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Repair of sphincter urethral strictures preserving urinary continence: surgical technique and outcomes

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Abstract:	Introduction Repair of post-TURP sphincter urethral strictures represents challenging problem, due to the risk of urinary incontinence after the repair. We described a surgical technique we use to repair these strictures preserving urinary continence in patients with incompetent bladder neck. Materials and methods An observational, retrospective study was conducted to include patients with post-TURP urethral strictures in the area of distal sphincter. We included only patients with complete clinical data and follow-up who previously underwent TURP or HOLEP or TUIP, and subsequently developed proximal bulbar urethral strictures close to the membranous urethra and the related distal urethral sphincter. Patients were included if they were fully continent after TURP or other procedures to treat BPH. The primary outcome of the study was treatment failure, defined as the need for any post-operative instrumentation. Secondary outcome was post-urethroplasty urinary continence. Patients showing stricture recurrence or post-operative incontinence were classified as failure. Results Overall, 69 patients were included in the study. Median patient's age was 67 years; median stricture length was 4 cm. Thirty-tree patients (47.8%) underwent previous urethrotomy. Median follow-up was 52 months. Out of 69 patients, 55 (79.7%) were classified success and 14 (20.3%) failure. Out of the whole cohort - thus 11/69 (16%) have a risk of recurrent strictures and 3/69 (4.3%) have incontinence. Conclusions The use of modified ventral onlay graft urethroplasty, using particular

	non-aggressive steps, is a suitable surgical technique for repair of sphincter urethral stricture in patients who underwent BPH transurethral surgery, using different procedures (TURP, HOLEP, TUIP).
Response to Reviewers:	Dear Editor, Please receive our revised manuscript entitled “Repair of sphincter urethral strictures preserving urinary continence: surgical technique and outcomes”. The current paper is a revised and extended draft of a previous original manuscript we submitted to your Journal. Here you can find our reply to reviewers’ comments. Reviewer #1: This paper refers to the surgical treatment of urethral stenosis at the external sphincter post BPH surgery. This is a very complex scenario because the internal sphincter mechanism has been removed and any surgery around membranous urethra may compromise postoperative continence. Although not very frequent, it is a real and unsolved dilemma, with very few information -if any- available to face these cases. For this reason, this is a very timely and interesting series, which proposes repair through an intra-sphincter ventral mucosa graft. The series is concise and well written, providing meaningful data. Some clarifications are necessary: - In the first paragraph of the Introduction the authors analyze the existing literature about post TURP strictures, but is important to note that most mentioned references relate to strictures at all locations along the urethra. Specific information about stenosis at the bulbo-membranous junction or membranous urethra (the specific issue of this communication) seems to be lacking, so it may be important to clarify this. RE: The current literature on this topic is poor and missing and the use of the term bulbo-membranous urethral strictures is also confusing. Mundy (reference 8 in the text) reported the following sentence: " A sphincter stricture is defined as a stricture of the membranous urethra..." and he never used the term bulbo-membranous stricture, reporting that if the stricture is more than 2 cm long is probably associated with strictured bulbar urethra. Kulkarni et al. (reference 2 in the text) reported the following sentence: " Most challenging is to manage are the proximal bulbar strictures. These strictures are very close to the membranous urethra. There is a risk of incontinence while treating these strictures. These are bulbar strictures and in the past, were erroneously described as membranous/sphincter strictures...But most studies describe membranous stricture or sphincter stricture frequently which to our experience has been the proximal bulbar strictures at large." and never used the term bulbo-membranous strictures. In conclusion, we fully agree we Kulkarni et al. suggestion that post-TURP urethral strictures are mainly located in the proximal bulbar urethra close to the membranous urethra. According to the reviewer's comment and review of these articles we avoid to use in the text the term "bulbo-membranous urethral strictures" and the following new sentence is now included in the Introduction: " Even though the anatomy suggests the classification of the male urethra as penile, bulbar, membranous, prostatic, may be very difficult, in the current clinical practice, to clearly identify the border between the proximal bulbar urethra and the membranous tract, mainly in patient with post-TURP stricture. We used the term sphincter strictures to define these proximal bulbar urethral strictures close to the membranous urethra and the related distal urethral sphincter." - By definition, urethral narrowing located in the bulbo-membranous junction or membranous urethra are referred as stenosis and not stricture. Please comment and correct if pertinent. RE: The American Urological Association guideline on male urethral stricture report the use of the term "stenosis" instead of "stricture" only for bladder neck contracture (J Urol 2017; 197:182-190). In the An International Consultation on Urethral Strictures (Marrakech, Morocco, October 13-16, 2010) published by SIU is reported: " The term stenosis is reserved for narrowing of the membranous urethra...the prostatic urethra, and the bladder neck, as they are not invested by corpus spongiosum. Important, the term stenosis does not imply spongiofibrosis." (Urethral Strictures, Edited by G. Jordan, C. Chapple, C. Heyns, Committee 1, pg. 6, 2012). Anyway, the term "stenosis" is rarely reported in the literature. Moreover, in our text, the strictures are now reported as proximal bulbar urethral stricture with spongiosum tissue.

- From the anatomic point of view, these stenosis are not all the same, because in some cases the lesion included the proximal bulbar and bulbo-membranous urethra, other involve mainly the membranous urethra and other mainly the prostato-membranous junction. In fact, the main length is 4cm and the range 1-7cm, so it is presumably that in most cases there was involvement of the proximal bulbar urethra and not only the bulbo-membranous junction. In addition, it is presumable that these cases have different degrees of fibrosis. Can you stratify your series considering these elements in order to find possible anatomic prognostic factors of failure?
RE: As we explained previously, it is not possible, in clinical practice, to classify the strictures as suggested by the reviewer. We agree with the reviewer that longer strictures are due to the extension of the stricture in the distal part of the proximal bulbar urethra. At present, it does not exist any reliable method to evaluate the prognostic factors of failure according to the degree of spongiofibrosis, because, currently, it does not exist any acceptable and reliable score-classification of urethral spongiofibrosis.

- This technique is suitable for cases with a patent urethra, therefore a totally obliterative stenosis may be a limiting condition. Please comment.
RE: In our present series, no patient had totally obliterative stricture. We fully agree with the reviewer that totally obliterative stricture may represent a serious limiting condition in using this technique. But, this topic is not the aim of our present study.

- Can you please specify the date range of your series?
RE: The following sentence is now included in the Methods: "...from October 2002 to July 2017."

- Your follow up time range was 14 to 191 months. Can you please specify what was the time to stenosis failure? Do you observed any failure after 14 months?
RE: The following sentence is now included in the Results: "Out of 11 failures, 4 (36.4%) were observed within first 12 months, 4 (36.4%) after 12-24 months, and 3 (27.2%) after more than 24 months"

- Do you give pelvic floor therapy to postoperative incontinent patients? How long after surgery you wait until declaring a patient incontinent?
RE: Pelvic floor exercises were not routinely recommended. For our purpose we defined post-op incontinence: “Urinary incontinence was defined as a subjective incontinence or use of pads reported by the patients. Clinically it was classified as stress urinary incontinence, mixed or urgency urinary incontinence”. The definition of post-operative incontinence is matter of debate. Unfortunately there is no reliable evidence for a specific a definitive reliable cut-off. In patients after radical prostatectomy for prostate cancer, urologists agree with a complex landscape. The definition of post-operative incontinence depends on different aspects such as timing, patient’s perception of incontinence, surgery, etc. The manuscript was changed accordingly: “Additionally, other limitations include the definition of post-operative urinary incontinence, which remains a matter of debate, the absence of neurophysiological tests to investigate the status of micturition arch reflex before and after the surgical repair”

- You said urodynamic was performed to post-operative incontinence, what were those results.
RE: Post-operative urodynamic was performed to role out detrusor overactivity and urgency urinary incontinence. Manuscript was changed accordingly.

