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PRIOR ENDOSCOPIC TREATMENT AND RECURRENCE AFTER ANTERIOR URETHROPLASTY IN MEN WITH URETHRAL STRICTURE DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT
Endoscopic treatment is frequently performed before definitive urethroplasty in men with anterior urethral stricture disease. However, the association between prior endoscopic intervention and postoperative recurrence or failure after urethroplasty remains clinically important, particularly among patients who undergo repeated dilation or direct vision internal urethrotomy. This systematic review and meta-analysis aimed to evaluate the association between prior endoscopic treatment and recurrence or failure following anterior urethroplasty, including the potential effect of repeated prior endoscopic procedures. A systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and registered in PROSPERO. PubMed, Scopus, and ScienceDirect were searched from database inception without publication-year restrictions. A total of 2,619 records were identified, of which 15 observational studies published between 2003 and 2022 were ultimately included in the systematic review. Eligible studies included adult men with anterior urethral stricture disease who underwent urethroplasty and reported extractable data on prior endoscopic treatment and postoperative recurrence or failure. Methodological quality was assessed using the Newcastle–Ottawa Scale. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for dichotomous outcomes, while adjusted hazard ratios (HRs) were pooled separately using the generic inverse variance method. Fifteen observational studies comprising 4,515 patients were included. Prior endoscopic treatment was associated with a higher risk of recurrence or failure after urethroplasty than no prior endoscopic treatment or primary urethroplasty (OR 1.58, 95% CI 1.13–2.21; $p = 0.008$; $I^2 = 0\%$). Time-to-event analyses similarly demonstrated an increased risk (HR 1.48, 95% CI 1.12–1.97; $p = 0.006$; $I^2 = 58\%$). Repeated prior endoscopic procedures were associated with an approximately twofold higher risk of recurrence or failure (OR 2.06, 95% CI 1.30–3.28; $p = 0.002$; $I^2 = 17\%$). Prior endoscopic treatment is associated with poorer outcomes following anterior urethroplasty, with a more pronounced risk among patients undergoing repeated endoscopic procedures. These findings support earlier referral for reconstructive evaluation in patients with recurrent anterior urethral stricture disease who are unlikely to benefit from further endoscopic management.

Keywords: anterior urethral stricture; direct vision internal urethrotomy; endoscopic treatment; recurrence; urethral dilation; urethroplasty

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INTRODUCTION

Male urethral stricture disease is one of the most common urological conditions in adult men and represents a substantial clinical burden because its recurrent nature often requires repeated evaluation and intervention. Management may involve endoscopic procedures, such as urethral dilation and direct vision internal urethrotomy (DVIU), or definitive reconstructive surgery performed by urologists (Payne et al., 2022). The burden of urethral stricture disease is particularly relevant in low- and middle-income countries, where access to reconstructive urologists, endoscopic equipment, and definitive treatment may be limited (Payne et al., 2022). Hospital-based studies have also demonstrated that urethral stricture disease contributes considerably to the urological workload and healthcare resource utilization among adult male patients (Okeke et al., 2023). The

recurrent nature of the disease has further encouraged the development of minimally invasive treatment modalities, including drug-coated balloon dilation, which aim to reduce recurrence and the need for repeated interventions after conventional endoscopic treatment (Hudson et al., 2025; Mahenthiran et al., 2024).

Treatment selection for urethral stricture disease is influenced by several factors, including stricture location, length, etiology, previous treatment history, patient characteristics, and the availability of reconstructive expertise (Madec et al., 2024). Anterior urethral strictures require individualized decision-making regarding definitive urethroplasty, conventional endoscopic treatment, or newer minimally invasive approaches. Urethral dilation and DVIU remain commonly used because they are relatively simple, minimally invasive, and widely available. However, their effectiveness is influenced by stricture characteristics and previous treatment history, with recurrent strictures generally associated with less favorable outcomes following repeated endoscopic management (Madec et al., 2024; Hudson et al., 2025). Repeated endoscopic manipulation may also increase the cumulative treatment burden and contribute to greater stricture complexity before definitive reconstructive surgery (Hudak et al., 2012; Viers et al., 2018).

Urethroplasty is generally considered the definitive treatment for recurrent anterior urethral stricture because it provides more durable outcomes than repeated DVIU or urethral dilation. Nevertheless, recurrence after urethroplasty remains a clinically relevant problem and may be influenced by stricture characteristics, patient-related factors, surgical factors, and previous treatment history (Chapman et al., 2017; Breyer et al., 2010). Previous endoscopic manipulation has received particular attention because repeated instrumentation may alter the local tissue environment and increase stricture complexity, potentially affecting subsequent reconstructive outcomes. (Hudak et al., 2012) reported that repeated transurethral manipulation of bulbar urethral strictures was associated with greater stricture complexity and longer disease duration. Similarly, (Viers et al., 2018) found that delayed reconstruction of bulbar urethral strictures was associated with multiple prior interventions, longer strictures, and more complex repairs. More recently, (Yildirim et al., 2022) specifically evaluated the relationship between previous urethral endoscopic procedures and recurrence following urethroplasty, highlighting the clinical importance of treatment history when assessing reconstructive outcomes.

