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Review – Benign Prostatic Obstruction

Management of Primary Bladder Neck Obstruction and Dysfunctional Voiding in Young Men: A Systematic Review and Meta-analysis

Massimiliano Creta [a,†,*], *Michael Baboudjian* [b,†], *Vasileios Sakalis* [c], *Nikita Bhatt* [d], *Cosimo De Nunzio* [e], *Mauro Gacci* [f,g], *Thomas R.W. Herrmann* [h], *Markos Karavitakis* [i], *Sachin Malde* [j], *Lisa Moris* [k,l], *Christopher Netsch* [m], *Malte Rieken* [n], *Natasha Schouten* [o], *Manuela Tutolo* [p], *Yuhong Yuan* [q], *Hashim Hashim* [r], *Jean-Nicolas Cornu* [s]

[a] *Department of Neurosciences, Reproductive Sciences and Odontostomatology, University of Naples "Federico II", Naples, Italy;* [b] *Department of Urology, APHM, North Academic Hospital, Marseille, France;* [c] *Department of Urology, Hippokrateion General Hospital, Thessaloniki, Greece;* [d] *Department of Urology, East of England Deanery, Urology, Cambridge, UK;* [e] *Department of Urology, Sapienza University, Ospedale Sant'Andrea, Rome, Italy;* [f] *Unit of Urological Robotic Surgery and Renal Transplantation, University of Florence, Careggi Hospital, Florence, Italy;* [g] *Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy;* [h] *Department of Urology, Spital Thurgau AG, Kantonsspital Frauenfeld, Frauenfeld, Switzerland;* [i] *Department of Urology, "CENTRAL UROLOGY", Lefkos Stavros the Athens Clinic, Athens, Greece;* [j] *Department of Urology, Guy's and St Thomas' NHS Foundation Trust, London, UK;* [k] *Department of Urology, University Hospitals Leuven, Leuven, Belgium;* [l] *Laboratory of Molecular Endocrinology, KU Leuven, Leuven, Belgium;* [m] *Department of Urology, Asklepios Klinik Barmbek, Hamburg, Germany;* [n] *University of Basel, Basel, Switzerland;* [o] *European Association of Urology Guidelines Office, Arnhem, The Netherlands;* [p] *Department of Urology, URI, IRCCS Ospedale San Raffaele, Milan, Italy;* [q] *Department of Medicine, London Health Science Center, Western University, London, ON, Canada;* [r] *Bristol Urological Institute, Bristol, UK;* [s] *Department of Urology, CHU Hôpitaux de Rouen - Hôpital Charles Nicolle, Rouen, France*

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Abstract

Background and objective: Management of young men with primary bladder neck obstruction (PBNO) and dysfunctional voiding (DV) is challenging. We systematically reviewed evidence on diagnostic strategies and treatment outcomes in men aged 18–50 yr with PBNO or DV.

Methods: We conducted a comprehensive bibliographic search on the Embase, Medline, and Cochrane Library databases in July 2024.

Key findings and limitations: Twenty-five publications were identified. Videourodynamics represents the standard diagnostic approach. Standard therapies for PBNO include alpha-blockers (ABs) as the first-line approach and bladder neck incision (BNI) in patients failing medical therapy. Pooled estimates of total International Prostate Symptom Score (IPSS) and maximum urinary flow rate (Q_{max}) improvements at 3 mo in patients receiving ABs are 7.0 points and 4.0 ml/s, respectively. The incidence of ejaculatory dysfunction (EjD) and failure rates range from 47% to 50% and from 23% to 52%, respectively. Corresponding figures in patients undergoing surgery are 11.2 points, 6.9 ml/s, 0–88.8%, and 11.1–13.3%, respectively. OnabotulinumtoxinA, as experimental second-line therapy in PBNO, provides 2-mo mean total IPSS and mean Q_{max}

* Corresponding author. Department of Neurosciences, Reproductive Sciences and Odontostomatology, University of Naples "Federico II", Naples, Italy. Tel. +39 082 497 1385.
E-mail address: max.creta@gmail.com (M. Creta).

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improvements of 14.1 points and 9.1 ml/s, respectively, with a 0% EjD rate. However, improvements deteriorate over time. Behavioral modifications plus biofeedback represent the only approach in patients with DV, providing symptom improvement of at least 50% in 83% of patients at 3 mo. Limits of evidence include few studies, mainly retrospective design, heterogeneous populations, small sample sizes, lack of direct comparisons, and short follow-up.

Conclusions and clinical implications: Diagnosis of PBNO/DV in young men requires the integration of anatomical and functional data. ABs represent the first-line approach for PBNO followed by BNI in cases of failure. Behavioral modification plus biofeedback represents the only strategy tested for DV. Given the low quality of evidence, a shared decision-making approach for diagnosis and treatment is required.

ADVANCING PRACTICE

What does this study add?

This systematic review summarizes evidence on diagnostic strategies and treatment outcomes for young men with primary bladder neck obstruction (PBNO) and dysfunctional voiding (DV), addressing the gap in age-specific recommendations. Standard therapies for PBNO include alpha-blockers as a first-line approach and bladder neck incision for patients failing medical therapy. Videourodynamics are highlighted as the most reliable diagnostic tool and analyzing outcomes across varied treatments. OnabotulinumtoxinA represents an experimental second-line therapy for PBNO, showing substantial but diminishing symptom relief over time, underscoring the need for ongoing management strategies. Behavior modifications plus biofeedback represents the only available option for DV.

Clinical Relevance

This systematic review and meta-analysis provide crucial insights into the diagnosis and management of primary bladder neck obstruction (PBNO) and dysfunctional voiding (DV) in young men, an often underrecognized and challenging subset of patients with lower urinary tract symptoms (LUTS). The findings highlight the need for specialized morpho-functional assessments, particularly video-urodynamics, to accurately differentiate PBNO and DV from other voiding dysfunctions. The study reinforces the role of alpha-blockers as the first-line treatment for PBNO, with bladder neck incision (BNI) reserved for refractory cases, while behavioral modifications and biofeedback remain the mainstay for DV management. Emerging therapies, such as onabotulinumtoxinA injections, show promise but require further validation. Importantly, the review underscores the lack of high-quality evidence guiding treatment decisions, emphasizing the necessity of shared decision-making to balance symptom relief with potential side effects, such as ejaculatory dysfunction. These findings provide valuable clinical guidance for urologists managing young men with PBNO and DV and highlight the need for future comparative studies to refine diagnostic and therapeutic strategies. Associate Editor: Dean Elterman, MD.

Patient Summary

We summarized evidence on the management of young men suffering from lower urinary tract symptoms related to primary bladder neck obstruction (PBNO) and dysfunctional voiding (DV), two frequent causes of bladder outflow obstruction in the age range of 18–50 yr. Diagnosis relies on a high index of suspicion followed by specialized tests. Available therapies for PBNO include drugs and surgery. Behavior modifications represent the only available option for DV. Unfortunately, the level of evidence is low and strong recommendations cannot be provided.

