

REVIEW

Functional and safety outcomes after benign prostatic enlargement surgeries in men with detrusor underactivity compared with normal detrusor contractility: Systematic review and meta-analysis

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Abstract

Introduction: Men with detrusor underactivity (DUA) and concomitant bladder outlet obstruction (BOO) due to benign prostatic enlargement (BPE) may present poorer functional outcomes after surgical desobstruction. This study aimed to evaluate the safety and efficacy of BPE surgery in men with DUA compared with those with normal detrusor contractility (NC).

Materials and Methods: This review was performed according to the 2020 PRISMA framework. A comprehensive literature search was performed until May 7, 2023, using MEDLINE, EMBASE, and Cochrane Database. No date limits were imposed. Only comparative studies were accepted. The primary endpoint was to assess if there was any difference in short- and long-term functional outcomes after BPE surgery in men with DUA and NC. The secondary endpoint was to evaluate the differences in perioperative outcomes and postoperative complications between the two groups. Meta-analysis was performed using Review Manager (RevMan) software.

Results: There were 5 prospective nonrandomized studies and 12 retrospective studies, including 1701 DUA and 1993 NC patients. Regarding surgical procedures, there were eight TURP (transurethral resection of the prostate) studies, four GreenLight PVP (photoselective vaporization of the prostate) studies, two HoLEP (Holmium laser enucleation of the prostate) studies, one GreenLight PVP/HoLEP study, one Holmium laser incision of the prostate study, and one study did not report the type of surgery. We did not find a statistically significant difference between the two groups in terms of perioperative outcomes, including postoperative catheterization time, hospitalization time, urinary

Marcelo Langer Wroclawski and Lucas Seiti Takemura contributed equally to this study and serve as the first authors.

Clinical Trial Registration: The protocol of the review was submitted for registration in PROSPERO (receipt 316311).

retention, need to recatheterization, transfusion rate, or urinary tract infections. Also, we found no significant differences in long-term complications, such as bladder neck stenosis or urethral stenosis. Posttreatment bladder recatheterization and retreatment rate for BPE regrowth could not be evaluated properly, because only one study reported these findings. When we analyzed functional outcomes at 3 months, those with NC had lower International Prostatic Symptom Score (IPSS), lower quality-of-life (QoL) score, better maximum flow rate (Qmax), and lower post-voiding residual (PVR) of urine. These results were maintained at 6 months postoperatively, with exception of PVR that showed no difference. However, at 12 and more than 12 months the functional outcomes became similar regarding IPSS and QoL. There were few data about Qmax and PVR at longer follow-up.

Conclusion: In this meta-analysis, data suggest that BOO surgical treatment in patients with concomitant BPE and DUA appears to be safe. Despite patients with DUA may present worse functional outcomes in the short postoperative term compared with the NC population, IPSS and QoL scores become comparable again after a longer follow-up period after surgery.

KEYWORDS

detrusor underactivity, lower urinary tract symptoms, prostate, prostatic hyperplasia, systematic review, transurethral resection of prostate, urodynamics

1 | INTRODUCTION

Normal voiding is achieved by a continuous detrusor contraction that leads to complete bladder emptying within a normal time span, in the absence of obstruction.¹ Therefore, lower urinary tract symptoms (LUTS), especially voiding symptoms, can be caused by impaired bladder contractility or bladder outlet obstruction (BOO). It is important to emphasize, however, that both conditions can coexist in the same patient, making treatment even more challenging.²

The prevalence of detrusor underactivity (DUA) in men with LUTS is 11%–40%.^{3,4} Alongside advancing age, benign prostatic enlargement (BPE) itself has been suggested as a risk factor for DUA and for that reason recommendations to reduce BOO and promote more efficient bladder emptying have emerged to avoid its development or stop its progression.^{5,6}

There remains a great concern in offering surgical treatment to these patients, since functional outcomes may be worse than in men with regular detrusor contractility.⁷

We aimed to systematically review the safety (i.e., complications) and efficacy (i.e., functional outcomes) of surgery for BPE in men with DUA as compared with those with normal contractility (NC).

2 | MATERIALS AND METHODS

2.1 | Aim of the review

The primary endpoint was to assess if there was any difference in short- and long-term functional outcomes after BPE surgery in men with DUA and NC, assessed with the International Prostatic Symptom Score (IPSS) comprising the quality-of-life item (QoL), maximum flow rate (Qmax), post-voiding residual (PVR) of urine, and number of patients catheter-free. The secondary endpoint was to evaluate the differences in perioperative outcomes (i.e., surgical time, postoperative catheterization time, and length of stay), and postoperative complications (fever, urinary tract infection, sepsis, blood transfusion, bladder neck, and urethral stenosis) between the two groups.

2.2 | Literature search

This review was performed according to the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework. A comprehensive literature search was performed until May 7, 2023, using MEDLINE, EMBASE, and Cochrane Central Controlled

Register of Trials (CENTRAL). Medical Subject Heading (MeSH) terms and keywords were used in the following string: (benign prostatic hyperplasia OR benign prostatic hypertrophy OR benign prostatic obstruction OR benign prostatic enlargement OR lower urinary tract symptoms OR bladder outlet obstruction OR LUTS OR BPH OR BPE OR BPO OR BOO) AND (detrusor underactivity OR hypocontractility OR detrusor contractility OR detrusor acontractility OR impaired contractility OR impaired bladder function OR bladder dysfunction OR bladder contractility OR hypocontractile OR acontractile) AND (transurethral resection OR vaporization OR photovaporization OR ablation OR enucleation OR prostatectomy). No date limits were imposed. The search was restricted to English papers only. Preclinical, animal, and pediatric studies were excluded. Only comparative studies were accepted. The protocol of the review was submitted for registration in PROSPERO (receipt 316311).

2.3 | Selection criteria

The PICOS (Patient, Intervention, Comparison, Outcome, Study type) model was used to frame and answer the question. P: men with BPE and surgical indication; I: patients with a preoperative diagnosis of DUA on pressure/flow study; C: patients with NC on a preoperative pressure/flow study; O: perioperative and functional outcomes, and complications after surgery; S: retrospective, prospective randomized and nonrandomized studies.

2.4 | Study screening and selection

Two independent authors screened all retrieved records through Covidence Systematic Review Management® (Veritas Health Innovation). A third author solved discrepancies. Studies were included based on PICOS eligibility criteria. Retrospective, prospective nonrandomized, and randomized studies were accepted. Meeting abstracts, reviews, case reports, letters to the editor, and editorials were excluded. The full text of the screened papers was selected if found relevant to the purpose of this study.

2.5 | Statistical analysis

Meta-analysis was performed using Review Manager (RevMan) 5.4 software by Cochrane Collaboration. Continuous variables were pooled using the inverse

variance of the mean difference with a random effect, 95% confidence intervals (CI), and *p* values. Incidence of complications, retreatment for BPE, and number of patients catheter free after surgery were assessed using Cochran-Mantel-Haenszel Method with the random effect model and reported as odd ratio (OR), 95% CI, and *p* values. Analyses were two-tailed. Significance was set at $p < 0.05$ and a 95% CI. Study heterogeneity was assessed utilizing the I^2 value. An I^2 value $> 50\%$ defined considerable heterogeneity. The quality assessment of the included studies was performed using the Cochrane Risk of Bias tool, ROBINS-I for retrospective and nonrandomized prospective studies.⁸

3 | RESULTS

The initial literature search retrieved 2454 papers. After removing 384 duplicates, 2070 studies were left for screening. Another 1967 papers were excluded against the title and abstract screening because they were unrelated to the purpose of this review. The full texts of the remaining 103 studies were screened and 87 papers were further excluded for lack of specificity of data or duplicate studies. Finally, 17 studies were accepted and included for meta-analysis.^{9–25} Figure 1 shows the PRISMA flow diagram.