Despite these findings, the relationship between previous endoscopic treatment and recurrence or failure following anterior urethroplasty remains incompletely established. Differences in patient characteristics, stricture location and length, definitions of recurrence, duration of follow-up, and the number of previous endoscopic procedures may contribute to variation across individual studies. Moreover, although repeated endoscopic treatment is commonly used before referral for urethroplasty, the extent to which repeated intervention may influence subsequent reconstructive outcomes remains an important clinical question. A clearer synthesis of the available evidence is therefore needed to support treatment decisions and determine whether patients with recurrent anterior urethral stricture may benefit from earlier referral for reconstructive evaluation. Therefore, this systematic review and meta-analysis aimed to evaluate the association between prior endoscopic treatment and recurrence or failure following anterior urethroplasty in adult men with urethral stricture disease. In addition, this study examined whether repeated prior endoscopic procedures were associated with a greater risk of postoperative recurrence or failure. By synthesizing the available observational evidence, this study seeks to provide clinically relevant evidence regarding the timing of referral for definitive urethroplasty and the potential consequences of repeated endoscopic management.

METHOD

Study Design and Registration

This systematic review and meta-analysis was registered in PROSPERO (CRD420261417442) and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021) The PECO (Population, Exposure, Comparison, and Outcomes) framework was used to formulate the research question and establish the eligibility criteria. The study was designed to assess whether a history of prior endoscopic treatment is associated with recurrence or treatment failure following anterior urethroplasty in adult men with urethral stricture disease.

Eligibility Criteria

Relevant studies included adult men with anterior urethral strictures who had a history of previous endoscopic procedures and reported failure or recurrence outcomes following urethroplasty. Anterior urethral strictures included bulbar, penobulbar, penile, and panurethral strictures. Endoscopic procedures included direct vision internal urethrotomy (DVIU), internal urethrotomy, and urethral dilation. The primary exposure of interest was endoscopic treatment performed before urethroplasty. The comparison group consisted of patients without prior endoscopic treatment, including those undergoing primary urethroplasty. Studies were included in the quantitative synthesis when recurrence or failure data were extractable. The primary outcomes were failure and recurrence following anterior urethroplasty. Recurrence was defined as radiographic recurrence, symptomatic recurrence requiring treatment, the need for postoperative instrumentation, urethral dilation, DVIU, repeat urethroplasty, or procedural failure. The studies included in this review were observational studies, including retrospective and prospective cohort studies, as well as comparative case series with extractable outcome data. Case reports, systematic reviews, animal studies, and in vitro studies were excluded. Studies were also excluded if they reported only recurrence following endoscopic procedures or if they included posterior or membranous urethral strictures without separate extractable data for anterior urethral strictures.

Information Sources and Search Strategy

A systematic literature search was conducted in PubMed, Scopus, and ScienceDirect. The search covered the period from database inception to the date of the final search, with no restriction on publication year. Only full-text articles published in English were included. The reference lists of included studies and relevant review articles were also manually screened to identify additional eligible studies. The search strategy combined terms related to urethral stricture, urethroplasty, prior endoscopic treatment, and recurrence or failure. The PubMed/MEDLINE search strategy included the following terms: “urethral stricture,” “urethral strictures,” “anterior urethral stricture,” “bulbar urethral stricture,” “penile urethral stricture,” “panurethral stricture,” “urethroplasty,” “anterior urethroplasty,” “bulbar urethroplasty,” “substitution urethroplasty,” “anastomotic urethroplasty,” “graft urethroplasty,” “direct vision internal urethrotomy,” “internal urethrotomy,” “optical urethrotomy,” “Sachse urethrotomy,” “DVIU,” “urethral dilation,” “urethral dilatation,” “endoscopic treatment,” “endoscopic management,” “recurrence,” “failure,” “treatment failure,” “stricture recurrence,” and “urethroplasty failure.” The search strategy was adapted for Scopus and ScienceDirect.

Study Selection

All records were exported to Rayyan.ai in RIS, CSV, and BibTeX formats for reference management and screening. Duplicate records were removed before screening. Two reviewers independently screened the titles and abstracts, followed by a full-text review of studies considered potentially eligible for data synthesis. Each record was categorized as either included or excluded. Any disagreements between reviewers were resolved through discussion. A total of 2,619 records were identified from PubMed (n = 1,601), Scopus (n = 784), and ScienceDirect (n = 234). After duplicate removal and eligibility assessment, 15 observational cohort studies published between

2003 and 2022 were included in the systematic review. The study selection process was summarized using a PRISMA flow diagram in accordance with the PRISMA 2020 reporting framework (Page et al., 2021).

Data Extraction

Data were extracted by the reviewers using a standardized Microsoft Excel spreadsheet. The extracted data included author names, year of publication, country, study design, population characteristics, lesion site, sample size, exposure relevant to the review, outcome definition, follow-up duration, and risk-of-bias assessment.

Risk of Bias Assessment

Methodological quality was assessed using the Newcastle–Ottawa Scale for cohort studies (Gualdi-Russo & Zaccagni, 2026). The assessment considered study selection, comparability between exposed and unexposed groups, and ascertainment of exposure and outcomes. Additional consideration was given to the completeness of reported data, outcome definitions, and control of potential confounding factors. Two researchers independently assessed the methodological quality of the included studies, and disagreements were resolved through discussion and consensus.

