Sexual Medicine, 2024, **12**, qfae064
https://doi.org/10.1093/sexmed/qfae064
Review

The urinary and sexual outcomes of buccal mucosal graft urethroplasty versus end-to-end anastomosis: a systematic review with meta-analysis

Xingming Zhao, MM[1,2], Qiang Guo, MM[1], Xi Zhang, MM[1], Qi Xing, MM[3], Sheng Ren, MM[2], Yuting Song, MM[4], Chengyong Li, MM[1], Chuan Hao, MM[1], Jingqi Wang, MD[1,*]

[1]Department of Urology, The Second Hospital of Shanxi Medical University, Taiyuan, Shanxi Province 030001, China
[2]Second Clinical Medical College, Shanxi Medical University, Taiyuan, Shanxi Province 030001, China
[3]Department of Urology, Shanxi Medical University, Taiyuan, Shanxi Province 030001, China
[4]Department of Histology and Embryology, Shanxi Medical University, Taiyuan, Shanxi Province 030001, China

*Corresponding author: Department of Urology, The Second Hospital of Shanxi Medical University, Xinghualing District, Taiyuan, Shanxi 030001, China. Email: drwangjq@126.com

Abstract

Background: The urinary and sexual outcomes after urethroplasty may be a concern for patients, but there are still some controversies regarding the consequences of buccal mucosal graft urethroplasty (BMG) in terms of erectile dysfunction (ED).
Aim: This meta-analysis aimed to compare urinary and sexual outcomes of BMG and end-to-end urethroplasty (EE).
Methods: The PubMed, Web of Science, Cochrane, and Embase databases were searched until February 31, 2023. Data extraction and quality assessment were performed by 2 designated researchers. Dichotomous data were analyzed as odds ratios with 95% confidence intervals (CIs). Heterogeneity across studies was assessed by the I^2 quantification, and publication bias using Begg's and Egger's tests. Meta-analysis was performed using RevMan software.
Outcomes: Outcomes included stricture recurrence, ED, penile complications, and voiding symptoms.
Results: Eighteen studies, including 1648 participants, were included in our meta-analysis. The meta-analysis revealed that there was no significant difference in stricture recurrence (OR = 0.74; 95% CI, 0.48–1.13; $P = .17$) and voiding symptoms (OR = 1.12; 95% CI, 0.32–3.88; $P = .86$) between the BMG group and the EE group. BMG was associated with lower risk of penile complications (OR = 0.40; 95% CI, 0.24–0.69; $P = .001$) and ED (OR = 0.53, 95% CI, 0.32–0.90, $P = .02$).
Clinical Implications: The study may help clinicians choose procedures that achieve better recovery of the urological and sexual function in the treatment of urethral stricture.
Strengths and Limitations: This meta-analysis is the first to evaluate the urinary and sexual outcomes of BMG vs EE. A limitation is that most of the included studies were retrospective cohort studies.
Conclusion: BMG is as effective as EE in the treatment of bulbar urethral stricture, but BMG has fewer complications and ED than EE.

Keywords: urethral stricture; end-to-end anastomosis; buccal mucosa graft; erectile dysfunction; PROSPERO: CRD42023406627.

Introduction

Urethral stricture is a common urological disease in clinical practice, which significantly affects the quality of life of patients.[1] The incidence of urethral structure in developed countries is 0.9%.[2] Urethral stricture is defined as the pathological narrowing of the urethral lumen secondary to scar formation in the subepithelial connective tissue.[3] Bulbar urethral stricture is mainly caused by trauma (especially straddle injury), iatrogenic injury, inflammation, and idiopathic factors.[4]

The management of bulbar urethral stricture requires consideration of various factors, such as the etiology of stricture, location, and length of fibrous tissue of the stricture. Conventional methods for treatment of urethral stricture include urethral dilatation, internal urethrotomy, urethral stent implantation, and urethroplasty.[5] Urethroplasty is the gold standard for treatment of urethral strictures, owing to its high-cost effectiveness and high success rates.[6] Urethroplasty procedure can be classified into end-to-end anastomosis and substitution urethroplasty.[7]