- You said that success in patients 31-69 years old was 81.4%, but 76.9 % in patients older than 70 years. Was this difference statistically significant?
RE: We did not perform any comparative statistical analysis, because it was not planned for the current study.

- You report better results in patients with shorter stenosis than in patients with strictures >5 cm. Was this difference statistically significant? Please refer to previous answer.

- The last sentence of the Abstract Conclusions is incomplete.

RE: The sentence was changed accordingly.

- There is no statistics on the tables. Please explain why.
RE: Tables report descriptive analysis and not comparative. We added a paragraph ad the end of M&M section.

- According to your results you obtained 55/69 overall success (79.7%), 58/69 stenosis free success (84%) and 66/69 (95.7%) continence-sparing rate. However, in the last sentence of the third paragraph of Discussion you said you avoided post-operative incontinence in 91.3% of the patients and only 4.3% of patients were incontinent. Please clarify.
RE: The sentence was changed accordingly: " All these sphincter-sparing maneuvers have allowed us to avoid post-operative incontinence in 66/69 patients (95.6%) who underwent repair of strictures in the area of the distal sphincter. Only 3/69 patients (4.3%) were incontinent after our surgery.

- The numbers also don't match in the Conclusions when you state a "79.7% success rate in terms of urethral patency, and 91.3% of post-operative urinary continence". Please clarify.
RE: The sentence was changed accordingly: " This technique provided 79.7% success rate in terms of urethral patency, and 95.6% of post-operative urinary continence.

Reviewer #2: Article describes a commonly used treatment option for treating urethral stricture disease and is not particularly novel or interesting. There are low numbers and short follow-up to allow for meaningful conclusions.
RE: Unfortunately, we disagree with the reviewer. The technique we fully described in any detail was never reported in the literature. The reviewer's comment refers probably to standard ventral onlay graft for bulbar urethral stricture, but the technique we present here is greatly different from the standard procedure and it was used to repair no common urethral strictures commonly managed by dilation, urethrotomy or end-to-end anastomosis (reference 7 in the text). The strengths of our paper may be found in: large number of patients, stricture type and etiology and the mean follow-up of 4.33 years; the latter is sufficient to widely evaluate the outcomes of this procedure.

Some additional points:

Denominator - how many TURPs to get this stricture rate in the authors referral base.
RE: We don't perform any prostatic surgery in our Center.

Very long median stricture length - any comments?
RE: The longer strictures are due to the extension of the stricture in the distal part of the proximal bulbar urethra. Please go to our reply to reviewer n. 1

Clarify why catheter left for one month, pros and cons of different catheterisation times.
RE: The complete urethral regeneration after any type of epithelial graft urethroplasty require long time over catheter to be completed, according to the Denis Browne principle and experimental studies on urethral regeneration (Proc.Roy.Soc.Med. 1949;42:466-468) (Surg.Gynec.Obstet. 1962;115:729-736) (J Urol 1965;93:247-254.). According to these important suggestions we prefer to leave the catheter for one month.

At one month, was the imaging performed a peri-catheter urethrogram?
RE: We don't use the peri-catheter urethrogram, because in our experience the incidence of post-operative fistula is very low (1%), and the peri-catheter urethrogram doesn't provide us with sure evaluation of the new urethral lumen and patency. We prefer to perform voiding cysto-urethrogram. In case of fistula we insert again a smoller catheter (Floley 12 F.) and we repeat the voiding cystourethrogram one month later.

In discussion, refer to rhabdosphincter being anterior but yet then stating anterior urethra safe to dissect into?
RE: We did not understand the issue the reviewer would like to address. In the second paragraph of discussion we reported a detaile description of neuroanatomy of rhabdosphincter, and we do not see any shortcoming.

Reviewer #3: This is a well done retrospective case series of 2 high volume centers. Presented is a series of post TURP membranous urethral strictures with a technique of ventral onlay urethroplasty. The technique is well described with accompanying pictures. The results regarding continence are encouraging. While no comparison is made with dorsal or transecting repairs in this manuscript, this is a good hypothesis generating article.

Introduction
1. 1st sentence of introduction should read "The incidence of urethral stricture after TURP is reported to range between 2.2% and 9.8 % [1,2]."
RE: The sentence was changed accordingly.

2. Please add an s to remains so the following sentence will read "However, the main cause of stricture after TURP remains undetermined to date [4]."
RE: The sentence was changed accordingly.

3. No hypothesis was included at the end of the introduction. Please add your hypothesis.
RE: The aim of the study was now re-phrased.

Methods

4. Section of Surgical Technique - were - should read "where"
RE: The sentence was changed accordingly.

Discussion

5. 1st sentence is run on and confusing, please revise and break into 2 sentence.
RE: The sentence was changed accordingly.

6. When describing reference #16 the authors state hardly any sphincter fibers can be found dorsal to the urethra. If I'm understanding the anatomy correctly, I think there are hardly any sphincter fibers ventrally, not dorsally.
RE: The figure 6 well depicts the anatomic distribution of the distal sphincter fibres around the dorsal aspect urethra. This suggestion is also reported in the literature (Reference 2 and 7 in the text).

7. Conclusion section reads "Cconclusion" Please remove "c"
RE: The sentence was changed accordingly.

Reviewer #4: Firstly - in abstract - the terminology "TURP or other anti BPH procedures" is odd. More appropriate terminology would be "TURP or other procedures to treat BPH."
Last paragraph of abstract should read "preserving urinary continence in 95.6% of patients."
RE: The sentences were changed accordingly.

Impressive result in terms of durable success in terms of stricture free rate (79.7%), as well as continence preservation (95.6%). However, definition of success is arbitrary (=no further procedures), and may miss clinical failures who didn't return for follow up. A more rigid and commonly used definition of success post urethroplasty would be the ability to pass a 16 Fr flexible cystoscope at a predetermined postoperative interval.
RE: We don't use a 16 Fr flexible cystoscope in evaluation of a recurrent stricture, because this procedure may produce a false-positive evaluation of any mucosal ring that don't cause any obstruction in passing the urine. In our daily experience the use of Uroflowmetry is more accurate to evaluate the stricture recurrence as reported in the literature:
(J Urol2010;184:1386-13909 (J Urol 2011;186:1934-1937) (Urology 2014;84:213-217).

From technical standpoint, initial dilation of stricture (to 16Fr) with subsequent incision of only the "mucosal ring" may limit damage to the distal urinary sphincter, however it may limit incision of truly spongiofibrotic tissue which has been dilated. The authors correctly note that anatomic studies reveal that membranous sphincter fibers are deficient ventrally (at the 6 O'Clock position) - where they incise the mucosa only.

Would a deeper incision into fibrotic spongy tissue where the sphincter is absent translate into a higher stricture free rate without compromising continence?
RE: We tanks the reviewer for this interesting question. In our experience, the incision of the fibrotic ring allowing the fully opening of the nasal speculum (see figures 3 and 4) is sufficient to obtain a stable opened urethral lumen without create a sphincter lesion, as the results of our study confirm.

