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To Transect or Not Transect: Results from the Scandinavian Urethroplasty Study, A Multicentre Randomised Study of Bulbar Urethroplasty Comparing Excision and Primary Anastomosis Versus Buccal Mucosal Grafting

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Abstract

Background: Open surgical treatment of short bulbar urethral strictures (urethroplasty) is commonly performed as transecting excision and primary anastomosis (tEPA) or buccal mucosa grafting (BMG). Erectile dysfunction and penile complications have been reported, but there is an absence of randomised trials.

Objective: To evaluate sexual dysfunction and penile complications after urethroplasty with tEPA versus BMG.

Design, setting, and participants: Centres in Finland, Sweden and Norway participated. Patients with a bulbar urethral stricture of ≤ 2 cm without previous urethroplasty were randomised. The primary endpoints were the degree of erectile dysfunction and penile complications. Follow-up was 12 mo.

Intervention: Patients were randomised to either tEPA or BMG urethroplasty.

Outcome measurements and statistical analysis: Sexual dysfunction was measured using the International Index of Erectile Function, 5-item version (IIEF-5) and a penile complications questionnaire (PCQ) designed for this study. Continuous data were analysed using analysis of covariance and categorical data were compared using a χ^2 test.

Results and limitations: A total of 151 patients were randomised to either tEPA ($n = 75$) or BMG ($n = 76$). The tEPA group reported more penile complications ($p = 0.02$),

This randomised study compared sexual dysfunction after urethroplasty with transecting excision and primary anastomosis or buccal mucosa grafting. No significant difference in erectile function was observed. More penile complications (reduced glans filling and penile shortening) were reported after the transecting technique.

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especially reduced glans filling ($p = 0.03$) and a shortened penis ($p = 0.001$). There were no differences in postoperative IIEF-5 total scores. Recurrence rates were similar in both groups (12.9%) but the study was not designed to detect differences in recurrence rates. The PCQ is not validated, which is a limitation.

Conclusions: More patients reported penile complications after urethroplasty with tEPA than with BMG. This should be considered when choosing the operative method, and patients should be informed accordingly.

Patient summary: This study compared two common operations for repair of narrowing of the male urethra. Neither of the two methods seems to cause worsened erections. However, penile problems are more common after the transection technique than after the grafting technique.

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1. Introduction

Open surgical treatment of short bulbar urethral strictures (urethroplasty) is commonly performed via either excision and primary anastomosis (EPA) or augmentation using a buccal mucosa graft (BMG) [1]. In transecting EPA (tEPA), the strictured urethra and surrounding corpus spongiosum are resected and the healthy ends are reanastomosed. In BMG urethroplasty, the urethra is incised along the stricture, but not transected, and the urethra is augmented with a graft. Traditionally, tEPA has been regarded as the gold standard for shorter strictures owing to its high success rates, while BMG is mainly used for longer strictures [2–4]. A meta-analysis comparing tEPA and BMG showed less sexual dysfunction but more recurrence with BMG [5]. However, similar recurrence rates for BMG and tEPA have also been reported [6].

Sexual dysfunction after urethroplasty has recently gained more attention but is reported to varying degrees [7–9]. It has been shown that transection is associated with a higher incidence of considerable penile shortening and impairment of erection and sexual life compared to other common urethroplasty methods [10]. In a retrospective review of 153 tEPAs, patients reported a cold glans during erection (1.6%), a glans that was neither full nor swollen during erection (11.6%), and a decrease in glans sensitivity (18.3%) [11]. Augmentation without transection of the spongiosal arteries may be beneficial by preserving blood flow, causing less penile or sexual dysfunction. However, the clinical significance of this hypothesis has not been compared in randomised controlled trials (RCTs), only several prospective nonrandomised studies [9,12–15].

The aim of this study was to compare tEPA and BMG urethroplasty in terms of postoperative sexual dysfunction and penile complications.

2. Patients and methods

The trial was designed as a multicentre randomised study to show superiority of either method regarding erectile dysfunction or penile complications evaluated using the International Index of Erectile Function, 5-item version (IIEF-5) and a penile complications questionnaire (PCQ), with a null hypothesis of no difference between the groups. To adjudicate the superiority of either treatment method, we considered two

primary endpoints. The first was the odds ratio of reporting one or more complications on the PCQ between the treatment arms. The second was the difference in mean change in IIEF-5 score between the treatment arms. Secondary endpoints were stricture recurrence and the rate of complications.