End-to-end urethroplasty (EE) was introduced by Hamilton in 1919 and is widely used in the treatment of bulbar and posterior urethral strictures, with surgical success rates ranging from 86% to 95%.[8] The EE procedure treats urethral strictures by removing the narrowed portion and directly connecting the healthy ends of the urethra. EE is widely performed in many health centers globally owing to technological advances, including better surgical instrumentation and improved perioperative management. Buccal mucosal graft (BMG) from the lower lip was first used in 1993 by El-Kasaby for the treatment of penile and bulbar urethral strictures.[9,10] The BMG procedure incises the narrowed segment of the

Received: June 24, 2024. **Revised:** August 24, 2024. **Accepted:** September 10, 2024

urethra and extends it to the normal urethral mucosa at both ends, using the buccal mucosa to augment or replace the narrowed portion of the urethra. Studies comparing EE and BMG procedures observed that BMG had a higher success rate and was associated with fewer complications than EE in the treatment of bulbar urethral strictures.[11]

Objectives

Currently, the effectiveness of methods for the treatment of bulbar urethral stricture is controversial, and there are few studies that compare the long-term efficacy of EE and BMG in the treatment of bulbar urethral stricture. We systematically reviewed the literature and utilized a meta-analysis to evaluate whether there were significant differences in urinary and sexual outcomes between BMG and EE for bulbar urethral stricture?

Materials and methods

This is a systematic review and meta-analysis of comparing the urinary and sexual outcomes of BMG urethroplasty and EE in the treatment of anterior urethral stricture. The study has been reported in line with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and AMSTAR (Assessing the methodological quality of systematic reviews) Guidelines.[12,13]

Search strategy

A comprehensive literature search of PubMed, Web of Science, Cochrane Central Controlled Register of Trials (CENTRAL), and EMBASE was performed by 2 independent reviewers up to February 31, 2023. The search strategies were as follows: ("Bulbar urethral stricture") AND ("Excision and Primary Anastomosis" OR "anastomotic urethroplasty" OR "end-to-end urethroplasty" OR "buccal mucosa graft"). The search was restricted to English papers, searching comparative studies between buccal mucosa graft urethroplasty and EE. Additional articles were added from relevant systematic reviews and references.

Inclusion and exclusion criteria

Inclusion criteria

The Patient Intervention Comparison Outcome Study type model was used to frame and answer the clinical question. Patient: patients with bulbar urethral stricture; Intervention: buccal mucosa graft urethroplasty; Comparison: EE; Outcome: stricture recurrence, incidence of erectile dysfunction (ED), penile complications (penile shortening, ejaculatory dysfunction, genital pain, and other complications occur in the penis), and voiding symptoms (post voiding dribbling, post void leak, and stream spraying); Study type: prospective cohort study, retrospective cohort study or randomized controlled trial (RCT).

Exclusion criteria

(1) Patients with a history of urethroplasty. (2) Animal and pediatric studies; (3) Review articles, case reports, letters to the editor, editorials, conference abstracts.

Literature selection and data extraction

Data were independently extracted by 2 designated researchers using predetermined inclusion and exclusion criteria, and disagreements were resolved reaching a consensus in group discussions. The contents included basic information of the study (first author, year of publication, and country), study design (prospective, retrospective study, and randomized controlled trials), baseline characteristics of patients (number of patients, mean age, and stricture length). The primary outcome was ED. The secondary outcomes were stricture recurrence, penile complications, and voiding symptoms. Regarding the evaluation of surgical outcomes, uroflowmetry and ultrasound residual urine volume are used to assess recurrence of urethral strictures, the International Index of Erectile Function is used to assess ED, and the Voiding Dysfunction Symptom Score and Voiding Diary are used to assess voiding symptoms. Penile complications were defined as including penile shortening, ejaculatory dysfunction, genital pain, abnormal penile erection, and a range of complications that occur in the penis. Frequency data were extracted for dichotomous outcomes, whereas mean and standard deviations were extracted for continuous outcomes.

Quality assessment

The quality of all studies was assessed and scored by 2 researchers independently. The quality assessments of randomized controlled trial were performed with the Cochrane Collaboration's tool.[14] All included non-randomized studies were evaluated by Newcastle–Ottawa Scale (NOS) system.[15] According to the NOS system, 7–9 score studies were thought of as high-level quality, 5–6 score studies were thought as moderate level, and 0–4 score studies were low-level quality. Low-level quality studies should not be involved in the meta-analysis. Any disagreement was discussed and resolved by a third reviewer.