Reviewer #5: As a matter of nomenclature, I would not call post-TURP strictures "sphincter urethral strictures". As the authors point out in the Introduction, "the post-TURP strictures in the bulbo-membranous tract are very close to the distal urinary sphincter". The strictures are not of the sphincter themselves. They are bulbomembranous and thus, just distal to the sphincter. I agree with the impetus for the paper - demonstrating that repairing bulbomembranous urethral strictures after TURP is safe and has a low chance of incontinence. However, I would read through the paper (including the title) and change the wording where appropriate - most notably the title. For example, the title should read more like "Ventral Onlay Urethroplasty after Transurethral Resection of the Prostate with a Focus on Continence Outcomes"
RE: Please also read the reply to reviewer 1. In replying to reviewer n. 1 we tried to address the issue of post-op incontinence definition. We would like to stress again the fact that there is scant concordance in literature. It is due to subjective and objective parameters, which sometime may be not concordant. One of the authors dealt with the topic for many years and all the authors are aware of: What does post-op incontinence mean?" (Costantini et al, Urol. Int. 2008)

Overall, I agree with the authors that outcomes in this patient population (post-TURP urethroplasty) are lacking.

Some of the authors (from the Reconstructive Urology Center in Pune, India) have previously published a series of post-TURP strictures from their center only (https://www.ncbi.nlm.nih.gov/pubmed/30267196). I found it interesting that the majority actually underwent dorsal onlay buccal mucosal graft urethroplasty in that study. Would the authors kindly discuss how these papers vary in inclusion criteria and how to decide what approach to take? My guess is preoperative RUG would inform your proximity to sphincter. If close to sphincter, then ventral onlay preferred. But this should be clear that many post-TUR strictures are actually done dorsally - perhaps not the focus of the paper but helpful when determining approach as the surgeon.
RE: As we report in the Discussion and as figure 6 depicts, the aggressive dorsal approach or the extensive fully circumferential mobilization of the urethra (to perform end-to-end anastomosis) may increase the risk of incontinence (Reference 7 in the text).

Specific comments -

Abstract - In the results, the percentages in the final sentence are more helpful if they are out of the whole cohort - thus 11/69 (16%) have a risk of recurrent strictures and 3/69 (4%) have incontinence. Those numbers are more helpful when counseling patients whether to embark on a post-TURP urethroplasty.
RE: The sentences were changed accordingly.

In the introduction, it states that patients were only included if fully continent after TURP. Though in the pre-operative investigations, "in patients with preoperative urinary incontinence, a urodynamic study was performed". Were these patients then excluded?

Results - there is a typo: in patients with "shorted" urethral strictures.
RE: It is not clear what the reviewer mean.

Discussion - I appreciate the discussion regarding their modification of technique and why they choose a ventral onlay approach.
No comments

Reviewer #6:

	Comments: Very interesting paper with important results and thoughtful presentation of the surgical technique. Few comments: 1) You found that the number of previous urethrotomies did not influence the success rate of urethroplasty, but what happen if you just consider previous urethrotomies as a single event (yes/no) instead of as continuously coded variable. Is this factor associate with urethroplasty failure? Indeed, ith the text you attested that "The number of previous urethrotomies didn't influence the outcomes of urethroplasty (Table 2". However, table 2 only presents rates of success and failure rather than a uni/multivariable examination. Regardless the result of this additional analysis, please state that no strong conclusion can be draw, since the analysis was underpowered. RE: Please refer to our previous answers about statistical analysis. We changed the limitation paragraph as well. 2) Despite a more extensive isolation of the trans-sphincter membranous urethra (Dalpiaz et al. doi:10.1111/j.1464-410X.2008.07772.x; Gomez et al. doi:10.21037/tau.2018.03.05) would be required for a better exposure of the stricture, the authors describe a more "conservative" approach for treating these strictures. Indeed, they present trans-bulbar approach for reaching the sphincteric membranous urethra. My concerns regard the limited visibility with this approach and the restricted space for suturing. How long did it take (in average) this procedure? There was any case where you had to abort the repair and proceed towards a more extensive isolation of the urethra? Moreover, you specified that the strictures were in the area of distal sphincter, but how many precisely were in the sphincteric urethra? How were the success and the incontinence rates of those patients? RE: The figures include in the paper depicts our technique as easy, with good visibility and conservative of the anatomy of the sphincter. I would like to congratulate with the authors for their efforts. Overall, this paper brings new and important insights in this filed and warrants publication.

Repair of sphincter urethral strictures preserving urinary continence: surgical technique and outcomes

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Abstract

Introduction Repair of post-TURP sphincter urethral strictures represents challenging problem, due to the risk of urinary incontinence after the repair. We described a surgical technique we use to repair these strictures preserving urinary continence in patients with incompetent bladder neck.
Materials and methods An observational, retrospective, study was conducted to include patients with post-TURP urethral strictures in the area of distal sphincter. We included only patients with complete clinical data and follow-up who previously underwent TURP or HOLEP or TUIP, and subsequently developed proximal bulbar urethral strictures close to the membranous urethra and the related distal urethral sphincter. Patients were included if they were fully continent after TURP or other procedures to treat BPH. The primary outcome of the study was treatment failure, defined as the need for any post-operative instrumentation. Secondary outcome was post-urethroplasty urinary continence. Patients showing stricture recurrence or post-operative incontinence were classified as failure.
Results Overall, 69 patients were included in the study. Median patient's age was 67 years; median stricture length was 4 cm. Thirty-tree patients (47.8%) underwent previous urethrotomy. Median follow-up was 52 months. Out of 69 patients, 55 (79.7%) were classified success and 14 (20.3%) failure. Out of the whole cohort - thus 11/69 (16%) have a risk of recurrent strictures and 3/69 (4.3%) have incontinence.
Conclusions The use of modified ventral onlay graft urethroplasty, using particular non-aggressive steps, is a suitable surgical technique for repair of sphincter urethral stricture in patients who underwent BPH transurethral surgery, using different procedures (TURP, HOLEP, TUIP).

Keywords Urethral stricture . Urinary incontinence . Urethroplasty. TURP

Introduction

The incidence of urethral stricture after TURP is reported to range between 2.2% and 9.8 % [1,2]. In 2004, Fenton et al. reported that out of 194 urethral strictures, 63 (32%) were classified as iatrogenic, and transurethral surgery accounted for most iatrogenic strictures (26/63, 41%) [3]. In 2009, Lumen et al. reported that transurethral surgery was the cause of strictures in 52 (19.4%) of the 268 patients [4]. These authors also suggested that transurethral surgery is the major cause of stricture in older patients and the second most common cause of bulbar urethral strictures [4]. In 2012, Heynes et al. reported an increase in incidence of iatrogenic strictures (mainly related to transurethral surgery) from 10% (in year 2001) to 36.8% (in year 2007) [5]. Interesting to note that some authors using a bipolar transurethral resection of the prostate (TURis) reported a significantly higher urethral stricture rate compared to standard monopolar TURP (M-TURP), in patients with a prostate volume > 70 ml (20% in TURis vs 2.2% in M-TURP) [6].

The most common sites of post-TURP urethral strictures have been meatus, fossa navicularis, penile urethra, peno-bulbar site and proximal bulbar tract [2]. The etiology of post-TURP bulbar urethral strictures are probably due to a multitude of causes, including improper traumatic insertion of the resectoscope (26F/28F), exacerbated by the narrow urethral caliber, monopolar current leakage due to insufficient resectoscope isolation, prolonged resection time, ischemia, protracted catheterization and infection. However, the main cause of stricture after TURP remains undetermined to date [4].

