)	417 (75)	189 (76)	0.9
Grade 1	114 (14)	82 (15)	32 (13)	0.5
Grade 2	61 (7.6)	39 (7.0)	22 (8.8)	0.4
Grade 3	24 (3.0)	18 (3.2)	6 (2.4)	0.7
Stricture-free survival estimates % (SD)				
1 y-SFS		94 (1.0)	88 (2.1)	
2 y-SFS		91 (1.2)	83 (2.4)	**<0.001**
5 y-SFS		86 (1.5)	75 (3.0)	
10 y-SFS		79 (2.1)	63 (4.2)	

PU = primary urethroplasty; RU = redo urethroplasty; min = minutes; IQR = interquartile range; VCUG = voiding cystourethrography; SD = standard deviation; SFS = stricture-free survival. p values comparing the PU group and RU group <0.05 are highlighted in bold.

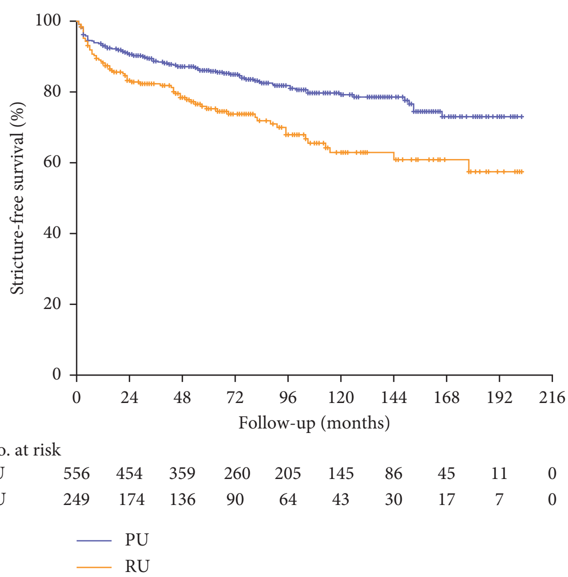

Figure 1: Kaplan–Meier curve for stricture-free survival in primary and redo urethroplasty. PU = primary urethroplasty; RU = redo urethroplasty; no. = numbers.

independent risk factors for failure in the multivariate analysis (Table 3).

4. Discussion

The aim of this study was to distinguish the primary and redo urethroplasty group and to compare the according SFS. Current literature shows similar success rates for primary and redo urethroplasty [7–14], although a majority of these papers indirectly compared the results of redo urethroplasty with success rates of primary procedures [8] or did not compare the results at all [7, 9, 12–14]. Since patient and stricture characteristics, definitions of failure and follow-up protocols vary among different patient series, indirect comparison is hazardous and insufficient to draw adequate conclusions. Two authors published a direct comparison between primary and redo urethroplasty, but these retrospective studies are underpowered in the amount of included redo procedures (37 and 49 respectively) [10, 11]. Hypothetically, considering 10% difference in SFS to be clinically relevant, a trial with a two-sided alpha of 0.05 and 80% power would require 248 patients per group to establish clinically relevant superiority for primary urethroplasty (assuming a SFS rate of 85% and 75% for the PU and RU group, respectively). To the best of our knowledge, this study is the first direct comparison between primary and redo urethroplasty with this amount of redo procedures and in our opinion, the results are noteworthy put the success rate of redo urethroplasty in perspective and contribute to more realistic patient expectations.

Several differences in baseline characteristics between the PU and RU groups existed. Penile strictures were significantly more frequent in the RU group, which could be explained by the fact that penile strictures are in most cases ineligible for anastomotic repair (AR) urethroplasty, which offers the highest success rate [18]. Usually, these strictures require a substitution urethroplasty and, as the success rate of these procedures deteriorates over time, the likelihood of being treated with a redo urethroplasty increases along [15, 18, 19]. Additionally, Lichen Sclerosus and failed hypospadias repair are associated with a higher failure rate and predominantly affect the penile urethra [7, 20, 21]. This in turn also explains why these etiologies were significantly more frequent in the RU group.

The redo stricture profile, as outlined above, warrants adapted operative strategies which are reflected in the applied surgical techniques [7, 20, 22]. Significantly fewer strictures were eligible for AR urethroplasty, whereas multistage procedures and definitive perineostomies were significantly more performed. This result is in line with the observations of Levine et al. [11]. Also, free graft urethroplasty was performed less frequently in the RU group. This may be explained by the fact that prior urethral surgery can impair the urethral blood supply and thus lead to a poorly vascularized, unsuitable graft bed for future urethral reconstructions. As regards the discrepancies in hospital stay

Table 3: Uni- and multivariate Cox regression analysis.

	Univariate		Multivariate	
	HR (95% CI)	p value	HR (95% CI)	p value
Age	1.00 (0.99–1.01)	0.7		
Stricture length	1.05 (1.02–1.08)	**0.003**	1.00 (0.95–1.06)	>0.9
Stricture location				
Penile	1.38 (0.99–1.92)	0.1		
Bulbar	0.51 (0.36–0.71)	**<0.001**	0.65 (0.42–1.01)	0.055
Posterior	0.76 (0.46–1.28)	0.3		
Multifocal	2.30 (1.47–3.58)	**<0.001**	1.71 (0.98–3.00)	0.059
Panurethral	1.45 (0.90–2.35)	0.1		
Stricture etiology				
Idiopathic	0.79 (0.56–1.11)	0.2		
Iatrogenic	1.37 (1.01–1.86)	**0.044**	1.11 (0.77–1.60)	0.6
External trauma	0.65 (0.39–1.09)	0.1		
Inflammatory	1.36 (0.85–2.18)	0.2		
Failed hypospadias repair	2.02 (1.32–4.10)	**0.001**	1.27 (0.70–2.29)	0.4
Previous interventions				
≥1 prior DVIU/dilatation	0.79 (0.58–1.07)	0.1		
≥1 prior urethroplasty	1.78 (1.30–2.43)	**<0.001**	1.52 (1.08–2.14)	**0.01**
Urethroplasty technique				
Anastomotic repair	0.46 (0.32–0.66)	**<0.001**	0.61 (0.36–1.03)	0.1
Free graft urethroplasty	1.23 (0.89–1.68)	0.2		
Pedicled flap urethroplasty	1.53 (0.88–2.66)	0.1		
Multistage urethroplasty	0.66 (0.27–1.61)	0.4		
Definitive perineostomy	1.20 (0.63–2.28)	0.6		
Comorbidity				
Smoking	1.02 (0.65–1.62)	0.9		
Diabetes	1.83 (1.09–3.08)	**0.04**	1.83 (1.07–3.11)	**0.03**
Cardiovascular comorbidity	1.22 (0.81–1.86)	0.3		
Suprapubic catheter	0.67 (0.45–1.00)	0.050		
UTI	0.91 (0.64–1.31)	0.6		

HR = hazard ratio; CI = confidence interval; DVIU = direct vision internal urethrotomy; UTI = urinary tract infection. p values comparing the PU group and RU group <0.05 are highlighted in bold.

between groups, patients often experience some degree of discomfort after harvesting an oral graft and this may contribute to the longer hospital stay, as observed in the PU group [23]. Meanwhile, staged procedures and perineostomies allow a relatively short hospital stay and even day surgery.

As regards surgical outcome, SFS was significantly lower in the RU group compared to the PU group, which distinctly contradicts prior literature suggesting that primary and redo urethroplasties have an equivalent outcome in terms of SFS [7–14]. However, our findings actually do corroborate the results from Blaschko et al., who described the largest redo urethroplasty series so far [7]. They reported a "primary success rate" of 67% after a median follow-up of 55 months, which is in line with our results as their definition of "primary success" corresponds with our definition of success. However, since an additional 12% of their patients remained stricture-free after the first salvage treatment, a total success rate of 78% was reported [7]. Rosenbaum et al. specifically focused on redo buccal mucosa graft urethroplasty and reported a success rate of 82% [8], albeit after a median follow-up of only 16 months, while it is established that the results of substitution urethroplasty strongly deteriorate over time [8, 19]. Siegel et al. directly compared primary and redo AR urethroplasties and described comparable results between both groups [10]. However, their sample of 37 redo procedures only contained patients with recurrent urethral strictures eligible for AR urethroplasty, representing only a favorable minority of the total patient population presenting with recurrent USD [10]. The fact that our dataset contains a mix of various techniques with different patient and stricture characteristics might explain these conflicting results. As for Levine et al., who reported the largest comparative series so far, redo urethroplasty succeeded in 92% of the cases, which was comparable with primary urethroplasty [11]. Their patient series, however, contained only 49 redo procedures and, despite the different stricture length, stricture location, and applied surgical techniques of their RU group, no Cox regression analyses were performed. Furthermore, our RU group contained substantially more penile, multifocal, panurethral, Lichen Sclerosus, and failed hypospadias repair cases which are all associated with increased stricture complexity [20–22]. Additionally, the higher success rate of Levine et al. could be explained by the fact that more than 20% of the failures of our RU group occurred after more than five years of follow-up. These failures may have been missed in their study as their mean follow-up was only 50 months [11]. Other researchers have investigated the redo urethroplasty setting as well, but their reports are characterized by a restricted sample size or a limited follow-up [9, 12–14]. Our patient series demonstrates that urethroplasty demands a prolonged follow-up since a significant amount of failures was observed after more than five years postoperatively, which is in line with the report from Han et al. [6]. An anatomical definition of failure (impossible passage of the cystoscope through the reconstructed area) could possibly detect more and earlier failures [17]. However, to date, no consensus about the definition of failure exists among urologic societies or expert panels [15].

Given the several differences in baseline characteristics between both groups, a Cox regression analysis was performed to investigate their prognostic value in the present dataset. However, in the multivariate analysis, only two characteristics remained statistically significant: prior urethroplasty and diabetes. This result underlines the observed differences in SFS between the PU and RU groups and confirms that, in this dataset, prior urethroplasty is predictive for urethroplasty failure, which corresponds with previous reports [5–7]. As for diabetes, it is known that the inherent microangiopathy contributes to a poorer vascularization, also at the urethral site, potentially impeding the healing of the urethra after surgery. This in turn can lead to an increased risk for failure [5]. Apart from these, other predictive factors for urethroplasty failure have been put forward as well, although significant differences in the investigated patient cohorts exist and might explain the inconsistent nature of these findings [3–6].

This study has various limitations. Before 2008, data were collected retrospectively and, since this cohort spans seventeen years, surgical techniques and perioperative management may have changed over time. Furthermore, every patient was offered a follow-up regimen at our institution, but a subset of patients was followed by the referring urologist, involving a risk of underreporting failures and potentially explaining a delayed detection of failures. No systematic endoscopic evaluation of urethral patency was performed and thus asymptomatic stricture formation after urethroplasty was not recorded. Also, this patient cohort represents a highly heterogeneous group involving several differences in baseline characteristics between the compared groups. The aim of this study was to explore these differences and to compare the according SFS in a patient cohort which is reflective for a tertiary reconstructive center with a minimum of exclusion criteria. Be that as it may, the aforementioned differences in SFS should be interpreted carefully, given the heterogenic nature of our comparison. However, none of the baseline characteristics, except for prior urethroplasty and diabetes, were found to be an independent risk factor for failure in the present dataset. Future studies ideally involving prospective multicenter data collection with a uniform follow-up protocol and definition of failure are required to corroborate these results in specific, more homogeneous patient subgroups and to enrich the evidence on managing recurrent USD.

5. Conclusions

In conclusion, several differences between primary and redo urethroplasties exist. Redo urethroplasty entails a distinct patient population to treat and is, in general, associated with lower stricture-free survival than primary urethroplasty, although more homogeneous series are required to corroborate these results. Prior urethroplasty and diabetes are independent risk factors for urethroplasty failure.

Abbreviations

AR: Anastomotic repair
CI: Confidence interval
cm: Centimeters
DVIU: Direct vision internal urethrotomy
HR: Hazard ratio
IQR: Interquartile range
min: Minutes
No.: Numbers
PU: Primary urethroplasty
RU: Redo urethroplasty
RUG: Retrograde urethrography
SD: Standard deviation
SFS: Stricture-free survival
USD: Urethral stricture disease
UTI: Urinary tract infection
VCUG: Voiding cystourethrography.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Review Article

Glans Resurfacing with Skin Graft for Penile Cancer: A Step-by-Step Video Presentation of the Technique and Review of the Literature

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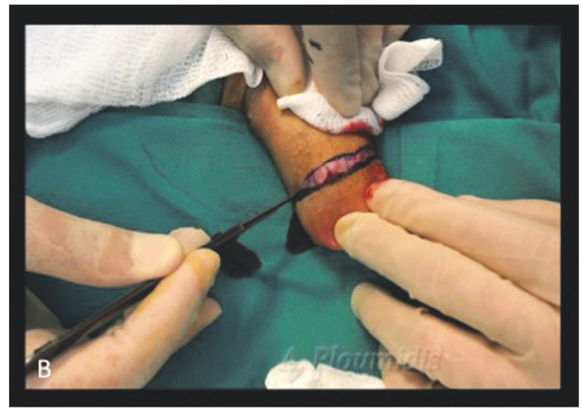
Introduction. Glans resurfacing has been suggested as a treatment option for the surgical management of superficial penile cancer (Tis, Ta, T1aG1, T1aG2). In this article we describe in detail the glans resurfacing technique with skin graft for penile cancer in a video presentation and we review the current knowledge of the literature. *Material and Methods*. The procedure is described in a stepwise fashion. Initially the patient is circumcised. The glans is marked in quadrants and completely stripped by dissecting and removing the epithelium and subepithelium layer of the glans. Deep spongiosal biopsies are taken to exclude invasion. Each quadrant is sent separately for biopsy. The surface of the graft size needed is estimated. A partial thickness skin graft is harvested from the thigh with a dermatome. The skin graft is then fenestrated. The graft is rolled over the glans and quilted with multiple sutures. A silicone 16F Foley catheter and a suprapubic catheter are placed. The penis is dressed with multiple gauzes and compressed with an elastic band. *Results*. The patient is discharged the next day. The dressing and Foley catheter are removed in 7 days. The patient continues to use the suprapubic catheter for 7 more days. The patient refrains from any sexual activity for 6 weeks and is closely followed. *Conclusions*. Glans resurfacing is an emerging new appealing surgical technique that is already a recommendation in the EAU guidelines for the treatment of premalignant and superficial penile lesions. The overall satisfaction rate and recovery of the sexual function are acceptable, and it can be considered an ideal procedure to treat superficial penile cancer.

1. Introduction

Penile cancer (PeCa), though uncommon, presents a geographical variation in incidence and a strong relation with the human papilloma virus (HPV) [1, 2]. One-third of the penile cancer cases are HPV-related, and even though the peak incidence is during the sixth decade of life, it can occur in younger patients [2]. Surgical management and the choice of infiltrative treatment depend on the stage and the invasiveness of the disease with penis sparing options reserved as a more overall suitable choice for the superficial disease up to T1a (TNM Classification) according to the European Urology Association (EAU) guidelines [3]. Radical surgical options, such as partial amputation and total penectomy, can impair sexual function or micturition, can affect genital sensibility, and can be detrimental for the psychology and the quality of life of the patient [3]. On the other hand, penile sparing surgery aims at complete excision of the primary tumor, with or without reconstruction, with the goal of preserving sexual function and improving cosmetic outcome [4]. Glans resurfacing is considered a new technique described since 2000 by Depasquale and was originally used for the treatment of extensive balanitis xerotica obliterans. Currently it has been suggested as a valid option for the surgical management of the superficial penile cancer (Tis, Ta, T1aG1, T1aG2) [4]. We describe in detail the glans resurfacing technique with skin

(a)



(b)

(c)

(d)

Figure 1: (a) Marking the circumcision line on the shaft of the penis. (b) Incising the marked skin, in order to perform the circumcision (sleeve technique). (c) Placing a tourniquet at the base of the penis. (d) The glans is marked in quadrants.

graft for penile cancer in a video presentation (available here) and we review the current knowledge of the literature on the procedure.

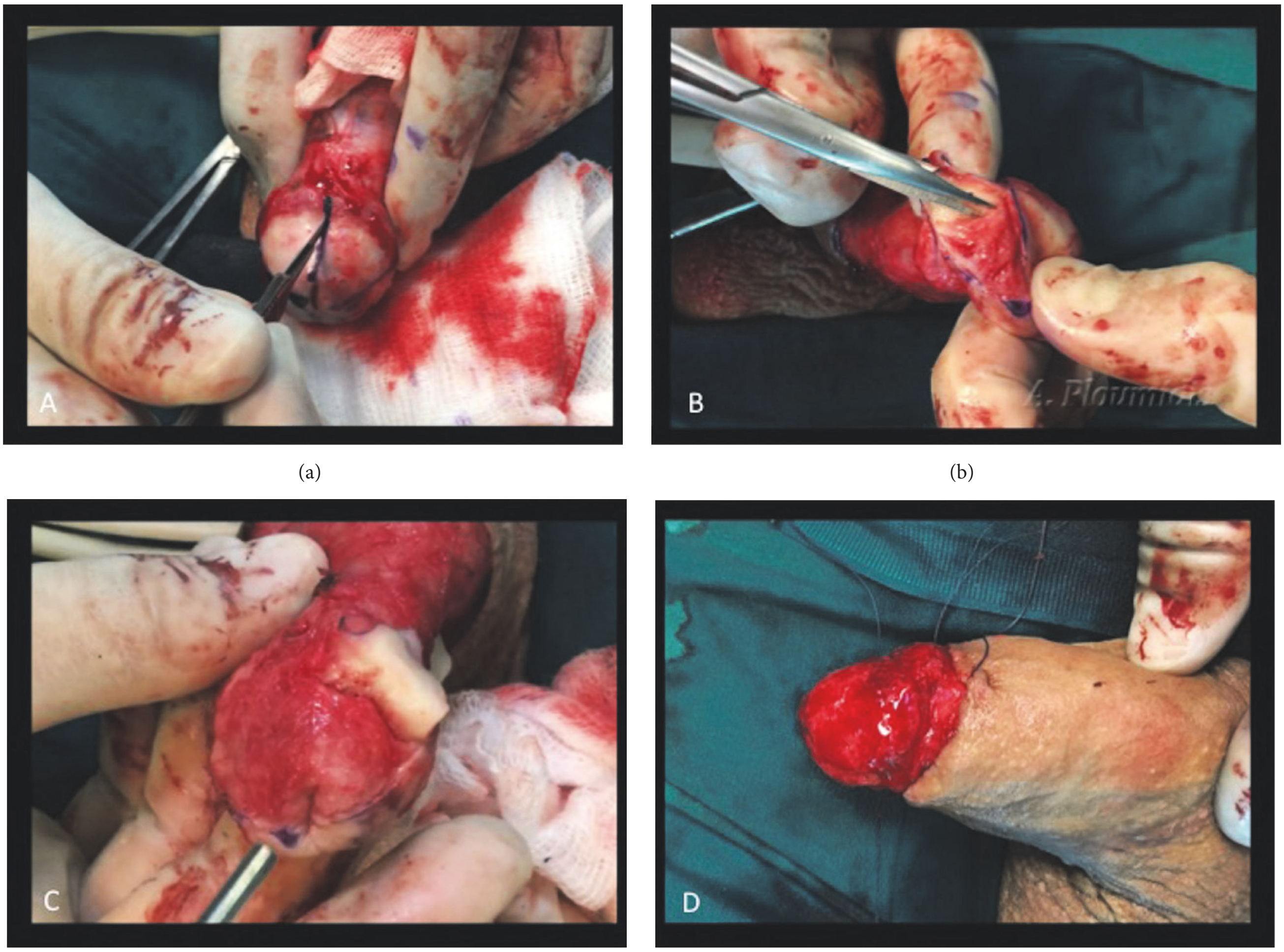
2. Surgical Technique

2.1. Step 1: General Preparation. The patient is placed in a supine position, with the legs slightly abducted. The procedure is performed under general anesthesia. Broad-spectrum antibiotics are administered preoperatively. The external genital organs and the inner thigh are shaved in the operating room and surgical skin preparation is performed using antiseptic solution. The surgical field is draped leaving the genitals and the thigh exposed. Usually the right thigh is preferred for a right-handed surgeon standing on the right side of the patient.

2.2. Step 2: Circumcision and Tourniquet Appliance. The prepuce skin is marked, just below the corona and on the shaft of the penis (Figure 1(a)). The excess foreskin is removed using the sleeve technique and the penis is circumcised (Figure 1(b)). Glans resurfacing begins by placing a tourniquet at the base of the penis (Figure 1(c)).

2.3. Step 3: Marking of the Glans in Quadrants and Dissecting of the Epithelium and Subepithelium Layer. The glans is marked in quadrants from the meatus to the corona (Figure 1(d)). The underlying spongiosum is exposed, by dissecting and removing the epithelium and subepithelium layer of the glans, from the meatus to the corona for each quadrant (Figure 2(a)). Dissection is undertaken with tenotomy scissors for better precision in dissection, or with a blade scalpel No 15 (Figure 2(b)). The plane of dissection lies between the thickened mucosa and the underlying spongy tissue. During the dissection the surgeon must take care that no affected mucosa is left on the glans especially near the meatus (Figure 2(c)). On the other hand, deep dissection down to the spongy tissue should be avoided not to cause unnecessary bleeding or to compromise the aesthetic outcome. The glans is completely stripped when all quadrants are removed and deep spongiosal biopsies can be taken to exclude invasion (Figure 2(d)). Each quadrant is sent separately for biopsy. After releasing the tourniquet compression, excessive bleeding is controlled with bipolar diathermy. Excessive cautery should be refrained in order to avoid necrotic tissue to the graft bed.

2.4. Step 4: Estimating Graft Size, Harvesting and Placement of the Skin Graft. The surface of the graft size needed is



(a) (b) (c) (d)

Figure 2: (a) Incising the epithelium and subepithelium of each quadrant of the glans. (b) Stripping the upper right quadrant of the glans, by removing the epithelium and subepithelium with tenotomy scissors (c) The upper right quadrant is completely peeled off. The upper left quadrant is semidetached and rolled backwards. The underlying spongiosum tissue is exposed. (d) The glans epithelium and subepithelium are completely removed.

estimated by accurately placing a white paper over the glans circumference. Blood is absorbed from the paper defining the size of the graft bed (Figure 3(a)). The paper is placed over the harvesting site, on the front or inner part of the thigh and the borders of the graft are marked taking into account graft contraction once removed (Figure 3(b)). A partial thickness skin graft is harvested from the thigh with a dermatome. The graft thickness ranges from 0,02 to 0.04 cm and is carefully trimmed (Figure 3(c)). The surgeon perforates the skin graft with a scalpel blade to allow blood and fluid accumulation to drain, thus improving graft survival (Figure 3(d)). The graft is rolled over glans starting from the ventral side (Figure 4(a)). Quilting sutures (5-0 absorbable polyglactin) are placed over the glans to secure the graft to its bed. In cases where a circumcision is performed due to the prepuce skin either being part of the disease or being strongly adhered to the glans, the proximal end of the graft is anastomosed with the distal shaft skin by everting the edges in order to recreate the corona sulcus (Figure 4(c)). A meatotomy is performed to compensate for possible stricture at the level of the meatus since the skin graft is inverted and approximated directly to the urethra (Figure 4(b)).

2.5. Step 5: Wound Dressing, Urinary Diversion, and Follow-Up. A silicone 16F Foley catheter and a suprapubic catheter are placed to prevent urine extravasation to the graft. The penis is dressed initially with a paraffin gauze and further covered with multiple gauzes and compressed with an elastic band (Figure 4(d)).

The patient is discharged the next day with instructions for bed rest for the following two days for better immobilization of the graft. The dressing and Foley catheter are removed in 7 days, and the graft is observed for inflammation or any necrotized tissue. The patient continues to use the suprapubic catheter for urine evacuation in order to keep the graft dry for 7 more days. The patient is advised to avoid any friction to the graft and refrain from sexual intercourse for 6 weeks.

(a) (b) (c) (d)

Figure 3: (a) Estimating the graft size needed by accurately placing a white paper over the glans circumference. Blood is absorbed from the paper defining the borders. (b) Marking the size of the skin graft over the harvesting site of the thigh taking into account graft contraction once removed. (c) A dermatome is used for the harvesting of the partial thickness skin graft. (d) Perforating the skin graft, in order to improve graft survival.

The patient is examined on a 3-monthly basis for 2 years, on a 6-monthly basis for a further two years, and then annually.

3. Discussion

PeCa diagnosis has a detrimental impact on the psychology of the patient, not only because a cancer has been diagnosed, but also due to the fact that the surgical management of the disease can affect adversely the cosmetic penile appearance, the sexual function, and the micturition of the patient [4]. The mainstay of surgical management is based on wide excision with partial or total penectomy involving the glans and the corpora cavernosa in cases of invasive PeCa [5, 6]. However, the difficulty patients have in accepting the amputative results of radical operations led to the emergence of new reconstructive surgical techniques with organ sparing orientation, not only for premalignant or superficial lesions but also for more advanced tumors. This approach aims to preserve the phallus and improve quality of life without compromising the oncological result [5, 6].

Glans resurfacing is considered a new technique in the field of reconstructive urology and it has been originally used for the treatment of severe lichen sclerosis of the glans [4]. Currently it is recommended from the EAU guidelines as a primary option for the management of the superficial non-invasive disease (PeIN) or as a secondary option after failure of topical chemotherapy or laser therapy. Furthermore, it is also recommended as a primary option for the management of superficial Ta, T1a (G1, G2) tumors [3].

The major studies referring to glans resurfacing technique with a median follow-up of at least 30 months reported no cancer-specific deaths, while the rates of the local recurrence fluctuated between 0 and 6% [3–7]. Glans resurfacing technique can be total (TGR) or partial (PGR) (excision of less than 50% of glans epithelium) [3, 4]. PGR is usually indicated in cases of localized CIS affecting less than 50% of the glans. During PGR only glans epithelium and subepithelium of

(a)

(b)

(c)

(d)

Figure 4: (a) The graft is rolled over glans starting from the ventral side. Quilting sutures are placed accordingly. (b) A meatotomy is performed to compensate for possible stricture at the level of the meatus due to sutures approximating the skin graft to the urethra. (c) The proximal end of the graft is sutured to the distal shaft skin by everting the edges in order to recreate the corona of a normal penis. Multiple quilting sutures secure the graft to its bed. (d) A suprapubic and a urethra catheter are placed. The penis is dressed with multiple gauzes and compressed with an elastic band for graft immobilization.

the locally affected area are dissected with a macroscopic clear margin [3]. The TGR technique has been described in detail in previous studies referring to the procedure but has never been presented as a step-by-step technique in a video presentation [3, 6–8].

After performing the circumcision, the first important step is the exposure of the spongiosum by removing the epithelium and subepithelium tissue of the glans, from the meatus to the corona for each quadrant (Step 3) [3, 6, 7, 9]. The significance of positive surgical margins in organ sparing surgery for PeCa is of utmost importance; thus each removed quadrant is sent separately for frozen section. Furthermore, a crucial part of this stage of the procedure is deep spongiosal biopsies acquisition, in order to confirm the absence of any invasion [3, 7, 9]. In case of a positive surgical margin, adjuvant treatment or surgical excision can be performed, although some authors have proposed following-up the patient in case of PeIN [3, 7]. It is important to stress that for the TGR technique the positive surgical margins (PSM) have been reported to be up to 20%, while when taking into consideration both the PGR and the TGR, the PSMs can reach 45% [3, 4]. Even though the overall recurrence rate was only 4%, the rate of secondary operation after performing TGR was 10% [3, 10]. Glansectomy was the preferred technique as a second procedure in most of the cases [3, 8, 9].

The next important stage of the operation is the estimation of the graft size, the harvesting and the "transplantation" of the selected graft (Step 4). Although graft-rejection in reconstructive operations is always a possibility, in TGR graft failure is not considered common [3, 6, 7]. The reduced rate of graft failure and the need for regrafting can be attributed to the increased vascularity of the underlying corpus spongiosum [5, 7]. In one study of 17 patients, two of them showed partial graft loss and wound separation that were managed successfully with conservative treatment [6]. Only in one case in a series of 25 patients, the graft failed to heal completely and the patient was submitted to a secondary glansectomy. The histology in this particular patient was an invasive grade II pT1 SCC [3].

A few key steps during this part of the operation can increase the success rate of inosculation. When the tourniquet is released, small bleeding vessels of the spongiosum should be coagulated meticulously and with accuracy in order to avoid any underlying hematoma, but at the same time taking care of the normal vascularity of the graft bed. Moreover, it is important to harvest a partial thickness graft ranging from 0,02 to 0.04 cm, carefully trimmed to fit and quilted with interrupted sutures in order to promote graft survival. Some authors have proposed immobilization of the skin graft without quilting but instead covering the neoglans with proflavine soaked gauge dressing anchored with tie-over sutures (TODGA-technique) [10]. Furthermore some surgeons suggest performing multiple small incisions (fenestration) on the graft to allow mild exudate to drain in order to prevent any underlying hematoma or seroma formation (Step 4) [6].

The procedure is completed with the placement of a Foley catheter and a compressive dressing to the penis [1–7]. We also recommend a placement of a suprapubic catheter in order to divert the urine when the Foley catheter is removed. This is especially performed in cases where PeCa is over the meatus and the excision of the glans epithelium leaves the urethra exposed. In this case, the graft healing can be compromised due to the urinary stream on the urethra-graft anastomosis at the fossa navicularis.