Statistical analysis

Statistical analyses were performed using RevMan 5.3 (The Cochrane Collaboration). Data from stricture recurrence, ED, penile complications, and voiding symptoms were pooled and analyzed as odds ratios (ORs) with 95% confidence intervals (CIs). I^2 quantification was used to determine inter-study heterogeneity. If there was no inter-study heterogeneity ($I^2 < 50\%$, $P > .10$), the fixed-effects model was used for meta-analysis. If there was significant between-study heterogeneity ($I^2 > 50\%$, $P < .10$), the source of heterogeneity was further analyzed and addressed using subgroup analysis or sensitivity analysis.[16] The random effects model was used for meta-analysis if heterogeneity could not be removed. A *P*-value less than .05 was considered statistically significant. Data are presented in the form of forest plots, and Begg's and Egger's tests were used to investigate the presence of publication bias.

Results

Literature screening

A total of 725 potentially eligible records were retrieved, of which 720 articles were identified from electronic databases (PubMed, 360; Cochrane, 23; Web of Science, 245 and EMBASE, 92) and 5 articles were added after a review of the references included in the study. After removing duplicates, the titles and abstracts of 476 records were screened. After a more detailed review, 387 papers that were deemed irrelevant to the study were excluded. After reading the text, 71 studies were

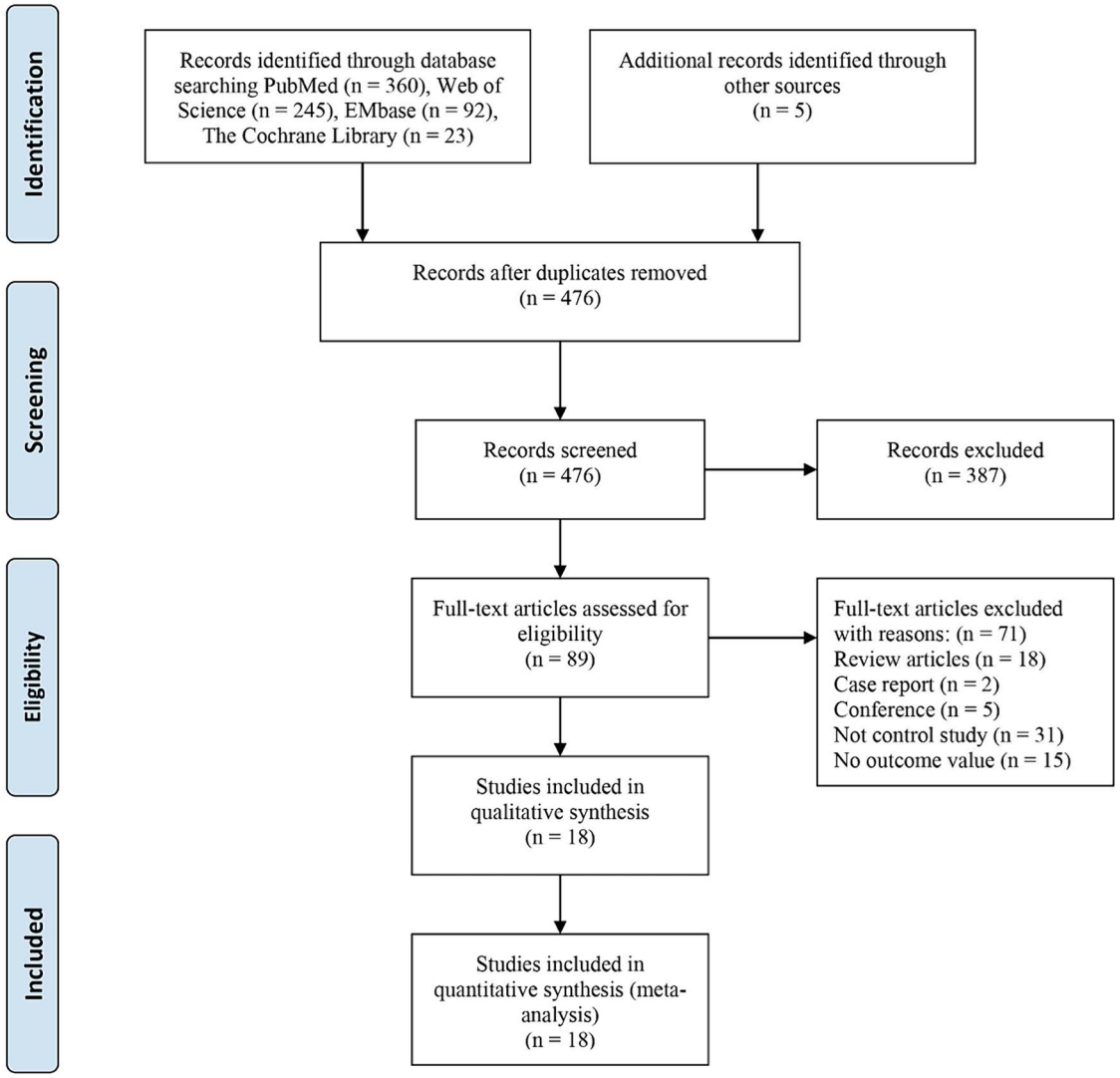

Figure 1. Flow chart of selection process in this meta-analysis.

further excluded for the following reasons: Review articles ($n = 18$), Case report ($n = 2$), Conference ($n = 5$), Not control study ($n = 31$), and No outcome value ($n = 15$). Finally, 18 studies, including 6 prospective studies,[17-22] 11 retrospective studies,[23-33] and 1 RCT,[11] met our selection criteria for meta-analysis (Figure 1).

Characteristics and quality of the included studies

