

Appendix

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1. Search strategy

We updated the search conducted by Wessels et al (1) for the American Urological Association (AUA) guideline for male urethral stricture. We searched MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews from January 1, 2014 to October 9, 2018.

- 1 (urethr* and (strictur* or stenosis* or narrow*)).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, dq, sh, tx, ct, nm, kf, px, rx, ui, sy] (14206)
- 2 limit 1 to yr="2014 -Current" (5949)
- 3 (uroflowmet* or cystourethrogra* or radiourethrograph* or rug or sonourethrograph* or urethrogram*).mp. (12284)
- 4 (cystoscop* or urethroscop* or (foley adj3 placement)).mp. (26210)
- 5 3 or 4 (36886)
- 6 2 and 5 (1467)
- 7 remove duplicates from 6 (1164)
- 8 (urethroplast* or urethrostom* or urethrotom*).mp. (7704)
- 9 end to end anastomosis.mp. (7539)
- 10 (urethroscop* or endoscop*).mp. (412283)
- 11 dilat*.mp. (228027)
- 12 or/8-11 (626961)
- 13 2 and 12 (3172)
- 14 remove duplicates from 13 (2336)
- 15 7 or 14 (2718)
- 16 limit 15 to (conference abstract or conference paper or editorial or erratum or letter or note or case reports or comment or news or newspaper article or patient education handout or webcasts) [Limit not valid in Embase, CCTR, CDSR, Ovid MEDLINE(R), Ovid MEDLINE(R) Daily Update, Ovid MEDLINE(R) In-Process, Ovid MEDLINE(R) Publisher; records were retained](1289)
- 17 15 not 16 (1429)

2. PICO study questions

PICO 1: Should men with suspected urethral stricture undergo cystoscopy as the most accurate method to diagnose a clinically significant urethral stricture?

POPULATION:	Men with suspected urethral stricture
INTERVENTION:	Cystoscopy
COMPARISON:	Urethrogram
ANTICIPATED OUTCOMES:	Stricture diagnosis versus the risk of urine infection, pain and patient discomfort

PICO 2: Should endoscopic management (dilation or DVIU) compared to urethroplasty be used for men with the initial diagnosis of urethral stricture?

POPULATION:	Men with recurrent urethral stricture
INTERVENTION:	Endoscopic treatment (either dilation or DVIU)
COMPARISON:	Urethroplasty
MAIN OUTCOMES:	Stricture recurrence and risk of complications

PICO 3: Should urethroplasty compared to endoscopic treatment (either dilation or DVIU) be used for men with recurrent urethral stricture?

POPULATION:	Men with recurrent urethral stricture
INTERVENTION:	Urethroplasty
COMPARISON:	Endoscopic treatment (either dilation or DVIU)
MAIN OUTCOMES:	Stricture recurrence and risk of complications

3. Detailed methods

Systematic review team

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Screening

Records identified by the updated search were uploaded to EndNote and duplicates removed. Titles and abstracts were initially screened by one reviewer (SD) to remove obviously irrelevant records. The remaining titles and abstracts were screened in duplicate by members of the CUA guideline panel (GB, TD, RK, KR, PV, BW) and a GRADE methodologist (NS). Full-texts of potentially eligible records were obtained and assessed for eligibility in duplicate by 3 reviewers (AB, SD, KS).

Inclusion and Exclusion Criteria

- Randomised controlled trials (RCTs) or non-randomised comparative or non-comparative studies
- Adult males with *initial or recurrent* urethral stricture, or at least 80% of included males meeting this criteria. Studies were excluded if more than 20% of the population had the following etiologies: i) trauma stenoses (pelvic fracture urethral injury, straddle trauma); ii) hypospadias associated urethral strictures; iii) bladder neck contracture; iv) vesicourethral anastomotic stenosis; v) radiation induced urethral stenoses; and vi) lichen sclerosus

- Outcomes included i) stricture recurrence; ii) symptoms; iii) quality of life; or iv) complications.
- English language publications

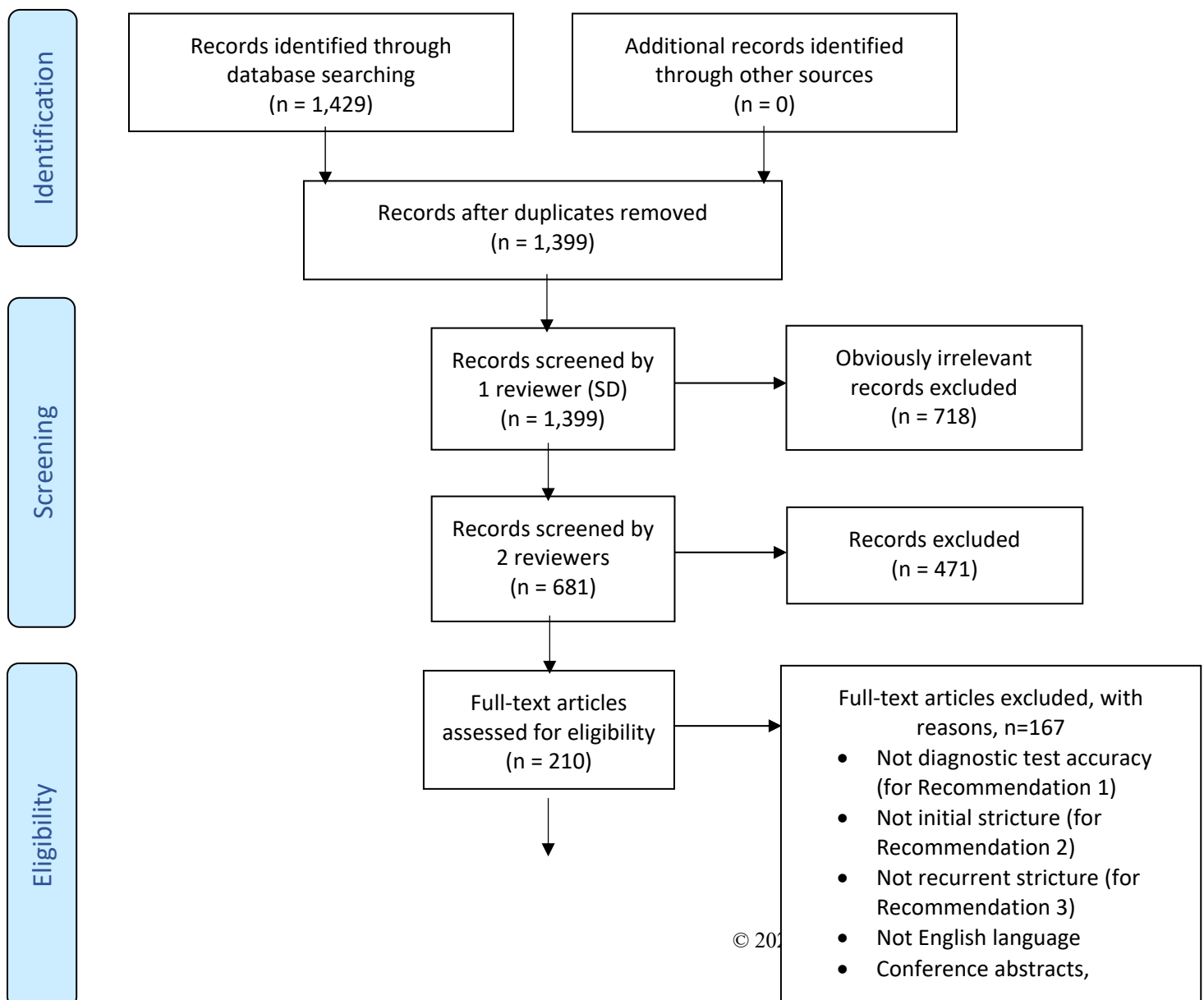
Risk of Bias Assessment

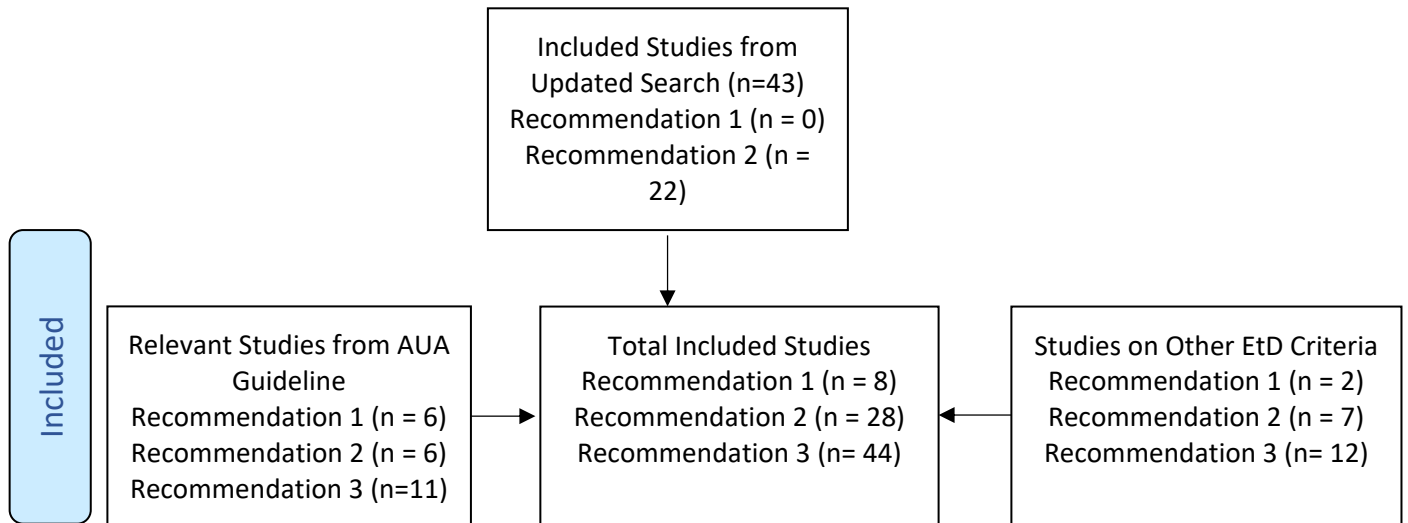
For studies identified from the AUA guideline (1) we used the risk of bias assessments as reported in the AUA guideline evidence report appendices. For studies identified from the updated search, RCTs were assessed using the Cochrane risk of bias tool, and we assumed risk of bias was very serious for all non-randomised comparative studies and non-comparative studies.

Statistical Analysis

Review Manager version 5.3 was used to conduct all analyses. Risk ratios and 95% confidence intervals were used to analyze data from direct comparisons. The proportion was averaged across non-comparative studies.

4. PRISMA Flow Diagram





5. Recommendations, Summaries of evidence and Evidence to Decision Tables

RECOMMENDATION 1

Summary of the Evidence

We did not identify any new studies from the updated search that assessed the diagnostic test accuracy of urethrography in men with suspected urethral stricture. We included six studies identified for the previous AUA guidelines (1) that assessed RUG and/or SUG compared to cystoscopy (and confirmation by surgery) as the reference standard. We assumed 100% sensitivity and specificity of cystoscopy to diagnose urethral stricture. Six studies assessed the diagnostic test accuracy of RUG (2-7) and three studies assessed SUG (4-6). Table 1 reports characteristics of included studies.

Table 1. Study details of included studies

Study	Country	Design	Total Enrolled	Age (years)	Quality score given by AUA
D'Elia 1996 (2)	Italy	Retrospective diagnostic case series	42 (only first 10 patients had RUG and MCU)	Median 53; range 24 to 81	Low
El-ghar 2010 (3)	Egypt	Retrospective diagnostic case series	30	Range 15 to 75	Low
Gupta 1993 (4)	India	Retrospective case series	30	Range 19 to 77	Low
Kostakopoulos 1998 (5)	Greece	Retrospective diagnostic case series	117	Range 25 to 85	Low
Mitterberger 2007 (6)	Austria	Diagnostic case series	93	Range 17 to 81	Low
Osman 2006 (7)	Egypt	Retrospective diagnostic case series	20	Range 17 to 77	Low

Risk of Bias

All 6 studies had low risk of bias as reported in the AUA guideline (1) and shown in Table 1.

Rourke KF, et al. Canadian Urological Association guideline on male urethral stricture. Can Urol Assoc J 2020;14(10).