Data Synthesis

The primary quantitative synthesis compared recurrence or failure following anterior urethroplasty between patients who had previously undergone endoscopic treatment and those without prior endoscopic treatment. For dichotomous outcomes, odds ratios (ORs) with 95% confidence intervals (CIs) were calculated from the reported event rates and sample sizes. A random-effects model was planned because clinical and methodological heterogeneity was anticipated across the included studies, particularly with respect to stricture characteristics, surgical techniques, previous endoscopic interventions, and definitions of recurrence. A fixed-effects model was considered when statistical heterogeneity was minimal. Statistical heterogeneity was assessed using the chi-square test and the I^2 statistic. To address potential confounding variables, including stricture length, etiology, and patient age, adjusted hazard ratios (aHRs) derived from multivariable models in the original studies were prioritized for time-to-event analyses. This approach enabled the association between prior endoscopic treatment and recurrence to be evaluated while accounting for relevant clinical predictors. Statistical heterogeneity was further addressed using a random-effects model to account for clinical differences in surgical techniques and outcome definitions across studies. A sensitivity analysis using the leave-one-out method was performed to evaluate the stability of the pooled estimates and identify studies that might disproportionately influence the overall findings. Other outcomes related to previous endoscopic treatments, including urethral dilation, DVIU, and internal urethrotomy, were summarized narratively because of the limited number of studies, inconsistent comparison groups, and differences in reported effect measures that prevented quantitative pooling. The meta-analysis was conducted using Review Manager (RevMan), version 5.4 (The Cochrane Collaboration, 2020). The software is the Cochrane platform used for preparing systematic reviews and conducting meta-analyses.

RESULT

Study Selection

A total of 2,619 records were identified from PubMed (n = 1,601), Scopus (n = 784), and ScienceDirect (n = 234). After removing 288 duplicate records, 2,331 records were screened based on their titles and abstracts. Of these, 1,716 records were excluded because they were not relevant to the review question. A total of 615 reports were assessed for eligibility. Among these, 600 reports were excluded because of an incorrect population (n = 196), incorrect exposure (n = 67), incorrect comparison (n = 128), incorrect outcome (n = 161), or inappropriate study design (n = 48). Consequently, 15 studies were included in the systematic review. The study selection process is presented in the PRISMA flow diagram in Figure 1, following the PRISMA 2020 reporting

framework (Page et al., 2021).

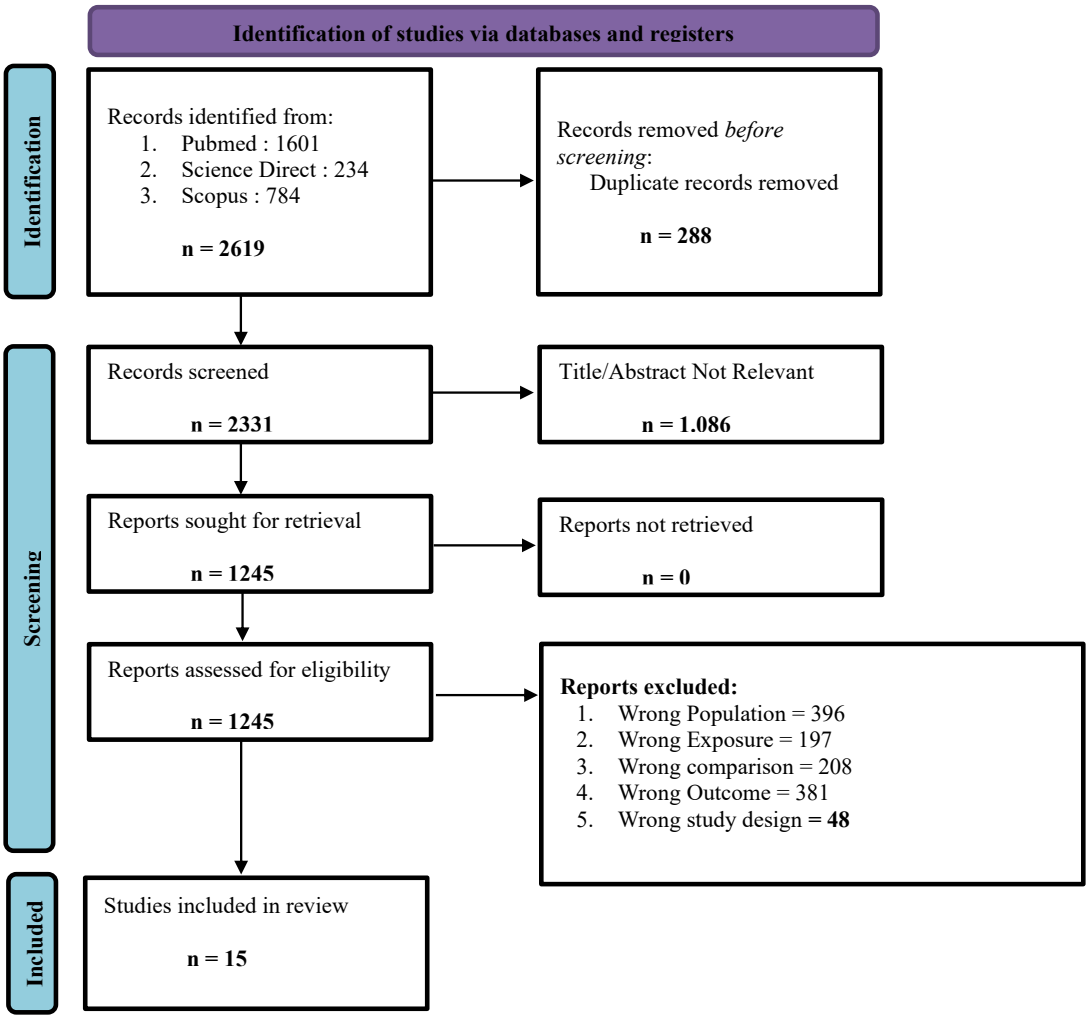

Figure 1. PRISMA flow diagram of study selection

Study Characteristics

A total of 15 studies were included in the systematic review. Of these, eight studies contributed data to the primary dichotomous meta-analysis, five studies contributed adjusted hazard ratios to the time-to-event analysis, and four studies were included in the subgroup analysis evaluating repeated prior endoscopic treatment. All included studies were observational cohort studies involving adult men with urethral stricture disease who underwent urethroplasty. The studies were conducted in Italy, Canada, the United States, Nigeria, the Netherlands, Germany, and multinational reconstructive urology centers. The total number of patients included in the systematic review was reported as 4,515. Sample sizes varied substantially between studies, ranging from 20 to 787 patients, depending on the study population and analytical approach. Follow-up duration ranged from approximately 1 year to 7 years. The characteristics of the included studies are summarized in Table 1.