A total of 18 studies were included, obtaining 1648 patients, of which 546 patients underwent BMG and 1102 patients underwent EE. The basic information and characteristics of the included literature are shown in Table 1. Twelve studies (including 1263 patients) compared stricture recurrence,[17,23-33] 9 studies (including 840 patients) compared postoperative sexual function (occurrence of ED),[17-19,21-23,26,27,30] 5 studies (including 378 patients) compared safety (occurrence of penile complications),[11,17,20,23,30] and 5 studies (including 331 patients) compared voiding symptoms.[17,20,21,23,26] Only one study did not describe the definition of surgical success in the text, the remaining studies did. A total of 13 high-quality studies[17-19,21-24,26-30,32] and 4 medium-quality studies[20,25,31,33] were included according to the NOS. The bias risk assessment of each included study is shown in Table 1. Only one RCT study was included in the meta-analysis,[11] and the bias risk assessment is shown in Figure 2. It does true randomization by using computer-generated tables. All studies reported complete outcome data.

Meta-analysis

Stricture recurrence

Twelve studies comparing 378 BMG with 885 EE procedures provided data on stricture recurrence, which were included in the meta-analysis. The combined results showed no significant difference between the BMG group and the EE group (OR = 0.74; 95% CI, 0.48–1.13; $P = .17$). No heterogeneity was found between studies ($I^2 = 0\%$; $P = .61$), and a fixed-effects model was used (Figure 3).

Penile complications

Five studies comparing 164 BMG with 214 EE procedures provided data on penile complications, which were included in the meta-analysis. The results showed a significantly lower risk of penile complications in the BMG group (OR = 0.40; 95% CI, 0.24–0.69; $P = .001$). There was a moderate heterogeneity among studies ($I^2 = 40\%$; $P = .15$), and a fixed-effects

Table 1. Baseline characteristics all included studies.