Patients with a bulbar urethral stricture of ≤ 2 cm in length were eligible for inclusion. The inclusion and exclusion criteria are listed in Table 1. Participating centres were located in Finland (Helsinki), Sweden (Gothenburg and Örebro), and Norway (Oslo). The study schedule is shown in Figure 1.

Patients admitted to the urological department for bulbar urethroplasty who met the study criteria were randomised before surgery after giving written informed consent to inclusion. Randomisation to either tEPA or BMG was carried out using the allocation method in a web-based, password-protected database (Viedoc). Randomisation was 1:1 at each study site.

The study was registered on ClinicalTrials.gov (NCT02321670) and approved by the relevant ethics committees. No external funding was received.

2.1. Patient-reported outcome measures

The PCQ designed for this study was based on questionnaires used previously [10,11]. It contains five questions addressing ejaculation (Q1), glans filling (Q2), glans sensation (Q3), penile length (Q4), and penile direction (Q5) (Supplementary material). The PCQ was completed by patients at follow-up.

The IIEF is a widely used self-reported instrument for evaluation of male sexual function [16,17]. The five-item version of the 15-item IIEF is known as IIEF-5 or the Sexual Health Inventory for Men (SHIM) [18]. Validated translations to the local language of each participating centre were used preoperatively and at follow-up (Supplementary material).

2.2. Surgical technique

Before study initiation, the group agreed on the operative techniques. In the tEPA group, the criterion was transection of the corpus spongiosum and excision of the stricture. The ends were anastomosed in two layers. In the BMG group, the corpus spongiosum was incised along the length of the stricture, ventrally or dorsally, depending on the surgeon's preference, and a BMG was placed on the urethral defect.

All patients had an indwelling Foley catheter for 2–3 wk postoperatively with antibiotic treatment, antithrombotic prophylaxis, and physical limitations implemented at the discretion of each centre. The postoperative treatment was the same for the two groups at every centre.

Table 1 – Inclusion and exclusion criteria

Inclusion criteria	
Patient with a bulbar urethral stricture of ≤ 2 cm in length as estimated via urethrography or endoscopy	
Age 18–70 yr	
Patient is able and willing to sign informed consent	
Patient is able and willing to complete all study requirements	
Exclusion criteria	
Previous open urethroplasty	
Previous hypospadias surgery	
Previous surgery for congenital curvature or Peyronie's disease	
Previous pelvic irradiation therapy	
Known grave psychiatric disorder	
Haemophilia or any other clotting disorder that causes bleeding diathesis	
Use of medication to increase erectile function, such as phosphodiesterase type 5 inhibitors and intracavernous injections, during the study	
Any condition or situation that, in the investigator's opinion, puts the patient at significant risk, could confound the study results, or could interfere significantly with the patient's participation in the study	

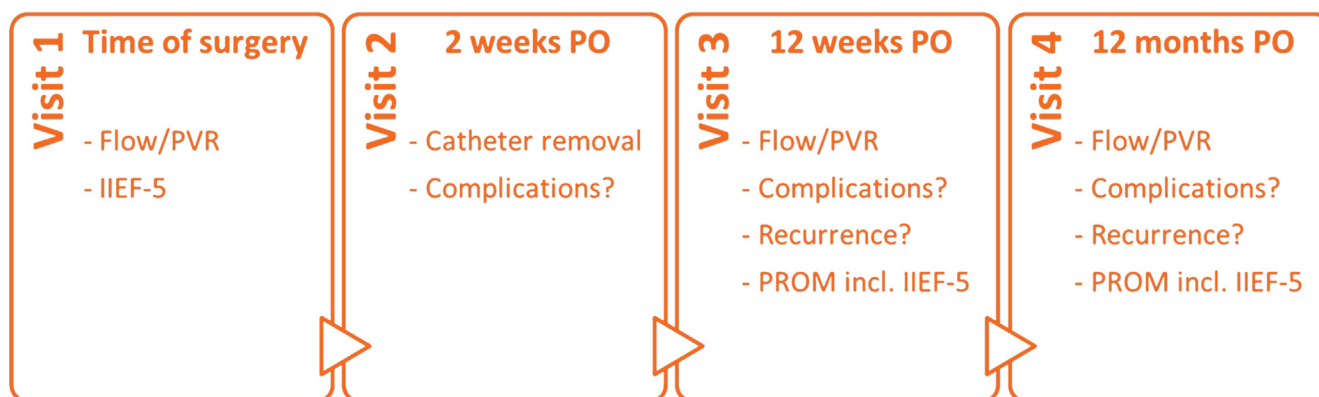


Fig. 1 – Study schedule. PVR = postvoid residual; PROM = patient-reported outcome measure; IIEF-5 = International Index of Erectile Function (5-item version); PO = postoperatively; incl. = including.