Generally the procedure is associated with minimal risk of intraoperative and postoperative complications like bleeding, infection, and hematoma [4, 5, 7]. The recovery of the patient is rapid, cosmetic result is acceptable, the restoration of glans sensation is expected to be prompt, and penile function is preserved [4, 6, 7, 11–13]. In the main studies for the TGR all the patients that were preoperatively sexual active regained the same sexual activity within 3-5 months [6, 7]. However, it is vital that the patients are informed about the possibility of a positive surgical margin and the potential need for a secondary auxiliary procedure [5].

4. Conclusions

Glans resurfacing is an emerging new appealing surgical technique that is already a recommendation in the EAU guidelines for the treatment of premalignant and superficial penile lesions. It is important to carefully select, harvest, and suture the graft to the recipient bed of the glans. Negative surgical margins are of great importance for oncological reasons and to avoid possible auxiliary procedure. The overall satisfaction rate and recovery of the sexual function are acceptable, and it could be considered an ideal treatment for the superficial penile cancer.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Supplementary Materials

Video presentation of a step-by-step surgical technique on glans resurfacing for penile cancer. *(Supplementary Materials)*

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Review Article

A Comprehensive Review Emphasizing Anatomy, Etiology, Diagnosis, and Treatment of Male Urethral Stricture Disease

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To date, urethral stricture disease in men, though relatively common, represents an often poorly managed condition. Therefore, this article is dedicated to encompassing the currently existing data upon anatomy, etiology, symptoms, diagnosis, and treatment of the disease, based on more than 40 years of experience at a tertiary referral center and a PubMed literature review enclosing publications until September 2018.

1. Introduction

Urethral stricture disease can develop throughout the entire length of the male urethra and can be caused by a large variety of etiologies. Also, urethral strictures give rise to a wide range of symptoms and warrant a specific diagnostic work-up before proceeding to any treatment modality.

The management of urethral stricture disease has a profound history and may embody one of the oldest documented urological entities known to mankind. In the second half of the 20th century, urologists have attempted to find solutions to treat both simple and complex urethral strictures and, over the last few decades, research has mainly been focused on refining the existing procedures to mitigate the negative postoperative consequences. However, despite the substantial scientific progress on this subject, a numerous amount of studies has revealed the insufficient knowledge about urethral stricture surgery among urologists and has shown that patients with urethral strictures are generally offered an inadequate treatment option [1–3].

Against this background, the article outlines the existing data about anatomy, etiology, symptoms, diagnosis, and treatment of male urethral stricture disease.

2. Anatomy

The terminology describing male urethral anatomy is often used incorrectly and thus needs clarification. In fact, the male urethra consists of the following segments (from bladder neck to meatus urethrae): the posterior urethra, containing the prostatic urethra and the membranous urethra, and the anterior or spongious urethra (embedded in corpus spongiosum), containing the bulbar urethra (between the membranous urethra and the penoscrotal angle) and the penile urethra (between the penoscrotal angle and the meatus urethrae) (Figure 1). Diseases of the prostatic urethra are beyond the scope of this article as they largely overlap with specific prostate diseases.

3. Etiology

The etiology of urethral stricture disease mainly involves the following: idiopathic, iatrogenic, external trauma, infection, and lichen sclerosus. In 2013, a comparative analysis showed that urethral strictures in India are proportionally more caused by an external trauma and less by an iatrogenic cause, when compared to the USA and Italy [4]. Meanwhile, in the Western World, the most important stricture etiology is iatrogenic [4–6] and developing countries primarily face

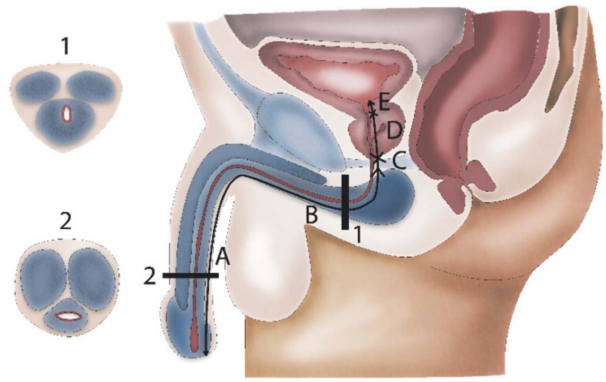


Figure 1: Anatomy of the male urethra. *1 = bulbar urethra (urethra runs dorsally through corpus spongiosum); 2 = penile urethra (urethra runs centrally through corpus spongiosum). A = penile urethra; B = bulbar urethra; C = membranous urethra; D = prostatic urethra; E = bladder neck.*

infectious strictures after venereal infections or after a nonspecific urethritis [7]. As regards lichen sclerosus, a skin condition with an important predilection for the anogenital region, its urethral involvement is a well-known aspect of the disease and potentially gives rise to urethral strictures at the penile or bulbar site [8, 9]. Furthermore, it must be underlined that a substantial amount of stricture etiologies remains unknown, even after thorough evaluation of the patient's history.

3.1. Iatrogenic Stricture Etiology. The medical world is responsible for a substantial amount of urethral strictures [5]. Every transurethral intervention (e.g., catheter insertion, introduction of surgical instruments, etc.) can damage the urethral mucosa and lead to subsequent stricture formation, even if performed adequately [5]. Therefore, all medical practitioners should keep this in mind and carefully consider their indications before proceeding to any transurethral manipulation. Failed hypospadias repair represents another important iatrogenic cause of strictures, especially in younger patients [5]. In a relatively older patient population, local prostate cancer treatments, mainly involving radical prostatectomy or radiation therapy, are an upcoming etiology and bring along strictures that are very challenging to treat [5]. Less frequently, strictures are due to ischemia of the corpus spongiosum which may occur after hypothermia or extracorporeal circulation, for instance, during cardiac or neurosurgery [5]. In these cases, strictures typically involve the complete anterior urethra because this entire segment strongly relies on the spongious blood supply.

3.2. External Trauma. External trauma leading to a pelvic fracture specifically threatens the membranous part of the male urethra either by a shear injury resulting from the movement of the pelvic bones or by a laceration injury caused by bony fragments cutting into the urethra. These phenomena may result in a partial or total rupture of the urethra. The associated hematoma formation then further separates both urethral ends and causes such a disruption defect in between.

Straddle injuries or a trauma directly impacting the perineum may damage the bulbar urethra as this part of the urethra gets crushed between the area of impact and the pubic bone. Generally, these injuries lead to stricture formation at the site of urethral damage and are usually accompanied by an important perineal hematoma due to an associated rupture in the surrounding spongious tissue.

In case of severe penile fractures, the rupture of the cavernous bodies can be associated with a rupture of the penile urethra which may lead to subsequent stricture formation.

4. Symptoms and Diagnosis

4.1. Patient History. Patients with a urethral stricture mostly complain about obstructive voiding symptoms. The most apparent symptom is weakening of the urinary stream. However, it is important to understand that all degrees of obstructive voiding can be present, ranging from a perfectly normal urinary stream to urinary retention. In case of a discrete urethral stricture and/or a slowly progressive onset of symptoms, the patient can indeed report a total absence of obstructive voiding symptoms as the detrusor muscle may compensate the lower urinary tract obstruction by hypertrophy. Other obstructive voiding symptoms may involve hesitancy, intermittency, straining, post-void dribbling, incomplete emptying of the bladder, and spraying (especially in meatal strictures). Apart from these, development of an overactive bladder is frequent as well and brings along complaints of urgency and frequency.

Other complaints such as hematuria or pollakisuria are also possible, although they are likely to be the result of a stricture related complication such as urinary stones, urethritis, or an infection of the prostate, epididymis, or testicle.

The presence of a urethral stricture should always be suspected in case of repetitive infections of the prostate, epididymis, or testicle.

Next to symptom assessment, history taking should focus on stricture etiology, previous interventions, relevant medical history and comorbidities.

4.2. Physical Examination. During physical examination, the clinician should palpate the urethra to identify fibrotic tissue and look for skin changes (e.g., lichen sclerosus), the presence of cellulitis, fistulas, or abscesses, the presence and quality of foreskin to potentially use in later urethral reconstruction and the presence of scars from prior surgery. These surgical scars may reveal important information about the type of prior reconstruction which is sometimes unknown to the patient.

Ideally, the examination of the patient also includes a digital rectal examination (benign prostatic hyperplasia; prostatitis) and an evaluation of the external genitals which might reveal (the consequences of) an epididymitis or an orchitis.

Be that as it may, imaging studies remain essential to evaluate the entire male urethra as only part of it can be evaluated by physical examination.

4.3. Technical Investigations

4.3.1. Uroflowmetry. The maximal urinary flow rate (Qmax) of an adult man with a healthy lower urinary tract is estimated to be >15 mL/s [10]. A Qmax of <15 mL/s is considered suspicious for lower urinary tract obstruction and requires further diagnostic evaluation. Apart from Qmax, it is also important to interpret the shape of the flow curve as in patients with a urethral stricture, uroflowmetry may typically reveal a curve with a plateau-shape at the level of the Qmax [11–13].

It must be underlined that uroflowmetry studies with a voided volume < 150 mL can lead to a less valuable interpretation [12].

4.3.2. Urethroscopy. Urethroscopy is a fast and relatively easy way to diagnose a urethral stricture. This investigation provides information about the location and the remaining caliber of the narrowed urethra (to pass or not to pass with the cystoscope). If the stricture is too narrow to allow passage of the cystoscope, no further information about the proximal urethra can be obtained with this diagnostic modality. In these cases it can be helpful to introduce a smaller caliber ureteroscope (4.5 or 6 Fr) which is able to pass through the strictured area and which thus provides further proximal information [14]. Apart from that, urethroscopy is also unable to provide any information about the surrounding spongiofibrosis. Given these drawbacks, urethroscopy alone is often considered insufficient for a thorough diagnostic work-up and additional imaging studies are mostly warranted.

4.3.3. Urethrography. A retrograde urethrography (RUG), in which contrast is injected through the urethral meatus, is capable of visualizing the entire urethra (except in cases with a total obliteration of the urethral lumen) up to the sphincter and even up to the bladder if patients can relax the sphincter enough to allow passage of contrast through the prostatic urethra and bladder neck (Figure 2). However, a RUG alone often results in insufficient distension of the urethra proximal to the stricture which may lead to incomplete information about the proximal stricture extent and the condition of the more proximal urethra. In this case, an additional voiding cysto-urethrography (VCUG) after filling the bladder with contrast (either after RUG or by instillation through a suprapubic catheter) may solve this problem and address the need for additional information.

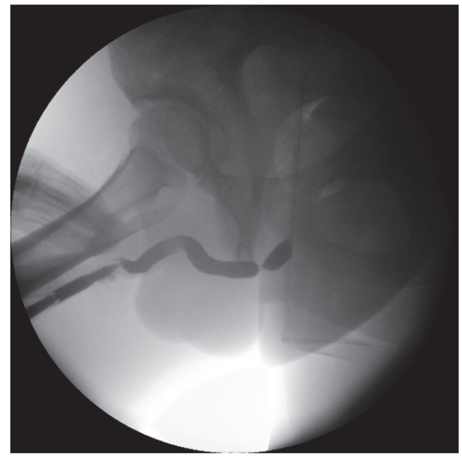


Figure 2: Retrograde urethrography. *Retrograde urethrography shows an isolated, short, bulbar urethral stricture.*

The combination of both RUG and VCUG provides a comprehensive image of the entire urethra and reveals valuable information about the number of strictures, stricture length, stricture location, and the remaining caliber of the narrowed urethra. Nonetheless, RUG and VCUG studies require careful interpretation and several drawbacks must be kept in mind. A prestenotic dilation, for instance, can mask the presence of a urethral stricture or interfere with the observed stricture length, especially in the bulbar urethra. In these cases, an additional image in profile view can be very useful. Furthermore, estimated stricture length, particularly at the bulbar site, should always be interpreted carefully as this result poorly correlates with the intraoperatively measured stricture length [15]. This can be explained by the fact that a 3-dimensional situation is projected on a 2-dimensional image and by the fact that the observed stricture length importantly depends on the patient's positioning and the provided penile traction during the investigation [15]. RUG and VCUG are further limited by the fact that—similar to urethroscopy—none of these studies provide any information about the surrounding spongiofibrosis.

4.3.4. Urethral Ultrasound. A urethral ultrasound may be useful in the diagnostic work-up of urethral strictures, particularly because it measures stricture length more adequately and because it reveals information about the surrounding spongiofibrosis [15]. During this investigation, a linear 7,5 MHz probe is placed sagitally against the region of interest: ventral penis for penile strictures, perineal for bulbar strictures. The urethra is then visualized as a hypoechogenic band with an 8 to 10 mm diameter (after instillation of a physiologic solution through a Foley catheter at the level of the meatus) and urethral strictures are represented as thick, irregular, and hyperechogenic zones in and around the depicted urethra (Figure 3).

Despite the aforementioned assets of urethral ultrasound, this imaging study is vastly underused in clinical practice

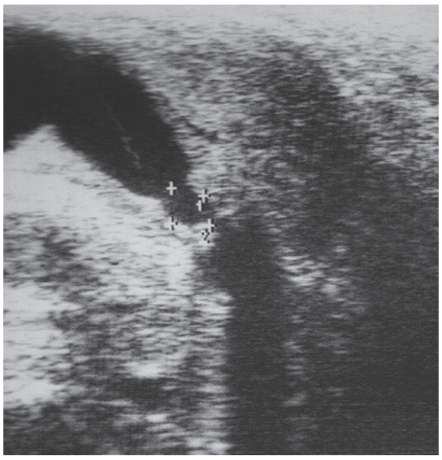


Figure 3: Ultrasound of the bulbar urethra. *Ultrasound shows an irregular, hyperechogenic zone in the bulbar urethra, representing a bulbar urethral stricture.*

and urethrography remains the routine diagnostic modality, principally because its rapid information is sufficient for the reconstructive urologist. Furthermore, as a urethral ultrasound takes longer to perform, there is a prolonged period of retrograde injection of a physiologic solution which is uncomfortable for the patient when awake.

4.3.5. Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) Scan. MRI is a very useful tool in case of tumor related urethral stricture disease. This imaging study can adequately demonstrate the extent of the disease in the surrounding tissues, for instance, into the cavernous bodies, which is of utmost importance for the subsequent surgical procedure. Further routine use in clinical practice is rather debatable. Nonetheless, Oh et al. advocate for MRI in case of complex trauma leading to a completely obliterated posterior urethra [16] and, more recently, Joshi et al. described a novel MRI protocol which leads to a reliable measurement of the urethral gap after pelvic fracture related urethral injuries [17]. This novel MRI technique could be very useful to plan and guide subsequent urethral reconstruction in these often complex cases [17].

A CT voiding urethrography can provide useful information in case of stricture related fistulas [18].

5. Treatment

5.1. Dilations. Urethral dilation represents one of the oldest urological procedures known to mankind. Throughout history, urologists have invented all sorts of instruments to progressively dilate urethral strictures up to a normal caliber. However, since the development of direct vision internal urethrotomy (DVIU), urethral dilation as a primary treatment for urethral stricture disease has decreased and research has started focusing on repetitive (auto)dilations as a strategy to prevent or delay stricture recurrence after DVIU (cf. infra) [19, 20].

As the mechanism of urethral dilation implies rupturing the urethral mucosa at the least scarred region of the stricture, it allows subsequent urine diffusion in the created defect and peri-urethral tissues which further nourishes the formation of scar tissue. Hence, a high stricture recurrence rate can be expected, either in the short or in the long term. Accordingly, durable success rates after urethral dilation for a primary, short urethral stricture lie between 50 and 60% but decrease to about 20% for strictures longer than 2.0 cm [21, 22]. Nonetheless, these results need to be put in perspective as DVIU can also cause urinary extravasation into the peri-urethral tissues and since Steenkamp et al. described no statistically significant difference in surgical outcome between DVIU and urethral dilation [21].

Potential risks that are associated with single or repetitive (auto)dilations include urethral hemorrhage, urinary tract infection, and sepsis. Furthermore, it is advised not to dilate the urethra in case of a present urinary tract infection.

5.2. Endoscopic Treatment

5.2.1. Direct Vision Internal Urethrotomy (DVIU). DVIU represents the basis of endoscopically treating urethral strictures and is inspired by a French idea, born in the 19th century (Civiale, 1817; Maisonneuve, 1848). This treatment principally differs from urethral dilation as it involves an intervention which is guided by the direct vision of the surgeon. During this procedure, a longitudinal incision is made over the entire stricture length into healthy urethral tissue, after which the gap between the wound edges is expected to be re-epithelialized.

Today, many urologists feel comfortable treating urethral strictures with endoscopic urethrotomy. Most likely, this popularity is mainly a result of its short learning curve, its relatively fast and simple character, and its paucity of major complications, rather than its intrinsic surgical outcome. Moreover, in many urology practices, a thorough knowledge of and/or experience with open urethral reconstruction are/is lacking [23].

(1) Indications. The sole indication for DVIU is a primary, isolated, short (<1.5 cm), bulbar urethral stricture. This recommendation is based upon several negative prognostic factors impeding success rates of DVIU: number of previous urethrotomies (and stricture-free interval hereafter), stricture length, number of strictures, stricture location, and the amount of surrounding spongiofibrosis [24, 25].

(2) Results. DVIU for primary urethral strictures <1.5 cm entails the best surgical outcome, with success rates ranging up to 80% in case of strictures <1 cm [26]. When performing DVIU for longer strictures, success rates drop to about 20% [26]. Moreover, Steenkamp et al. have shown that every additional centimeter to be treated with DVIU brings along an extra risk factor (RR: 1.22) for stricture recurrence [21].

(3) Therapeutic Options to Prevent or Delay Stricture Recurrence after Urethrotomy

Repetitive (Auto)Dilation. Repetitive (auto)dilation is frequently administered as an adjuvant therapy after DVIU to prevent or delay stricture recurrence. This strategy has been evaluated by several retrospective series which have shown a limited benefit over DVIU only and these findings have been corroborated by a recent systematic review and meta-analysis [27–30]. These studies, however, provide no data about which specific patient groups might benefit more or less from these adjuvant dilations and it has been described that repetitive (auto)dilations are associated with a poor quality of life [31].

Injection or Instillation with Corticosteroids. Post-urethrotomy injection or instillation with corticosteroids has been evaluated by two randomized [32, 33] and two nonrandomized [34, 35] series, three of which have shown a clear benefit over DVIU only in strictures <2 cm [32, 34, 35]. However, all of these reports are based on a poor-quality study design and thus no clear conclusions can be drawn about the true value of corticosteroids in this setting.

Injection with Low-Dose Mitomycin C (MMC). Low-dose MMC (0.1 mg in 2 mL, 5%) injections in the freshly incised urethral stricture have been described with beneficial results in an initial small randomized, controlled trial (n=20) [36]. The rationale behind this strategy lies within the antifibrotic and anticollagen properties of the MMC substance. More recent studies, involving a large randomized, controlled trial [37] and a descriptive study in 37 patients [38], have confirmed the benefit of adding these injections over DVIU only.

Nevertheless, the use of post-urethrotomy MMC injections has not exactly found its way into routine clinical practice. The experienced serious adverse events following extravasation of MMC after intravesical instillations, even though these concentrations of MMC are 20 times higher, might be an explanation for this. Furthermore, this trend may be further encouraged by the presence of all valuable alternatives, as mentioned above.

5.2.2. Metallic Endoluminal Stents. Metallic endoluminal stents are endoscopically inserted after incision of the urethral stricture and are manufactured to maintain a sufficient caliber at the level of the diseased urethra. These stents may be particularly interesting in short urethral strictures as they allow re-epithelization from both extremities. In more extensive stricture disease, however, the formation of granulation tissue may overgrow the meshes of the inserted stent and thus lead to a partial or complete obliteration of the stent's endolumen.

These endoluminal stents were enthusiastically introduced in the 1990s, especially for short, recurrent bulbar strictures as they offered promising short-term success rates [39]. However, in the long-term, devastating problems occurred in patients after endoluminal stent implantation including restenosis due to overgrowth, stent migration, encrustation, and infection [39]. Thereafter, endoluminal stents rapidly decreased in popularity and several reconstructive techniques were advocated for urethroplasty after endoluminal stent failure [39].

5.2.3. Laser Evaporation of the Stricture. The laser technique is capable of evaporating the entire urethral stricture, but it destroys the epithelium of the urethra at the same time. Considering this, holmium laser urethrotomy is specifically indicated for short urethral strictures, because, in these cases, re-epithelization may be expected even sooner than in classic urethrotomy. Moreover, there is limited evidence that, for these strictures, the recurrence rates within 1 year of follow-up are significantly lower after laser urethrotomy, when compared to cold-knife incision [40]. In case of longer urethral strictures, less favorable results are to be expected from this treatment modality, particularly when the urethral epithelium has been disintegrated over the entire length of the treated stricture. However, these auspicious results should be put in perspective as they are supported by a limited amount of studies, with small sample size, short follow-up and poor description of the study design and methods [40].

5.3. Open Reconstructive Treatment. Urethroplasty, the open reconstructive treatment for urethral strictures, is associated with significantly better long-term success rates than dilation or any endoscopic treatment option [26]. Over time, a tremendous amount of surgical techniques has been described and gradually refined, providing a very rich armamentarium for the reconstructive urologist. The exact choice of technique for a particular patient with a particular case of urethral stricture disease will depend on numerous factors, at least including the following: previous urethral treatments, number of strictures, stricture length, stricture location, stricture etiology, comorbidities and the quality of the corpus spongiosum, the surrounding tissues, and potential graft sites. Hence, a thorough diagnostic work-up is indispensable and of utmost importance when selecting the most adequate treatment option.

5.3.1. Timing of Surgery. Urethroplasty should be timed adequately and needs to take place after full maturation of the stricture. Following this logic, the authors believe that postponing urethral reconstruction until 3 months after the latest transurethral manipulation is the ideal approach, although there is no true evidence to support this specific statement. The rationale behind our timing is that the introduction of even a small caliber instrument may rupture the strictured area, causing a significant problem in the intra-operative determination of the distal extent of the stricture as a transurethral catheter or Beniqué might fluently pass through the dilated, but diseased urethra. This in turn could lead to an insufficient urethroplasty procedure, leaving fibrotic tissue, and thus stricture disease, behind.

Considering this, urinary diversion will need to be guaranteed by placing a suprapubic catheter in case of acute urinary retention.

5.3.2. Preoperative Work-Up. The key-point in preoperative work-up is to assure that the patient's urine is sterile during urethroplasty as a urinary tract infection can complicate the postoperative course and might contribute to urethroplasty failure. Therefore, it is advised to perform a urinalysis with

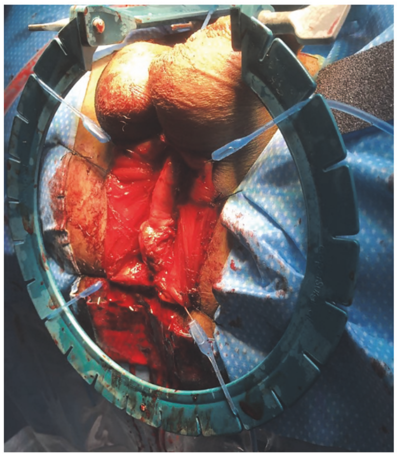


Figure 4: Exposure of the bulbar urethra. *The bulbar urethra is exposed using 4 stay sutures and a Lone Star retractor.*

urine culture and antibiogram one week preoperatively and to start with appropriate antibiotics 24 hours before surgery. This is especially important in patients with a suprapubic catheter, in whom the risk of contaminated urine is substantially higher. In case of a sterile urine portion, a single dose of cefazoline or a quinolone is administered at the start of the operation. In these cases, it is unnecessary to routinely perpetuate the antibiotic treatment regimen after any urethroplasty since this would only endorse the increasing problem of resistant microorganisms.

5.3.3. Urethral Access. For a long period of time, the authors have been using a midline perineal skin incision to access the bulbar and posterior urethra. This incision gives an excellent exposure with a minimal risk of wound dehiscence after closure and it has the advantage to be less painful than an inverted-U or λ incision [41]. After the skin incision, the subcutaneous fat tissue is further dissected until the level of the bulbospongiosus muscle, which is then incised longitudinally on the midline and separated from the corpus spongiosum. Further exposure can be obtained by fixating the muscle to the perineal skin with 4 stay sutures and by applying a self-retaining retractor with multiple stay hooks (Figure 4).

To access the penile urethra, a circumferential skin incision about 0.5 cm below the glans is an excellent approach (Figure 5). This incision will provide an excellent, well vascularized coverage of the reconstructed area and minimizes the risk of postoperative fistulation. After this skin incision, the penis can be degloved along Buck's fascia, following the virtually avascular plane in between, which results in an easy exposure of the entire penile urethra [42, 43].

An alternative approach to access the penile urethra was described by Kulkarni et al. and involves invagination of the penis through a perineal skin incision, thus accessing the entire penile urethra without the need for a penile skin incision [44]. This approach offers a perfect coverage of the penile site of reconstruction and allows total anterior urethral reconstruction through one perineal incision.

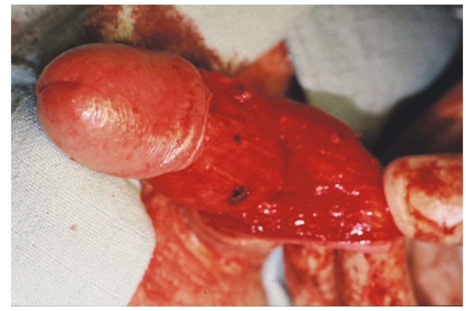


Figure 5: Exposure of the penile urethra. *After a circumferential incision, the penis is degloved along Buck's fascia providing exposure of the entire penile urethra.*

5.3.4. Surgical Techniques

(1) End-to-End Urethroplasty. End-to-end urethroplasty or excision and primary anastomosis (EPA) urethroplasty represents the surgical technique with the best long-term surgical success, entailing a composite success rate of 93.8% [45, 46]. During this procedure, the diseased segment of the urethra is excised and replaced by adjacent healthy urethral tissue, without the need for grafts or flaps to bridge the gap (Figure 6) [47].

Be that as it may, the indications for this surgical technique are restricted by the limited elasticity of the bulbar urethra. In fact, only strictures up to 3.0 cm are to be treated with end-to-end urethroplasty because the excision of longer segments would hamper the creation of a well vascularized and tension-free anastomosis, which is crucial for a successful procedure. The intrinsic elasticity of the bulbar urethra is estimated to be around 25% and, assuming an average bulbar urethral length of 10 cm, a gap of up to 2.5 cm can be bridged. Further length can be gained progressively by performing additional maneuvers involving extensive proximal and distal urethral mobilization, cleavage of the cavernous bodies, supracrural rerouting, and inferior pubectomy [48]. If, even after these length-gaining maneuvers, the gap between both urethral ends remains too large, an augmentation using free grafts or pedicled flaps will be inevitable [47].

Recommendations regarding urethroplasty of the bulbar urethra are currently highly inconsistent and controversial opinions are reported in literature: the International Consultation on Urologic Diseases (ICUD) advises end-to-end urethroplasty as the technique of first choice in all isolated, short ($\leq$ 3.0 cm), bulbar urethral strictures while others may argue that it is only indicated after bulbar trauma [48–50]. Apart from that, end-to-end urethroplasty is also recommended for posterior urethral strictures after pelvic fractures or after prostate surgery or radiation [47, 51–53]. Herein, the scar tissue is entirely excised and a bulbomembranous or bulboprostatic anastomosis is created. A cystoscope or a curved sound may be introduced in the suprapubic tract, down to the proximal urethral portion, to guide the surgeon in his/her surgical dissection and creation of the anastomosis [47, 51]. In very unusual circumstances, a combined abdominoperineal approach might be necessary [51]. In most of these patients with posterior urethral strictures, the elaborated anastomotic repair technique defined by Webster et al. will suffice to restore urethral continuity [48]. If this would not be the case, substitution or staged urethroplasty remains a viable option.

End-to-end urethroplasty is contraindicated in most penile urethral strictures, even in short ones, as EPA in this segment may lead to penile shortening and chordee.

Nontransecting End-to-End Urethroplasty. Traditionally, end-to-end urethroplasty included full thickness transection of the corpus spongiosum at the level of the stricture. However, as EPA only requires the excision of the narrowed segment and the surrounding spongiofibrosis, a full thickness transection of the corpus spongiosum, with the bulbar/urethral arteries within it, is usually unnecessary [47]. Against this background, Jordan et al. introduced the idea of a "nontransecting" or "vessel-sparing" technique in 2007 [54] which was later slightly modified and popularized by Andrich and Mundy (Figure 6) [55]. Many urethroplasty centers have adopted this technique ever since and promising results—in line with the success rates of the transecting technique—have been reported [47, 56–59]. This nontransecting technique aims to reduce surgical trauma, especially to the bulbar/urethral arteries embedded in the corpus spongiosum. Preserving these arteries potentially reduces the risk of postoperative erectile dysfunction or glans ischaemia. Apart from that, vessel-sparing could also be beneficial for subsequent urethral interventions requiring a well sustained vascular milieu, such as free graft urethroplasty or the implantation of an artificial urinary sphincter [47]. So far, these potential benefits are only assumptions as there is only one retrospective series suggesting a functional benefit for nontransecting EPA over transecting EPA [59]. Prospective randomized, controlled trials with validated questionnaires will be needed to corroborate these suggestions.