3.1 | Study characteristics and quality assessment

Table 1 shows characteristics of the included studies. There were 5 prospective nonrandomized studies^{14,17,18,22,25} and 12 retrospective studies,^{9–13,15,16,19–21,23,24} including 1701 DUA and 1993 NC patients. Regarding surgical procedures and in accordance with the ICS (International Continence Society) report on the terminology for male lower urinary tract surgery,²⁶ there were eight TURP studies, four GreenLight PVP (photoselective vaporization of the prostate; also known as GreenLight laser vaporization of the prostate) studies, two HoLEP studies, one GreenLight PVP/HoLEP study, one Holmium laser incision of the prostate study, and one study did not report the type of surgery. DUA was diagnosed on preoperative pressure/flow study using the bladder contractility index (PdetQmax+5Qmax) less than 100 in 11 studies, Schafer nomogram (weak and very weak bladder contractility) in 5 studies, and PdetQmax of <30 cm H₂O with Qmax <12 mL/s in the remaining one.

Supporting Information: Figure 1 shows the details of quality assessment in the retrospective and prospective nonrandomized studies. Seven studies showed a low

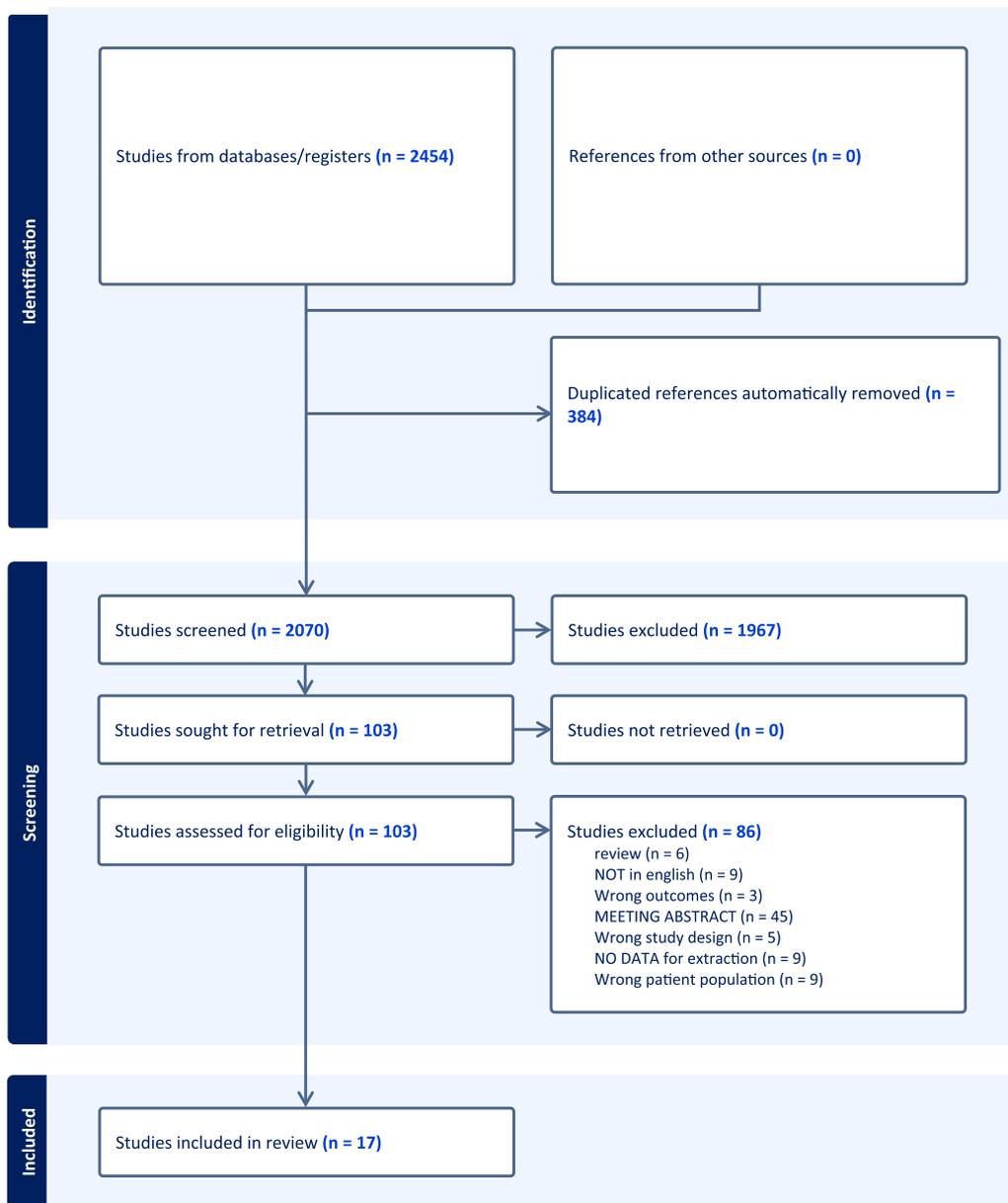


FIGURE 1 PRISMA flow diagram.

overall risk of bias, nine studies had a moderate overall risk of bias, and the remaining one had a serious overall risk of bias. The most common reason for the risk of bias was in selection of the reported results, followed by risk in measurement of outcomes.

3.2 | Meta-analyses of operative and perioperative outcomes

Meta-analysis from four studies (1100 cases in DUA and 965 cases in NC group) showed a significant shorter surgical time in the DUA group (MD -9.02 min 95% CI

-15.69 to 2.35 , $p = 0.008$). Study heterogeneity was considerable (I^2 87%) (Figure 2).

Meta-analysis of three studies (987 cases in DUA and 807 cases in NC group) showed no significant difference in postoperative catheterization time between the groups (MD 0.01 day 95% CI -0.05 to 0.06 , $p = 0.85$). There was no study heterogeneity (I^2 0%) (Figure 3).

Meta-analysis of two studies (855 cases in DUA and 568 cases in NC group) showed no significant difference in postoperative stay between the groups (MD 0.09 day 95% CI -0.10 to 0.29 , $p = 0.34$). There was moderate study heterogeneity (I^2 38%) (Figure 4).

TABLE 1 Characteristics of included studies.

Reference	Type of study	Type of surgery	Inclusion criteria	Exclusion criteria	Definition of DUA	Mean age \pm standard deviation, DUA group, years	Mean age \pm standard deviation, normal contractility group, years
Cho et al. ⁹	Retrospective	HoLEP and Green-Light PVP	LUTS/BPH refractory to medical treatment	Previous diagnosis of urethral stricture, prostate carcinoma, or neurogenic bladder disease, or a previous history of urological surgery	BCI < 100	69.2 \pm 6.6 (HoLEP) 67.9 \pm 8.3 (PVP)	68.3 \pm 6.7 (HoLEP) 67.7 \pm 7.4 (PVP)
Choi et al. ¹⁰	Retrospective	GreenLight PVP	Persistent LUTS even after medical therapy for longer than 3 months and cases in which medications were avoided because of the side effects	Neurogenic bladder, prostate cancer, or urethral stricture	Contractility was lower than weak by the Schäfer nomogram	71.18 \pm 7.87	68.7 \pm 7.3
Dobberfuhl et al. ¹¹	Retrospective	NA	Patients who had desobstructing procedure with complete preoperative urodynamics	Patients whose urodynamics records were not complete	BCI < 100	69 \pm 12	68 \pm 10
Gotoh et al. ¹²	Retrospective	TURP	50–86 years. LUTS and Qmax < 15 mL/s	Neurogenic disorder, neurogenic bladder	Schafer nomogram: very weak, weak, normal, and strong	Not reported	Not reported
Han et al. ¹³	Retrospective	TURP	Patients who underwent TURP for LUTS suggestive of BPH, had preoperative pressure-flow study and were followed-up for at least 12 months after surgery	Underlying neurologic disorders; urinary calculi, urethral stricture, and prostate cancer	BCI < 100	68.5 \pm 8.5	68.0 \pm 6.8
Javlé et al. ¹⁴	Prospective not randomized	TURP	Age > 50 years, IPSS greater than 12, Qmax < 13 mL/s, and residual urine greater than 60 mL	Prostatic cancer, PSA > 4 ng/mL, prior prostatic surgery, residual urinary volume > 300 mL, or neuropathic vesicourethral dysfunction	Schafer nomogram: weak versus normal	Not reported	Not reported
Lebani et al. ²⁵	Prospective not randomized	Monopolar or bipolar TURP	Men with IPSS > 8 who failed to clinical treatment and have been indicated to prostatic surgical procedure	Suspicious or diagnosed prostate cancer, urethral stenosis, and neurological diseases	BCI < 100	70.1 \pm 8.03	69.6 \pm 8.4
Masumori et al. ¹⁵	Retrospective	TURP	Patients with LUTS/BPH aged \geq 50 years	Prostate cancer, neurological diseases, and the impossibility of symptomatic examination	Schafer nomogram: weak/very weak versus normal	Not reported	Not reported