First author and year	Country	Type of study	Number of patients	Median/mean age, years	Median/mean stricture length (cm)	Median/mean follow-up (months)	NOS score
Al-Qudah 2006[23]	USA	Retrospective study	43 (BMG: 19, EE: 24)	46 (18–78)	2.8 (0.5–11)	2 9 (10–53)	7
Anderson 2017[24]	USA	Retrospective study	152 (BMG: 50, EE: 102)	NR	BMG: 3.9 (1–10) EE: 2.3 (0.5–8)	BMG: 48 EE: 72	7
Barbagli 1997[25]	Italy	Retrospective study	43 (BMG: 19, EE: 24)	NR	NR	NR	5
Choudhary 2015[17]	India	Prospective study	90 (BMG: 45, EE: 45)	NR	NR	BMG:3 2.8 EE: 28.4	8
Coursey 2001[18]	USA	Prospective study	82 (BMG: 26, EE: 56)	45.7	1.875	36	8
Dogra 2011[19]	India	Prospective study	53 (BMG: 21, EE: 32)	BMG: 38.10 EE: 37.66	BMG: 6.13 EE: 2.95	BMG: 15.29 EE: 15.19	7
Furr 2019[26]	USA	Retrospective study	179 (BMG: 40, EE: 139)	BMG: 42.8 EE: 40.5	BMG: 3.98 EE: 1.7	BMG: 51.4 EE: 63.3	7
Granieri 2014[27]	USA	Retrospective study	305 (BMG: 103, EE: 202)	BMG: 41.2 EE: 43.3	BMG: 2.8 EE: 1.4	16.8	7
Hussain 2020[28]	Pakistan	Retrospective study	199 (BMG: 33, EE: 166)	NR	NR	43.5	7
Joseph 2002[20]	UK	Prospective study	27 (BMG: 14, EE: 13)	36	2.8	32	6
Kessler 2003[21]	Germany	Prospective study	43 (BMG: 23, EE: 20)	BMG: 36 EE: 35	NR	BMG: 18 EE: 46	8
Lewis 2002[29]	USA	Retrospective study	53 (BMG: 22, EE: 31)	NR	3	23	8
Lozano 2009[30]	Spain	Retrospective study	67 (BMG: 10, EE: 57)	NR	BMG: 2–5 EE: 1–2.5	NR	7
MacDonald 2005[31]	USA	Retrospective study	54 (BMG: 20, EE: 34)	NR	NR	NR	6
Nilsen 2022[11]	Norway	RCT	151 (BMG: 76, EE: 75)	35	1	12	RCT
Omar 2020[22]	Egypt	Prospective study	29 (BMG:8, EE:21)	BMG: 47.8 (9.1) EE: 33.2 (12.1)	BMG: 4.3 (0.9), EE: 2.04 (0.5)	6	7
Pallares 2022[32]	Mexico	Retrospective study	21 (BMG: 12, EE: 9)	51.6 (14.22)	2.57 (1.3)	18	7
Park 2004[33]	USA	Retrospective study	57 (BMG: 5, EE: 52)	NR	2.8	53	6

Abbreviation: BMG, buccal mucosal graft urethroplasty; EE, end-to-end urethroplasty; NR, not reported; RCT, randomized controlled trial; NOS, Newcastle–Ottawa Scale system.

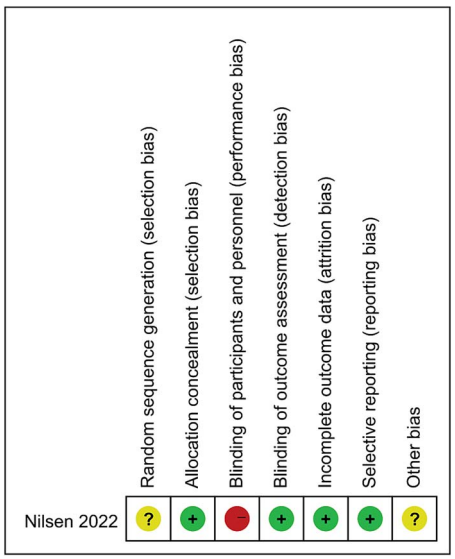

Figure 2. Risk of bias in randomized controlled trials.

model was used (Figure 4). Of these, poor voiding symptoms had sufficient meta-analysis data available. Five studies comparing 133 BMG with 198 EE procedures provided data on poor voiding symptoms. The results showed no significant difference between the BMG group and the EE group (OR = 1.12; 95% CI, 0.32–3.88; $P = .86$). Heterogeneity was significant ($I^2 = 69\%$; $P = .01$), and a random-effects model was used (Figure 5).

Erectile dysfunction

Nine studies comparing 184 BMG with 351 EE procedures provided data on ED, which were included in the meta-analysis. The results showed a significantly lower incidence of ED in the BMG group (OR = 0.53, 95% CI, 0.32 – 0.90, $P = .02$). No heterogeneity was found between studies ($I^2 = 4\%$; $P = .40$), and a fixed-effects model was used (Figure 6).

