



Evidence Review:

Urethroplasty for benign urethral strictures in adult men

NHS England

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1. Introduction

A urethral stricture is a narrowing of the anterior urethra as a consequence of ischaemic spongiobrosis caused by scarring, injury, infection, or non-infectious forms of urethritis, which can lead to reduced flow or blockage of urine (retention), and other complications such as penile swelling and pain, and pain in the pelvic or lower abdominal area. Strictures are the most common cause of difficulty passing urine in younger and middle aged men.

Urethral strictures can be divided into a) anterior urethral strictures, and b) the less common and complex posterior urethral strictures that are caused by the disruption of the urethra by injury.

Typically, patients experiencing a benign anterior urethral strictures are subject to either an urethrotomy or urethral dilation as first-line treatment options. Where patients show incomplete response and/or are contraindicated or have a stated preference, an urethral reconstruction via urethroplasty is potential second line treatment. This policy proposition considers the latter; urethral reconstruction for benign anterior urethral stricture disease.

Urethroplasty is the open repair of a stricture in the urethra; the most common site is the bulbar urethra, followed by the penile urethra. A one-stage repair is the most common form of repair. Depending on the length and location of the stricture, different options are available: 1) excision of the stricture and reconnection of healthy urethra; 2) augmentation of the urethra, with or without excision of the strictures segment.

The policy proposition is in line with European Association of Urology (EAU) and International Consultation on Urological Disease (ICUD) guidelines (both 2010).

Greater availability of trained urethroplasty surgeons, use of managed care pathways to reduce hospital stay, and adoption of oral mucosa as graft material has broadened its application.

2. Summary of results

Summary

The body of evidence for this review comprised of two systematic reviews including one Cochrane review, one case control study and a few large and small case series. The overall evidence was limited in direct comparison of urethroplasty with other interventions. The Cochrane review was low quality with the entire body of evidence based on an abstract of a single non published study (Wong et al. 2010, updated 2012). Two studies comparing the current surgical practice and beliefs were included in the evidence review to provide background information but not summarised.

In summary, the current clinical evidence review provides low level but supportive evidence in favour of urethroplasty compared to urethrotomy with reduction in recurrence rates ranging from 11 to 24% over 1 to 4 years and significant improvement in peak urinary flow in up to 86% of patients. Success in terms of stricture recurrence may be impacted by stricture length, and anatomical location of the stricture segment. Some studies appear to identify patients with longer stricture lengths as an ideal subgroup for primary urethroplasty. Additionally, there appears to be a volume-outcome relationship with a continuous learning curve beyond 600 patients/surgeon. The literature search did not find any studies on patient-reported outcomes or cost-effectiveness for urethroplasty.

Detailed Evidence

Part 1: Clinical effectiveness of urethroplasty versus endoscopic therapy for the treatment of urethral strictures

The clinical effectiveness of a urethral stricture treatment was defined in most studies in terms of rate of stricture recurrence and improvement in urinary peak flow.

Meeks et al. (2009) evaluated clinical outcomes of urethroplasty based on stricture recurrence in a systematic review of 86 studies published between 2000 and 2008. Recurrence was defined as the need for a repeat surgical procedure or dilation after urethroplasty. The time period for follow-up was not reported and is likely to be varied

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across studies, which should be noted given the tendency towards recurrence over time. Average stricture recurrence rate for urethroplasty was found to be 15.6%, with significantly higher rates for longer strictures (>5 cm) ($p=0.0006$). Additionally, the recurrence rate was lowest for bulbar urethral strictures (13.9%) compared with that for penile strictures (18.4%, $p=0.00001$) and posterior urethral strictures (17.5%, $p=0.0006$). The reconstructive technique did not appear to affect the recurrence rate (15.6% for graft vs 16.4% for anastomotic, $p=0.37$).

A recent large case series by Warner et al. (2015) updated these findings, reporting recurrence rate of 22.5% at average follow-up of 20 months (12-344 months) for urethroplasty on long-segment urethral strictures in 466 patients treated at 8 international centres. Lowest recurrence rate was reported for one-stage buccal mucosal graft at 17.5%. However, given the retrospective nature of the study and non-random allocation of treatment, there is significant risk of patient selection bias between different sub-types of urethroplasty.