(Continues)

TABLE 1 (Continued)

Reference	Type of study	Type of surgery	Inclusion criteria	Exclusion criteria	Definition of DUA	Mean age \pm standard deviation, DUA group, years	Mean age \pm standard deviation, normal contractility group, years
Monoski et al. ¹⁶	Retrospective	GreenLight PVP	Urinary retention attributed to BPH. Urinary retention was defined as having a postvoiding urine residual >400 mL, the need for an indwelling urethral catheter or suprapubic tube, or the need for clean intermittent catheterization at least once daily. All patients had failed at least one voiding trial and were taking at least one medication for BPH.	Not reported	Pdet Qmax of 30 cm H ₂ O or less and a Qmax of 12 mL/s or less.	Not reported	Not reported
Paick et al. ¹⁷	Prospective not randomized	GreenLight PVP	Age >50 years IPSS > 8 or Qmax <10 mL/s	5-alpha-reductase inhibitor use, presence of an indwelling urinary catheter, previous prostate surgery, urethral stricture, prostate malignancy, and neurogenic bladder disease	BCI < 100	70.8 \pm 6.5	69.6 \pm 3.4
Plata et al. ¹⁸	Prospective not randomized	GreenLight PVP	LUTS/BPH refractory to medical treatment	pelvic radiotherapy, neurogenic bladder, history of previous prostatic intervention, urethral stricture, and prostate cancer	BCI < 100	65 \pm 9.01	65 \pm 7.48
Pyun et al. ¹⁹	Retrospective	HoLEP	Patients undergoing HoLEP	Patients with a known previous neurogenic etiology	BCI < 100	71.8 \pm 8.1	70 (6.9)
Ryoo et al. ²⁰	Retrospective	HoLEP	LUTS due to BPH	Underlying neurologic disorders or other urologic diseases	BCI < 100	69.2 \pm 6.2	67.2 \pm 8.1
Tanaka et al. ²²	Prospective not randomized	TURP	Patients with LUTS/BPH aged >50	Patients with urinary retention, prostate cancer, and a history of prostatic surgery	Using Schäfer's diagram provided by the maximum flow rate and detrusor pressure at maximum flow	Not reported	Not reported

TABLE 1 (Continued)

Reference	Type of study	Type of surgery	Inclusion criteria	Exclusion criteria	Definition of DUA	Mean age \pm standard deviation, DUA group, years	Mean age \pm standard deviation, normal contractility group, years
Zhong et al. ²³	Retrospective	TURP	Patients having received TURP for BPH	History of prostatic and/or urethral surgery; history of pelvic mass and pelvic surgery; neurogenic bladder dysfunction; bladder neoplasm, bladder neck contracture, bladder stones, or urethral stricture; prostate cancer; inability to void during the pressure flow study; LUTS medications within 2 weeks before the evaluation	BCI < 100	Not reported	Not reported
Zhu et al. ²⁴	Retrospective	TURP	Patients with LUTS as a result of BPO who underwent TURP	History of prostate surgery, or urethral surgery, urethral stricture, prostate cancer, bladder cancer, bladder stone, neurogenic bladder, history of neurological disease, acute or chronic bladder or prostatic inflammation, pharmaceutical treatment for LUTS at least 2 weeks before a urodynamic study and failure to undergo a urodynamic study	BCI < 100	Not reported	Not reported
Suh et al. ²¹	Retrospective	Holmium TUIP	BPH patients unresponsive to medical treatment	Neurologic disorders or concomitant urinary calculi, urethral stricture, or prostate cancer	BCI < 100	60.0 \pm 10.1	60.6 \pm 10.7

Abbreviations: BCI, bladder contractility index (BCI = PdetQmax + 5Qmax); BPH, benign prostatic hyperplasia; DUA, detrusor underactivity; HoLEP, holmium laser enucleation of the prostate; LUTS, lower urinary tract symptoms; PVP, prostate photo vaporization; TUIP, transurethral incision of the prostate; TURP, transurethral resection of the prostate.

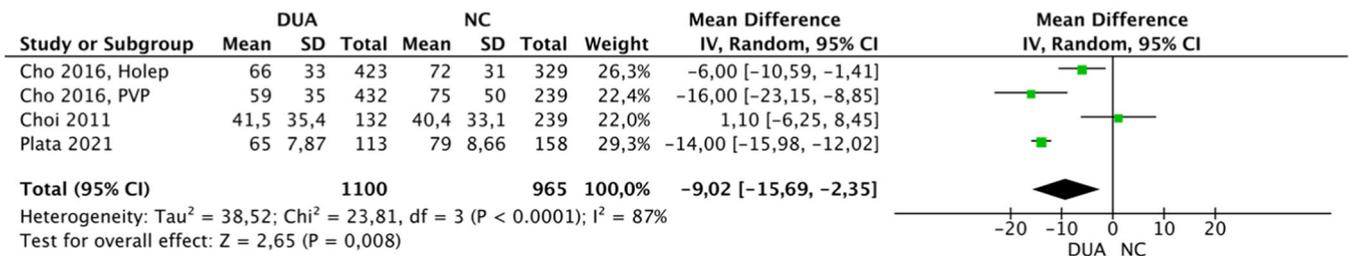


FIGURE 2 Comparison of surgical time between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility.

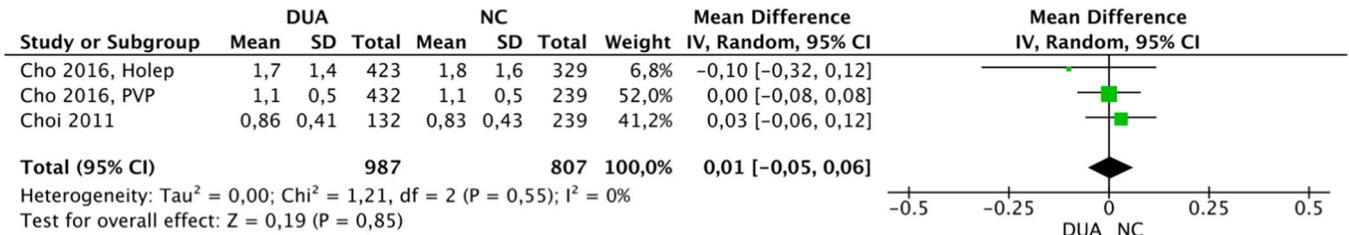


FIGURE 3 Comparison of postoperative catheterization time between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility.

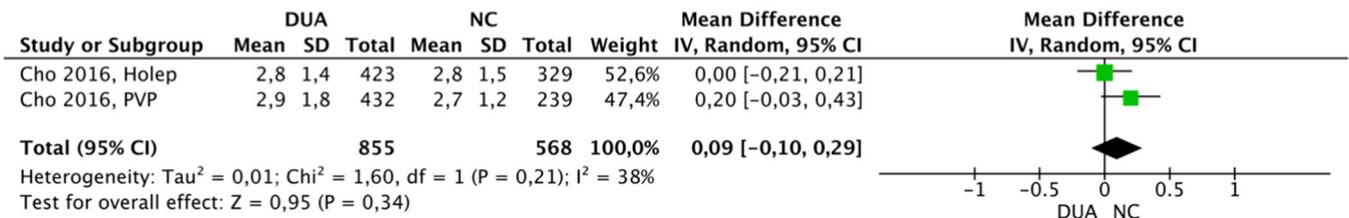


FIGURE 4 Comparison of postoperative stay between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility.