2.3. Statistical analysis

Estimates of the occurrence of penile complications were based on previous studies addressing penile complications [10,11]. Estimating that 30% of the tEPA group and 15% of the BMG group would experience one or more penile complications, the groups should each include 134 patients to achieve 80% statistical power at an α level of 0.05. Thus, the study aimed to include 300 patients.

Statistical analyses were carried out with SPSS v26 and $p < 0.05$ was considered statistically significant. Continuous data were analysed via linear regression with baseline measurements as covariates and the operative technique as a fixed factor (analysis of covariance). Risk differences between the treatment arms for categorical data are reported with the 95% confidence interval (CI) and tested using a Pearson χ^2 test. The p values reported are not corrected for multiple testing.

Table 2 – Number of patients included at each site

	tEPA	BMG	Total
Helsinki	16	16	32
Oslo	47	48	95
Gothenburg	8	8	16
Örebro	4	4	8
Total	75	76	151

tEPA = transecting excision and primary anastomosis; BMG = buccal mucosal graft.

3. Results

In total, 151 patients were enrolled between September 1, 2015, and December 31, 2019 (Table 2). A total of 75 patients were randomised to tEPA and 76 to BMG. The final follow-up visit was February 9, 2021. There were no differences in preoperative characteristics between the two groups (Table 3).

Three patients (2%) did not undergo surgery according to their randomisation assignment. Two patients randomised

Table 3 – Preoperative characteristics

Variable ^a	tEPA	BMG
Patients (n)	75	76
Median age, yr (IQR)	35 (29–44)	35 (25–48)
Median body mass index, kg/m ² (IQR)	26 (23–28)	25 (24–29)
Median stricture length, mm (IQR)	10 (7–15)	10 (8–15)
Median maximum flow, ml/s (IQR)	8 (6–10)	9 (6–12)
Median residual urine volume, ml (IQR)	67 (23–137)	90 (32–176)
Suprapubic tube, n (%)	12 (16)	10 (13)
Median IIEF-5 score, points (IQR)	25 (23–25)	25 (21–25)

tEPA = transecting excision and primary anastomosis; BMG = buccal mucosal graft; IQR = interquartile range.

^a There were no significant differences between the groups for any of the variables.

to tEPA underwent BMG because of unexpectedly long strictures, one of them with an augmented end-to-end anastomosis. One patient randomised to BMG underwent tEPA. Thus, tEPA was performed in 74 patients and BMG in 77 patients (59 ventral and 18 dorsal).

In total, 144 patients completed 12-mo follow-up; four were lost to follow-up and three left the study because of early recurrence of stricture. The results presented were analysed on an intention-to-treat basis, but as the number of patients not operated on according to protocol is very small, the changes when analysed according to the actual operating method are negligible.

3.1. Penile complications

Data from the PCQ were available for 139 patients at 3 mo and 144 patients at 12 mo. Table 4 summarises the PCQ results. The risk of reporting one or more of the complications in Q2–Q5 was greater in the tEPA group at both 3 mo and 12 mo. The question regarding ejaculation (Q1) was excluded from the analysis of one or more penile complications, as it was considered not to be a penile problem. The risk of reporting a complication was greater in the tEPA group for Q1 (ejaculation) and Q5 (penile direction) at 3 mo and for Q2 (glans filling) and Q4 (penile length) at both 3 mo and 12 mo. There was a difference in Q3 (glans sensation) between the two groups at either visit. Subgroup analyses showed no difference in penile complications between dorsal and ventral BMG.

3.2. Sexual dysfunction

IIEF-5 scores were available for 150 patients preoperatively, 137 patients at 3 mo, and 142 patients at 12 mo. The mean scores and differences in mean score between the treatment arms are reported in Table 5. There were no differences in total IIEF-5 score between the two groups at any visit.