In a much smaller retrospective case series of patients who underwent bulbar end-to-end anastomosis urethroplasty ($n=33$), stricture recurrence was observed in 12% of patients at average 42.6 months (8 – 96 months) follow-up. All recurrences were limited to patients with non-traumatic strictures (Suh et al., 2013). This could indicate the potential role of the underlying aetiology (e.g. if there is an ongoing disease process, recurrence is more likely). Similarly, Xu et al. (2014) reported a recurrence rate of 11% with mean postoperative urinary peak flow rate of 24.2mL/s over a long follow up (mean 38.7 months, range 12-110 months) in a case series of 36 patient with relatively long strictures (median length 12.5cm) secondary to genital lichen sclerosis.

The Cochrane systematic review comparing simple urethral dilatation, endoscopic urethrotomy, and urethroplasty for urethral stricture disease in adult men was limited to a review of one unpublished study comparing urethroplasty with urethrotomy (Wong et al. 2010, update on 2012). The review reported a study by Ravichandran et al. (2003) on 50 males who were randomised to initial treatment by urethroplasty (anastomotic technique) or urethrotomy. More men in the urethrotomy (64%) group were likely to require further surgery or dilation compared with the urethroplasty group (24%). These findings need to be treated with extreme caution given that the review was based on an abstract of this study which has not been published in any peer reviewed journal.

More definitive evidence for comparative effectiveness of urethroplasty comes from a retrospective case control study ($n=45$) in Spain which reported that urethroplasty was significantly successful ($p=0.01$) in 86.4% of the patients compared with 47.8% for urethrotomy, using urinary peak flow > 15mL/s after surgery as the definition for successful outcome. The urethroplasty ($n=31$) group included 9 patients (20%) in whom the previous urethrotomy had failed. This subgroup had longer strictures (3.4 ± 3.1) compared to primary urethroplasty (1.6 ± 1.6) and primary urethrotomy (1.1 ± 0.5) subgroups. Based on these findings the authors concluded that urethroplasty would be an ideal choice for patients with stricture length >1.5cm. The retrospective nature of the study, non-randomised assignment of procedures and small number of patients are likely to limit the representativeness of the study population and hence generalisability of the findings. (Tinaut-Ranera et al. 2014).

In conclusion, there is currently low level but supportive evidence for greater effectiveness of urethroplasty in treatment of urethral strictures compared to urethrotomy, with reduction in recurrence rates ranging from 11% to 24% (mean follow up time period 20-42.6 months) and significant improvement in urinary peak flow in up to 86% of patients. Success in terms of stricture recurrence may be impacted by stricture length. The studies appear to identify patients with longer stricture lengths as an ideal subgroup for primary urethroplasty.

Part 2: Patient-reported outcome measures for urethroplasty

The literature search did not find any studies on patient-reported outcomes for urethroplasty.

Part 3: Safety issues or adverse events (complications)

Warner et al. (2015) indicate early complications including infection (UTI), local pain, inflammation, numbness, oedema, and penile skin ischemia in up to 15 out of 466 patients. More serious side effects were wound dehiscence in 8 cases and one case each of fistula and scrotal abscess. Late complications mainly included penile chordee (11), persistent hypoesthesia (7), fistula (6), and erectile dysfunction (3). Authors report that occurrence of a complication conferred no statistical impact on stricture recurrence ($p=0.29$). The complication rate was higher in the cases with fasciocutaneous flap urethroplasty compared with those without a flap (32% vs 14%, respectively; $p=0.02$).

Suh et al. (2013) reported that early complications with the open surgery were minor and limited to one case each

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of catheter-related infection and epididymitis (2/33 patients). Late complications included intermittent perineal or scrotal pain, which affected 8/33 patients and responded to analgesics.

Xu et al. (2014) report postoperative complications occurred in approximately 11% of patients with one patient developing urinary fistula secondary to infection and three patients developing meatal stenosis 3-11 months postoperatively which required correction with meatoplasty.