This nontransecting variant of end-to-end urethroplasty has also been introduced to treat posterior urethral strictures [60, 61]. However, in these strictures, the bulbar arteries and the cavernous vasculonervous bundles may already be obliterated or damaged due to the pelvic fracture or previous prostate treatments, abolishing the potential benefits of vessel preservation. Furthermore, the anatomical proximity of the membranous urethra to the urinary sphincter and the cavernous vasculonervous bundles should be taken into account and, if possible, a sphincter-sparing variant of nontransecting end-to-end urethroplasty may be superior in terms of continence preservation [62].

For short (<1.0 cm) and not too narrow strictures, a Heineke-Mikulicz urethroplasty can be performed with excellent success rates (Figure 7) [63]. In this subtype of nontransecting procedure, the stricture is longitudinally incised and then closed transversely without excising the fibrotic tissue. Some call this technique a stricturoplasty, rather than a true urethroplasty.

(2) Free Graft Urethroplasty. From the moment a stricture is no longer an indication for end-to-end urethroplasty, a substitution urethroplasty is unavoidable [64]. Herein, the use of a free graft represents the easiest and most straightforward technique to treat strictures from the meatus urethrae up to the posterior urethra. These free grafts can be harvested from several sites such as the preputium, the penile shaft, the oral cavity (buccal or lingual mucosa), the tunica vaginalis, and exceptionally the bladder mucosa [64]. Various manners have been described to suture the harvested graft onto or into the opened urethra (ventral onlay, dorsal onlay, dorsolateral onlay, dorsal inlay, and combinations), but tubularized grafts are to be avoided since these results are far less favorable than the aforementioned substitution techniques [64]. Furthermore, it is well known that free graft procedures provide worse outcomes at the penile urethra than at the bulbar urethra [64]. Most likely, this is the result of a more limited amount of corpus spongiosum at the penile site and its proximity to the urethral meatus and external, colonized milieu.

Preputial Grafts versus Buccal Mucosa Grafts. Nowadays, the trend is to use buccal mucosa grafts over preputial grafts (Figure 8). However, this choice is mainly based upon expert opinion as convincing evidence to support this is currently lacking. Some retrospective reports have attempted to investigate this issue but could not justify to choose one over the other [65, 66]. Prospective, randomized, controlled trials will be necessary to truly justify this trend and to bring forward an evidence-based recommendation.

Despite its excellent success rates, buccal mucosa graft urethroplasty also brings along some drawbacks. In contrast to the use of preputial grafts, for instance, a second surgical site—the oral cavity—needs to be disinfected and prepared with sterile drapes, which lengthens the duration of the procedure. Also, the surgeon taking the oral graft needs to be familiar with the anatomy of the oral cavity. Furthermore, it cannot be denied that the created defect in the buccal mucosa may cause important pain and/or discomfort in these patients, possibly resulting in a longer hospital stay. Persisting oral symptoms may involve pain, swelling, numbness, diminished taste, speech problems, and/or an impairment of the mouth opening, smiling, or eating [67–69]. Nonetheless, the use of buccal mucosa grafts has been a major asset in the surgical repertoire to treat urethral stricture disease.

Lingual Mucosa Grafts. Lingual mucosa grafts can be utilized as an alternative to buccal mucosa grafts (Figure 9). They are harvested from the sublingual region, respecting the sublingual nerve and the lingual papillae, which are important in the perception of taste. The main advantage of this graft site lies within its easy exposure, in contrast to an inner cheek. However, the graft length that can be obtained is limited to about 6.0-7.0 cm, depending on the size of the tongue. A randomized, controlled trial performed by Lumen et al. showed similar success and oral morbidity rates in buccal and lingual mucosa graft use, but the type of oral discomfort differed: lingual mucosa harvesting caused significantly more dysgeusia and problems with eating and speaking whereas buccal mucosa harvesting led to more oral tightness [70]. Be that as it may, the use of lingual mucosa grafts has also been an important asset in the armentarium of the reconstructive urologist.

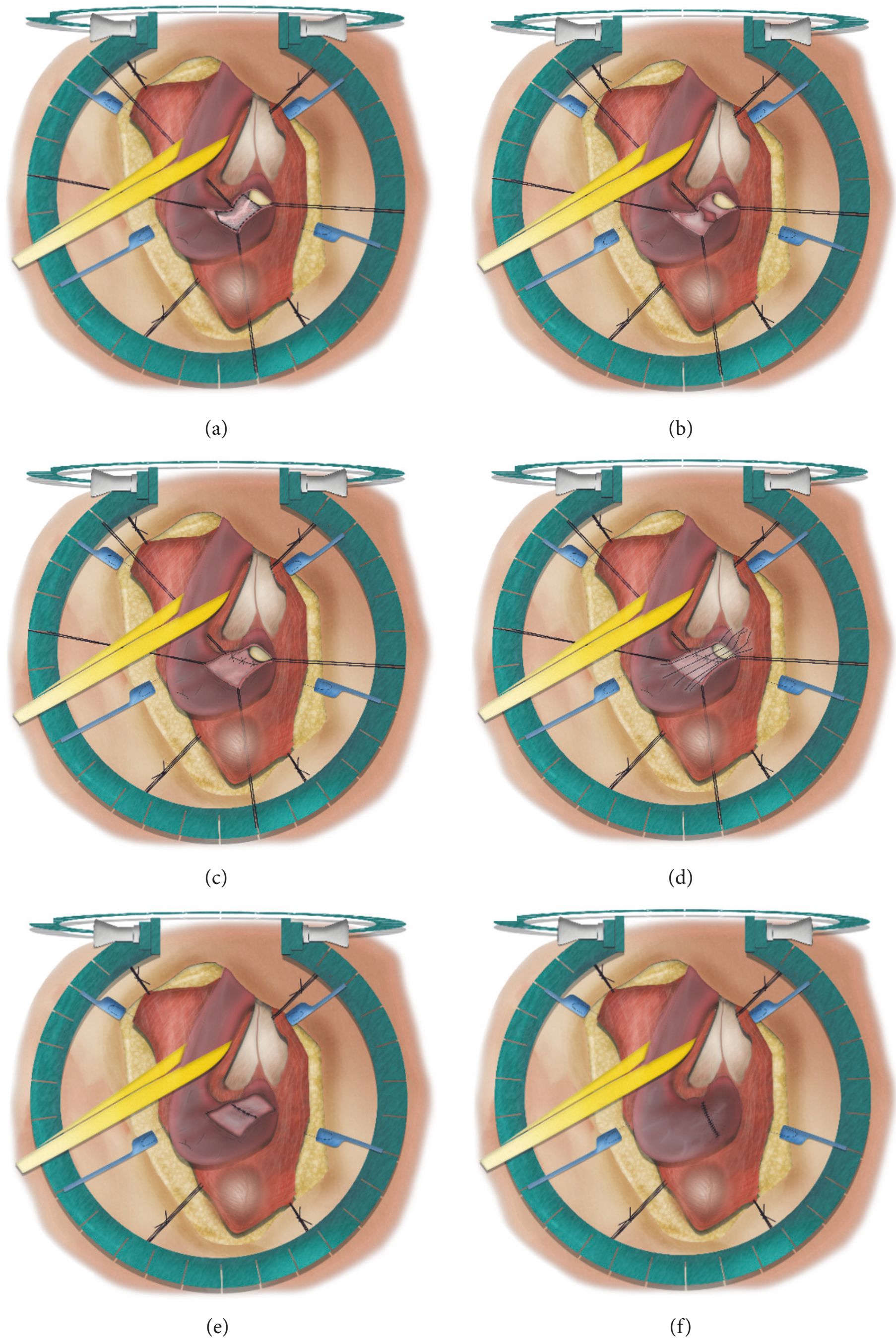
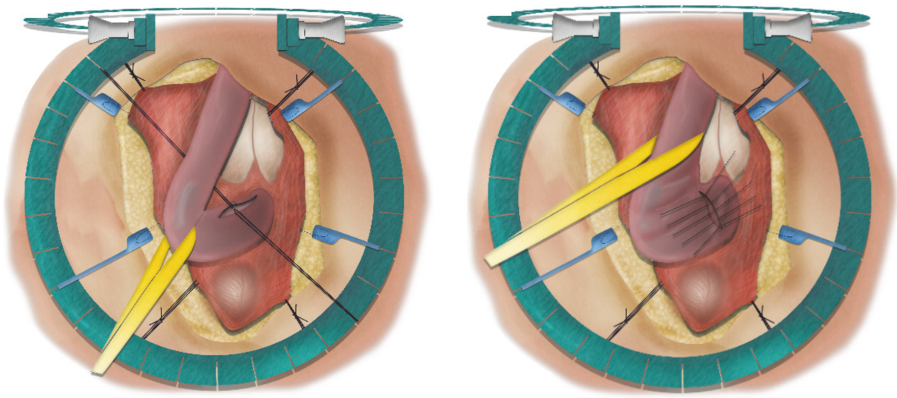


Figure 6: Nontransecting end-to-end urethroplasty. *(a) = excision of the stricture and surrounding spongiofibrosis after dorsal, longitudinal incision; (b) = ventral spatulation of the proximal and distal urethral end; (c) = transverse closure of the ventral urethral plate; (d, e) = transverse closure of the dorsal urethra; (f) = spongioplasty.*

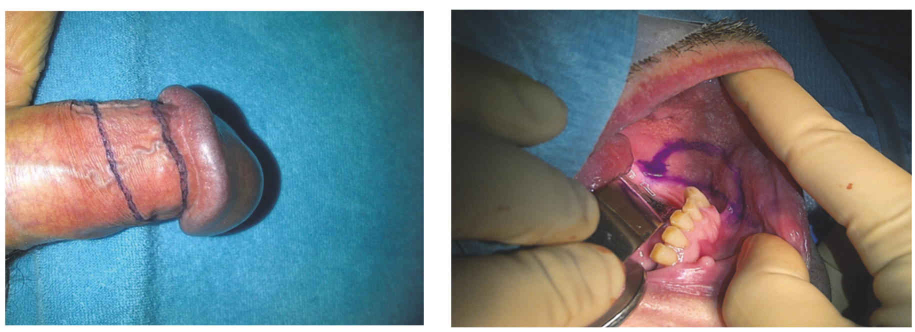
To Close or Not to Close the Oral Graft Site. A recent randomized, controlled trial by Soave et al. has shown that no closure of the donor site is noninferior to closure of the donor site regarding quality and intensity of oral pain (Figure 10) [69].

Graft Placement. Originally, free graft urethroplasty always involved a ventral placement of the graft on the longitudinally opened urethral stricture: the so-called "ventral onlay" free graft urethroplasty. Later, Barbagli et al. modified this technique and started placing grafts dorsally, against the cavernous bodies: the so-called "dorsal onlay" free graft urethroplasty [71]. This technique seemed to have the advantage of better graft fixation against its vascular bed and tended to cause less sacculation than ventral onlay procedures. A recent randomized, controlled trial, however, could not withhold any differences between both types of graft placement in the treatment of bulbar urethral strictures [72]. Hence, the



(a) (b)

Figure 7: Heineke-Mikulicz stricturoplasty. *(a) = longitudinal incision over the stricture; (b) = transverse closure of the incision.*



(a) (b)

Figure 8: Preputial graft versus buccal mucosa graft. *(a) = preputial graft; (b) = buccal mucosa graft.*

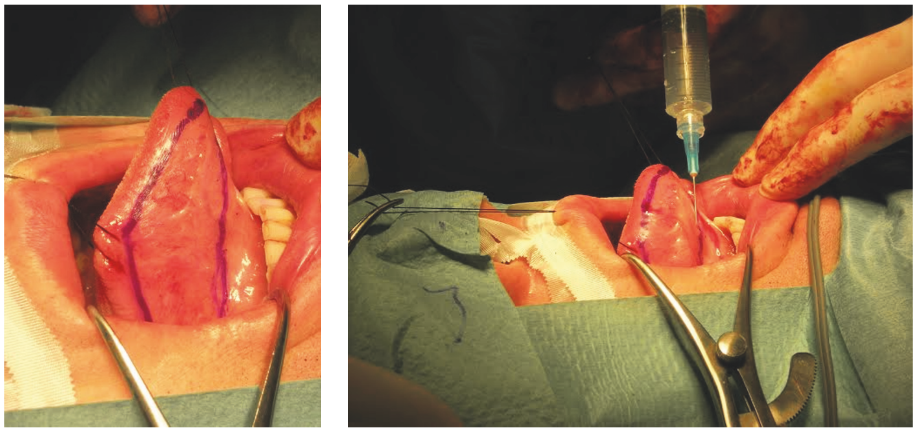
choice between a ventral and a dorsal onlay urethroplasty is mainly left upon the surgeon's discretion, but it remains very case-specific and importantly driven by multiple patient and stricture characteristics (e.g., previous urethral surgery, stricture location, and quality of the local tissues). It is even possible to combine both ventral and dorsal graft placement in case of long-segment strictures or in case of very narrow strictures, as described by Hudak et al. [73] and Palminteri et al. [74].

Asopa has further modified this technique to a "dorsal inlay" free graft urethroplasty in which the urethra must not be dissected circumferentially to allow a dorsal onlay of the free graft [75]. In fact, this technique involves a ventral opening of the urethra followed by incising the dorsal urethral plate from the inside of the lumen. This adjusted approach has the advantage to be faster than a Barbagli procedure and can efficiently be administered when the surgeon intraoperatively finds that a ventral onlay procedure will not be possible. The success rates of a Barbagli procedure and an Asopa procedure are shown to be comparable [76].

It is a well-known fact that free graft urethroplasties at the penile urethra entail lower success rates than more proximal free graft procedures [64]. This observation may largely be explained by the relative paucity of corpus spongiosum at the more distal penile urethra. Hence, the graft almost fully depends on the vascular supply of the subcutaneous tissue in this region, which is strongly variable and much more tenuous than at the bulbar site. Against this background, it is assumed that dorsal graft placement is superior at the penile urethra, because then the cavernous bodies can act as a good vascular graft bed.

Later in the quest for minimally invasive urethroplasty, Kulkarni et al. described a new technique: the one-sided anterior urethroplasty with dorsolateral placement of the graft [44]. As such, only one side of the anterior urethra is dissected to allow graft augmentation while, on the other side, the vascular, neural, and muscular structures of the urethra are fully spared, which contributes to less tissue damage during urethroplasty. This may be particularly interesting at the penile urethra, where the vascular supply is more tenuous and rather vulnerable.

Failure after Free Graft Urethroplasty. The success of a free graft urethroplasty importantly depends on the relationship between the graft and its vascular bed. The graft has to be well in contact with a rich vascular bed in absence of any infection in order to survive. If one of these parameters is disturbed in any way, the risk of graft necrosis, and thus failure, exists. Even if none of these variables is disturbed, graft contracture can occur and may lead to restenosis of the urethra [77].



(a) (b)

Figure 9: Lingual mucosa graft harvesting. *(a) = right, sublingual graft site; (b) = submucosal fluid injection to allow hydrodissection*.

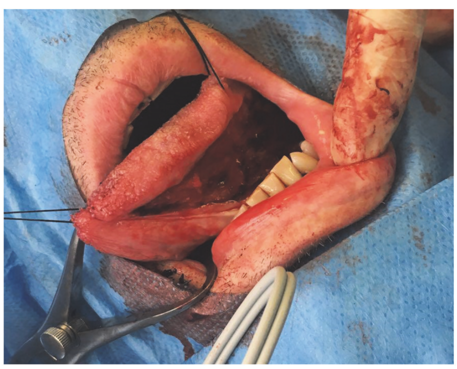


Figure 10: Nonclosure of the graft site. *The left, sublingual donor site is left open after thorough hemostasis.*

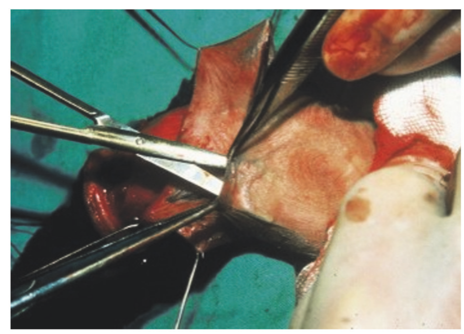


Figure 11: Duckett flap. *Mobilization of a pedicled Duckett flap (inner preputium).*

(3) Pedicled Flap Urethroplasty. Pedicled flaps carry their own vascular supply in the pedicle and therefore can survive independent of the surrounding tissues. The preputium (Figure 11) and penile shaft skin (Figure 12) are both ideal sites to mobilize a pedicled flap from to augment the penile and/or the bulbar urethra up to the bulb of the corpus spongiosum. In complicated cases, scrotal flaps can also be administered, preferably after destruction of the hair follicles [78], and, exceptionally, even intestinal flaps may be used for extraordinary reconstructions [79].

Pedicled flap urethroplasty can be administered in basically every urethral stricture case, from the meatus up to the posterior urethra, and is associated with excellent success rates [64, 80–82]. Moreover, it is shown that tubularized flaps perform as well as patch procedures, in contrast to free graft procedures [80–82].

Undeniably, pedicled flap urethroplasty also brings along several postoperative side-effects, such as sacculation and intra-urethral hair growth, and should not be considered a first-choice treatment for relatively simple cases. However, though technically challenging, every urethral surgeon should master this variety of techniques, because, sooner or later, this will be the only pertinent option left.

(4) Multistage Urethroplasty. Given the outstanding success rates of one-stage urethroplasty, the indications for multistage procedures have diminished remarkably. Nowadays, staged interventions are mostly reserved for redo cases in which there's a complete lack of healthy tissue and only very precarious vascularization.

Almost every multistage urethroplasty technique is derived from the original Johanson technique [83]. The general principle of this technique is to first open the diseased urethra longitudinally and then suture the created urethral edges to the borders of penile/scrotal skin (depending on stricture location). As such, the diseased urethra is left open and a neo-meatus originates in a hypospadias position. This is considered the first stage of a Johanson procedure. The second stage of Johanson's procedure basically consists of retubularizing this marsupialized urethra around a transurethral catheter and is performed at earliest 3 months after the first stage. In some patients, however, the urethral plate will be of poor quality, even after several months. In these cases, it might be necessary to incise this fibrotic or ischemic plate dorsally and to augment the urethra with a free graft, placed against the corporal bodies [84–88].

After Johanson, several surgeons—Turner-Warwick [89], Gil-Vernet [90], and Blandy [91]—have further adapted the

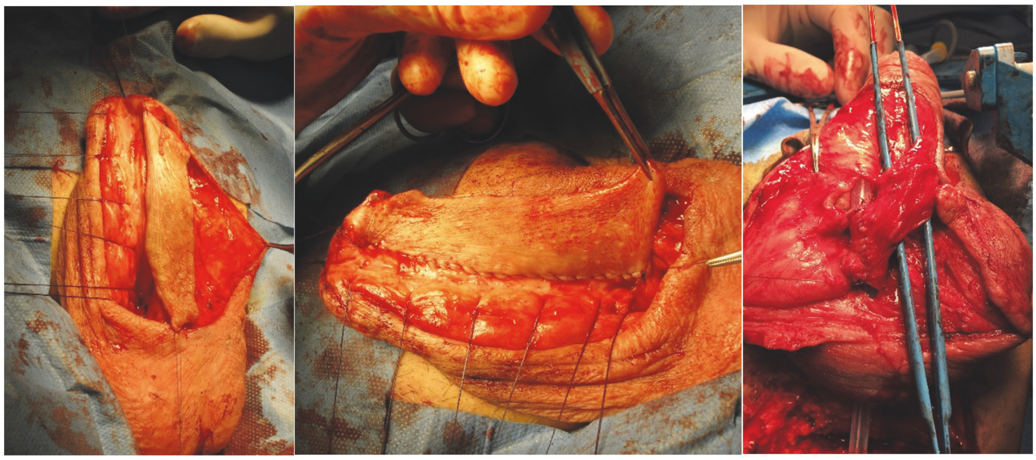


FIGURE 12: Orandi flap. *Mobilization of a pedicled Orandi flap (ventral longitudinal island; penile shaft skin).*

technique of staged urethroplasty, but the same idea is basically always respected.

(5) Mesh Graft Urethroplasty or Multistage Oral Mucosa Graft Urethroplasty. Mesh graft urethroplasty and multistage oral mucosa graft urethroplasty both represent a variation of multistage urethroplasty in which the disadvantages of tubularizing hairy skin segments (stone formation; infection) are avoided. With the mesh graft urethroplasty, a split thickness skin graft is harvested using a dermatome and meshed, and, with the multistage oral mucosa graft urethroplasty, a piece of oral mucosa is harvested and prepared as described above. The mesh graft or oral mucosa graft is then sutured in between the created urethral edges (after opening of the urethra) and the borders of the skin and, subsequently, during the second stage, there is no need to tubularize hair bearing skin, but only hairless graft material. These techniques are mostly reserved for complex reconstructions and mesh grafts are particularly interesting in cases with restricted graft/flap options [92, 93].

(6) Definitive Perineostomy. Nowadays, multistage urethroplasty is almost exclusively preferred in rather complex cases and in patients that have had numerous urethral interventions already. Often, these patients are perfectly happy to void without any problems after the first stage of an intended multistage procedure and wish to retain the created perineostomy without a second-stage procedure. This definitive perineal urethrostomy represents a well-accepted situation for many patients, especially multioperated and older ones.

For the creation of a definitive perineostomy, the Johanson and Blandy techniques are most frequently used and entail similar success rates [92]. With the Blandy technique, a perineal inverted-U incision is performed and the tip of this inverted-U flap is sutured against the deepest, most proximal part of the opened urethra (Figure 13). An alternative technique is the use of a 7-shaped flap, as described by French et al. [94]. In complex cases it might even be necessary to administer free grafts or mesh grafts in the creation of a perineostomy [95].

(7) Tissue-Engineering in Urethroplasty. Urethral reconstruction using matrix-bred tissue out of the patient's own urothelium or oral mucosa has recently been introduced as an alternative approach which mainly addresses the limitations inherent to the classic substitution urethroplasty. So far, tissue engineering with urothelium has been described in laboratory studies [96, 97] and, in 2018, Barbagli et al. have reported a success rate of 86% after MukoCell® graft urethroplasty in a clinical study (median stricture length of 5.0 cm and median follow-up of 55 months) [98]. In their technique, a 0.5 cm^2 oral mucosa biopsy was harvested and sent to the laboratory for tissue engineering. After 3 weeks, the manufactured piece of tissue was sent back to the hospital and administered during urethroplasty (ventral onlay, dorsal onlay, dorsal inlay, and combinations).

Today, the largest limit of tissue engineering lies within its cost, but, definitely, this technique involves several advantages, especially when the classic substitution materials become scarce or even totally absent. Furthermore, it reduces the amount of donor tissue that is required for reconstruction and could therefore potentially reduce the side-effects of the graft site that are seen after a classic free graft urethroplasty [98]. Nonetheless, to date, there is no data to support this statement and future studies will be required to elucidate this issue. Also, the same conditions as in a classic free graft urethroplasty (close, immobile contact with a well vascularized graft bed in absence of infection) will be required to allow a successful procedure.

(8) Combination of Techniques. In case of multiple urethral strictures or very long, often complicated urethral strictures, a combination of the aforementioned techniques might be necessary to offer the patient a one-stage solution [99, 100]. In order to do so, a combined perineal and penile skin incision might be necessary. The most popular combination is probably represented by a free graft urethroplasty at

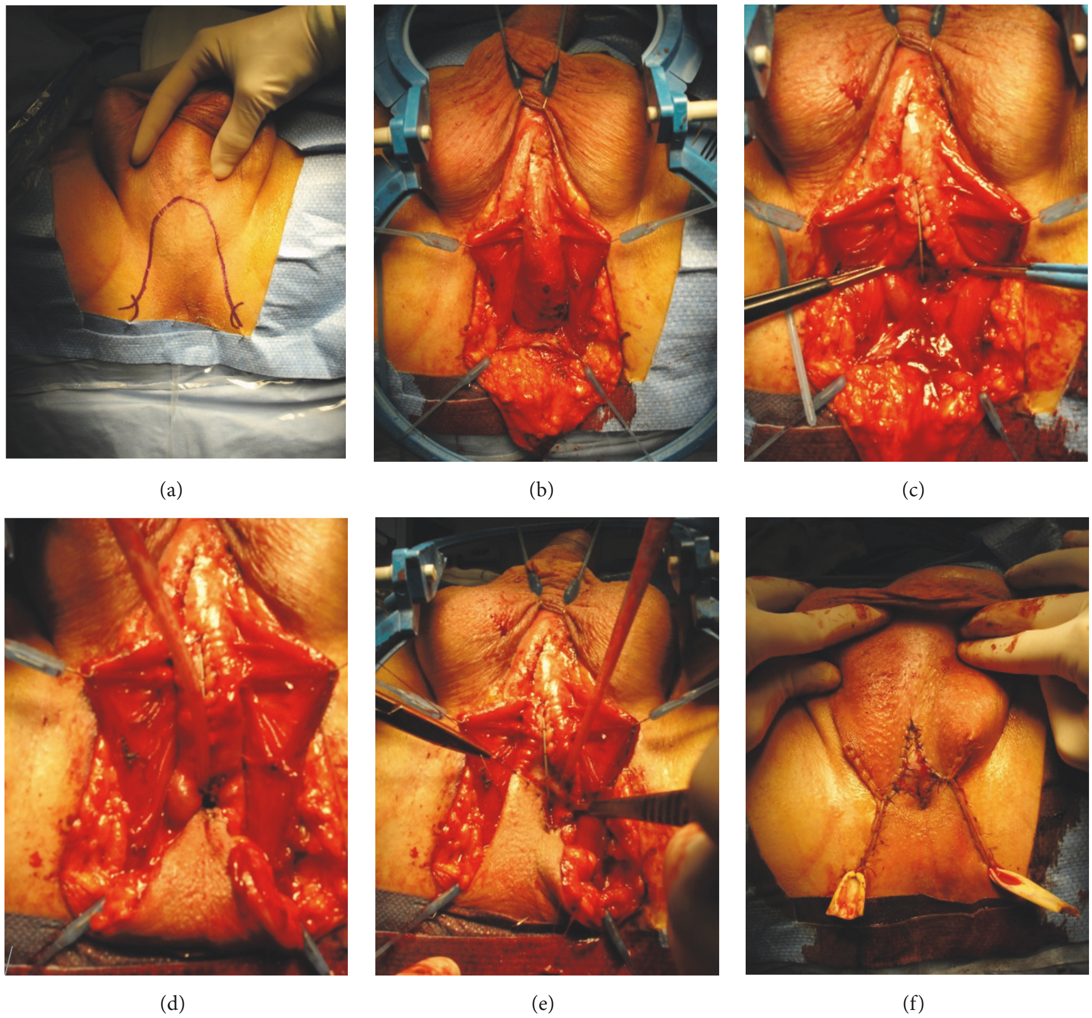


Figure 13: Blandy perineostomy. *(a) = inverted-U incision to create the Blandy flap; (b) = mobilized Blandy flap and exposure of the bulbar urethra; (c) = opening of the strictured area until patent proximal urethra is reached; (d) = suturing the tip of the Blandy flap to the deepest point of the opened urethra; (e) = further suturing the edges of the Blandy flap to the urethral edges; (f) = end-result of the Blandy perineostomy.*

the bulbar urethra, combined with a pedicled flap at the less vascularized penile urethra. However, basically every combination is possible but should be administered with common sense and respect to the urethral vascularization.

5.3.5. Choice of Surgical Technique. For a primary urethroplasty, the surgeon should always opt for the simplest and most straightforward technique that yields the highest success rates. Ideally, the chosen technique also represents the treatment option that least compromises the therapeutic armamentarium that might be needed in the future as there is always a risk for urethroplasty failure requiring one or more salvage treatments [101].

For isolated, short (≤3.0 cm), bulbar urethral strictures, the authors follow the end-to-end urethroplasty recommendation of the ICUD, although a lot of controversy exists as mentioned above [46, 49, 50]. From the moment a stricture can no longer be treated with anastomotic repair, substitution urethroplasty will be required, in which a free graft urethroplasty represents the easiest and most evident technique to treat stricture disease from the meatus up to the posterior urethra [64]. Herein, penile urethral strictures are preferably augmented dorsally because of the rich vascular bed that is provided by the corporal bodies. In most cases, a free graft procedure will be favored over a pedicled flap procedure since flap urethroplasties are technically more demanding and interfere more with the external appearance of the genitals. Furthermore, free graft urethroplasties importantly rely on the quality of the urethral vascularization, which will be progressively impoverished, surgery after surgery. Hence, it makes sense to administer free grafts earlier in the treatment cascade, thus fully utilizing its window of opportunity.

The more redo procedures a patient has undergone, the harder it gets to choose between surgical approaches, as the options become sparser and gradually less favorable. In these cases, it is hard to stipulate general rules as these treatment decisions are very case-specific and need to be well deliberated. In long, complex and multioperated urethral strictures, a preputial or scrotal skin flap could remain a viable option, at least if this tissue is still available. An alternative is to perform a multistage urethroplasty or to construct a definitive perineostomy, which is often well-tolerated by patients with an elaborate history of urethral stricture treatments.

It should be underlined that this decision-making process may not be universal and that there is a lot of controversy about treatment algorithms for urethral reconstruction, especially in the bulbar urethra [46, 49, 50]. However, no matter which algorithm is used, it is of utmost importance that every surgeon eager to perform a urethroplasty masters the variety of techniques as described above, especially because an intraoperative shift from one technique to another is sometimes unavoidable. Hence, it must be stressed that urethroplasty should only be performed in recognized referral centers with sufficient volume.