Table 1.
Characteristics of the included studies

No	Study	Country	Design	Population	Sample Size	Exposure	Outcome	Follow Up
1	Barbagli, 2008	Italy	Retrospective cohort	dorsal skin graft urethroplasty	38	Prior dilation/urethrotomy/associated treatment	Postoperative instrumentation / recurrence	Mean 111 month
2	Barbagli, 2019	Italy	Retrospective	Sphincter bulbar	69	Previous urethrotomy/dilatio	Recurrence or postoperative	Median 52 month

No	Study	Country	Design	Population	Sample Size	Exposure	Outcome	Follow Up
			cohort			n/ associated treatment	instrumentation	
3	Benson, 2019	USA	Retrospective cohort	Anterior and posterior urethroplasty	420 anterior; 367 posterior	1–2 or ≥3 prior endoscopic treatments	Any subsequent stricture procedure >30 days after urethroplasty	Median 22.7 month anterior, 23.9 month posterior
4	Breyer, 2010	USA	Retrospective cohort	Anterior and posterior urethroplasty	443	Prior DVIU and prior dilation	Need for recurrent intervention, DVIU,or repeat urethroplasty	Median 5.8 years
5	Chapman, 2017	Canada	Retrospective cohort	Bulbar urethral stricture	596	Previous DVIU/dilation	Anatomic recurrence; inability to pass 16Fr cystoscope	Mean 65.4 month
6	Figler, 2013	USA	Retrospective cohort	Bulbar stricture, BMG urethroplasty	102	Prior procedure; DVIU/ dilation reported separately	Need for endoscopic/ open revision or suprapubic catheter	Mean 36 month
7	Fossati, 2016	Italy	Retrospective cohort	One-stage anterior urethroplasty	641	Dilation, urethrotomy, or associated treatments	Any postoperative instrumentation, including dilation	Median 69 month
8	Hudak, 2012	USA	Retrospective cohort	Primary bulbar urethral stricture	101	≥2 vs 0–1 transurethral manipulations	Additional procedure/instrumentation after Urethroplasty	Median 26 month
9	Kahokehr, 2018	USA	Retrospective cohort	Bulbar urethroplasty cohort	395	Prior endoscopic treatment	Recurrence diagnosed by cystoscopy and/or RUG requiring intervention	Median 28 month
10	Kessler, 2003	Germany	Retrospective cohort	Surgery for urethral stricture; mixed sites	238	≥2 urethrotomies vs 0–1 urethrotomy	Failure based on urethrogram/endoscopy, Qmax ≤15 mL/s, recurrent UTI, or reintervention	Up to 7.5 years
11	Ofoha, 2019	Nigeria	Retrospective cohort	Urethroplasty cohort	20	Prior urethral dilatation	Return of LUTS within 1 year	≥1 year
12	Sawyer, 2022	USA	Retrospective cohort	Adult male urethroplasty cohort	234	Prior dilation/DVIU	Revision surgery or recurrence on imaging/cystoscopy	Median 289 days
13	Viers, 2018	USA	Retrospective multinational cohort	Primary bulbar urethroplasty	278	Number of prior DVIU/endoscopic treatments	Need for recurrent intervention, catheterization,or repeat urethroplasty	Median 64 month
14	Warner, 2015	Multinational, 8 centers	Retrospective cohort	urethral stricture ≥8 cm	466	Prior dilation/urethrotomy	Any intervention for recurrence: dilation, urethrotomy,	Mean 20 month
15	Yildirim, 2022	Netherlands	Retrospective cohort	anterior urethroplasty for bulbar	106	Number of prior endoscopic treatments and ISD	Need for reintervention	Median 12 month

Note. BMG = buccal mucosa graft; DVIU = direct vision internal urethrotomy; ISD = intermittent self-dilatation; LUTS = lower urinary tract symptoms; RUG = retrograde urethrogram; UTI = urinary tract infection.

The Benson et al. (2019) study included both anterior and posterior urethroplasty populations. The eligibility and pooled-analysis dataset should be checked to confirm which subgroup was included in the present meta-analysis.

The study populations differed in terms of stricture location and clinical characteristics. Several studies focused specifically on anterior or bulbar urethral strictures, whereas others included broader urethroplasty populations involving anterior and posterior strictures or long-segment disease. The urethroplasty techniques also varied and included anastomotic urethroplasty, dorsal skin graft urethroplasty, buccal mucosa graft urethroplasty, single-stage anterior urethroplasty, staged urethroplasty, and substitution urethroplasty (Barbagli et al., 2008, 2019; Figler et al., 2013; Fossati et al., 2016). Previous endoscopic exposure also varied across studies. Some studies analyzed urethral dilation, DVIU, or urethrotomy separately, whereas others combined previous endoscopic procedures or categorized patients according to the number of previous interventions. Definitions of recurrence or failure similarly varied and included repeat urethroplasty, radiographic or endoscopic evidence of recurrence, postoperative instrumentation, repeat dilation, DVIU, inability to pass a 16-Fr cystoscope, recurrence of lower urinary tract symptoms, or any subsequent procedure related to urethral stricture (Chapman et al., 2017; Hudak et al., 2012; Kahokehr et al., 2018; Yildirim et al., 2022).