Part 4: Volume-outcome relationship of urethroplasty

The only evidence on the relationship between volume and outcomes was from the study by Fossati et al. (2015). This study evaluated the surgical learning curve for one-stage anterior urethroplasty in 641 patients performed by one surgeon over 20 years in Italy. The outcome measure was treatment failure, defined as any postoperative instrumentation needed after urethroplasty. Surgical experience was a significant predictor of failure-free survival after adjusting for case mix (hazard ratio per 20 procedures: 0.98; 95% CI, 0.97–0.99; $p=0.008$). The 5-year failure-free survival increased from 70% to 80% over the first 400 procedures and to 85% from procedure number 400 to 600. Probability between surgical success and surgical experience was nearly linear with improvement in outcomes by approximately 5% per 200 procedures. The learning curve did not reach plateau after 600 procedures.

In the absence of further validation from other multi-centre and multi-surgeon studies, this study indicates a volume-outcome relationship for urethroplasty and highlights the need for minimum volume per surgeon and good training.

Part 5: Cost-effectiveness of urethroplasty

The literature search did not identify any studies on cost-effectiveness analysis for urethroplasty.

3. Research questions

1. What is the clinical effectiveness of urethroplasty (open repair) versus endoscopic therapy for the treatment of urethral strictures?
2. What are the patient-reported outcome measures for urethroplasty?
3. Are there any safety issues or adverse events associated with urethroplasty?
4. Is there a volume-outcome relationship of urethroplasty for the treatment of urethral strictures?
5. What is the cost-effectiveness of urethroplasty for the treatment of urethral strictures?

4. Methodology

A review of published, peer reviewed literature has been undertaken based on the research questions set out in Section 3 and a search strategy agreed with the lead clinician and public health lead for this policy area. This has involved a PubMed search and search of the Cochrane database for systematic reviews, in addition to review of any existing NICE or SIGN guidance. The evidence review has been independently quality assured.

An audit trail has been maintained of papers excluded from the review on the basis of the inclusion and exclusion criteria agreed within the search strategy. The full list has been made available to the clinicians developing the policy where requested.

5. Results

A detailed breakdown of the evidence is included in the Appendix.

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Appendix One

Grade	Study design and intervention			Population		Outcomes					Reference	Other		
Grade of evidence	Study design	Study size	Intervention	Population characteristics	Sub group	Category	Primary Outcome	Primary Result	Secondary Outcome	Secondary Result	Reference	Complications noted	Benefits noted	Comments
3	Case series	36 patients	36 underwent one-stage urethroplasty using a lingual musococcal graft (LMG) (n=22), buccal mucosal graft (BMG) (n=5) or combined LMG and BMG (n=9)	Patients with urethral strictures associated with genital lichen sclerosis Median stricture length of 12.5 (range 6-18 cm)	Lichen sclerosis induced strictures	Clinical effectiveness of the intervention	The primary outcome measure was the objective result (success vs failure), defined as the absence of stricture recurrence at follow-up. The objective outcome was considered a failure when any postoperative instrumentation was needed, including dilation.	Success rate was 88.9% with a mean follow up of 38.7 months (range 12-110 months) In patients classified as successful, the mean postoperative urinary peak flow rate was 24.2 mL/s (range, 15.3-47 mL/s) Study concluded that both LMG and BMG are suitable and effective urethroplasty techniques for patients with urethral stricture diseases associated with genital lichen sclerosis	Postoperative complications	Postoperative complications occurred in 11.11% of patients a) One patient developed a urinary fistula secondary to infection b) Three patients developed meatal stenosis 3-11 months postoperatively and all voided well after meatoplasty	Xu, Yue-Min; Feng, Chao; Sa, Ying-Long; Fu, Qiang; Zhang, Jiong; Xie, Hong. Outcome of 1-stage urethroplasty using oral mucosal grafts for the treatment of urethral strictures associated with genital lichen sclerosis. Urology. 2014.	Not stated	Not stated	Small prospective case series with high potential for selection bias. Single centre outcomes which may not be representative. Only descriptive analysis provided.
3	Systematic	1) 210 patients in study comparing outcomes of surgical urethral dilation and optical urethrotomy (not relevant to the PICO) 2) 50 patients in study comparing outcomes of urethrotomy and urethroplasty	Urethroplasty carried out using an anastomotic technique (n=25)			Clinical effectiveness of the intervention compared to existing interventions	1) Proportion of men suffering from stricture recurrence as defined in repeat urethrography by a reduction in urethral calibre to less than 16 French (French is a unit for calibre measurement = external circumference in mm and divided by Pi to get diameter)	In the first six months, men were more likely to require further surgery in the urethrotomy group than in the primary urethroplasty group (RR 3.39, 95% CI 1.62 to 7.07). After two years, 16 of 25 (64%) men initially treated by urethrotomy required continued self-dilatation or further surgery for stricture recurrence compared to 6 of 25 (24%) men treated by primary urethroplasty.	Not stated	Not stated	Wong, Susan S. W.; Aboumarzouk, Omar M.; Narahari, Radhakrishna; O'Riordan, Anna; Pickard, Robert. Simple urethral dilatation, endoscopic urethrotomy, and urethroplasty for urethral stricture disease in adult men. Cochrane Database Syst Rev. 2012.	Not stated	Not stated	The review is based on a single 50 patient study for which only abstract was available.

