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Review – Bladder Outlet Obstructions

Diagnostic Tests for Female Bladder Outlet Obstruction: A Systematic Review from the European Association of Urology Non-neurogenic Female LUTS Guidelines Panel

Karl H. Pang [a,†], Riccardo Campi [b,c,†], Salvador Arlandis [d], Kari Bo [e], Christopher R. Chapple [f], Elisabetta Costantini [g], Fawzy Farag [h,i], Jan Groen [j], Markos Karavitakis [k], Marie Carmela Lapitan [l], Margarida Manso [m,n], Serenella Monagas Arteaga [o], Arjun K. Nambiar [p], Aisling U. Nic An Ríogh [q], Eabhann M. O'Connor [r], Nadir I. Osman [f], Benoit Peyronnet [s], Véronique Phé [t], Vasileios I. Sakalis [u], Néha Sihra [v], Lazaros Tzelves [w], Huub van der vaart [x,y], Yuhong Yuan [z], Muhammad Imran Omar [aa,bb,‡,], Christopher K. Harding [p,‡]*

[a] *Academic Urology Unit, University of Sheffield, Sheffield, UK;* [b] *Unit of Urological Robotic Surgery and Renal Transplantation, University of Florence, Careggi Hospital, Florence, Italy;* [c] *Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy;* [d] *Urology Department, La Fe University and Polytechnic Hospital, Valencia, Spain;* [e] *Department of Sports Medicine, Norwegian School of Sport Sciences, Oslo, Norway;* [f] *Section of Functional and Reconstructive Urology, Department of Urology, Royal Hallamshire Hospital, University of Sheffield, Sheffield, UK;* [g] *Department of Medicine and Surgery, University of Perugia, Perugia, Italy;* [h] *Department of Urology, Sohag University Hospital, Sohag, Egypt;* [i] *Department of Urology, East Suffolk and North Essex NHS Foundation Trust, UK;* [j] *Department of Urology, Erasmus MC, Rotterdam, The Netherlands;* [k] *Department of Urology, University General Hospital of Heraklion, Medical School, University of Crete, Heraklion, Crete, Greece;* [l] *College of Medicine/Philippine General Hospital/National institutes of Health, University of the Philippines Manila, Manila, Philippines;* [m] *Department of Urology, São João University Hospital Center, Porto, Portugal;* [n] *Faculty of Medicine of Porto, Porto, Portugal;* [o] *Department of Urology, University Hospital of San Agustín, Avilés, Spain;* [p] *Department of Urology, Freeman Hospital, Newcastle-upon-Tyne, UK;* [q] *Department of Urology, Cork University Hospital, Cork, Ireland;* [r] *Department of Urology, Beaumont Hospital, Dublin, Ireland;* [s] *University of Rennes, Rennes, France;* [t] *Department of Urology, Assistance Publique-Hôpitaux de Paris, Pitié-Salpêtrière Academic Hospital, Sorbonne University, Paris, France;* [u] *Department of Urology, Agios Pavlos General Hospital of Thessaloniki, Thessaloniki, Greece;* [v] *Guy's and St Thomas' NHS Foundation Trust, London, UK;* [w] *Second Department of Urology, National and Kapodistrian University of Athens, Sismanogleio General Hospital, Athens, Greece;* [x] *Division Woman & Baby, University Medical Center Utrecht, Utrecht, The Netherlands;* [y] *Bergman Clinics Women's Health, The Netherlands;* [z] *Division of Gastroenterology, Department of Medicine, McMaster University, Hamilton, ON, Canada;* [aa] *University of Aberdeen, Aberdeen, UK;* [bb] *European Association of Urology, Arnhem, The Netherlands*

† Karl H. Pang and Riccardo Campi should be considered joint first authors.
‡ Muhammad Imran Omar and Christopher K. Harding should be considered joint senior authors.
* Corresponding author. Academic Urology Unit, Health Sciences Building (second floor), University of Aberdeen, Foresterhill, Aberdeen AB25 2ZD, UK. Tel. +44-1224-438126.
E-mail addresses: m.i.omar@abdn.ac.uk, m.i.omar@uroweb.org (M.I. Omar).

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Abstract

Context: Female bladder outlet obstruction (fBOO) is a relatively uncommon condition compared with its male counterpart. Several criteria have been proposed to define fBOO, but the comparative diagnostic accuracy of these remains uncertain.
Objective: To identify and compare different tests to diagnose fBOO through a systematic review process.
Evidence acquisition: A systematic review of the literature was performed according to the Cochrane Handbook and Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist. The EMBASE/MEDLINE/Cochrane databases were searched up to August 4, 2020. Studies on women $\geq$18 yr of age with suspected bladder outlet obstruction (BOO) involving diagnostic tests were included. Pressure-flow studies or fluoroscopy was used as the reference standard where possible. Two reviewers independently screened all articles, searched reference lists of retrieved articles, and performed data extraction. The risk of bias was assessed using Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2).
Evidence synthesis: Overall, 28 nonrandomised studies involving 10 248 patients were included in the qualitative analysis. There was significant heterogeneity regarding the characteristics of women included in BOO cohorts (ie, mixed cohorts including both anatomical and functional BOO). Pressure-flow studies $\pm$ fluoroscopy was evaluated in 25 studies. Transperineal Doppler ultrasound was used to evaluate bladder neck dynamics in two studies. One study tested the efficacy of transvaginal ultrasound. The urodynamic definition of fBOO also varied amongst studies with different parameters and thresholds used, which precluded a meta-analysis. Three studies derived nomograms using the maximum flow rate (Q_{max}) and voiding detrusor pressure at Q_{max}. The sensitivity, specificity, and overall accuracy ranges were 54.6–92.5%, 64.6–93.9%, and 64.1–92.2%, respectively.
Conclusions: The available evidence on diagnostic tests for fBOO is limited and heterogeneous. Pressure-flow studies $\pm$ fluoroscopy remains the current standard for diagnosing fBOO.
Patient summary: Evidence on tests used to diagnose female bladder outlet obstruction was reviewed. The most common test used was pressure-flow studies $\pm$ fluoroscopy, which remains the current standard for diagnosing bladder outlet obstruction in women.
Take Home Message: The available evidence on diagnostic tests for female bladder outlet obstruction is limited and heterogeneous. The most common test used was video-urodynamics, which remains the current standard for diagnosing bladder outlet obstruction in women.

1. Introduction

Female bladder outlet obstruction (fBOO) is an uncommon condition that can be caused by anatomical or functional abnormalities [1]. The estimated prevalence is 2–23% depending on diagnostic criteria [2]. The International Continence Society (ICS) defines fBOO as "the generic term for obstruction during voiding, characterised by a reduced urine flow rate (FR) and/or presence of a raised post-void residual (PVR) and an increased detrusor pressure (P_{det})" [3]. Female patients typically present with lower urinary tract symptoms (LUTS), which are rarely isolated voiding symptoms [4]. The urodynamics (UDS) criteria and diagnostic cut-off values for fBOO are not defined, and vary in the literature. This is in stark contrast to bladder outlet obstruction (BOO) in males, which is well defined and has a greater evidence base [5]. The objective of the current systematic review (SR) was to identify and compare different diagnostic tests, which have been proposed for the diagnosis of fBOO.