Even though the anatomy suggests the classification of the male urethra as penile, bulbar, membranous, prostatic, may be very difficult, in the current clinical practice, to clearly identify the border between the proximal bulbar urethra and the membranous tract, mainly in patient with post-TURP stricture. We used the term sphincter strictures to define these proximal bulbar urethral strictures close to the membranous urethra and the related distal urethral sphincter. Because of the stricture proximity to the sphincter, and the bladder neck compromised by prior BPH surgery, there is an inherent risk of causing urinary incontinence by attempts to repair these strictures [2,7]. In a limited series of patients with post-TURP sphincter strictures who underwent urethroplasty, Mundy reported a high incidence of postoperative incontinence [8].

The aim of this study was to investigate the clinical outcome of surgical repair of post-TURP sphincter urethral strictures and to report the rate of post-operative urinary continence.

Methods

Patient population and study design

We performed an observational, retrospective, descriptive study on a cohort of patients who underwent surgical repair of post-TURP proximal bulbar urethral strictures, close to the membranous urethra and the related distal urethral sphincter, at the Centers for Reconstructive Urethral Surgery in Arezzo, Italy and Pune, India from October 2002 to July 2017. The study was approved by the Institutional Review Board. Patients were requested to read and sign the informed consent explaining the surgical procedure and the complications. We included only patients with complete clinical data who previously underwent TURP or HOLEP or TUIP, and later developed sphincter urethral stricture. All patients included in the study were fully continent after TURP or other procedures. Patients with traumatic or penile strictures, or posterior urethral disruption, lichen sclerosus (LS), failed hypospadias repair (FHR), previous radiotherapy, or incomplete clinical records or inadequate follow-up (minimum follow-up 12 months) were excluded. Patients with history or clinical records reporting treatment of urethral stricture prior to the TURP were excluded as well. Furthermore, patients with pre-operative urgency or urgency incontinence, with neurological diseases impacting on micturition reflex were excluded from the study. The primary outcome of the study was treatment failure, defined as the need for any post-operative instrumentation. Secondary outcome was evaluation of post-surgery urinary continence. Patients showing stricture recurrence or post-operative incontinence were classified as failure. Urinary incontinence was defined as a subjective incontinence or use of pads reported by the patients. Clinically it was classified as stress urinary incontinence, mixed or urgency urinary incontinence.

Pre-operative investigations

The clinical history and charts of patient were reviewed in order to evaluate the etiology of stricture (TURP, HOLEP, TUIP), and the presence of urinary incontinence, and the previous treatment of the stricture (dilation, urethrotomy, urethroplasty). The genitalia were inspected to exclude the presence of LS or FHR. Preoperative tests included urine culture, post-void residual (PVR), retrograde urethrogram (RUG) and voiding cystourethrogram (VCUG), sonourethrography and urethroscopy.

Surgical technique

A 3F. guide-wire is inserted with small instrument (7 F.) through the stricture (Fig. 1). Atraumatic plastic Nelaton 16 F. is gently inserted through the external urinary meatus into the urethra to the site of stricture where the catheter stops to progress, and the area is marked on perineum (Fig. 2A). A midline perineal incision is made, the bulbo-spongiousum muscles are separated at the midline and the bulbar urethra is fully exposed. The site of stricture is again marked (Fig. 2B). About 2 cm proximal to the stricture a site is also marked were the bulbar urethra will be opened (Fig. 2B). The bulbar urethra is longitudinally opened and a previously placed 3F. guide-wire is exposed as it traverses through the stricture (Fig. 2C). Under the guidance of the guide-wire the stricture is gently progressively dilated from 8F. to 16F using atraumatic plastic Nelaton catheters. (Fig. 3ABC). After the final 16F. catheter dilation, a nasal speculum is gently inserted across the stricture (Fig. 4AB) and the mucosal ring is incised at the 6 o'clock position using a special ophthalmic scalpel (Fig.4CD) until the nasal speculum could be fully opened without tension (Fig. 4E). A J-shaped needle (Fig. 5A), is inserted through the spongy tissue in front to the verumontanum, and the tip of the needle is delivered towards the bladder and then pulled back using a second needle driver (Fig. 5BCD). Using this technique, three stitches (Vicryl 4/0) are inserted at the 5-6-7 o'clock just distal to the verumontanum (Fig. 5E). Oral mucosal graft is then placed into the ventral urethrotomy according to the standard technique of ventral onlay urethroplasty. At the completion of the procedure a grooved silicone Foley catheter 18F. is left in place for one month.

Post-operative course and follow-up criteria

One month after the surgery, a voiding cysto-urethrography was performed and the catheter was removed. Follow-up visits were scheduled every 6 months and included uroflowmetry and post-micturition residual urine evaluation. Patients were queried in detail regarding their urinary continence status in different body positions (supine, standing, under stress) and were asked to report on their use of pads (small, medium, large). For patients who have reported any degree of post-operative incontinence, urodynamic study was performed to rule our detrusor overactivity. Data were described as number and percentage, or mean and standard deviation, or median and range, when appropriated. Differences between groups were not compared.

Results

Overall, 69 patients were included in the study of whom 63 (91.4%) previously underwent TURP, 3 (4.3%) HOLEP and 3 (4.3%) TUIP. Median patient's age was 67 years (range 31-81 years), and median stricture length was 4 cm (range 1-7 cm). Overall, 33 patients (47.8%) underwent previous urethrotomy, median 1 (range 1-10). Following urethroplasty a median follow-up was 52 months (range 14-191 months). Out of 69 patients, 55 (79.7%) were classified as a success and 14 (20.3%) as a failure. Among the 43 (62.3%) patients 31-69 years old, the success rate was 81.4%, while among the 26 patients older than 70 years the success was 76.9%. Stratified by prior BPH treatment, for the patients with strictures after TURP the urethroplasty success rate was 79.4%, after HOLEP 100% and after TUIP 66.7%. In patients with urethral strictures between 1 and 5 cm the success rate was ranging from 76.2% to 100%. In comparison, in patients with strictures 5/6 cm the successful outcome was achieved in 66.7% (Table 1). The number of previous urethrotomies didn't influence the outcomes of urethroplasty (Table 2). Overall, out of the 14 failures, 11 (78.6%) were due to recurrent strictures, and 3 (21.4%) were due to post-operative incontinence. **Out of 11 failures, 4 (36.4%) were observed within first 12 months, 4 (36.4%) after 12-24 months, and 3 (27.2%) after more than 24 months.**
One of the 3 patients developed urge incontinence due to overactive bladder, as it was showed by urodynamic assessment, and was successfully treated with medical therapy. The treatments of 11 patients with recurrent strictures were summarized in Table 3. In summary, out of 69 patients, 5 (7.2%) were included in periodic dilation program, and 1(1.4%) was suggested to leave a permanent urethral catheter.

Discussion

The repair of post-TURP proximal bulbar urethral strictures close to the membranous urethra and the related distal urethral sphincter still represents a challenging problem, due to the risk of urinary incontinence after the repair. Indeed, due to incompetent bladder neck, the residual urinary continence is only guaranteed by the functioning distal urinary sphincter. To repair these difficult urethral strictures, we used the ventral onlay oral mucosa graft technique originally described by Morey and McAninch in 1996 [9,10,11]. This technique was greatly modified with important non-aggressive surgical steps to avoid the sphincter damage.