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2+	Case-control	<p>1) 37 patients</p> <p>a) 18 randomised to receive penile skin circular graft (PCG)</p> <p>b) 19 randomised to receive penile skin circular flap (PCF)</p>	<p>Urethroplasty: Penile circular skin graft (all cases between the two intervention group performed by 2 surgeons)</p>			<p>Clinical effectiveness of the intervention compared to existing interventions</p>	<p>1) Operative time</p> <p>2) Complications</p>	<p>1) Operative time was significantly shorter in the PCG than in the PCF group PCG 203.3 (range: 160-280) minutes versus PCF 281.6 (range: 240-320) minutes in the PCG and the PCF groups, respectively (P = 0.000)</p> <p>2) Complications</p> <p>a) Early postoperative complications were similar across both groups except for superficial skin necrosis, which occurred in PCF group only</p> <p>b) Most common early complication seen was scrotal edema - occurred in 28% of PCG patients and 37% of PCF patients (P = 0.174)</p> <p>c) Hematoma and wound infection were similar across both groups (P = 1.0) d) Superficial skin necrosis in 1 case of PCF</p> <p>3) Complications - late</p> <p>a) Mild post void dribbling occurred similarly in both groups (28% in PCG and 32% in PCF) (P = 0.76)</p> <p>b) Stricture recurred in 27.7% and 21% in PCG and PCF groups, respectively, but did not reach statistical significant (P = 0.249) c) Urethro-cutaneous fistula occurred in one case of PCF</p>	Not stated	Not stated	<p>Hussein, Mohamed M.; Moursy, Essam; Gamal, Wael; Zaki, Mohamed; Rashed, Ahmed; Abozaied, Abdelmonem. The use of penile skin graft versus penile skin flap in the repair of long bulbo-penile urethral stricture: a prospective randomized study. Urology. 2011.</p>	Refer outcomes	Refer outcomes	<p>This study provides insight into the effectiveness of two different urethroplasty intervention. It concluded that distal penile circular skin graft urethroplasty is less time-consuming than distal penile circular skin flap. Both procedures have a good and similar success rate at intermediate follow-up with similar rate of complications. The variation between two subgroups was reduced through identification of as homogenous group as possible e.g. patients who had stricture that included the bulbo-penile urethra and by random assignment of procedures. However, given the criteria for selection of patients for urethroplasty versus other.</p>
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2-	Systematic	5,617 patients	Urethroplasty (various methods)			Clinical effectiveness of the intervention	Recurrence after urethroplasty	<p>1) Recurrence was defined as the need for additional surgical procedure (75% of studies) or dilation (52% of studies). The methods used to determine stricture recurrence after urethroplasty were widely variable</p> <p>2) Overall reported stricture recurrence rate was 15.6% between 2000-2008</p> <p>a) Lowest average recurrence rate was 8.3% in 2002 and the highest recurrence rate was 18.7% in 2006 - this may reflect trend towards completing more challenging strictures over time</p> <p>b) Recurrence rate was lowest for bulbar urethral strictures (13.9%) compared for penile strictures (18.4%, P = 0.00001) and posterior urethral strictures (17.5%, P = 0.0006)</p> <p>c) Recurrence rate was significantly higher for longer strictures (5 cm or greater, 16.6%) compared to that of shorter strictures (less than 5 cm, 12.4%, P = 0.0006)</p> <p>d) Reconstructive technique did not appear to affect the recurrence rate (15.6% for graft vs. 16.4% for anastomotic, P = 0.37)</p>	<p>1) Complication rate</p> <p>2) Strategy to evaluate stricture recurrence</p>	<p>1) The complication rate after urethroplasty was 19% (0% to 72% range) (this depended on the definition of 'complication')</p> <p>2) Study proposes a 2 tier system to evaluate stricture recurrence after urethroplasty:</p> <p>a) First tier involves obtaining an AUA-Symptom Score based on clinical history provided by the patient- a cost effective, non-invasive screening method can be considered a first line screen for structure recurrence</p> <p>b) Followed by flexible cystoscopy in symptomatic patients - this evaluation method has the highest sensitivity and specificity to detect and characterise extent of possible stricture recurrence</p>	Meeks, Joshua J.; Erickson, Bradley A.; Granieri, Michael A.; Gonzalez, Chris M.. Stricture recurrence after urethroplasty: a systematic review. J. Urol.. 2009.	Not stated	The use of a standardised surveillance protocol to define stricture recurrence after urethroplasty will allow more effective comparison across institutions	This study partially answers the PICO in that it looks at complications associated with urethroplasty and identifies a way forward for standardising the identification of stricture recurrence. The methodology for the systematic review was documented but with limitation information on the studies reviewed.