RECOMMENDATION 1 - GRADE Evidence to Decision Framework

Should urethrogram: RUG vs. urethrogram: SUG be used to diagnose urethral stricture in men with suspected urethral stricture?	
POPULATION:	men with suspected urethral stricture
INTERVENTION:	urethrogram: RUG
COMPARISON:	urethrogram: SUG
ANTICIPATED OUTCOMES:	Urine infection, pain or patient comfort
BACKGROUND:	<p>Background</p> <p>From the American Urological Association (AUA) 2006 guidelines: Clinicians should use urethro-cystoscopy, retrograde urethrography, voiding cystourethrography, or ultrasound urethrography to make a diagnosis of urethral stricture. (Moderate Recommendation; Evidence Strength Grade C)</p> <p>Endoscopy and/or radiological imaging of the urethra is essential for confirmation of the diagnosis, assessment of stricture severity (e.g. staging), and procedure selection. History, physical examination, and adjunctive measures described above in Statements One and Two cannot definitively confirm a urethral stricture. Urethroscopy identifies and localizes urethral stricture and allows evaluation of the distal caliber, but the length of the stricture and the urethra proximal to the urethral stricture cannot be assessed in most cases. When flexible cystoscopy does not allow visual assessment proximal to the urethral stricture, small caliber cystoscopy with a flexible ureteroscope or flexible hysteroscope can be useful adjuncts. MRI can provide important detail in select cases (i.e., PFUI, diverticulum, fistula, cancer).</p>

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know 	<p>The AUA recommendation does not specify which test to use or imply superiority of one individual test to make a definitive diagnosis.</p> <p>The AUA recommendation also does not address MRU in the Canadian context.</p> <p>In practice, urologists are not always certain that a patient has a potential urethral stricture. Typically, a cystoscopy is done and the other tests recommended by AUA will not be undertaken. A urethrogram will only be ordered if a clinician is very certain that the patient has a urethral stricture. Therefore, the AUA recommendation is not sufficiently instructive or actionable.</p> <p>The recommendation should consider patient history of urethral structure and provide guidance on whether it is an initial diagnosis versus an existing stricture (requiring staging) and/or recurrence.</p>	<p>Diagnostic interventions include:</p> <ul style="list-style-type: none"> ● Cystoscopy ● Retrograde Urethrogram (RUG) ● Voiding Cystourethrogram (VCUG) ● Sonourethrogram (SUG) ● MR Urethrogram (MRU) <p>The panel recognized that specific investigative tests are used for initial diagnosis (cystoscopy) versus staging (RUG or SUG).</p>

Test accuracy How accurate is the test?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Very inaccurate ○ Inaccurate 	<p>We did not identify any new studies from the updated search that assessed the diagnostic test accuracy of urethrography in men with suspected urethral stricture.</p> <p>We included six studies identified for the previous AUA guidelines that assessed RUG</p>	<p>For most of the studies, the prevalence of included population was approximately 80% or higher.</p>

<ul style="list-style-type: none">● Accurate○ Very accurate○ Varies○ Don't know	<p>and/or SUG compared to cystoscopy (and confirmation by surgery) as the reference standard. We assumed 100% sensitivity and specificity of cystoscopy to diagnose urethral stricture. Six studies assessed the diagnostic test accuracy of RUG (D’Elia 1996, El-ghar 2010, Gupta 1993, Kostakopoulos 1998, Mitterberger 2007, Osman 2006) and three studies assessed SUG (Gupta 1993, Kostakopoulos 1998, Mitterberger 2007).</p> <p>Table 2: Test accuracy data for RUG and SUG based on 40% and 60% prevalence of urethral stricture by clinical suspicion</p> <p>NOTE: the comparisons for all tests was to cystoscopy (and confirmation by surgery) - assumption is 100% sensitivity and specificity of cystoscopy to diagnose urethral stricture:</p> <table><tr><th colspan="2">urethrogram: RUG</th><th colspan="2">urethrogram: SUG</th></tr><tr><td>Sensitivity</td><td>0.94</td><td>Sensitivity</td><td>0.90</td></tr><tr><td>Specificity</td><td>0.90</td><td>Specificity</td><td>1.00</td></tr></table>	urethrogram: RUG		urethrogram: SUG		Sensitivity	0.94	Sensitivity	0.90	Specificity	0.90	Specificity	1.00	<p>The panel considered this to be quite high if based on clinician suspicion of urethral stricture. This may be a biased estimate, due to selections or reporting bias, e.g., inclusion of a very select population, based on age, recurrence, urethral flow pattern, etc. The panel agreed that prevalence of 40% to 60% may be more appropriate.</p> <p>The panel also considered the setting in which these diagnostic tests were undertaken. For example, the SUG may be done in a specialist center rather than an academic hospital or community practice. The RUG may be more commonly or widely performed.</p> <p>Because MRU is performed to determine the length or diameter of the urethral stricture, it is best reserved for select cases (and not for routine initial diagnosis of suspected stricture), including: complex trauma (PFUI, straddle), suspected malignancy, radiotherapy induced urethral stenosis, associated rectourethral fistula.</p> <p>The panel agreed that they should also consider whether RUG or SUG were preferable to the actual use of the gold standard (cystoscopy).</p>
urethrogram: RUG		urethrogram: SUG												
Sensitivity	0.94	Sensitivity	0.90											
Specificity	0.90	Specificity	1.00											

Rourke KF, et al. Canadian Urological Association guideline on male urethral stricture. Can Urol Assoc J 2020;14(10).

Desirable Effects How substantial are the desirable anticipated effects?																																																			
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS																																																	
<ul style="list-style-type: none">○ Trivial● Small○ Moderate○ Large○ Varies○ Don't know	<table><tr><th rowspan="3">Outcome</th><th colspan="4">Effect per 100 patients tested</th></tr><tr><th colspan="2">pre-test probability of 60%</th><th colspan="2">pre-test probability of 40%</th></tr><tr><th>urethrogram: RUG</th><th>urethrogram: SUG</th><th>urethrogram : RUG</th><th>urethrogram: SUG</th></tr><tr><td rowspan="2">True positives</td><td>56 (0 to 0)</td><td>54 (0 to 0)</td><td>38 (0 to 0)</td><td>36 (0 to 0)</td></tr><tr><td colspan="2">2 more TP in urethrogram: RUG</td><td colspan="2">2 more TP in urethrogram: RUG</td></tr><tr><td rowspan="2">False negatives</td><td>4 (60 to 60)</td><td>6 (60 to 60)</td><td>2 (40 to 40)</td><td>4 (40 to 40)</td></tr><tr><td colspan="2">2 fewer FN in urethrogram: RUG</td><td colspan="2">2 fewer FN in urethrogram: RUG</td></tr><tr><td rowspan="2">True negatives</td><td>36 (0 to 0)</td><td>40 (0 to 0)</td><td>54 (0 to 0)</td><td>60 (0 to 0)</td></tr><tr><td colspan="2">4 fewer TN in urethrogram: RUG</td><td colspan="2">6 fewer TN in urethrogram: RUG</td></tr><tr><td rowspan="2">False positives</td><td>4 (40 to 40)</td><td>0 (40 to 40)</td><td>6 (60 to 60)</td><td>0 (60 to 60)</td></tr><tr><td colspan="2">4 more FP in urethrogram: RUG</td><td colspan="2">6 more FP in urethrogram: RUG</td></tr></table>	Outcome	Effect per 100 patients tested				pre-test probability of 60%		pre-test probability of 40%		urethrogram: RUG	urethrogram: SUG	urethrogram : RUG	urethrogram: SUG	True positives	56 (0 to 0)	54 (0 to 0)	38 (0 to 0)	36 (0 to 0)	2 more TP in urethrogram: RUG		2 more TP in urethrogram: RUG		False negatives	4 (60 to 60)	6 (60 to 60)	2 (40 to 40)	4 (40 to 40)	2 fewer FN in urethrogram: RUG		2 fewer FN in urethrogram: RUG		True negatives	36 (0 to 0)	40 (0 to 0)	54 (0 to 0)	60 (0 to 0)	4 fewer TN in urethrogram: RUG		6 fewer TN in urethrogram: RUG		False positives	4 (40 to 40)	0 (40 to 40)	6 (60 to 60)	0 (60 to 60)	4 more FP in urethrogram: RUG		6 more FP in urethrogram: RUG		
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Compared to performing SUG at initial diagnosis, the use of RUG may lead to fewer missed cases of urethral stricture (2 fewer per 100 men), but more unnecessary treatment (4 to 6 more per 100 men).																																																			

Undesirable Effects How substantial are the undesirable anticipated effects?																			
JUDGEMENT	RESEARCH EVIDENCE		ADDITIONAL CONSIDERATIONS																
<ul style="list-style-type: none">○ Large○ Moderate○ Small● Trivial○ Varies○ Don't know	<p>False negatives (missed cases) will likely return to the clinic after one month because they continue to have symptoms. However, false positives will receive unnecessary treatment incurring costs, and experience side effects of treatment.</p> <p>Very low certainty evidence (due to risk of bias and small number of patients) from one non-randomized study (Choudhary 2004) found that there may be less pain with RUG versus SUG, but bleeding and intravasation may be similar. In Canada, SUG is provided under local anaesthesia, and when providing SUG positioning is invasive, more gel is required, and the probe must be pushed quite hard against the perineum.</p> <p>D'Elia 1996 reported no infective or traumatic complications with RUG (non-comparative case series).</p> <table><thead><tr><th>Complications</th><th>RUG</th><th>SUG</th><th>P value</th></tr></thead><tbody><tr><td>Pain during procedure</td><td>40/70 (57.1%)</td><td>15/70 (21.4%)</td><td>< 0.001</td></tr><tr><td>Urethral bleeding</td><td>3/70 (5.7%)</td><td>1/70 (1.4%)</td><td>< 0.5</td></tr><tr><td>Contrast Intravasation</td><td>3/70 (4.3%)</td><td>0</td><td>-</td></tr></tbody></table>		Complications	RUG	SUG	P value	Pain during procedure	40/70 (57.1%)	15/70 (21.4%)	< 0.001	Urethral bleeding	3/70 (5.7%)	1/70 (1.4%)	< 0.5	Contrast Intravasation	3/70 (4.3%)	0	-	<p>The panel acknowledged that undesirable effects may result in poor outcomes and costs for incorrect treatments.</p> <p>The panel determined that the risk of death is very low.</p>
Complications	RUG	SUG	P value																
Pain during procedure	40/70 (57.1%)	15/70 (21.4%)	< 0.001																
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Contrast Intravasation	3/70 (4.3%)	0	-																

Certainty of the evidence of test accuracy What is the overall certainty of the evidence of test accuracy?			
JUDGEMENT	RESEARCH EVIDENCE		ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Very low● Low○ Moderate○ High○ No included studies	<p>The overall certainty of the evidence of test accuracy is low.</p>		<p>Patient factors will also impact the results of the diagnostic tests.</p>

Certainty of the evidence of effects What is the overall certainty of the evidence for any critical or important direct benefits, adverse effects or burden of the test?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Very low <input checked="" type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input type="radio"/> No included studies		
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Important uncertainty or variability <input type="radio"/> Possibly important uncertainty or variability <input checked="" type="radio"/> Probably no important uncertainty or variability <input type="radio"/> No important uncertainty or variability		The panel felt that practicality, availability of resources, acceptability and patient burden were as important as the evidence on test accuracy.

Resources required How large are the resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know 	<p>We did not search for studies that compared the costs of RUG versus SUG for diagnosis of urethral stricture.</p> <p>Cystoscopy is widely available in most clinical settings and requires fewer resources (such as costs, equipment and training) than RUG or SUG. SUG may be costlier than RUG due to equipment costs, and SUG is likely less available in most clinics, and less accessible to urologists.</p>	<p>The panel acknowledged the additional costs for SUG, in which an ultrasound machine is required (unlike for RUG) and is not available in most clinics. The RUG is more accessible to urologists.</p>
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know 		<p>See acceptability, resources, and feasibility sections.</p>

Acceptability Is the intervention acceptable to key stakeholders?					
JUDGEMENT	RESEARCH EVIDENCE				ADDITIONAL CONSIDERATIONS
<div><div><div>○ No</div><div>○ Probably no</div><div>● Probably yes</div><div>○ Yes</div><div>○ Varies</div><div>○ Don't know</div></div></div>		Cystoscopy	RUG	SUG	Most urologists are more comfortable and experienced with doing cystoscopy first for diagnosis. Patients may experience more pain and discomfort with SUG, because it must be done under local anesthesia in Canada, positioning is more invasive, more gel is required for distending, and must push quite hard against the perineum with the probe.
	Burden to patient	Low	Moderate	High	
	Discomfort for patient	Low	Moderate	High	
	Invasiveness	Moderate	Moderate	High	
	Need for anesthesia	Low	Low	High	
	Difficulty performing	Low	Moderate	High	
	Performer dependent	Low	High	High	
	Most urologists in Canada are likely more comfortable and experienced using cystoscopy for diagnosis.				
Feasibility Is the intervention feasible to implement?					
JUDGEMENT	RESEARCH EVIDENCE				ADDITIONAL CONSIDERATIONS
<div><div><div>○ No</div><div>○ Probably no</div><div>○ Probably yes</div><div>● Yes</div><div>○ Varies</div><div>○ Don't know</div></div></div>	Cystoscopy is widely available in most clinical settings and feasible to provide. Bach 2014: The image quality and accuracy of RUG is operator-dependent; surgical planning should be based on high quality images generated by experienced practitioners or the surgeon him/herself.				<div>The panel considered the impracticality of most urologists to conduct an SUG for initial diagnosis, due to:<ul style="list-style-type: none">limited access to the set-up and equipment neededmore burden to the patients</div>

		<ul style="list-style-type: none"> • interpretation is more difficult than RUG • less clinician experience in Canada. <p>For most urologists, it is easier to do cystoscopy first for diagnosis, then RUG (optional or for staging), and lastly, SUG.</p> <p>Clinicians must have access to a highquality RUG in order to get a good diagnosis.</p> <p>The panel also acknowledged that we must consider who is interpreting the test results, e.g., radiologist, community urologist, or specialist.</p> <p>The panel agreed there was enough reasons to recommend against using an MRU for initial diagnosis (regardless of the scientific evidence), such as: expense, lack of resources, impracticality, better used for operative planning rather than diagnosis.</p>
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SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
TEST ACCURACY	Very inaccurate	Inaccurate	Accurate	Very accurate		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF THE EVIDENCE OF TEST ACCURACY	Very low	Low	Moderate	High			No included studies
CERTAINTY OF EFFECTS	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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CONCLUSIONS

Recommendation

We suggest using cystoscopy rather than urethrography for the initial diagnosis of suspected stricture
Conditional recommendation, low certainty in evidence of effects

We suggest performing retrograde urethrography to further stage a urethral stricture or referral to a centre of expertise in reconstructive urology, when a recurrent stricture is suspected
Conditional recommendation, low certainty in evidence of effects

We suggest against using magnetic resonance urethrography for routine initial diagnosis of suspected stricture.
Conditional recommendation, low certainty in evidence of effects

MRI is best reserved for select cases:

- Complex trauma (PFUI, Straddle)
- Suspected malignancy
- Radiotherapy induced urethral stenosis
- Associated rectourethral fistula

Justification

Cystoscopy is widely available in most clinical settings, and requires fewer resources (such as costs, equipment and training) than Urethrography or MRU.

The use of Urethrography or MRU at initial diagnosis may lead to greater numbers of missed cases of urethral stricture (2 to 4 more per 100 men) and unnecessary treatment (0 to 6 more per 100 men) than when performing cystoscopy.

Rourke KF, et al. Canadian Urological Association guideline on male urethral stricture. Can Urol Assoc J 2020;14(10).

RECOMMENDATION 2

Summary of the Evidence

There were 28 relevant non-randomised studies (6 from the AUA guidelines and 22 new studies). Five compared endoscopic management to urethroplasty (8-12). Twenty-three were non-comparative (13-35). Table 3 reports characteristics of included studies.