5.3.6. Peculiar Urethral Stricture Conditions and Locations

(1) Posterior Urethral Strictures. These strictures are characterized by the following:

(i) An anatomical proximity to the urethral sphincter and possible extension deeper than the urogenital diaphragm

(ii) A distraction defect between the prostatic apex and the distal urethral portion

(iii) Concomitant hematoma formation, infection, and/or previously failed urethral realignment procedures (endoscopic or open) which might lead to extensive stricture formation in the entire zone between both disrupted urethral ends, which makes it hard to recognize the local anatomy. Furthermore, in strictures related to a pelvic fracture, the displacement of bony fragments might hamper the exposure, which further complicates the surgical procedure

(iv) In traumatic strictures, the possibility of coexisting damage to the penis, scrotum, and/or perineum, which may heavily compromise the available surgical options to restore the urethral continuity

The standard approach after trauma related urethral injuries involves the immediate placement of a suprapubic catheter [52] followed by a delayed urethroplasty, generally after 3 months, although, in reserved cases, a delay of 6 weeks may be enough [102]. Placement of the suprapubic tube should always be guided by imaging studies as the bladder may have been displaced in all possible directions depending on the impact of the trauma. Then, 3 months later, the ideal moment for an end-to-end urethroplasty is reached because the hematoma will have been resorbed and the distraction defect between both urethral ends will beat its minimum.

(2) Meatal Strictures. Meatal strictures may be located only at the meatus urethrae but can also expand in the navicular fossa or the entire transglandular segment. In some cases, the meatal stricture is part of an entire diseased anterior urethra.

A meatal stricture is often considered as a minor and rather benign condition, although, in every case, the clinician has to consider the possibility of underlying lichen sclerosus. Furthermore, obtaining a perfectly functional and esthetic result is harder than it may seem. Herein, the severe deviation of the urinary stream represents the most bothersome complication as it will obligate the patient to void in a sitting position.

The true extent of a meatal stricture is often difficult to estimate preoperatively. In pronounced strictures, a RUG will usually be impossible to perform and, during a VCUG, the entire proximal urethral segment will dilate but will only poorly reveal the true length of the stricture. In fact, the most reliable length measurement takes place in the operating theatre. Hence, the surgeon starting the meatoplasty should always master a variety of techniques as every patient will need an individualized surgical approach.

Several techniques have been described to reconstruct the urethral meatus [103]. Many of these techniques, however, do not involve a closure of the glans and thus leave behind a hypospadias neo-meatus. From both a functional and an esthetic point of view, one should always attempt to close the glans and to restore the distal penile anatomy as meticulously as possible. Penile skin flap meatoplasty represents one of the suggested techniques but is nowadays gradually abandoned as it often leads to a slightly hypospadias meatal position afterwards. During this technique, a small pedicled penile skin flap can easily be mobilized after a subglandular incision to access the meatal urethra. An alternative approach is to cleave the glans and to dorsally incise the urethral plate into healthy, well vascularized tissue. Thereafter, an according graft can be harvested and dorsally laid in, according to Asopa [75], and the glans wings can be closed in two firm layers to prevent fistulas and glandular dehiscence (Figure 14). More recently, another alternative for meatal reconstruction has been described by Nikolavsky and involves transmeatal buccal mucosa graft repair of the meatus and navicular fossa [104]. During this procedure a wedge of scar tissue is cut out ventrally through the meatus and the tip of the buccal mucosa graft is put into the apex of the created defect using a double-armed suture following the inside-out principle. Thereafter, both sutures are tied externally and the same principle is used for the edges of the graft until adequate fixation is obtained.

The use of genital skin must be avoided in all patients with a lichen sclerosus related stricture as it can lead to a failed procedure [9]; in these cases, oral mucosa must be administered [105].

(3) Lichen Sclerosus Related Strictures. Lichen sclerosus is a chronic, inflammatory skin condition with a specific predilection for the genital region. Furthermore, this disease may importantly affect the penile as well as the bulbar urethra [8, 9]. These strictures are associated with higher failure rates after urethroplasty than strictures of any other etiology and require a specific therapeutic approach [9].

As mentioned above, it is generally accepted that lichen sclerosus related strictures are not to be treated with skin as substitution material, but with oral grafts [105]. Nonetheless, it remains unclear whether oral mucosa grafts are actually resistant to this disease or not.

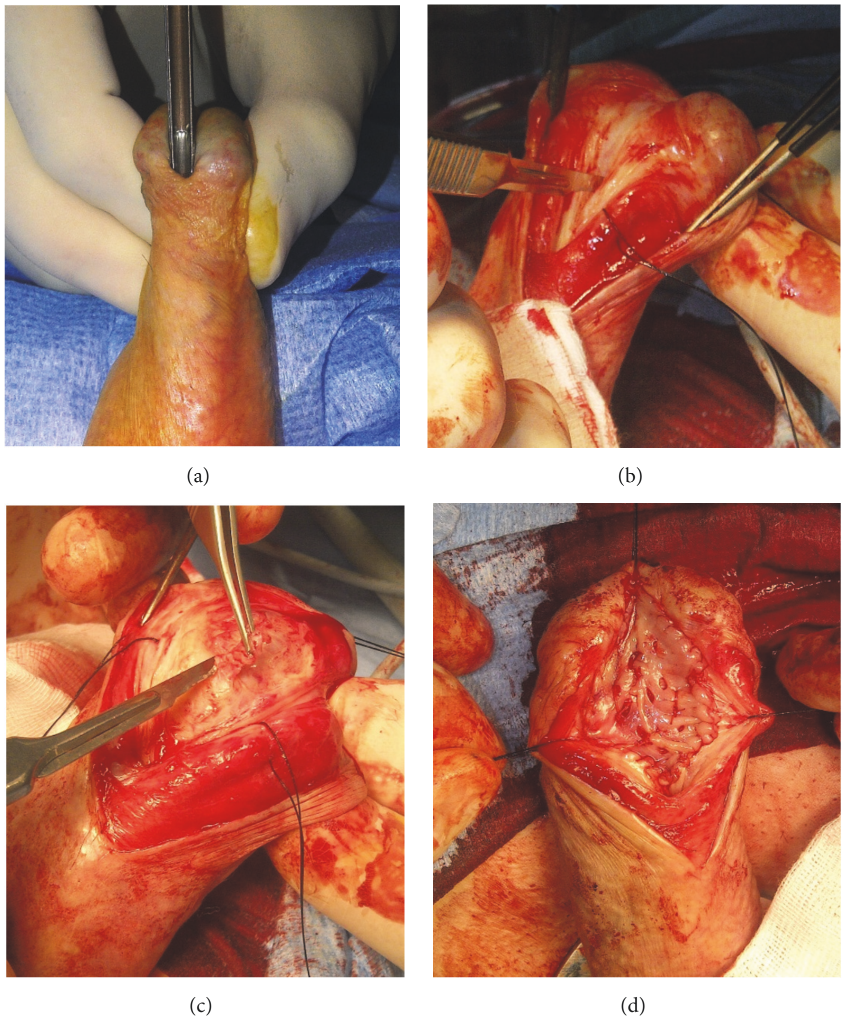


Figure 14: Asopa technique for meatal and navicular strictures. *(a) = opening of the meatal stricture with a grooved director; (b) = incision of the dorsal urethral plate; (c) = excision of fibrotic tissue; (d) = dorsal inlay of buccal mucosa graft.*

Based on good dermatological results after high-dosed, locally applied corticosteroids, its value has also been evaluated for intra-urethral administration and has shown satisfying results in small patient series [106, 107]. It makes sense that these substances would also be beneficial as an adjuvant to urethroplasty, but so far there is no evidence to support this statement.

(4) Urethral Strictures after Local Prostate Cancer Treatment. All local treatment options for prostate cancer (radical prostatectomy, external radiation therapy, brachytherapy, and focal prostate cancer treatments like high intensity focused ultrasound (HIFU) or cryotherapy) may contribute to subsequent stricture formation, located between the bladder neck and bulbar urethra [108]. These strictures are usually characterized by intense fibrosis and poorly vascularized surrounding tissues which may hamper a successful and uncomplicated surgical procedure. In most of the cases, an end-to-end urethroplasty is the technique of choice, especially because these urethral strictures are usually rather short [109–112]. The authors believe that if one of both urethral ends is well vascularized, a decent to good success rate may be expected [111]. Substitution urethroplasties have also been described for this indication and seem to bring along a successful surgical outcome [109, 112, 113]. However, these numbers are based on highly selected patient series and the true success of these procedures may have been overestimated.

It must be acknowledged that, overall, these patients are hard to treat and that urethroplasty in these cases holds an important risk for failure. Furthermore, the presence of a stricture may have concealed a problem of underlying incontinence, which may suddenly appear after a successful procedure in which the urethral patency has been restored. Hence, all patients should be thoroughly informed preoperatively and well counseled about the potential consequences of treating their stricture.

5.3.7. Impact of Urethroplasty on Sexual Life. In a literature review incorporating 36 studies with a total of 2323 patients, persisting de novo erectile dysfunction has been described in 1% of the patients after urethroplasty [114]. This number strongly varied between different studies and ranged from 0% to 38%, which may be attributed to differences in patient and stricture characteristics, types of repair, definitions of erectile dysfunction, and methods of questioning. On the other hand, a transitional decline in erectile function shortly postoperative (6 weeks) has been described with spontaneous resolution after 6 to 12 months [115].

With the classic transecting end-to-end urethroplasty, the erectile tissue is directly damaged during surgery and thus one could expect that erectile function importantly decreases after this procedure. This assumption has been illustrated by a study of Ekerhult et al., although they could only withhold a 5% incidence rate of de novo erectile dysfunction after end-to-end procedures [116]. Herein, the question remains whether nontransecting end-to-end urethroplasty is linked to lower postoperative sexual dysfunction without impeding the surgical success rates of urethroplasty by excision and primary anastomosis [59]. As regards free graft urethroplasty with buccal mucosa, studies have shown that these procedures do not impact the patients' postoperative erectile function [117, 118].

Ejaculatory function is often better after urethroplasty than before, provided the use of a technique in which the continuity of the bulbospongiosus muscle is actively restored during the multilayered closure of the perineum [119, 120].

5.3.8. Postoperative Course. After urethral reconstruction, it is important to provide urinary derivation as urine extravasation at the recently operated region might lead to important complications, such as abscess formation and phlegmon. When a free graft has been used, the authors routinely leave a 20 Fr transurethral catheter in place to avoid prolapse of the graft into the urethral lumen and to allow close contact between the graft and its vascular bed. In other cases, urinary derivation is assured through a 16 Fr transurethral catheter or a suprapubic tube. Nonetheless, it should be underlined that catheter use after urethral reconstruction is extremely variable between different urethroplasty centers, without clear data if one regimen is truly better than the other.

Most patients are discharged from the hospital on the second or third postoperative day with the indwelling catheter in place. At that moment, instructions for wound care are provided, which are specifically important in patients with a perineal wound. These wounds need to be kept dry and clean. Therefore, the use of a hair dryer (3 to 4 times a day) and repeated disinfection is advised, a method that was copied from wound care principles after episiotomy in females.

Routine perpetuation of the antibiotic treatment regimen must be limited to those patients in which a preoperative urinary tract infection has been established. In these cases, appropriate antibiotics (according to the antibiogram) are continued for a maximum of 5 days since any longer use will only contribute to the problem of resistant microorganisms. There is no clear evidence to support this advice in urethroplasty, although the authors base this recommendation upon the general rules and principles of antibiotic therapy.

After 7 to 14 days, the first postoperative visit is scheduled and involves the execution of a VCUG, after filling the bladder with contrast medium through the indwelling catheter. Some authors argue the value of a routine postoperative urethrography as only few patients will show contrast extravasation requiring a catheter replacement [121, 122]. However, these authors routinely leave the catheter for 3 weeks instead of 1 or 2 weeks. It has been established that indwelling catheters bring along important side-effects and complications and thus it might certainly benefit the patient to remove the catheter as early as possible [123]. Moreover, it has been demonstrated in our department that catheter removal after 8 days is as safe as prolonged catheter dwell-time and that extravasation at first VCUG has an important negative prognostic value [124].

5.3.9. Follow-Up after Urethroplasty. To date, the ideal follow-up of patients after urethroplasty remains poorly defined. At Ghent University Hospital, patients are scheduled to revisit after 3 months, after 12 months, and annually thereafter. During these visits, anamnesis, physical examination, uroflowmetry, and Urethral Stricture Surgery Patient Reported Outcome Measures (USS-PROM) questionnaires are routinely administered [125, 126]. Additional urethrography and/or cystoscopy are/is only performed in case of obstructive voiding symptoms or a maximal flow rate of < 15 mL/s.

To date, there is no clear consensus about standard administration of urethrography and/or urethroscopy during follow-up. There is, however, a remarkable trend to use patient-reported outcome measures (PROMs) after urethral reconstruction. In 2011, Jackson et al. created and validated the USS-PROM, a questionnaire specifically made for patients after urethroplasty [125]. Later, numerous validated translations have been reported and implemented in routine clinical practice [125–132].

The optimal follow-up schedule will need further elucidation in the future. Presumably, this will not be a story of "one-size-fits-all" as urethral stricture disease entails a very heterogeneous patient cohort which certainly demands patient-adapted follow-up strategies.

6. Conclusion

Male urethral stricture disease embodies a very heterogeneous condition in which thorough knowledge about anatomy, etiology, symptoms, diagnosis, and treatment aspects is crucial in optimizing care of these patients. Future prospective research will be warranted to gain further evidence and to refine the current practice of managing male urethral stricture disease.

Abbreviations

CT: Computed tomography
DVIU: Direct vision internal urethrotomy
EPA: Excision and primary anastomosis
HIFU: High intensity focused ultrasound

ICUD: International Consultation on Urologic Diseases
MMC: Mitomycin C
MRI: Magnetic resonance imaging
Qmax: Maximal urinary flow rate
RR: Relative risk
RUG: Retrograde urethrography
USS-PROM: Urethral Stricture Surgery Patient Reported Outcome Measures
VCUG: Voiding cystourethrography.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Research Article

Urogynecological and Sexual Functions after Vecchietti Reconstructive Surgery

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Hypothesis/Aims of Study. Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome is the second most common cause of primary amenorrhea. The ESHRE/ESGE categorizes this disorder within the class 5 uterine malformation of the female genital tract anomalies. It is characterized by congenital absence of the uterus, cervix, and upper part of the vagina in otherwise phenotypically normal 46XX females. These patients have normal ovaries, biphasic ovarian cycle, and female psychosexual identification. Laparoscopic Vecchietti's operation—surgical method in which the vagina increases in size by gradually applying traction to the vaginal vault—is one of the methods used to treat MRKH. The aim of this study was to establish the urogynecological and sexual functions after Vecchietti's operation. *Study Design, Materials and Methods.* Fifteen patients with MRKHS who underwent laparoscopic Vecchietti's operation were included. A control group of 15 age-matched, childless, sexually active women were examined during the same period. All patients underwent the basic evaluation of anatomical outcomes. Sexual outcomes were established by the Polish validated Female Sexual Function Index (FSFI) questionnaire. Continence status was assessed by Polish validated Urinary Distress Inventory (UDI-6) and the Incontinence Impact Questionnaire (IIQ-7). *Results.* Mean age of MRKH group was 22.06±5.13 yrs. Mean follow-up after surgery was 8.02±3.43 yrs. Mean age of women from control group was 22.4±4.35. Mean FSFI scores show good quality of sexual life in both groups. UDI-6 scores showed that patients after Vecchietti surgery have urogynecological problems significantly more often than healthy women do. Based on the IIQ-7, it is evident that one patient from the MRKH group (6,6%) suffers from stress urinary incontinence and the rest (20%) have rather irritative problems with the functioning of the lower urinary tract. *Conclusion.* Quality of sexual life after the Vecchietti's operation in long-term follow-up does not differ from that of healthy women, but these patients suffer more frequent from urogynecological complaints. The trial is registered with NCT03809819.

1. Introduction

Mayer–Rokitansky–Küster–Hauser syndrome (MRKHS) is the second most common cause of primary amenorrhea. Indeed, the European Society of Human Reproduction and Embryology (ESHRE) and the European Society for Gynaecological Endoscopy (ESGE) categorize this disorder within the class 5 uterine malformation category of the female genital tract anomalies [1]. It is characterized by the congenital absence of the uterus, cervix, and upper part of the vagina in otherwise phenotypically normal 46XX females [2]. These patients have normal ovaries, biphasic ovarian cycles, and female psychosexual identification. While vaginal aplasia is detectable with the physical examination of babies, it is usually diagnosed during adolescence with primary amenorrhea, and, rarely, in the beginning of the sexual life, as complaints of dyspareunia or unsuccessful intercourse [3]. Laparoscopic Vecchietti's operation—a surgical method in which the vagina is increased in size by steadily applying traction to the vaginal vault—is one of the methods used to treat MRKH [4]. This approach involves gentle stretching of the patient's own vaginal skin. An oval device is placed on the vaginal dimple and drawn up gradually by threads that run through the oval from the perineum into the pelvis and out through the abdomen, where they are attached to a traction device. To create a neovagina, the tension is increased on the traction device to pull the thread and stretch the vagina by approximately 1 to 1.5 cm/d until the vagina reaches approximately 7-8 cm in depth [4]. Postoperative management including repeated dilatation of the vaginal dimple is established at least for 6 months: during initial 3 months the dilator is placed on the vaginal dimple using firm pressure for 10 minutes two times a day, for successive 3 months 2-3 times per week. Treatment with dilators was ceased when it was successful; satisfactory intercourse was achieved. Initial supervision and education of proper dilatation were essential to avoid the urethra and anus dilatation [5]. The created neovagina is then covered by nonkeratinized squamous epithelium. MRKHS compromises sexual life and makes natural reproduction impossible. Moreover, associated upper urinary tract malformations are found in approximately 30% of all cases of MRKHS. Among these are unilateral renal agenesis, ureter malformation, ectopia of one or both kidneys, renal hypoplasia, horseshoe kidney, and hydronephrosis [6]. Available literature is insufficient in the area of urogynecological dysfunction such as urinary incontinence in patients treated for MRKHS.

The aim of this study was to establish the degree of urogynecological and sexual functions after the Vecchietti's operation.

2. Materials and Methods

Between 2009 and 2015, thirty-five women underwent Vecchietti's operation performed by the same surgeon in our department. For the purposes of this study, we sent 35 letters inviting them for a check-up. Of these, fifteen patients arrived for examination; hence, fifteen patients with MRKHS who had undergone laparoscopic Vecchietti's operation were included. A control group of 15 age-matched, childless, sexually active women were examined during the same period. Those patients came for routine check-up to our outpatient department. All patients provided written informed consent to participate in the study.

All patients underwent the basic evaluation of anatomical outcomes. Pelvic Organ Prolapse Quantification (POPQ) was assessed for every patient. Additionally, we performed the cough stress test (CST) with comfortably full bladder in supine and standing position—recommended in the evaluation of uncomplicated female patients with the complaint of stress urinary incontinence (SUI) [7]. We determined the patient's bladder volume at the time of CST via an ultrasound bladder scan prior to examination. Test was performed in a range of bladder volumes between 200 and 400 ml.

Urine test strip was also done to determine possible pathological changes in patient's urine.

Sexual outcomes were established by the Polish validated Female Sexual Function Index (FSFI) questionnaire, of 19 questions. These enable an assessment of sexual function over the previous 4 weeks. The subscale scores ranged from 0 to 6, with higher scores indicating better sexual function. Subjects obtaining a total PL-FSFI score of 27.50 or lower were considered to have sexual dysfunction [8].

Continence status was assessed by 2 questionnaires: Polish validated Urinary Distress Inventory (UDI-6) and the Incontinence Impact Questionnaire (IIQ-7). IIQ-7 measures the impact of urinary incontinence on activities, roles, and emotional states, whereas the UDI-6 measures how troubling the symptoms are. UDI-6 consists of 6 items, which are subdivided into 3 domains: IS-irritative symptoms, SS-stress symptoms, and OS-obstructive/discomfort symptoms. IIQ-7 consists of 7 items, which are subdivided into 4 domains: PA, physical activity; TR, travel; SA, social activities; and EH, emotional health. For both UDI-6 and IIQ-7, a higher score equals higher disability (completely compromised by urinary symptoms =100). Over all, these questionnaires result in a 0-400 scale: the greater the score, the more problematic the incontinence [9].

3. Statistical Analysis

Statistical analysis was performed using Statistica v. 12.0 software (StatSoft, Poland). P values less than 0.05 were considered significant. Variables that were not normally distributed (P <0.05 by Shapiro-Wilk test) were analyzed via the Mann-Whitney U test.

4. Results

Mean age of MRKH group was 22.06±5.13 yrs. Mean follow-up after surgery was 8.02±3.43 yrs. Mean age of women from the control group was 22.4±4.35.

All patients included in the study did not experience intraoperative complications. During examination, we did not observe evidence of postoperative complications or vaginal scarring. In the study group, vaginal length was 7±1.2 cm and all women were in the POPQ-0 stage. In the control group, all women were also in the POPQ-0 stage.

Urine test strip tests were normal for patients from both groups.

All women were in a stable relationship. 14 women (93%) from the MRKH group declared a satisfactory sexual life and this was confirmed by the FSFI questionnaire results. In the control group, sexual satisfaction was declared by 100% of all patients, but the FSFI results confirmed this in 14 (93%) cases.

FSFI and UDI-6, IIQ-7 results are shown in Table 1.

4.1. Interpretation of Results. FSFI scores show good quality of sexual life in both groups. Indeed, women from both groups have scores higher than the mean result for the general Polish population (= 27.5).

UDI-6 scores showed that patients after Vecchietti surgery have urogynecological problems significantly more often than healthy women do. Declared problems started about 7 months after surgery. Based on the IIQ-7, it is evident that one patient from the MRKH group (6,6%) suffers from stress urinary incontinence and the rest (20%) have rather irritative problems with the functioning of the lower urinary tract.

Table 1: FSFI and UDI-6, IIQ-7 results.

QUESTIONNAIRE GROUP	FSFI Me (min-max)	UDI-6 Me (min-max)	II Q7 Me (min-max)
MRKH (n=15)	29.55 (6.80-32.6)	116.55 (0.00-333.00)	0.00 (0.00-366.3)
CONTROL (n=15)	30.95 (21.9-35.4)	33.3 (0.00-199.8)	0.00 (0.00-133.2)
Test U Mann-Whitney (p)	0.43	0.05	0.34

4.2. Discussion. Vecchietti's operation is one of the leading treatment options for MRKHS. The resulting neovagina enables women with this syndrome to have sexual intercourse. In our study, we confirmed that this method is well accepted by patients in the aspect of sexual satisfaction; however, urogynecological problems affect this group more often than do the healthy population. Previous studies have evaluated the aspect of megalourethra and urinary incontinence due to urethral coitus [10], but stress urinary incontinence problems after the Vecchietti's operation have been only shown in case reports [11, 12]. We agree with Bianchi et al. that the creation of a neovagina can alter the previous anatomy, modifying the balance in the pelvic floor. This leads to the change in the urethrovesical angle and a lack of suburethral support, allowing hypermobility of the urethra [11]. The aforementioned can be the reasons for urinary incontinence. In our study, however, we also observed irritative problems that cannot be explained by pelvic organ prolapse (POP) or bladder infection. Huebner et al. describe the support structures in pelvis before and after Vecchietti's surgery in magnetic resonance imaging. The support ligaments are present in these women preoperatively and the Vecchietti's procedure simply extends the vagina into these areas. Scar tissue at the apex as a result of the peritoneal tunneling during the Vecchietti procedure might enforce apical support of both cardinal and uterosacral ligaments. Missing scar tissue can explain why prolapse has been described quite often after self-dilatation [13].

The FSFI scale used in our study assesses all aspects of a woman's sexual functioning in 4 domains: desire, excitement, lubrication, and orgasm. In our study, the sexual function self-declared by our study group was good. This is no surprise, as a large majority of published studies show similar results [14–16]. We observed problems in only 1 out of 15 women. She was the oldest participant of the study and was 33 at the time of operation; she was observed for 6 years afterwards and usually declared lack of satisfaction in all aspects of sexual life apart from desire.

5. Study Limitations

This study includes only a small group of patients; this is partly the result of a limited population of women with MRKHS. The second reason for an insufficient study group in terms of population is the fact that only 15 out of 35 operated women came for evaluation. Most women are operated on when they are 18 years old; they finish secondary schools and travel to study in different towns and sometimes other countries, so it is difficult to contact them.

6. Conclusion

Quality of sexual life after the Vecchietti's operation in long-term follow-up does not differ from that of healthy women, but these patients suffer more frequent from urogynecological complaints.

These findings support the need for further research in a larger study group to assess urogynecological outcomes of the Vecchietti's operation.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Disclosure

An abstract (#346) with preliminary results of this study was presented at the International Continence Society Annual Meeting, September 12-15, 2017, in Florence, Italy.

Conflicts of Interest

The authors declare no conflicts of interest.

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Review Article

Female Urethroplasty: A Practical Guide Emphasizing Diagnosis and Surgical Treatment of Female Urethral Stricture Disease

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Female urethral strictures are rare. Guidelines on how to diagnose and treat these strictures are lacking. At present, only expert opinion is available to guide clinical practice. Once the diagnosis is suspected based on obstructive voiding symptoms and uroflowmetry, most clinicians will use in addition video-urodynamics (including urethrography), urethral calibration and cystourethroscopy for confirmation of the diagnosis. Clinical inspection and gynaecological examination are also important. Urethral dilation is usually the first-line treatment despite the lack of long-term success. Female urethroplasty is associated with higher success rates. A multitude of techniques are described but not one technique has shown superiority above another. This narrative review aims to provide a clinical guide for diagnosis and treatment to the urologist motivated to perform female urethroplasty.

1. Introduction

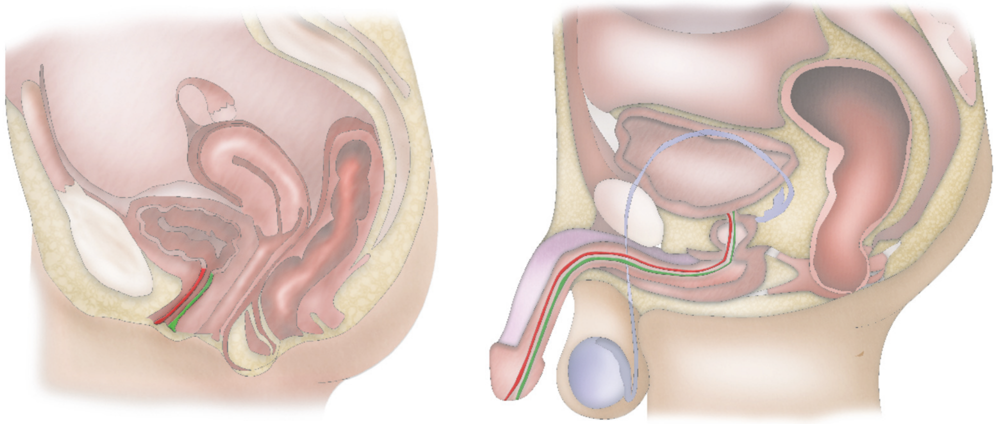
Female urethral strictures are rare but can cause severe symptoms impacting the patient's quality of life. About 10% of women with obstructive voiding will have a true ("anatomical") urethral stricture [1–3]. First-line treatment usually consists of dilation(s) but long-term cure rates are disappointing [4]. In males, several techniques of urethral reconstruction (urethroplasty) have been described and entail extensive experience at high-volume centers with high cure rates [5]. On the contrary, experience with female urethroplasty and the literature about it are scarce with only a few case series with limited follow-up. The rarity of the disease, the lack of experience, and the fear of functional complications (e.g., urinary incontinence) might hamper urologists to perform female urethroplasty. The aim of this narrative review is to provide the urologist treating female urethral strictures a practical guide in which diagnostic modalities are available and to provide a well-illustrated summary of the most commonly used techniques of female urethroplasty.

2. Surgical Terminology

The terminology used in female urethroplasty can be confusing and needs further clarification. The definition of dorsal and ventral to describe the location at the urethra is derived from male urethroplasty but is from an anatomical point of view not logic in females [3]. In males, the ventral part of the pendulous urethra is the part pointing forward during erection whereas the ventral part of the bulbar urethra is pointing downwards and even backward at the membranous urethra (Figure 1). In females, the ventral part of the urethra is the part pointing backward, towards vagina. The dorsal part is pointing forward towards the pubic bone. The anterior vaginal wall is the part of the vagina in direct contact with the urethra and bladder whereas the posterior wall is in contact with the rectum (Figure 1). A proximal stricture is a stricture close to the bladder neck, whereas a distal stricture is located close to the urethral meatus.