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3	Case series	641 patients	One-stage anterior urethroplasty using substitute tissues (85% (n=546); one-stage oral mucosa urethroplasty 15% (n=95); Penile skin flap		Other	Change in surgical outcomes over time (same surgeon). Treatment failure was defined as recurrence requiring any postoperative instrumentation including dilation. Uroflowmetry and urine culture were repeated every 6 months in the first 2 years and annually thereafter. When symptoms of decreased voiding flow were present and uroflowmetry was <12 ml/s, retrograde and voiding urethrography, urethral ultrasound, and urethroscopy were repeated to fully document re-stricture features.	1. Probability of 5-year failure-free survival increased from 70% to 80% after the first 400 cases and from 80% to approximately 85% from procedure number 400 to procedure number 600 a) Surgeon experience was significantly associated with a lower probability of treatment failure (hazard ratio per 20 procedures: 0.98; 95% CI, 0.97–0.99; p = 0.008.) b) There was nearly linear relationship between surgical success and surgical experience - success increased 5% per 200 procedures 2) Learning curve did not reach plateau after 600 procedures and continued to show improvement	Not stated	Not stated	Fossati, Nicola; Barbagli, Guido; Larcher, Alessandro; Dell'Oglio, Paolo; Sansalone, Salvatore; Lughezzani, Giovanni; Guazzoni, Giorgio; Montorsi, Francesco; Lazzeri, Massimo. The Surgical Learning Curve for One-stage Anterior Urethroplasty: A Prospective Single-surgeon Study. Eur. Urol. 2015.	Not stated	Better results are achieved only after a long learning curve that may not be justifiable for late-career and low-volume surgeons.	Strengths - single centre and single surgeon learning curve with large number of patients and long follow-up. Limitations: difficult to generalise the findings given the variability in baseline surgical skills, learning pace and surgical infrastructure as well as access to alternate treatment modalities. Information about postoperative examinations, such as uroflowmetry, as well as quality-of-life questionnaires, was not available for a significant proportion of patients. Therefore, the definition of treatment failure could not take into account those functional data. Furthermore, only one type of urethroplasty (one stage anterior urethroplasty) were included in this study.
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2++	Cross-sectional	1) 6,320 urologists a) 2,287 newly certifying b) 4,597 recertifying	Urethroplasty		Other	1) Case volume characteristics among certifying urologists associated with treatment of urethral structure to compare practice patterns of recent graduates to recertifying attending urologists and trends over time	<p>1) Over the study period, urologists performed a total of 95,747 (86.2%) urethral dilations, 10,986 (10.0%) DVIU, and 4349 (3.9%) urethroplasties</p> <p>a) Of the strictures managed with urethroplasty, 90.7% (3,944 cases) were excision and primary anastomosis, whereas 99 (0.9%) used graft tissue and 405 (9.3%) were performed in a stage fashion</p> <p>2) The overall ratio of dilation/direct vision internal urethrotomy to urethroplasty 24.5:1 for all urologists in the study (N = 6,320)</p> <p>3) The ratio of dilation/direct vision internal urethrotomy to urethroplasty for urologists applying for new certification was 8.5:1, as compared to urologists applying for first recertification (10 years) (20.0:1), second certification (20 years) (63.3:1), and third certification (30 years) (99.5:1) (P < 0.001)</p> <p>4) Newly certifying urologists performed urethroplasty 3.7 times more often than those recertifying</p> <p>a) Urethroplasty cases comprised 10.6% of all male urethral stricture cases logged during new certification</p> <p>5) Academically affiliated urologists were 8 times more likely to perform urethroplasty than endoscopic treatments (P < 0.001)</p> <p>a) Academics were also 1.9 times as likely to choose a staged procedure (P = 0.001), and 2.3 times as likely to use graft as their counterparts (P < 0.001)</p> <p>6) 10% of urologists in the study performed > = five urethroplasties (54.1% of all urethroplasty procedures)</p>	Not stated	Not stated	Liu, Joceline S.; Hofer, Matthias D.; Oberlin, Daniel T.; Milose, Jaclyn; Flury, Sarah C.; Morey, Allen F.; Gonzalez, Chris M.. Practice Patterns in the Treatment of Urethral Stricture Among American Urologists: A Paradigm Change?. Urology. 2015.	1) The reason for underuse of urethroplasty is likely to be multifactorial, including relative ease of endoscopic management, unfamiliarity with the procedure, referral patterns, patient preference etc.	Not stated	The study confirms that newly certifying urologists performed urethroplasty more often than their more experienced urologists. The major limits of the study include that the American Board of Urology (ABU) database does not document etiology of stricture and therefore could not comment on how stricture characteristics may have influenced individual treatment decisions, patient outcomes, or patterns of referral. Incorrect or incomplete coding is a possibility and therefore another limitation.
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3	Case series	466 patients	Surgical outcomes of 5 different types of urethroplasty were evaluated: a) Fasciocutaneous (FC) flap b) 1-stage buccal mucosal graft (BMG) c) 2-stage Johanson urethroplasty: defined as the closure of the previously opened urethra with or without the use of grafts to augment the diameter of the urethral lumen d) Definitive first-stage Johanson urethroplasty (including perineal urethrotomy): defined as opening the urethra through the strictured portion and securing the cut edge of the urethra to the penile skin, or perineal skin in the case of perineal urethrotomy e) Combination of grafts and flaps			Clinical effectiveness of the intervention	1) Surgical complications 2) Recurrence	<p>1) Overall success rate was 77.5%, with recurrence rate of 22.5%.</p> <p>2) Previous dilation or urethrotomy was found to have a statistically significant negative impact on success. Previous urethroplasty did not appear to significantly affect outcome.</p> <p>3) Ventral or dorsal BMGI urethroplasty most successful type.