Table 3. Characteristics of Included Studies

Study (Reference)	Study Design	Stricture Instance			Stricture Type	Stricture Etiology	Comparison		Relevant Outcomes				Quality Score from AUA Guideline
		Initial Only	Recurrent Only	Initial & Recurrent (% Initial)			Urethroplasty Procedure(s) (number of patients)	Endoscopic Management Procedure(s) (number of patients)	Stricture Recurrence	Symptoms	Quality of Life	Complications	
AUA Evidence (n=6)													
Atak 2011 (30)	RCT			✓ (84%)	Single, anterior (bulbous urethra) or posterior annular urethral strictures	posterior strictures: iatrogenic bladder neck contraction after transurethral resection of the prostate (35.3%); anterior strictures: iatrogenic, such as history of prolonged or traumatic urethral catheterization (64.7%)	N/A	holmium:yttrium-aluminium-garnet (HO:YAG) laser (n=21) vs. cold-knife urethrotomy (n=30)	✓			✓	Low
Hussein 2011 (31)	RCT	✓			anterior bulbo-penile urethral stricture	Post-instrumentation (catheter/endoscopy; 54%) or idiopathic (45.9%)	ventral onlay urethroplasty using distal penile circular fasciocutaneous flap (PCF) (n=19) vs. ventral onlay urethroplasty using a distal penile full-thickness circular graft (PCG) (n=18)	N/A	✓			✓	Low
Kulkarni 2012 (32)	NRS			✓ (89%)	panurethral stricture	Lichen sclerosus (70%), catheter induced (11.9%), idiopathic (10.2%), instrumentation	1-stage dorsal onlay oral mucosa graft urethroplasty (n=117)	N/A	✓				Low

*Rourke KF, et al. Canadian Urological Association guideline on male urethral stricture.
Can Urol Assoc J 2020;14(10).*

Study (Reference)	Study Design	Stricture Instance			Stricture Type	Stricture Etiology	Comparison		Relevant Outcomes				Quality Score from AUA Guideline
		Initial Only	Recurrent Only	Initial & Recurrent (% Initial)			Urethroplasty Procedure(s) (number of patients)	Endoscopic Management Procedure(s) (number of patients)	Stricture Recurrence	Symptoms	Quality of Life	Complications	
						(5.3%), failed hypospadias repair (1.8%), trauma (0.8%)							
Mandhani 2005 (33)	NRS	✓			Short-segment bulbar urethral stricture	Inflammation (79%), trauma (21%)	N/A	visual internal urethrotomy (Sachse) (n=105)	✓				Low
Mazdak 2010 (34)	RCT	✓			bulbar urethral stricture	Trauma (46.7%), inflammation (15.6%), unknown (37.8%)	N/A	cold knife DVIU + triamcinolone (n=23) vs. cold knife DVIU (n=22)	✓				Low
Pansadoro 1996 (35)	NRS			✓ (88%)	bulbar, penile, or penile bulbar urethral stricture	Iatrogenic (40%) ^a , infective (29%) ^a , traumatic (4%) ^a , congenital (2%) ^a , unknown (25%) ^a	N/A	Cold-knife internal endoscopic urethrotomy (Sachse) (n=224)	✓				Low
Search Update (n=22)													
Al Taweel 2015 (13)	NRS			✓ (46%)	Bulbar, penile urethra, combined penile & bulbar, or fossa navicularis stricture	NR	N/A	Visual internal urethrotomy (n=140)	✓				N/A
Barbagli 2018 (8) *	NRS			✓ (30%)	bulbar stricture	Idiopathic (63%), catheter (13.4%), instrumentation (11.8%), trauma (9.7%), infection (1.2%), congenital (0.6%), radiotherapy (0.3%)	Various types of urethroplasty (n=894)	Cold knife internal urethrotomy (n=348)	✓				N/A

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		Initial Only	Recurrent Only	Initial & Recurrent (% Initial)			Urethroplasty Procedure(s) (number of patients)	Endoscopic Management Procedure(s) (number of patients)	Stricture Recurrence	Symptoms	Quality of Life	Complications	
Cecen 2014 (14)	RCT	✓			penile, bulbar and membranous urethral strictures	Iatrogenic (80%), trauma (20%)	N/A	PlasmaKinetic urethrotomy (n=77) vs. cold-knife urethrotomy (n=66)	✓			✓	N/A
Choudhary 2015 (15)	NRS	✓			Location not reported; stricture length (<2cm vs. >2cm) determined procedure	Trauma (76.6%), infection (13.3%), non-specific cause (10%)	Buccal mucosa graft augmented dorsal onlay urethroplasty (n=45) vs. Excision and end to end anastomosis (n=45)	N/A	✓			✓	N/A
Das 2017 (9) *	NRS			✓ (84%)	Meatal, fossa navicularis, penile, bulbar, or pan-anterior stricture	Trauma (35.4%), Balanitis xerotica obliterans (23.6%), infection (19.1%), idiopathic (7.3%), catheterization (5.5%), post-transurethral resection (TUR; 5.5%), instrumentation (1.8%), post-hypospadias (1.8%)	Fossa navicularis & distal penile stricture: BMG urethroplasty (n=5) Meatal stricture: BMG meatoplasty (n=6) Pan-anterior urethral stricture: two-stage Johanson urethroplasty	Fossa navicularis & distal penile stricture: extended meatotomy (n=5) or clobetasol + dilatation (n=5) Meatal stricture: meatotomy + dilatation (n=12) or clobetasol + tacrolimus + dilatation (n=12) Pan-anterior urethral stricture: clobetasol +	✓				N/A

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Study (Reference)	Study Design	Stricture Instance			Stricture Type	Stricture Etiology	Comparison		Relevant Outcomes				Quality Score from AUA Guideline
		Initial Only	Recurrent Only	Initial & Recurrent (% Initial)			Urethroplasty Procedure(s) (number of patients)	Endoscopic Management Procedure(s) (number of patients)	Stricture Recurrence	Symptoms	Quality of Life	Complications	
							(n=8) or BMG urethroplasty (n=10) Bulbar urethral stricture: anastomotic urethroplasty (n=26) or BMG urethroplasty (n=5)	tacrolimus + dilatation (n=5) Bulbar urethral stricture: optical internal urethrotomy (n=9)					
Ekeke 2017 (10) *	NRS			NR	Bulbar, prostatic, membranous, fossa navicularis, female urethral, or long segment	Iatrogenic (catheterization or endoscopy, 19.1%), trauma (55.2%), inflammation (24.8%), malignancy (1%)	Urethroplasty substitution (n=24) or anastomotic (n=71)	Dilatation (n=37) or DVIU (n=61)	✓			✓	N/A
Fall 2014 (16)	NRS			✓ (49%)	Bulbar, penile, membranous or multiple urethral stricture	Sexually transmitted infection (60%), pelvic trauma (20%), iatrogenic (1.3%), unknown (18.7%)	Various types of urethroplasty (n=75)	N/A	✓				N/A
Holzhauser 2018 (17)	NRS			✓ (69%)	Bulbar, penile, panurethral strictures	Traumatic, idiopathic or iatrogenic (?% ^b), inflammatory or hypospadias (2.1%)	N/A	endoscopic urethrotomy with knife (n=127) vs. endoscopic urethrotomy with Ho:Yag laser (n=65)	✓			✓	N/A
Hyn 2015 (11) *	NRS			NR	Anterior or posterior stricture	NR	urethroplasty (n=32)	internal endoscopic	✓				N/A

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Study (Reference)	Study Design	Stricture Instance			Stricture Type	Stricture Etiology	Comparison		Relevant Outcomes				Quality Score from AUA Guideline
		Initial Only	Recurrent Only	Initial & Recurrent (% Initial)			Urethroplasty Procedure(s) (number of patients)	Endoscopic Management Procedure(s) (number of patients)	Stricture Recurrence	Symptoms	Quality of Life	Complications	
								urethrotomy (n=44)					
Jain 2014 (18)	RCT	✓			Short segment strictures (<2cm)	Inflammatory (46.7%), post-catheterization (32.2%), trauma (11.1%), unknown (10%)	N/A	Holmium (Ho: YAG) laser DVIU (n=45) vs. Sachse cold knife DVIU (n=45)	✓			✓	N/A
Jhanwar 2016 (19)	NRS	✓			short-segment bulbar urethral stricture (≤1.5cm)	NR	N/A	Holmium laser DVIU (n=54) vs. Sachse cold knife DVIU (n=58)	✓			✓	N/A
Kluth 2017 (20)	NRS			✓ (66%)	Penile, bulbar	Trauma (3.9%) ^c , infection (7.0%) ^c , radiation (14.8%) ^c , iatrogenic (24.2%) ^c , unknown (50.0%) ^c	N/A	DVIU (n=85)	✓				N/A
Kulkarni 2016 (21)	NRS			✓ (89%)	panurethral stricture	Lichen sclerosus (57.9%), catheterization, idiopathic, iatrogenic, failed hypospadias, or trauma (42.1%)	one-stage oral mucosal graft urethroplasty (n=318)	N/A	✓				N/A
Kunz 2018 (22)	NRS			✓ (17%)	Anterior strictures (Bulbar, penile, penobulbar, fossa navicularis)	Unknown (60.6%), iatrogenic (28.9%), trauma (8.4%), lichen sclerosus (4.2%), inflammation (2.8%)	Augmented anastomotic repair with oral mucosa graft (n=12)	N/A	✓				N/A
Ozcan 2015 (23)	NRS	✓			NR	NR	N/A	plasmakinetic urethrotomy (n=30) vs. cold	✓		✓		N/A

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Study (Reference)	Study Design	Stricture Instance			Stricture Type	Stricture Etiology	Comparison		Relevant Outcomes				Quality Score from AUA Guideline
		Initial Only	Recurrent Only	Initial & Recurrent (% Initial)			Urethroplasty Procedure(s) (number of patients)	Endoscopic Management Procedure(s) (number of patients)	Stricture Recurrence	Symptoms	Quality of Life	Complications	
								knife urethrotomy (n=30)					
Pal 2017 (24)	NRS			✓ (63%)	Single or multiple bulbar stricture	Inflammatory (26.3%), traumatic (5.1%), iatrogenic (10.2%), idiopathic (58.5%)	N/A	DVIU (n=118)	✓				N/A
Redon-Galvez 2016 (25)	NRS			✓ (89%)	Single or multiple; penile, bulbar, urethrovessical or membranous stricture	Idiopathic (32.8%), iatrogenic (67.2%)	N/A	Sachse internal urethrotomy (n=60)	✓				N/A
Sachin 2017 (26)	NRS	✓			Anterior urethral stricture	Pelvic fracture urethral injury (16.7%), inflammatory (83.3%)	substitution urethroplasty (n=22) vs. end-to-end anastomotic urethroplasty (n=18)	N/A				✓	N/A
Tinaut-Ranera 2014 (12) *	NRS	✓		✓ (80%)	Bulbar, meatus, membranous, proximal penile, distal penile or panurethral	Trauma (4.4% ^d), infection (4.4% ^d), congenital disorder (11.1% ^d), catheterization (11.1% ^d), prostatic/bladder transurethral resection (22.2% ^d), balanitis (2.2% ^d), unknown (44.4% ^d)	Urethroplasty (n=22)	Endoscopic urethrotomy (n=14)	✓				N/A

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Study (Reference)	Study Design	Stricture Instance			Stricture Type	Stricture Etiology	Comparison		Relevant Outcomes				Quality Score from AUA Guideline
		Initial Only	Recurrent Only	Initial & Recurrent (% Initial)			Urethroplasty Procedure(s) (number of patients)	Endoscopic Management Procedure(s) (number of patients)	Stricture Recurrence	Symptoms	Quality of Life	Complications	
Tolkach 2016 (27)	NRS	✓			Single or multiple; Penile, Prebulbar, Bulbar, Anastomosis (RPE), bladder neck, combination, or unclear location	TURP (34.8%), Idiopathic (36.2%), Trauma (4.2%), Hereditary (0.1%), Urethroplasty (1.6%), RPE (9.4%), Infection (2.6%), Catheterization (11%)	N/A	Internal cold-knife urethrotomy (n=961)	✓				N/A
Yenice 2018 (28)	RCT	✓			bulbar stricture	Iatrogenic (66.7%), traumatic (19.0%), urethritis (9.5%), idiopathic (4.8%)	N/A	Holmium:YAG laser internal urethrotomy (HIU) (n=34) vs. cold-knife optical internal urethrotomy (OIU) (n=29)	✓			✓	N/A
Yuruk 2016 (29)	NRS	✓			Bulbar stricture	Unknown/Idiopathic (37.3%), transurethral intervention (62.7%)	N/A	DVIU (n=193)	✓				N/A

Abbreviations: N/A = Not Applicable; NR = Not Reported; NRS = non-randomized study; RCT = randomized controlled trial

Footnotes:

* studies that made a direct comparison of endoscopic management to urethroplasty

^a percentages based on total number of potentially eligible patients (n=450) rather than the total number of analysed patients (n=224)

^b reported numerator (as reported by study authors in Table 2) exceeds the denominator, so percentage cannot be accurately reported

^c percentages based on total number of included participants (n=128) rather than the total number of participants in the subgroup of interest, i.e., primary DVIU (n=85)

^d percentages based on total number of included participants (n=45) rather than the total number of participants in the treatment arms of interest (n=36)

Table 4. Summary of Findings

Outcomes № of participants (studies)	Certainty of the evidence (GRADE)	Study Event Rates			Anticipated absolute effects	
		With urethroplasty	With endoscopic management (dilation or DVIU)	Relative effect (95% CI)	Risk with urethroplasty	Risk difference with endoscopic management (dilation or DVIU)
Stricture Recurrence - COMPARATIVE 1655 (5 observational studies) ^{1,2,3,4,5}	⊕○○○ VERY LOW a,b,c	231/1103 (20.9%)	189/552 (34.2%)	RR 2.19 (1.46 to 3.27)	209 per 1,000	249 more per 1,000 (96 more to 475 more)
Complications - Initial & Recurrent Stricture - COMPARATIVE 193 (1 observational study) ²	⊕○○○ VERY LOW a,d,e	8/95 (8.4%)	12/98 (12.2%)	RR 1.45 (0.62 to 3.40)	84 per 1,000	38 more per 1,000 (32 fewer to 202 more)
Stricture Recurrence - NON COMPARATIVE 2616 (22 observational studies) ^{6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27}	⊕○○○ VERY LOW f,g	87/563 (15.5%)	790/2053 (38.5%)	not pooled	not pooled	not pooled
Quality of Life (post-op scores) - NON COMPARATIVE 60 (1 observational study) ⁸	⊕○○○ VERY LOW f,i	-	-	-	not pooled	not pooled
Complications - NON COMPARATIVE 1976 (9 observational studies) ^{6,7,9,11,12,17,18,19,28}	⊕○○○ VERY LOW f,j	87/622 (14.0%)	32/1354 (2.4%)	not pooled	not pooled	not pooled