1. Introduction

Up to 20% of men younger than 50 yr report at least moderate lower urinary tract symptoms (LUTS) [1]. They represent a group distinct from the elderly counterpart. Indeed, although bladder outlet obstruction (BOO) secondary to benign prostatic enlargement (BPE), idiopathic overactive/underactive bladder, and nocturnal polyuria represent relevant pathophysiological mechanisms leading to non-neurogenic LUTS in older males, the spectrum of etiologies in younger ones is different [1–4]. Primary bladder neck obstruction (PBNO) and dysfunctional voiding (DV) represent the two commonest voiding disorders in men aged 18–50 yr, leading to functional BOO and non-neurogenic LUTS [4–18]. PBNO is defined as the inability of the bladder neck smooth muscle to open adequately during voiding, with a subsequent increase of detrusor pressure to try to overcome the resistance of the bladder neck and allow urine

to flow [4–11]. DV is a condition characterized by an intermittent and/or fluctuating flow due to inadequate or variable relaxation generally of the sphincters during voiding in neurologically normal men [11]. The exact prevalence of PBNO and DV in the general population is largely unknown. Schifano et al [12] predicted a probability of suffering from PBNO for a 40-yr man with mild and severe LUTS of 26% and 47%, respectively. Epidemiological studies involving videourodynamics (VUDS) in selected populations of men aged 18–50 yr with non-neurogenic LUTS showed a prevalence of PBNO and DV up to 54% and 43%, respectively [4–13].

Young men suffering from LUTS secondary to PBNO or DV represent a diagnostic and therapeutic challenge. Indeed, there are no currently available recommendations from international guidelines, and management is highly discretional.

We aimed to perform a systematic review addressing diagnostic strategies and outcomes of treatments in men aged 18–50 yr suffering from LUTS secondary to PBNO or DV.

2. Methods

The protocol was registered in the PROSPERO database (ID: CRD42024552024) and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidance [19].

2.1. Search strategy

We conducted a comprehensive bibliographic search on the Embase, Medline, and Cochrane Central Register of Controlled Trials (CENTRAL; Ovid) databases on July 26, 2024. Initial screening was performed independently by two investigators (M.B. and M.C.) based on the titles and abstracts of the articles to identify ineligible reports. Potentially relevant reports were subjected to a full-text review, and the relevance of the reports was confirmed after the data extraction process. Disagreements were resolved by consultation with a third coauthor (V.S.).

2.2. Study selection

We used the population, intervention, comparator, outcome, study (PICOS) model to define study eligibility [20]. PICOS criteria were set as follows: population—populations composed of $\geq$90% men aged 18–50 yr, presenting with LUTS related to obstruction (proven by urodynamics or presumed by the trialist) secondary to PBNO or DV; intervention—observation, physical therapies, medical therapies, surgical therapies, sacral neuromodulation, and onabotulinumtoxinA (BoNTA) injection therapy; comparator—none; outcome—variations in terms of maximum urinary flow (Q_{max}), detrusor pressure at maximum urinary flow ($P_{det}Q_{max}$), postvoid residual volume (PVR), symptom score, complications, and discontinuation rates; and study—retrospective and prospective human studies enrolling at least 15 patients reporting original research. Only English-language articles were assessed for eligibility. No restrictions for date of publication were applied. Reviews, meta-analyses, editorials, commentaries, authors' replies, meeting abstracts of unpublished studies, and case reports were excluded. Reference sections were checked to identify relevant articles.

2.3. Data extraction

Data on studies, patients, and treatment characteristics were extracted independently by two authors (M.C. and M.B.). We recorded the following items: first author, study period, study design, sample size, age, diagnosis, duration of symptoms, type of treatment, follow-up duration, baseline and follow-up symptom scores, and baseline and follow-up urodynamic parameters (Q_{max}, $P_{det}Q_{max}$, Bladder Outlet Obstruction Index [BOOI], PVR, and number of patients with detrusor overactivity [DO]). Incidence and reasons for treatment discontinuation, complications, and second-line treatments were also recorded.

2.4. Data analysis and synthesis

The meta-analysis was performed using ProMeta 3 software (https://idostatistics.com/) when there were two or more studies reporting the same outcome under the same definition. The effect size was estimated by means, mean differences, and rates, as appropriate, with 95% confidence interval (95% CI). Statistical pooling for means, mean differences, and rates estimate was performed according to a random-effect model. Whenever possible, data were stratified by a therapeutic approach and subgroup analyses were conducted. We assessed heterogeneity using the Cochrane Q test and quantified it using I^2 values. A p value of <0.10 was considered statistically significant. Data unsuitable for a meta-analysis were presented only in a narrative fashion.

2.5. Risk of bias

Two authors (M.C. and M.B.) assessed the risk of bias, and discrepancies were resolved by a third author (V.S.). For single-arm studies, we assessed the risk of bias with the tool suggested by the European Association of Urology (EAU) Guidelines Office using the following criteria: a priori protocol, selection of participants, missing data handled adequately, specification of outcomes/selective reporting, and measurement of outcomes [21].

3. Results

3.1. Description of the studies included

A total of 4311 abstracts were screened and 68 full-text articles were assessed. Finally, 25 studies were included in the review (Supplementary Fig. 1) [6–10,12,13,22–39]. Of these, 13 studies described diagnostic evaluations [6–10,12,21–27] and 14 studies (ten retrospective and four prospective) enrolling a total of 695 patients (PBNO: 652; DV: 43; mean age ranging from 27.3 to 43.0 yr) described outcomes of treatments [22,25,28–39]. In details, one study (nine patients), seven studies (267 patients), seven studies (331 patients), and on study (30 patients) investigated the efficacy of no treatment, alpha-blockers (ABs), surgery, and BoNTA, respectively, in patients with PBNO. One study (43 patients) investigated the role of behavior modifications plus biofeedback in patients with DV. Ten studies were included in the quantitative synthesis. The risk of bias

assessment of included studies is reported in Supplementary Table 1.

3.2. Diagnostic evaluation

3.2.1. Medical history

Clinical presentation of PBNO and DV in men aged 18–50 yr is highly variable [25,39]. Typically, most patients complain of long-lasting LUTS, with a mean duration of symptoms before diagnosis reaching up to 53.8 mo and nearly 88% of patients complaining of symptoms for >1 yr in series involving both PBNO and DV patients [4,10,22]. Series selectively focusing on PBNO and DV patients reported a mean duration of urinary symptoms before diagnosis of 100.2 and 33.6 mo, respectively [22,23]. However, no significant differences in terms of symptom duration have been observed by some authors [4,6]. Although PBNO and DV are disorders of the voiding phase and voiding symptoms are more frequently reported in some series, there is no pivotal symptom, and the spectrum of LUTS may include storage, voiding, and postmicturition symptoms [23]. A study evaluating the symptomatology in 46 male patients with PBNO found poor stream (70%), frequency (50%), dribbling (37%), and nocturia (30%) to represent the most common symptoms [24]. Jeong et al [6] reported storage, voiding, and postmicturition symptoms in 80%, 71.3%, and 46.3% of PBNO patients, respectively. Nocturia was reported to be significantly higher in PBNO patients with a higher degree of obstruction [23]. Chronic pelvic pain was evident in up to 24.5% of PBNO patients, while recurrent urinary tract infections were observed in 28% of cases [23,24]. The prevalence of storage, voiding, and postmicturition symptoms in DV patients has been reported to be 79.2%, 48.6%, and 40.3%, respectively [6]. Although patients suffering from PBNO were reported to have a lower body mass index (23.4 vs 25; $p < 0.0001$), lower Charlson comorbidity index (CCI) scores (CCI $\geq$ 1: 10% vs 19%; $p = 0.004$), and lower prostate-specific antigen (0.8 vs 2.5 ng/ml; $p < 0.0001$) than those suffering from LUTS from other reasons, these factors were not the predictors of PBNO at the multivariable analysis [12]. Additionally, no differences were observed in terms of depressive symptoms [12].

