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# De novo erectile dysfunction after anterior urethroplasty: a systematic review and meta-analysis

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# **Abstract**

- To evaluate the likelihood of developing *de novo* erectile dysfunction (ED) after anterior urethroplasty and to determine if this likelihood is influenced by age, stricture length, number of previous procedures or timing of evaluation.
- PubMed, Embase, Cochrane, and Google Scholar databases were searched for the terms `urethroplasty', `urethral obstruction', `urethral stricture', `sexual function', `erection', `erectile function', `erectile dysfunction', `impotence' and `sexual dysfunction'.
- Two reviewers evaluated articles for inclusion based on predetermined criteria.
- In a meta-analysis of 36 studies with a total of 2323 patients, de novo ED was rare, with an incidence of 1%.
- In studies that assessed postoperative erectile function at more than one time point, ED was transient and resolved at between 6 and 12 months in 86% of cases.
- Men should be counselled regarding the possibility of transient or permanent *de novo* ED after anterior urethroplasty procedures.
- Increasing mean age was associated with an increased likelihood of *de novo* ED, but this was not statistically significant.

## **Keywords**

erectile dysfunction; m	ieta-analysis; systemat	ic review; urethrop	lasty

## Introduction

Urethroplasty is the `gold standard' for treatment of urethral stricture disease. Recently, an increased focus has been placed on the potential risk of erectile dysfunction (ED) after urethroplasty procedures. *De novo* ED after urethroplasty is thought to be attributable to cavernous and[1] perineal nerve injury, or to the disruption of bulbar artery flow[2]. Proposed surgical methods for reducing injury to these structures during urethroplasty include bulbospongiosus and perineal nerve preservation[3], bulbar artery preservation[4], and non-transection of the corpus spongiosum[5].

The objective of the present study was to assimilate and summarize the available data on *de novo* ED stemming from anterior urethroplasty procedures. We wanted to determine the incidence of *de novo* ED after anterior urethroplasty and assess if this incidence was

associated with age or number of previous urethroplasty procedures, and to determine whether all patients were questioned about postoperative erectile function. We also wanted to assess if *de novo* ED resolved or persisted over time. To our knowledge no guideline-based[6,7] systematic review or meta-analysis has been completed on this topic.

## **Materials and Methods**

# Systematic review

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and Meta-analysis of Observational Studies in Epidemiology (MOOSE) criteria were followed for systematic review [6,7]. All inclusion and exclusion criteria were determined by author consensus before the literature search was begun.

#### Literature search

Electronic searches of PubMed, EMBASE, Google Scholar and Cochrane databases were conducted using the search terms, `urethroplasty', `urethral obstruction', `urethral stricture', `sexual function', `erectile function', `erectile dysfunction', `impotence' and `sexual dysfunction'. The search strategy and search terms were constructed with the assistance of an experienced medical librarian. The search was limited to human studies. A manual search of reference lists from the articles selected for inclusion in this study was also performed. Abstracts presented at national urology meetings appropriate for inclusion in the present study were identified through EMBASE and Google Scholar searches to identify additional studies (`grey material') and studies that may have a negative result. These abstracts were matched with the corresponding articles written later by the same groups when a complete article was available for inclusion, and only the completed article was included for review. Experts in reconstructive urology were also queried to identify any additional articles that should be included for review.

# Eligibility criteria

Eligibility criteria were determined before the literature search was begun. We included only English-language studies on patients who underwent anterior urethroplasty procedures because of difficulties obtaining standardized translation of non-English-language studies. As urethroplasty techniques have evolved over time and systematic standards for assessing surgical complications have become more universal, we included studies from the last 15 years. Manuscripts with a cohort that included both adult and paediatric patients were included, with efforts made to extract data on adult patients only when possible as little to no assessment on erectile function has been performed on paediatric patients.

Exclusion criteria consisted of patients undergoing posterior urethroplasty, case reports/case series with nine or fewer patients, and studies with only paediatric patients aged 18 years. Studies in which the majority of patients had ED owing to pelvic trauma before urethroplasty, and studies comparing urethroplasty with primary realignment in pelvic fracture urethral distraction defects were excluded. Abstracts with incomplete data about the number of patients with postoperative ED were also excluded, as these data could not be properly interpreted.

## Study selection process

Our initial search using English-language and human participant limits identified 736 articles. An additional 20 articles were included based on identification from the references of the included articles. The titles and abstracts of these articles were reviewed by two authors, and a final 36 articles were selected for inclusion based on independent review and consensus discussion between the authors of the present study. Articles were excluded

owing to lack of relevance (391), not meeting defined inclusion criteria (159), and duplication or incomplete information (14) (Fig. 1). Manuscripts for all selected articles were obtained and analysed.