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio; **MD:** Mean difference

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GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

- a. non-randomized studies
- b. Only 1 of 5 studies in patients with initial stricture: n=32, RR = 1.57 (0.37 to 6.72)
- c. wide CI for absolute effect (despite adequate number of events)
- d. study not clear on whether patients had initial or recurrent stricture
- e. few events & wide CI for absolute effect
- f. not direct comparison of endoscopic management to urethroplasty
- g. proportion of events varied greatly between studies (0% to 87.9%)
- h. few events
- i. few participants
- j. proportion of events varied greatly between studies (0% to 61%)

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Figure 2. Comparative Studies – Stricture Recurrence

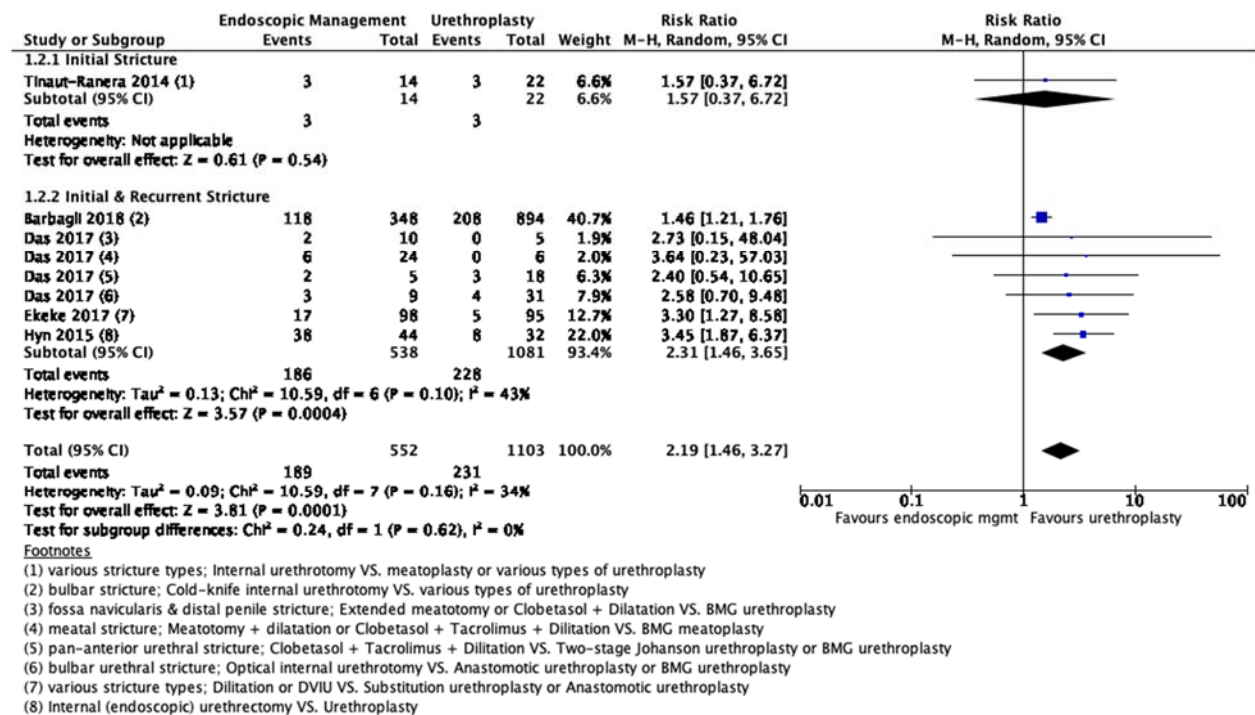


Figure 3. Comparative Studies – Complications

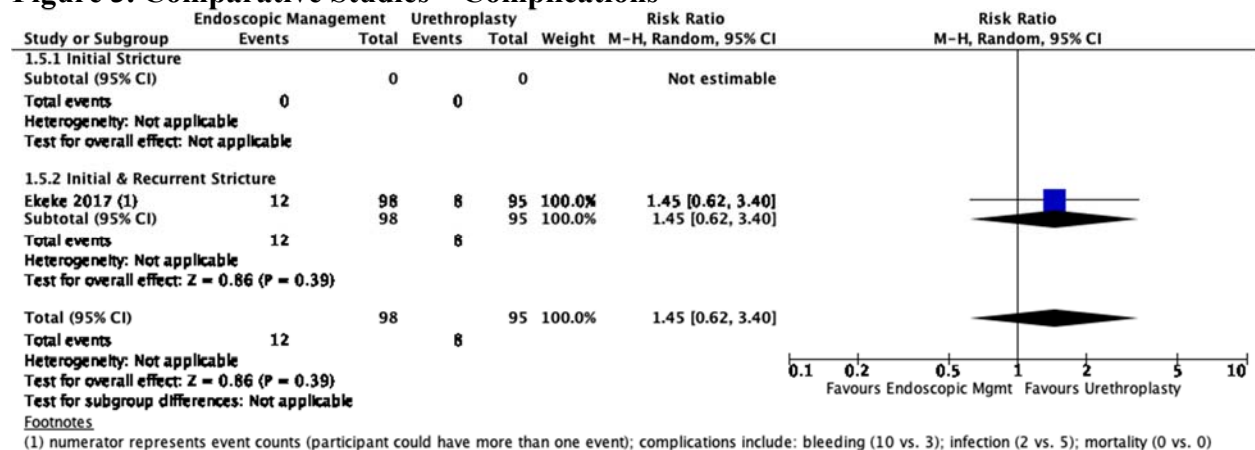


Table 5. Non-Comparative Studies – Stricture Recurrence by Procedure

Study or Subgroup	Endoscopic Management			Urethroplasty		
	Events	Total	%	Events	Total	%
Oral Mucosa Graft Urethroplasty						
Choudhary 2015 ^a				7	45	15.6%
Kulkarni 2012				14	104	13.5%
Kulkarni 2016				39	283	13.8%
Subtotal				60	432	13.9%
Anastomotic urethroplasty						
Choudhary 2015 ^b				6	45	13.3%
Kunz 2018				0	12	0.0%
Subtotal				6	57	10.5%
Scrotal or Penile Island Flap (Graft) Urethroplasty						
Hussein 2011 ^c				4	19	21.1%
Hussein 2011 ^d				5	18	27.8%
Subtotal				9	37	24.3%
Other Urethroplasty						
Fall 2014				12	37	32.4%
Subtotal				12	37	32.4%
Cold knife urethrotomy						
Atak 2011	14	30	46.7%			
Cecen 2014	22	66	33.3%			
Holzhauser 2018	41	95	43.2%			
Jain 2014	0	45	0.0%			
Jhanwar 2016	4	55	7.3%			
Kluth 2017	50	85	58.8%			
Mandhani 2005	41	105	39.0%			
Mazdak 2010 ^e	11	22	50.0%			
Mazdak 2010 ^f	5	23	21.7%			
Ozcan 2015	11	30	36.7%			
Pal 2017	83	118	70.3%			
Pansadoro 1996 ^g	69	129	53.5%			

Study or Subgroup	Endoscopic Management			Urethroplasty		
	Events	Total	%	Events	Total	%
Pansadoro 1996 ^h	58	69	84.1%			
Redón-Gálvez 2016	22	60	36.7%			
Tolkach 2016	108	470	23.0%			
Yenice 2018	6	29	20.7%			
Yuruk 2016	45	193	23.3%			
Subtotal	590	1624	36.3%			
Laser Urethrotomy						
Atak 2011	4	21	19.0%			
Holzhauser 2018	21	37	56.8%			
Jain 2014	6	45	13.3%			
Jhanwar 2016	4	52	7.7%			
Yenice 2018	11	34	32.4%			
Subtotal	46	189	24.3%			
Cold-knife or Laser Urethrotomy						
Al Taweel 2015	123	140	87.9%			
Subtotal	123	140	87.9%			
PlasmaKinetic Urethrotomy						
Cecen 2014	24	70	34.3%			
Ozcan 2015	7	30	23.3%			
Subtotal	31	100	31.0%			
TOTAL	790	2053	38.5%	87	563	15.5%

Footnotes

^a BMG augmented dorsal onlay urethroplasty

^b EPA

^c Ventral onlay urethroplasty using distal penile circular fasciocutaneous flap (PCF)

^d Ventral onlay urethroplasty using a distal penile full-thickness circular graft (PCG)

^e cold knife DVIU

^f cold knife DVIU + triamcinolone

^g bulbar stricture

^h penile & penile bulbar stricture

Table 6. Non-Comparative Studies – Quality of Life

Study or Subgroup	Endoscopic Management			Urethroplasty		
	Mean	SD	Total	Mean	SD	Total
Ozcan 2015 ^a	1.9	0.7	30	-	-	-
Ozcan 2015 ^b	1.4	0.5	30	-	-	-
TOTAL	-	-	60	-	-	-

Footnotes:

^a plasmakinetic urethrotomy; pre-op scores 5.3, 0.7

^b cold knife urethrotomy; pre-op scores 5.2, 0.6

Table 7. Non-Comparative Studies – Complications by Type

Study or Subgroup	Endoscopic Management			Urethroplasty		
	Events	Total	%	Events	Total	%
Erectile Dysfunction						
Choudhary 2015 ^a	-	-	-	3	45	6.7%
Choudhary 2015 ^b	-	-	-	1	45	2.2%
Sachin 2017 ^c	-	-	-	11	22	50.0%
Sachin 2017 ^d	-	-	-	11	18	61.1%
Subtotal	0	0	0.0%	26	130	20.0%
Urinary Incontinence						
Choudhary 2015 ^a	-	-	-	2	45	4.4%
Choudhary 2015 ^b	-	-	-	7	45	15.6%
Subtotal	0	0	0.0%	9	90	10.0%
Other Urinary						
Atak 2011 ^{e, f}	0	30	0.0%	-	-	-
Atak 2011 ^{e, g}	0	21	0.0%	-	-	-
Cecen 2014 ^{e, f}	0	66	0.0%	-	-	-
Cecen 2014 ^{e, h}	0	70	0.0%	-	-	-
Choudhary 2015 ^{a, i}	-	-	-	6	45	13.3%
Choudhary 2015 ^{b, i}	-	-	-	8	45	17.8%
Hussein 2011 ^{j, l}	-	-	-	5	18	27.8%
Hussein 2011 ^{k, l}	-	-	-	6	19	31.6%
Yenice 2018 ^{g, m}	1	34	2.9%	-	-	-
Subtotal	1	221	0.5%	25	127	19.7%

Study or Subgroup	Endoscopic Management			Urethroplasty		
	Events	Total	%	Events	Total	%
Infection						
Atak 2011 ^{f, n}	0	30	0.0%	-	-	-
Atak 2011 ^{g, n}	0	21	0.0%	-	-	-
Cecen 2014 ^{f, n}	0	66	0.0%	-	-	-
Cecen 2014 ^{h, n}	0	70	0.0%	-	-	-
Hussein 2011 ^j	-	-	-	2	18	11.1%
Hussein 2011 ^k	-	-	-	2	19	10.5%
Jhanwar 2016 ^{p, o}	2	52	3.8%	-	-	-
Jhanwar 2016 ^{f, o}	0	55	0.0%	-	-	-
Subtotal	2	294	0.7%	4	37	10.8%
Bleeding						
Atak 2011 ^{g, q}	0	21	0.0%	-	-	-
Atak 2011 ^{f, q}	0	30	0.0%	-	-	-
Cecen 2014 ^{h, q}	0	70	0.0%	-	-	-
Cecen 2014 ^{f, q}	0	66	0.0%	-	-	-
Hussein 2011 ^{k, r}	-	-	-	3	19	15.8%
Hussein 2011 ^{j, r}	-	-	-	2	18	11.1%
Jain 2014 ^{f, s}	7	45	15.6%	-	-	-
Jhanwar 2016 ^p	0	52	0.0%	-	-	-
Jhanwar 2016 ^f	5	55	9.1%	-	-	-
Yenice 2018 ^f	3	29	10.3%	-	-	-
Subtotal	15	368	4.1%	5	37	13.5%
Fluid Extravasation						
Jain 2014 ^{p, t}	4	45	8.9%	-	-	-
Jhanwar 2016 ^p	3	52	5.8%	-	-	-
Jhanwar 2016 ^f	2	55	3.6%	-	-	-
Subtotal	9	152	5.9%	-	-	-
Swelling						
Hussein 2011 ^{j, u}	-	-	-	5	18	27.8%
Hussein 2011 ^{k, u}	-	-	-	7	19	36.8%
Subtotal				12	37	32.4%

Study or Subgroup	Endoscopic Management			Urethroplasty		
	Events	Total	%	Events	Total	%
Fistula Complications						
Hussein 2011 ^j	-	-	-	0	18	0.0%
Hussein 2011 ^k	-	-	-	1	19	5.3%
Subtotal				1	37	2.7%
Overall/Any						
Holzhauser 2018 ^v	1	37	2.7%	-	-	-
Holzhauser 2018 ^w	4	95	4.2%	-	-	-
Subtotal	5	132	3.8%	-	-	-
Other						
Atak 2011 ^{g, x}	0	21	0.0%	-	-	-
Atak 2011 ^{f, x}	0	30	0.0%	-	-	-
Cecen 2014 ^{h, y}	0	70	0.0%	-	-	-
Cecen 2014 ^{f, y}	0	66	0.0%	-	-	-
Choudhary 2015 ^{b, z}	-	-	-	2	45	4.4%
Choudhary 2015 ^{a, z}	-	-	-	0	45	0.0%
Hussein 2011 ^{k, aa}	-	-	-	3	19	15.8%
Hussein 2011 ^{j, aa}	-	-	-	0	18	0.0%
Subtotal	0	187	0.0%	5	127	3.9%
TOTAL	32	1354	2.4%	87	622	14.0%

Footnotes:

^a EPA

^b BMG augment dorsal onlay

^c substitution urethroplasty

^d end-to-end anastomotic urethroplasty

^e urinary retention

^f cold-knife urethrotomy

^g holmium:yttrium-aluminium-garnet (HO:YAG) laser

^h PlasmaKinetic urethrotomy

ⁱ thin stream of urine

^j ventral onlay urethroplasty using a distal penile full-thickness circular graft (PCG)

^k ventral onlay urethroplasty using distal penile circular fasciocutaneous flap (PCF)

^l post-void dribbling

^m urine extravasation

ⁿ bacteremia

^o fever

^p holmium laser DVIU

^q hemorrhage

^r hematoma

^s intra-operative bleeding

^t extravasations of irrigating fluid in perineum

Rourke KF, et al. Canadian Urological Association guideline on male urethral stricture. Can Urol Assoc J 2020;14(10).