Sensitivity analysis

A sensitivity analysis of voiding symptoms was performed by excluding one study at a time to detect the source of heterogeneity. The analysis showed that after excluding the study by Furr et al.,[26] the heterogeneity of voiding symptoms decreased to 11%, suggesting that this study may be the potential source of heterogeneity. Combined data demonstrated still

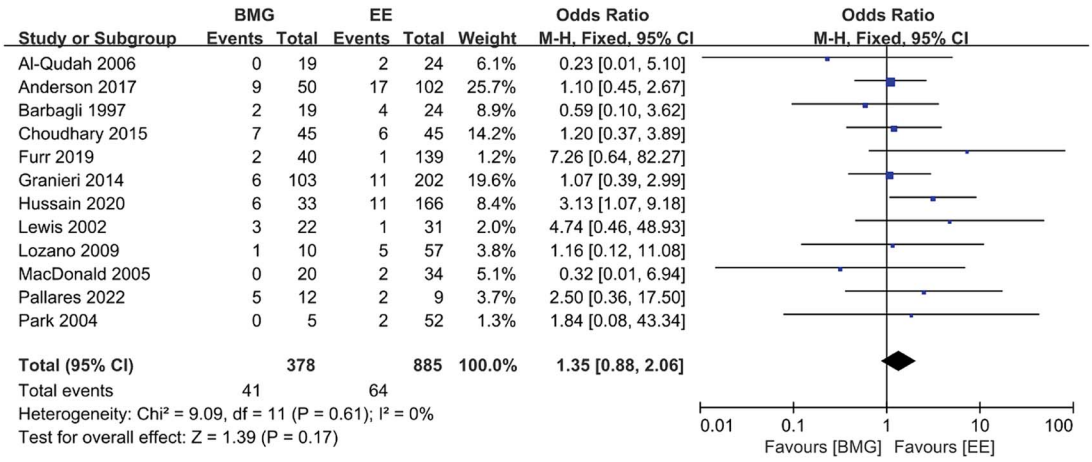

Figure 3. Forest plots illustrating postoperative stricture recurrence.

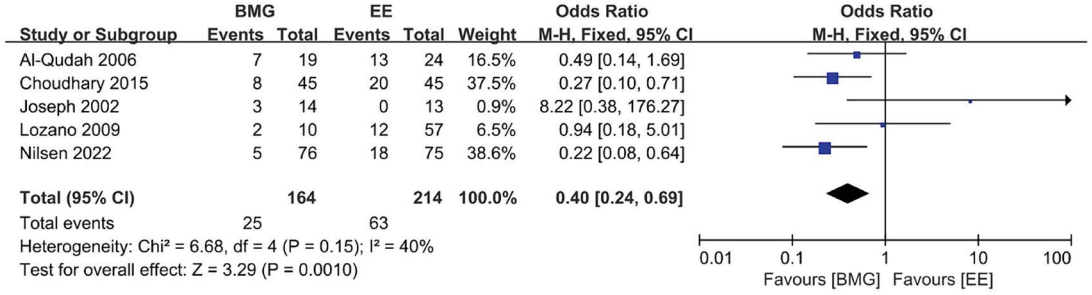

Figure 4. Forest plots illustrating postoperative penile complications.

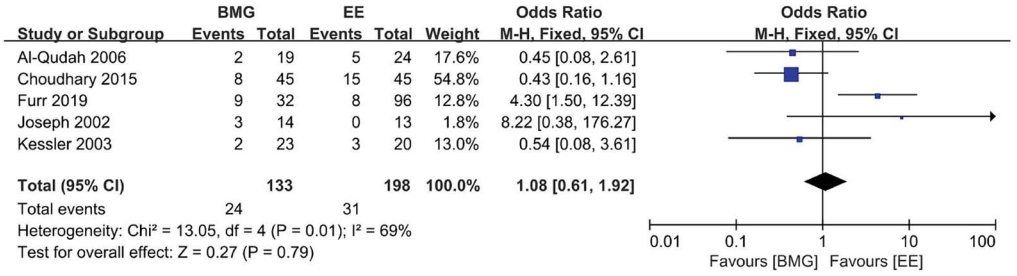

Figure 5. Forest plots illustrating postoperative poor voiding symptoms.

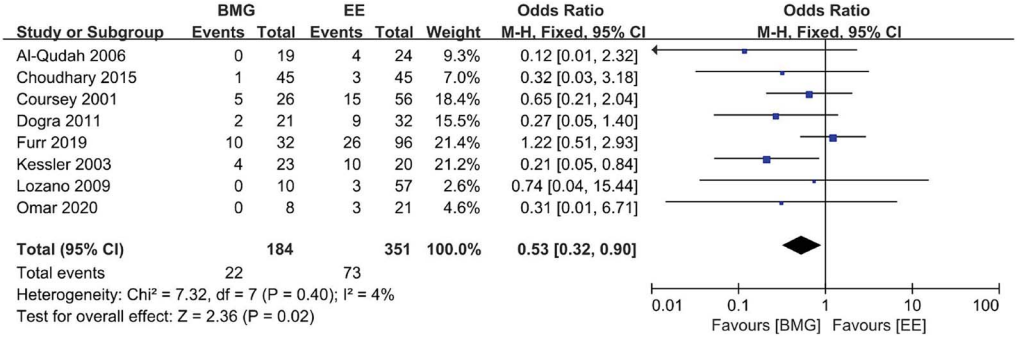

Figure 6. Forest plots illustrating postoperative erectile dysfunction.