3. Preoperative Evaluation

A urethral stricture will cause obstructive voiding which is clinically translated into a weak urinary stream, sensation of



(a) (b)

Figure 1: Female versus male urethral anatomy. *(a) = female urethral anatomy; (b) = male urethral anatomy. Green = ventral urethra; red = dorsal urethra.*

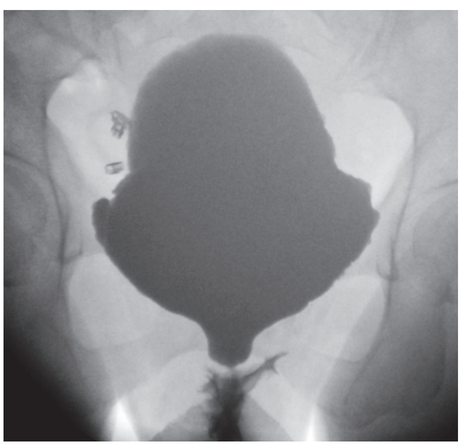


Figure 2: Wine glass image. *Voiding cystourethrography with a distal female urethral stricture and prestenotic dilation.*

incomplete voiding, straining, frequency, and nocturia [6, 7]. Many women also experience pain during micturition and urgency [1, 3, 7, 8]. Because of residual urine, these women are at risk for developing recurrent urinary tract infections [3, 6, 7, 9]. In women with lower urinary tract symptoms, uroflowmetry must be part of the diagnostic work-out and a plateau-shaped curve is suggestive for a stricture [10]. A gynaecological examination is indispensable as it might directly reveal a meatal stenosis and the presence of lichen sclerosus, pelvic organ prolapse, or periurethral abnormalities. This examination must also emphasize the quality of local tissues which might be used for urethral reconstruction [1, 2]. The inability to pass a 14 Fr urethral catheter is almost pathognomonic for the presence of a urethral stricture, although there is no strict definition of the normal caliber of the female urethra [3, 4, 11]. Cystourethroscopy might directly visualize the stricture but provides no information about the stricture length. In case of meatal or distal urethral strictures, insertion of the scope might not be possible, especially for the very narrow strictures [4]. Postvoidal ultrasonography can show residual volume inside the bladder [8]. Vaginal ultrasound using an 8 MHz probe can show the presence of the stricture after instillation of gel through the meatus. Retrograde urethrography, the standard evaluation in males, is not practical in females [8, 12]. Instead, antegrade voiding cystourethrography (VCUG) must be used. Filling of the bladder is accomplished by either suprapubic access, if a suprapubic catheter has been placed, or passing a small-caliber (e.g., 5Fr feeding tube) catheter through the stricture inside the bladder. Images are made at start, with full bladder, during voiding and after voiding. Bladder diverticula might be present as well as vesicoureteral reflux. During voiding, the urethra proximal to the stricture will show dilation with abrupt narrowing at the stricture site (Figure 2, "wine glass image") [6, 13]. Thus, VCUG will provide information about both the location (proximal, mid, and distal) and the length of the stricture.

Video-urodynamics combines this imaging with pressure-flow studies and provides as such a more complete evaluation [1, 4, 7, 9, 10]. In case of any doubt of concomitant abnormalities (urethral diverticula, abscess formation, etc.), pelvic MRI will provide useful anatomical information [2, 4, 10] (Figure 3).

A few days before operation, a urine culture must be performed and antibiotics must be started in case of infection the day before surgery according to the antibiogram.

No guidelines exist on which diagnostic modalities must be used during the work-out [3], but before start of urethroplasty, the surgeon must have obtained sufficient information on the presence, extent, and location of the stricture as well as on the quality of surrounding structures in order to be prepared for the urethroplasty.

4. Surgical Guide

4.1. Patient Positioning and Preparation. In postmenopausal women, intravaginal estrogens may be administrated to treat

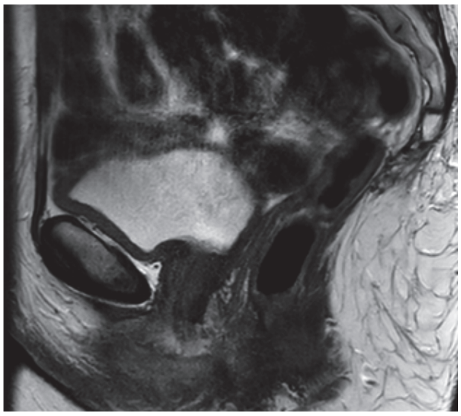


Figure 3: MRI of the female pelvis. *The urethra is clearly visible without the presence of a urethral diverticulum or periurethral abscess.*

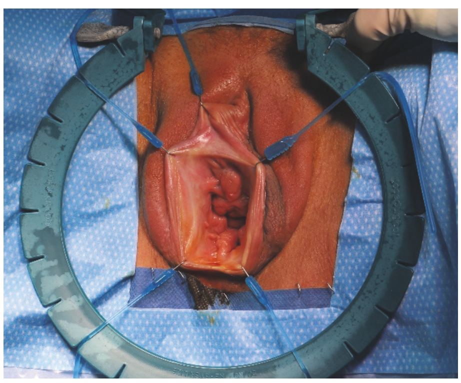


Figure 4: Exposure of the female urethra and vagina using the lone-star retractor.

vaginal mucosa atrophy [14]. In order to have a stable and mature stricture, urethroplasty must be postponed 3 months after the last dilation or urethrotomy [15]. All patients are placed in the lithotomy position. If a suprapubic catheter is present, the bladder is instilled with 100cc of 1:1 diluted povidone-iodine solution. The labia minora are retracted by sutures or a lone-star retractor in order to have a good exposure of the vestibulum, the urethral meatus, and the vaginal introitus (Figure 4) [9, 10]. Vaginal access (and access to the more proximal urethra) is facilitated using Doyen's vaginal blade retracting the posterior vaginal wall [16]. A guidewire is placed through the urethra inside the bladder in order to avoid creation of false passage during opening of the stricture [17]. Suture materials for urethral reconstruction are absorbable sutures 4.0 (adults) or 5.0 (children–adolescents).

4.2. Surgical Technique

4.2.1. Heineke-Mikulicz Meatoplasty. The stenotic meatus is ventrally incised in a longitudinal fashion until healthy urethral mucosa is reached that allows passage of a 20Fr catheter. The borders of the urethral mucosa are sewed to the borders of the vaginal mucosa in a transverse fashion with separate sutures [1].

4.2.2. Flap Urethroplasty

Anterior Vaginal Wall Flap ("Blandy Flap") (Figure 5). An inverted U-incision is made at the anterior vaginal wall, just below the ventral urethral meatus. The flap is dissected away from the ventral urethra over 3 cm with preservation of the submucosal layer containing the vascular pedicle of this flap. The ventral side of the urethra is incised until healthy proximal urethral mucosa is identified allowing passage of a 20Fr catheter. Stay sutures are placed on both sides of the opened urethra in order to facilitate exposure. The flap is turned towards the opened urethra and the tip of the U-flap is sutured to the proximal part of the opened urethra with 3 sutures. The edges of the flap are further sutured to the edges of the urethra with running or interrupted sutures on both sides until the level of the external meatus. The remaining base of the flap is sutured to the borders of the vaginal mucosa with separate Donati sutures [15].

Vestibular Flap ("Montorsi Flap") (Figure 6). An inverted-Y incision is made at the dorsal urethral meatus. The distal urethra is dissected away from the clitoris and surrounding suburethral tissues but without accessing the ventral urethrovaginal plane. Once the dorsal urethral wall has been sufficiently exposed, a dorsal urethral incision is made. The strictured urethra is further opened until healthy proximal urethra is encountered allowing passage of a 20 Fr catheter. Stay sutures are placed as described above. According to the length of the stricture, a 1.5-3cm long and 1 cm wide vestibular flap is mobilized from the right or left side, just aside the vertical vestibular incision. A flap with rich blood supply is needed and as a consequence superficial submucosal dissection must be avoided. The tip of the flap is sutured to the proximal end of the opened urethra with 3 separate absorbable sutures. The borders of the flap are further sutured to the borders of the opened urethra on both sides with a running suture. The base of the flap is finally sutured to the vestibular mucosa with interrupted absorbable Donati sutures [7].

Lateral Vaginal Wall Flap ("Orandi Flap") (Figure 7). This technique is inspired by the ventral longitudinal island penile skin flap in male urethroplasty and hypospadias reconstruction [14, 16]. A midline [14] or slightly lateral C-shaped [16] incision is made at the anterior vaginal wall. Dissection is directed towards the ventral urethra and the urethra is opened at the level of the stricture. The stricture is further opened along the guidewire until healthy proximal urethra is identified. A 2 cm wide flap with a length according to the length of the opened urethra is harvested from the lateral vaginal wall. Medially, the dissection of the flap is performed deep along the periurethral tissues. Laterally, the dissection is done along a superficial submucosal plane. This creates a laterally based vascular pedicle. The mobilization of this pedicle must be done sufficiently in order to allow the mucosal flap to be turned and sutured into the opened urethra. If hemostasis is needed, meticulous bipolar hemostasis is advised in order not to damage the vascularization of the flap. The medial surface of the flap is sutured towards the ipsilateral side of

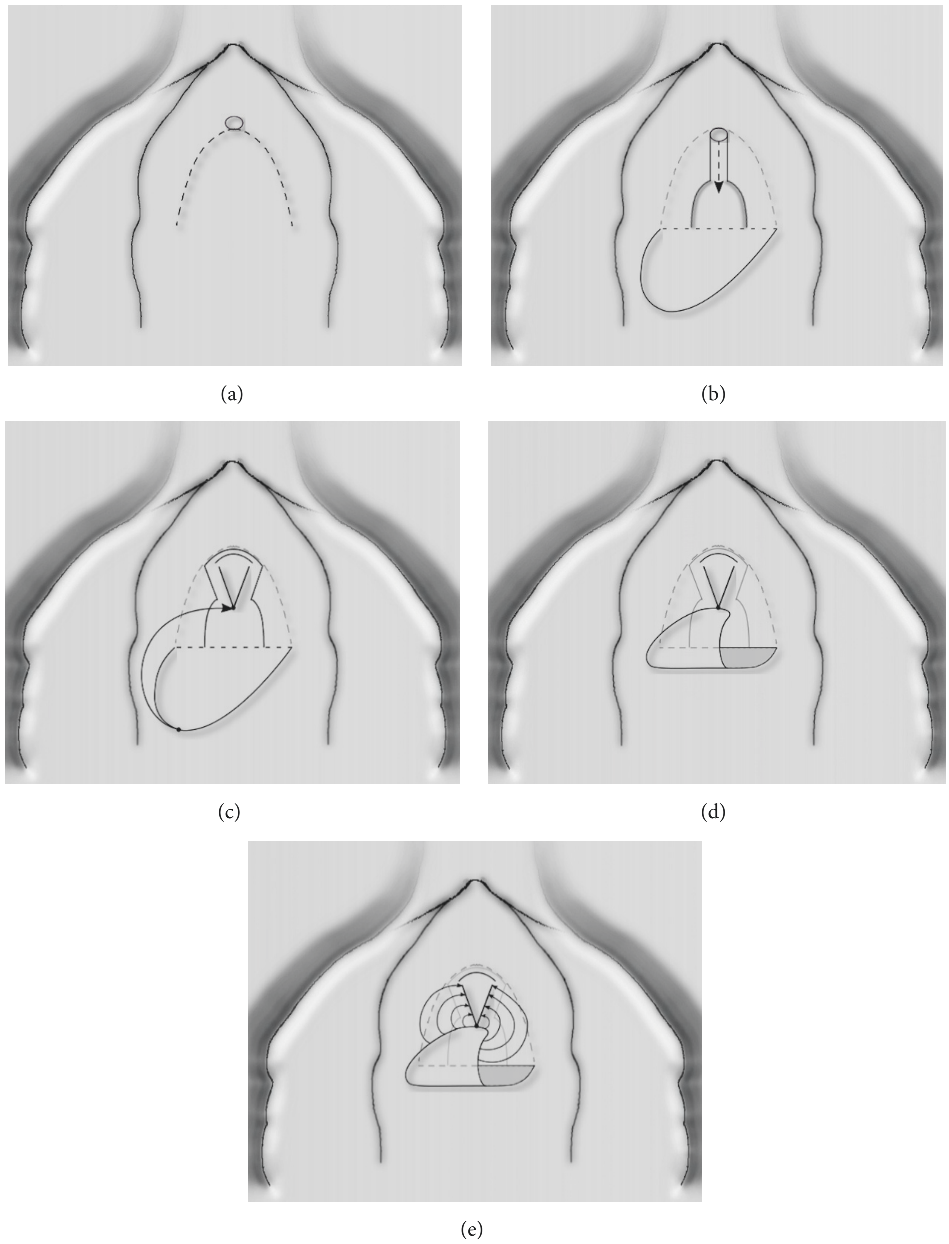


Figure 5: Anterior vaginal wall flap ("Blandy flap"). *(a) = inverted U-incision; (b) = ventral stricturotomy; (c) & (d) = suturing the tip of the U-flap to the proximal part of the opened urethra; (e) = further suturing the edges of the flap to the urethral edges.*

the urethra. The mucosal surface of the flap is turned towards the urethral lumen and the initial lateral side of the flap is sutured to the contralateral side of the urethra. The vaginal wall is closed with interrupted Donati sutures 2.0 above this reconstruction.

4.2.3. Free Graft Urethroplasty. A multitude of grafts (vaginal, labial, buccal, or lingual mucosa) have been described in female urethroplasty [4]. In order to promote imbibition and inosculation, grafts require suturing onto a well-vascularized graft bed and the graft itself needs to be carefully defatted.

Dorsal Onlay (Figures 8 and 9). A semilunar suprameatal incision is made. The plane between the clitoris bodies and the dorsal urethra is dissected. The pubic bone is digitally palpated and marks the point of proximal dissection [18]. The dorsal urethra is incised and the stricture is opened along the guidewire until healthy proximal urethra is encountered. Stay sutures are placed at the urethral edges immediately after opening of the stricture. A graft is harvested according to the dimensions of the stricture. The graft is placed with its mucosal surface towards the urethral lumen. The edges of the graft are sutured to the edges of the opened urethra with a bilateral running suture. Suturing is started at the proximal

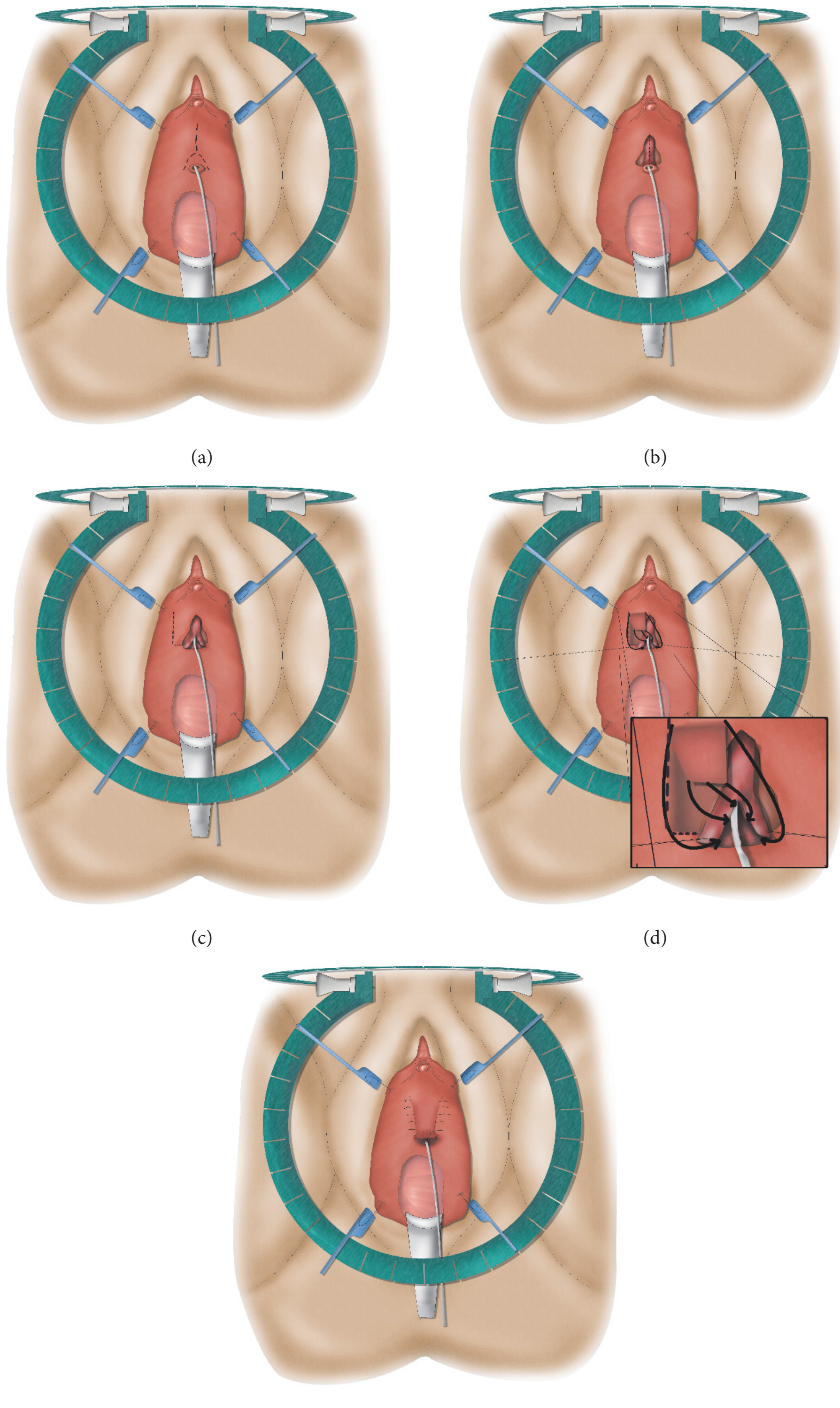
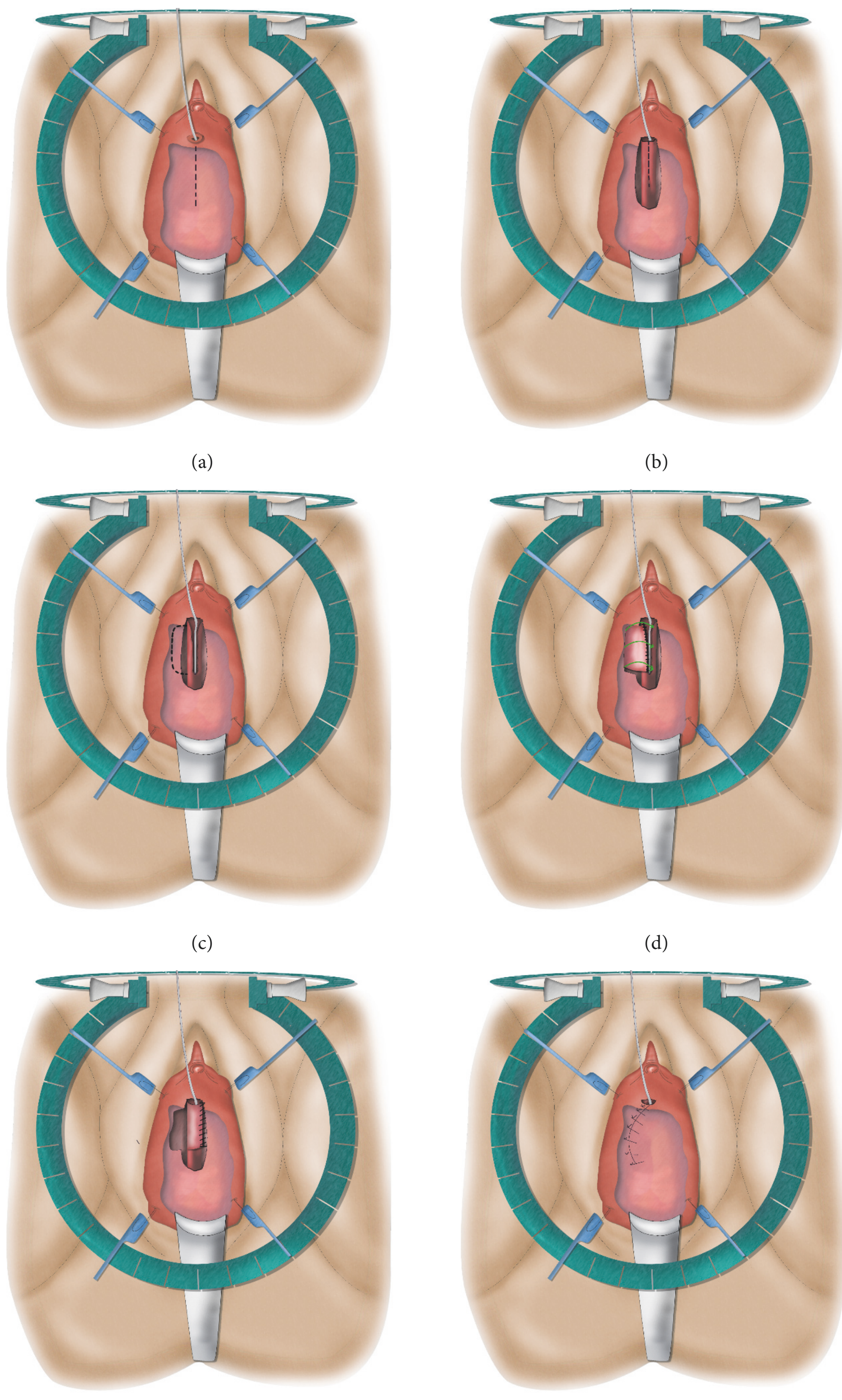


Figure 6: Vestibular flap ("Montorsi flap"). *(a) = inverted-Y incision; (b) = dorsal stricturotomy; (c) = mobilization of the vestibular flap; (d) = suturing the tip of the flap to the proximal end of the opened urethra and the edges of the flap to the urethral edges; (e) = suturing the base of the flap to the vestibular mucosa.*

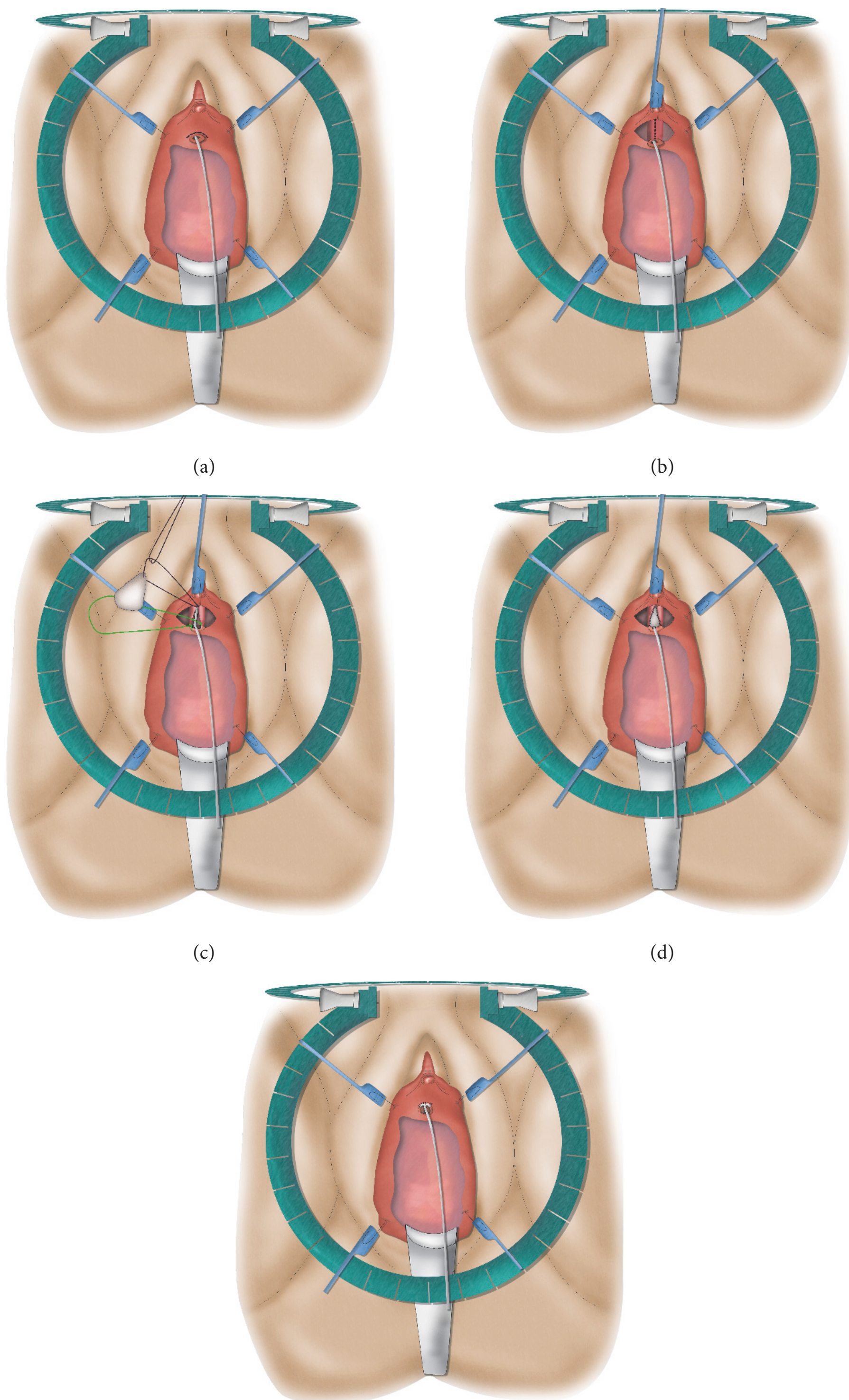


(a) (b)

(c) (d)

(e) (f)

Figure 7: Lateral vaginal wall flap ("Orandi flap"). *(a) = longitudinal midline incision at anterior vaginal wall; (b) = ventral stricturotomy; (c) = mobilization of the lateral vaginal wall flap; (d) = suturing the medial surface of the flap towards the ipsilateral side of the urethra; (e) = turning the mucosal surface of the flap towards the urethral lumen and suturing the lateral side of the flap to the contralateral side of the urethra.*



(a) (b) (c) (d) (e)

Figure 8: Dorsal onlay free graft urethroplasty. *(a) = semilunar suprameatal incision; (b) = dorsal stricturotomy; (c) & (d) = suturing the edges of the graft to the urethral edges; (e) = suturing the distal edges of the graft to the edge of the suprameatal incision.*

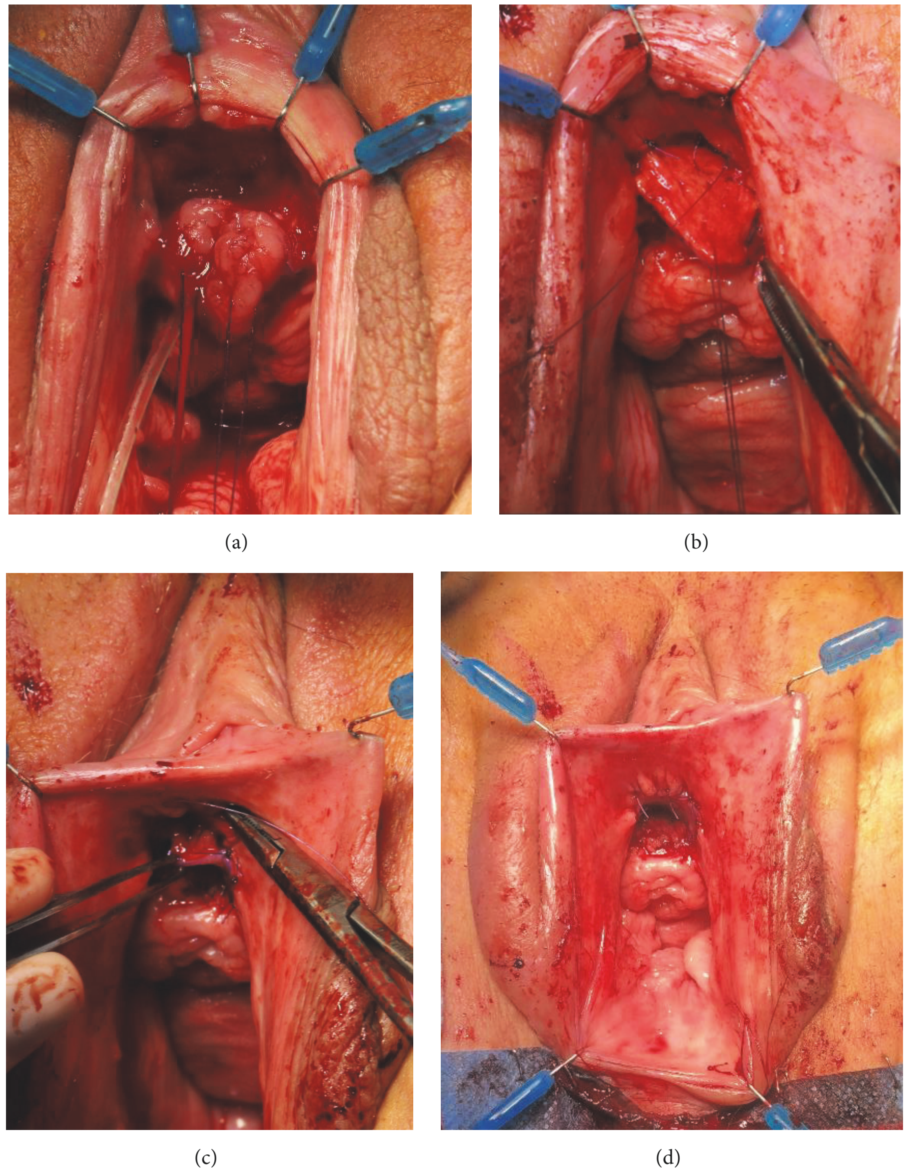
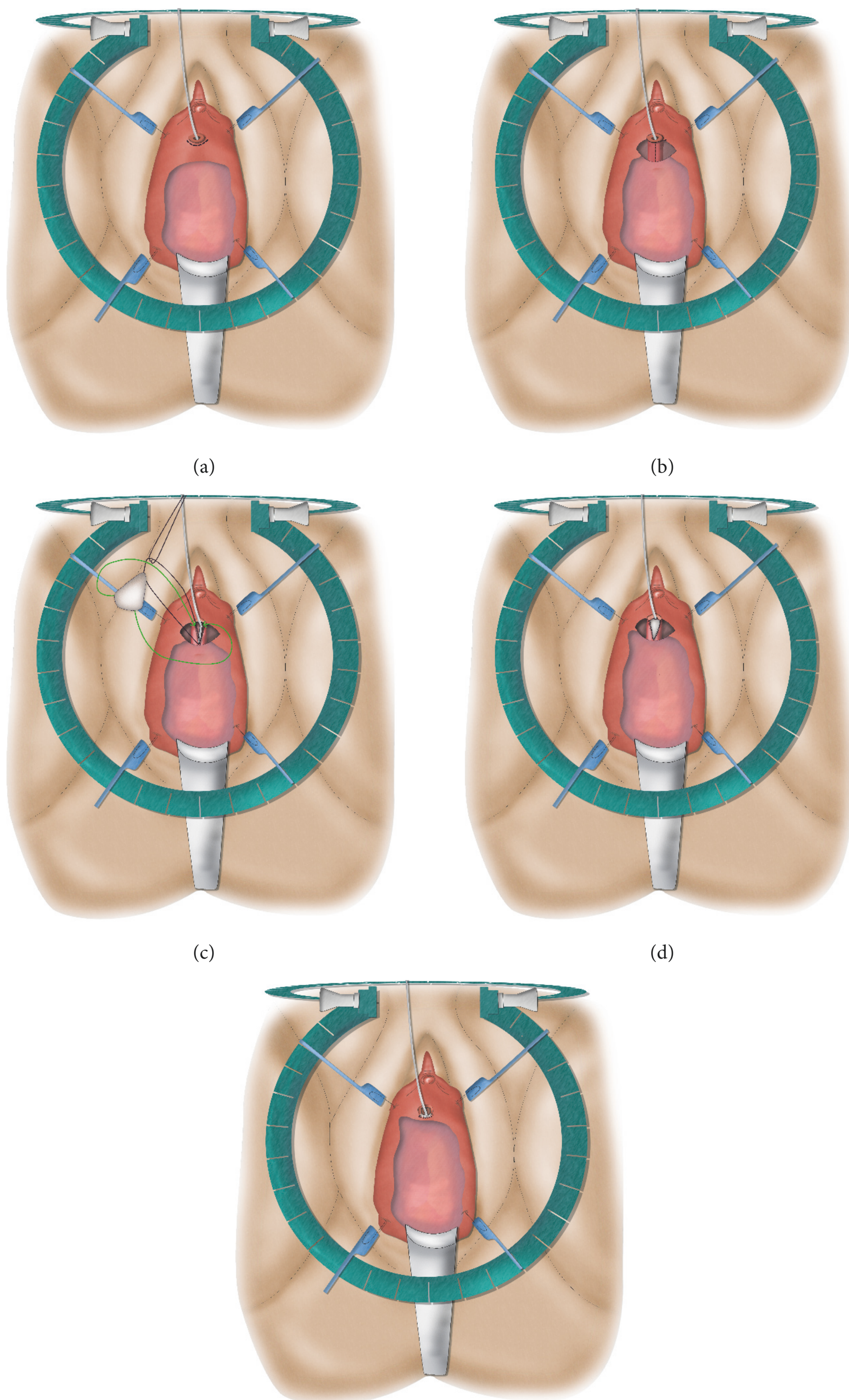


FIGURE 9: Dorsal onlay buccal mucosa graft urethroplasty. *(a) = semilunar dorsal incision and stricturotomy with stay sutures placed at the opened urethra; (b) = quilting the graft against the surface of the clitoral bodies and suturing the edges of the graft against the urethral edges; (c) = suturing the distal edges of the graft to the edge of the suprameatal incision; (d) = final result.*

urethra and continued up to the meatus. This suturing must also include the periurethral tissues in order to have a good fixation of the graft to the surrounding tissues. In addition to this, the graft is quilted to the clitoral bodies at the midline with resorbable sutures [8, 18]. At the meatus, the edges of the distal graft are approximated to the edge of the suprameatal incision with separate simple sutures [8].