2. Evidence acquisition

2.1. Review protocol and search strategy

The review followed the methods detailed in the *Cochrane Handbook* and followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist (Supplementary Table 1), guided by the European Association of Urology (EAU) Guidelines Office Methods Committee [6–8].

Medline, Embase, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials databases were searched without language or other restrictions for all relevant publications up to August 4, 2020. The search strategy is detailed in the Supplementary material. Reference lists of the included studies were screened, and included for full-text screening and data extraction if they fulfilled our a priori inclusion criteria.

Two review authors (K.H.P. and R.C.) screened all abstracts and full-text articles independently. Any

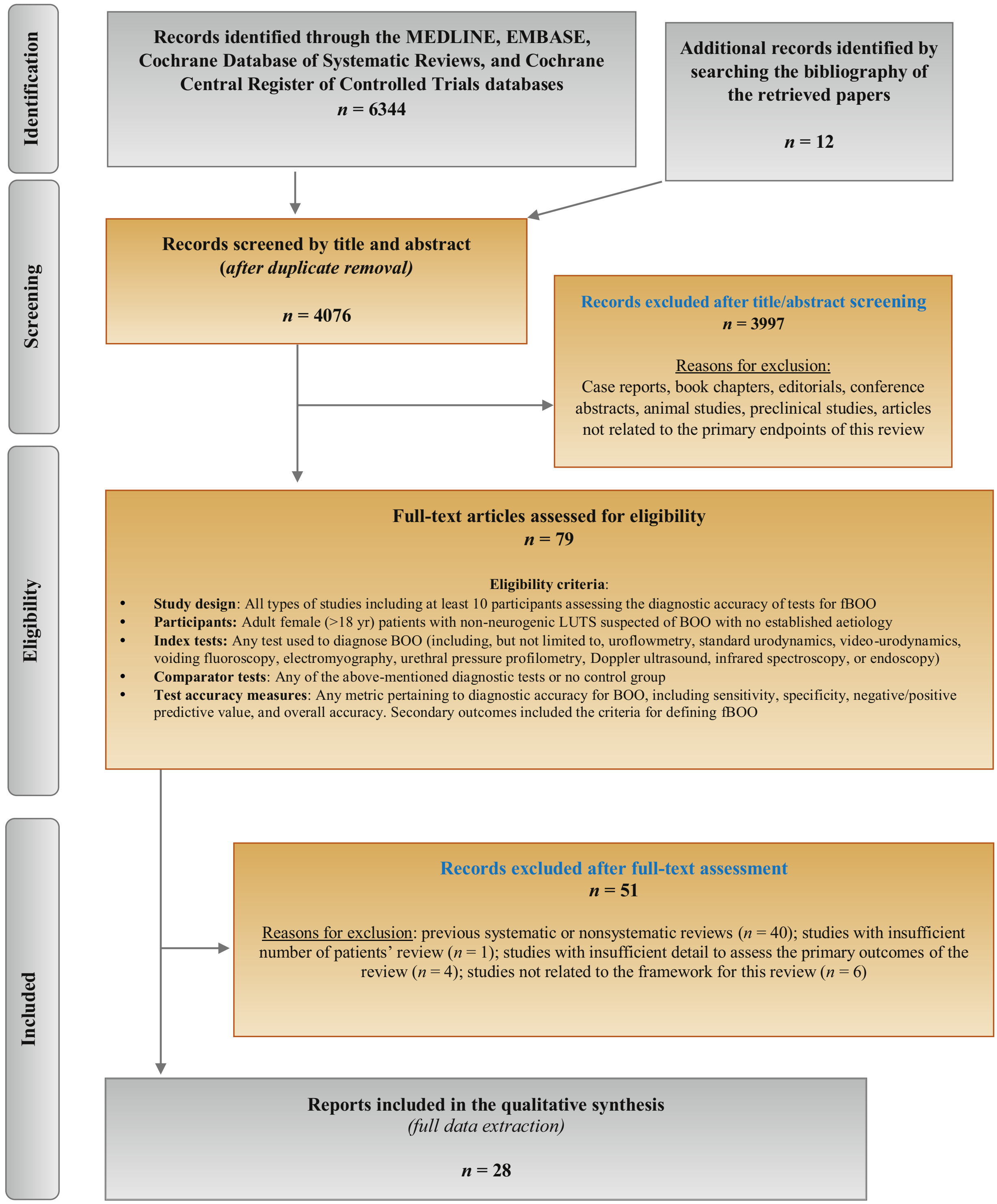

Fig. 1 – Flowchart showing the main steps of the review process according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement recommendations. BOO = bladder outlet obstruction; fBOO = female bladder outlet obstruction; LUTS = lower urinary tract symptoms.

disagreement was discussed and resolved by the senior authors (M.I.O. and C.K.H.). Standardised data extraction was performed by the same two review authors who performed screening. The flowchart depicting the overall review process according to the PRISMA statement is shown in Figure 1.

2.2. *Eligibility criteria*

Eligibility criteria of this SR are the following:

1. *Study design:* All types of studies including at least ten participants assessing diagnostic accuracy of tests for fBOO

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2. *Participants:* Adult female (≥18 yr) patients with non-neurogenic LUTS suspected of BOO with no established aetiology
3. *Index tests:* Any test used to diagnose BOO (including, but not limited to, uroflowmetry, standard UDS, video-urodynamics [VUDS], voiding fluoroscopy, electromyography, urethral pressure profilometry, Doppler ultrasound, infrared spectroscopy, or endoscopy)
4. *Comparator tests:* Any of the abovementioned diagnostic tests or no control group