Despite numerous anatomical and radiological studies, the anatomy of the distal male urinary sphincter is still a controversial subject.[8,12,13,14,15,16] In summary, the full male urinary continence is guaranteed by two different sphincter components: 1. the proximal smooth muscle component composed of condensation of detrusor fibers (bladder neck); 2. the distal rhabdosphincter, a striated muscle that extends sleeve-like from the base of the bladder to the urogenital diaphragm. [8,12,13] The distal rhabdosphincter is not a circumferential ring around the urethra, but is omega-shaped inserting dorsally at the perineal body via a tendinous rafe. [6,7,13] Innervation of the rhabdosphincter comes from pelvic (autonomic) and pudendal (somatic) nerve branches, which enter the rhabdosphincter postero-laterally. [15] In 1996, Strasser H. et al. fully described the anatomy and innervation of the rhabdosphincter of the male urethra, by means of anatomical dissections and serial anatomical as well as histological sections of 12 male pelves.[16] The authors have clearly shown that in an adult male, hardly any striated muscle fibers can be found dorsal to the urethra, forming an omega-shaped loop around the anterior and lateral aspects of the urethra.[16] (Fig. 6).This pattern of muscle position leaves the ventral anterior and anterolateral surface of the membranous urethra relatively safe for dissection without sphincter damage.

To preserve urinary continence in patients with strictures in the area of the distal sphincter is fundamental to fully respect and preserve the true anatomy of this sphincter. Fully circumferential dissection or complete transection of the proximal bulbar/membranous urethra or aggressive dorsal dissection of the urethra may damage the sphincter fibers and potentially cause incontinence.[6,7,8] For these reasons, we greatly modified our surgical technique of ventral onlay graft urethroplasty. In our approach the bulbar urethra is opened along its ventral surface, avoiding any circumferential dissection, the stricture is gently progressively dilated avoiding damage to the sphincter fibers and the incision of the stricture is made at 6 o'clock were the sphincter fibers are absent. Moreover, we make the urethrotomy incision only through the mucosal ring sparing the underlying spongiosum tissue. All these sphincter-sparing maneuvers have allowed us to avoid post-operative incontinence in 91.3% of the patients who underwent repair of strictures in the area of the distal sphincter. Only 4.3% of patients were incontinent after our surgery.

There are some weaknesses in this study. The sample size is relatively small, notwithstanding the multicenter international setting. No statistical comparative analysis was done. Additionally, other limitations include the definition of post-operative urinary incontinence, which remains a matter of debate, the absence of neurophysiological tests to investigate the status of micturition arch reflex before and after the surgical repair. Somatosensory evoked potentials of the pudendal nerves were not investigated and we could not detect presence or absence of neurogenic sphincter deficiency. Finally, when we evaluated existing literature for articles on similar topics, we failed to find data to consider in a discussion.

Conclusion

The use of modified ventral onlay graft urethroplasty is a suitable surgical technique for repair of sphincter urethral stricture in patients who underwent BPH transurethral surgery. This technique provided 79.7% success rate in terms of urethral patency, and 95.6% of post-operative urinary continence.

References

1. Rassweiler J, Teber D, Kuntz R, Hofmann R (2006) Complications of transurethral resection of the prostate (TURP) - incidence, management, and prevention. Eur Urol 50:969-980

2. Kulkarni SB, Joglekar O, Alkandari M, Jhosi PM (2018) Management of post TURP strictures. World J Urol Sep 28. https://doi.org/10.1007/s00345-018-2498-x

3. Fenton AS, Morey AF, Aviles R, Garcia CR (2005) Anterior urethral strictures: etiology and characteristics. Urology 65:1055-1058

4. Lumen N, Hoebeke P, Willemsen P, De Troyer B, Pieters R, Oosterlinck W (2009) Etiology of urethral strictures disease in 21st Centrury. J Urol 182:983-987

5. Heynes CF, van der Merwe J, Basson J, van der Merve A (2012) Etiology of male urethral strictures - Evaluation of temporal changes at a single center, and review of the literature. African J Urol 18:4-9

6. Komura K, Inamoto T, Takai T et al (2015) Incidence of urethral stricture after bipolar transurethral resection of the prostate using TURis: results from a randomized trial. BJU Int 115:644-652

7. Blakely S, Caza T, Landas S, Nikolawski D (2016) Dorsal onlay urethroplasty for membranous urethral strictures: urinary and erectile functional outcomes. J Urol 195:1501-1507

8. Mundy AR (1989) The treatment of sphincter strictures. BJU 64:626-628

9. Morey AF, McAninch JW (1996) When and how to use buccal mucosa grafts in adult bulbar urethroplasty. Urology 48:194-198

10. Barbagli G, Sansalone S, Romano G, Lazzeri M (2011) Sugery Ilustrated - Surgical Atlas - Ventral onlay oral mucosal graft bulbar urethroplasty. BJU 108:1218-1231

11. Barbagli G, Montorsi F, Guazzoni G et al (2013) Ventral oral mucosal graft urethroplasty in nontraumatic bulabr urethral strictures: surgical technique and multivariable analysis of the results. Eur Urol 64:440-447

12. Wang XD, Liu S, Xiong LX, Sun PY, Wang XS (2014) Normal anatomy of urethral sphincter complex in young Chinese males on MRI. Int Urol Nephrol 46:1469-1476

13. Strasser H, Bartsch G (2000) Anatomy and innervation of the rhabdosphincter of the male urethra. Semin Urol Oncol 18:2-8

14. Oelrich TM (1980) The urethral sphincter muscle in the male. Am J Anat 158:229-246

15. Hollabaugh RS Jr, Dmochowski RR, Steiner MS (1997) Neuroanatomy of the male rhabdosphincter. Urology 49:426-434

16. Strasser H, Klima G, Poisel S, Horninger W, Bartsh G (1996) Anatomy and innervation of the rhabdosphincter of the male urethra. The Prostate 28:24-31

LEGEND OF FIGURES

Figure 1AB: The 3F. guide-wire is inserted by urethroscopy through the stricture.

Figure 2: A. Nelaton 16 F. is inserted and the site of stricture is marked into perineum. **B.** The bulbar urethra is exposed, and the site of stricture is marked. Two cm before the stricture site is also marked the site were the bulbar urethra will be opened. **C.** The bulbar urethra is opened and the 3F. guide-wire is exposed inside the stricture.

Figure 3: A. Under the guidance of the guide-wire the stricture is gently progressively dilated by inserting Nelaton catheter 8F. **B.** After progressive 10,12,14 F. dilation a 16F. Nelaton catheter is inserted. **C.** View of stricture after progressive dilation.