#### **Data extraction**

Two authors independently extracted predetermined categorical information data from the selected articles. This information included: study dates; number and age of patients; mean stricture length; location of the stricture; type of urethroplasty performed; number of patients with *de novo* ED after urethroplasty; whether or not this ED resolved during the timeframe of the study; length of study follow-up whether or not all patients were questioned about erectile function; whether or not patients were questioned about erectile function before their operation; whether or not a standardized questionnaire such as the International Index of Erectile Function (IIEF) was used; and whether the study was prospective or retrospective (Table 1[2,5,8–41]).

# Statistical analysis

A random effects meta-analysis was performed using the metan command in Stata Version 12.1 (StataCorp, College Station, TX, USA)[42]. The inputs to the meta-analysis were the proportion of patients with *de novo* ED and associated 95% CI for each of the studies. As a number of the studies had zero patients with *de novo* ED, CIs were derived using the Jeffreys method[43] as implemented in the ci command in Stata 12. Analyses were conducted on the log-transformed scale and then back-transformed for display purposes in the forest plot. Associations of the proportion of *de novo* ED with study-level characteristics were evaluated by both meta-regression and subgroup forest plots. Statistical analyses were performed by the University of California San Francisco Clinical and Translational Science Institute Biostatistics Consultation Service.

# Results

Thirty-six articles with 2323 total patients who underwent anterior urethroplasty procedures met the inclusion criteria for meta-analysis. The incidence of post-urethroplasty *de novo* ED ranged from 0 to 38%. The present meta-analysis found that *de novo* ED was rare, with an incidence of 1% (CI 1–3%)(Fig.2). The five studies that reported a *de novo* post-urethroplasty ED incidence of >20% were all conducted after 2001, all used a questionnaire to assess ED, and all patients were directly questioned about ED postoperatively.

Interestingly, the *de novo* ED incidence was not increased when patients were directly asked about erectile function (odds ratio [OR] 0.83 [CI 0.06–10.90]). Five of the 12 studies that stated all patients were asked about erectile function reported 0% *de novo* postoperative ED. Additionally, de novo ED was not associated with stricture location or type of repair (Table 1).

In many cases *de novo* ED resolved 6–12 months after surgery. Seven of the 21 studies that reported *de novo* ED reported resolution of ED in 86% (50/58) of cases (Table 1). Fourteen of the studies did not report resolution of ED over time and did not assess ED postoperatively at more than one time point.

Before initiating the present study, we hypothesized that patients who had undergone multiple failed previous procedures for their urethral stricture disease would have a higher risk of *de novo* ED. This was not demonstrated in our statistical analysis. There was no statistically significant association between number of failed previous direct vision internal urethrotomies, urethral dilations or urethroplasty procedures and *de novo* ED (OR 1.003 [CI 0.994–1.012 per every additional failed previous procedure]). There was also no association

between mean stricture length and de novo ED (OR 0.91 [CI 0.66–1.25 per each additional 1 cm mean stricture length]).

Since ED increases with age, we hypothesized that older patients would have an increased risk of *de novo* ED. There was a slight association between mean age in the study group and *de novo* ED with an OR 1.12 (CI 0.97–1.31) for each additional year in mean age, but this was not significant.

# **Discussion**

This systematic review and meta-analysis of urethroplasty and ED examining articles from 1997 to 2012 with 2323 total patients found that the incidence of *de novo* ED was low (1%, CI 1–3%). Although this incidence is low, there was substantial heterogeneity in the studies (I-squared=93%, *P*<0.001) indicating that there was more variation than would be expected by chance alone (Fig. 2). The substantial heterogeneity in these studies has a large impact on the result and may underestimate the risk of *de novo* ED after urethroplasty. This heterogeneity may be attributable, in part, to the variation in how ED was reported and assessed in each study. Although not explicitly stated, some studies that did not question all patients postoperatively about erectile function may have relied on patient volunteered self-reporting, which may underestimate *de novo* ED. Future studies on urethroplasty outcomes should include pre- and postoperative analysis of ED to allow better future analyses and comparisons across studies.