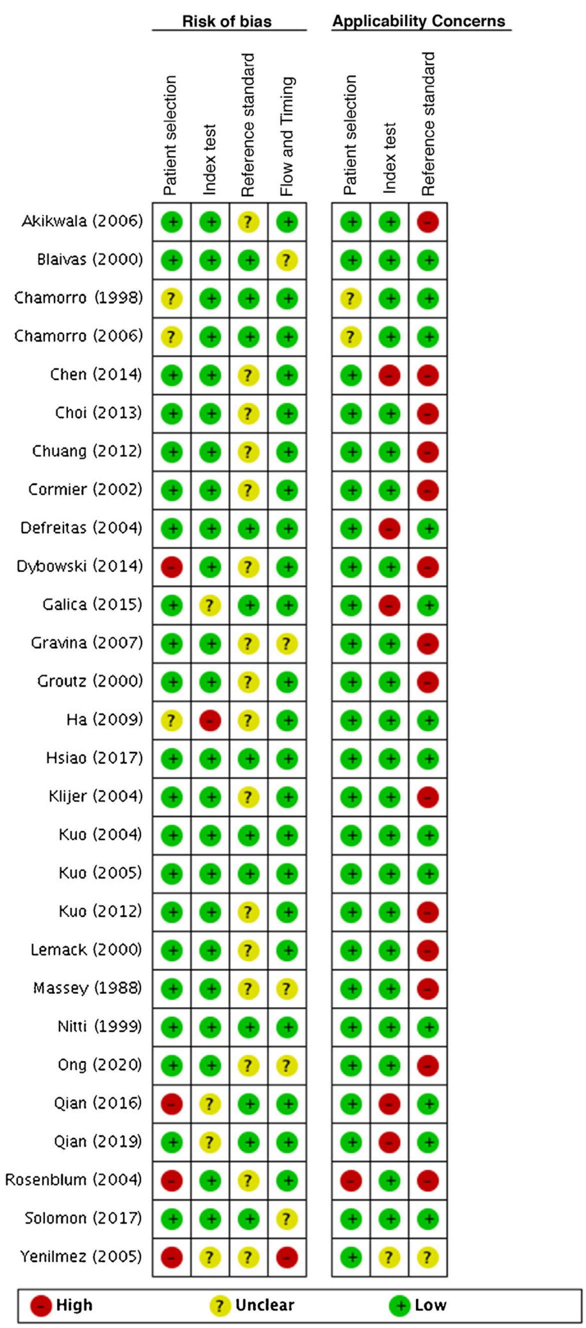

Fig. 2 – Summary of risk of bias and applicability concerns. The figure shows the reviewers' judgements on each domain for each included study according to the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) 2 tool.

5. *Test accuracy measures:* Any metric pertaining to diagnostic accuracy for BOO, including sensitivity, specificity, negative/positive predictive value (NPV/PPV), and overall accuracy
6. Secondary outcomes including the criteria for defining fBOO

2.3. *Assessment of risk of bias in individual studies*

Risk of bias (RoB) assessment within the included studies was performed independently by two authors (K.H.P. and R. C.) according to the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool (Fig. 2 and 3) [9]. This tool provides a measure for RoB and applicability over four domains of interest (patient selection, index test, reference standard, and timing of the index test and the reference standard). A list of the most important potential confounders for outcomes was developed a priori with clinical content experts (EAU Non-neurogenic Female LUTS Guidelines Panel). Confounder assessment included whether each prognostic confounder was considered and whether, if necessary, it was controlled for in the analysis. Potential confounding factors assessed were the following: (1) whether indices for UDS were determined automatically or manually, and (2) whether the UDS adhered to contemporaneous quality standards (ICS standards for studies from 2002 onwards; for studies before 2002, judgement was made by reviewers). Disagreement was solved by a third review author (M.I.O.).

2.4. *Data analysis*

Owing to the expected heterogeneity in definitions and thresholds of the index tests for diagnosing fBOO, a quantitative analysis and meta-analysis was not feasible, and therefore a qualitative (narrative) synthesis of all included studies was performed. Where elements of diagnostic accuracy were not reported by study authors, we calculated these by using a two-by-two contingency table consisting of true positive, false positive, false negative, and true negative rates based on the data reported by study authors. True positive cases were those diagnosed by VUDS used as the reference standard. Measures of test performance included sensitivity, specificity, PPV, NPV, and overall accuracy.

3. Evidence synthesis

3.1. *Study selection*

The search identified 6344 citations. After duplicate report removal, 4076 were screened by abstract and 79 were assessed for full-text eligibility. Overall, 28 studies fulfilled the inclusion criteria set for this review, and 10 248 patients were included in the qualitative analysis (Fig. 1) [4,10–32].

3.2. *Characteristics of the included studies*

The characteristics of the 28 included studies are detailed in Table 1 and Supplementary Table 2. Of these, 25 evaluated

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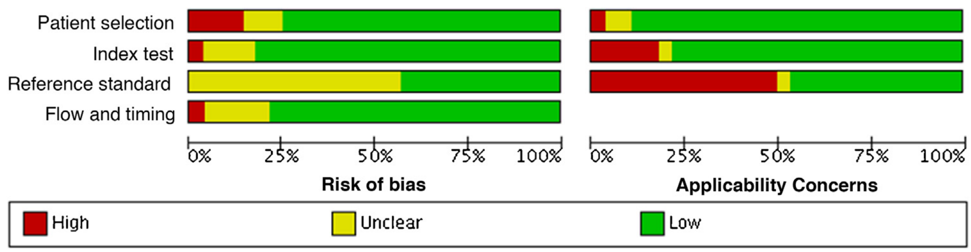

Fig. 3 – Graph of risk of bias and applicability concerns. The figure shows the reviewers' judgements on each domain presented as percentages across included studies according to the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) 2 tool.

the use of UDS ± fluoroscopy [4,10–22,26–36], two of which evaluated pre-existing nomograms [35,36], one evaluated the use of transvaginal ultrasound scan (TVUS) and voiding UDS [23], and two looked at transperineal Doppler ultrasound scan (TPUS) [24,25]. Five studies defined cut-offs for UDS parameters [17,26,29,31,32], one study described fluoroscopic characteristics for fBOO [20], one study evaluated the area under the curve (AUC) of detrusor pressure [18], and three studies derived a nomogram to diagnose fBOO [10,14,19].

3.3. *RoB assessment*

The QUADAS-2 tool was used to assess RoB within studies. Results are graphically illustrated in Figures 2 and 3. The proportions of studies with a low RoB in the "patient selection", "index test", "reference standard", and "flow and timing" domains were 75%, 82.1%, 42.9%, and 78.6%, respectively. The domain showing the highest proportion of studies with an "unclear" RoB was the "reference standard" domain (57.1%). Overall, there were low levels of concern about the applicability of the studies' findings to the review question regarding the "patient selection" and "index test" domains, while there was a high level of concern regarding the "reference standard" domain in more than half of the included studies (54%).

3.4. *Results of individual studies: a narrative synthesis*

The UDS parameter cut-offs, and nomogram and diagnostic details for each study are summarised in Table 2. The overall ranges of diagnostic performance across all tests were as follows: sensitivity, 54.6–92.5%; specificity, 64.6–93.9%; PPV, 50–95.5%; NPV, 33.3–97.1%; and overall accuracy, 64.1–92.2%.