^u scrotal oedema

^v endoscopic urethrotomy with laser

^w endoscopic urethrotomy with knife

^x false route or epididymitis

^y false route

^z chordae

^{aa} superficial skin necrosis

Other factors

Fourteen studies addressed other EtD factors (11, 16, 18, 19, 23, 28, 36-43). We did not identify cost-effectiveness studies.

RECOMMENDATION 2 - GRADE Evidence to Decision Framework

Should endoscopic management (dilation or DVIU) vs. urethroplasty be used for men with (undifferentiated) initial diagnosis of urethral stricture?	
POPULATION:	men with (undifferentiated) initial diagnosis of urethral stricture
INTERVENTION:	endoscopic management (dilation or DVIU)
COMPARISON:	urethroplasty
MAIN OUTCOMES:	Stricture Recurrence, Symptoms, Quality of Life, Complications

ASSESSMENT

Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know 	<p>In total, 28 eligible studies were identified when combining relevant studies from the AUA guideline (n=6) with studies identified from our updated search (2014-2018; n=22). Amongst the 28 studies, only 5 studies directly compared endoscopic management to urethroplasty. All 5 were observational studies identified by our updated search. Only 1 in 5 comparative studies included patients with initial stricture. Quality of life and symptoms were not addressed in the comparative studies.</p> <p>23/28 studies provided data on either endoscopic management or urethroplasty. Amongst the 23 studies at least 80% of patients received treatment for initial stricture (or results for initial stricture are reported separately). Stricture recurrence rates reported in non-comparative studies are shown in Table 5 stratified by procedure. Complications reported in non-comparative studies are shown in Table 7 stratified by complication type.</p> <p>See Tables 5, 6, 7</p>	<p>The guideline panel agreed that endoscopic management may increase stricture recurrence by approximately 25% more compared to urethroplasty, and there may be a greater proportion of stricture recurrence.</p> <p>However, the proportion of recurrence and differences between the procedures are likely overestimated since it was not the initial diagnosis of urethral stricture for all participants, and men were likely selected to be treated by a specific procedure based on other characteristics not adjusted for in the analyses.</p> <p>There was very little data for symptoms after the procedures.</p>

Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know 	<p>Complications reported in non-comparative studies are shown in Table 7 stratified by complication type.</p> <p>See Table 7</p>	
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ● Very low ○ Low ○ Moderate ○ High ○ No included studies 		
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability 	<p>Breyer 2017: Patients and clinicians had a low agreement rate (53%) with respect to which symptoms, functions and impacts of urethral stricture disease were most important. Twenty patients were most bothered by: anxiety about being unable to void, post-void dribbling, trouble aiming the stream, sitting to urinate and the need to plan ahead. Twenty-two reconstructive urologists rated the following as most important for making treatment decisions: straining to urinate, weak stream, anxiety about being unable to void, full bladder and discomfort urinating in public. Patients included one sexual item (slow force of ejaculation) in their top 15 items, but clinicians did not include any sexual symptoms.</p> <p>Hampson 2017a: 169 patients with urethral stricture disease completed an anonymous online survey consisting of decisional conflict regarding surgical management and a choice-based conjoint analysis exercise. Prior to completing the choice-based survey, 50% reported having decisional conflict about what treatment option to pursue, whereas after the conjoint analysis only 44% had decisional conflict (< .01). Seventy percent of participants felt that the choice-based conjoint analysis exercise was helpful in deciding what was important in making a</p>	

	treatment decision, and 82% felt that it helped them express their priorities and preferences for side effects and outcomes of surgical management. Of those participants with decision conflict before the choice-based conjoint analysis exercise, 66% agreed that the survey helped them decide on what was important and 82% agreed that it helped them express their priorities.	
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input checked="" type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input type="radio"/> Don't know	Benefits may slightly favour urethropasty - small benefits Harms favoured endoscopy - smaller harms with endoscopy Overall, probably favours endoscopy	
Resources required How large are the resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Large costs <input checked="" type="radio"/> Moderate costs <input type="radio"/> Negligible costs and savings <input type="radio"/> Moderate savings <input type="radio"/> Large savings <input type="radio"/> Varies <input type="radio"/> Don't know		Relative - the costs are relatively small compared to other procedures for other conditions However, the initial costs of urethroplasty may be greater than endoscopic procedures due to operating time and post-operative stay.

Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know 		<p>endoscopy widely available with usual training.</p> <p>urethroplasty less widely available</p>
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ● Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know 	<p>Hampson 2017b: Endoscopic incision was preferred by younger men and men with college education or higher. Open reconstruction was preferred by older men and men with less education. Both age groups preferred to maximize the procedure success rate, although the older group had a stronger negative preference against the 25% success rate procedure, suggesting that they are less likely to accept a poor success rate. Compared to the higher income group, the lower income group had a stronger preference against higher copayment cost, against poorer success rates and against possible future procedures.</p> <p>Choudhary 2015: Most patients who had BMG dorsal onlay urethroplasty were satisfied during a four-year follow-up.</p>	<p>The guideline panel agreed that most patients will do something first before needing to be referred and to wait</p>
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ● Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know 	<p>Fall 2014: The success rate of urethroplasty was 81% (17/21) in patients operated on by experienced surgeons in urological reconstructive surgery and 53.7% (29/54) in those operated on by younger surgeons (p=0.02).</p> <p>Faris 2016: Analyzed early urethroplasty outcomes from six recently trained reconstructive urologic fellows. The average number of cases performed per surgeon per year averaged 21.8 (range 14 to 53), which increased significantly with years in practice (p = 0.0036). Controlling for stricture location, years out</p>	<p>The guideline panel agreed that urethroplasty is less available than endoscopy</p>

	<p>of fellowship and repair type, success rates between surgeons were statistically different ($p = 0.0014$). Overall success rates improved significantly with time ($p = 0.0422$ for trend), with improvements being most pronounced with bulbar urethroplasties. Overall success rates for penile repairs did not appear to improve with time. This group of surgeons averaged approximately 100 cases before obtaining proficiency (defined as success rate of > 90%) for all types of urethroplasty. The odds of complications decreased 3% (OR 0.97) and 4% (OR 0.96) for every month out of fellowship for bulbar and penile cases respectively. Blood loss did not appear to be affected by time from fellowship or case number.</p> <p>Jain 2014: Clinicians were not able to negotiate telescope completely into the urinary bladder in 8/45 (17.78%) patients who underwent internal urethrotomy with Holmium laser, which was indicative of incompleteness of the procedure. On the other hand, internal urethrotomy was completed successfully in all patients (45/45) who underwent the cold knife procedure.</p> <p>Obi 2017: Delay in undergoing surgery was a common observation in a review of 48 short segment bulbar urethral strictures cases in Nigeria. Authors attributed the delay to due to poor finance. The mean time to surgery from presentation was 10.20 (± 4.96) months (range 3-22). Comorbidities tended to increase with the treatment delay. Patients operated on after 6 months of presentation had significantly more associated comorbidity, 24/26 patients (92.3%) compared to those operated on within 6 months, 8/16 cases (50%), $p=0.003$.</p> <p>Hyn 2015: Operative time was shorter with endoscopic urethrectomy compared to urethroplasty: mean 55.7 \pm 18.6 minutes versus 103.7 \pm 45.7.</p> <p>Huang 2017: Operative time was significantly shorter operative time with endoscopic realignment by modified technique under flexible urethroscope compared to conventional endoscopic realignment surgery: mean 29.1 \pm 9.5 minutes vs 58.1 \pm 11.2, $p<0.001$.</p> <p>Three studies found that operative time was shorter for cold knife urethrotomy compared to Holmium laser urethrotomy: Jain 2014: mean 7.44 minutes (range 5-10) versus 19.8 (15-30) Jhanwar 2016: mean 16.3 \pm 1.78 minutes versus 20.96 \pm 2.23, $p<0.0001$ Yenice 2018: mean 18.4 \pm 2.3 minutes versus 21.9 \pm 3.8, $p < 0.05$.</p>	
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	<p>Ozcan 2015: Operative time was shorter for plasmakinetic urethrotomy compared to cold knife urethrotomy: mean 15.6 ± 3.3 minutes versus 19.5 ± 4.2, p<0.05.</p> <p>Zou 2017: Operative time was shorter for endoscopic realignment compared to cystostomy: mean 115 minutes versus 142, p<0.05.</p>	
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SUMMARY OF JUDGEMENTS

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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CONCLUSIONS

Recommendation

We suggest endoscopic management as the initial treatment of the symptomatic undifferentiated stricture (Conditional Recommendation, Very Low levels of certainty of evidence).

Justification

The benefits are likely similar between endoscopic management and urethroplasty. For most complications, including erectile dysfunction, urinary incontinence, infection, bleeding, swelling, and fistula complications, the risk was often 4% greater with urethroplasty than endoscopic management.

There may be cost savings with urethroplasty due to fewer recurrences, but greater costs due to increased training, operating time and post-operative stay. Urethroplasty is also less available than endoscopic management resulting in longer wait times which may make endoscopic management more preferable to men.

RECOMMENDATION 3

Characteristics of included studies

Data from 32 studies involving 4587 patients were included in the review of urethroplasty versus endoscopic management for urethral stricture recurrence. Of those included studies, we found one comparative nonrandomized study (44); and 31 noncomparative studies (30 case series and one combined analysis of trial groups) (20, 24, 33, 45-72). Of 31 noncomparative studies, 21 studies assessed urethroplasty (46, 48-52, 54-58, 60, 63-71) and 10 assessed endoscopic treatment (20, 24, 33, 45, 47, 53, 59, 61, 62, 72).

The median sample size was 68 (range, 4-596) patients. In total, 3840 men received urethroplasty and 747 men received endoscopic management. In studies evaluating urethroplasty, 63% (2422/3840) had previous endoscopic and 19% (718/3840) had previous urethroplasty. In studies evaluating endoscopic, 56% (415/747) men had previous endoscopic and 33% (249/747) had previous urethroplasty. From studies that reported details of stricture site, 76% (2827/3733) men had bulbar urethra and 17% (617/3733) had penile urethra. Most studies had a mean follow-up of two years or longer. The overall study characteristics are detailed in Table 8.

Other factors

Twelve studies reported on other EtD factors (16, 30, 38, 73-82). Costs are mainly driven by operating time, postoperative stay, and long-term complications. There may be cost savings with urethroplasty due to fewer recurrences, but greater costs due to increased training, operating time and post-operative stay. Urethroplasty is also less available than endoscopic management. Repeat endoscopic management procedures may be less acceptable to men with multiple recurrences, however more acceptable to men who want to avoid in-hospital procedures, scheduling, timing or hospital stay.

Risk of Bias

All of the included studies had high risk of bias owing to selection bias, confounding bias, and selective reporting bias.

Table 8. Characteristics of Included Studies

Study ID	Study Design	Interventions (n _p /n _i)	Stricture site (%)	Previous treatments (%)	Number of previous treatments	Duration of follow-up	Definition of event*
Ekerhult 2017(44)	Comparative NRS	Urethroplasty (NR/55 urethroplasties)	Bulbar (73%), Penile (27%)	Prior urethroplasty (100%)	NR	Median, 70-82 mth	Need for an additional surgical procedure
		Endoscopic (NR/124 endoscopies)					
Sukumar 2018(45)	Retrospective case series	Endoscopic management (53 pts/NR)	NR	Prior urethroplasty (100%)	NR	Median, 5 mth	Anatomic definition of urethral stricture recurrence (i.e., the ability to navigate past the endoscopically managed stricture recurrence with a cystoscope without force)
Vetterlein 2018(46)	Retrospective case series	Urethroplasty (98 pts/NR)	NR	Prior endoscopy (NR); Prior urethroplasty (100%)	All patients had at least one urethroplasty.	Median, 33 mth	Recurrence was defined as the symptomatic need for any instrumentation during follow-up, including dilation, endoscopic, or reconstructive surgery.
Rosenbaum 2015(47)	Retrospective case series	Endoscopic (43 pts/NR)	Bulbar (81%) Penile (14%)	Prior endoscopic + urethroplasty (81%); Prior urethroplasty (100%)	All patients had at least one urethroplasty and 81% had at least one urethroplasty and DVIU	Mean, 12 mth	Stricture recurrence was determined when urinary flow rate <15 ml/s and verified. In a combined retro- and antegrade voiding cystography or cystoscopy
Siegel 2015(48)	Retrospective case series	Urethroplasty (37 pts/898 urethroplasties)	Bulbar (100%)	Prior endoscopy + urethroplasty	All patients had at least one	Mean, 42 mth	Need for an additional urethral procedure except diagnostic cystoscopy

Study ID	Study Design	Interventions (n _p /n _i)	Stricture site (%)	Previous treatments (%)	Number of previous treatments	Duration of follow-up	Definition of event*
				(84%); Prior urethroplasty (100%)	urethroplasty and 84% had at least one endoscopy and urethroplasty		
Rosenbaum 2016(49)	Retrospective case series	Urethroplasty (50 pts/NR)	Bulbar (71%), Penile (29%)	Prior urethroplasty (100%)	All patients had at least one urethroplasty	Mean, 14 mth	Need for an additional urethral procedure and when maximum urinary flow rate <15 ml/s and stricture was verified in a combined RUG/AUG or cystoscopy.
Pal 2017(24)	Retrospective case series	Endoscopic (68 pts/NR)	Bulbar (100%)	Prior endoscopic (100%)	NR	Mean, 6 mth	Symptoms or signs of recurrent stricture and ability to pass freely 18Fr catheter during urethral calibration
Mellon 2014(50)	Retrospective case series	Urethroplasty (107 pts/NR)	NR	Not specified	NR	Mean, 39 mth	Urethral stricture recurrence; no definition.
Levine 2014(51)	Retrospective case series	Urethroplasty (49 pts/NR)	Bulbar (63%), Penile (22%)	Prior urethroplasty (100%)	NR	Mean, 49 mth	Urethral patency, defined as ≥16F urethral caliber with the absence of voiding symptoms
Kluth 2017(20)	Retrospective case series	Endoscopic (43 pts/NR)	NR	Prior endoscopic (100%)	NR	Median, 16 mth	First subjective or objective sign of recurrence, defined as increased postvoid residual urine volume, decreased force of urinary stream, obstructive patterns in uroflowmetry (urinary flow rate <15 mL/s), and definitive urethrographic or