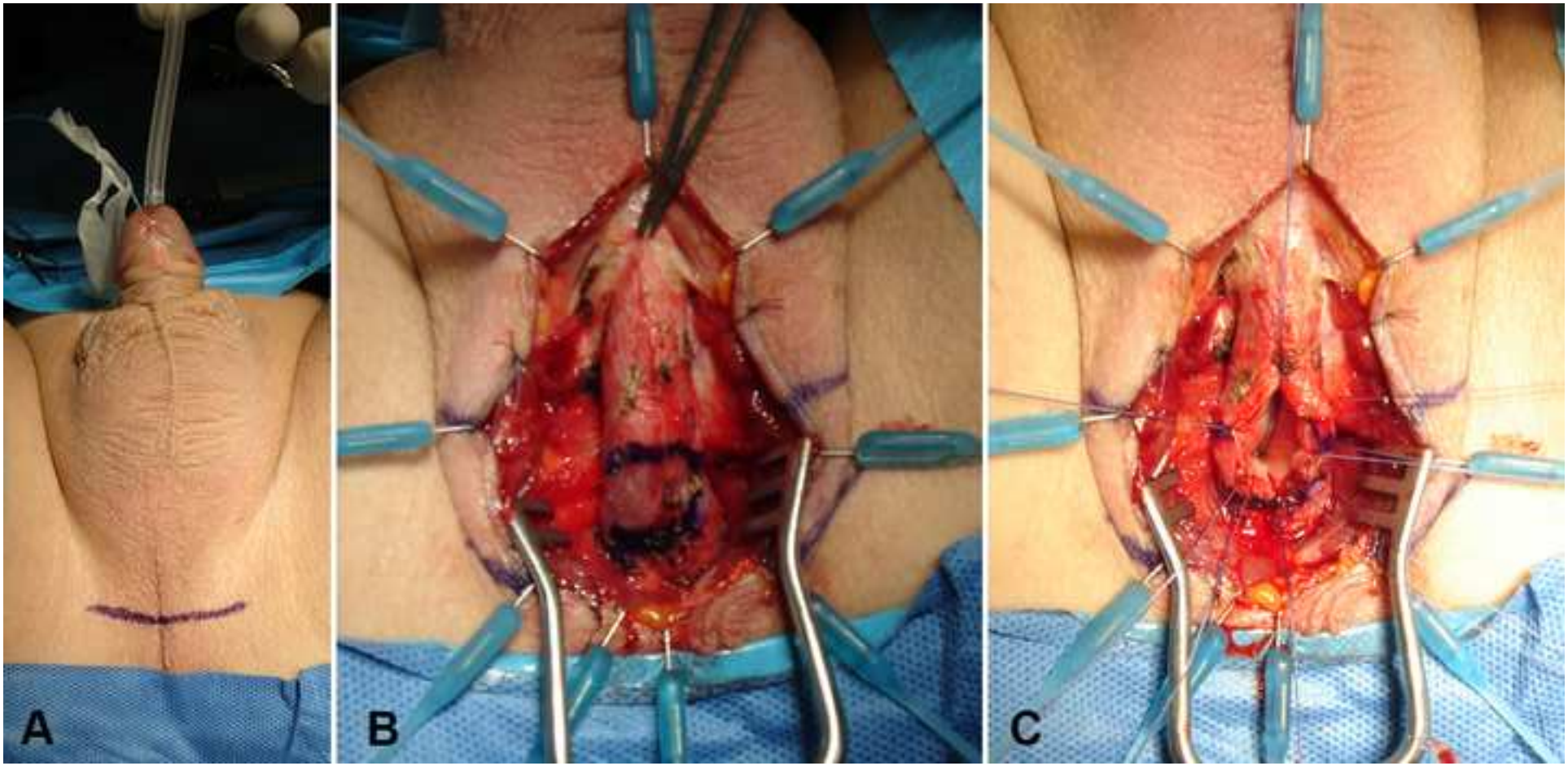
Figure 4: A. View of the nasal speculum with modified tip. **B.** The nasal speculum is inserted in the stricture. **C.D.** The white mucosal ring is incised at 6 o'clock using a special ophthalmic scalpel. **E.** The nasal speculum is fully opened.

Figure 5: A. The J-shaped needle. **B.C.D.E.** The J-shape needle is inserted through the spongy tissue in front to the veru-montanu, the tip of the needle is pushed on the bladder and pulled back. **F.** Using this maneuver, three stitches are inserted at 5,6 7, o'clock in front to the veru montanu.

Figure 6: Schematic drawing of the rhabdosphincter of the male urethra: BL = urinary bladder, PR = prostate. U = urethra, SUS = striated urinary sphincter = rhabdosphincter (Reprinted with permission.[16]).

Figure

Click here to access/download;Figure;FIGURE 2.jpg



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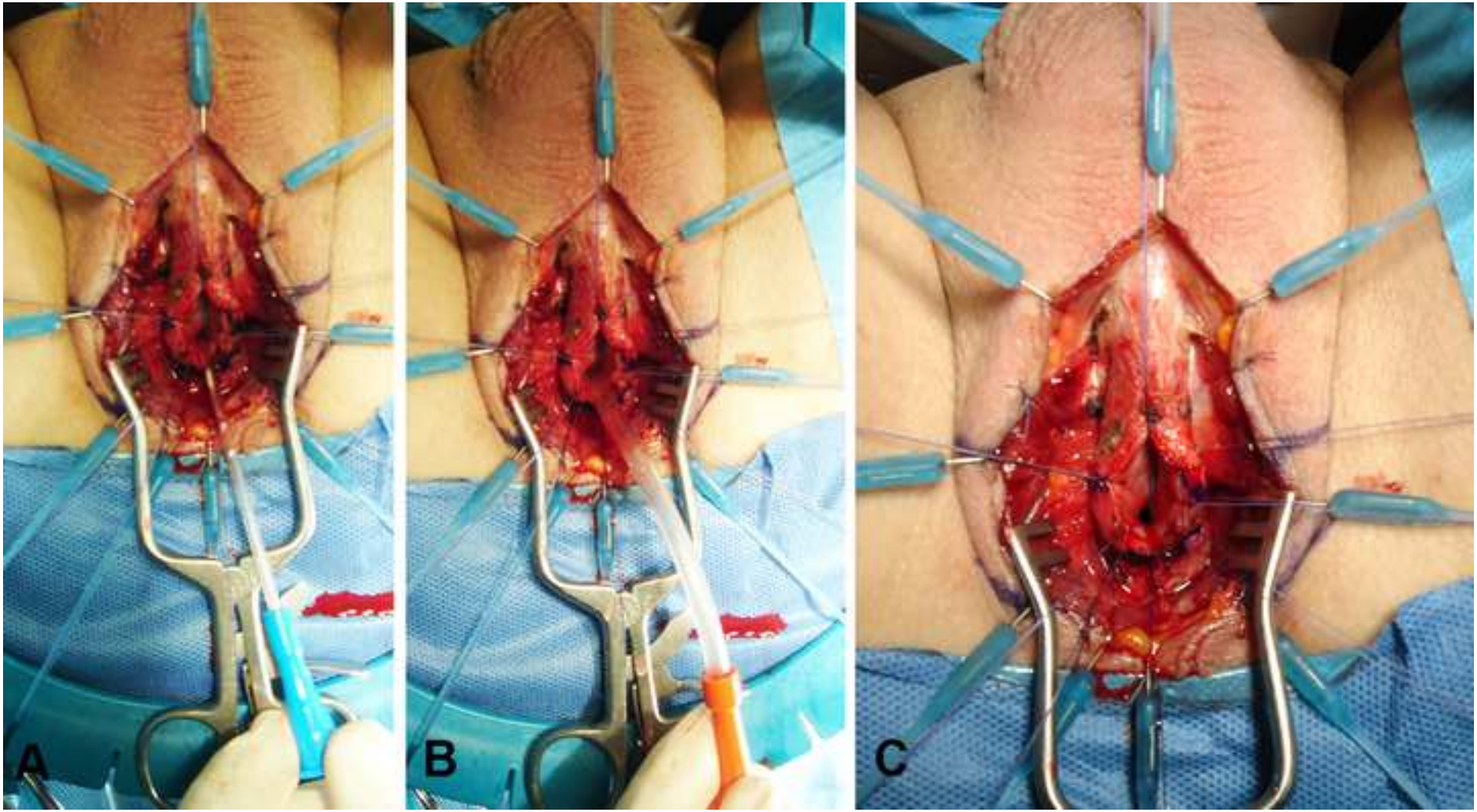