3.4.1. *Defining UDS cut-off values*

Massey and Abrams [32] defined cut-offs of Q_{max} <12 ml/s, $P_{det.Qmax}$ >50 cmH_2O, and urethral resistance >0.2 to diagnose fBOO. In 5948 consecutive patients presenting with LUTS, 163 (2.74%) were found to have fBOO based on these criteria. Lemack and Zimmern [31] performed receiver-operator characteristic analyses from UDS on female patients with voiding LUTS. All patients had prior voiding cystourethrography, and cut-off values of Q_{max} ≤11 ml/s and $P_{det.Qmax}$ ≥21 cmH_2O optimised the diagnostic accuracy for fBOO. These cut-offs provided sensitivity, specificity, and overall accuracy of 91.5%, 73.6%, and 81%, respectively. Defreitas et al [29] found in women with a range of LUTS that the $P_{det.Qmax}$ value with high specificity and the greatest sensitivity for detecting fBOO was 25 cmH_2O, and the Q_{max} value resulting in equal sensitivity, specificity, and accuracy (68%) was close to 12 ml/s. Kuo [17] analysed VUDS data from 580 patients with a range of LUTS, and proposed thresholds of Q_{max} ≤15 ml/s and $P_{det.Qmax}$ ≥35 cmH_2O improving sensitivity, specificity, and overall accuracy for fBOO to 81.6%, 93.9%, and 92.2%, respectively. Gravina et al [26] found that Q_{max} ≤15 ml/s was associated with sensitivity of 78.9% and specificity of 85.9% in a cohort of women with a range of LUTS. A $P_{det.Qmax}$ of ≥28 cmH_2O resulted in poor sensitivity of 64.2% and specificity of 64.6%. However, when using a BOO index ($P_{det.Qmax}$ – $2Q_{max}$) of >–8, the sensitivity and specificity increased to 80.8% and 86.1%, respectively. Cormier et al [18] used the previously defined Q_{max} of <12 ml/s, but evaluated additional UDS parameters: (1) AUC of P_{det} during voiding (AUCdet) and (2) AUC of P_{det} during voiding adjusted for voided volume (AUCdet/Vol), in a cohort of women with a clinical diagnosis of dysfunctional voiding. Dysfunctional voiding is defined by the ICS as "an intermittent and/or fluctuating flow rate due to involuntary intermittent contractions of the peri-urethral striated or levator muscles during voiding in neurologically normal women" [3]. Using linear discriminant analysis, AUCdet/Vol was confirmed as a relevant parameter to classify patients into obstructed, equivocal, and nonobstructed groups. A cut-off value of 5.83 $cmH_2O/s/ml$ separated obstructed from equivocal cases and 2.56 $cmH_2O/s/ml$ distinguished equivocal from unobstructed cases.

3.4.2. *Fluoroscopy*

Nitti et al [20] proposed VUDS criteria, based mainly on fluoroscopic appearance, for diagnosing fBOO. In a study of 261 women with "non-neurogenic voiding dysfunction", BOO was defined as radiographic evidence of obstruction between the bladder neck (BN) and distal urethra in the presence of a sustained detrusor contraction of any magnitude, which was usually associated with a reduced urinary flow rate. Bladder neck obstruction (BNO) was diagnosed when the BN was closed/narrowed during attempted voiding. Radiographic obstruction of the urethra was diagnosed as a discrete area of narrowing with proximal dilatation. Strict pressure-flow criteria were not used to classify cases as obstructed or unobstructed in their study. Overall, 76 (29.1%) patients met the fluoroscopic criteria for

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Table 1 – Overview of the design, patient population, and diagnostic criteria for bladder outlet obstruction among the studies included in the review

First author (year)	Study design	Country	Clinical presentation	Total no. of patients analysed	BOO, *n* (%)	Age (yr), mean (SD or range)	Test evaluated	Reference test	Diagnostic criteria for BOO as reported by authors
Akikwala (2006) [27]	Prospective—single centre	USA	LUTS	91	40 (44.0)	62.3 (16–90)	VUDS, PF EMG	Fluoroscopy	Five criteria, including (1) fluoroscopy, (2) Q_{max} ≤15 ml/s and $P_{det.Qmax}$ ≥20 cmH_2O, (3) Q_{max} ≤11 ml/s and $P_{det.Qmax}$ ≥21 cmH_2O, (4) Q_{max} ≤12 ml/s and $P_{det.Qmax}$ ≥25 cmH_2O, and (5) the Blaivas-Groutz nomogram
Blaivas (2000) [19]	Retrospective—single centre	USA	LUTS	100	50 (50)	BOO: 64.4 (17.6); unobstructed: mean 64.8 (10.7)	VUDS, EMG, endoscopy	Fluoroscopy	One or more: (1) free Q_{max} ≤12 ml/s and $P_{det.Qmax}$ ≥20 cmH_2O, (2) radiographic evidence BOO with sustained detrusor contraction ≥20 cmH_2O and poor Q_{max} regardless of free Q_{max}, (3) inability to void with transurethral catheter in place despite a sustained detrusor contraction of ≥20 cmH_2O
Chen (2014) [22]	Retrospective—single centre	Taiwan	LUTS	440	168 (38.2)	DV: 67.8 (18.1); control: 58.9 (18.4)	VUDS	Fluoroscopy	DV: high P_{det}, intermittent or increased external sphincter EMG activity and a "spinning top" urethral appearance on cinefluoroscopy during voiding
Choi (2013) [11]	Prospective—multicentre	Korea	LUTS	792	89 (11.2)	Voiding difficulty: 61.8 (12.1); LUTS: 62.7 (10.2)	UDS	Clinical assessment	Q_{max} <15 ml/s and $P_{det.Qmax}$ >20 cmH_2O
Chuang (2012) [16]	Retrospective—single centre	Taiwan	LUTS	781	405 (51.9)	NR	VUDS	Fluoroscopy	BND: VUDS revealing narrow BN with high/normal detrusor contractility; DV: high P_{det} with open BN and narrow mid urethra during voiding; stricture: narrow distal urethra with low FR regardless high/normal VP; PRPF: could not relax their PF muscle with low VP and intermittent flow
Cormier (2002) [18]	Prospective—single centre	France	VD	85	21 (24.7)	55 (18-83)	VUDS, UP	Fluoroscopy	Q_{max} <12 ml/s and PVR > 150 ml
Defreitas (2004) [29]	Prospective—single centre	USA	LUTS	313	169 (54.0)	BOO: 60 (15); control: 42 (7)	UDS	Clinical assessment	Q_{max} <12 ml/s and $P_{det.Qmax}$ >25 cmH_2O
Dybowski (2014) [14]	Retrospective—multicentre	Poland	Voiding LUTS	67	21 (31.3)	Median 53	UDS	Clinical assessment	BOO = ($P_{det.Qmax}$ – 1.5 × Q_{max}) > 10
Galica (2015) [23]	Retrospective—single centre	Italy	BOO symptoms	15	3 (20)	NR	TVUS, VUDS, EMG	Fluoroscopy	Q_{max} <12 ml/s and $P_{det.Qmax}$ >20 cmH_2O, no images for urethral stricture at fluoroscopy, silent EMG
Gravina (2007) [26]	Retrospective—single centre	Italy	LUTS	170	133 (78.2)	BOO, median (IQR): 62 (56–69); unobstructed: 57.5 (48.3–63.5)	UDS	Clinical assessment	1. Q_{max} cut-off <15 ml/s
									2. BOOI cut-off >–8
									3. $P_{det.Qmax}$ ≥28 cmH_2O

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Table 1 (*Continued*)