Ventral Onlay (Figure 10). Development of the plane between the vaginal wall and the urethra can be facilitated by hydrodissection using a diluted solution of lidocaine with epinephrine [10]. A midline incision in the anterior vaginal wall is made above the region of the stricture. Dissection is performed towards the urethra and semilunar from the 3-o'clock to the 9-o' clock position around the ventral urethra. A ventral midline stricturotomy is performed at the level of the stricture. This stricturotomy can be started distally at the tip of a catheter or metal sound inserted through the meatus. Alternatively, stricturotomy can be started at the proximal end of the stricture. This is identified by the inflated balloon of a Fogarty embolectomy catheter that was inserted in the bladder and retracted up to the proximal end of the stricture [10]. The proximal and distal end of the stricture must allow passage of a 20Fr catheter after spatulation. Stay sutures are placed at the urethral edges to facilitate exposure. A graft is harvested according to the dimensions needed to augment the strictured urethra. The surrounding spongiosal tissue is sutured above this graft to provide a vascular bed. In case of



(a) (b) (c) (d) (e)

Figure 10: Ventral onlay free graft urethroplasty. *(a) = semilunar inframeatal incision; (b) = ventral stricturotomy; (c and d) = suturing the edges of the graft to the urethral edges; (e) = suturing the distal edges of the graft to the edge of the inframeatal incision.*

insufficiency or poor quality of the vascular bed, a Martius flap must be mobilized towards the urethral reconstruction in order to provide an additional healthy vascular bed for the graft, to prevent urethra-vaginal fistula formation, and to ensure a healthy layer if subsequent suburethral sling insertion might be necessary (Figures 11 and 12) [10].

To harvest the Martius flap [19], a sagittal incision is made at the most dependent line of the labium majus. Dissection is proceeded until the deep fibrofatty tissue ("bright yellow") is identified. This fibrofatty pad is laterally and medially mobilized following a natural tissue plane under the subcutaneous fat. Laterally, the flap is mobilized until the labiocrural fold. Medially, one should take care not to dissect into the bulbospongiosus and ischiocavernosus muscles. The flap is provided by a branch of the internal pudendal artery coming from posteriorly and a branch of the external pudendal artery coming from anteriorly. In most cases, the flap is pedicled at its posterior branch and the anterior pedicle is ligated with mobilization of the anterior part. The deep aspect of dissection takes place alongside the surface of the pubic bone [20]. A subcutaneous tunnel (2 fingers wide) is created between the vaginal and the labial incision and the flap is transposed to the site of urethral reconstruction [19]. The flap is quilted to the graft with interrupted absorbable sutures 5.0. Abundant tissue of the flap is resected. A suction drain is left in place at the labial incision and the wound is closed in layers above this [19]. The vaginal epithelium is closed over the flap with 3.0 absorbable sutures (running suture or Donati) (Figures 11 and 12).

5. Postoperative Care

Vaginal packing during 24 h is advised for hemostatic reasons [10, 18].

At the end of the procedure, a 16 to 20 Fr urethral catheter is inserted through the reconstructed urethra. In case of a vestibular flap, the catheter can be removed early, even after 1 day [9]. After an anterior vaginal wall flap, the catheter is maintained for 7-10 days [17]. After a lateral vaginal wall flap, the catheter is maintained for 3 weeks [14, 16]. For ventral and dorsal onlay graft urethroplasty, the catheter remains for 2-3 weeks [8, 10, 18]. The catheter is removed if there is no contrast extravasation on urethrography.

6. Choice of Technique

At present, there are no guidelines on how to treat female urethral strictures despite the multitude of techniques that have been published [18]. In general, a trial of internal urethrotomy and/or dilation is performed initially [3]. Based on a systematic review of Osman et al., the composite success rate is 47% with a 58% and 27% success rate in case of, respectively, no previous dilations or previous dilations [4]. As most of these women were performing intermittent catheterization afterwards, this success rate is too optimistic. This practice must be considered as a form of repetitive dilations and should be discouraged in symptomatic women. All types of urethroplasty are associated with a higher success rate. Vaginal flap urethroplasty, vaginal/labial graft urethroplasty, and oral mucosa graft urethroplasty have a composite success rate of, respectively, 91%, 80%, and 94% [4]. No large and well-conducted comparative trials have been performed to evaluate whether one technique is superior to another, whether the dorsal location is better than the ventral one or whether a specific type of graft performs better than the others. The choice of technique therefore is mainly dictated by the treating surgeon's experience and preference. Nevertheless, based on the general principles of surgery and wound healing, based on the experiences in male urethroplasty and based on expert opinion, some advices can be suggested:

(i) *Heineke-Mikulicz meatoplasty*: Despite the high success rate (96%) [11], this technique can only be used for very short (<0,5 cm) meatal strictures [3]. When applied for longer strictures, it will result in a hypospadiac meatus with vaginal voiding and irritation. Furthermore, this technique is not advised in case of lichen sclerosus as this disease will further affect the reconstructed meatus [21].

(ii) *Use of genital mucosa (vaginal/labial)*: In male urethroplasty, the use of genital skin in case of lichen sclerosus resulted in an up to 100% failure rate [21]. Based on this observation, genital mucosa should be avoided in females with lichen sclerosus as stricture etiology. Instead, the use of oral mucosa is advised as it is more resistant to lichen sclerosus. In case of vaginal atrophy, vaginal mucosa (graft or flap) is not suitable for urethral reconstruction [3, 4, 8, 10]. Even in women with normal genital mucosae, atrophic changes will occur after the menopause. This might affect the reconstruction as well and can be a cause of future stricture recurrence [10]. Long-term follow-up after urethroplasty with genital mucosa is needed to accept/reject this hypothesis. Vaginal mucosa graft is also not advised in case of a narrow vaginal introitus as this will further exacerbate this [8]. No matter what type of graft is used, it must be sutured onto a well-vascularized graft bed to ensure graft survival and success of the urethral reconstruction. In addition, the graft must be immobilized at the graft bed as much as possible. Quilting sutures to the graft bed are important for this purpose.

(iii) *Anterior vaginal wall and vestibular flaps* can be used for meatal stricture and short (<2cm) distal urethral strictures [14]. The anterior vaginal wall flap can cause an inward urine stream with vaginal voiding [14, 22]. The vestibular flap has the potential disadvantage of spraying and anterior deflection of the urinary stream. Longer strictures (>2cm) or proximal stricture must be treated with graft procedures or lateral vaginal flap urethroplasty [10, 16].

(iv) *Ventral procedures* are technically more easy to perform [4]. Furthermore, due to the omega-shape of the female urethral sphincter with its ventral midline deficiency, ventral stricturotomy and subsequent

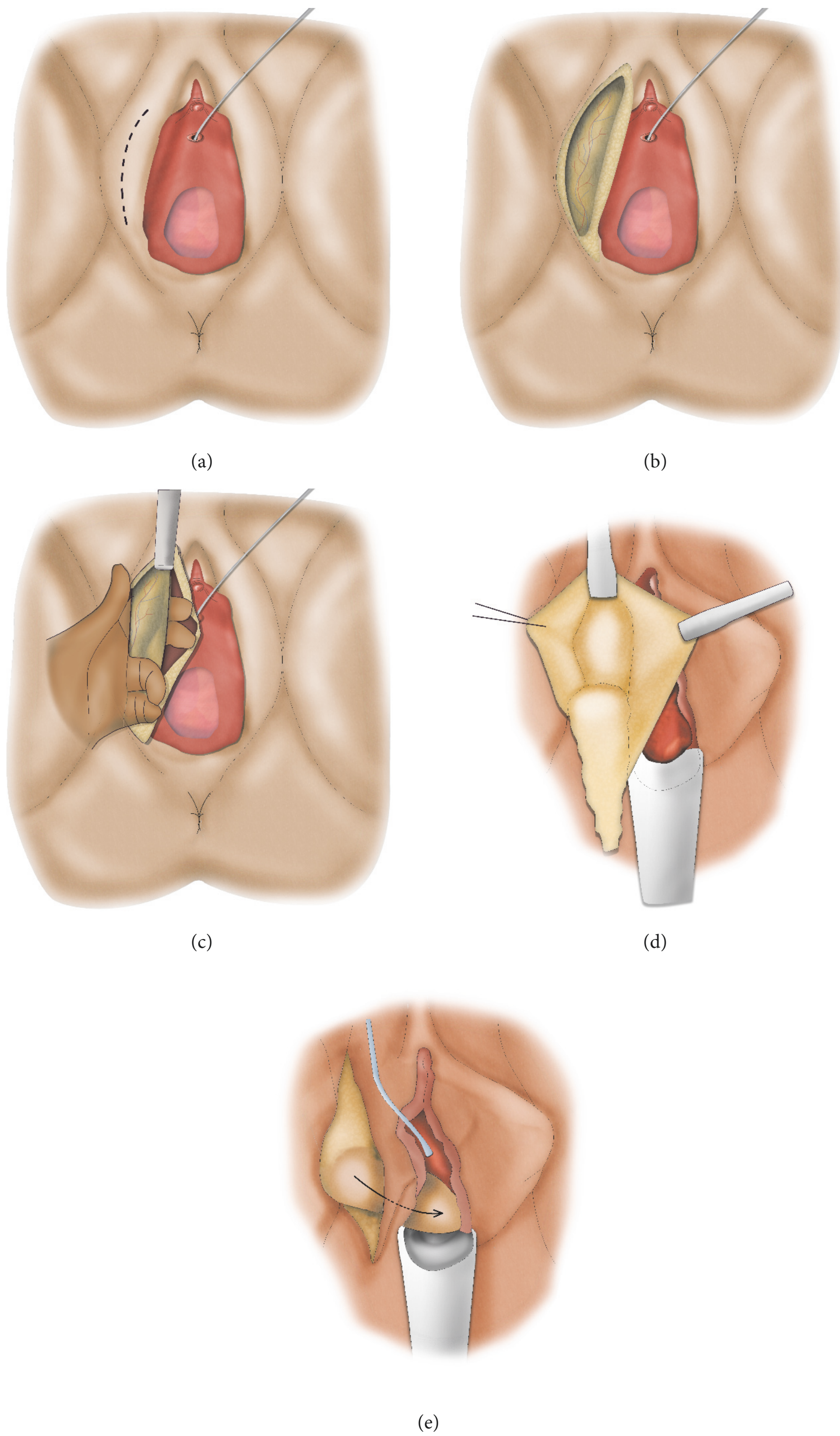


Figure 11: Martius flap. *(a) & (b) = sagittal incision at the most dependent line of the labium majus; (c) & (d) = mobilizing fibrofatty tissue; (e) = transposition of the Martius flap to the reconstructed area through a subcutaneous tunnel.*

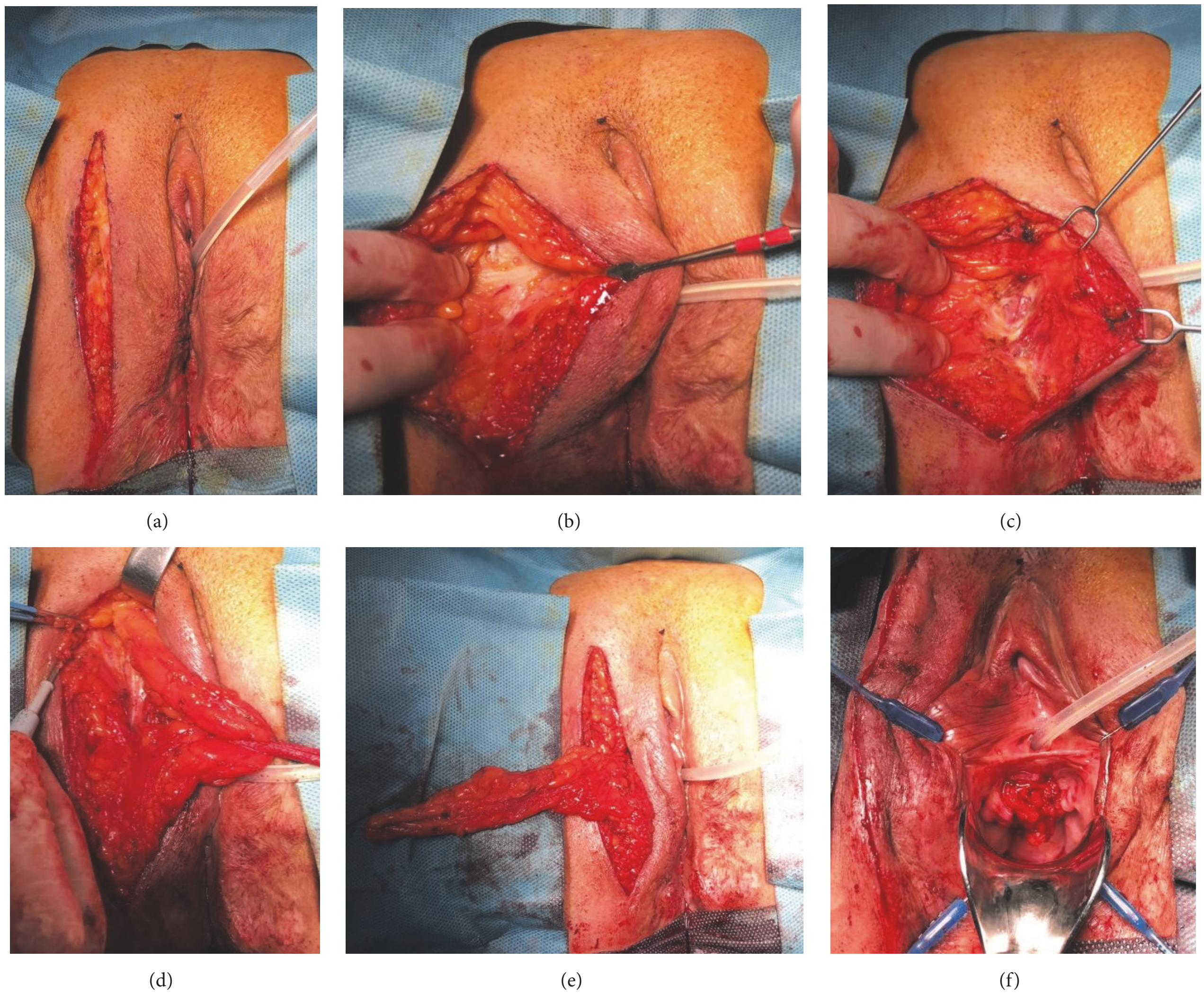


FIGURE 12: Martius flap procedure after ventral urethral repair. *(a) = sagittal incision line; (b) = lateral dissection to the labiocrural fold; (c) = medial dissection up to the bulbospongiosus muscle; (d) = mobilization of the flap; (e) = division of the anterior pedicle; (f) = transposed Martius flap to the ventrally reconstructed area.*

urethroplasty should have less risk of stress urinary incontinence [3, 10]. However, this hypothesis seems to be solely theoretical as no excess in stress urinary incontinence has been reported with dorsal procedures as well [4]. The paucity of ventral muscular tissue and overlapping suture lines after reconstruction pose a risk for the development of urethrovaginal fistula formation [3, 4]. In ventral free graft procedures, a low burden for the use of the Martius flap should be maintained especially in case of poor quality of the ventral local tissues. In addition, the use of a Martius flap makes subsequent insertion of a suburethral sling possible [4]. Its use should be balanced against the complications of the Martius flap which are in general minor (labial hematoma, cosmetic labial problems, decreased sensitivity, and local pain) [19, 20].

(v) *Dorsal procedures* are technically more challenging with more risk of bleeding and damage to the clitoral bodies [3]. The fear of injury to the clitoral neurovascular bundle seems not to be justified [4]. On the other hand, the dorsal approach has less risk of fistula formation and graft sacculation and is preferred if future insertion of a suburethral sling is expected and in case of fibrosis or unhealthy appearance of the ventral vaginal wall [2, 4, 8, 15, 18].

7. Conclusions

Female urethroplasty provides excellent cure rates and must be performed in case of recurrence after dilation. Before urethroplasty, diagnostic modalities are needed to confirm the presence, the location, and length of the stricture and to provide insight into the quality of surrounding tissues.

The choice of technique depends on stricture length, stricture location, and the quality of local tissues. Nevertheless, the optimal treatment strategy in female urethral strictures needs further clarification, preferably with larger and comparative series.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

Bram Nevejans created the surgical drawings.

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Clinical Study

Excision and Primary Anastomosis for Bulbar Urethral Strictures Improves Functional Outcomes and Quality of Life: A Prospective Analysis from a Single Centre

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Background. Excision and primary anastomotic (EPA) urethroplasty remains the gold standard definitive treatment for short urethral stricture disease. For patients, postoperative erectile function and quality of life are the main goals of the surgery. Patient-reported outcome measures (PROMs) are therefore of major importance. *Objective*. The objective of this study was to prospectively analyse functional outcomes and patient satisfaction. *Design, Settings, and Participants*. We prospectively evaluated 47 patients before and after EPA from August 2009 until February 2017. The first follow-up visit occurred after a median of 2.2 months (n = 47/47), with the second and third follow-ups occurring at a median of 8.5 months (n = 38/47) and 20.2 months (n = 31/47). Before surgery and at each follow-up visit, the patients received five questionnaires: the International Prostate Symptom Score (IPSS), the International Prostate Symptom Score with the Quality of Life (IPSS-QOL) score, the Urogenital Distress Inventory Short Form (UDI-6) score, the International Index of Erectile Function-5 (IIEF-5) score, and the ICIQ-Lower Urinary Tract Symptoms Quality of Life (ICIQ-LUTS-QOL) score. *Surgical Procedure*. Surgery was performed in all cases using the same standardized EPA technique. *Outcome Measurements and Statistical Analysis*. Voiding symptoms, erectile dysfunction, and quality of life were analysed using paired sample t-tests, with a multiple-testing Bonferroni correction. Any requirement for instrumentation after surgery was considered treatment failure. *Results and Limitations*. Patients with mild or no baseline erectile dysfunction showed significant decline in erectile function at first follow-up (mean IIEF-5 of 23.27 [standard deviation; SD: 2.60] vs. 13.91 [SD: 7.50]; p=0.002), but this had recovered completely at the third follow-up (IIEF-5: 23.25 [SD: 1.91]; p=0.659). Clinically significant improvements were noted in IPSS, IPSS-QOL-score, UDI-6-score, and ICIQ-LUTS-QOL-score at the first follow-up (p<0.0001). These improvements remained significant at the second and third follow-ups (p<0.0001) for all PROMs. Three of the patients experienced stricture recurrence. The main limitations of this study were incomplete questionnaires, loss to follow-up, and low number of patients. *Conclusions*. EPA results in an initial decline in erectile function, but full recovery occurred at a median of 20 months. Voiding improved significantly, and a major improvement in quality of life was noted, which persisted for up to 20 months after surgery. *Patient Summary*. This study showed the importance of patient-reported outcome measures in indicating the actual outcome of urethral stricture disease surgery.

1. Introduction

Urethral stricture disease has an incidence of 0.6%–0.9% in developed countries [1, 2], and it impacts patients' quality of life significantly [2]. Furthermore, when treated endoscopically, the disease has a high recurrence rate, necessitating repeat procedures with costly repercussions for healthcare [1]. Treatment depends on the aetiology, location, and length of the stricture. To identify all aspects of the stricture anatomy, preoperative assessment is essential, including retrograde urethrography, uroflowmetry, and cystoscopy [3].

The most common initial procedures used to treat short (< 1.5 cm), isolated bulbar urethral strictures are internal urethrotomy and dilatation [4, 5]. However, the recurrence-free rates of these procedures are only 39%–73%; repeated urethrotomies or dilatations have even lower success rates and so are not cost effective [6–9]. For this reason, urethroplasty should be considered the procedure of choice in patients with strictures which have recurred after initial endoscopic management or which fail to meet the criteria for single internal urethrotomy or dilatation [9, 10].

The management of bulbar urethral strictures depends on the length of the stricture and the amount of associated spongiofibrosis. For strictures less than 2 cm in length, excision and primary anastomosis (EPA) has shown excellent long-term results [10]. Longer strictures may require substitution urethroplasty [11], which aims to minimize stricture recurrence and the need for further instrumentation. Although the definition of long-term success and the follow-up methods have varied, EPA has shown an overall high level of success (> 90%) across different series [12, 13].

The impact of urethral strictures and subsequent urethroplasty on sexual function, as well as on voiding, should be evaluated postoperatively. Several larger studies have stated that EPA has no significant long-term impact on erectile function [14, 15]. When erectile dysfunction was reported, it tended to be transient, with full recovery 6 months after surgery [15]. However, some recent prospective series have reported that erectile function is poorer after EPA than after stricturotomy and augmentation [16–18], and many surgeons have therefore ceased using classic transecting EPA in favour of nontransecting EPA or augmented urethroplasty. These findings highlight the need for further prospective studies with validated outcome measures. In 2011, the validated Urethral Stricture Surgery Patient Reported Outcome Measure (USS PROM) was developed to assess patient-centred functional outcomes after urethroplasty [19]. This questionnaire assesses lower urinary tract symptoms (LUTS), general health status, and treatment satisfaction. After 2 years' follow-up, it seemed that the USS PROM could generate adequate patient-centred evidence and establish an international consensus on outcome reporting after urethral reconstruction surgery [20].

The present study aimed to use patient-reported outcome measures (PROMs) to prospectively analyse voiding symptoms, erectile function, and quality of life after classic transecting EPA urethroplasty.

2. Materials and Methods

We prospectively evaluated 47 patients who underwent EPA between August 2009 and February 2017 in University Hospitals Leuven [Figure 1]. All patients provided written and oral informed consent prior to participating in this trial. Men with short (< 2 cm) bulbar urethral strictures were included in the study. Before surgery, the aetiology and characteristics of the strictures were assessed using urethrography, uroflowmetry, urethroscopy (to evaluate the stricture and distal urethra), and urine culture. All procedures were performed by 2 surgeons using the same, standardized classic transecting EPA.

Follow-up visits were organized by the urologist, residents, and secretaries, with the first at 3 months, the second at 9 months, and the third at 18 months. Functional outcomes and impact on quality of life were ascertained by physical examination, uroflowmetry, and validated PROMs. Before surgery and at each follow-up visit, all patients filled out five PROM questionnaires [Figure 1]. Any need for urethral instrumentation following urethroplasty was considered a treatment failure. At each follow-up, complications were recorded using the Clavien–Dindo grading classification system.

The following PROMs were used:

(1) The International Prostate Symptom Score (IPSS) [21]

(2) The International Prostate Symptom Score with Quality of Life score (IPSS-QOL) [21]

(3) The Urogenital Distress Inventory Short Form score (UDI-6) [22]

(4) The International Index of Erectile Function-5 score (IIEF-5) [23, 24], with only sexually active men who had intercourse being asked to fill in this questionnaire

(5) The ICIQ-Lower Urinary Tract Symptoms Quality of Life score (ICIQ-LUTS-QOL) [25]

The completed questionnaires were scanned into the patients' files and a prospective database was created. All new data was added to this database at each follow-up visit. In February 2017, a total of 47 patients were included. Statistical analysis was performed using the paired-sample t-test, with a multiple-testing Bonferroni correction. To this end, commercially available software (IBM® SPSS® Statistics) was used. The alpha significance level was set at $\alpha = 0.05$ (5%). Kaplan-Meier survival analysis was performed to assess stricture recurrence events in time. The study was approved by the hospital's ethics committee (S55868/B322201319205) and registered at www.clinicaltrials.gov (NCT01982136).