</p> <p>4) Recurrence rates for 5 urethroplasty interventions as follows: a) FC flap 37.5% b) One-stage BMG 17.5% c) First- and second-stage Johanson urethroplasty 37.5% d) Perineal urethrotomy or definitive first stage 24.1% e) Combination FC and graft 23.5%</p> <p>The study concludes that one-stage repairs with BMG offer an excellent option for patients with long segment and panurethral stricture disease. In cases with obliterative or absent urethral plate, a 2-stage Johanson urethroplasty with BMG offers a viable alternative. In cases of lichen sclerosis, 1-stage BMG has better outcomes than a 2-stage repair. If BMGs are not available, FC flaps offer similar success; however, these are associated with higher rates of complications. Skin grafts should be avoided, unless no alternatives exist.</p>	Complications	<p>Early complications included local pain, numbness, edema, UTI, penile skin ischemia, epididymis inflammation and scrotal abscess. Late complications mainly included fistula, chordee, persisting numbness.</p> <p>Occurrence of a complication conferred no statistical impact on stricture recurrence (P = .29). Patients with an FC flap (alone or in combination) were compared with those without a flap. The complication rate was higher in the FC group compared with those without a flap (32% vs 14%, respectively; P = .02).</p>	Warner, Jonathan N.; Malkawi, Ibraheem; Dhradkeh, Mohammad; Joshi, Pankaj M.; Kulkarni, Sanjay B.; Lazzeri, Massimo; Barbagli, Guido; Mori, Ryan; Angermeier, Kenneth W.; Storme, Oscar; Campos, Rodrigo; Velarde, Laura; Gomez, Reynaldo G.; Han, Justin S.; Gonzalez, Christopher M.; Martino, David; Sandul, Anatoliy; Martins, Francisco E.; Santucci, Richard A. A Multi-institutional Evaluation of the Management and Outcomes of Long-segment Urethral Strictures. Urology. 2015.	Not stated	Not stated	Limitations of observational retrospective study with data collected from different centres. It is not clear as which international centres contributed the data. Patient selection criteria, baseline patient characteristics, differences in diagnosis, investigations and intra-surgical variations have not been addressed.
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2-	Cross-sectional	1) 92,448 procedures	Urethroplasty for male urethral stricture disease			Other	1) Utilisation of interventions	<p>1) A total of 92,448 procedures were performed, there were 50,875 urethral dilations (55.03%), 39,785 urethrotomies (43.03%), and 1,788 urethroplasties (0.19%)</p> <p>2) Both the total number and relative percentage of urethroplasties performed increased over the course of the study, showing a consistent trend toward increased utilization of urethroplasty in this population.</p> <p>3) Changes in the relative use were statistically significant for each quintile (P <.0001).</p> <p>4) Effect of geographic location and proximity to teaching hospital had effect on utilisation of the intervention; a total of 80.4% of these urethroplasties were performed in locations with a residency program</p> <p>*One of the possible reasons for the increase in urethroplasty is increase in referrals to centres of excellence</p>	Not stated	Not stated	Lacy, John M.; Cavallini, Maximiliano; Bylund, Jason R.; Strup, Stephen E.; Preston, David M.. Trends in the management of male urethral stricture disease in the veteran population. Urology. 2014.	Not stated	Not stated	The study is a retrospective review and there are several limitations. For example, patient age was evaluated but comorbidities were neither taken into account, nor were the complexity of the urethral strictures among the patients. There also may have been selection bias in the VA population relative to the general public as VA patients on the whole are an older population with potential higher numbers of comorbidities; this may account for the relatively high number of urethral dilations.
2-	Case-control	45 patients	<p>1) Urethroplasty (n=22), urethroplasty after urotomy (n=9)</p> <p>a) 32.3% underwent meatoplasty (repairing stricture of meatus and navicular fossa)</p> <p>b) 41.9% underwent end-to-end anastomosis,</p> <p>c) 12.9% received a penile skin flap</p> <p>d) 6.5% received a scrotal flap</p> <p>e) 3.2% received a preputial flap</p> <p>f) 3.2% underwent a two-stage surgery without receiving a graft</p>			Clinical effectiveness of the intervention compared to existing interventions	<p>Surgical outcomes (Results analysed 6 months after surgery through performing flowmetry and serial voiding urethrography; Success considered to be with peak flow of 15 mL/s)</p>	<p>1) Surgical success: 86.4% for urethroplasty vs. 47.8% urethrotomy (P = 0.01)</p> <p>2) 20% of patients in whom the initial urethrotomy had failed subsequently underwent urethroplasty</p> <p>3) The presence of concomitant diseases, such as diabetes mellitus, smoking or cardiovascular disease, had no influence on the results obtained after treatment</p> <p>4) The baseline length of urethral strictures varied across patients in three categories: urethrotomy (1.1 ± 0.50, urethroplasty (1.6 ± 1.6), urethroplasty after urethrotomy) 3.4 ± 3.1</p> <p>The study concludes that urethroplasty is ideal for urethral stricture with a length greater than 1.5cm or in cases where internal urethrotomy is not indicated and treatment failure occurs. Urethrotomy may be an option that does not worsen the outcome after a subsequent urethroplasty.</p>	Not stated	Refer outcome	Tinaut-Ranera, Javier; Arrabal-Polo, Miguel Ángel; Merino-Saías, Sergio; Nogueras-Ocaña, Mercedes; López-León, Víctor Manuel; Palao-Yago, Francisco; Arrabal-Martín, Miguel; Lahoz-García, Clara; Alaminos, Miguel; Zuluaga-Gomez, Armando. Outcome of urethral strictures treated by endoscopic urethrotomy and urethroplasty. Can Urol Assoc J. 2014.	Not stated	Refer outcomes	The limitations of this study are small number of patients and retrospective design with potential for significant selection bias and representativeness of study population.