First author (year)	Study design	Country	Clinical presentation	Total no. of patients analysed	BOO, *n* (%)	Age (yr), mean (SD or range)	Test evaluated	Reference test	Diagnostic criteria for BOO as reported by authors
Groutz (2000) [4]	Retrospective—single centre	USA	Voiding LUTS	587	38 (6.5)	63.9 (17.5)	VUDS, EMG, endoscopy	Fluoroscopy	Q_{max} <12 ml/s and $P_{det.Qmax}$ >20 cmH_2O; site of obstruction: narrowest point in the urethra during VCUG; urethral obstruction: (1) visible signs of narrowed urethra, analogous to urethral stricture in men; (2) the urethra felt narrow because it "gripped" the cystoscope; or (3) the bladder neck and proximal urethra appeared to be compressed, analogous to benign prostate hyperplasia in men
Ha (2009) [34]	Retrospective—multicentre	Korea	LUTS	320	39 (12.2)	BOO: 55.4 ± 14.7; non-BOO: 55.2 ± 12.4	UDS	Clinical assessment	Q_{max} ≤12 ml/s and $P_{det.Qmax}$ ≥25 cmH_2O
Hsiao (2017) [21]	Retrospective—single centre	Taiwan	VD	1914	1858 (97.1)	Anatomic BOO: 57.8 (16.7); functional BOO: 59.4 (13.8); bladder dysfunction: 64.7 (16.2); normal tracings: 54.0 (14.3)	VUDS, urethral EMG	Fluoroscopy	$P_{det.Qmax}$ cut-off = 30 cmH_2O for differentiating BOO from bladder dysfunction and normal tracings; cystoscopy was used in conjunction with the VUDS findings for differential diagnosis of the aetiology of BOO
Klijer (2004) [30]	Prospective—single centre	Poland	Chronic bladder symptoms	53	19 (35.9)	Median (range): 37.5 (16–70)	Uroflowmetry, UDS, VCUG	Fluoroscopy	Q_{max} <15 ml/s and $P_{det.Qmax}$ >40 cmH_2O; site determined by fluoroscopy
Kuo (2004) [17]	Retrospective—single centre	Taiwan	LUTS	580	76 (13.1)	BOO: 50.2 (15.1); SUI: 51 (12.7); asymptomatic: 44.6 (16.4)	VUDS	Fluoroscopy	1. Obstructive voiding and irritative symptoms
									2. Sustained detrusor contraction during voiding phase in UDS
									3. Radiological evidence of narrow BN or distal urethra during voiding phase
									4. DSD: increased sphincter EMG during voiding; PRPF: no concomitant relaxation of EMG activity during micturition
Kuo (2005) [12]	Retrospective—single centre	Taiwan	BOO signs and symptoms	207	194 (93.7)	57 (23)	VUDS, urethral EMG	Fluoroscopy	BOO: radiological evidence of obstruction in the bladder outlet on voiding cystourethrography plus voiding detrusor pressure >35 cmH_2O in combination with Q_{max} <15 ml/s. DSD: increased sphincter EMG during voiding; PRPF: no concomitant relaxation of EMG activity during micturition

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Table 1 (***Continued***)

First author (year)	Study design	Country	Clinical presentation	Total no. of patients analysed	BOO, *n* (%)	Age (yr), mean (SD or range)	Test evaluated	Reference test	Diagnostic criteria for BOO as reported by authors
Kuo (2012) [15]	Retrospective—single centre	Taiwan	LUTS and pain	1605	314 (19.6)	58 (18–98)	VUDS	Fluoroscopy	BND: VUDS revealing narrow BN with high/normal detrusor contractility; DV: high P_{det} with open BN and narrow midurethra during voiding; stricture: narrow distal urethra with low FR regardless of high/normal VP; PRPF: could not relax their PF muscle with low VP and intermittent flow
Lemack (2000) [31]	Prospective—single centre	USA	Voiding LUTS	211	87 (41.2)	NR	UDS, PF EMG	Clinical assessment	$Q_{max} \le 11$ ml/s and $P_{det.Qmax} \ge 21$ cmH_2O
Massey (1988) [32]	Retrospective—single centre	UK	LUTS	163	163 (100)	51.6 (8–81)	Uroflowmetry, UDS, UP, EMG	Fluoroscopy	Two or more of the following parameters: (1) $Q_{max} < 12$ ml/s, (2) $P_{det.Qmax} > 50$ cmH_2O, (3) urethral resistance > 0.2 (P/F^2), (4) "significant" residual urine in the presence of raised $P_{det.Qmax}$ or urethral resistance
Nitti (1999) [20]	Retrospective—single centre	USA	Non-neurogenic VD	261	76 (29.1)	BOO: 57.5; unobstructed: 55	VUDS	Fluoroscopy	BOO: radiographic evidence of obstruction between BN and distal urethra with sustained detrusor contraction of any magnitude, which was usually associated with reduced or delayed urinary flow rate; radiographic obstruction at the BN was diagnosed when BN was closed/narrow during voiding; radiographical obstruction of the urethra was diagnosed as a discrete area of narrowing with proximal dilatation
Ong (2020) [13]	Retrospective—single centre	Taiwan	LUTS	530	474 (89.4)	BOO: 57.8 (16.7); BND: 63.9 (17.1); DV: 61.1 (16.5); normal VUDS: 54.0 (14.3)	VUDS, EMG, VCUG	Fluoroscopy	High voiding pressure: $P_{det.Qmax} \ge 35$ cmH_2O
Qian (2016) [24]	Retrospective—single centre	China	LUTS	66	36 (54.6)	BNO: 55 (13); control: 50 (14)	TPUS and Virtual Touch tissue quantification	UDS	1. Polyuria, urgency, frequency, nocturia, dysuria
									2. BN enlarged on USS, PVR > 50 ml
									3. Cystoscopy: resistance on insertion, BN thickened, apophysis on anterior or posterior lip
									4. BOO: $Q_{max} < 12$ ml/s with $P_{det.Qmax} > 20$ cmH_2O
Qian (2019) [25]	Retrospective—single centre	China	LUTS	51	27 (52.9)	FBNO: 56 (10); control: 47 (16)	TPUS	UDS	Best ROC cut-off for FBNO: SWV 2.38 m/s

Table 1 (*Continued*)