3. Surgical Technique

Most procedures were performed under general anaesthesia, with perioperative administration of intravenous cefazolin (2 g). Patients were placed in a modified dorsal lithotomy position. Through a midline perineal incision, sharp dissection was performed to the level of the bulbospongiosus muscle. This muscle was cleaved, and the urethra was dissected circumferentially, distally, and proximally, with sufficient mobility to ensure a tension-free anastomosis. A flexible urethrocystoscopy was performed to assess the stricture location, which was marked by a suture (Monocryl 2/0). At this site, the urethra was transected and the stricture was excised. The urethra was spatulated on both sides within the well-vascularized, healthy tissue. The diseased part was sent for pathological examination. When the stricture was too short to allow traction free anastomosis, the plane between the corpora cavernosa was cleaved to obtain space. An end-to-end anastomosis was performed using eight separate sutures (Monocryl 3/0), and a transurethral 16 Fr. silicone catheter was placed. Haemostasis was induced, the wound was closed in layers, and a compressive bandage was applied. After 24 hours, the compressive bandage was removed, the wound was inspected, and the patient was discharged. When voiding urethrocystography with the transurethral catheter

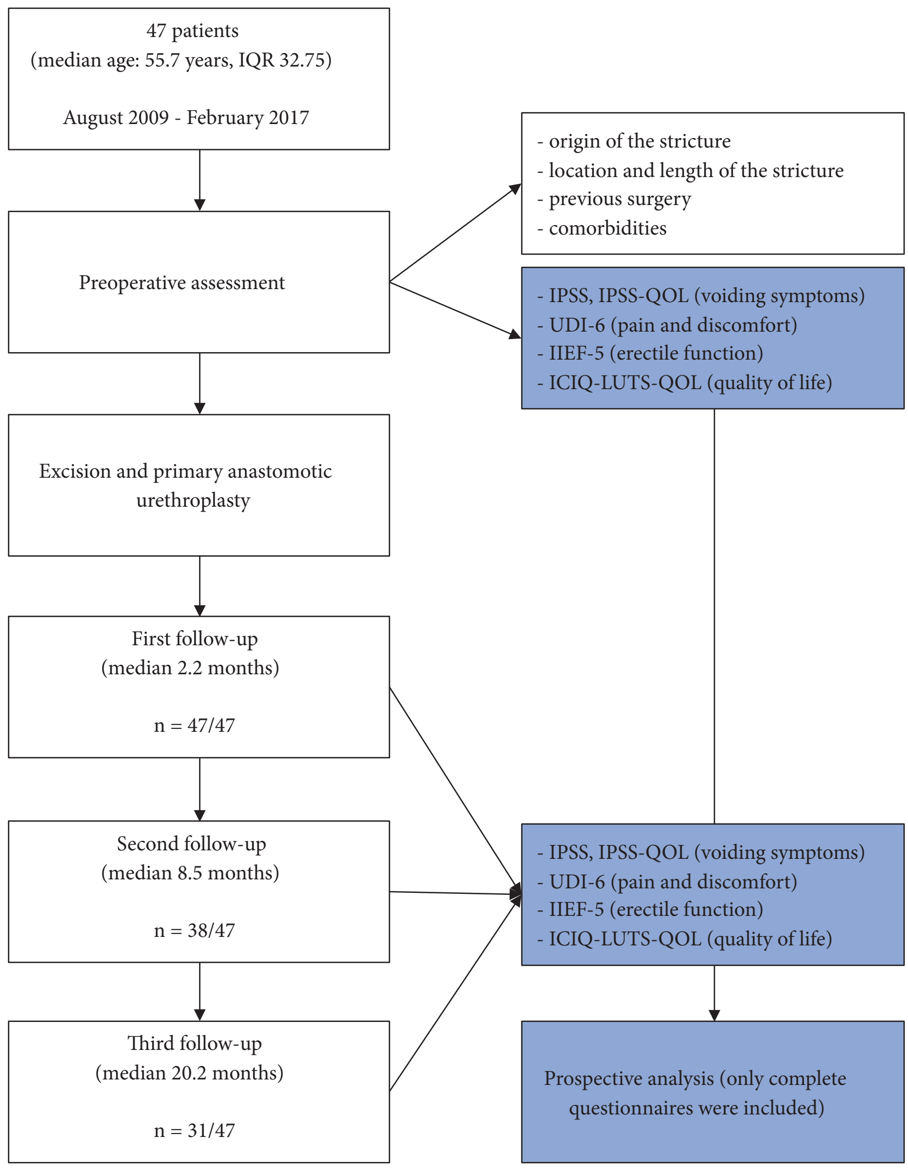


Figure 1: **Flowchart and study design.** *IQR: interquartile range, IPSS: International Prostate Symptom Score, IPSS-QOL: International Prostate Symptom Score with Quality of Life, UDI-6: Urogenital Distress Inventory Short Form score, IIEF-5: International Index of Erectile Function-5 score, and ICIQ-LUTS-QOL: ICIQ-Lower Urinary Tract Symptoms Quality of Life score.*

in situ showed no leakage after 2 weeks, the catheter was removed.

4. Results

A total of 47 patients were included. The first follow-up took place after a median of 2.2 months (n = 47/47), with the second and third follow-ups occurring at a mean of 8.5 months (n = 38/47) and 20.2 months (n = 31/47), respectively [Figure 1]. The patients' median age at surgery was 55.7 years (interquartile range [IQR]: 32.75 years). The median stricture length was 1.0 cm (IQR: 0.7 cm) [Table 1].

The causes of the stricture were trauma (n = 8), infection (n = 1), and iatrogenic (n = 22). In 16 patients, the cause was unknown [Table 1]. The iatrogenic causes were previous transurethral resection (n = 11), catheterization (n = 5), radical prostatectomy (n = 4), and radiotherapy/brachytherapy (n = 2).

All strictures were located in the bulbar urethra (n = 47). A total of 11 patients had undergone no previous surgery, whereas 6 patients had previously undergone only one urethrotomy or dilatation. In total, 29 patients had undergone multiple dilatations or urethrotomies [Table 1], among whom 22 patients had a history of more than 3 previous interventions.

In total, 3 stricture recurrences were noted; all occurred within the first 9 months [Figure 2]. Postoperative complications were recorded in 3 patients and consisted of accidental

Table 1: Patient and stricture demographics.

Preoperative characteristics of the study population (47 patients)	
Median age	55.7 years (IQR: 32.75 years)
Median stricture length	1 cm (IQR: 0.7 cm)
Median follow-up (months)	1st follow-up: 2.2 months (IQR: 1.1 months) 2nd follow-up: 8.5 months (IQR: 2.4 months) 3rd follow-up: 20.2 months (IQR: 9.4 months)
Stricture location	47/47: bulbar (100%)
Stricture aetiology	8/47: traumatic (17%) 22/47: iatrogenic (47%) 16/47: idiopathic (34%) 1/47: infection (2%)
Previous surgery	29/47: repetitive urethrotomy/dilatation (62%) 1/47: open surgery + dilatation (2%) 11/47: no previous surgery (23%) 6/47: one urethrotomy or dilatation (13%)

IQR: interquartile range.

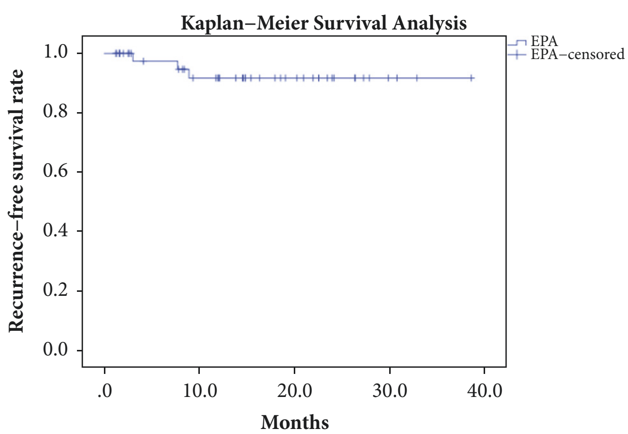


Figure 2: **Kaplan-Meier statistical analysis curve.** *EPA: excision and primary anastomosis.*

suture-fixing of the catheter (n = 2) and acute bacterial prostatitis (n = 1). Accidental stitching of the catheter should be recorded as a technical failure of surgery. All these complications were observed within the first days and weeks after surgery. The median catheterization duration was 14 days (IQR: 5 days).

5. Specific Outcome Measures

5.1. Voiding Symptoms (IPSS and Maximal Flow Rate Q_{max}). The mean preoperative IPSS-score was 18.16 (standard deviation [SD]: 6.35). This had decreased significantly at the first follow-up visit, with a mean score of 4.33 (SD: 3.87) ($p < 0.0001$). This difference remained significant at the second ($p < 0.0001$) and third visits ($p < 0.0001$), with mean scores of 3.21 (SD: 4.46) and 3 (SD: 4.53), respectively. There were no significant differences among the first, second, and third visits in this regard [Figure 3].

There was a significant difference between the preoperative mean Q_{max} (8.43 mL/s, SD: 7.05 mL/s, mean voided volume: 231 mL) and the mean Q_{max} at the first follow-up (25.09 mL/s, SD: 16.61 mL/s, mean voided volume: 272 mL; $p < 0.0001$). This difference remained significant at the second ($p < 0.0001$) and third follow-up visits ($p < 0.0001$), with mean scores of 20.63 mL/s (SD: 11.69 mL/s, mean voided volume: 240 mL) and 23.47 mL/s (SD 9.37, mean voided volume 259 mL), respectively.

5.2. Urogenital Distress and Discomfort (UDI-6). Significant differences were noted between the preoperative mean UDI-6-score of 34.39 (SD: 20.45) and the mean score at first follow-up of 8.99 (SD: 13.66; $p < 0.0001$). These differences remained significant at the second ($p < 0.0001$) and third follow-up visits ($p = 0.0001$), with mean scores of 5.38 (SD: 15.04) and 5.72 (SD: 11.59), respectively. There were no significant differences between the UDI-6 scores at first, second, and third follow-up visits [Figure 4].

5.3. Erectile Dysfunction (IIEF-5). Only 23 of the 47 patients were sexually active before surgery and completed the IIEF-5 questionnaire.

Patients with mild or no baseline erectile dysfunction (IIEF-5: 17–25) had a significant decline in erectile function at the first follow-up (IIEF-5: 23.27, SD: 2.60 vs. 13.91, SD 7.50; $p = 0.002$; n = 15/23). At the second follow-up, erectile function still differed significantly from preoperative values [IIEF-5: 20.31, SD: 5.15; $p = 0.045$; n = 15/23). By the third follow-up, a full recovery was seen, and erectile function did not differ significantly from the preoperative value [IIEF-5: 23.25, SD: 1.91; $p = 0.659$; n = 15/23) [Figure 5].

Patients with mild/moderate to severe ED (IIEF-5: 5–16) at baseline (n = 8/23) experienced no significant difference in erectile function at the first follow-up [IIEF-5: 8.75, SD: 4.53 vs. 7.73, SD: 2.55; $p = 0.453$; n = 8/23), second follow-up [IIEF-5: 6.67, SD: 0.82; $p = 0.187$; n = 8/23), or third follow-up [IIEF-5: 6.40, SD: 1.52; $p = 0.477$; n = 8/23) [Figure 6].

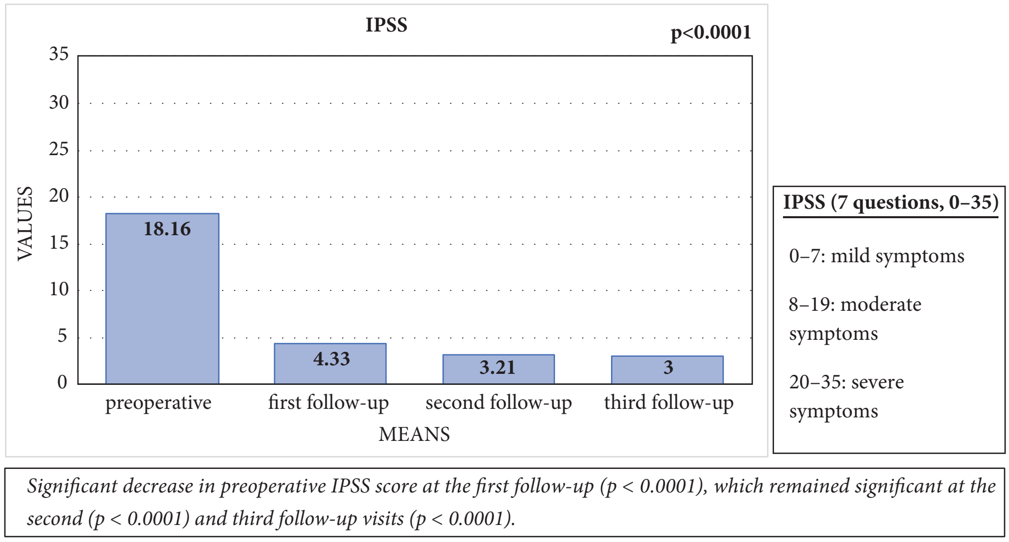


Figure 3: Comparison of the mean preoperative IPSS with the IPSS at the first, second, and third follow-up visits.

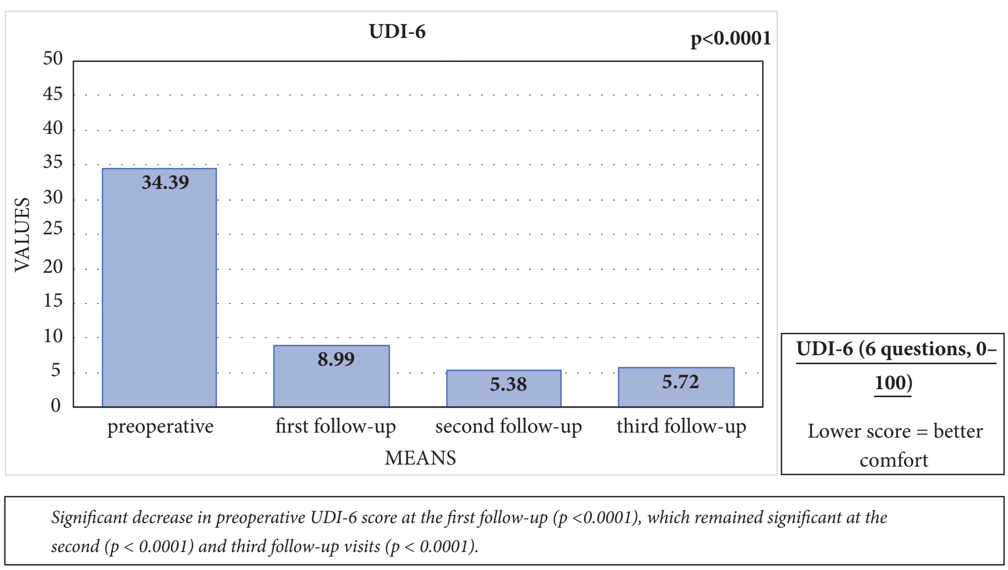


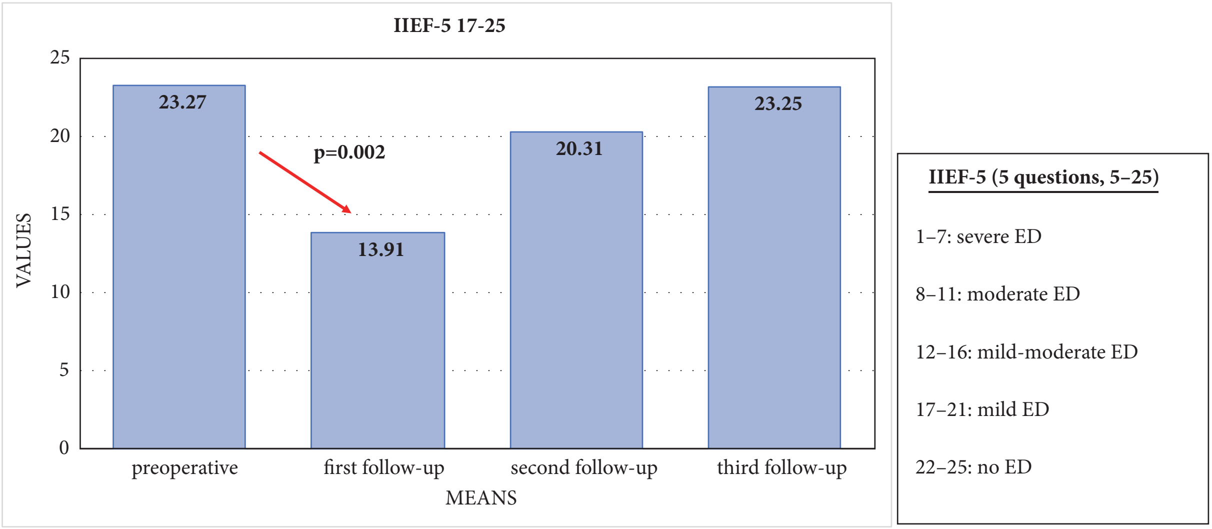
Figure 4: Comparison of the mean preoperative UDI-6 score with the UDI-6 scores at the first, second, and third follow-up visits.

5.4. Quality of Life (IPSS-QOL and ICIQ-LUTS-QOL). A significant improvement was noted between the preoperative mean IPSS-QOL score of 4.30 (SD: 1.17) and the mean score of 1.17 (SD: 1.03) at the first follow-up visit ($p < 0.0001$). This improvement remained significant at the second ($p < 0.0001$) and third follow-up visits ($p < 0.0001$), with mean scores of 1 (SD: 1) and 0.94 (SD: 1.21), respectively. There were no significant differences between the first, second, and third follow-up visits in this regard [Figure 7].

The mean preoperative ICIQ-LUTS-QOL score was 36.5 (SD: 10.34), and it had decreased significantly at the first follow-up visit, with a score of 23.26 (SD: 6.13; $p < 0.0001$). This improvement also remained significant at the second ($p < 0.0001$) and third follow-up visits ($p < 0.0001$), with mean scores of 22.34 (SD: 6.72) and 21.90 (SD: 6.97), respectively. There were no significant differences between the first, second, and third follow-up visits [Figure 8].

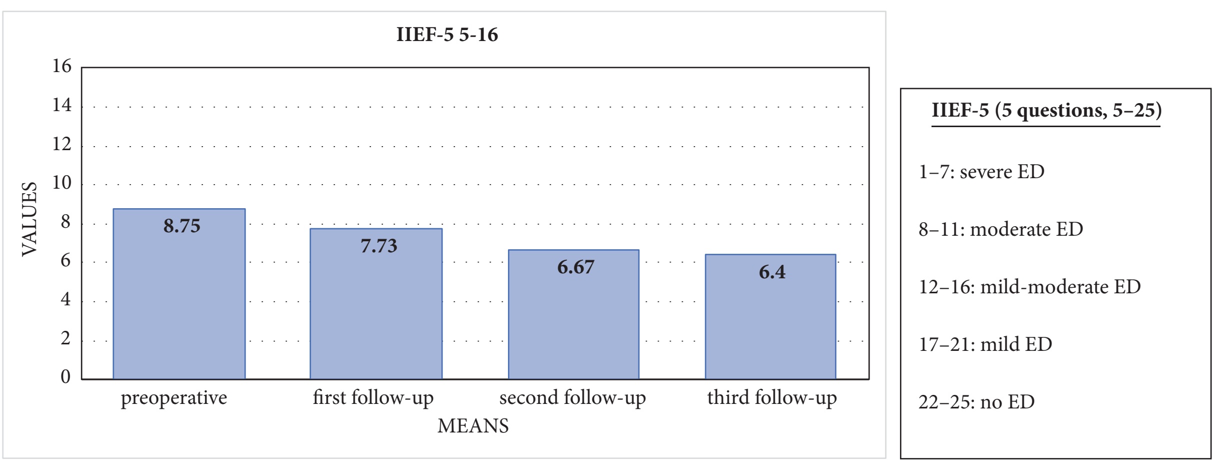
6. Discussion

6.1. Voiding Symptoms and Urogenital Distress. In the present study, EPA led to a significant decrease in IPSS score, as measured at the first, second, and third follow-up visits, indicating an improvement in LUTS. Furthermore, we noticed a significant improvement in Q_{max} after surgery. The main voiding complaints of urethral stricture disease are weak stream, dribbling, and incomplete emptying [26]. The IPSS assesses most of these symptoms. In addition, there was a



A significant decrease can be seen from preoperative IIEF-5 score at the first follow-up (p = 0.002), which remained significant at the second follow-up (p = 0.045) but had recovered at third follow-up (p = 0.659).

Figure 5: Comparison of the mean preoperative IIEF-5 score with the IIEF-5 scores at the first, second, and third follow-up visits in patients with mild-to-no erectile dysfunction at baseline.



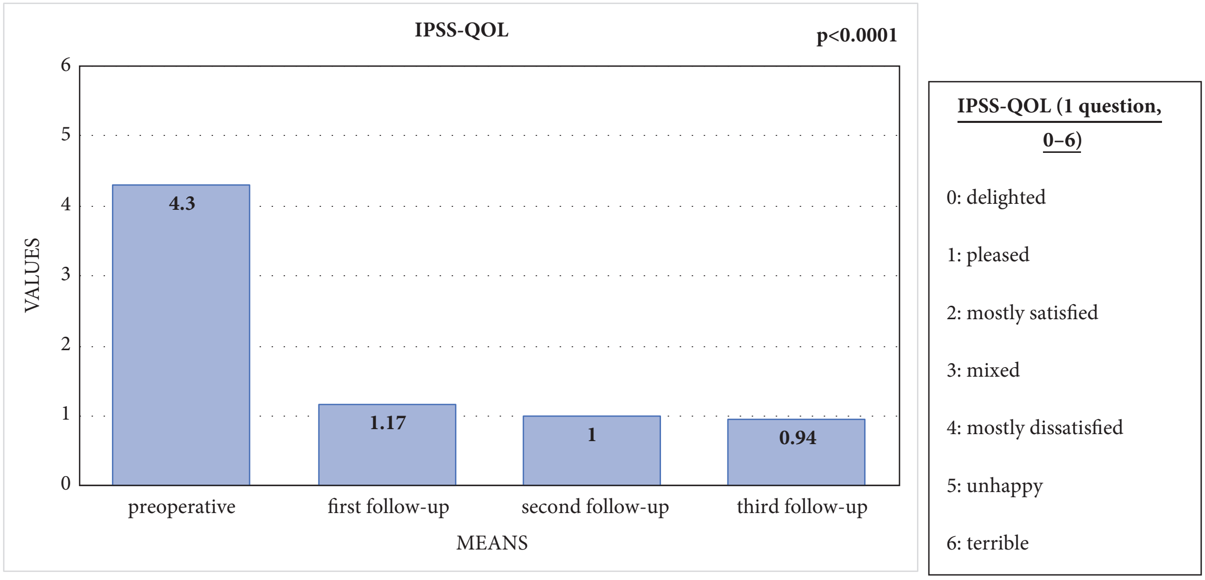
No significant changes can be seen from preoperative IIEF-5 score and scores at the first follow-up, the second follow-up and the third follow-up.

Figure 6: Comparison of the mean preoperative IIEF-5 score with the IIEF-5 scores at the first, second, and third follow-up visits in patients with moderate-to-severe erectile dysfunction at baseline.

significant decrease in UDI-6 score during follow-up in the present study, highlighting an improvement in dribbling, incontinence, and pain after surgery. These findings are similar to those described by Jackson et al., who used the USS PROM questionnaire [19, 20].

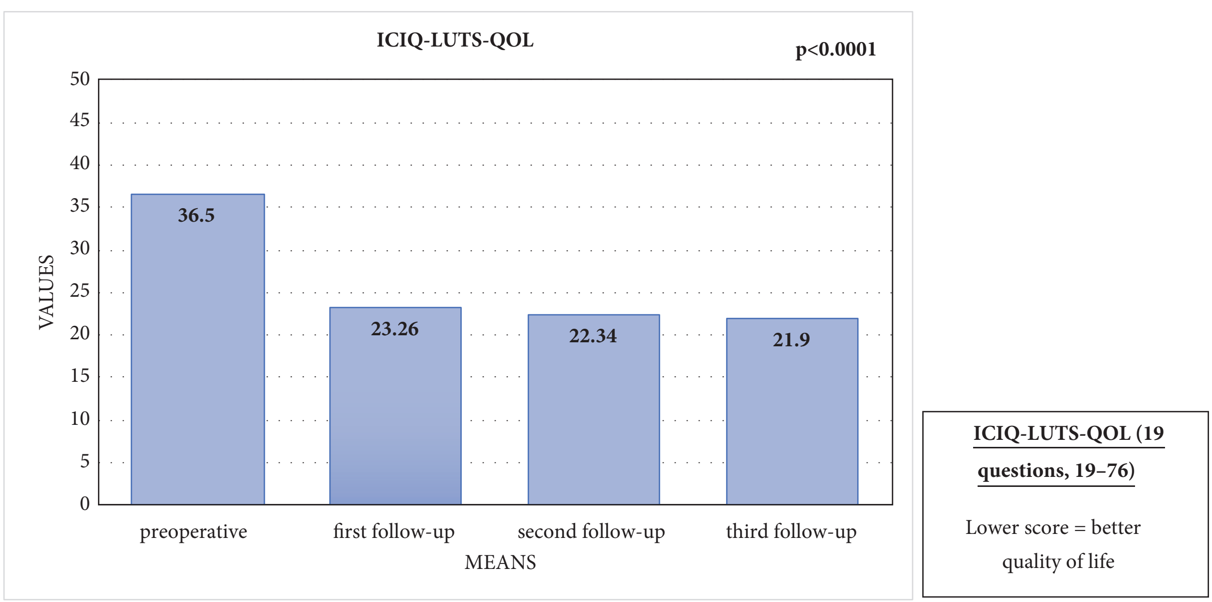
EPA aims to remove the urethral stricture and associated spongiofibrosis, as well as to reconstruct the urethra with an adequate and sufficient diameter. In the present study, there was a significant decline in IPSS and a significant improvement in Q_{max} after surgery. Therefore, we conclude that EPA resolves obstructive voiding symptoms and improves urinary flow.

6.2. Erectile Dysfunction. We noticed a significant decline in the IIEF-5 score at the first follow-up in sexually active patients who had good erectile function before surgery (n = 15/23). This first decline could be attributed to pain and catheterization during the first weeks after surgery [15, 16]. Full recovery of erectile function was seen at the third follow-up. In contrast, patients with moderate to severe erectile



A significant decrease can be seen from preoperative IPSS-QOL score at the first follow-up ($p < 0.0001$), which remained significant at the second ($p < 0.0001$) and third follow-up visits ($p < 0.0001$).

Figure 7: Comparison of the mean preoperative IPSS-QOL score with IPSS-QOL scores at the first, second, and third follow-up visits.



A significant decrease can be seen from preoperative ICIQ-LUTS-QOL score at the first follow-up ($p < 0.0001$), which remained significant at the second ($p < 0.0001$) and third follow-up visits ($p < 0.0001$).

Figure 8: Comparison of the mean preoperative ICIQ-LUTS-QOL score with ICIQ-LUTS-QOL scores at the first, second, and third follow-up visits.

dysfunction at baseline experienced no significant difference over time.

This transient decline in erectile function was also described by Erickson et al., with a similar return to baseline erectile function during follow-up [15]. Minimally invasive urethroplasty is becoming more popular, and recent studies have suggested that transection of the corpus spongiosum leads to less favourable outcomes with regard to erectile function [17, 18], perhaps because there is a close anatomical relationship between the bulbar urethra and the erectile innervation [18]. The nontransecting technique preserves the well vascularised underlying spongiosum and thus has a lesser impact on sexual function [18]. Consequently, nontransecting EPA has shown potential benefits. Our data, although involving only a small subgroup of patients with good baseline erections (n = 15/23), showed no differences in erectile function at longer follow-up. Thus, patients with normal erectile function should be counselled before surgery regarding the possibility of early erectile dysfunction, and patients with moderate to severe erectile dysfunction before surgery are unlikely to develop improved erectile function.

6.3. Quality of Life. Following reconstruction, patients were pleased with their voiding function, and a significant improvement was noted between the preoperative and postoperative IPSS-QOL scores. We noticed a similar change in the ICIQ-LUTS-QOL questionnaire, which extensively questioned quality of life before and after surgery and explores in detail the impact of different treatment modalities on the patients' lives [25]. Our findings are consistent with a prospective series published by Jackson et al. in 2013, wherein most patients (87%) were satisfied or very satisfied after surgery, with significant improvement in their health state index [20]. Therefore, our data show that EPA has a significant positive impact on quality of life.

6.4. Stricture Recurrence and Complications. Three patients experienced stricture recurrence in the present study, and all of these failures occurred in the first 9 months. Kaplan-Meier survival analysis was carried out to ensure that surgical success was correctly reported, since 16 patients were lost to longer follow-up [Figure 2]. At long follow-up, we noticed no new stricture recurrences, and no patients have yet required repeat urethroplasty. Ultimately, we achieved a high recurrence-free rate, and our findings were similar to those of previous studies, which have reported high levels of overall success (> 90%) [12, 13].

Only 3 complications were recorded, and these were also comparable with previous studies [10, 13]. According to the Clavien–Dindo grading classification system, we had 1 Grade II complication (bacterial prostatitis requiring pharmacological treatment) and 2 "Grade IIIb" complications (suture-fixed catheter requiring endoscopic intervention under short general anaesthesia) [27]. All these complications were seen in the first 3 weeks after surgery.

7. Strengths and Limitations

The key strengths of this study were its prospective nature and the availability of preoperative values. All the patients were asked to complete the questionnaires as stated above and these data were accurately recorded. However, there were some limitations. It was a single centre series with a relative low number of patients and a short follow-up. Consequently, the study lacked statistical power. Furthermore, several incomplete questionnaires were submitted: 3 at the first follow-up, 3 at the second follow-up, and 5 at the third follow-up. Some patients were also lost to follow-up, mainly because some patients were followed by the referring urologist. In 2011, Jackson et al. published a validated, patient-reported outcome measure to analyse patient satisfaction and relief of symptoms after urethroplasty [19]. In the present study, we did not use this validated questionnaire, because our analysis began in 2009. Thus, to prospectively evaluate our patients, we used other validated questionnaires, as detailed above. The UDI-6 score to assess urinary incontinence, pain, and discomfort was initially established for use in clinical and research studies in women [22]. However, in 2015, this questionnaire was also validated in men [28]. In 2017, Verla et al. published a validated Dutch version of the USS PROM questionnaire [29]. Since our centre is located in the Dutch speaking part of Belgium, this validated questionnaire may have been beneficial, since it also includes questions about the patients' general health status and ejaculatory dysfunction, which were not assessed in this trial.