3.3. Stricture recurrence

Data for stricture recurrence were available for 147 patients. Stricture recurrence was defined as a need for additional surgery. A total recurrence rate of 12.9% (19 patients) was observed, with nine patients (12.0%) in the tEPA group and ten (13.2%) in the BMG group (risk difference -0.01 , 95% CI -0.12 to 0.10 ; $p = 0.8$).

There were no differences in postoperative maximum flow or residual urine between the groups at any of the visits (Table 6).

3.4. Complications

Complication results are shown in Table 7. Postoperative bleeding was defined as a scrotal or perineal haematoma and was more frequent in the tEPA group ($p < 0.001$). The bleeding complications were classified as Clavien-Dindo grade I in all except three patients, all of whom were in the tEPA group (one grade II, one grade IIIa, and one grade IIIb).

There were no significant differences in the rates of urinary tract infection (all grade I–II) or of perineal wound infection. Wound infections were reported for three patients in the tEPA group after discharge or at catheter removal, classified as grade II ($n = 2$) and grade IIIa ($n = 1$).

No deep venous thrombosis or compartment syndromes were observed. One patient had a myocardial infarction 6 d after surgery that required coronary stenting (grade IVa). Abnormal pain, anaesthesia, or dysaesthesia in the perineum or lower extremities was reported by six patients during the early postoperative period, by ten patients at 3 mo, and by three patients at 12 mo, all classified as grade I–II.

Retrograde urethrography was performed in 136 patients at the first attempt of catheter removal at 2–3 wk after surgery. Leakage of contrast was observed in eight patients, with no difference between the groups. In these

Table 4 – Patients answering “Yes” on the penile complications questionnaire

	Patients, n (%)		RD (95% CI)	p value
	tEPA	BMG		
Q1. Has ejaculation become worse after your operation?				
3 mo	18 (26)	2 (2.8)	0.24 (0.12–0.35)	<0.001
12 mo	5 (7.1)	6 (8.1)	-0.01 (-0.10 to 0.08)	0.8
Q2. Do you experience less stiffness of the penis head during erection?				
3 mo	18 (26)	5 (7.0)	0.19 (0.07–0.31)	0.002
12 mo	13 (19)	5 (6.8)	0.12 (0.01–0.23)	0.03
Q3. Have you lost any feeling on the head of your penis after the operation?				
3 mo	11 (16)	8 (11)	0.05 (-0.07 to 0.16)	0.4
12 mo	9 (13)	9 (12)	0.007 (-0.101 to 0.115)	0.9
Q4. Has your erect penis become shorter after the operation?				
3 mo	11 (16)	1 (1.4)	0.15 (0.06–0.24)	0.002
12 mo	18 (26)	4 (5.4)	0.20 (0.09–0.32)	0.001
Q5. When erect, does your penis now point in a different direction?				
3 mo	7 (10)	0	0.10 (0.03–0.18)	0.005
12 mo	4 (5.7)	3 (4.1)	0.017 (-0.054 to 0.087)	0.6
Any Q2–Q5. One or more complication				
3 mo	26 (38)	10 (14)	0.24 (0.10–0.38)	0.001
12 mo	23 (33)	12 (16)	0.17 (0.03–0.30)	0.02

tEPA = transecting excision and primary anastomosis; BMG = buccal mucosal graft; RD = risk difference for tEPA – BMG; CI = confidence interval.

Table 5 – Total IIEF-5 scores at follow up

Time	Mean score		MD (95% CI)	p value ^a
	tEPA	BMG		
3 mo	21.1	22.3	1.2 (–0.01 to 2.4)	0.051
12 mo	21.8	23.0	1.2 (–0.4 to 2.7)	0.14

tEPA = transecting excision and primary anastomosis; BMG = buccal mucosal graft; MD = mean difference; CI = confidence interval.
^a There was no significant difference between the groups at either visit.

Table 6 – Maximum flow and residual volume at follow-up

Variable	Time	Mean value		MD (95% CI)	p value ^a
		tEPA	BMG		
Max flow (ml/s)	3 mo	29	29	0 (–5 to 4)	0.9
	12 mo	28	27	1 (–4 to 6)	0.8
Residual volume (ml)	3 mo	54	69	15 (–8 to 39)	0.2
	12 mo	64	81	17 (–10 to 44)	0.2

tEPA = transecting excision and primary anastomosis; BMG = buccal mucosal graft; MD = mean difference; CI = confidence interval.
^a There were no significant differences between the groups at either visit.