First author (year)	Study design	Country	Clinical presentation	Total no. of patients analysed	BOO, *n* (%)	Age (yr), mean (SD or range)	Test evaluated	Reference test	Diagnostic criteria for BOO as reported by authors
Rosenblum (2004) [28]	Retrospective—single centre	USA	LUTS	57	2 (3.5)	30 (19–47)	VUDS, PF EMG, CMG	Fluoroscopy	BOO: fluoroscopy; DV: increased external sphincter activity during voluntary voiding, as evidenced by EMG tracing and/or fluoroscopy, with a sustained detrusor contraction
Solomon (2018) [10]	Retrospective—single centre	UK	LUTS	535	125 (23.4)	Obstructed: 51.9 (12.3); unobstructed: 49.1 (16.1)	VCMG	Fluoroscopy	BOO likely if $P_{det.Qmax} > 2.2 \times Q_{max} + 5$
									BOOIf = $P_{det.Qmax} - 2.2 \times Q_{max}$, that is, BOOIf <0, <10% probability of obstruction; BOOIf >5, likely obstructed (50%); and BOOIf >18, obstruction almost certain (>90%)
Vírseda Chamorro (1998) [35]	Retrospective—single centre	Spain	LUTS	80	56 (70)	62.19 (13.29); range (18–84)	Standard UDS, urethral resistance	Clinical assessment	Noninvasive Q_{max} ≤10th percentile in Haylen nomogram
						Women with VD: 64.39 (11.62)			
						Women without VD: 56.36 (15.76)			
Vírseda Chamorro (2006) [36]	Cross-sectional study	Spain	LUTS	52	25 (48.1)	48.7 (14.4; range 20–81)	VUDS, Blaivas-Groutz nomogram	Fluoroscopy	High P_{det} associated with one of the following: (1) absence of BNO, (2) decrease in urethral diameter with proximal dilatation (urethral obstruction)
Yenilmez (2005) [33]	Retrospective—single centre	Turkey	LUTS	122	39 (32.0)	Group 1 urethral stricture (*n* = 19): 58.6 ± 10.5; group 2 DV (*n* = 13): 46.8 ± 15.2; group 3 pelvic prolapse (*n* = 7): 56.1 ± 9.4; controls (SUI group; *n* = 83): 54.1 ± 9.7	UDS, endoscopy	Clinical assessment	Q_{max} ≤15 ml/s and $P_{det.Qmax}$ >20 cmH_2O (endoscopic measures and clinical symptoms should also be considered)

BN = bladder neck; BND = bladder neck dysfunction; BNO = bladder neck obstruction; BOO = bladder outlet obstruction; BOOI = BOO index; BOOIf = bladder BOOI female; CMG = cystometrogram; DSD = detrusor sphincter dyssynergia; DV = dysfunctional voiding; EMG = electromyography; FBNO = female BNO; FR = flow rate; IQR = interquartile range; LUTS = lower urinary tract symptoms; NR = not reported; P_{det} = detrusor pressure; $P_{det.Qmax}$ = detrusor pressure at Q_{max}; PF = pelvic floor; PRPF = poor relaxation of pelvic floor; PVR = postvoid residual; Q_{max} = maximum flow rate; ROC = receiver operating characteristic curve; SD = standard deviation; SUI = stress urinary incontinence; SWV = shear wave velocity; TPUS = transperineal two-dimensional Doppler ultrasound; TVUS = transvaginal ultrasound; UDS = urodynamics; UP = urethral profiling; USS = ultrasound scan; VD = voiding dysfunction; VCMG = video cystometrogram; VCUG = voiding cystourethrography; VP = vesical pressure; VUDS = video urodynamics.

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Table 2 – Overview of the accuracy metrics (including sensitivity, specificity, negative predictive value, positive predictive value, and overall accuracy) of different tests used to diagnose bladder outlet obstruction among the studies included in the review

First author (year)	Q_{max} (ml/s)	$P_{det.Qmax}$ (cmH_2O)	Nomogram	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Overall accuracy (%)
(Video)urodynamics								
Akikwala (2006) [27]	≤15, ≤11, ≤12	≥20, ≥21, ≥25	NA	NR	NR	NR	NR	NR
Chen (2014) [22]	DV ≥15	>35	NA	NR	NR	NR	NR	NR
Choi (2013) [11]	<15	>20	NA	NR	NR	NR	NR	NR
Chuang (2012) [16]	NR	>35	NA	NR	NR	NR	NR	NR
Cormier (2002) [a] [18]	<12	NR	NA	NR	NR	NR	NR	NR
Defreitas (2004) [a] [29]	<12	>25	NA	Q_{max}: 68; $P_{det.Qmax}$: NA	Q_{max}: 68; $P_{det.Qmax}$: NA	Q_{max}: 71.4; $P_{det.Qmax}$: NA	Q_{max}: 64.5; $P_{det.Qmax}$: NA	Q_{max}: 68; $P_{det.Qmax}$: NA
Gravina (2007) [a] [26]	≤15	≥28	NA	Q_{max}: 78.9; BOOI: 80.8; $P_{det.Qmax}$: 64.2	Q_{max}: 85.9; BOOI: 86.1; $P_{det.Qmax}$: 64.6	Q_{max}: 95.4; BOOI: 95.5; $P_{det.Qmax}$: 86.7	Q_{max}: 53.3; BOOI: 56.1; $P_{det.Qmax}$: 33.3	Q_{max}: 80.5; BOOI: 82.3; $P_{det.Qmax}$: 64.1
Groutz (2000) [4]	<12	>20	NA	NR	NR	NR	NR	NR
Ha (2009) [34]	≤15 Maximal voided volume ≤350 ml	–	NA	Q_{max}: 82 Maximal voided volume: 71	Q_{max}: 72 Maximal voided volume: 46	Q_{max}: 34.4 Maximal voided volume: 28.2	Q_{max}: 96.5 Maximal voided volume: 91.2	Q_{max}: 73.1 Maximal voided volume: 49.0
Hsiao (2017) [21]	≤15	>30	NA	54.6	91.8	82.9	73.4	76.0
Klijer (2004) [30]	<15	>40	NA	NR	NR	NR	NR	NR
Kuo (2004) [a] [17]	≤15	≥35	NA	$P_{det.Qmax}$ ≥35 cmH_2O and Q_{max} ≤15 ml/s: 81.6	$P_{det.Qmax}$ >35 cmH_2O and Q_{max} <15 ml/s: 93.9	66.7	97.1	92.2
Kuo (2005) [12]	<15	>35	NA	NR	NR	NR	NR	NR
Kuo (2012) [15]	NR	>35	NA	NR	NR	NR	NR	NR
Lemack (2000) [a] [31]	≤11	≥21	NA	91.5	73.6	50.0	96.8	81
Massey (1988) [a] [32]	<12	>50	NA	NR	NR	NR	NR	NR
Nitti (1999) [20]	NR	NR	NA	NR	NR	NR	NR	NR
Ong (2020) [13]	NR	≥35: high-pressure BND; <35: low-pressure BND	NA	NR	NR	NR	NR	NR
Rosenblum (2004) [28]	NR	NR	NA	NR	NR	NR	NR	NR
Vírseda Chamorro (1998) [35]	≤10 percentile	–	Used the Haylen (Liverpool) nomogram	91	45	79.6	68.7	77.5
Vírseda Chamorro (2006) [36]	≤12	≥20	Used Blaivas-Groutz nomogram	100	67.5	71.4	100	80.8
Yenilmez (2005) [33]	≤15	>20	NA	84.6	84.3	76.7	92.1	
Nomograms								

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Table 2 (*Continued*)