no statistical significance (OR = 0.56, 95% CI, 0.24– 1.31, $P = .18$) (Table 2).

Publication bias

Begg's and Egger's tests were used to investigate the presence of publication bias. No significant publication bias was observed regarding stricture recurrence, ED, or voiding symptoms, and minimal publication bias was detected in terms of penile complications (Table 3).

Discussion

A total of 18 studies involving 546 patients who underwent BMG and 1102 patients who underwent EE were included in this meta-analysis. In this study, various outcomes

Table 2. Sensitivity analysis of poor voiding symptom.

References	OR (95% CI)	*h*	I^2 (%)
Al-Qudah[23]	1.42 [0.32 to 6.31]	.65	75
Choudhary[17]	1.58 [0.38 to 6.47]	.53	60
Furr[26]	0.56 [0.24 to 1.31]	.18	11
Joseph[20]	0.88 [0.24 to 3.27]	.85	74
Kessler[21]	1.34 [0.30 to 6.01]	.7	76

Table 3. Assessment of publication bias.

Outcomes	Begg's test	Egger's test
Stricture recurrence	0.945	0.952
Erectile dysfunction	0.711	0.089
Penile complications	0.086	0.007
Voiding symptom	0.462	0.887

including stricture recurrence, penile complications, ED, and international index of erectile function-5 scores were analyzed. Overall, both BMG and EE were effective in the treatment of urethral strictures, but BMG had a lower complication rate, especially in the ED.

End-to-end urethroplasty is the treatment of choice for bulbar urethral stricture. The EE procedure involves partial incision of the urethral stricture, and then the 2 healthy ends are anastomosed.[34] The application of this procedure was previously limited to short-segment strictures of approximately 1 cm in length due to concerns of potential complications, such as recurrence of the stricture, caused by tension of the anastomosis.[35] However, EE is currently used in longer strictures owing to technological advances. BMG has several advantages, such as simple operability, high efficacy, and few complications, and it can be performed through 3 approaches: ventral, dorsal, and lateral. The dorsal approach is also known as the Barbagli procedure.[36-38] Awad et al. conducted a study comprising 60 patients with anterior urethral stricture who had undergone buccal mucosa graft urethroplasty, and the results showed a 90% success rate.[39] In this meta-analysis, no statistically significant difference was observed between BMG and EE procedures regarding stricture recurrence, and the 2 procedures resulted in a good treatment outcome for urethral strictures. Previous investigations have indicated that EE is associated with a lower rate of recurrence compared to buccal urethroplasty in the management of bulbar urethral strictures. We believe that the reason for the difference in results may be the different definitions of surgical success in different article series.

We compared the postoperative penile complications between the 2 groups and the results showed that patients in the BMG group had a lower rate of penile complications. Nilsen et al. randomly assigned 151 patients who had not undergone urethroplasty into 2 groups and conducted a 12-month follow-up. The results showed a higher rate of penile complications, and significantly reduced glans filling and penile shortening in subjects who had undergone EE compared with BMG urethroplasty.[11] The findings in the present study showed no statistically significant differences in the incidence of voiding symptoms between the 2 groups. Minute urinary leakage after voiding is common in patients who have undergone urethroplasty and can be attributed to reduced urinary tract elasticity due to stricture disease or the treatment effects. This side effect can be effectively alleviated if patients manually drain this urine from the perineum after the procedure.