The strengths of the present study include that fact that it provides a comprehensive review of the urethroplasty literature with broad inclusion criteria. To our knowledge, this is the first systematic review of ED related to urethroplasty procedures that follow the standardized systematic review PRISMA and MOOSE criteria[6,7]. Study limitations include the limiting of the search criteria to English-language studies and lack of specific data on whether or not all patients had been questioned regarding erectile function before surgery in some series. Little information was available on patient characteristics that may influence ED risk, such as vascular disease and diabetes. There was also a lack of a standardized validated questionnaires administered to patients in most series. In studies that used a validated questionnaire such as the IIEF, the authors of those studies determined whether the decline in IIEF constituted ED and did not all use a standardized decrease in IIEF score to determine de novo ED. In some studies, it was unclear as to whether all patients were evaluated for ED or if only patients who self-reported ED were included. Many studies did not clearly delineate the number of patients who underwent previous urethroplasty procedures vs internal urethrotomy or dilation procedures, so all previous procedures had to be assessed together. We have addressed these limitations by including information on these variables for each study included for meta-analysis (Table 1), but we do acknowledge that these limitations may greatly influence the outcomes of the present study, especially with potential under-reporting of de novo ED in studies that did not question all patients about ED pre- and postoperatively.

The present article shows the change in urethroplasty outcome reporting over time. More recent studies were more likely to use a questionnaire and were more likely to assess ED both pre- and postoperatively. This stresses the importance of assessing all patients before and after urethroplasty operations to obtain similar results across studies. It also suggests that older studies that did not question all patients pre- and postoperatively may be underreporting the true incidence of *de novo* ED.

Most studies evaluating ED after urethroplasty do not include a control surgery for comparison. A study comparing ED after anterior urethroplasty to ED in age-matched

control patients receiving circumcision found 30.9% of urethroplasty patients and 27.3% of circumcision patients reported ED[20]. While circumcision incision may alter penile sensation, it does not significantly alter penile blood flow or erectile innervation, and psychogenic effects on erectile function associated with any penile surgery must be taken into consideration.

For most patients who underwent urethroplasty and who experienced *de novo* ED, ED resolved over time, with the majority of patients returning to baseline erectile function between 5 and 12 months after treatment [2,5,8,19]. This suggests that ED after urethroplasty may be attributable to both long-term and short-term effects. Long-term effects include neurovascular damage from the operation itself and may include postoperative alterations in blood supply unmasking vasculogenic ED in older patients. Shortterm effects are more likely to be caused by the psychological impact of surgery and catheterization. Short-term effects may also include alterations in blood supply that are compensated for by revascularization during healing.

We propose that future urethroplasty studies include prospectively collected validated questionnair on ED and that standardized follow-up periods for evaluation of ED be used. This will allow a more systematic assessment of ED after urethroplasty that will be comparable across cohort studies. This may allow for alterations in urethroplasty technique based on ED risk in particular cases. Additionally, patients may be better counselled preoperatively on possible risks of ED in the short and long term.

In conclusion, the present meta-analysis found that the risk of *de novo* ED after anterior urethroplasty was low at 1%. Many cases of *de novo* ED resolved within 6–12 months; however, the possibility of *de novo* post-urethroplasty ED, even if transient from the psychological impact of surgery or during revascularization, should be discussed during preoperative evaluation.

# **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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# **Abbreviations**

**ED** erectile dysfunction

**PRISMA** Preferred Reporting Items for Systematic Reviews and Meta-Analyses

MOOSE Meta-analysis of Observational Studies in Epidemiology

**IIEF** International Index of Erectile Function.

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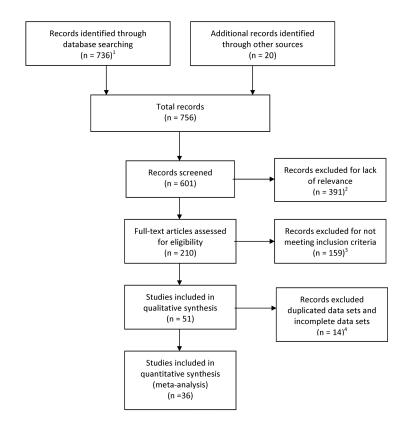
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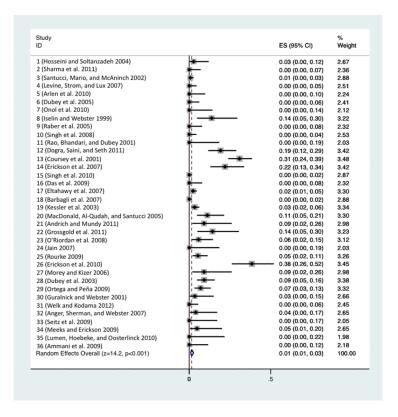
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#### **Article Selection**



- Articles from sources: PubMed 236, Embase 483, Google 17
- i.e. not about urethroplasties or ED
- Case report 9, editorial comment 34, review article 15, children 19, <9 patients 3, PFUDD 63, Posterior urethroplasty 16
   Duplicated data sets 5, incomplete data sets 7

Fig. 1. Flow chart of inclusion and exclusion of studies for the meta-analysis.