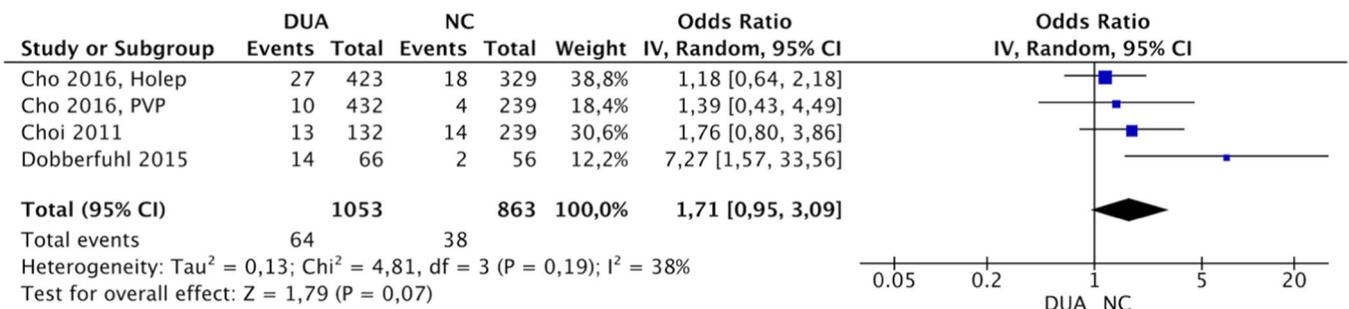


FIGURE 5 Comparison of postoperative recatheterization for urinary retention between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility.

3.3 | Meta-analyses of postoperative complications

Meta-analysis from four studies (1053 cases in DUA and 863 cases in NC group) showed that the

incidence of postoperative recatheterization for urinary retention did not reach statistical significance between the two groups (OR 1.71 95% CI 0.95–3.09, $p = 0,07$) Study heterogeneity was moderate (I^2 38%) (Figure 5).

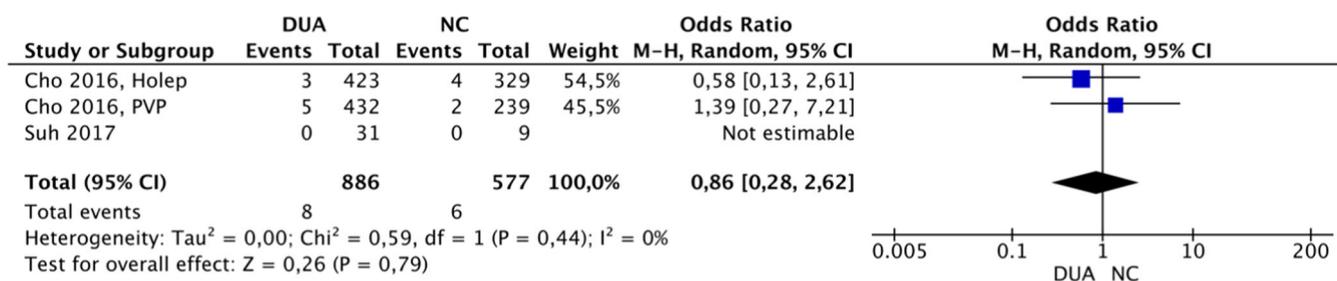


FIGURE 6 Comparison of blood transfusion rate between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility.

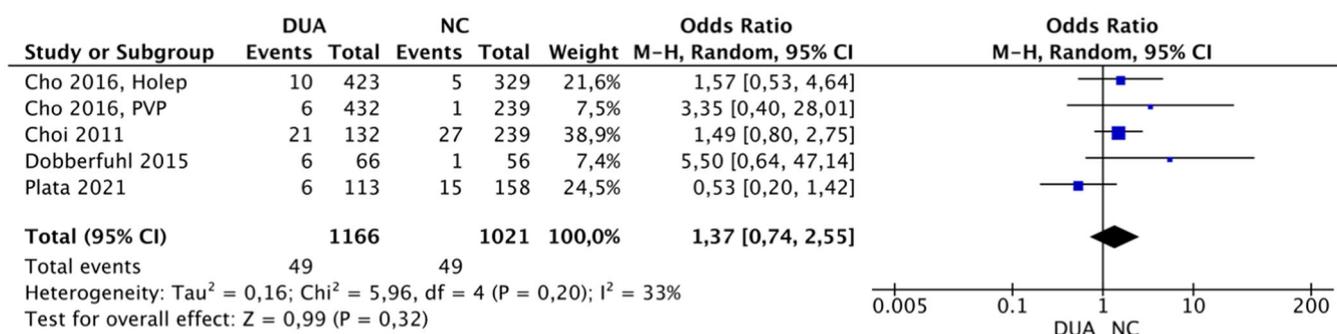


FIGURE 7 Comparison of urinary tract infection rate between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility.

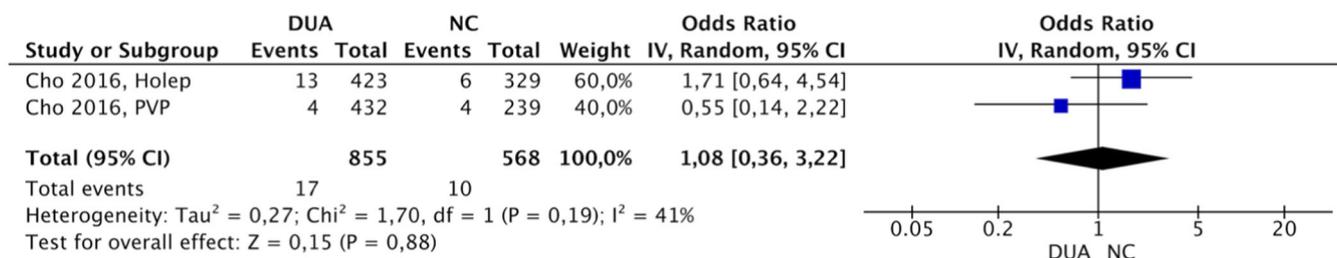


FIGURE 8 Comparison of urethral stenosis rate between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility.

Meta-analysis from three studies (886 cases in DUA and 577 cases in NC group) showed that blood transfusion rate did not differ between the two groups (OR 0.86 95% CI 0.28–2.62, $p = 0.79$). There was no study heterogeneity (I^2 0%) (Figure 6).

Meta-analysis from five studies (1166 cases in DUA and 1021 cases in NC group) showed that urinary tract infection rate did not differ significantly between the groups (OR 1.37 95% CI 0.74–2.55, $p = 0.32$). Study heterogeneity was moderate (I^2 33%) (Figure 7).

There was only one study reporting the incidence of fever and sepsis, making meta-analysis not feasible.

3.4 | Meta-analyses of postoperative long-term complications

Meta-analysis from two studies (855 cases in DUA and 568 cases in NC group) showed no significant difference in the occurrence of urethral stenosis between the two groups (OR 1.08 95% CI 0.36–3.22, $p = 0.88$). Study heterogeneity was moderate (I^2 41%) (Figure 8).

Meta-analysis from two studies (855 cases in DUA and 568 cases in NC group) showed no significant difference in the occurrence of bladder neck stenosis between the two groups (OR 1.98 95% CI 0.49–7.97, $p = 0.34$). Study heterogeneity was low (I^2 8%) (Figure 9).

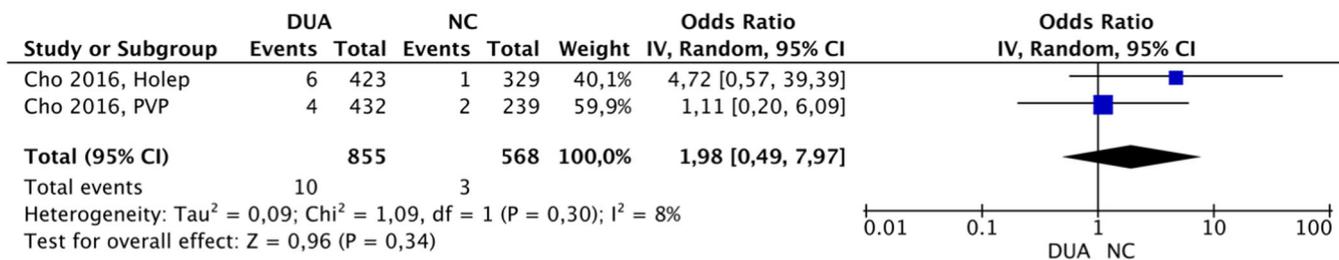


FIGURE 9 Comparison of bladder neck stenosis rate between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility.