Study ID	Study Design	Interventions (n _p /n _i)	Stricture site (%)	Previous treatments (%)	Number of previous treatments	Duration of follow-up	Definition of event*
							cystoscopic evidence of stricture recurrence
Kahokehr 2018(52)	Retrospective case series	Urethroplasty (373 pts/NR)	Bulbar (100%)	Prior endoscopic (100%)	59% has more than one endoscopic	Median, 28 mth	Need for further intervention in the postoperative period as diagnosed with cystoscopy and/or RUG
Farrell 2017(53)	Retrospective case series	Endoscopic (44 pts/NR)	Bulbar (100%)	Prior endoscopic (61%); Prior urethroplasty (39%)	median of 1 previous procedure	Median, 26 mth	Inability to pass a 16 Fr flexible cystoscope through the stricture or need for additional procedures based on obstructive voiding symptoms
Chapman 2017(54)	Retrospective case series	Urethroplasty (596 pts/NR)	Bulbar (100%)	Prior endoscopic (88%); Prior urethroplasty (11%)	88% pts had at least one endoscopic	Mean, 65 mth	Stricture recurrence, defined anatomically as the inability to easily pass a 16Fr cystoscope.
Cordon 2014(55)	Retrospective case series	Urethroplasty (102 pts/637 urethroplasties)	Bulbar (56%)	Prior endoscopic (75%); Prior urethroplasty (10%)	NR	Mean, 40 mth	Need for subsequent open or endoscopic operative intervention
Ekerhult 2015(56)	Retrospective case series	Urethroplasty (90 pts/109 urethroplasties)	Penile (100%)	Prior endoscopic (44%); Prior urethroplasty (51%)	NR	Median, 40-63 mth	Stricture recurrence, diagnosed with cystoscopy, combined with patient's symptoms such as poor urine stream, dribbling,

Study ID	Study Design	Interventions (n _p /n _i)	Stricture site (%)	Previous treatments (%)	Number of previous treatments	Duration of follow-up	Definition of event*
							leakage, low urinary flow or a urinary retention episode.
Fossati 2016(57)	Prospective case series	Urethroplasty (546 pts/NR)	Bulbar (80%), Penile (16%)	Prior endoscopic (50%); Other* (47%)	NR	Median, 69 mth	Need for an additional surgical procedure (including dilation)
Fuchs 2018(58)	Retrospective case series	Urethroplasty (403 pts/NR)	Bulbar (48%), Penile (42%)	Prior endoscopic (72%); Prior urethroplasty (43%)	NR	Median, 51 mth	Need for additional surgical procedure or management
Kizilay 2017(59)	Retrospective case series	Endoscopic (185 pts/NR)	NR	Prior endoscopic (100%)	NR	Mean, 6 mth	Stricture recurrence; no definition
Xu 2017(60)	Retrospective case series	Urethroplasty (81 pts/NR)	Penile (46%)	Prior endoscopic (47%); Others* (76%)	NR	Mean, 41 mth	Stricture recurrence; no definition
Mandhani 2005(33)^	Retrospective case series	Endoscopic (28 pts/NR)	Bulbar (100%)	Prior endoscopic (100%)	NR	Mean, 46 mth	Recurrence of symptoms, failure to self-calibrate and the need for secondary procedures (dilation, internal urethrotomy, or urethroplasty)
Heyns 1998(61)^	A combined analysis of trial groups	Endoscopic (68 pts/NR)	NR	Prior endoscopic (94%); Prior urethroplasty (12%)	NR	Median, 21 mth	Stricture recurrence; no definition

Study ID	Study Design	Interventions (n _p /n _i)	Stricture site (%)	Previous treatments (%)	Number of previous treatments	Duration of follow-up	Definition of event*
Ketabchi 2017(62)	Prospective case series	Endoscopic (87 pts/NR)	Bulbar (44%), Penile (40%)	Not specified	NR	Median, 6 mth	Need for an additional urethral procedure and when maximum urinary flow rate <15 ml/s
Rigatti 1993^(63)	Prospective case series	Urethroplasty (62 pts/NR)	Bulbar (100%)	Prior endoscopic (100%); Prior urethroplasty + endoscopic (10%)	90% had at least one urethrotomy	Mean, 12 mth	Stricture recurrence; no definition
Viers 2018(64)	Retrospective case series	Urethroplasty (492 pts/514 urethroplasties)	Bulbar (68%), Penile (14%)	Prior endoscopic (76%); Prior urethroplasty (18%)	NR	Median, 31 mth	Need for recurrent urethral intervention
Barbagli 2014(65)^	Retrospective case series	Urethroplasty (296 pts/NR)	Bulbar (85%); Penile (15%)	Prior endoscopic (58%); Prior urethroplasty (5.7%); Others* (36%)	NR	Median, 118 mth	Need for an additional urethral procedure (including dilation)
Welk 2012(66)^	Retrospective case series	Urethroplasty (44 pts/NR)	Bulbar (100%)	Prior endoscopic (98%); Prior urethroplasty (5%)	98% had at least one prior dilation, 93% had at least prior DVIU, and 5% had a prior urethroplasty	Median, 32 mth	Need for an additional urethral procedure (including dilation)

Study ID	Study Design	Interventions (n _p /n _i)	Stricture site (%)	Previous treatments (%)	Number of previous treatments	Duration of follow-up	Definition of event*
Barbagli 2001(67)^	Retrospective case series	Urethroplasty (47 pts/NR)	Bulbar (100%)	Prior endoscopic (100%)	NR	Mean, 63 mth	Need for additional urethral procedure (including dilation)
Barbagli 2008(68)^	Retrospective case series	Urethroplasty (22pts/NR)	Bulbar (100%)	Prior endoscopic (64%); Other* (36%)	NR	Mean, 111 mth	Need for additional urethral procedure (including dilation)
Elgammal 2009(69)^	Retrospective case series	Urethroplasty (22 pts/NR)	Bulbar (100%)	Prior endoscopic (100%)	NR	Mean, 42 mth	Symptoms of infravesical obstruction, urinary flow rate <15 mL/s, postvoiding residual urine volume >50 mL, and poor urethral caliber on ascending urethrography
Figler 2013(70)^	Retrospective case series	Urethroplasty (87 pts/NR)	Bulbar (100%)	Prior endoscopic (82%); Prior urethroplasty (16%)	NR	Mean, 36 mth	Need for endoscopic or open revision of the reconstruction or placement of a suprapubic catheter for urinary retention.
Kluth 2013(71)^	Retrospective case series	Urethroplasty (140 pts/NR)	Bulbar (64%); Penile (20%)	Not specified	NR	Median, 10 mth	Need for an additional urethral procedure (except scheduled follow-up endoscopy)
Park 2004(72)^	Retrospective case series	Endoscopic (4 pts/NR)	NR	Prior urethroplasty (100%)	NR	Median, 25 mth	Stricture recurrence; no definition

*event: failure or recurrence stricture defined as per study author. ^Included study from AUA Evidence. NR: Not reported. n_p: total number of participants. n_i: total number of interventions. *Other previous stricture treatments may include hypospadias repair, US repair, optical internal urethrotomy, meatotomy, suprapubic cystostomy, or other associated treatments.

Table 9. Summary of Findings

No of participants (studies) Follow-up	Overall certainty of evidence	With endoscopic treatment (either dilation or DVIU)	With urethroplasty
Stricture (comparative NRS)			
179 (1 observational study)(44)	⊕○○○ VERY LOW ^{a,b}	74 per 100	19 fewer per 100 (from 32 fewer to 3 fewer)
Stricture (noncomparative NRS)			
4408 (31 observational studies) (20, 24, 33, 45-72)	⊕○○○ VERY LOW ^{c,d,e,f,g}	306/623 (49.1%)	603/3785 (15.9%)
Complications (counts)			
681 (11 observational studies) (44, 47, 49-51, 53, 60, 62, 63, 66, 70)	⊕○○○ VERY LOW ^{c,d,e,g}	47/174 (27.0%)	133/507 (26.0%)

Explanations

- a. Comparative study, unadjusted analyses
- b. Few participants
- c. Studies were not comparative; loss to follow-up unknown in most studies.
- d. Proportions were inconsistent across studies.
- e. Not direct comparison of endoscopic management to urethroplasty
- f. Definition of failure in a few studies did not exclusively measured by recurrence stricture
- g. Different outcome definitions across studies

Table 10. Study-specific Recurrence Stricture

Study or Subgroup	Endoscopic Management			Urethroplasty		
	Events	Total	%	Events	Total	%
Chapman 2017	-	-	-	40	596	6.7%
Cordon 2014	-	-	-	18	102	18%
Ekerhult 2015*	-	-	-	26	109	24%
Fossati 2016	-	-	-	142	546	26%
Fuchs 2018	-	-	-	68	403	17%
Kahokehr 2018	-	-	-	24	373	6.4%
Levine 2014	-	-	-	4	49	8.2%
Mellon 2014	-	-	-	27	107	25%
Rigatti 1993	-	-	-	9	62	15%
Rosenbaum 2016	-	-	-	9	50	18%
Siegel 2015	-	-	-	2	37	5.4%

Study or Subgroup	Endoscopic Management			Urethroplasty		
	Events	Total	%	Events	Total	%
Vetterlein 2018	-	-	-	18	98	18%
Viers 2018*	-	-	-	74	514	14%
Xu 2017	-	-	-	10	81	12%
Barbagli 2014	-	-	-	79	296	27%
Welk 2012	-	-	-	3	44	6.8%
Barbagli 2001	-	-	-	6	47	13%
Barbagli 2008	-	-	-	9	22	41%
Elgammal 2009	-	-	-	1	22	4.5%
Figler 2013	-	-	-	15	87	17%
Kluth 2013	-	-	-	19	140	14%
Ekerhult 2017*	92	124	74%	30	55	55%
Farrell 2017	11	44	25%	-	-	-
Heyns 1998	34	68	50%	-	-	-
Park 2004	0	4	0%	-	-	-
Ketabchi 2017	41	87	47%	-	-	-
Kizilay 2017	87	185	47%	-	-	-
Kluth 2017	12	43	28%	-	-	-
Mandhani 2005	15	28	54%	-	-	-
Pal 2017	54	68	79%	-	-	-
Rosenbaum 2015	21	43	49%			
Sukumar 2018	31	53	58%	-	-	-
TOTAL	398	747	53%	633	3840	16%

*unit of analysis is per procedure (not per patient)

Table 11. Recurrence Stricture by Study Design

Study or Subgroup	Endoscopic Management			Urethroplasty		
	Events	Total	%	Events	Total	%
Comparative NRS						
1 study (179 patients)	92	124	74%	30	55	55%
Noncomparative NRS						
31 studies (4410 patients)	306	623	49%	603	3785	16%
TOTAL	398	747	53%	633	3840	16%

Table 12. Study-specific Recurrence Stricture by Prior Baseline Characteristics

Study or Subgroup	Endoscopic Management†			Urethroplasty†		
	Events	Total	%	Events	Total	%
Prior Endoscopy (DVIU and/or dilation)						
Chapman 2017	-	-	-	36	525	6.9%
Kahokehr 2018	-	-	-	24	373	6.4%
Rigatti 1993	-	-	-	9	62	15%
Barbagli 2014	-	-	-	40	171	23%
Barbagli 2001	-	-	-	6	47	13%
Barbagli 2008	-	-	-	9	14	64%
Elgammal 2009	-	-	-	1	22	4.6%
Figler 2013	-	-	-	12	71	17%
Farrell 2017	6	27	22%	-	-	-
Kizilay 2017	87	185	47%	-	-	-
Kluth 2017	12	43	28%	-	-	-
Mandhani 2005	15	28	54%	-	-	-
Pal 2017	54	68	79%	-	-	-
Rosenbaum 2015*	18	35	51%	-	-	-
Subtotal	192	386	50%	137	1285	11%
Prior Urethroplasty						
Chapman 2017	-	-	-	7	64	11%
Levine 2014	-	-	-	4	49	8.2%
Rosenbaum 2016	-	-	-	9	50	18%
Siegel 2015	-	-	-	2	37	5.4%
Vetterlein 2018	-	-	-	18	98	18%
Barbagli 2014	-	-	-	3	17	18%
Figler 2013	-	-	-	2	14	14%
Ekerhult 2017	92	124	74%	30	55	55%
Farrell 2017	5	17	29%	-	-	-
Park 2004	0	4	0%	-	-	-
Rosenbaum 2015	21	43	49%	-	-	-
Sukumar 2018	31	53	58%	-	-	-
Subtotal	149	241	62%	75	384	20%
TOTAL	341	627	54%	212	1669	13%

*All patients had prior endoscopy and urethroplasty. †Patients may have had multiple previous procedures (prior endoscopy alone or in combination with prior urethroplasty). Cordon 2014, Ekerhult 2015, Fossati 2016, Heyns 1998, Ketabchi 2017, Mellon 2014, Rosenbaum 2016, Viers 2018, Xu 2017, Welk 2012, Kluth 2013 did not provide subgroup data by prior procedure.