**Fig. 2.** Forest plot of *de novo* ED after anterior urethroplasty across all studies.

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Table 1

icteristics of studies included for analysis

Comments	Moderate ED that resolved spontaneously in three patients at 6-month at 6-month patient required PDE5i	Worse ED associated with longer stricture length, no significant difference in ED rates when compared with circumcision	-	-	-	No significant ED difference in dorsal vs ventral onlay	
Stricture location	Bulbar	Anterior	Bulbar	Bulbar: 5 Bulbopenile: 5 Penile: 2	Bulbar	Bulbar: 56 Bulbopenile: 39 Penile: 14	Membranous: 13 Membranobulbar: 12 Bulbar: 59 Bulbopenile: 67 Penile: 54 Fossa: 20
Urethroplasty type	DO: 12 DO + EPA: 13 DO + PF: 4 27 used MG, 2 used BMG	EPA: 56 BMG: 26 PF: 44 Other: 26	DO augmented anastomosis: 20 VO augmented anastomosis: 9 7 used PF, 22 used BMG or MG	PF	EPA	Ventral PF: 52 Dorsal PF: 23 VO + BMG or MG: 18 DO BMG or MG: 16	BMG: 30 PF: 100 EPA: 40 MG: 68
de novo postoperative ED, n (%)	4 (14)	47 (30.9)	1 (3.4)	0	1(1)	10 (9)	8 (3.4)
Questionnaire	°Z	Internally validated questionnaire	Non-standardized questionnaire	Not stated	Not stated	Not stated	Not stated
All Patients questioned about ED, pre-/ postoperatively?	Not stated/Not stated	No/Yes	No/Yes	Not stated/Not stated	Not stated/Not stated	Not stated/Not stated	Yes/Not stated
Months follow-up (range)	19 (10–37)	36 (3–149)	28 (3–126)	15.6 (5–25)	70 (6–291)	33.5 (11.4–58.7)	28.9 (12–73)
Age (range), years	43 (10–81)	45.7 (17–83)	44 (15–79)	40.5 (20–66)	38 (6-82)	39.5 (11–62)	43 (28-59)
No. of pati ents	29	152	29	12	168	109	238
Study Type	etrospective BJU Int. A	umpor manuscript; available	PMC 2014 S	eptember eptember	retrospecti <del>ve</del>	retrospective	retrospective
ors, year	CE, ster GD, [15]	sey JW, 2001	lnick Webster 2001 [35]	4S, et al., [18]	cci RA, 2002	y D, et )03 [33]	er TM, 2003

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ors, year	Study Type	No. of pati	Age (range), years	Months follow-up (range)	All Patients questioned about ED, pre-/ postoperatively?	Questionnaire	de novo postoperative ED, n (%)	Urethroplasty type	Stricture location	Comments
son BA, 2007	BJU.	59	41.7 (15–65)	22.3 (7.5–37.1)	No/Yes	O'Leary	13 (25)	EPA: 23 DO or VO + BMG: 22 2 stage w/BMG: 7	Anterior	No significant ED difference pre- vs postoperatively; postoperative EF scores improved 1 year after repair did not affect EF scores
OK, et 007 [30]	retrospective Section	12	38.9 (17–58)	14.2 (2–26)	Not stated/Not stated	Not stated	0	DO + BMG	Bulbar: 2 Bulbopenile: 4 Penile: 6	
ne LA, et 307 [11]	retrospecti <del>u</del> .	53	45 (21–75)	53 (15–120)	Not stated/Not stated	Not stated	(0) 0	DO + BMG: 24 VO + BMG: 22 2 stage: 7	Bulbar: 35 Penile: 18	
ordan, A, 2008	ips available in I	52	39 (19–61)	34 (12–80)	Not stated/No	Not stated	3 (6)	DO + BMG	Bulbar	Postoperative ED resolved in two patients, not in one patient with DM
n PB, et 008 [17]	MC 2014	55	29 (18–58)	17.5 (not stated)	Not stated/Not stated	Not stated	(0) 0	DO + BMG	Bulbar: 14 Penile: 11 Bulbopenile: 30	ı
ani A, et 309 [41]	Prospective Spanner	20	34 (19–45)	32 (14–68)	Not stated/Yes	IIEF	(0) 0	EPA	Bulbar	1
k, et al., [23]	retrospectique	30	28 (18–58)	9 (4–12)	Not stated/Not stated	Not stated	(0) 0	DO + BMG	Bulbar: 6 Bulbopenile: 6 Penile: 18	
s JJ, son B, [39]	not stated	21	46 (18–77)	18 (5–42)	Not stated/Not stated	Not stated	1 (4.7)	Full thickness abdominal skin grafts	Bulbar: 11 Penile: 13 Fossa: 8 Bulbopenile: 4	1
ça JLL, CP 2009	retrospective	100	41 (18–79)	Not stated (5–125)	Not stated/Not stated	Not stated	(1)	EPA: 57 DO or VO + BMG: 20 PF: 23	Bulbar: 78 Penile: 22	1
ke K [31]	prospective	93	Not stated	12 (12–57)	Not stated/Not stated	Subjective symptom analysis	5 (5)	DO + BMG augmented anastomosis	Bulbar	