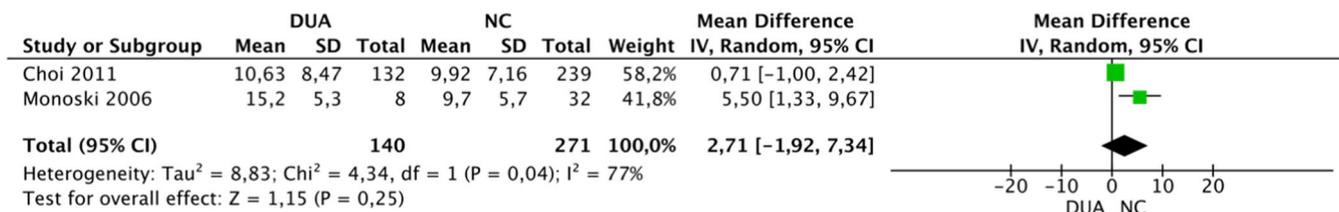


FIGURE 10 Comparison of IPSS score 1 month after surgery between DUA and NC groups. DUA, detrusor interactivity; IPSS, International Prostatic Symptom Score; NC, normal contractility.

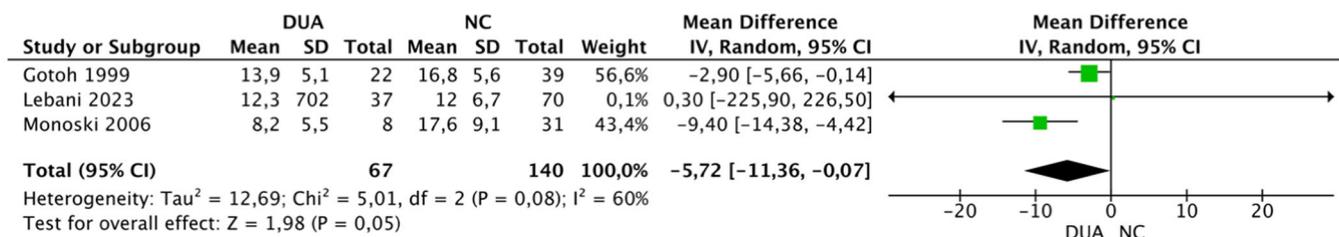


FIGURE 11 Comparison of Qmax 1 month after surgery between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility; Qmax, maximum flow rate.

There was only one study reporting the reoperation rate for BPE regrowth and the number of patients catheter free at follow-up, making meta-analysis not feasible.

3.5 | Meta-analyses of functional outcomes at 1 month

Meta-analysis from two studies (140 cases in DUA and 271 cases in NC group) showed that there was no difference in IPSS score between the two groups (MD 2.71 points 95% CI -1.92 to 7.34, $p = 0.25$). Study heterogeneity was considerable (I^2 77%) (Figure 10).

Meta-analysis from three studies (67 cases in DUA and 140 cases in NC group) showed that Qmax difference between groups did not reach statistical

significance (MD -5.72 mL/s 95% CI -11.36 to 0.07, $p = 0.05$). Study heterogeneity was considerable (I^2 60%) (Figure 11).

Meta-analysis from two studies (30 cases in DUA and 70 cases in NC group) showed that PVR did not differ between the two groups (MD 89.26 mL 95% CI -118.76 to 297.29, $p = 0.40$). Study heterogeneity was considerable (I^2 74%) (Figure 12).

There was only one study reporting QoL, making meta-analysis not feasible.

3.6 | Meta-analyses of functional outcomes at 3 months

Meta-analysis from seven studies (309 cases in DUA and 519 cases in NC group) showed that IPSS score was

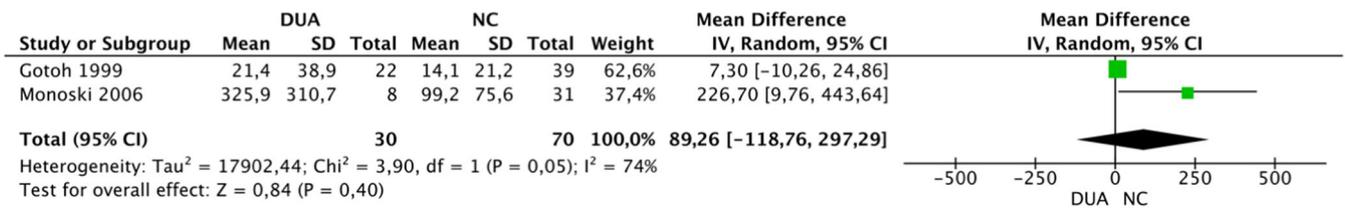


FIGURE 12 Comparison of PVR 1 month after surgery between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility; PVR, post-voiding residual.

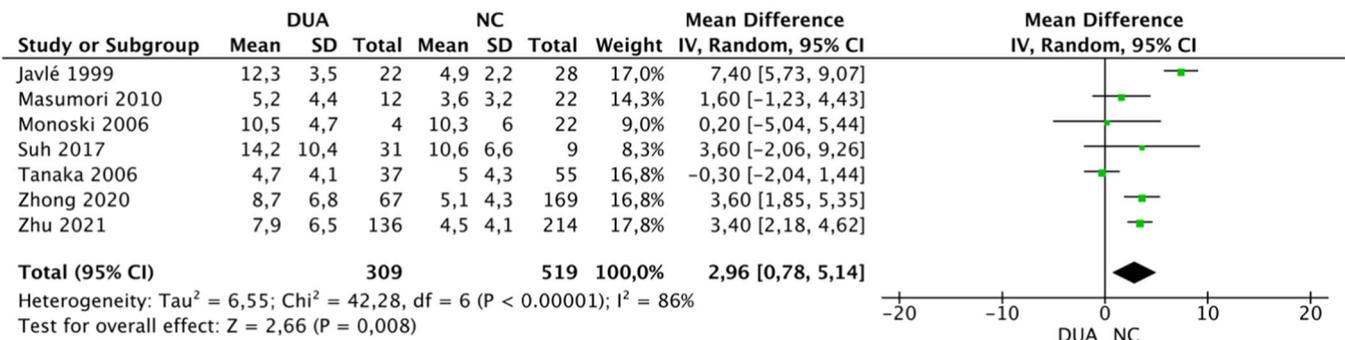


FIGURE 13 Comparison of IPSS score 3 months after surgery between DUA and NC groups. DUA, detrusor interactivity; IPSS, International Prostatic Symptom Score; NC, normal contractility.

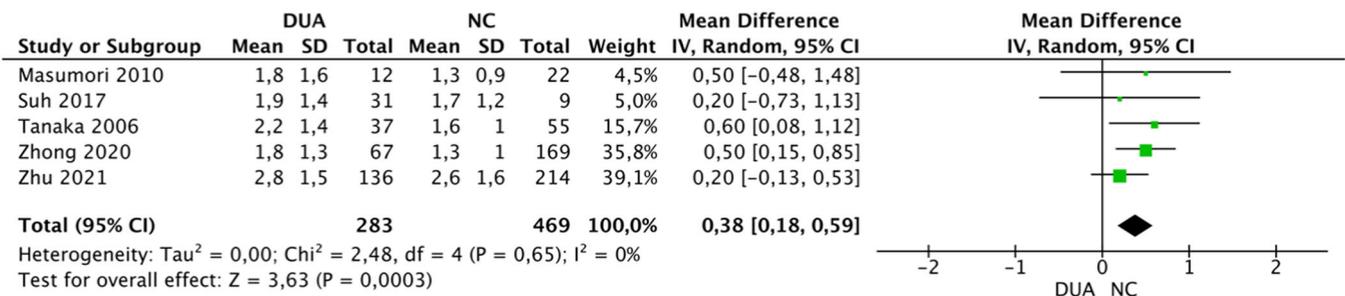


FIGURE 14 Comparison of QoL score 3 months after surgery between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility; QoL, quality-of-life.

significantly lower in the NC group (MD 2.96 points 95% CI 0.78–5.14, $p = 0.008$). Study heterogeneity was considerable (I^2 86%) (Figure 13).