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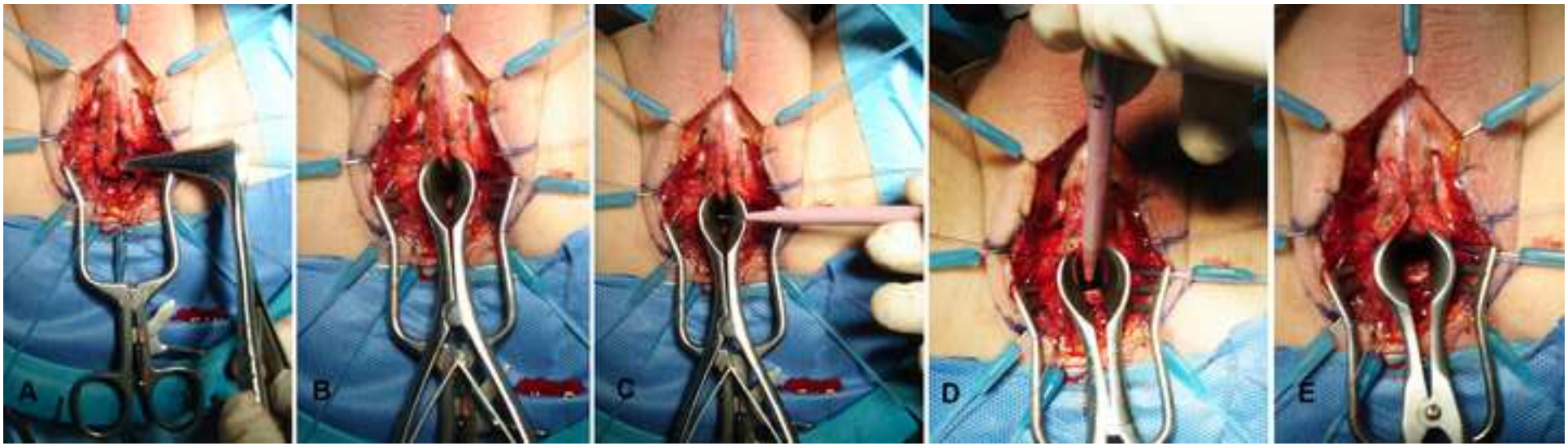

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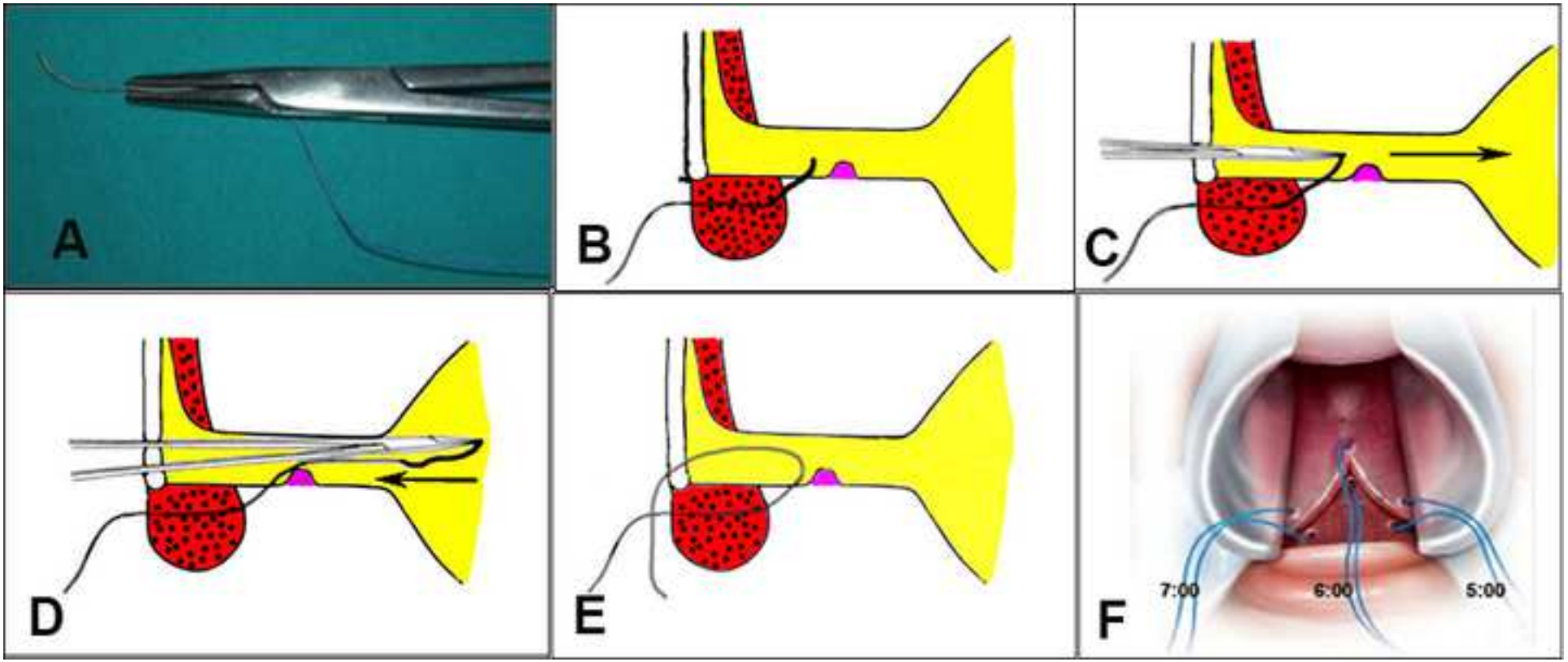

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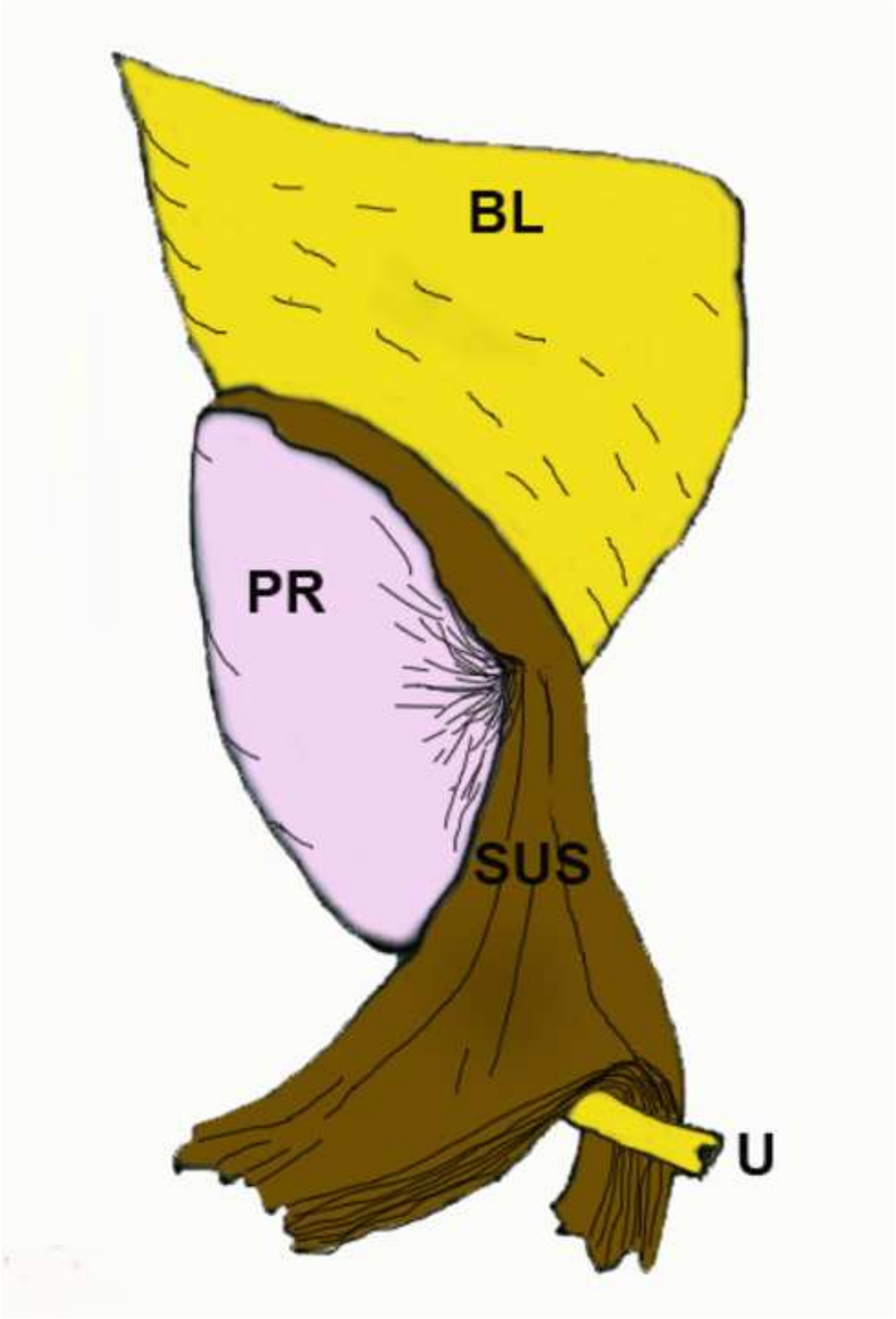