First author (year)	Q_{max} (ml/s)	$P_{det.Qmax}$ (cmH_2O)	Nomogram	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Overall accuracy (%)
Blaivas (2000) [19]	≤12	≥20	Classify into no, mild, moderate, severe obstruction: (1) between unobstructed and minimally obstructed: a line with slope 1.0 and intercept 7 cmH^2O; (2) between minimally and moderately obstructed: a horizontal line at P_{detmax} 57 cmH_2O; (3) between moderately and severely obstructed: a horizontal line at $P_{det.Qmax}$ 107 cmH_2O	NR	NR	NR	NR	NR
Dybowski (2014) [14]	≤12	NR	$P_{det.Qmax} = 1.5 \times Q_{max} + 10$; BOO = $(P_{det}(Q_{max}) - 1.5 \times Q_{max}) > 10$	90.5	65.2	54.3	94	73.1
Solomon (2018) [10]	NR	NR	If $P_{det.Qmax} = 2.2 \times Q_{max} + 5$ or BOOIf = $P_{det.Qmax} - 2.2 \times Q_{max}$ (<0 = <10%, >5 = 50%, >18 = >90% obstructed)	86	93	78.8	95.7	91.4
Transvaginal USS								
Galica (2015) [26]	<12	>20	NA	NR	NR	NR	NR	NR
Transperineal Doppler USS								
Qian (2016) [24]	<12	>20	NA	Anterior lip SWV 2.11 m/s: 69.4 (AUC 0.782); posterior lip SWV 2.06 m/s: 66.7 (AUC 0.831)	Anterior lip SWV 2.11 m/s: 81.5 (AUC 0.782); posterior lip SWV 2.06 m/s: 85.2 (AUC 0.831)	Anterior: 80.7; posterior: 85.7	Anterior: 68.6; posterior: 68.4	Anterior: 74; posterior: 80.6
Qian (2019) [25]	NA	NA	NA	ARFI: 88.9; SWE: 81.5; combined: 92.5	ARFI: 79.2; SWE: 79.2; combined: 87.5	ARFI: 82.8; SWE: 81.5; combined: 89.3	ARFI: 86.4; SWE: 79.2; combined: 91.3	ARFI: 84.3; SWE: 80.4; combined: 90.2

ARFI = acoustic radiation force impulse; AUC = area under the curve; BND = bladder neck dysfunction; BOO = bladder outlet obstruction; BOOIf = BOO index female; DV = dysfunctional voiding; NA = not applicable; NPV = negative predictive value; NR = not reported or necessary information required to calculate this test accuracy measure not reported; $P_{det.Qmax}$ = detrusor pressure at Q_{max}; PPV = positive predictive value; Q_{max} = maximum flow rate; SWE = shear wave elastography; SWV = shear wave velocity; USS = ultrasound scan.

[a] Defined Q_{max} and $P_{det.Qmax}$ cut-offs.

obstruction, but diagnostic performance statistics in comparison with pressure-flow thresholds were not reported.

3.4.3. UDS and fluoroscopy

The ranges of diagnostic values for all VUDS studies included were as follows: sensitivity, 54.6–91.5%; specificity, 64.6–93.9%; PPV, 50–95.5%; NPV, 33.3–97.1%; and overall accuracy, 64.1–92.2%. Several studies have used predefined UDS cut-offs to evaluate their cohorts.

Groutz et al [4] used Q_{max} ≤15 ml/s and $P_{det.Qmax}$ >20 cmH_2O (Chassagne et al's [37] criteria) to diagnose BOO in 6.5% of 587 women presenting with voiding symptoms. Klijer et al [30] used a Q_{max} of <15 ml/s and a $P_{det.Qmax}$ of >40 cmH_2O, and diagnosed BOO in 18.9% of 53 women with "chronic bladder symptoms". Choi et al [11] analysed 792 women with a range of LUTS and diagnosed BOO in 11.2%, using Q_{max} <15 ml/s and $P_{det.Qmax}$ >20 cmH_2O. Rosenblum et al [28] evaluated voiding dysfunction in 57 nulliparous women with a range of LUTS, and female BNO (fBNO) was diagnosed in 3.5% using Nitti et al's [20] radiological criteria.

Yenilmez et al [33] examined a UDS database of 412 women with various LUTS and analysed 122 with complete data. Testing different Q_{max} and $P_{det.Qmax}$ cut-offs, Q_{max} ≤15 ml/s and $P_{det.Qmax}$ >20 cmH_2O gave sensitivity and specificity of 84.6% and 84.3%, respectively.

Ha et al [34] conducted UDS on 320 women with LUTS and diagnosed 39 (12.2%) with BOO using cut-offs of Q_{max} ≤12 ml/s and $P_{det.Qmax}$ >25 cmH_2O. They found that the use of a Q_{max} of ≤15 ml/s resulted in sensitivity and specificity of 83% and 72%, respectively.

Six studies from the same group used VUDS to evaluate females with LUTS [15], voiding dysfunction [13,16,21], dysfunctional voiding [22], and signs and symptoms of BOO [12]. Nitti et al's [20] criteria were used for the radiological definition of BOO, and the Q_{max} (<15 ml/s) and $P_{det.Qmax}$ (>35 cmH_2O) cut-offs were used as pressure-flow thresholds [17]. In another study, VUDS findings from 1914 women with suspected voiding dysfunction were examined and BOO was diagnosed in 42.3%. Using diagnostic thresholds of $P_{det.Qmax}$ >30 cmH_2O for fBOO, sensitivity, specificity, and overall accuracy of, respectively, 54.6%, 91.8%, and 76% were obtained. Using an Abrams-Griffiths BOO index cut-off of 30 for differentiating anatomic BOO from functional BOO yielded sensitivity of 46.9% and specificity of 76.5% [21]. Ong et al [13] identified bladder neck dysfunction (BND) in 12.3% of 810 women with voiding dysfunction. They further classified BND into high ($P_{det.Qmax}$ ≥35 cmH_2O) or low (<35 cmH_2O) pressure.

Akikwala et al [27] compared five UDS definitions and determined their correlation in women with a clinical suspicion of fBOO:

1. Nitti et al's [20] radiological definitions
2. Q_{max} ≤15 ml/s and $P_{det.Qmax}$ ≥20 cmH_2O (Chassagne et al's [37] criteria)
3. Q_{max} ≤11 ml/s and $P_{det.Qmax}$ ≥21 cmH_2O (Lemack and Zimmern's [31] criteria)
4. Q_{max} ≤12 ml/s and $P_{det.Qmax}$ ≥25 cmH_2O (Defreitas et al's [29] cut-offs)
5. Blaivas-Groutz nomogram [19]

A total of 91 women were evaluated and 40 (44%) had fBOO by at least one criterion. Overall, 38 (42%) were diagnosed with fBOO using the Blaivas-Groutz nomogram, 28 (31%) using Chassagne et al's [37] criteria, 26 (29%) using Nitti et al's [20] criteria, 18 (20%) using Lemack and Zimmern's [31] criteria, and 13 (14%) using Defreitas et al's [29] proposed thresholds. The study concluded that Nitti et al's [20] radiological criteria and Chassagne et al's [37] pressure-flow criteria have the highest concordance, the Blaivas-Groutz nomogram overestimated fBOO, whereas Defreitas et al's [29] cut-offs tended to underestimate it [27].