Table 13. Study-specific Complications by Type

Study or Subgroup	Endoscopic Management			Urethroplasty		
	Events	Total	%	Events	Total	%
Erectile Dysfunction						
Levine 2014	-	-	-	9	49	19%
Mellon 2014	-	-	-	1	107	0.9%
Rosenbaum 2016	-	-	-	24	50	48%
Subtotal	-	-	-	34	206	17%
UTI						
Levine 2014	-	-	-	5	49	10%
Rigatti 1993	-	-	-	5	62	8.1%
Ketabchi 2017	8	87	9.0%	-	-	-
Rosenbaum 2015	10	43	23%	-	-	-
Subtotal	18	130	14%	10	111	9.0%
Urinary Incontinence						
Levine 2014	-	-	-	0	49	0%
Rosenbaum 2016	-	-	-	14	50	28%
Figler 2013	-	-	-	3	103	2.9%
Rosenbaum 2015	6	43	14%	-	-	-
Subtotal	6	43	14%	17	202	8.4%
Bleeding						
Xu 2017	-	-	-	0	81	0%
Ketabchi 2017	6	87	6.9%	-	-	-
Subtotal	6	87	6.9%	0	81	0%
Extravasation						
Ketabchi 2017	10	87	11%	-	-	-
Subtotal	10	87	11%	-	-	-
Fistula complications						
Mellon 2014	-	-	-	2	107	1.9%
Ekerhult 2015	-	-	-	10	109	9.2%
Ekerhult 2017	-	-	-	7	11	64%
Subtotal	-	-	-	19	227	8.4%
Diverticulum						

Study or Subgroup	Endoscopic Management			Urethroplasty		
	Events	Total	%	Events	Total	%
Mellon 2014	-	-	-	1	107	0.9%
Figler 2013	-	-	-	4	103	3.8%
Subtotal	-	-	-	5	210	2.4%
Other						
Levine 2014 (a)	-	-	-	5	49	10%
Levine 2014 (b)	-	-	-	7	49	14%
Welk 2012 (b)	-	-	-	1	44	3.8%
Levine 2014 (c)	-	-	-	6	49	12%
Levine 2014 (d)	-	-	-	7	49	14%
Mellon 2014 (e)	-	-	-	4	107	3.7%
Xu 2017 (e)	-	-	-	5	81	6.2%
Mellon 2014 (f)	-	-	-	0	107	0%
Rigatti 1993 (g)	-	-	-	3	62	4.8%
Rigatti 1993 (h)	-	-	-	4	62	6.5%
Rosenbaum 2016 (i)	-	-	-	13	50	26%
Farrell 2017 (j)	0	44	0%	-	-	-
Ketabchi 2017 (k)	8	87	9.0%	-	-	-
TOTAL COMPLICATIONS	47	174	27%	133	507	26%

Footnotes:

- (a) Scrotal pain
- (b) Chordee
- (c) Post-void dribble
- (d) LUTS (lower urinary tract system)
- (e) Meatal stenosis
- (f) Mortality
- (g) Pouches of skin
- (h) Stones
- (i) No improvement in quality of life
- (j) Long term complications
- (k) Dysuria

RECOMMENDATION 3- GRADE Evidence to Decision Framework

QUESTION

Should urethroplasty vs. endoscopic treatment (either dilation or DVIU) be used for men with recurrent urethral stricture?	
POPULATION:	Men with recurrent urethral stricture
INTERVENTION:	Urethroplasty
COMPARISON:	Endoscopic treatment (either dilation or DVIU)
MAIN OUTCOMES:	Recurrence stricture and risk of complications
BACKGROUND:	In men with previous endoscopic management, the use of repeat endoscopic management for treating urethral stricture may increase stricture complexity with high failure rates of >80%. Current guidelines therefore have recommended urethroplasty instead of repeated endoscopic management for recurrence anterior urethral stricture following failed endoscopic management (AUA recommendation; Moderate Recommendation; Evidence Strength Grade C). The American Urological Association (AUA) also recommends the use of urethroplasty for patients with recurrent meatal or fossa navicular of strictures (Moderate Recommendation; Evidence Strength Grade C). In patients who are unable to undergo, or who prefer to avoid, urethroplasty, repeated endoscopic procedures are considered palliative measures.

ASSESSMENT

Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know 	We did not identify any randomized controlled trials (RCTs) comparing urethroplasty vs endoscopic treatment (either dilation or DVIU) for men with recurrent urethral stricture. We found 1 comparative study (Ekerhult 2017); and 31 noncomparative studies (30 case series and one combined analysis of trial groups). 21 noncomparative studies assessed urethroplasty (Levine 2014, Mellon 2014, Rosenbaum 2016, Siegel 2015, Vetterlein 2018, Rigatti 1993, Viers 2018, Xu 2017, Chapman 2017, Cordon 2014, Ekerhult 2015, Fossati 2016, Fuchs 2018, Kahokehr 2018, Barbagli 2014, Welk 2012, Barbagli 2001, Barbagli 2008, Elgammal 2009, Figler 2013, Kluth 2013) and 10 noncomparative studies assessed endoscopic	The panel noted that it is reasonable to expect a higher rate of recurrence stricture with endoscopic treatment when compared with urethroplasty in patients with recurrent urethral stricture.

treatment (Farrell 2017, Ketabchi 2017, Kluth 2017, Pal 2017, Rosenbaum 2015, Sukumar 2018, Kizilay 2017, Mandhani 2005, Heyns 1998, Park 2004).

The benefits of urethroplasty may be moderately greater than endoscopic management with 16% recurrence versus 53%, respectively. For studies that reported details of previous treatment, repeat endoscopic treatment may increase stricture complexity and, hence, recurrence (50% versus 11%) in patients who had prior endoscopy when compared with urethroplasty; but the evidence is very uncertain owing to high risk of bias, imprecision, and indirectness. Data for subgroup by stricture site were not available.

A summary of the findings from these studies is provided below:

Table 9:

No of participants (studies) Follow-up	Overall certainty of evidence	With endoscopic treatment (either dilation or DVIU)	With urethroplasty
Stricture (comparative NRS)			
179 (1 observational study)(44)	⊕○○○ VERY LOW ^{a,b}	74 per 100	19 fewer per 100 (from 32 fewer to 3 fewer)
Stricture (noncomparative NRS)			
4408 (31 observational studies) (20, 24, 33, 45-72)	⊕○○○ VERY LOW ^{c,d,e,f,g}	306/623 (49.1%)	603/3785 (15.9%)
Complications (counts)			
681 (11 observational studies) (44, 47, 49-51, 53, 60, 62, 63, 66, 70)	⊕○○○ VERY LOW ^{c,d,e,g}	47/174 (27.0%)	133/507 (26.0%)

Summary of Recurrence stricture by prior baseline characteristics (see full Table 12)

It is important to consider location of stricture and type of previous procedure when planning patient care as the panel considers the possibility that the effect of interventions could differ according to stricture site and previous procedure type.

	<table><tr><th rowspan="2">Study or Subgroup</th><th colspan="3">Endoscopic Management*</th><th colspan="3">Urethroplasty*</th></tr><tr><th>Events</th><th>Total</th><th>%</th><th>Events</th><th>Total</th><th>%</th></tr><tr><td colspan="7">Prior endoscopy (DVIU and/or dilation)</td></tr><tr><td>14 studies (1671 patients)</td><td>192</td><td>386</td><td>50%</td><td>137</td><td>1285</td><td>11%</td></tr><tr><td colspan="7">Prior Urethroplasty</td></tr><tr><td>12 studies (625 patients)</td><td>149</td><td>241</td><td>62%</td><td>75</td><td>384</td><td>20%</td></tr><tr><td colspan="7">*patients may have had multiple previous procedures (multiple previous endoscopies with or without prior urethroplasty)</td></tr></table>	Study or Subgroup	Endoscopic Management*			Urethroplasty*			Events	Total	%	Events	Total	%	Prior endoscopy (DVIU and/or dilation)							14 studies (1671 patients)	192	386	50%	137	1285	11%	Prior Urethroplasty							12 studies (625 patients)	149	241	62%	75	384	20%	*patients may have had multiple previous procedures (multiple previous endoscopies with or without prior urethroplasty)							
Study or Subgroup	Endoscopic Management*			Urethroplasty*																																														
	Events	Total	%	Events	Total	%																																												
Prior endoscopy (DVIU and/or dilation)																																																		
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*patients may have had multiple previous procedures (multiple previous endoscopies with or without prior urethroplasty)																																																		
Undesirable Effects How substantial are the undesirable anticipated effects?																																																		
JUDGEMENT	RESEARCH EVIDENCE		ADDITIONAL CONSIDERATIONS																																															
<ul style="list-style-type: none">○ Large○ Moderate○ Small● Trivial○ Varies○ Don't know	<p>Overall, there may be a slight reduction in complications (1% fewer) with urethroplasty than with endoscopic treatment. A total of 133 complications (26%) in 507 patients in the urethroplasty group and 47 complications (27%) occurred in 174 patients with endoscopic management group. Fistula and diverticulum occurred in 8.4% and 2.4% of patients treated with urethroplasty, respectively. Incontinence was higher with endoscopic than with urethroplasty (14% versus 8.4%, respectively). The evidence was very low certainty due to double counting (patients counted twice or more for complications), small number of patients, and selective outcome reporting.</p> <p>Summary of Table 13: Complications after treatment in patients with recurrent urethral stricture</p>		<p>The panel noted that it is important to consider fistula, diverticulum, and other complications that require re-operation and cause permanent disability.</p>																																															

Outcome No of studies (participants)	Endoscopic Management			Urethroplasty		
	Events	Total	%	Events	Total	%
Erectile Dysfunction						
3 studies (206 patients)	-	-	-	34	206	17%
UTI						
4 studies (241 patients)	18	130	14%	10	111	9.0%
Urinary Incontinence						
4 studies (245 patients)	6	43	14%	17	202	8.4%
Bleeding						
2 studies (168 patients)	6	87	6.9%	0	81	0%
Extravasation						
1 study (87 patients)	10	87	11%	-	-	-
Fistula Complications						
3 studies (227 patients)	-	-	-	19	227	8.4%
Diverticulum						
2 studies (210 patients)	-	-	-	5	210	2.4%
Certainty of evidence What is the overall certainty of the evidence of effects?						
JUDGEMENT	RESEARCH EVIDENCE					ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ● Very low ○ Low ○ Moderate ○ High ○ No included studies 	Certainty of the evidence of effects was judged as 'very low'. All studies are observational by nature (high risk of bias). 30 studies were case series (high risk of bias), one study randomized patients to different endoscopic treatments but not with urethroplasty (a combined analysis of trial groups, high risk of bias), and one comparative nonrandomized study with unadjusted analysis (high risk of bias).					

Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability 	A longitudinal study (Betrand 2016) showed that cystoscopic recurrence was a strong predictor of dissatisfaction after urethroplasty followed by postoperative sexual function, postoperative pain, and postoperative voiding complaints; whereas, stricture length, absence of postvoid dribble, postoperative penile shortening, absence of chordee, and improved perceived overall health may influence postoperative patient satisfaction (Maciejewski 2017).	The panel agreed that the risk of chordee may increase with presence of post void dribble and long-term stricture complications, which further decreases postoperative patient satisfaction.
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention 	Probably favours urethroplasty	

or the comparison ● Probably favors the intervention ● Favors the intervention ○ Varies ○ Don't know		
Resources required How large are the resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	<p>Retrospective analysis of 2298 male urethroplasties from the 2001-2010 Healthcare Cost and Utilization Project – Nationwide Inpatient Sample showed median charges of USD \$19,866 (IQR, \$14,346–\$29,382) with calculated costs of \$7,321 (\$5,677–\$10,000). The mean annual cost of urethroplasty did not change significantly over time with a median increase of USD \$616 per year (Harris 2016).</p> <p>Patients age 45-65 years incurred more cost of urethroplasty than patients age 18-45 years. In addition to older age, other factors associated with increased cost include higher hospital volume, rural hospital setting, use of graft, multiple comorbid conditions, patients with obesity or renal failure, increased length of hospital stay, and inpatient/postoperative complications (Harris 2016).</p>	<p>The panel acknowledged the importance of societal perspective for making optimal societal decisions. Costs are mainly driven by operating time, postoperative stay, and long-term complications. Additionally, age, patient important outcomes, and number of treatment failures should be considered when choosing DVIUs vs urethroplasty as a treatment (e.g., which age group should receive urethroplasty? which intervention should be given first to avoid and reduce costs for repeat procedures?)</p>

		<p>Urethroplasty is often given after two failed DVIUs. In this case, it is probably cheaper to choose urethroplasty as a first-line treatment over multiple DVIUs.</p> <p>The panel noted that cost is relatively small compared to other procedures for other conditions</p>
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Very low ● Low ○ Moderate ○ High ○ No included studies 	Data for cost were based on a large inpatient data from the 2001-2010 Healthcare Cost and Utilization Project – Nationwide Inpatient Sample (Harris 2016).	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Reduced ○ Probably 	No research evidence found. (see feasibility for possible barriers to access)	

reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know		
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	Patients: A longitudinal study showed that among 433 adult men with urethral strictures who underwent urethroplasty, 83% who responded would repeat the operation. Of those who had previous DVIU, 66% and 65% reported being satisfied and unsatisfied, respectively (Betrand 2016). In a low resource setting, dorsal and ventral onlay graft urethroplasties were fairly easy to perform with high patient satisfaction and minimal number of complaints (Kaggwa 2014, Pahwa 2013). Surgeons: US data from 2007-2011 involving 2,700 patients underwent repeat endoscopic management and 1,444 underwent urethroplasty showed that compared to patients treated with repeat endoscopic management, those treated with urethroplasty were younger (median age 44 vs 54 years), less likely to have comorbidity, more likely to have travelled out of the metropolitan area for care (34% vs 17%) and more likely to have a reconstructive urologist in the metropolitan area where care was provided (76% vs 62%) (Figler 2015). Although urethroplasty was underused, there was an increase in utilization of urethroplasty from 1999 to 2013 among the Veterans Affairs population (Lacy 2014). US national data from 1998 to 2011 also showed that in 240,108 urethral procedures, 91% underwent urethral incision/dilation; there was a declining rate of urethral incision and dilation (10.74/1,000 per year); and urethral reconstruction showed a gradual increase with time (1.654/1,000 per	Both interventions are acceptable to patients, but the panel believed that acceptability varies by number of repeat procedures, recurrences, quality of life, co-morbidities, but not age. Some patients may not accept multiple repeat procedures. Most men who have multiple recurrences may prefer urethroplasty, however, preferences may be variable. Most men who have poor quality of life due to recurrent stricture will likely choose urethroplasty. Men who are frail with multiple co-morbidities, who want to avoid an in-hospital operative procedure, scheduling, timing or hospital

	year). Urethral reconstruction was favored in younger patients, and at larger hospitals and teaching hospitals (Buckley 2016).	stay, may choose DVIU or dilation for a recurrent stricture. Furthermore, repeat endoscopic treatment may be appropriate for poor urethroplasty candidates (comorbidities, patient preference, etc) or select short (<2 cm) bulbar strictures with “durable” prior response
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know 	<p>A survey of 88 practicing urologists in the Mid-Atlantic region of the American Urological Association (AUA) showed that 68% who reported had no barriers to referring patients for urethroplasty. Those who reported believed that formal training in urethroplasty influences urologists’ decision to recommend urethroplasty. Another common provider-level barrier to urethroplasty included long distance to urethroplasty surgeon (15%), followed by concern about postoperative complications (9%), lack of reconstructive urologist in the insurance network (5%), not knowing a reconstructive urologist (2%), and concern about losing patients (1%) (Consolo 2016).</p> <p>Better outcomes following urethroplasty are associated with greater surgeon experience (Fall 2014, Helmy 2014, Faris 2016) though with a longer operative time with BMG substitution urethroplasty by dorsal urethrotomy approach when compared to ventral sagittal urethrotomy (142 vs 125 minutes) (Pahwa 2013). For those who received endoscopic management, operative time was longer for the conventional cold knife urethrotomy compared to Holmium laser DVIU (mean 23.83 ± 5.47 versus 16.42 ± 8.04 minutes) (Atak 2011).</p>	<p>Urethroplasty is less widely available than endoscopic management likely because urethroplasty requires additional training, which is a barrier to accessibility. The panel however believed urethroplasty should be offered, regardless of the barrier. Physicians with less experience can refer patients to surgeons who can perform urethroplasty.</p>

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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CONCLUSIONS

Recommendation

In the setting of men with recurrent urethral stricture failing prior endoscopic treatment, we suggest performing urethroplasty rather than repeat endoscopic management (DVIU or dilation) (*Conditional recommendation, very low certainty in evidence of effects*).