Risk of Bias Assessment

The methodological quality of the included studies was assessed using the Newcastle–Ottawa Scale (NOS) for cohort studies (Gualdi-Russo & Zaccagni, 2026). Overall, the methodological quality varied from low to high, with most studies demonstrating moderate to high methodological quality. The main methodological strengths included clearly defined urethroplasty cohorts, clinically relevant recurrence or failure outcomes, and ascertainment of previous endoscopic treatment history from medical records. The principal limitations involved the retrospective design of most studies, differences in recurrence and failure definitions, variation in follow-up duration, and incomplete adjustment for potential confounding factors. These factors included stricture length and location, etiology, urethroplasty technique, follow-up duration, and comorbidities. No study was excluded solely on the basis of its risk-of-bias assessment. The detailed assessment is presented in table 2.

Table 2.
Risk of bias assessment using Newcastle–Ottawa Scale

Study	Selection	Comparability	Outcome	Total NOS
Barbagli,2008	4/4	½	2/3	7/9
Barbagli, 2019	4/4	0/2	2/3	6/9
Benson,2019	4/4	½	2/3	7/9
Breyer, 2010	4/4	2/2	3/3	9/9
Chapman, 2017	4/4	2/2	3/3	9/9
Figler, 2013	4/4	½	2/3	7/9
Fossati, 2016	4/4	2/2	2/3	8/9
Hudak, 2012	4/4	0/2	2/3	6/9
Kahokehr, 2018	4/4	0/2	3/3	7/9
Kessler, 2003	4/4	2/2	3/3	9/9
Ofoha, 2019	3/4	0/2	1/3	4/9
Sawyer, 2022	4/4	½	1/3	6/9
Viers, 2018	4/4	½	3/3	8/9
Warner, 2015	4/4	½	3/3	8/9
Yildirim, 2022	4/4	½	2/3	7/9

Note. NOS = Newcastle–Ottawa Scale. Risk-of-bias assessment was based on the cohort-study version of the Newcastle–Ottawa Scale (Gualdi-Russo & Zaccagni, 2026).

Primary Meta-Analysis

The primary meta-analysis evaluated the association between previous endoscopic treatment and recurrence or failure following urethroplasty. Eight studies contributed dichotomous outcome data. Among 1,511 patients who had undergone previous endoscopic treatment, 201 experienced recurrence or treatment failure, compared with 57 of 409 patients in the comparison group. The pooled analysis demonstrated that previous endoscopic treatment was associated with a higher risk of recurrence or failure following urethroplasty (OR = 1.58, 95% CI [1.13, 2.21], p = .008). Statistical heterogeneity was minimal ($\chi^2 = 6.39$, p = .50, $I^2 = 0\%$), indicating a consistent direction of association across the included studies despite differences in patient characteristics, stricture location, previous interventions, and urethroplasty techniques. The forest plot for the primary dichotomous analysis is presented in Figure 2.

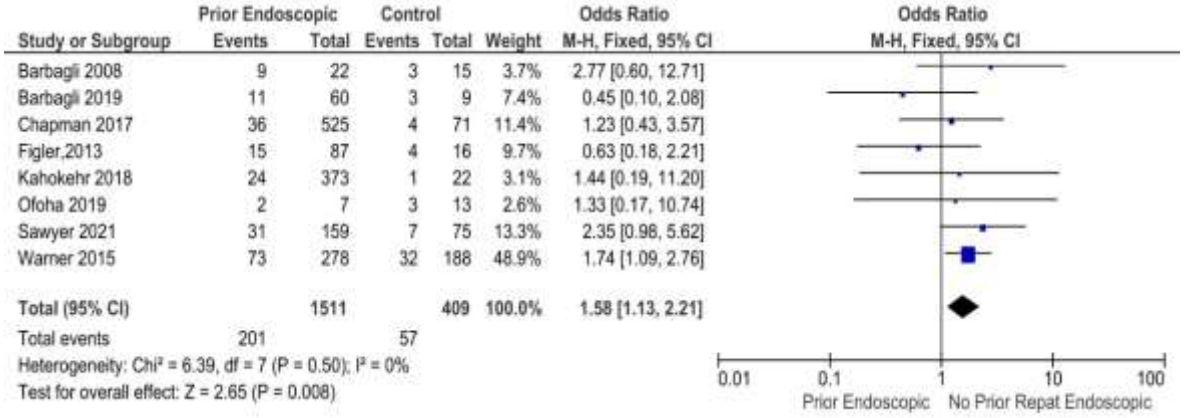

Figure 2. Forest plot of the primary dichotomous meta-analysis evaluating the association between prior endoscopic treatment and recurrence or failure after urethroplasty.

These findings are consistent with observations from individual cohort studies indicating that previous endoscopic manipulation may be associated with more complex stricture characteristics and subsequent treatment challenges (Hudak et al., 2012; Viers et al., 2018; Yildirim et al., 2022).

Time-to-Event Analysis

The primary dichotomous analysis provided evidence of an association between previous endoscopic treatment and poorer urethroplasty outcomes. To further account for differences in follow-up duration and the timing of recurrence, a complementary time-to-event analysis was conducted.