3.2.2. Questionnaires

There is no specific validated questionnaire for the assessment of patients with PBNO and DV. Physicians can refer to a validated questionnaire for male LUTS such as the International Consultation on Incontinence Questionnaire for Male LUTS, or the IPSS or the American Urological Association (AUA) questionnaire. However, their utility to monitor symptom changes and treatment outcomes is uncertain. One study assessing potential predictors of PBNO diagnosis found a higher IPSS and younger age to be independent predictors [12]. On the contrary, Wang et al [13] failed to find statistically significant differences in terms of mean IPSS scores between patients with PBNO, DV, and benign prostatic obstruction (BPO). In detail, the authors reported a mean total IPSS of 18.1, 20.3, and 19.1 in patients with PBNO, DV, and BPO, respectively [13]. Storage subscores were 8.1, 8.8, and 6.9, while voiding subscores were 10.1, 11.4, and 12.2 in patients with PBNO, DV, and BPO, respectively [13].

3.2.3. Uroflowmetry and PVR measurement

Although a Q_{max} of <15 ml/s has frequently been observed in patients diagnosed with PBNO and DV, this finding is not specific [13,39]. Wang et al [13] failed to find statistically significant differences in terms of Q_{max} between patients with PBNO, DV, and BPO (12.0, 11.8, and 9.8 ml/s, respectively). Similarly, Schifano et al [12] failed to find statistically significant differences in terms of Q_{max} between patients with PBNO and LUTS for other reasons. Intermittent increases and decreases of flow in an undulating fashion observed when voiding in a private setting have been considered by some authors as a criterion for DV [22]. An elevated PVR has also been observed frequently. However, similarly to Q_{max}, it lacks specificity. Wang et al [13] failed to find statistically significant differences in terms of PVR between patients with PBNO, DV, and BPO (91, 77, and 77 ml, respectively).

3.2.4. Ultrasound scan

The value of prostate volume (PV) in predicting PBNO and DV from other causes of LUTS in men is controversial. Young men with PBNO and DV generally have a PV of <30 cm^3 [12]. In their series, Wang et al [13] found statistically significant differences in terms of PV between patients with PBNO, DV, and BPO (23.7, 24.4, and 38.2 ml, respectively). Schifano et al [12] found lower PV values in men with PBNO than in men with LUTS from other reasons (26 vs 61 ml; $p < 0.0001$). However, the predictive value of PV was not confirmed after adjusting for other clinical variables.

3.2.5. Magnetic resonance imaging

A group investigated whether magnetic resonance imaging (MRI) and MR voiding cystourethrography (MR-VCU) could identify PBNO in 21 male patients with a urodynamic diagnosis of PBNO [26]. MRI was able to analyze both urethral lumen and muscular structures of the bladder neck. The diagnostic accuracy of MRI was 87%. In 13 patients who were able to perform MR-VCU, the diagnostic accuracy was 100%, based on the following features: reduction of the bladder neck relaxation during micturition, kyphosis of the prostatic urethra, a mild focal dilation of the prostatic urethra (due to the hypertonicity of the urogenital diaphragm), and patency of distal urethra. The value of MRI for the diagnosis of PBNO remains to be established, and additional studies are necessary before any clinical use.

3.2.6. VUDS and electromyography

VUDS represents the gold standard for the diagnosis of PBNO and DV [11,12,23,26].

VUDS criteria for PBNO are as follows: a high-pressure/low-flow voiding pattern, radiographic evidence of obstruction at the bladder neck, relaxation of the striated sphincter, and no evidence of distal obstruction. Currently, however, there are no commonly accepted urodynamic threshold parameters in this subset of patients. Additionally, although a significant association has been observed between the extent of bladder neck opening impairment on voiding cystourethrography and the magnitude of urodynamic measures of obstruction and contraction, no association with the severity of symptoms and voiding efficiency has been found [23]. VUDS has also been used to assess response to treatment [27]. Typically, electromyography (EMG) during

micturition, or an attempt at micturition, demonstrates relaxation of the striated sphincter concomitant with the detrusor contractions in PBNO patients [6,24]. However, although increased EMG activity is not expected in PBNO, its presence should not in and of itself exclude the diagnosis of PBNO due to false-positive results that can occur with surface EMG, which assesses pelvic floor activity rather than sphincter activity.

The criteria adopted to diagnose DV include the following: electrical activity of the external sphincter during voiding detected on EMG in the absence of abdominal straining, brief and intermittent closing of the membranous urethra during voiding detected on fluoroscopy, and intermittent increases and decreases of flow in an undulating fashion detected on uroflowmetry performed in a private setting [22].

3.2.7. Urethrocystoscopy

The role of urethrocystoscopy in the diagnostic workup of PBNO and DV is controversial. Although some authors consider it a useful test to rule out urethral strictures or enlarged prostate in selected cases, its role has been considered questionable by others [6,8,12,34,35,37].

3.3. Outcomes of therapies

Table 1 describes study features and baseline characteristics of patients enrolled in studies evaluating treatment options for PBNO/DV.

3.3.1. No treatment

The outcomes of no treatment were assessed only in one retrospective study involving nine PBNO patients who failed therapy with ABs and refused further treatments [25]. At a mean follow-up of 36 mo, the mean AUA-6 score improved by 5.9 points, mean Q_{max} improved by 4.7 points, and mean PVR improved by 56 ml (not statistically significant variations in all cases; Table 2) [25].

3.3.2. Behavioral modifications plus biofeedback

The outcomes of behavioral modifications (instructions to relax the pelvic floor muscles during voiding) plus biofeedback were assessed in one study involving 43 patients who received the diagnosis of DV after an unsuccessful trial of ABs [21]. Treatment success, defined as a decrease of symptoms of at least 50% in two consecutive visits, was observed in 35 patients (83%) at 3 mo (Tables 2 and 3) [22]. Sexual adverse events were not assessed.

3.3.3. Alpha-blockers

Outcomes of therapy with ABs were assessed only in PBNO patients. The pooled estimate in terms of the mean baseline total IPSS score was 22.5 (95% CI: 14.3–30.7; Supplementary Fig. 2). The mean total IPSS variation following therapy ranged from –1 to –12 points (pooled estimate at 3 mo: –7.0 [95% CI: –8.3 to –5.8; $p < 0.000$]; Supplementary Fig. 3). The mean IPSS quality of life (QoL) subscore improvement ranged from –1.5 to –1.9 points (pooled estimate at 3 mo: –1.7 points [95% CI: –2.0 to –1.3; $p < 0.000$]; Supplementary Fig. 4). The mean Q_{max} variation ranged from 3.7 to 11.1 ml/s (pooled estimate at 3 mo: 4.0 ml/s [95% CI: 3.1–4.9; $p < 0.001$]; Supplementary Fig. 5). The mean PVR variation ranged from to 26.9 to –70 ml (pooled estimate at 3 mo: –31.1 ml [95% CI: –36.3 to –25.9; $p < 0.001$]; Supplementary Fig. 6). Two studies evaluated BOOI variation after treatment with ABs [37,38]. Sudrania et al [37] reported a median BOOI improvement of 21 points, while Sureka et al [38] reported a mean BOOI improvement of 34.5 points. Overall, unsuccessful outcomes were reported in a percentage of patients ranging from 23% to 52%. Systemic adverse events were reported by 0–16.1% of patients, with giddiness being the most frequent adverse event. The incidence of EjD ranged from 47% to 50% (Table 3). One study assessed the incidence of erectile dysfunction, and none of the patients reported this adverse event [25]. None of the studies assessed variations in terms of mean International Index of Erectile Function (IIEF).