Table 7 – Complications

	Postoperatively		At catheter removal		At 3 mo		At 12 mo	
	n/N (%)	RD (95% CI)	n/N (%)	RD (95% CI)	n/N (%)	RD (95% CI)	n/N (%)	RD (95% CI)
Bleeding								
tEPA	18/75 (24)	0.20 (0.09–0.31) ^a	NA	NA	NA	NA	NA	NA
BMG	3/76 (3.9)		NA		NA		NA	
UTI								
tEPA	0/75	0.15 (–0.06 to 0.01)	1/75 (1.3)	–0.07 (–0.13 to 0.00)	2/71 (2.8)	–0.01 (–0.07 to 0.05)	1/71 (1.4)	–0.05 (–0.12 to 0.01)
BMG	2/76 (2.6)		6/76 (7.9)		3/74 (4.1)		5/75 (6.7)	
Wound infection								
tEPA	0/75	NA	3/75 (4.0)	0.04 (–0.004 to 0.084)	0/71	NA	0/71	NA
BMG	0/76		0/76		0/74		0/75	

tEPA = transecting excision and primary anastomosis; BMG = buccal mucosal graft; RD = risk difference for tEPA – BMG; CI = confidence interval; UTI = urinary tract infection; NA = not applicable.
^a Postoperative bleeding was more common in the tEPA group ($p < 0.001$).

patients, the catheter was kept in place for another 2 wk, and the catheter was removed without additional urethrography in six patients. Urethrography in the remaining two patients showed no leakage of contrast.

3.5. BMG donor site complications

No occlusion of Stensen's duct or donor site infection was observed. Bleeding from the donor site was reported for one patient (1.3%; grade I). Oral discomfort was graded as none, mild, moderate, or severe, and was reported by 26 patients (34%) during their hospital stay, 15 of mild and 11 of moderate grade. At catheter removal, four patients (5.2%) reported mild oral discomfort, and at 3- and 12-mo follow-up, three patients (3.9%) reported mild oral discomfort.

4. Discussion

Our study is the first randomised trial comparing two different bulbar urethroplasty techniques [12]. The results show that penile complications, especially reduced glans filling and penile shortening, are more common after tEPA than after BMG urethroplasty. The fact that differences were observed in glans filling, but not in sensation, supports the hypothesis that this is caused by reduced blood supply due to transection of the corpus spongiosum. These findings should be taken into account while counselling patients scheduled for bulbar urethroplasty.

Neither method showed superior results in erectile function as measured in terms of the IIEF-5 score.

According to our study, both methods showed similar results regarding stricture-free rates, and the rates did not differ from those in the literature [4,19,20].

Patient-reported outcome measures (PROMs) are important to acknowledge postoperative outcomes besides keeping the urethral lumen patent, including impact on symptoms, daily functioning, and health-related quality of life. When initiating our study, the USS-PROM questionnaire, designed for urethral stricture surgery, was available [21]. Other PROMs, such as the Brief Male Sexual Function Inventory and Coursey's questionnaire from 2001, have also been used [22,23]. However, these do not completely address sexual function and were therefore not chosen for this study.

The IIEF-5 questionnaire was originally developed to measure improvements in erection for sexually active men following sildenafil treatment and is not validated for urethral surgery. Premature ejaculation or the absence of a sexual partner may falsely lower the IIEF-5 score, and the questionnaire may not be optimal in this setting. It is, however, widely used and validated in all Scandinavian languages. There were no differences between the groups at each follow-up visit. The differences in penile complications did not result in differences in IIEF-5 scores.

The PCQ is not a validated questionnaire. However, as the randomisation of patients limits bias caused by any misinterpretation of the questionnaires, we interpret the differences between the groups as clinically relevant. The questions investigate impairment of penile function and do not reveal if the condition was stable or improved. If the urethra is obstructed, re-establishing a patent lumen may enhance the outflow of semen. On the contrary, division of the bulbospongiosus muscle may have an impact in the opposite direction.

Sexual dysfunction after urethroplasty may be more common than previously reported [19]. A review of sexual dysfunction in urethral reconstruction found that it is underappreciated [24]. In the report by Barbagli et al [11], 23% of the patients interviewed experienced ejaculatory dysfunction after tEPA, in line with our results (18%). Another analysis of ejaculation after anterior urethroplasty using the Male Sexual Health Questionnaire showed no change in ejaculation [25]. Although the authors reported that surgery had a minimal effect on ejaculatory function, four patients out of 28 had impaired ejaculation after surgery. Ejaculation improved in seven out of 28 patients, showing that an open lumen is also important for ejaculation.