Five studies reported adjusted hazard ratios assessing the association between previous endoscopic treatment and recurrence or failure following urethroplasty. The estimates were pooled using the generic inverse variance method with a random-effects model. The pooled analysis demonstrated that patients with a history of previous endoscopic treatment had a higher hazard of recurrence or failure following urethroplasty (HR = 1.48, 95% CI [1.12, 1.97], p = .006). Moderate heterogeneity was observed across the studies ($\chi^2 = 9.52$, p = .05, $I^2 = 58\%$). This heterogeneity may reflect differences in study design, follow-up duration, stricture characteristics, surgical techniques, definitions of previous endoscopic exposure, and covariates included in the multivariable models. The forest plot of the time-to-event analysis is presented in Figure 3.

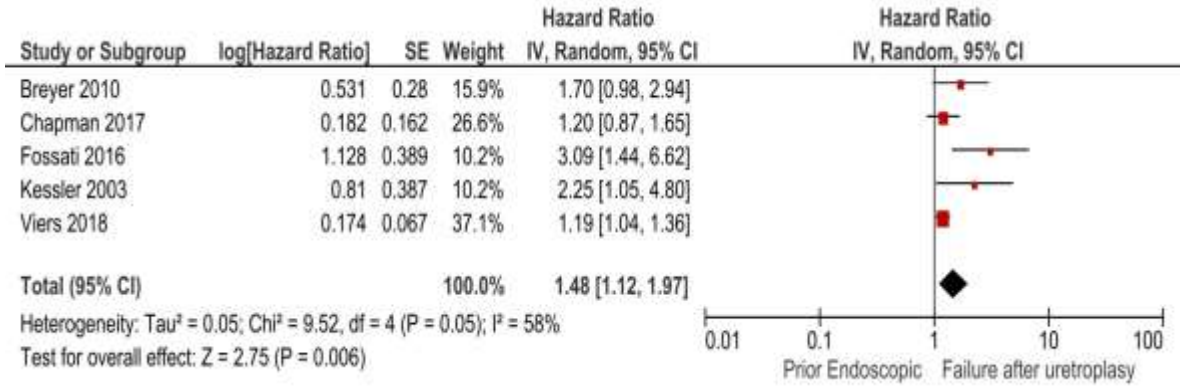

Figure 3. Forest plot of the time-to-event analysis using adjusted hazard ratios to evaluate the association between prior endoscopic treatment and recurrence or failure after urethroplasty.

Subgroup Analysis of Repeated Prior Endoscopic Treatment

Because the time-to-event analysis demonstrated moderate heterogeneity, a prespecified subgroup analysis was conducted to examine whether the number of previous endoscopic interventions influenced postoperative outcomes. Four studies were included in the subgroup analysis comparing patients with repeated prior endoscopic treatment with those without previous endoscopic treatment or with fewer previous procedures. The pooled analysis demonstrated a higher risk of recurrence or failure among patients who had undergone repeated endoscopic treatment (OR = 2.06, 95% CI [1.30, 3.28], p = .002). Statistical heterogeneity was low (χ^2 = 3.64, p = .30, I^2 = 17%), indicating relatively consistent findings across the included studies.

The approximately twofold increase in risk suggests that repeated urethral manipulation before definitive urethroplasty may be associated with less favorable postoperative outcomes. This finding is clinically relevant because previous studies have reported that repeated transurethral manipulation may be associated with greater stricture complexity and prolonged disease duration (Hudak et al., 2012), while delayed reconstruction has been associated with multiple prior interventions and more complex repairs (Viers et al., 2018). The forest plot for the subgroup analysis is presented in Figure 4.

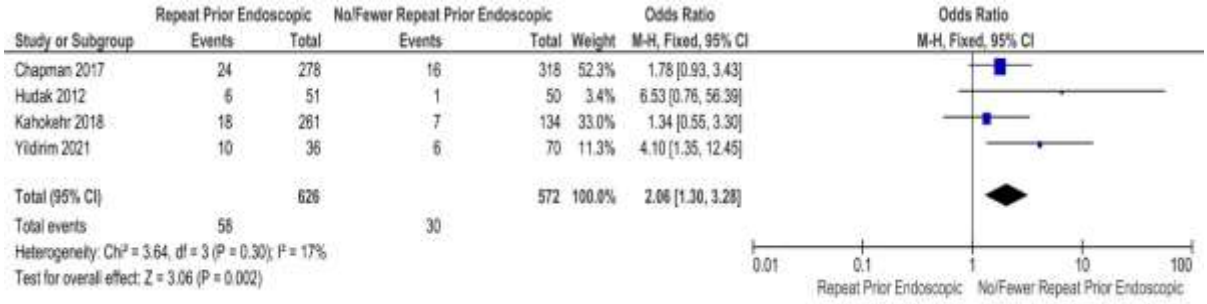

Figure 4. Forest plot of the subgroup analysis comparing repeated prior endoscopic treatment with no or fewer prior endoscopic procedures for recurrence or failure after urethroplasty.

Taken together, the primary dichotomous analysis, time-to-event analysis, and subgroup analysis demonstrate a consistent association between previous endoscopic treatment and poorer outcomes following urethroplasty. The association was more pronounced among patients who had undergone repeated endoscopic procedures, supporting consideration of earlier reconstructive evaluation in patients with recurrent urethral stricture disease.