In addition to focusing on penile complications after BMG urethroplasty, the patients' donor area (oral site) should be evaluated. Common short-term oral complications of this procedure include altered taste, difficulty in eating, and speech disorders. Common long-term complications include oral tightness, probably due to the deeper location of the buccal mucosa in the oral cavity, which impairs tissue elasticity and extensibility after retrieval.[40,41] Akpayak et al. conducted a 2-year follow-up for 24 patients with long bulbar urethral stricture who had undergone dorsal onlay BMG urethroplasty. The results revealed that 21 patients had unobstructed urination after surgery, and 3 patients exhibited recurrence of postoperative strictures, with only short-term complications such as swelling, bleeding, and pain in the donor area, indicating high efficacy and safety of BMG procedure.[42]

Despite the high efficacy of urethroplasty in the treatment of urethral strictures, ED is a common complication, with incidence ranging from 0% to 40%.[43] Some urologists postulate that aggressive dissection and excessive cautery of the bulbar urethra damage the cavernous nerve, bulbar artery, or collateral vessels, leading to ED.[44,45] Omar et al. evaluated the changes in erectile function after bulbar urethral stricture anastomosis vs substitution surgery in 34 men with urethral stricture. The results showed that 3 patients undergoing routine anastomosis presented with persistent ED at 6 months postoperatively during follow-up.[22] In the present study, BMG significantly reduced the incidence of ED. The BMG procedure involves incision of the corpus spongiosum ventrally or dorsally along the length of the stricture and placing the BMG in the urethral defect, which protects the blood supply to the penis and urethral corpus spongiosum, which in turn protects postoperative sexual function.

Graft substitution urethroplasty is a procedure used to treat urethral strictures and can be performed with different body tissues, such as tipped penile flaps, bladder mucosa, and

oral mucosa. The buccal mucosa is a widely used alternative material for urethroplasty and was initially used in the surgical treatment of urethral strictures in the bulb and penis.[46] Buccal mucosa is a non-keratinized, complex squamous epithelium that shares structural similarities with the urethral mucosa and is easily accessible under local anaesthesia.[47] The buccal mucosa has a high content of elastic fibers, good tissue elasticity, a thin lamina propria, and a thick epithelial layer, so the reconstructed urethra is resistant to infection and trauma.[48] In addition, bilateral harvesting of the buccal mucosa provides longer graft material for patients with long stenotic segment lengths.

However, extensive extraction area is associated with a higher incidence of oral complications. Therefore, it is important to consider both the convenience of extraction and the impact of postoperative rehabilitation at the extraction site during oral mucosal harvesting. Smoking and tobacco chewing reduce graft quality.[49] Kurtzman et al. observed that deterioration in oral health is associated with altered mucosal histology, which may lead to thinning of the lamina propria and poor surgical outcomes.[50]

Careful mucosal sampling and surgical details can significantly reduce the occurrence of stricture recurrence and various complications during buccal mucosal urethroplasty. The whole mucosa, including a small amount of submucosal connective tissue, is usually collected, as thin mucosa has poor survival rates and can quickly shrink. Separation of the mucosa should be carefully conducted as the operation is delicate, and the vascular tip should be protected. The acquired buccal mucosa should have a moderate width because too wide mucosal duct will form diverticulum, whereas insufficient width will easily form urethral stricture. The length of the stricture determines the surgical technique used for repairing bulbar urethral strictures. End-to-end anastomosis is recommended for 1–2 cm strictures, whereas substitution urethroplasty is recommended for longer strictures. Staged urethroplasty is preferred for patients with strictures associated with poor local conditions.[51]

Due to the ambiguity in the definition of success after urethroplasty, this meta-included study used different results. In this study, a quality assessment of the included studies was performed, but the results were limited because they were not blinded due to the nature of surgical studies. Data such as the incidence of penile shortening or ED after urethroplasty are reported subjectively and may be susceptible to significant recall bias.

Conclusions

The BMG procedure significantly reduced the incidence of penile complications and postoperative ED in patients with bulbar urethral strictures compared with the EE procedure. However, the incidence of stricture recurrence and voiding symptoms was not significantly different between the BMG and EE groups.

Author contributions

X.M.Z. and Q.G. contributed equally. X.M.Z. and Q.G.: Conceptualization-Equal. Q.G. and X.Z.: Methodology.

Y.T.S., Q.X., and S.R.: Investigation. X.M.Z. and X.Z.: Writing–original draft. . C.Y.L., J.Q.W., and C.H.: Writing–review and editing. Q.G. and J.Q.W.: Supervision.

Funding

None declared.

Conflicts of interest

The authors disclose no financial or personal conflicts.

Data availability

Data availability is not applicable to this article as no new data were created or analyzed in this study.

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