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ors, year	Study Type	No. of pati ents	Age (range), years	Months follow-up (range)	All Patients questioned about ED, pre-/ postoperatively?	Questionnaire	de novo postoperative ED, n (%)	Urethroplasty type	Stricture location	Comments
M, et al., [38]	not stated	13	53.8 (24–76)	12 (not stated)	Not stated/Yes	Non-standardized questionnaire	0	EPA: 8 DO + MG: 5	Bulbar: 9 Penile: 4	1
AM, et 010 [12]	retrospective	24	43.2 (26–71)	10.5 (1–72)	Not stated/Not stated	No	(0) 0	BMG	Anterior	1
son BA, 2010 [2]	BJU BJU	52	40.67 (26–56)	7.2 (17 days to 22.8mo)	Yes/Yes	IIEF	20 (38)	EPA: 20 Augmented EPA: 15 VO: 11 2 stage: 6	Bulbar: 35 Penile: 17	Recovery of EF in all but two patients between 92 and 398 days
on N, et	Author manuscrip	10	36.5 (16-60)	46.6 (15–79)	Not stated/Yes	Non-standardized questionnaire	0	Ventral longitudinal stricturotomy w/ transverse closure 4 pts had concurrent urethroplasty at another site: PF (2 penile), BMG (2; 1 bulbar, 1 penile)	Bulbar: 6 Fossa: 4	
SY, et )10	retrospectiæe	16	Not stated	24.6 (4–96)	Not stated/Not stated	Not stated	0	Circular BMG	Meatal	1
uP, et )10 [22]	retrospecti <del>ae</del> ui u M	150	40 (18–73)	33 (4–72)	No/Yes	O'Leary	(0) 0	EPA: 59 DO + BMG: 55 PF: 36	Bulbar: 95 Bulbopenile: 47 Penile: 8	1
ich DE, ly AR [5]	retrospective	22	34 (21–65)	12 (6–21)	No/Not stated	No	2 (9)	Non-transecting EPA	Bulbar	Temporary ED, resolved spontaneously
a PN, et )11 [19]	prospectiving of the prospectivity of the prospecti	78	37.9 (21–71)	15.5 (13.2–17.8)	Yes/Yes	IIBF	15 (20)	PF: 14 DO + BMG: 29 DO + MG: 3 EPA: 32	Bulbar: 53 Penile: 25	96% recovery at 6 months, three who did not recover EF were older and had mild-to- moderate ED preoperatively.
sgold E, 2011	retrospective	28	46 (not stated)	28.7 (1–114)	No/No	No	4 (14)	DO + BMG augmented anastomosis for recurrent stricture	Bulbar	
na V, et 11 [9]	prospective	34	34.6 (18–60)	8.4 (3–13)	Yes/Yes	O'Leary	8 (24)	EPA: 18 Progressive perineal: 9 DO + BMG: 9 Staged: 7	Bulbomembranous: 2 Bulbar: 18 Penile: 7 Entire length: 7	

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Blasc	chko et al.
Comments	
Stricture location	Prox bulbar: 31 Distal bulbar: 10 Penile: 3
Urethroplasty type	Non-transecting EPA: 21 DO + BMG: 23
de novo postoperative ED, n (%)	(0) 0
Questionnaire	Non-standardized questionnaire
All Patients questioned about ED, pre-/ postoperatively?	Not stated/No
ors, year Study Type No. Age (range), years Months follow-up (range) All Patients of questioned a pati ents postoperativ	27.6 (14.4–45.6)
Age (range), years	40 (34–55)
No. of pati ents	44
Study Type	retrospective 44 40 (34–55)
ors, year	BK, ma RT [36]

nuccal mucosa graft; DM, diabetes mellitus; DO, dorsal onlay; EPA, excision and primary anastomosis; EF, erectile function; MG, mesh graft; PDE5i, phosphodiesterase 5 inhibitor.

icled flap; VO, ventral onlay.

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