Meta-analysis from five studies (283 cases in DUA and 469 cases in NC group) showed that QoL score was significantly lower in the NC group (MD 0.38 points 95% CI 0.18–0.59, $p = 0.0003$). There was no study heterogeneity (I^2 0%) (Figure 14).

Meta-analysis from six studies (298 cases in DUA and 513 cases in NC group) showed that Qmax was significantly lower in the DUA group (MD -13.58 mL/s 95% CI -22.54 to -4.63 , $p = 0.003$). Study heterogeneity was considerable (I^2 94%) (Figure 15).

Meta-analysis from six studies (298 cases in DUA and 513 cases in NC group) showed that PVR was

significantly lower in the NC group (MD 19.21 mL 95% CI 2.82–35.60, $p = 0.02$). Study heterogeneity was considerable (I^2 83%) (Figure 16).

3.7 | Meta-analyses of functional outcomes at 6 months

Meta-analysis from three studies (170 cases in DUA and 297 cases in NC group) showed that IPSS score was significantly lower in the NC group (MD 3.05 points 95% CI 0.90–5.20, $p = 0.005$). Study heterogeneity was moderate (I^2 57%) (Figure 17).

Meta-analysis from three studies (170 cases in DUA and 297 cases in NC group) showed that QoL score was

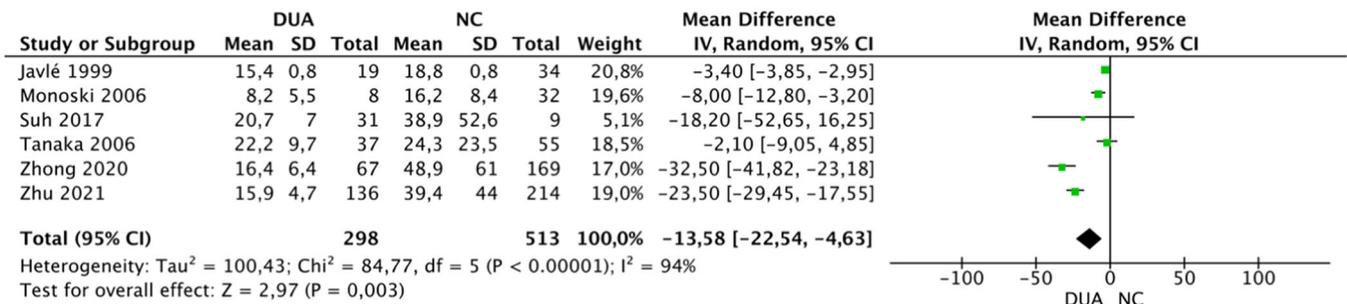


FIGURE 15 Comparison of Qmax 3 months after surgery between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility; Qmax, maximum flow rate.

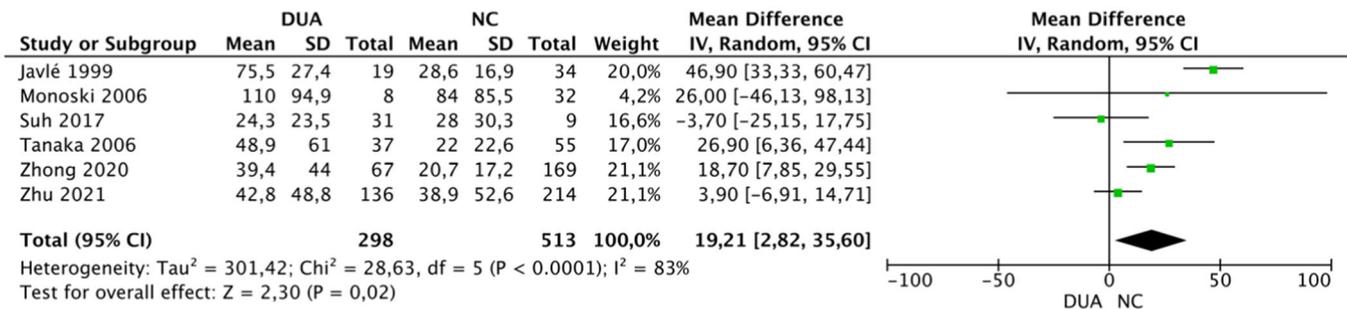


FIGURE 16 Comparison of PVR 3 months after surgery between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility; PVR, post-voiding residual.

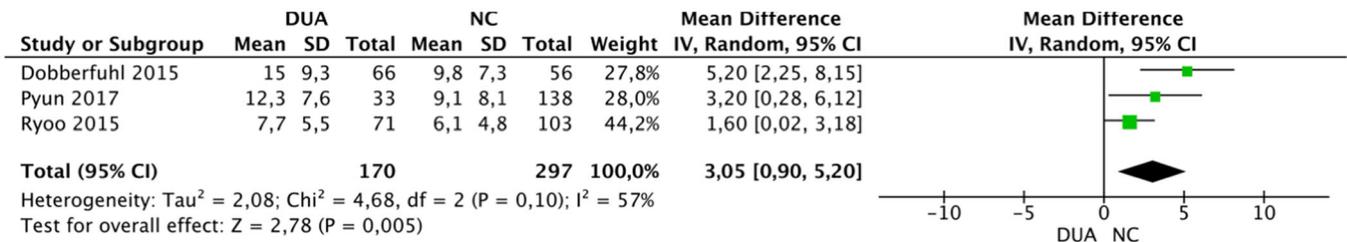


FIGURE 17 Comparison of IPSS score 6 months after surgery between DUA and NC groups. DUA, detrusor interactivity; IPSS, International Prostatic Symptom Score; NC, normal contractility.

significantly lower in the NC group (MD 0.61 points 95% CI 0.16–1.05, $p = 0.007$). Study heterogeneity was moderate (I^2 59%) (Figure 18).

Meta-analysis from four studies (207 cases in DUA and 367 cases in NC group) showed that Qmax was significantly lower in the DUA group (MD -4.92 mL/s 95% CI -7.52 to -2.32 , $p < 0.0002$). Heterogeneity was significant (I^2 71%) (Figure 19).

Meta-analysis from three studies (170 cases in DUA and 297 cases in NC group) showed that PVR did not differ significantly between the two groups (MD 1.59 mL 95% CI -11.06 to 14.25 , $p = 0.81$). Study heterogeneity was low (I^2 12%) (Figure 20).

3.8 | Meta-analyses of functional outcomes at 12 months

Meta-analysis from two studies (166 cases in DUA and 273 cases in NC group) showed that IPSS score did not differ between the two groups (MD 0.94 points 95% CI -0.60 to 2.48 , $p = 0.23$). There was no study heterogeneity (I^2 0%) (Figure 21).

Meta-analysis from two studies (166 cases in DUA and 273 cases in NC group) showed that QoL score did not differ between the two groups (MD 0.36 points 95% CI -0.99 to 1.70 , $p = 0.60$). Study heterogeneity was significant (I^2 94%) (Figure 22).

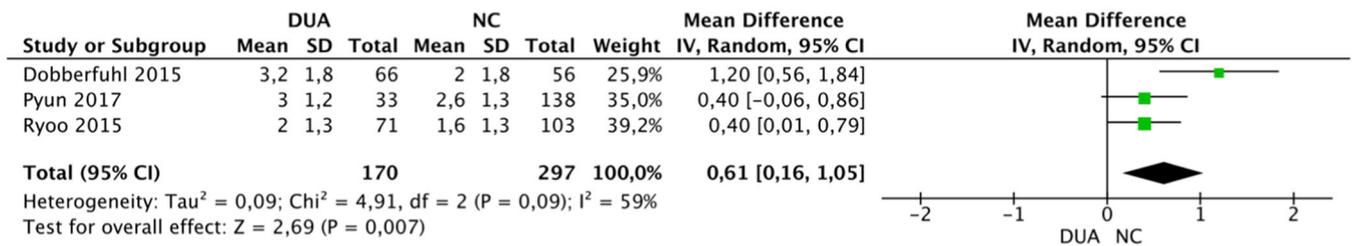


FIGURE 18 Comparison of QoL score 6 months after surgery between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility; QoL, quality-of-life.