3.3.4. BoNTA injection

A single study assessed the outcomes of a transurethral bladder neck injection of BoNTA (200 U diluted in 4 ml of saline and injected at 3, 6, 9, and 12 o'clock positions [1 ml per site] at about 1 cm from the bladder-neck rim, using a 23-gauge needle through a 22F rigid cystoscope) in 30 patients with PBNO after unsuccessful AB therapy [35]. The mean total IPSS varied from 21.9 at baseline to 7.8, 10.3, 16.6, and 19.9 at 2-, 6-, 9-, and 12-mo follow-up, respectively. The mean Q_{max} varied from 7.8 ml/s at baseline to 16.9, 15.5, 12.7, and 8.6 ml/s at 2-, 6-, 9-, and 12-mo follow-up, respectively (Table 2). None of the patients reported EjD (Table 3). Erectile dysfunction was not assessed.

3.3.5. Surgery

The outcomes of surgery were described only in PBNO patients. The following procedures were assessed: single bladder neck incision (BNI; $n = 243$), bilateral BNI ($n = 96$), transurethral resection of the prostate ($n = 9$), the transurethral resection of the bladder neck ($n = 1$). The pooled estimate in terms of the mean baseline total IPSSs was 26.4 (95% CI: 15.2–37.6; Supplementary Fig. 2). The mean total IPSS improvement ranged from –8.8 to –23.3 points (pooled estimate at 3 mo: –11.2 points [95% CI: –16.12 to –6.33; $p < 0.0001$]; Supplementary Fig. 3). The mean IPSS QoL subscore improvement ranged from –1.9 to –2.2 points. The mean Q_{max} improvement ranged from 4.2 to 18.5 ml/s (pooled estimate at 3 mo: 6.9 ml/s [95% CI: 1.4–12.5; $p = 0.014$]; Supplementary Fig. 5). The mean PVR variation ranged from to 7.6 to –156 ml. One study evaluated $P_{det}Q_{max}$ variation after treatment by reporting an improvement in terms of the mean $P_{det}Q_{max}$ by 68 cmH_2O [25]. An unsuccessful outcome was reported in 0–15.3% of patients. Overall, EjD rates ranged from 0% to 88.8% (pooled estimate following BNI: 3.0% [95% CI: 1–6%]). Results stratified according to the type of BNI revealed pooled EjD rates of 0% (95% CI: 0–1%) and 9% (95% CI: 2–21%) following single and bilateral BNI, respectively ($p = 0.128$; Supplementary Fig. 7). The incidence of erectile dysfunction was assessed only in one study and was 0% [25]. Two studies described variations in terms of the mean IIEF score [33,36]. Yang et al [33] reported a mean IIEF variation of 1.9 points (mean [standard deviation] preoperative IIEF: 22.6 [2.6], mean [standard deviation] postoperative IIEF: 20.7 [4.3], $p = 0.08$). Mattioli et al [36] failed to find variations in terms of the mean IIEF score (mean IIEF: 24). Recurrent obstruction was reported after 1 yr in two patients with a history

Table 1 – Study features and baseline characteristics of patients enrolled

Study	Study period	Study design	Sample size (*n*)	Age (yr), mean (SD/range)	Diagnosis	Symptom duration (mo), mean (SD/range)	Treatment	Follow-up evaluations (mo)
ABs								
Trockman [25]	NA	R	7	NA	PBNO	NA	Terazosin (5 mg daily or prazosin 2 mg twice daily	25.0 (14.0) [a]
Yang [29]	1998–2001	R	24	39.3 (7.4/26–55)	PBNO [b]	18.1 (11.6)	Doxazosin 1 mg daily titrated to 2 mg daily as needed for >3 mo	3
Suri [31]	1988–1996	R	45	33.4 (6.5)	PBNO [c]	45.6 (49.2)	Prazosin or terazosin + CIC	96.0 (46–140) [a]
Cisternino [d] [32]	1995–2001	R	29	43.0 (31–49) [e]	PBNO	18.0 (6–20) [e]	Alfuzosin 5 mg or tamsulosin 2 mg for at least 6 mo	6, 12, 18, 24
Cisternino [f] [32]	1995–2001	R	12	43.0 (31–49) [e]	PBNO	8.0 (6–20) [e]	Alfuzosin 5 mg or tamsulosin 2 mg for at least 6 mo	6, 12, 18, 24
Li [34]	2005–2009	R	30	27.3 (18–35)	PBNO [g]	26.4 (3–65)	Doxazosin 4 mg daily for at least 12 mo	3, 12
Sudrania [37]	2013–2015	P	21	41.0 (18–50)	PBNO [h]	NA	Tamsulosin 0.4 mg daily for 3 mo	3
Sureka [38]	2014–2022	R	99	32.1 (5.2)	PBNO [h]	38.4 (12.5)	Tamsulosin 0.4 mg or alfuzosin 10 mg daily for 3–6 mo	6
Surgery								
Norlen [39]	1981–1983	R	18	41.0 (25.0–52.0)	PBNO [i]	144.0 (3–240)	TURP: 9 TURBN: 1 bBNI: 6 sBNI (5 o'clock): 2	NA
Kaplan [28]	NA	R	31 [j]	NA	PBNO	38.3 (25–126)	sBNI (5 o'clock): 31	3, 6, 12
Trockman [25]	NA	R	18 [j]	NA	PBNO	NA	bBNI: 18	30.0 (18.0) [a]
Kochakarn [30]	1998–2001	R	35	40.3 (2.4/36–46)	PBNO	NA	sBNI: 35	3, 6, 12
Suri [31]	1988–1996	R	18 [j]	NA	PBNO [c]	NA	sBNI (12 o'clock): 18	96.0 (46–140) [a,e]
Yang [33]	2000–2004	P	33 [k]	41.9 (6.9/27–50)	PBNO [l]	26.1 (19.4)	bBNI (downward to 0.5–1.0 cm proximal to the verumontanum): 33	3, 24
Mattioli [36]	2012–2015	P	196 [m]	42.0 (21–45)	PBNO	NA	sBNI (7 o'clock): 157 bBNI: 39	6, 12, 24
BoNTA								
Sacco [35]	2010–2011	P	30 [j]	33.8 (19–48)	PBNO [n]	55.2 (12–84)	BoNTA	2, 6, 9, 12
Behavior modifications plus biofeedback								
Kaplan [22]	1990–1996	R	43 [j]	36.7 (23–50)	DV [o]	33.6 (17–146)	Biofeedback + behavior modifications	3, 6
No treatment								
Trockman [25]	NA	R	9 [j]	NA	PBNO	NA	No treatment	36.0 (16.0) [a]

ABs = alpha-blockers; bBNI = bilateral bladder neck incision (5 and 7 o'clock positions); BoNTA = onabotulinumtoxinA; BOO = bladder outlet obstruction; BOOI = Bladder Outlet Obstruction Index; CIC = clean intermittent catheterization; DV = dysfunctional voiding; NA = not available; P = prospective; PBNO = primary bladder neck obstruction; $P_{det}Q_{max}$ = detrusor pressure at maximum urinary flow; PVR = postvoid residual volume; Q_{max} = maximum urinary flow rate; R = retrospective; sBNI = single bladder neck incision; SD = standard deviation; TURBN = transurethral resection of the bladder neck; TURP = transurethral resection of the prostate.