8. Conclusion

At presentation, the questionnaires indicated that the patients had bothersome voiding symptoms and impaired quality of life. After classic transecting EPA urethroplasty, their voiding symptoms had improved significantly, without significant impact on erectile function. Furthermore, we noticed an improvement in quality of life which remained significant for up to 20 months after surgery. This prospective study emphasizes the importance of patient-reported outcome measures when assessing the results of reconstructive urethral surgery. Operative success should not merely be defined in terms of the need for stricture-related interventions, as erectile dysfunction and voiding symptoms contribute to quality of life, and thus to overall surgical success.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Disclosure

No financial support was received; this study was performed as part of employment at the Department of Urology, University Hospitals Leuven, under the guidance of Prof. Van der Aa. The abstract of this study was presented at the 33rd annual EAU Congress in Copenhagen.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Research Article

Excision and Primary Anastomosis for Short Bulbar Strictures: Is It Safe to Change from the Transecting towards the Nontransecting Technique?

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Objective. To explore whether it is safe to change from transecting excision and primary anastomosis (tEPA) towards nontransecting excision and primary anastomosis (ntEPA) in the treatment of short bulbar urethral strictures and to evaluate whether surgical outcomes are not negatively affected after introduction of ntEPA. *Materials and Methods*. Two-hundred patients with short bulbar strictures were treated by tEPA (n=112) or ntEPA (n=88) between 2001 and 2017 in a single institution. Failure rate and other surgical outcomes (complications, operation time, hospital stay, catheterization time, and extravasation at first cystography) were calculated for both groups. Potentially predictive factors for failure (including ntEPA) were analyzed using Cox regression analysis. *Results*. Median follow-up for the entire cohort was 76 months, 118 months, and 32 months for, respectively, tEPA and ntEPA ($p<0.001$). Nineteen (9.5%) patients suffered a failure, 13 (11.6%) with tEPA and 6 (6.8%) with ntEPA ($p=0.333$). High-grade (grade ≥3) complication rate was low (1%) and not higher with ntEPA. Median operation time, hospital stay, and catheterization time with tEPA and ntEPA were, respectively, 98 and 87 minutes, 3 and 2 days, and 14 and 9 days. None of these outcomes were negatively affected by the use of ntEPA. Diabetes and previous urethroplasty were significant predictors for failure (Hazard ratio resp. 0.165 and 0.355), whereas ntEPA was not. *Conclusions*. Introduction of ntEPA did not negatively affect short-term failure rate, high-grade complication rate, operation time, catheterization time, and hospital stay in the treatment of short bulbar strictures. Diabetes and previous urethroplasty are predictive factors for failure.

1. Introduction

The International Consultations on Urologic Diseases (ICUD) recommends urethroplasty by excision and primary anastomosis (EPA) for short and isolated bulbar urethral strictures as it provides an excellent success rate (93.8%) with a low complication rate [1]. After EPA, the diseased segment is entirely removed and replaced by own healthy urethra without the need for urethral substitution material (grafts or flaps), which is probably the reason for the high success rate. During the "classic" transecting EPA (tEPA), the corpus spongiosum containing the urethra is transected full thickness at the level of the stricture [2]. As EPA only requires excision of the narrowed urethra and the surrounding spongiofibrosis, a full thickness transection is usually not necessary. To avoid this and to preserve the dual blood supply of the urethra, Jordan et al. introduced the concept of vessel-sparing or nontransecting EPA (ntEPA) [3], later slightly modified by Andrich et al. [4]. This nontransecting variant is an attempt to reduce the surgical trauma of tEPA and several centers have introduced this technique in their reconstructive repertoire[4–6]. A prerequisite to use ntEPA is that the outcomes are at least not inferior compared to the standard technique of tEPA. Case series of ntEPA have a promising short-term success rate of 94.5-100% [3, 5–7], which is in line with the composite success rate of 93.8% for the tEPA reported by the ICUD[1]. However, indirect comparison of series is hazardous as patient and stricture characteristics, follow-up schedules, and reporting of outcomes might vary among series. Therefore, the primary objective of this study is to evaluate whether the change in practice from tEPA to ntEPA yielded surgical outcomes that are not inferior to the patient. To the best of our knowledge, this is the first paper to report this.

2. Material and Methods

2.1. Study Population. A database was collected of all male patients (n=852) who underwent urethroplasty at Ghent University Hospital starting from 2001 (start of electronic medical file). Since 2008, this collection was done prospectively. Patients who underwent EPA, either by the transecting or nontransecting technique, for isolated short bulbar strictures (ranging from the penoscrotal angle up to the urogenital diaphragm) were selected from this database until December 2017. Exclusion criteria were EPA performed for posterior or penile strictures, EPA with concomitant urethroplasty at another part of the urethra, EPA in transgender patients, and EPA in patients on clean intermittent catheterization. All patients underwent preoperative evaluation including history taking (with emphasis on stricture etiology and previous urethral interventions), clinical examination, uroflowmetry, and urethrography. According to our in-home algorithm to treat urethral strictures, EPA is the preferred technique for short (≤3cm) bulbar strictures [8]. After attendance at a masterclass on urethroplasty we became familiar with the technique and being convinced of the theoretical advantages of ntEPA, we performed our first cases in November 2011. Starting from January 2012, ntEPA became the standard technique.

2.2. Surgical Technique. A detailed description of the operative techniques is beyond the scope of this article as it has been published previously [6, 9]. In brief, the patient is placed in the social lithotomy position, a midline perineal incision is made, and the bulbospongiosus muscle is incised at the midline and dissected away from the corpus spongiosum containing the bulbar urethra. The bulbar urethra is circumferentially detached from the corporal bodies and mobilized from the penoscrotal angle up to the urogenital diaphragm. With tEPA, the perineal body ("centrum tendineum") is incised for further mobilization of the ventral bulbar urethra. With this technique, the spongious tissue is transected full thickness at the level of the stricture which is marked after introduction of a metal sound through the meatus. The narrowed urethra and surrounding spongiofibrosis are fully excised, the healthy urethral ends are spatulated, and a tension-free anastomosis is made by 8 resorbable sutures 4.0. For ntEPA, the modification described by Andrich et al. was used [4]. The urethra is incised dorsally at the level of the stricture. Again, the stricture and surrounding fibrosis are excised but with preservation of the ventral spongiosum. The urethral edges are also spatulated and connected end-to-end with 8 resorbable sutures 4.0. In case of any difficulties to ensure a complete resection of the fibrosis or if the fibrosis encompasses the entire thickness of the spongious tissue, conversion to tEPA is done. The spongious tissue is closed with resorbable sutures 4.0 over the urethral anastomosis. This second layer ("spongioplasty") is circumferential with tEPA and at the dorsolateral side with ntEPA. For both techniques, a 20Fr silicone catheter is left in place as well as a perineal suction drain.

2.3. Follow-Up and Evaluation. The suction drain is removed after 24-48 hours. The patient is discharged when his clinical condition allows for it, which is usually after 2 days. The catheter is removed 1 to 2 weeks later on ambulatory base if voiding cystourethrography confirms absence of extravasation [10]. In case of extravasation, the examination is repeated after one week. Follow-up including history taking and uroflowmetry was advised every 3 months during the 1st year, and annually thereafter. Surgical complications (≤90 days) were scored according to the Clavien-Dindo classification. Patients were asked to come on earlier visit if they experience obstructive urinary symptoms or had a urinary tract infection. In case of suspicion of recurrence (clinical symptoms or maximum urinary flow <15ml/s), retrograde urethrography or urethroscopy was performed. Referred patients were sent back to and followed by their local urologist. A functional definition of failure was used, namely, obstructive symptoms with the need for additional urethral instrumentation (including simple dilation) [11]. Other surgical outcomes analyzed are operation time, hospital stay, catheterization time, and extravasation at first cystography. Functional outcomes (incontinence, erectile function, and genital sensitivity) are not the scope of this study as these parameters were not systematically questioned and in those where it was done, different questionnaires were used over the years. The study was approved by the local ethics committee (EC UZG 2008/234). All operations were done by 2 surgeons (W.O., N.L.).

2.4. Statistical Analysis. A first analysis was done per surgical technique (tEPA versus ntEPA). As mentioned above, since 2012 ntEPA became the standard technique. However, in case of difficulties or severe spongiofibrosis, conversion to tEPA was possible. As these are presumably more complex cases, a selection bias between surgical groups since 2012 is imminent. In order to minimize this, a second analysis was done using the intention-to-treat (ITT) principle in which all conversions to tEPA since 2012 remained classified as ntEPA cases (further called "ITT-ntEPA"). Statistical tests were done using IBM™ SPSS software version 25.0. All tests were done 2-sided and a p value <0.05 indicates statistical significance. Next to descriptive statistics, categorical variables were compared using Fischer's exact test. Continuous variables were analyzed for parametric distribution using the Shapiro-Wilk test and as all variables had a nonparametric distribution, the Mann-Whitney *U* test was used for comparison. Failure-free survival (FFS) was calculated using Kaplan-Meier survival analysis with log rank statistics. To evaluate whether ntEPA was an independent predictor for failure, uni- and multivariate Cox regression analysis with calculation of the Hazard Ratio (HR) was performed.

Table 1: Patient and stricture characteristics (IQR: interquartile range; tEPA: transecting excision and primary anastomosis; ntEPA: nontransecting excision and primary anastomosis).

	Total (n=200)	tEPA (n=112)	ntEPA (n=88)	p-value
age (years); median (IQR)	49 (32-65)	49 (34-66)	47 (30-64)	0,216
follow-up (months); median (IQR)	76 (32-122)	118 (93-148)	32 (17-57)	**<0,001**
stricture length (cm); median (IQR)	1,5 (1-2)	1,5 (1-2)	1,25 (1-2)	**0,004**
diabetes; n(%)	11 (5,5%)	6 (5,4%)	5 (5,7%)	1
presence of suprapubic catheter; n(%)	44 (22%)	29 (25,9%)	15 (17%)	0,169
previous urethroplasty; n(%)	37 (18,5%)	19 (17%)	18 (20,5%)	0,584
etiology; n(%)				
idiopathic/congenital	102 (51%)	52 (46,4%)	50 (56,8%)	
iatrogenic	72 (36%)	43 (38,4%)	29 (33%)	0,508
external trauma	20 (10%)	13 (11,6%)	7 (8%)	
inflammatory	6 (3%)	4 (3,6%)	2 (2,3%)	

Table 2: Surgical outcome per surgery technique (IQR: interquartile range; FFS: failure-free survival; tEPA: transecting excision and primary anastomosis; ntEAP: nontransecting excision and primary anastomosis).

	Total (n=200)	tEPA (n=112)	ntEPA (n=88)	p-value
operation time (mintues); median (IQR)	92 (79-108)	98 (80-115)	87 (71-100)	**<0,001**
hospital stay (days); median (IQR)	2 (2-3)	3 (2-4)	2 (1-2)	**<0,001**
extravasation at first cystography; n(%)	12 (6%)	6 (5,4%)	6 (6,8%)	0,768
catheterization time (days); median (IQR)	13 (9-14)	14 (13-15)	9 (8-13)	**<0,001**
complications; n(%)				
none	170 (85%)	100 (89,3%)	70 (79,5%)	
G1	20 (10%)	8 (7,1%)	12 (13,6%)	0,147
G2	8 (4%)	3 (2,7%)	5 (5,7%)	
G3	2 (1%)	1 (0,9%)	1 (1,1%)	
Failure, n(%)	19 (9,5%)	13 (11,6%)	6 (6,8%)	0,333
Estimated failure free survival, % (standard deviation)				
1y-FFS	97 (±1,2)%	98,2 (±1,3)%	95,5 (±2,2)%	
3y-FFS	95,2 (±1,6)%	95,5 (±2)%	95,5 (±2,2)%	0,356
10y-FFS	85,6 (±3,5)%	86,9 (±3,7)%	NR	

The following variables were included: type of urethroplasty (tEPA versus ntEPA), previous urethroplasty, presence of suprapubic catheter, stricture length, and diabetes. For every surgical parameter (failure rate, complication rate, operation time, hospital stay, extravasation at first cystography, and catheterization time) the null hypothesis (H_0) was as follows: "the surgical parameter is not worse with ntEPA compared to tEPA."

3. Results

3.1. Per Surgery Analysis. A total of 200 patients underwent EPA, 112 by tEPA and 88 by ntEPA. Median follow-up for the entire cohort was 76 months, with a significant longer follow-up for tEPA compared to ntEPA (resp., 118 versus 32 months; p<0.001). There were no significant differences between both groups for patient's age, presence of diabetes, stricture etiology, presence of a suprapubic catheter, and previous urethroplasty (Table 1). Median stricture length with tEPA and ntEPA was 1,5 and 1,25 cm, respectively (p=0.004). The following hypotheses concerning surgical outcomes were evaluated (Table 2).

3.1.1. H_0: Operation Time Is Not Longer with ntEPA Compared to tEPA. Median operation time with tEPA and ntEPA was, respectively, 98 and 87 minutes (p<0.001). The null hypothesis cannot be rejected.

Table 3: Surgical outcome per intention-to-treat cohort (IQR: interquartile range; FFS: failure-free survival; ITT-tEPA: intention-to-treat transecting excision and primary anastomosis; ITT-ntEAP: intention-to-treat nontransecting excision and primary anastomosis; NA: not available).

	ITT-tEPA (n=101)	ITT-ntEPA (n=99)	p-value
follow-up (months); median (IQR)	122 (97-150)	33 (17-59)	**<0,001**
age (years); median (IQR)	50 (34-67)	44 (31-63)	0,102
stricture length (cm); median (IQR)	1,5 (1-2)	1,5 (1-2)	0,07
diabetes; n(%)	6 (5,9%)	5 (5,1%)	1
presence of suprapubic catheter; n(%)	26 (25,7%)	18 (18,2%)	0,233
operation time (minutes); median (IQR)	95 (80-110)	88 (73-100)	**0,009**
previous urethroplasty; n(%)	15 (14,9%)	22 (22,2%)	0,205
hospital stay (days); median (IQR)	3 (2-4)	2 (1-2)	**<0,001**
extravasation at first cystography; n(%)	4 (4%)	8 (8,1%)	0,248
catheterisation time (days); n(%)	14 (13-14)	9 (8-14)	**<0,001**
failure; n(%)	12 (11,9%)	7 (7,1%)	0,336
complications; n(%)			
none	92 (91,1%)	78 (78,8%)	**0,024**
G1	7 (6,9%)	13 (13,1%)	
G2	1 (1%)	7 (7,1%)	
G3	1 (1%)	1 (1%)	
Estimated failure free survival, % (standard deviation)			
1y-FFS	98 (±1,4)%	96 (±2)%	0,256
3y-FFS	95 (±2,2)%	96 (±2)%	
10y-FFS	87,4 (±3,7)%	NA	

3.1.2. H_0: Hospital Stay Is Not Longer with ntEPA Compared to tEPA. Patients treated by tEPA had a median hospital stay of 3 days compared to 2 days with ntEPA (p<0.001). The null hypothesis cannot be rejected.

3.1.3. H_0: ntEPA Is Not Associated with More Extravasation at First Cystography Compared to tEPA and There Is No Longer Catheterization Time with ntEPA Compared to tEPA. Extravasation at first cystography requiring catheter reinsertion was observed in 5.4% and 6.8% of patients treated, respectively, by tEPA and ntEPA (p=0.768). Median catheterization time with tEPA and ntEPA was, respectively, 14 and 9 days (p<0.001). The null hypothesis cannot be rejected.

3.1.4. H_0: ntEPA Is Not Associated with More Complications Compared to tEPA. No complications were reported in 89.3 and 79.5% for, respectively, tEPA and ntEPA (p=0.147). Low-grade complication rate was not significantly different among groups. Two patients (1%) suffered a grade 3 complication (requiring intervention), one in each group. The null hypothesis cannot be rejected.

3.1.5. H_0: ntEPA Has No Higher Failure Rate Compared to tEPA. 13 (11.6%) and 6 (6.8%) patients, respectively, suffered a failure with tEPA and ntEPA (p=0.333). The estimated 1- and 3-year FFS is 98.2 and 95.5% for tEPA and 95.5 and 95.5% for ntEPA (p=0.356) (Table 2). The null hypothesis cannot be rejected.

3.2. Intention-to-Treat (ITT) Analysis. Patient and stricture characteristics did not significantly differ between these 2 cohorts (Table 3). As mentioned above, all patients in the ITT-tEPA cohort (n=101) underwent tEPA. However, conversion towards tEPA was performed in 11 of 99 (11.1%) patients of the ITT-ntEPA cohort. Table 4 provides information about the characteristics of the patients converted to tEPA and those treated by ntEPA. In the ITT-ntEPA cohort, patients finally treated with tEPA had a median stricture length of 2 cm compared to 1,25 cm for ntEPA (p=0.019) whereas other preoperative characteristics were comparable. Median operation time for ITT-tEPA and ITT-ntEPA was, respectively, 95 and 88 minutes (p<0.009). in the ITT-ntEPA cohort, patients finally treated by tEPA had a median operation time of 155 minutes compared to 87 minutes with ntEPA (p=0.01). Median hospital stay was 3 and 2 days for, respectively, ITT-tEPA and ITT-ntEPA (p<0.001). In the ITT-ntEPA cohort, patients finally treated by tEPA and ntEPA both had a median hospital stay of 2 days (p=0.088). Extravasation at

Table 4: Characteristics and surgical outcomes of patients treated by tEPA and ntEPA in the intention-to-treat ntEPA cohort (IQR: interquartile range; FFS: failure-free survival; ITT-tEPA: intention-to-treat transecting excision and primary anastomosis; ITT-ntEAP: intention-to-treat nontransecting excision and primary anastomosis; NA: not available).

	tEPA (n=11)	ntEPA (n=88)	p-value
follow-up (months); median (IQR)	36 (23-73)	32 (17-57)	0,308
age (years); median (IQR)	44 (36-52)	47 (30-64)	0,676
stricture length (cm); median (IQR)	2 (1,25-2,5)	1,25 (1-2)	**0,019**
diabetes; n(%)	0 (0%)	5 (5,7%)	1
presence of suprapubic catheter; n(%)	3 (27,3%)	15 (17%)	0,415
previous urethroplasty; n(%)	4 (36,5%)	18 (20,5%)	0,256
operation time (minutes); median (IQR)	115 (88-158)	87 (71-100)	**0,01**
hospital stay (days); median (IQR)	2 (2-3)	2 (1-2)	0,088
extravasation at first cystography; n(%)	2 (18,2%)	6 (6,8%)	0,217
catheterization time (days); median (IQR)	15 (12-15)	9 (8-13)	**0,005**
failure; n(%)	1 (9,1%)	6 (6,8%)	0,574
complications; n(%)			
none	8 (72,7%)	70 (79,5%)	0,339
G1	1 (9,1%)	12 (13,6%)	
G2	2 (18,2%)	5 (5,7%)	
G3	0 (0%)	1 (1,1%)	

Table 5: Uni-and multivariate Cox regression analysis to predict for failure (HR: Hazard Ratio; CI: confidentiality interval; tEPA: transecting excision and primary anastomosis; ntEPA: nontransecting excision and primary anastomosis).

	Univariate			Multivariate		
	HR	95% CI	p-value	HR	95% CI	p-value
type of urethroplasty (tEPA vs ntEPA)	0,593	0,193-1,822	0,361	0,671	0,212-2,122	0,497
previous urethroplasty (no versus yes)	0,368	0,139-0,973	**0,044**	0,355	0,130-0,970	**0,043**
suprapubic catheter (no versus yes)	1,613	0,469-5,539	0,448	1,468	0,409-5,259	0,556
Stricture length	0,784	0,383-1,605	0,505	0,743	0,340-1,623	0,456
diabetes (no versus yes)	0,185	0,053-0,651	**0,009**	0,165	0,046-0,596	**0,006**

first cystography was reported in 4% and 8.1% of ITT-tEPA and ITT-ntEPA cases, respectively (p=0.248). Median catheterization time with ITT-tEPA and ITT-ntEPA was, respectively, 14 and 9 days (p<0.001). In the ITT-ntEPA cohort, patients treated by tEPA had a longer catheterization time compared to ntEPA (15 versus 9 days; p=0.005). More low-grade (G1-G2) complications were reported in the ITT-ntEPA cohort compared to ITT-tEPA (20,2% versus 7,9%; p=0.024). In the ITT-ntEPA cohort, patients finally treated by tEPA had a complication rate of 27,3% compared to 20,5% for patients treated by ntEPA (p=0.339). 12 (11.9%) and 7 (7.1%) patients, respectively, suffered a failure with ITT-tEPA and ITT-ntEPA (p=0.336). The estimated 1- and 3-year FFS are 98 and 95% for tEPA and 96 and 96% for ntEPA (p=0.256).

3.3. Additional Analyses. In total, 19 (9.5%) patients suffered a failure. Of the 19 failed cases, 6 (31.6%) cases were observed within the 1st year, 6 (31.6%) between the 2nd and 5th year and 7 (36.8%) after the 5th postoperative year. For tEPA, 2 (15.4%), 4 (30,8%), and 7 (53,8%) failures were detected within the 1st year, between the 2nd and 5th year, and after 5 years, respectively. For ntEAP, 4 (66.7%) cases were detected during the 1st year after operation and 2 (33.3%) between the 2nd and 5th year.

Cox regression analysis could not identify ntEPA as a predictor for failure (Table 5). In univariate analysis, previous urethroplasty (HR 0.369; p=0.044) and diabetes (HR 0.185; p=0.009) were predictive for failure. Both previous urethroplasty (HR 0.355; p=0.043) and diabetes (HR 0.165;

p=0.006) remained negative predictive factors in multivariate analysis.

4. Discussion

The success rate of 88.4% for tEPA in this series might appear somewhat lower compared to the 93.8% composite success rate for tEPA reported in the ICUD-review [1]. However, the median follow-up of 115 months in this paper is substantially longer compared to the papers included in that review [1]. Andrich et al. reported an 87% success rate after 10-year follow-up [12]. Although this series reported durable results on the long term with most of the recurrences occurring with the first years after surgery [12], this could not be confirmed by the present series as 53.8% of failures with tEPA were found even after the 5th postoperative year. In two other series, where time-related events are available, a steady decline in the success rate of tEPA was observed as well [13, 14]. As for substitution urethroplasty, this indicates that EPA also needs prolonged follow-up as late recurrences are possible. Some of our late failures were detected on occasion in an asymptomatic patient for which access to the bladder was needed (e.g., urethral catheter during surgery and cystoscopy because of hematuria). It has indeed been described that a stricture only becomes symptomatic once the urethral diameter is less than 10Fr. It is likely that a strict follow-up schedule with standard cystoscopy would have detected these failures earlier [11]. Some of the late failures might also be attributed to progression of the stricture disease as almost 20% of patients already underwent previous urethroplasty. The shorter follow-up with ntEPA in this series is explained by the change in practice since 2012 where it became the standard technique. The 93.2% success rate with ntEPA is in line with previous reports [3–7]. Estimated 1- and 3-FFS could not demonstrate inferiority of ntEPA versus tEPA nor could uni- and multivariate Cox regression analysis identify ntEPA as an independent predictive factor for failure. With ntEPA, 2 failures were detected between the 2nd and 5th postoperative year, also underlining the need for prolonged follow-up to evaluate whether this noninferiority remains on the long term (>5 years follow-up). With ntEPA, the operation time was on average 11 minutes shorter. With ntEPA, no need for ventral dissection deeper than the perineal body is needed which saves time. Furthermore, full transection of the corpus spongiosum with tEPA leads to substantial bleeding through the bulbar arteries with need for additional hemostasis (and time to achieve this). On the other hand, we perceive that the anastomosis itself is somewhat more difficult to perform and more time-consuming with ntEPA. However, other factors might bias operation time. By the standard introduction of ntEPA in 2012, both surgeons already had a large experience with urethral anatomy and urethroplasty. This experience probably has facilitated the introduction of ntEPA. In the earlier stages when uniformly tEPA was performed, this experience was less and surgery could have taken more time. Furthermore, since 2012 an important selection bias is present at the expense of tEPA: the more complex cases are still treated with tEPA and this complexity might account for a longer operation time. Nevertheless, even with ITT-analysis, operation time remained in favor of ntEPA. At least, this indicates that a shift in practice towards the use of ntEPA does not negatively affect operation time in surgeons already proficient with tEPA. The more complex nature of tEPA cases since 2012 might also be apparent by the longer stricture length and the longer catheterization time compared to the contemporary ntEPA cases. This selection bias might be the reason why strictures treated by ntEPA were shorter in the per surgery analysis but no longer in the ITT-analysis. This selection bias might in part explain the longer catheterization time with tEPA. However, the longer catheterization time is undoubtedly related to a change in our practice for catheter stay since 2010 when it was decided to remove the catheter after 1 week for simple cases (whereas this was 2 weeks before) [10]. With ntEPA, a one-day shorter hospital stay was observed. Although this might indicate a quicker recovery with ntEPA, this cannot by assumed as such. In recent years, budgetary reasons have urged us to discharge the patients as early as possible which probably attributed towards the shorter hospital stay since 2012. The observation that the tEPA cases since 2012 had an equal hospital stay despite a probably more complex stricture supports the latter hypothesis. The complication rate in this series is low and confirms the finding of other colleagues [5, 14]. High-grade (≥grade 3) complications were not more frequent with ntEPA. With ITT-analysis (but not per surgery analysis), low-grade complications were somewhat more frequent with ntEPA. This is likely due to the mainly retrospective data collection with risk of underreporting of low-grade complications in tEPA versus the prospective data collection with ntEPA. Nevertheless, this observation must raise a concern and warrants further evaluation.

Despite introduction of ntEPA, we needed to convert towards a tEPA in approximately 10% of cases. A more distal location of the stricture within the bulbar urethra was not a reason for conversion to tEPA in this series. The main reason for conversion was extensive spongiofibrosis ("full thickness") in which it was no longer valuable to spare the ventral spongious tissue. This conversion to tEPA is not at all jeopardized by an approach to go for ntEPA as all initial surgical steps are the same. From this series, it is clear that tEPA must remain in the repertoire of the urethral surgeon. Furthermore, tEPA remains indispensable in the delayed treatment of pelvic fracture related injuries [15, 16] and iatrogenic posterior urethral injuries [17]. However, the applicability of ntEPA for posterior strictures is currently explored as well [6, 18].

The aim of ntEPA is to reduce the surgical trauma with preservation of the dual blood supply of the urethra. This might offer an advantage for subsequent urethral interventions, e.g., redo-urethroplasty with free graft in which a well-vascularized graft bed is essential or implantation of an artificial urinary sphincter with less risk of cuff erosion [3]. Furthermore, ntEPA might offer a benefit regarding the reported vascular deficiency of the glans penis and the risk of erectile dysfunction with tEPA [19, 20]. The present dataset lacks information to evaluate these potential advantages. Nevertheless, despite the theoretical benefit, at least a transient decline in erectile function in 6-21.9% of cases has already been reported with ntEPA as well [4–7].

Diabetes and previous urethroplasty were identified as independent predictors for failure. With both techniques of EPA and the associated need for extensive mobilization of the bulbar urethra, the "3th" vascular supply (small arterial connections between the corporal bodies and the corpus spongiosum) of the urethra is sacrificed. Diabetes with its associated microangiopathy further increases the risk of ischemia at the urethral ends which is a reason for failure of the anastomosis [21]. In addition, diabetes might be a contributing factor in the development of ischemic strictures, which might explain some late failures. Diabetes as risk factor for failure was identified by another series as well [21]. A previous failed urethroplasty usually reflects a more complex urethral pathology with a higher risk of failure [22]. EPA for a failure after previous urethroplasty is possible in case of a previous EPA in which the urethral mobilization was insufficient for tension-free anastomosis (technical error). EPA is also possible for a short recurrence after graft urethroplasty, usually at one of the ends of the graft [23]. Other series have also identified previous urethroplasty as a negative predictive factor [14, 21], whilst others have not [23].

This study has several limitations. Until 2008, data collection was retrospective with its inherent risk of bias. Although a follow-up schedule is proposed to the patients and the referring urologists, this is not systematically followed. This might also explain delayed detection of failure or underreporting of (minor) complications. A functional definition of failure was used, but at the moment, an anatomical definition is advised as it is more accurate and objective [11]. Validated patient reported outcome measures as suggested by Jackson et al. [24] were not systematically used, as it lasted to 2017 until a Dutch validation was available [25]. This prohibits any meaningful further evaluation. The follow-up of ntEPA is relatively short. Another important limitation is that this paper is an evaluation of basically 2 noncontemporary cohorts. Changes in practice, increasing surgical experience, selection of more challenging cases, etc. might have a major impact on outcome parameters. Therefore, any direct comparison of these 2 cohorts must be avoided. To overcome all the above-mentioned shortcomings, it is necessary to conduct a prospective randomized study comparing tEPA with ntEPA evaluating surgical and functional outcomes using a strict protocol. Because important surgical parameters were not negatively affected in this series after introduction of ntEPA, it appears justified to start up such a trial. In this perspective and to elucidate the definitive role of ntEPA, our center has initiated the VeSpAR-trial: a prospective randomized controlled trial comparing Vessel-Sparing Anastomotic Repair and transecting anastomotic repair in isolated short bulbar urethral strictures (ClinicalTrials.gov NCT03572348).

5. Conclusion

Introduction of ntEPA for short bulbar strictures by experienced urethral surgeons does not negatively affect short-term failure rate, high-grade complication rate, operation time, hospital stay, and catheterization time. Late recurrences are possible with both types of EPA underlining the need for continued follow-up in these patients. tEPA must remain in the surgical repertoire for challenging cases. Diabetes and previous urethroplasty are independent predictors for failure of EPA.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors have no conflicts of interest related to the present series. The authors received no funding for this study.

Authors' Contributions

M. Waterloos and W. Verla contributed equally

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