Publication Bias

Funnel plots were used to visually assess potential publication bias for the primary odds-ratio analysis, the time-to-event analysis, and the subgroup analysis of repeated prior endoscopic treatment. No marked asymmetry was observed in the available funnel plots. However, interpretation of funnel plot symmetry was limited by the small number of studies included in each analysis. Formal statistical tests for funnel plot asymmetry were therefore not performed because each analysis included fewer than 10 studies. Consequently, the possibility of publication bias and small-study effects cannot be completely excluded. The funnel plots are presented in Figure 5

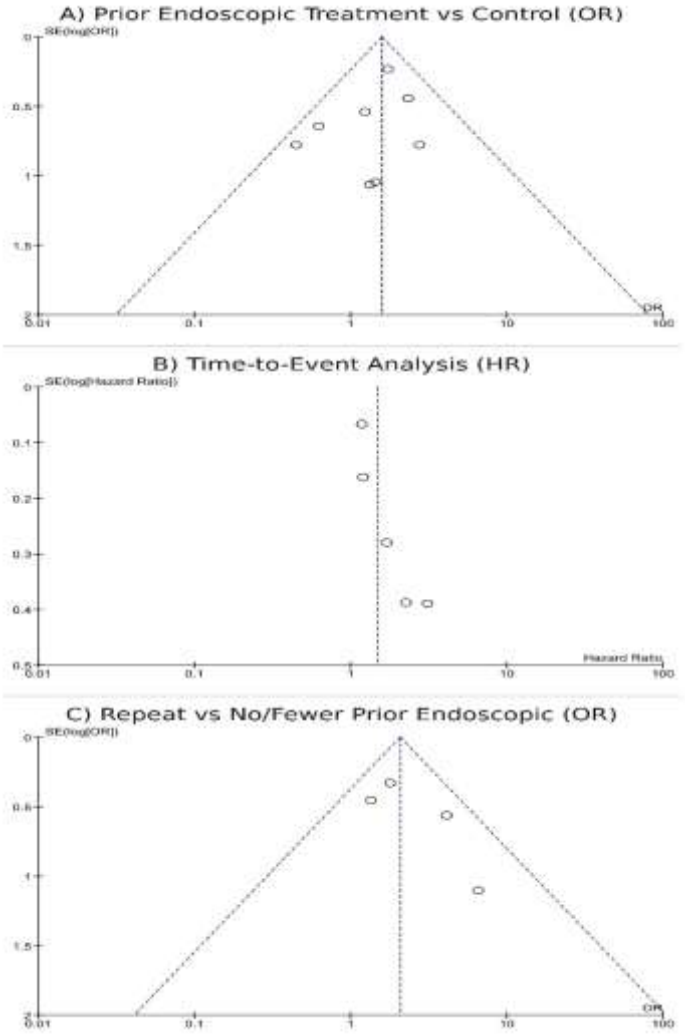

Figure 5. Funnel plots for publication bias assessment. A, primary analysis of prior endoscopic treatment and recurrence or failure after urethroplasty; B, time-to-event analysis using adjusted hazard ratios; C, subgroup analysis of repeated prior endoscopic treatment versus no or fewer prior endoscopic procedures.

DISCUSSION

The primary meta-analysis showed that prior endoscopic treatment was significantly associated with recurrence or failure after anterior urethroplasty (OR = 1.58, 95% CI [1.13, 2.21], p = .008), with no substantial statistical heterogeneity (I^2 = 0%). This finding indicates a relatively consistent association across the included studies despite differences in patient populations, stricture characteristics, and surgical techniques. The consistency of the pooled estimate strengthens the evidence that previous endoscopic intervention may be an important factor to consider when assessing the prognosis of patients undergoing anterior urethroplasty.

This finding was further supported by the time-to-event analysis, which demonstrated an increased risk of recurrence or failure over time among patients with previous endoscopic treatment (HR = 1.48, 95% CI [1.12, 1.97], p = .006). Moderate heterogeneity was observed in this analysis (I^2 = 58%), which may reflect differences in follow-up duration, surgical techniques, stricture characteristics, and covariates included in the adjusted models. Nevertheless, the direction of the pooled association remained consistent with the primary dichotomous analysis, suggesting that the relationship between previous endoscopic treatment and urethroplasty outcomes was not solely attributable to differences in follow-up duration.

The subgroup analysis demonstrated an even stronger association among patients who had undergone repeated prior endoscopic treatment. Patients with repeated endoscopic procedures had approximately twice the risk of recurrence or failure after urethroplasty compared with those with no or fewer prior procedures (OR = 2.06, 95% CI [1.30, 3.28], p = .002; I^2 = 17%). The low heterogeneity observed in this subgroup indicates relatively consistent findings among the contributing studies. These results suggest that the cumulative number of previous endoscopic interventions may have prognostic relevance and should be considered when determining the timing of definitive reconstructive treatment.

The pooled findings are supported by several individual studies. (Chapman et al., 2017) reported that previous DVIU or urethral dilation was associated with recurrence following bulbar urethroplasty (HR = 1.60, p = .03). (Breyer et al., 2010) found that each additional DVIU increased the risk of urethroplasty failure (OR = 1.11 per procedure, p = .04). Similarly, (Hudak et al., 2012) demonstrated lower success rates among patients who had undergone two or more previous transurethral manipulations compared with those who had undergone fewer procedures (66% vs. 91%, p = .01). (Viers et al., 2018) also reported that each additional endoscopic procedure was associated with an increased risk of recurrence (HR = 1.17, 95% CI [1.03, 1.33]). Collectively, these findings are consistent with the present subgroup analysis, which demonstrated an approximately twofold higher risk of recurrence or failure among patients with repeated prior endoscopic treatment.