[a] Mean (standard deviation/range) follow-up.

[b] Relaxed external sphincter electromyography during voiding, no distal urethral obstruction, and narrowing only at the vesical neck on voiding cystourethrography under fluoroscopic guidance. Associated findings were a sustained detrusor contraction during voiding with detrusor pressure ≥20 cmH_2O, Q_{max} ≤15 ml/s, and an obstructive flow pattern.

[c] Detrusor pressure during voiding >40 cmH_2O, Q_{max} <10 ml/s, opening pressure >40 cmH_2O with a relaxed external sphincter, and PVR >100 ml. Inadequate funneling of the bladder neck.

[d] Successful group.

[e] Overall study population.

[f] Unsuccessful group.

[g] Radiographic evidence of inadequate funneling of the bladder neck with relaxation of the external sphincter during voiding and no distal urethral obstruction, $P_{det}Q_{max}$ >20 cmH_2O and Q_{max} <15 ml/s.

[h] Type 1 PBNO: BOOI >40 with videourodynamic evidence of an obstructed, nonopening bladder neck in patients with clinical features of BOO.

[i] Sustained detrusor contraction ≥30 cmH_2O, Q_{max} ≤15 ml/s, complete relaxation of the external urethral sphincter (electromyographic silence), radiographic and manometric evidence of obstruction at the vesical neck or proximal 1–2 cm of the urethra, and absence of distal obstruction.

[j] Unsuccessful previous medical therapy.

[k] Fourteen patients had a poor response to medication and the other 19, who had beneficial effects of medication, were unwilling to take long-term medication.

[l] Narrowing only at the bladder neck on voiding cystourethrography. Associated findings were as follows: sustained detrusor contraction during voiding with detrusor pressure ≥30 cmH_2O, Q_{max} <15 ml/s, relaxed external sphincter electromyography during voiding, and no distal urethral obstruction radiologically.

[m] Failure of medical treatment or interruption of therapy for adverse events.

[n] Evidence of incomplete or delayed opening of bladder neck during voluntary detrusor contraction on videourodynamic studies; no voiding pressure criteria were used.

[o] Electrical activity of the external sphincter during voiding in the absence of abdominal straining and brief, intermittent closing of the membranous urethra during voiding detected on electromyography, and fluoroscopy + intermittent increases and decreases of flow in an undulating fashion.

Table 2 – Symptoms and urodynamic parameters at baseline and follow-up evaluations

Study	Baseline									Follow-up							
	Urodynamic parameters Mean (SD)/median (range)					IPSS/AUA score Mean (SD)/median (range)				Urodynamic parameters Mean (SD)/median (range) [follow-up, mo]				IPSS/AUA score Mean (SD)/median (range) [follow-up, mo]			
	Q_{max} (ml/s)	$P_{det}Q_{max}$ (cmH_2O)	BOOI	PVR (ml)	DO (*n*)	T	S	V	QoL	Q_{max} (ml/s)	$P_{det}Q_{max}$ (cmH_2O)	BOOI	PVR (ml)	T	S	V	QoL
ABs																	
Trockman [25]	11.0 (3.6)	60.0 (NA) [a]	NA	65.0 (62.0)	NA	18.6 (4.6) [b]	NA	NA	NA	22.1 (13.9) [I]	49.0 (NA) [I] [a]	NA	45.0 (30.0) [I]	10.3 (9.9) [I] [b]	NA	NA	NA
Yang [29]	11.8 (3.2)	57.1 (23.4)	33.5 (NA)	80.2 (17.1)	12	18.3 (4.6)	7.5 (2.1)	10.7 (3.1)	4.1 (1.1)	15.9 (3.9) [3]	NA	NA	48.5 (10.3) [3]	11.6 (5.2) [3]	4.7 (1.5) [3]	6.8 (2.1) [3]	2.6 (1.0) [3]
Suri [31]	7.5 (2.5)	100.0 (35.8)	85.0 (NA)	275.4 (200.0)	NA	NA	NA	NA	NA	+4 (NA) [I] [c]	NA	NA	−70 (NA) [I] [c]	−12 (NA) [c]	NA	NA	NA
Cisternino [d] [32]	8.5 (3.0–11.0)	71.2 (14.0) [e]	54.2 (NA) [e]	63.5 (0–90.0)	14 [e]	18.6 (15.0–28.0)	NA	NA	NA	14.0 (12.5–18.3) [12]	NA	NA	40.0 (20.0–60.0) [12]	10.3 (8.0–13.0) [12]	NA	NA	NA
Cisternino [f] [32]	8.5 (3.0–11.0) [e]	71.2 (14.0) [e]	54.2 (NA) [e]	63.5 (30.0–100.0)	14 [e]	19.0 (16.0–18.0)	NA	NA	NA	NA	NA	NA	55.0 (50.0–80.0) [12]	18.0 (16.0–20.0) [12]	NA	NA	NA
Li [34]	11.4 (2.9)	NA	NA	79.3 (33.4)	NA	17.4 (4.2)	NA	NA	4.2 (1.1)	15.4 (3.6) [3] 15.1 (3.2) [12]	NA	NA	49.8 (22.7) [3] 47.1 (21.3) [12]	10.1 (4.7) [3] 10.4 (4.8) [12]	NA	NA	2.3 (1.2) [3] 2.4 (1.3) [12]
Sudrania [37]	8.0 (5.5–10.0)	71.0 (61.5–107.5)	59.0 (47.5–94.5)	82.0 (40.5–232.0)	NA	22.0 (16.0–30.5)	7.0 (5.0–12.5)	15 (10.0–19.0)	5 (4.0–5.5)	10.0 (8.0–12.0) [3]	56.0 (45.5–94.5) [3]	38.0 (30.0–74.5) [3]	NA	12.0 (7.0–19.5) [3]	4.0 (2.0–7.5) [3]	8.0 (4.0–11.0) [3]	4.0 (2.0–5.0) [3]
Sureka [38]	7.9 (2.6)	81.2 (11.3)	65.9 (4.7)	138.1 (21.2)	NA	26.7 (3.6)	NA	NA	NA	15.7 (4.3) [6]	63.3 (10.9) [6]	31.4 (4.1) [6]	165.0 (25.3) [6]	19.8 (3.7) [6]	NA	NA	NA
Surgery																	
Norlen [39]	9.1 (NA) [e]	110.0 (NA) [e]	91.8 (NA) [e]	159.0 (NA) [e]	8 [e]	NA	NA	NA	NA	26.3 (NA) [I]	NA	NA	NA	Marked relief of voiding symptoms in all patients	NA	NA	NA
Kaplan [28]	9.2 (NA)	76.6 (NA)	58.2 (NA)	NA	27	16.4 (NA) [g]	NA	NA	NA	16.4 (NA) [3] 15.7 (NA) [6] 16.8 (NA) [12]	NA	NA	NA	7.2 (NA) [g] [3] 6.4 (NA) [g] [6]	NA	NA	NA
Trockman [25]	8.2 (4.5)	116.0 (NA) [h]	NA	161.0 (132.0)	NA	17.1 (5.2) [b]	NA	NA	NA	26.7 (11.8) [I]	48.0 (NA) [I] [h]	NA	23.0 (33.0) [I]	4.3 (4.5) [I] [b]	NA	NA	NA
Kochakarn [30]	7.8 (2.2)	NA	NA	NA	NA	32.1 (2.0)	NA	NA	5.0 [i]	12.0 (2.1) [3] 14.3 (1.8) [6] 15.2 (1.6) [12]	NA	NA	NA	23.3 (3.1) [3] 19.9 (3.0) [6] 14.4 (3.6) [12]	NA	NA	NA
Suri [31]	8.5 (NA)	NA	NA	NA	NA	26.9 (NA)	NA	NA	NA	19.6 (NA) [I]	NA	NA	−156 (NA) [I] [j]	3.6 (NA) [I]	NA	NA	NA
Yang [33]	10.7 (3.7)	61.8 (29.9)	40.4 (NA)	107.0 (77.0)	13	20.7 (5.4)	9.1 (2.9)	11.5 (4.0)	4.2 (1.0)	20.6 (5.8) [3] 19.2 (4.6) [24]	NA	NA	37.0 (31.0) [3] 48.0 (25.0) [24]	6.9 (5.9) [3] 8.7 (4.7) [24]	3.2 (2.9) [3] 8.7 (4.7) [24]	3.7 (3.3) [3] 4.4 (3.0) [24]	2.0 (1.3) [3] 2.3 (1.3) [24]
Mattioli [36]	8.3 (NA)	NA	NA	NA	NA	25.0 (NA)	NA	NA	NA	24.0 (NA) [12]	NA	NA	NA	7.0 (NA) [12]	NA	NA	NA
BoNTA																	
Sacco [35]	7.8 (0.6)	48.0 (2.9)	32.4 (NA)	55.4 (6.0)	NA	21,9 (1.6)	8.3 (0.9)	13.6 (1.1)	5.0 (0.2)	15.5 (0.8) [6] 8.6 (0.6) [12]	NA	NA	36.5 (5.9) [6] 51.2 (6.4) [12]	10.3 (1.3) [6] 19.9 (1.5) [12]	4.3 (0.9) [6] 7.3 (1.0) [12]	6.0 (0.7) [6] 12.6 (1.0) [12]	2.6 (0.3) [6] 4.9 (0.2) [12]
Behavior modifications plus biofeedback																	
Kaplan [22]	13.3 (4.2)	46.3 (13.7)	19.7 (NA)	NA	17	18.4 (NA) [k]	NA	NA	NA	NA	NA	NA	NA	7.6 (NA) [3] 8.1 (NA) [6]	NA	NA	NA
No treatment																	
Trockman [25]	9.9 (2.7)	130.0 (NA) [i]	NA	45.0 (30.0)	NA	16.4 (4.2) [b]	NA	NA	NA	14.6 (6.9) [I]	93.0 (NA) [I] [i]	NA	47.0 (48.0) [I]	10.5 (6.8) [I] [b]	NA	NA	NA