Remarks: Most men who have poor quality of life due to strictures which recur multiple times per year will likely choose urethroplasty. However, men who may want to avoid an in-hospital operative procedure, scheduling, timing and hospital stay may choose DVIU or dilation for a recurrent stricture. A shared decision-making model will help to understand patients' values and preferences.

Justification

The evidence of effectiveness of urethroplasty compared to endoscopic management for recurrence stricture was of very low certainty. Data from 32 studies (1 comparative study and 31 noncomparative studies) involving 3840 men with urethroplasty and 747 with endoscopic management were identified. Of 31 noncomparative studies, 21 studies assessed urethroplasty and 10 assessed endoscopic treatment. The findings indicate that men with recurrent stricture may experience more recurrence and complications following endoscopic management when compared to urethroplasty. Recurrence was particularly high in those who received repeat endoscopic treatment. Costs are mainly driven by operating time, postoperative stay, and long-term complications. There may be cost savings with urethroplasty due to fewer recurrences, but greater costs due to increased training, operating time and post-operative stay. Urethroplasty is also less available than endoscopic management. Repeat endoscopic management procedures may be less acceptable to men with multiple recurrences, however more acceptable to men who want to avoid in-hospital procedures, scheduling, timing or hospital stay.

6. All References to included studies

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7. References Excluded from AUA Guideline

Excluded References	Reason for Exclusion
RECOMMENDATION 1 (n=14)	
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3. Choudhary S, Singh P, Sundar E, Kumar S, Sahai A. A comparison of sonourethrography and retrograde urethrography in evaluation of anterior urethral strictures. Clin Radiol. 2004 Aug 1;59(8):736-42.	Non comparative
4. Das S. Ultrasonographic evaluation of urethra stricture disease. Urology 1992;40(3): 237.	Non comparative
5. de Kort LM, Uiterwaal CS, Beek EJ, et al. Reliability of voiding cystourethrography to detect urethral obstruction in boys. Urology 2004;63: 967–71.	Non comparative
6. Gong EM, Arellano CMR, Chow JS, Lee RS. Sonourethrogram to manage adolescent anterior urethral stricture. J Urol. 2010 Oct;184(4):1699-702	Non comparative
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11. Peskar DB, Perovic AV. Comparison of radiographic and sonographic urethrography for assessing urethral strictures. Eur Radiol. 2004 Jan;14(1):137-44.	Non comparative
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14. Yekeler E, Suleyman E, Tunaci A, Tunaci M, Balci NC, Onem K, Tunc M, Acunas G. Contrast-enhanced 3D MR voiding	Non comparative

urethrography: preliminary results. Magn Reson Imaging. 2004 Nov;22(9):1193-9.	
RECOMMENDATION 2 (n=34)	
1. Aldaqadosi H, El Gamal S, ElNadey M, El Gamal O, Radwan M, Gaber M. Dorsal onlay (Barbagli technique) versus dorsal inlay (Asopa technique) buccal mucosal graft urethroplasty for anterior urethral stricture: a prospective randomized study. Int J Urol. 2014 Feb;21(2):185-8.	Pg. 186: "Of the 47 patients, 34 (72.3%) had a total of 78 internal urethrotomy procedures (average 1.7 per patient)."
2. Andrich DE, Leach CJ, Mundy AR. The Barbagli procedure gives the best results for patch urethroplasty of the bulbar urethra. BJU Int. 2001;88(4):385-9.	No evidence to suggest prior procedures were done, but also not explicitly stated that patients had initial stricture
3. Barbagli G, Palminteri E, Guazzoni G, Montorsi F, Turini D, Lazzeri M. Bulbar urethroplasty using buccal mucosa grafts placed on the ventral, dorsal or lateral surface of the urethra: Are results affected by the surgical technique? J Urol. 2005 Sep;174(3):955-7.	A total of 47 patients (94%) had undergone previous urethrotomy or dilation.
4. Barbagli G, Kulkarni SB, Fossati N, Larcher A, Sansalone S, Guazzoni G, Romano G, Pankaj JM, DellAcqua V, Lazzeri M. Long-term followup and deterioration rate of anterior substitution urethroplasty. J Urol. 2014 Sep;192(3):808-13.	$(20+151+17)/359 = 188/359=52\%$ with prior dilation, urethrotomy, urethroplasty
5. Brede C, Angermeier K, Wood H. Continence outcomes after treatment of recalcitrant postprostatectomy bladder neck contracture and review of the literature. Urology. 2014;83(3):648-52.	At least $21/63=33.3\%$ have already undergone dilation at baseline
6. Chen ML, Odom BD, Johnson LJ, Santucci RA. Combining ventral buccal mucosal graft onlay and dorsal full thickness skin graft inlay decreases failure rates in long bulbar strictures (≥ 6 cm). Urology. 2013 Apr;81(4):899-902.	Authors do not explicitly state that included patients had first instance of stricture; no information on previous procedures. EXCLUDE since population not clear.
7. Figler BD, Malaeb BS, Dy GW, Voelzke BB, Wessells H. Impact of graft position on failure of single-stage bulbar urethroplasties with buccal mucosa graft. Urology. 2013 Nov;82(5):1166-70.	Not initial stricture
8. Giannakopoulos X, Grammeniatis E, Gartzios A, Tsoumanis P, Kammenos A. Sachse urethrotomy versus endoscopic urethrotomy plus transurethral resection of the fibrous callus (Guillemin's technique) in the treatment of urethral stricture. Urology. 1997 Feb;49(2):243-7.	All 80 patients with urethral stricture and a history of prior surgery in the lower urinary tract: open transvesical prostatectomy (28 cases), TUR of the prostate (32 cases), and a history of bladder catheterization (20 cases).
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preservation: efficacy and impact on urinary continence status. European Urology. 2008;54(3):647-56.	prostatectomy with bladder neck preservation
10. Goel A, Goel A, Jain A. Buccal mucosal graft urethroplasty for penile stricture: Only dorsal or combined dorsal and ventral graft placement? Urology. 2011 Jun;77(6):1482-6.	Pg. 1483: "history of previous interventions" was recorded, so likely not initial stricture.
11. Hafez AT, ElAssmy A, Dawaba MS, Sarhan O, Bazeed M. Long-term outcome of visual internal urethrotomy for the management of pediatric urethral strictures. J Urol. 2005 Feb;173(2):595-7.	35.5% underwent previous urethroplasty
12. Heyns CF, Steenkamp JW, De Kock ML, Whitaker P. Treatment of male urethral strictures: Is repeated dilation or internal urethrotomy useful? J Urol. 1998 Aug;160(2):356-8.	All patients with recurrent stricture, so EXCLUDE
13. Hosseini J, Kaviani A, Hosseini M, Mazloomfard MM, Razi A. Dorsal versus ventral oral mucosal graft urethroplasty. Urol J. 2011;8(1):48-53. PMID: 21404203	Authors excluded patients with previously failed urethroplasty; no info to suggest patients received previous procedures but also not explicitly stated that patients had initial diagnosis so EXCLUDE
14. Kaggwa S, Galukande M, Dabanja H, Luweesi H. Outcomes of dorsal and ventral buccal graft urethroplasty at a tertiary hospital in Uganda. ISRN Urology 2014; 316819.	Not explicitly stated that patients had initial diagnosis, but no information to suggest otherwise. EXCLUDE
15. Kostakopoulos et al. 2004¹⁵³	Cannot Locate Full-Text
16. Kumar S, Kapoor A, Ganesamoni R, Nanjappa B, Sharma V, Mete UK. Efficacy of holmium laser urethrotomy in combination with intralesional triamcinolone in the treatment of anterior urethral stricture. Korean J Urol. 2012 Sep;53(9):614-8.	primary or secondary stricture [17+11]/50 = 56%
17. Launonen E, Sairanen J, Ruutu M, Taskinen S. Role of visual internal urethrotomy in pediatric urethral strictures. J Pediatr Urol. 2014;10(3):545-9.	100% pediatric urethral stricture
18. Levine LA, Strom KH, Lux MM. Buccal mucosa graft urethroplasty for anterior urethral stricture repair: evaluation of the impact of stricture location and lichen sclerosus on surgical outcome. J Urol. 2007 Nov;178(5):2011-5.	Not initial stricture
19. Magera et al. 2009¹⁵¹ -	Title is : Outcome Analysis of Urethral Wall Stent Insertion With Artificial Urinary Sphincter Placement for Severe Recurrent Bladder Neck Contracture Following Radical Prostatectomy; 7/25

	had prior failed endoscopic treatments
20. Mathur RK, Sharma A. Tunica albuginea urethroplasty for panurethral strictures. Urol J. 2010 Spring;7(2):120-4.	87% (75/86) patients had some form of intervention (urethrotomy, dilation, or urethroplasty) before referring to “us” (the author’s clinic)
21. Meeks et al. 2011⁸⁷	- 54% people with previous (?) dilation; 11 with urethrotomy
22. Morey AF, Lin HC, DeRosa CA, Griffith BC. Fossa navicularis reconstruction: impact of stricture length on outcomes and assessment of extended meatotomy (first stage Johanson) maneuver. J Urol. 2007 Jan;177(1):184-7.	Cannot Locate Full-Text
23. Nikolavsky D, Blakely SA, Hadley DA, Knoll P, Windsperger AP, Terlecki RP, Flynn BJ. Open reconstruction of recurrent vesicourethral anastomotic stricture after radical prostatectomy. Int Urol Nephrol. 2014 Oct 25;46(11):2147-52.	Pg 2148: “The mean number of transurethral procedures (dilation/urethrotomy) prior to VUAR was 4.5.” Prior procedures, so EXCLUDE.
24. Pahwa M, Gupta S, Pahwa M, Jain BD, Gupta M. A comparative study of dorsal buccal mucosa graft substitution urethroplasty by dorsal urethrotomy approach versus ventral sagittal urethrotomy approach. Adv Urol. 2013;2013:124836.	Patients with previously failed urethroplasty were excluded; no evidence presented to suggest patients had any other procedures, but also not explicitly stated that patients had first diagnosis of stricture so EXCLUDE
25. Pfalzgraf D, Beuke M, Isbarn H, Reiss CP, Meyer-Moldenhauer WH, Dahlem R, Fisch M. Open retropubic reanastomosis for highly recurrent and complex bladder neck stenosis. J Urol. 2011 Nov;186(5):1944-7.	Title is Open Retropubic Reanastomosis for Highly Recurrent and Complex Bladder Neck Stenosis
26. Ramchandani P, Banner MP, Berlin JW, Dannenbaum MS, Wein AJ. Vesicourethral anastomotic strictures after radical prostatectomy: Efficacy of transurethral balloon dilation. Radiology. 1994 Nov;193(2):345-9.	Not clear whether patients had initial stricture so EXCLUDE
27. Steenkamp JW, Heyns CF, De Kock ML. Internal urethrotomy versus dilation as treatment for male urethral strictures: A prospective, randomized comparison. J Urol. 1997 Jan;157(1):98-101.	No. with previous stricture treatment: Dilation: 31/104 DVIU: 37/106 Total: 68/210 =32% EXCLUDE

28. Stormont TJ, Suman VJ, Oesterling JE. Newly diagnosed bulbar urethral strictures: Etiology and outcome of various treatments. J Urol. 1993;150(5):1725-8.	Cannot Locate Full-Text
29. Surya BV, Provet J, Johanson KE, Brown J. Anastomotic strictures following radical prostatectomy: risk factors and management. J Urol. 1990 Apr;143(4):755-8.	Cannot Locate Full-Text
30. Tunc et al. 2002¹³⁹	Not initial stricture (had previous DVIU)
31. Vicente J, Salvador J, Caffaratti J. Endoscopic urethrotomy versus urethrotomy plus Nd-YAG laser in the treatment of urethral stricture. Eur Urol. 1990;18(3):166-8.	prior urethrotomy
32. Wang et al. 2009²³⁶	Systematic review
33. Yesil et al. 2013¹³⁸	Cannot Locate Full-Text
34. Zehri AA, Ather MH, Afshan Q. Predictors of recurrence of urethral stricture disease following optical urethrotomy. Int J Surg. 2009;7(4):361-4.	Pg 362: "Correlation of previous treatments with recurrence rate indicated that; optical urethrotomy (p . 0.000), dilatation (p . 0.000) and self intermittent catheterization (p. 0.001) found to have significantly higher recurrence rate." So looks like they included patients with previous treatments, so EXCLUDE.
RECOMMENDATION 3 (n=3)	
1. Terlecki RP, Steele MC, Valadez C, Morey AF. Grafts are unnecessary for proximal bulbar reconstruction. J Urol. 2010;184(6):2395-9.	Unclear population
2. Tinaut-Ranera J, Arrabal-Polo MA, Merino-Salas S, Nogueras-Ocana M, Lopez-Leon VM, Palao-Yago F, et al. Outcome of urethral strictures treated by endoscopic urethrotomy and urethroplasty. Canadian Urological Association Journal. 2014;8(1-2):E16-9.	No outcome data