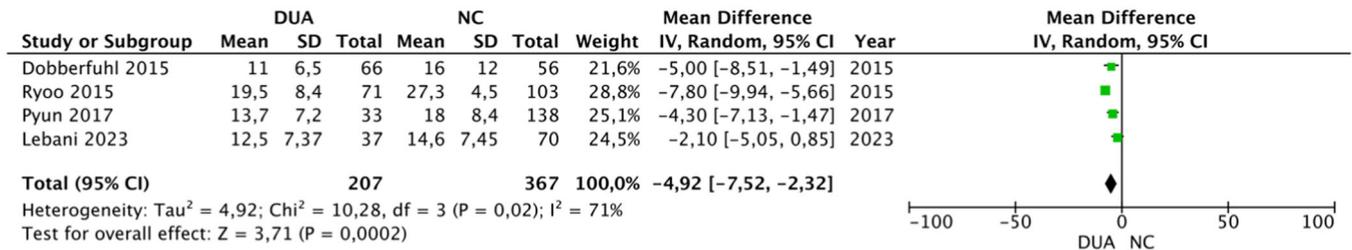


FIGURE 19 Comparison of Qmax 6 months after surgery between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility; Qmax, maximum flow rate.

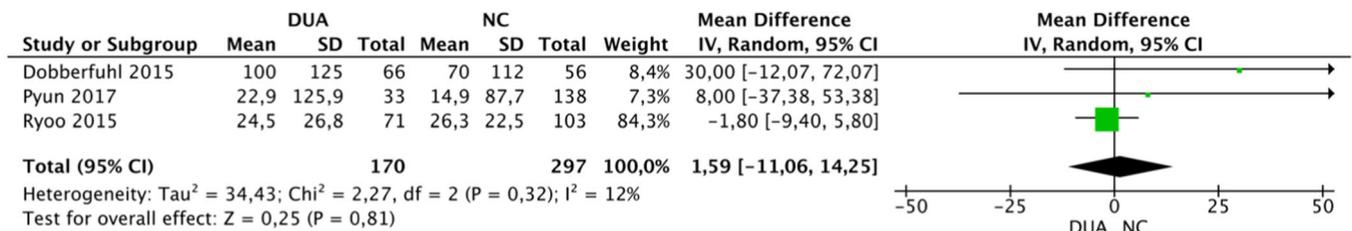


FIGURE 20 Comparison of PVR 6 months after surgery between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility; PVR, post-voiding residual.

There was only one study reporting Qmax and PVR, making meta-analysis not feasible.

There was only one study reporting Qmax and PVR, making meta-analysis not feasible.

3.9 | Meta-analyses of functional outcomes at more than 12 months

Meta-analysis from two studies (37 cases in DUA and 68 cases in NC group) showed that IPSS score did not differ significantly between the two groups (MD 4.88 points 95% CI -3.21 to 12.97 , $p = 0.24$). Study heterogeneity was considerable (I^2 77%) (Figure 23).

Meta-analysis from two studies (37 cases in DUA and 68 cases in NC group) showed that QoL score between groups was not statistically significant (MD 1.00 point 95% CI -0.07 to 2.07 , $p = 0.07$). Study heterogeneity was moderate (I^2 33%) (Figure 24).

4 | DISCUSSION

Diagnosing DUA without the use of pressure/flow study (PFS) is challenging. Unlike overactive bladder (OAB), where the presence of urgency and increase of frequency can define it, there is no pathognomonic symptom that can define the diagnosis of DUA. Patients with DUA may have symptoms that overlap those seen in OAB and in BOO, such as straining, weak stream, hesitancy, urinary frequency, and nocturia. These symptoms make the distinction between these two entities problematic without an invasive PFS, and it is important to emphasize that DUA and BOO can coexist in some patients, especially in the elderly.²

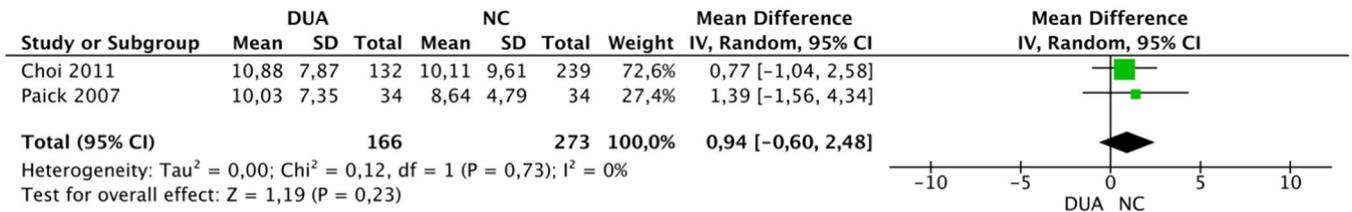


FIGURE 21 Comparison of IPSS score 12 months after surgery between DUA and NC groups. DUA, detrusor interactivity; IPSS, International Prostatic Symptom Score; NC, normal contractility.

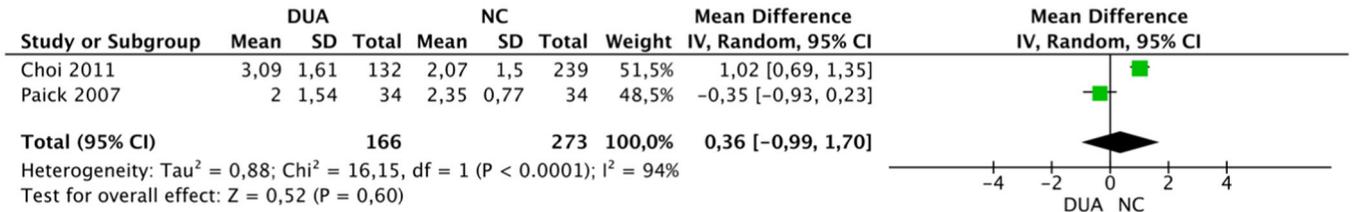


FIGURE 22 Comparison of QoL score 12 months after surgery between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility; QoL, quality-of-life.

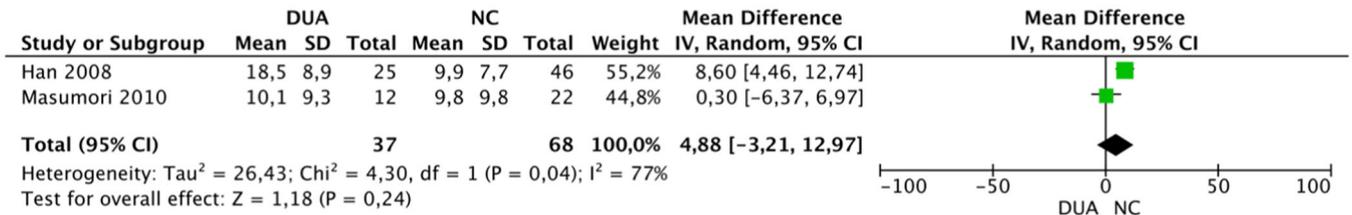


FIGURE 23 Comparison of IPSS score more than 12 months after surgery between DUA and NC groups. DUA, detrusor interactivity; IPSS, International Prostatic Symptom Score; NC, normal contractility.

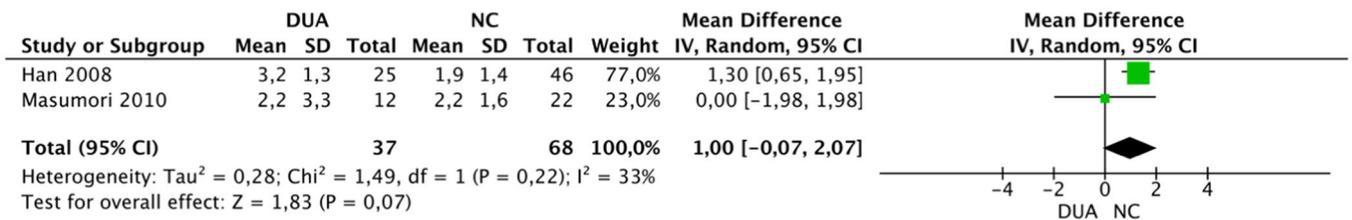


FIGURE 24 Comparison of QoL score more than 12 months after surgery between DUA and NC groups. DUA, detrusor interactivity; NC, normal contractility; QoL, quality-of-life.