ABs = alpha-blockers; AUA = American Urological Association; BoNTA = onabotulinumtoxinA; BOOI = Bladder Outlet Obstruction Index; DO = detrusor overactivity; IPSS = International Prostate Symptom Score; I = last follow-up; NA = not available; $P_{det}Q_{max}$ = detrusor pressure at maximum urinary flow; PVR = postvoid residual volume; Q_{max} = maximum urinary flow rate; QoL = quality of life; S = storage subscore; SD = standard deviation; T = total score; V = voiding subscore.

[a] Data available for one patient.
[b] AUA-6 symptom score.
[c] Compared with baseline values (not available) in the subgroup of 22 patients responding to alpha-blockers.
[d] Successful group.
[e] Overall study population.
[f] Unsuccessful group.
[g] Boyarsky symptom score.
[h] Data available for nine patients.
[i] Data available for two patients.
[j] Compared with baseline values (not available) in the subgroup of 18 patients undergoing bladder neck incision.
[k] Data relative to 35 patients experiencing improvement.

Table 3 – Adverse event/retreatment rates reported by studies

Study	Systemic AE Type: *n* (%)	Perioperative complications Type: *n* (%)	EjD *n* (%)	Patients not achieving successful outcome *n* (%), reason	Treatment discontinuation *n* (%), reason	Subsequent treatment Type: *n* (%)	Recurrent obstruction *n* (%)
ABs							
Trockman [25] [a]	NA	–	NA	16 (44.4), NA	16 (44.4), NA	BNI: 8 (22.2)Observation: 8 (22.2)	–
Yang [29]	0	–	NA	11 (45.8), NA [b]	4 (14.2), unknown reason [c]	NA	–
Suri [31]	Orthostatic hypotension: 2 (4.4)	–	NA	23 (51.1), NA	23 (51.1), unsuccessful outcome 2 (4.4), orthostatic hypotension	BNI: 18 (40.0) CIC: 5 (11.1)	–
Cisternino [32]	0	–	NA	12 (29.2), NA	NA	Surgery (offered)	–
Li [34]	Slight dizziness and somnolence: 2 (6.6)	–	NA	8 (33.3), NA [d]	3 (10.0), lack of efficacy 3 (10.0), unknown reason	BNI: 5 (16.6) CIC: 1 (3.3)	–
Sudrania [37]	Giddiness: 3 (14.2)	–	10 (47.6)	5 (23.8), NA	1 (4.7), giddiness [c]	BNI: 5 (23.8)	–
Sureka [38]	Giddiness: 16 (16.1)	–	50 (50.5)	21 (21.1), failure at 3 mo [e] 31 (31.3), recurrent symptoms	52 (52.5)	BNI: 52 (52.5)	–
Surgery							
Norlen [39]	NA	NA	16 (88.8) sBNI: 0 Other surgical procedures: 16	0	–	–	NA
Kaplan [28]	NA	NA	0	1 (3.2) [f]	–	–	0
Trockman [25]	0	0	4 (26.6)	NA	–	–	2 (13.3)
Kochakarn [30]	NA	NA	Reduction of sperm count (63% at 6 mo and 69% at 1 yr)	0 [g]	–	NA	NA
Suri [31]	NA	NA	NA	0 [g]	–	NA	2 (11.1)
Yang [33]	NA	0	0	4 (15.3) [f]	–	Anticholinergics: 2 (7.6) PFMT: 2 (7.6)	NA
Mattioli [36]	NA	0	3 (1.5) [h] Reduced semen volume: 14 (7.1) [h]	NA	–	NA	NA
BoNTA							
Sacco [35]	0	Painful micturition: 19 (63.3) Hematuria: 13 (43.3) Urinary retention: 4 (13.3)	0	NA (20.0) at 2 mo [i] NA (55.2) at 12 mo [i]	–	0	NA
Behavior modifications plus biofeedback							
Kaplan [22]	NA	NA	NA	8 (18.6) [j]	NA	NA	NA
No treatment							
Trockman [25]	–	–	–	NA	NA	NA	NA

ABs = alpha-blockers; AE = adverse event; BNI = bladder neck incision; BoNTA = onabotulinumtoxinA; CIC = clean intermittent catheterization; EjD = ejaculatory dysfunction; IPSS = International Prostate Symptom Score; NA = not available; PFMT = pelvic floor muscle training; sBNI = single bladder neck incision; – = not applicable.

[a] Overall cohort of 36 patients.

[b] : Successful outcome: Q_{max} increase ≥2.5 ml/s and >50% decrease in total IPSS.

[c] Excluded from the analysis.

[d] Successful outcome: Q_{max} increase ≥3 ml/s and >40% decrease in total IPSS.