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-	Other	523 urologists	1) Urethroplasty			Other	<p>1) Survey results on national practice patterns in Italy</p> <p>1) Minimally invasive methods confirmed to be performed more frequently than any open urethroplasty technique (P = 0.012)</p> <p>2) Most practiced treatments was internal urethrotomy (81.8%), followed by palliative dilation (62.5%)</p> <p>3) 60.8% of responders did not perform urethroplasty surgery a) Of those that did, 30.8% performed 1-5 urethroplasties yearly, and only 8.4% performed >5 urethroplasty surgeries yearly</p> <p>4) Only 33.8% consider urethroplasty as a primary treatment option and 65.4% believed that thought that urethroplasty is best option only after failed minimally invasive treatments</p> <p>* Maximum stricture length for internal urethrotomy is 1.5cm * Most commonly used urethroplasty procedure was the one-stage graft technique, particularly using oral mucosa and ventrally placed (21.2%) (P < 0.001)</p>	Not stated	Not stated	<p>Palminteri, Enzo; Maruccia, Serena; Berdondini, Elisa; Di Pierro, Giovanni Battista; Sedigh, Omid; Rocco, Francesco. Male urethral strictures: a national survey among urologists in Italy. Urology. 2014.</p>	Not stated	Not stated	<p>In Italy, minimally invasive procedures are most commonly used for urethral stricture disease and only a small portion of urologists perform urethroplasty surgery. Major limitation of the study is that was based on a questionnaire mailed to selected urologists, with a response rate of 75%. As such, findings may not be representative.</p>
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Appendix Two