Even in the setting of invasive urodynamics there is no single, universally accepted criterion for diagnosing DUA,²⁷ with multiple methods being applied, such as maximum Watt Factor (WFmax) of $<7-10$,^{28,29} Bladder Contractility Index (BCI) of <100 ,³⁰ and association of absolute values of urodynamic parameters, such as a PdetQmax <40 cm H₂O associated with a Qmax <15 mL/s. All of these criteria have their own advantages and limitations, as does the indication of invasive urodynamics

before surgery for LUTS, since the results may not impact surgical decision.³¹

The rationale of performing PFS before endoscopic treatment for BOO is to diagnose concomitant DUA, which is present in 11%–40% of men with LUTS.^{3,4} The presence of DUA in men with LUTS has been postulated to be associated with long-term treatment failure and lower Qmax after surgery,⁷ an important finding when counseling patients before the procedure. However, since

PFS is an invasive exam, it may be unpractical to be performed in all patients with LUTS, being strictly recommended for those with a higher risk of having DUA, such as patients in age extremes (>80 years and <50 years), associated neurological conditions and those with bladder emptying issues (PVR > 300 mL or patients who cannot void more than 150 mL).³²

In this meta-analysis, however, we did not find a statistically significant difference between DUA and NC groups in the postoperative catheterization time, hospitalization time, urinary retention, need to recatheterization, transfusion rate, or urinary tract infections. This highlights that BPE surgery in DUA patients is as safe as in NC patients in the immediate postoperative period. Nonetheless, surgery in DUA group was statistically shorter. Three studies reported surgical time (one of those, had stratified data on PVP and HoLEP groups)^{9,10,18} and differences might be explained by a greater total prostate volume consistently reported on the NC groups in all three comparisons that found a shorter surgical time on DUA group.^{9,10,18} This is consistent with clinical practice, and it is assumed that less prostate tissue can be retrieved in a shorter surgical time.

We found no significant differences between long-term complications, such as bladder neck stenosis or urethral stenosis. Unfortunately, retreatment rate for BPE regrowth was reported in only one trial. Taken together, our results suggest that BPE surgery seems to be equally safe regarding long-term complications between DUA and NC patients.

When we analyze functional outcomes at 1 month, three studies were included and both groups showed similar results regarding IPSS score, Qmax, and PVR. At 3 months, on the other hand, a larger number of patients were evaluated and those with NC had lower IPSS score, lower QoL score, better Qmax, and lower PVR. These results were maintained at 6 months postoperatively, with exception of PVR that showed no difference between groups. It is hard to say if a mean difference of two to three points in IPSS score between groups is clinically significant, but the fact is that Qmax mean difference at 3 months was relevant (13.58 mL/s), favoring the NC group. However, at 12 and more than 12 months after surgery, the functional outcomes become similar again regarding IPSS and QoL. There were few data about Qmax and PVR at longer follow-up. Paick¹⁷ showed that when KTP (Potassium-Titanyl-Phosphate) PVP was performed in patients with DUA, the Qmax went from 9.7 mL/s at baseline to 13.8 mL/s at 12-month follow-up, while patients with NC had a baseline Qmax of 10 mL/s and a postoperative Qmax of 17.9 mL/s. This difference at 12 months was statistically significant ($p = 0.023$). Conversely, Choi¹⁰ studied 120 W Greenlight

HPS Laser PVP and reported a Qmax of 15.53 mL/s in NC group and a Qmax of 13.94 mL/s in DUA group at 12-month follow-up, without statistical significance. Unfortunately, standard deviation was not informed in this later study and, therefore, it could not be included in our meta-analysis. Other studies reported only the delta values regarding treatment outcomes, and we could not perform statistical analysis properly either.

According to our findings, patients with DUA that proceed to surgery may have worse functional outcomes in the short-term postoperative course compared with the NC population, but the results at long-term follow-up seem to be comparable between these groups. The main hypothesis here is that bladder contractility tends to improve after BOO relief,³³ but it takes time. Unfortunately, none of the prospective studies focused on re-evaluating the BCI in postoperative urodynamics to confirm this theory. However, a retrospective analysis evaluated men with urodynamic DUA who underwent TURP or TUIP (transurethral incision of the prostate) and found that 81.7% of the participants achieved a satisfactory outcome, defined as improved quality of life and having a voiding efficiency of >50% after treatment. In the satisfactory treatment group, mean BCI significantly increased from 16.4 at baseline to 61.0 postsurgery.³⁴

Although the exact etiology of DUA remains elusive, a variety of pathophysiological processes, including BOO and advanced age, has been suggested as risk factors.⁵ The impact of an increase in bladder outlet resistance on voiding can be more significant in men with both BPE and DUA,¹² and a strong recommendation has been made that a reduction of any degree of BOO can promote more efficient bladder emptying preventing worsening of DUA. Therefore, patients diagnosed with DUA should probably have surgery to relieve outlet resistance and perhaps improve their contractility or at least improve voiding. Among surgical interventions for BPE, TURP is still the most performed procedure.^{35,36} However, endoscopic enucleation is emerging as a potential new gold standard.^{37,38} However, there has been no consensus on which of these techniques have the best outcomes in patients with DUA.

An interesting prospect of improving outcomes of patients with DUA would be to offer potential treatments targeted to improve detrusor function and then offer a BPE surgery as the first step to maximize the outcomes in these patients. This could range from the use of pharmacogenetic therapies,³⁹ stem cells or regenerative therapy,⁴⁰ gene therapy,⁴¹ and neuromodulation.⁴²

This study has its limitations. This study lacks the inclusion of randomized controlled trials. While there was a total of 17 studies included, most of our meta-analysis

have evaluated only two or three studies to evaluate the outcomes. This affected our meta-analysis due to the small number of studies/sample sizes available to qualitatively measure some outcomes. Furthermore, the heterogeneity in the composite studies, variability in patients in terms of selection bias due to comorbidity and prostate volume and other factors, as well as an array of procedures (HoLEP, TURP, and PVP), hampered the capacity for extrapolation. We also do not have data on reoperation rate for BPE regrowth and the number of patients catheter-free at long-term follow-up.

5 | CONCLUSION

In this meta-analysis, we found that BOO surgical treatment in patients with concomitant BPE and DUA appears to be safe. DUA patients have similar perioperative outcomes compared with NC ones.

Despite patients with DUA may present worse functional outcomes in the short postoperative term compared with the NC population, IPSS and QoL scores become comparable again after a longer follow-up period after surgery.

AUTHOR CONTRIBUTIONS

Study concept and design: Marcelo Langer Wroclawski, Vineet Gauhar, Jeremy Yuen-Chun Teoh, and Daniele Castellani. *Acquisition of data:* Marcelo Langer Wroclawski, Lucas Seiti Takemura, Hugo Octaviano Duarte Santos, Flavio Lobo Heldwein, Vineet Gauhar, Ee Jean Lim, Yu Xi Terence Law, Jeremy Yuen-Chun Teoh, and Daniele Castellani. *Analysis and interpretation of data:* Lucas Seiti Takemura, Hugo Octaviano Duarte Santos, Flavio Lobo Heldwein, and Daniele Castellani. *Drafting of the manuscript:* Marcelo Langer Wroclawski, Lucas Seiti Takemura, Hugo Octaviano Duarte Santos, Flavio Lobo Heldwein, Vineet Gauhar, Ee Jean Lim, Yu Xi Terence Law, Jeremy Yuen-Chun Teoh, and Daniele Castellani. *Critical revision of the manuscript for important intellectual content:* Marcelo Langer Wroclawski, Vineet Gauhar, Jeremy Yuen-Chun Teoh, Thomas Reinhard William Herrmann, and Daniele Castellani. *Statistical analysis:* Daniele Castellani. *Supervision:* Marcelo Langer Wroclawski. All authors read and approved the final draft and manuscript before submission.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The study is a systematic review and meta-analysis that retrieved and analyzed data from already published studies. The study is a systematic review and meta-analysis that retrieved and analyzed data from already published studies. Informed consent should have been obtained by primary investigators.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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