[e] Failure: <30% improvement in total IPSS.

[f] Successful outcome: Q_{max} increase ≥2.5 ml/s and ≥25% decrease in total IPSS, and ≥1 point increase in quality of life.

[g] Successful outcome: symptom improvement.

[h] All patients undergoing bilateral incision.

[i] Patients not achieving overall satisfaction.

[j] Successful outcome: decrease in symptoms ≥50% on two consecutive office visits.

of single BNI (treated successfully with repeated procedure) and after 2 and 4 yr in another two patients with a history of bilateral BNI (one required transurethral resection of the prostate and the other refused further interventions) [25,31].

3.3.6. Results from subgroup analyses

3.3.6.1. Total IPSS variation. A statistically significant difference in terms of the total IPSS reduction was evident between ABs, BoNTA injection, and BNI at both 6 mo (–6.9, –11.6, and –12.2 points, respectively) and 12 mo (–7.0, –2.0, and –17.7 points, respectively; Supplementary Fig. 3).

3.3.6.2. IPSS QoL. A statistically significant difference in terms of IPSS QoL score reduction was evident between ABs and BoNTA at 12 mo (–1.8 and –0.1 points, respectively; Supplementary Fig. 3 and 4).

3.3.6.3. Maximum urinary flow rate. A statistically significant difference in terms of Q_{max} variation was evident between ABs, BoNTA, and BNI at 6 mo (7.8, 7.7, and 6.5 ml/s, respectively) and 12 mo (3.7, 0.8, and 7.4 ml/s, respectively; Supplementary Fig. 5).

3.3.6.4. Postvoid residual volume. A statistically significant difference in terms of PVR variation was evident between ABs and BNI at 3-mo follow-up (–31.1 and –70.0 ml, respectively) and between ABs and BoNTA at both 6 mo (26.9 and –18.9 ml, respectively) and 12 mo (–32.2 and –4.2 ml, respectively; Supplementary Fig. 6).

4. Discussion

Herein, we performed a comprehensive assessment of the diagnostic strategies and treatment outcomes in males aged 18–50 yr complaining of LUTS related to PBNO and DV. Given the high prevalence of these disorders in this age range and the nonspecific clinical presentation, the clinical suspicion is crucial. Indeed, PBNO and DV are often underdiagnosed, and many patients initially receive an empirical diagnosis of chronic prostatitis or neurogenic/psychogenic bladder voiding dysfunctions, thus leading to a frequent delay in the delivery of adequate treatments [28,36]. Therefore, a careful diagnostic workup is required, mainly in patients complaining of long-lasting LUTS. Exclusion of neurological disorders and conventional assessments for nonneurogenic male LUTS should be considered as the first-line approach. Although noninvasive predictors have been proposed for PBNO, the definitive diagnosis of PBNO and DV formally relies on the findings from in-depth morphofunctional assessments, with VUDS representing the gold standard approach [11,12,23,26]. However, VUDS is expensive, time consuming, unpleasant to the patient, and often unavailable in everyday clinical practice [23,26]. Additionally, some patients fail to void during the study due to psychological and physical discomfort, and the proportion of nonvoiders among patients receiving VUDS is greater than among those undergoing standard urodynamic study [40]. Therefore, evaluation of data separately collected by standard urodynamic investigations and voiding cystourethrography has been considered a reliable alternative approach by some authors [23,26]. Although being a poorly standardized procedure, concomitant EMG provides additional data concerning the activity of the striated urethral sphincter-pelvic floor complex concomitant with the detrusor contractions. Recently, MRI has been proposed for the evaluation of PBNO as an "all-in-one" multiplanar and multiparametric assessment of both urethral lumen and muscular structures of the bladder neck without using ionizing radiation [26]. Urethral pressure profilometry has also been proposed by some authors for the evaluation of men with voiding LUTS [27]. However, in the absence of clinical trials, its use remains experimental [27].

The goals of therapies in young men with LUTS secondary to PBNO and DV include improvement of symptoms and QoL, relief of obstruction, prevention of disease-related complications, and preservation of sexual/reproductive health.

Currently, therapeutic options for PBNO include observation, ABs, BoNTA, and surgery.

Although observation has been proposed by some authors as an option for PBNO patients with minimal symptom bother and without clinical or urodynamic evidence of upper or lower urinary tract decompensation, available evidence in young men aged 18–50 yr was derived from only one study describing the outcomes of no treatment in nine patients unresponsive to ABs who refused surgery [25,41,42]. The authors demonstrated not statistically significant variations in terms of the mean AUA-6 score, mean Q_{max}, and mean PVR at a mean follow-up of 36 mo [25].

ABs act primarily by relaxing the smooth muscle of the bladder neck and are commonly prescribed as first-line treatment in patients with PBNO [41–44]. Overall, these provide clinically meaningful symptomatic improvements, with the magnitude of mean total IPSS and Q_{max} being comparable with those obtained in older patients suffering from LUTS related to BPO [44,45]. A major drawback of ABs is the considerable discontinuation rate, ranging from 4.7% to 55%, mainly due to unsuccessful outcomes or adverse events. A higher baseline urodynamic obstruction grade and younger age have been identified as predictors of AB failure [29,32,37,38].

Surgery, typically involving BNI, is mostly performed in patients failing therapy with ABs and aims at relieving the obstruction by interrupting muscular fibers of the internal sphincter located at the bladder neck [31,38,41,42]. The classical procedure proposed initially by Turner-Warwick et al [46] in 1973 involves two incisions from the bladder neck to the verumontanum at 5 and 7 o'clock positions. Technical variations including single incision and preservation of part of the supramontanal prostate have been introduced to preserve ejaculatory function [28,33,36,39]. Although based on indirect comparisons, the magnitudes of both total IPSS and Q_{max} improvements are higher than those for ABs. Of note, this finding is line with the results from indirect comparisons in older patients suffering from LUTS-related BPO [47,48]. Permanent EjD and fertility impairments are major drawbacks of surgery. A lower, although not statistically significant, incidence of EjD was observed following single BNI. However, a reduction of sperm count was evident despite this approach [30].

Transurethral injection of BoNTA at the level of bladder neck was evaluated as an alternative option for young men with medically refractory PBNO in a preliminary single, open-label, noncomparative study [35]. Although

satisfactory symptomatic and urodynamic improvements were observed at 2-, 6-, and 9-mo follow-up, in the absence of significant adverse effects or EjD, a loss of efficacy was evident over time with loss of benefits at 12-mo follow-up and need for repeated injections.

Evidence about the management of DV mainly derives from pediatric populations [49]. Data focusing on male patients aged 18–50 yr are limited to a single, small-sized study showing the short-time efficacy of behavioral modifications plus biofeedback. Data concerning strategies to adopt in cases of treatment failure in this subset of patients are lacking. Sacral neurostimulation (SNM) is considered by some authors an exciting new treatment for refractory voiding disorders including DV [50,51]. Jonas et al [52] evaluated the efficacy of SNM in patients with idiopathic urinary retention secondary to underactive or acontractile detrusor, or functional outlet obstruction due to urethral overactivity and refractory to standard therapy. The study included 177 patients (74% females) with a mean age of 42.9 (range: 17.4–81) yr. Of note, 69% of implanted patients eliminated catheterization at 6 mo and an additional 14% had a ≥50% reduction in catheter volume per catheterization [52]. Clean intermittent catheterization remains a further option in patients with both PBNO and DV refractory to first-line therapy.