Figure

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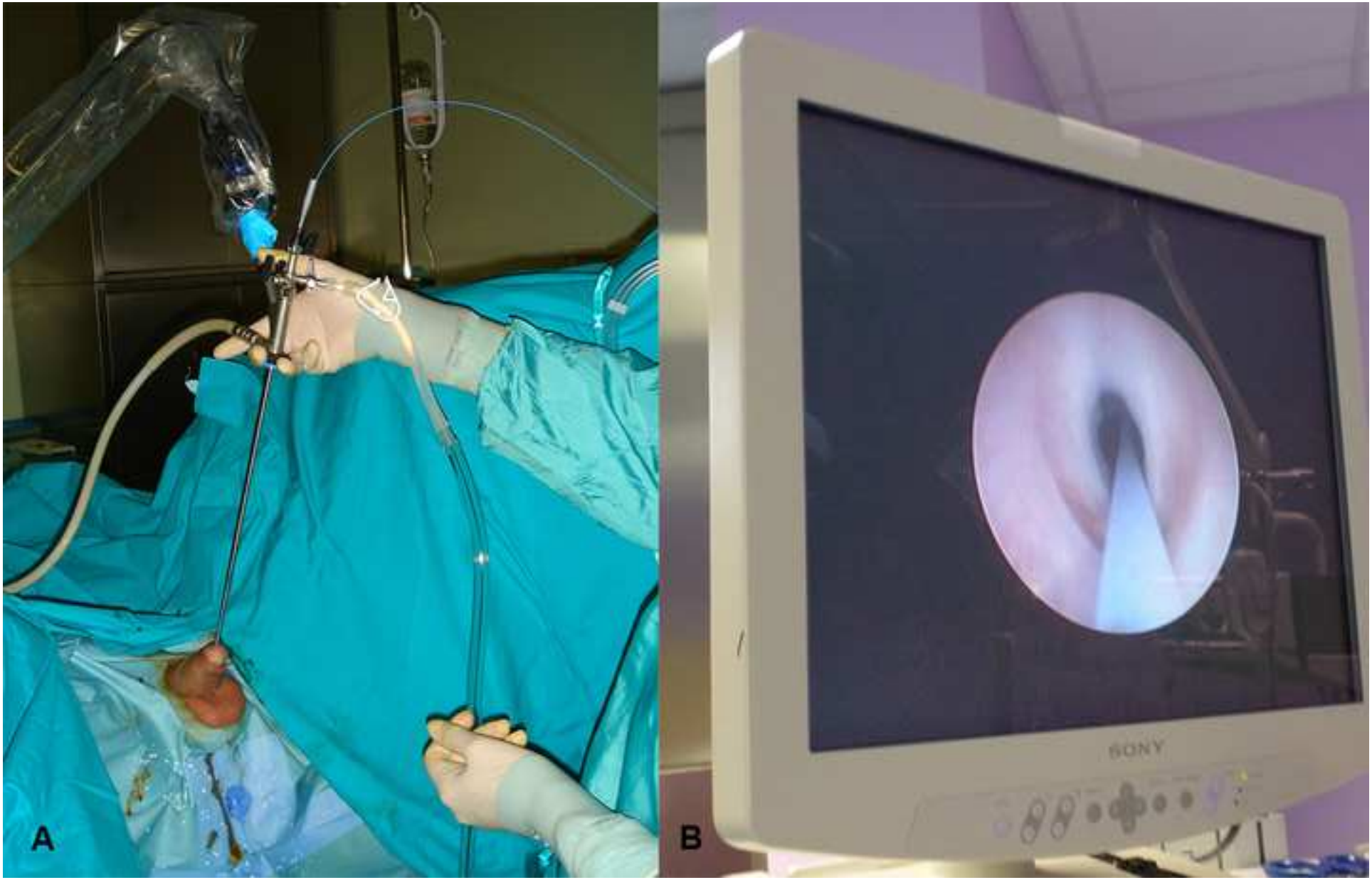

Table 1: Success rate according to the stricture length.

stricture length	N° patients	success	failure
1-2 cm	2 (2.9%)	2 (100%)	-
2-3 cm	11 (16%)	9 (81.8%)	2 (18.2%)
3-4 cm	21 (30.4%)	16 (76.2%)	5 (23.8%)
4-5 cm	25 (36.2%)	20 (80%)	5 (20%)
5-6 cm	6 (8.7%)	4 (66.7%)	2 (33.3%)
> 6 cm	4 (5.8%)	4 (100%)	-
total	**69**	**55 (79.7%)**	14 (20.3%)

Table 2: Success rate according to the previous treatments.

treatment of failures	N° patients	success	failure
periodic dilation	2 (18.2%)	-	-
urethrotomy	7 (63.6%)	4 (57.1%)	3 (42.9%) periodic dilation
oral mucosa urethroplasty	2 (18.2%)	1 (50%)	1 (50%) permanent catheter
total	**11**	**5**	**4**

Table 3: Treatment of 11 failures.

previous treatment	N° patients	success	failure
1 urethrotomy	14 (20.3%)	12 (85.7%)	2 (14.3%)
2 urethrotomies	11 (16%)	10 (90.9%)	1 (9.1%)
3 urethrotomies	2 (2.9%	2 (100%)	-
4 urethrotomies	1 (1.4%)	1 (100%)	-
5 urethrotomies	1 (1.4%)	1 (100%)	-
6 urethrotomies	3 (4.3%)	3 (100%)	-
10 urethrotomies	1 (1.4%)	1 (100%)	-
none	9 (13%)	6 (66.7%)	3 (33.3%)
dilations	8 (11.6%)	6 (75%)	2 (25%)
associated treatment	19 (27.5%)	13 (68.4%)	6 (31.6%)
total	**69**	**55 (79.7%)**	**14 (20.3%)**