In a retrospective cohort of 233 patients after a wide variety of urethral stricture surgical procedures, men were remotely asked about sexual life and penile complaints [10]. In this report, 30% of patients had marked or severe penile shortening after tEPA, 14% had penile curvature, 49% had deterioration of erectile function, and 43% had impaired sexual life. The results for penile shortening are in line with our findings.

In one prospective cohort, 97 patients undergoing BMG urethroplasty were evaluated using the IIEF-5 [26]. There was no change in IIEF-5 scores over longer follow-up after an initial slight drop at the first follow-up visit. A prospec-

tive nonrandomised study from 2017 showed no change in IIEF-5 for either transecting or nontransecting urethroplasty [27].

Preservation of sexual function after bulbar urethroplasty has received more attention in the last couple of decades. Preserving the proximal blood supply of the urethra has been proposed as a potential advantage, and nontransecting anastomotic techniques have gained in popularity after our study commenced. In 2007, Jordan et al [28] introduced vessel-sparing EPA. Further results were published by Andrich and Mundy in 2012 [29] and by Lumen et al in 2016 [30]. A review of the literature on the subject published between 2000 and 2018 concluded that nontransecting bulbar urethroplasty is favoured over transecting techniques, although without extensive evaluation of penile and erectile complications [31]. A retrospective study from 2019 compared transecting and nontransecting anastomotic urethroplasty and found less sexual dysfunction in the nontransecting group [32]. However, nontransecting techniques have a weak recommendation in the European guidelines [1]. The VeSpAR trial is an ongoing randomised study comparing nontransecting and transecting urethroplasty of short bulbar strictures, but does not include assessment of penile complications [33].

4.1. Strengths and limitations

The results must be considered in light of some strengths and limitations. The study was designed as an RCT comparing two common surgical methods for repair of short bulbar urethral strictures, the first of its kind. The multicentre design can be both a strength and a limitation.

The study included fewer patients than estimated to achieve necessary power to compare sexual dysfunction. This was because of a slower inclusion rate than planned as the Danish site did not join and the Swedish sites were not able to operate on as many patients as intended. After more than 4 yr, it was deemed not feasible to continue the study, as it would have taken 8–10 yr to reach the intended number. Inclusion was stopped without interim analysis. Data were not available for analysis until after the decision to stop inclusion.

A majority of the participants included were from one centre, and neither the patients nor the surgeons were blinded in the study since the use of oral grafts means that this is not feasible. This leaves the possibility for bias due to patient or surgeon preferences or surgeon experience. However, subgroup analysis comparing Oslo with the other centres did not show major differences in complication rates.

Lumen patency was not evaluated via endoscopy or urethrography at follow-up. The number of patients included may be too small and the follow-up too short to detect a difference in recurrence.

We used both validated and nonvalidated PROMs, the latter being a major limitation. The use of validated PROMs evaluating the impact of treatment on symptoms, daily function, or health-related quality of life with an emphasis on sexual problems is warranted in future studies. At present, application of several questionnaires is needed to obtain data for the whole spectrum of effects [34,35].

5. Conclusions

More penile complications were reported after urethroplasty with tEPA than after BMG, especially reduced glans filling and penile shortening. When performing urethral surgery, transection of the corpus spongiosum should be avoided if possible, and patients should be informed accordingly.

The differences in penile complications are not reflected in a clinically significant reduction in IIEF-5 scores, and this questionnaire may not be suitable for evaluation of sexual dysfunction after urethroplasty. Validated PROMs encompassing all aspects of results after urethral surgery should be developed.

Author contributions: Ole Jacob Nilsen had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Nilsen, Sairanen, Ekerhult, Lindqvist, Persson.
Acquisition of data: Nilsen, Veiby Holm, Sairanen, Ekerhult, Lindqvist, Persson, Grabowska.

Analysis and interpretation of data: Nilsen, Veiby Holm, Sairanen, Ekerhult, Lindqvist, Persson, Grabowska.

Drafting of the manuscript: Nilsen, Sairanen.

Critical revision of the manuscript for important intellectual content: Nilsen, Veiby Holm, Sairanen, Ekerhult, Lindqvist, Persson, Grabowska.

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Peer Review Summary

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