Literature search terms

Assumptions / limits applied to search:	
Original search terms:	None
Updated search terms - Population	Urethral stricture OR Urethral stenosis OR Spongiofibrosis
Updated search terms - Intervention	Urethroplasty OR Urethral reconstruction
Updated search terms - Comparator	Urethrotomy OR Urethral dilatation OR Intermittent self dilation
Updated search terms - Outcome	bleeding OR complication rates OR compromise of diameter of urethra OR cost effectiveness OR flow symptoms OR frequency OR infection OR pain OR quality of life OR recovery time OR re-intervention OR return to work OR storage symptoms OR stricture recurrence OR symptom improvement OR urgency OR voiding

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Inclusion criteria	General inclusion criteria
	<p>In order of decreasing priority, articles will be selected based on the following criteria.</p> <ol style="list-style-type: none"> 1. All relevant systematic reviews and meta-analysis in the last 5 years and those in 5-10 years period which are still relevant (e.g. no further updated systematic review available) 2. All relevant RCTs and those in the 5-10 years period which are still relevant (e.g. not superseded by a next phase of the trial/ the RCT is one of the few or only high quality clinical trials available) <p>>>>> If studies included reaches 30, inclusion stops here</p> <ol style="list-style-type: none"> 3. All relevant case control and cohort studies, that qualify after exclusion criteria <p>>>>> If studies included reaches 30, inclusion stops here</p> <ol style="list-style-type: none"> 4. All relevant non analytical studies (case series/ reports etc.) that qualify after exclusion criteria <p>>>>> If studies included reaches 30, inclusion stops here</p>
	Specific inclusion criteria
	None
Exclusion criteria	General exclusion criteria
	<p>Studies with the following characteristics will be excluded:</p> <ol style="list-style-type: none"> 1. Does not answer a PICO research question 2. Comparator differs from the PICO 3. < 50 subjects (where studies with >50 subjects exist) 4. No relevant outcomes 5. Incorrect study type 6. Inclusion of outcomes for only one surgeon/doctor or only one clinical site (where studies with > one surgeon/doctor or one clinical site exist) 7. Narrative / non-systematic reviews (relevant referenced studies to be included)
	Specific exclusion criteria
	Urethroplasty or urethral reconstruction in females