Limitations of the present systematic review should be acknowledged. These mainly reflect the drawbacks related to the primary literature: a small number of studies, limited sample sizes, retrospective design in many cases, a lack of direct comparisons, considerable heterogeneity in terms of populations (a lack of uniform diagnostic criteria, duration of symptoms, and a lack of adherence to the more recent technical standard methods defined by the International Continence Society), interventions (type and duration of medical treatments, and type of surgery), timing and modality of outcome assessments, arbitrary and heterogeneous definitions of successful outcomes, and short follow-up [53]. Relevant outcomes such as IPSS subscores and follow-up urodynamic data were collected only rarely. The criteria we adopted for inclusion/exclusion also deserve considerations: the cutoff age of 50 yr was chosen arbitrarily based on epidemiological data. Although up to 25% of men aged 40–50 yr suffer from benign prostatic hyperplasia, the adoption of VUDS criteria for the diagnosis of PBNO/DV in the majority of studies included in our analysis contributes toward mitigating this potential limitation [54]. Additionally, we excluded male/female studies involving <90% of male population and mixed populations not providing subgroup data specific to our inclusion criteria. Although this approach could result in the exclusion of studies with potentially valuable insights, especially in areas where data are scarce, such as DV, it aimed to ensure consistency and relevance while minimizing the risk of bias. Finally, we can hypothesize that some published series may include PBNO/DV patients misdiagnosed as BPE patients and treated as such. A suggested algorithm helping in the diagnosis and treatment of PBNO and DV in men aged 18–50 yr is provided in Fig. 1. Given the lack of high-level evidence, as well as limits inherent to specialized tests, types and timing of additional morphofunctional assessments remain partially discretional. Accordingly, current EAU guidelines on non-neurogenic LUTS recommend performing urodynamics in men with bothersome, predominantly voiding LUTS, aged <50 yr only, when considering invasive treatments [44]. Similarly, the type and sequence of treatments should be discussed in a case-by-case fashion within a

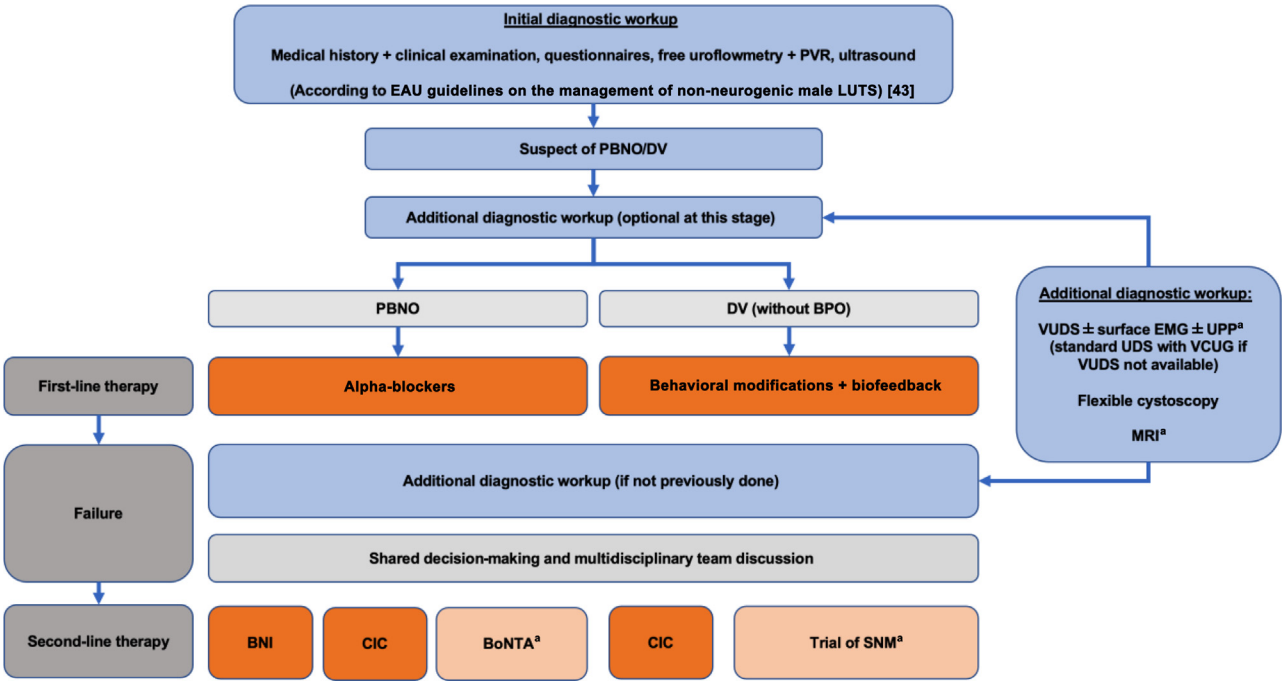

Fig. 1 – Algorithm summarizing the diagnosis and treatment of PBNO/DV in men aged 18–50 yr. BNI = bladder neck incision; BoNTA = onabotulinumtoxinA; BPO = benign prostatic obstruction; CIC = clean intermittent catheterization; DV = dysfunctional voiding; EAU = European Association of Urology; EMG = electromyography; LUTS = lower urinary tract symptoms; MRI = magnetic resonance imaging; PBNO = primary bladder neck obstruction; PVR = postvoid residual volume; SNM = sacral neurostimulation; UDS = urodynamics; UPP = urethral pressure profilometry; VCUG = voiding cystourethrography; VUDS = videourodynamics. [a] Experimental.

shared decision-making process and a multidisciplinary approach. Unfortunately, data looking at the natural history of PBNO and DV as well as at risk factors for developing detrusor and/or renal complications due to prolonged obstruction are lacking [12]. Therefore, due to the long-life expectancy of these patients, the long-lasting symptoms before diagnosis, and the unpredictable natural history of these conditions, a careful follow-up is advisable.

Future multi-institutional comparative studies are needed to identify the predictors of PBNO/DV among men aged 18–50 yr suffering from non-neurogenic LUTS, to shed light on the role of alternative diagnostic modalities such as MRI, urethral pressure profilometry, and machine learning models, to address the comparative efficacy and safety of available treatments, and to identify the predictors of response [5,55].

5. Conclusions

The diagnosis of PBNO and DV in young men relies on a high index of suspicion and a careful morphofunctional diagnostic workup. ABs and behavioral modifications plus biofeedback represent first-line approaches in patients with PBNO and DV, respectively. BNI should be discussed with patients with PNBO mainly when first-line approaches fail. However, the level of evidence is currently low; thus, strong diagnostic and therapeutic recommendations cannot be provided. Therefore, careful counseling about the benefits and risks of standard and experimental therapies within a shared and multidisciplinary decision-making process is required.

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Study concept and design: Creta, Cornu, Baboudjian, Hashim, Sakalis.
Acquisition of data: Creta, Cornu, Baboudjian, Hashim, Sakalis.
Analysis and interpretation of data: Creta, Cornu, Baboudjian, Hashim, Sakalis.
Drafting of the manuscript: Creta, Cornu, Baboudjian, Hashim, Sakalis.
Critical revision of the manuscript for important intellectual content: Cornu, Baboudjian, Bhatt, Creta, De Nunzio, Gacci, Hashim, Herrmann, Karavitakis, Malde, Moris, Netsch, Rieken, Sakalis, Tutolo, Yuan.
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