The association between previous endoscopic treatment and poorer urethroplasty outcomes may be explained by the cumulative effects of repeated urethral manipulation. Repeated instrumentation may contribute to tissue injury, progressive fibrosis, and increased stricture complexity, potentially making subsequent reconstruction more technically demanding. (Hudak et al., 2012) reported that repeated transurethral manipulation was associated with increased stricture complexity and longer disease duration. Similarly, (Viers et al., 2018) found that delayed reconstruction was associated with multiple prior interventions, longer strictures, and more complex repairs. These observations provide a potential clinical explanation for the stronger association observed in the subgroup of patients who underwent repeated endoscopic treatment.

Stricture-related characteristics may also contribute to poorer postoperative outcomes. Longer strictures, penile or penobulbar location, dense spongiofibrosis, inflammatory etiology, and recurrent or complex disease may reduce tissue quality and increase the technical difficulty of urethral reconstruction. Previous studies have identified stricture characteristics as important determinants of urethroplasty outcomes (Breyer et al., 2010; Chapman et al., 2017). Therefore, the observed association between prior endoscopic treatment and recurrence should not necessarily be interpreted as an isolated treatment effect, because repeated endoscopic intervention may also be a marker of more severe or complex underlying stricture disease.

Patient-related factors may provide additional explanations for variation in postoperative outcomes. Conditions such as diabetes mellitus, smoking, obesity, older age, and vascular comorbidities may theoretically affect tissue perfusion and wound healing. However, the evidence regarding these

factors as independent predictors of urethroplasty recurrence is not entirely consistent (Breyer et al., 2010; Chapman et al., 2017). Accordingly, these variables should be regarded as potential contributors rather than definitive predictors of recurrence or treatment failure.

The clinical importance of recurrence is further supported by postoperative surveillance studies. (Anderson et al., 2022) reported recurrence requiring further treatment in 27 of 144 patients (18.75%) following urethroplasty, including diaphragm-type recurrence in 13 patients and significant restenosis in 14 patients. These findings demonstrate that recurrence is not merely an anatomical outcome but may lead to additional postoperative interventions. Similarly, (Vetterlein et al., 2021) reported an 84% satisfaction rate and 85% recurrence-free survival among 534 men undergoing anterior buccal mucosal graft urethroplasty. Among dissatisfied patients, functional recurrence and oral morbidity were important contributors to dissatisfaction, accounting for 28% and 20%, respectively. Impaired postoperative ejaculatory function was also independently associated with dissatisfaction (OR = 2.35, p = .029). Thus, recurrence or treatment failure following urethroplasty may have broader consequences for patient satisfaction, sexual function, and perceived treatment success.

An important strength of the present meta-analysis is the separate synthesis of adjusted hazard ratios. By prioritizing estimates derived from multivariable models, the analysis accounts for potentially important covariates reported in the primary studies, such as stricture length, etiology, and patient characteristics. The pooled adjusted analysis remained statistically significant (HR = 1.48, p = .006), suggesting that the association between previous endoscopic treatment and recurrence was not completely explained by the covariates included in the original models. However, the interpretation should remain cautious because the adjustment sets differed among studies and residual confounding cannot be excluded.

Several limitations should be considered when interpreting these findings. First, all included studies were observational, and most used retrospective designs; therefore, selection bias and residual confounding cannot be excluded. Second, recurrence and failure were analyzed as a composite outcome, although definitions varied among studies and included anatomical recurrence, symptomatic recurrence, postoperative instrumentation, dilation, DVIU, repeat urethroplasty, and other forms of reintervention. Third, previous endoscopic treatment was not uniformly defined, and the number, type, and timing of previous procedures varied across studies. Fourth, the included studies differed in stricture location, length, etiology, urethroplasty technique, follow-up duration, and adjustment for confounding variables. Finally, the limited number of studies in each quantitative analysis restricted the assessment of publication bias and prevented robust evaluation of secondary outcomes, including urinary flow rate, complications, sexual function, patient satisfaction, and operative difficulty.

Directly comparable meta-analytic evidence remains limited because previous studies have largely focused on the durability of endoscopic treatment, comparisons of urethroplasty techniques, or general predictors of stricture recurrence. The present study addresses this evidence gap by specifically evaluating previous endoscopic treatment as a prognostic factor for recurrence or failure following anterior urethroplasty and by separately examining the effect of repeated endoscopic procedures. The findings indicate that previous endoscopic treatment, particularly repeated intervention, is associated with poorer outcomes after urethroplasty. Future prospective studies using standardized definitions of endoscopic exposure, recurrence, and treatment failure are needed to determine whether this association represents a causal effect of repeated instrumentation or partly reflects the greater baseline severity and complexity of the underlying stricture disease.

CONCLUSION

This systematic review and meta-analysis demonstrates that prior endoscopic treatment is significantly associated with an increased risk of recurrence or failure after anterior urethroplasty in adult men with urethral stricture disease. This association was consistent across the primary dichotomous analysis, time-to-event analysis, and subgroup analysis. Importantly, repeated prior endoscopic treatment was associated with an approximately twofold higher risk of recurrence or failure, suggesting that cumulative urethral manipulation before definitive reconstruction may adversely affect urethroplasty outcomes. These findings support earlier referral for urethroplasty in patients with recurrent anterior urethral strictures rather than repeated endoscopic management. However, because the available evidence is derived mainly from observational studies with variable definitions of recurrence, exposure, and follow-uphttps://chatgpt.com/library?entry_point=sidebar.

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