3.4.4. Nomograms to define fBOO

Nomograms are commonly used for the diagnosis of male BOO and most show good concordance [5]. However, there is greater disparity in diagnostic methods for fBOO. The Blaivas-Groutz nomogram used free Q_{max} and $P_{det.max}$ to define four groups: severe, moderate, mild, and no obstruction. Using this nomogram, 50 obstructed patients (Q_{max} ≤12 ml/s and $P_{det.Qmax}$ ≥20 cmH_2O) were reclassified into those with severe (*n* = 4, 8%), moderate (*n* = 12, 24%), and mild (*n* = 34, 68%) BOO. Of the 50 unobstructed controls, 40 (80%) women were classified as those having no obstruction by the nomogram, six (12%) having between no obstruction and mild obstruction, and the remaining four (8%) being mildly obstructed [19]. Vírseda Chamorro et al [36] categorised 52 women with LUTS according to the Blaivas-Groutz nomogram and compared the results with VUDS findings. Using the nomogram, the sensitivity for BOO was 100%, but its specificity was 67.5%. In addition, Vírseda Chamorro et al [35] also used the Liverpool uroflowmetry nomogram [38] to categorise women with Q_{max} percentile ≥50 or ≤10, and, using UDS, found that the urethral resistance average was the only significant UDS parameter to diagnose voiding dysfunction in women.

Dybowski et al [14] proposed a new nomogram following the observation that when Q_{max} and $P_{det.Qmax}$ of individual patients were plotted on a pressure-flow graph, a distinctive distribution of patients with clinical signs and symptoms of BOO was noted, enabling a straight line to be drawn. The straight line separating obstructed women from the rest (described by the equation $P_{det.Qmax} = 1.5 \times Q_{max} + 10$) was tested on 67 women, and the sensitivity, specificity, PPV, NPV, and overall accuracy were 90.5%, 65.2%, 54.3%, 94%, and 73.1%, respectively.

The Solomon-Greenwell nomogram used Q_{max} and $P_{det.Qmax}$ based on radiographic evidence of increased urethral resistance and a Bayesian approach rather than suggesting discrete pressure-flow thresholds. In a cohort of 535 women with various LUTS, the sensitivity, specificity, PPV, NPV, and overall accuracy were 86%, 93%, 78.8%, 95.7%, and 91.4%, respectively. The authors proposed a female BOO index (BOOIf) calculated using the following formula: BOOIf = $P_{det.Qmax}$ – 2.2x Q_{max}. The percentages of fBOO were <10%, 50%, and >90% if the BOOIf values were <0, >5, and >18, respectively [10]. This nomogram was tested for

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correlation with symptoms in 1014 women with LUTS, and the most common symptom in the 19% diagnosed with fBOO was increased daytime urinary frequency [37]. Treatment validation was also examined in a study of 21 women treated at the authors' own institution [38]. Sensitivity to change was demonstrated with consistent reductions in indices and probability of fBOO after treatment.

3.4.5. Transvaginal ultrasound scan

Galica et al [23] investigated the role of TVUS in women with LUTS suggestive of BOO, and Q_{max} <12 ml/s and $P_{det.Qmax}$ >20 cmH_2O. A mean distance of 1.3 cm from the BN to the vaginal wall was found in women with BNO (fBNO). The authors concluded that VUDS remains the principal diagnostic method and did not propose a diagnostic method based on ultrasonographic indices.

3.4.6. Transperineal Doppler ultrasound scan

Two separate studies in women with a range of LUTS evaluated TPUS in diagnosing fBNO. In one study, transperineal sonography and Virtual Touch tissue quantification were used. BOO was defined as Q_{max} <12 ml/s and $P_{det.Qmax}$ >20 cmH_2O. The thickness and shear wave velocity (SWV) of the BN were higher in the fBNO group. For the anterior and posterior lips of the BN, SWVs of 2.11 m/s (AUC 0.78; sensitivity 69.4%; specificity 81.5%) and 2.06 m/s (AUC 0.83; sensitivity 66.7%; specificity 85.2%) were the best thresholds for diagnosing fBNO [24]. In another study, fBNO was diagnosed with cystoscopy and/or UDS, and the diagnostic efficacy of shear wave elastography (SWE) and acoustic radiation force impulse imaging (ARFI) was compared. Using both in combination was better than using either ARFI or SWE alone. This provided sensitivity, specificity, PPV, NPV, and overall accuracy of 92.5%, 87.5%, 89.3%, 91.3%, and 90.2%, respectively [25].

3.4.7. Excluded studies

A couple of earlier studies were not included in the current SR because the inclusion criteria were not met. Axelrod and Blaivas [39] in a study of three patients defined fBNO as Q_{max} <12 ml/s, sustained detrusor contraction ≥20 cmH_2O, and radiological evidence of obstruction at the vesical neck. Chassagne et al [37] in a study that was not included, as a proportion of patients had stress urinary incontinence, used thresholds of Q_{max} ≤15 ml/s and $P_{det.Qmax}$ >20 cmH_2O to diagnose fBOO, and reported sensitivity and specificity of 74.3% and 91.1%, respectively. These cut-off values were also used in a number of studies included in this SR.

3.5. Discussion

3.5.1. Principal findings

This is the first SR to summarise evidence from 28 studies involving 10 248 patients comparing the diagnostic measures of different tests used to diagnose fBOO. It is evident that studies within this topic area are difficult to compare for a number of reasons. Firstly, the included studies show considerable variation in inclusion criteria. Some studies have looked at a general population of women with LUTS, whereas others have concentrated on those with predominant voiding symptoms, and some have investigated groups with a poorly defined range of clinical diagnoses such as “voiding dysfunction” or “chronic bladder symptoms”. This results in a wide range of prevalence rates, and consequently the true incidence of fBOO is difficult to define.

Further heterogeneity is encountered due to a lack of consensus and consistency regarding reference UDS criteria used to diagnose fBOO. This variation has ultimately precluded any meta-analysis of these data. Nitti et al's [20] radiological definition of fBOO and the UDS thresholds of Q_{max} <12 ml/s and $P_{det.Qmax}$ >20 cmH_2O appear to be the most widely used diagnostic cut-offs, indicating that VUDS is the current standard investigation for fBOO, which is reflected in the recommendations of contemporary guidelines [1].

Novel diagnostic measurements and parameters have not enjoyed widespread uptake. The AUC/volume method proposed by Cormier et al [18] has not been replicated in larger studies. Similarly, the BOO index cut-off of ≥–8 to diagnose fBOO, proposed by Gravina et al [26], is derived from the work in males by Abrams and Griffiths and may not be applicable in women. Urethral pressure profile studies and surface electromyography are not utilised widely in contemporary clinical practice and considered optional, perhaps due to a poor correlation between results from different centres and continuing scepticism regarding the additional value provided by these tests [1,40].

Three nomograms (Blaivas-Groutz, Dybowski, and Solomon-Greenwell) were identified in this SR, and were based on Q_{max} and P_{detmax} or $P_{det.Qmax}$ [10,14,19]. However, there have been no head-to-head studies, and hence strong recommendations cannot be made regarding their comparative utility.

3.5.2. Implications for clinical practice

At present, there are no standardised UDS parameters and hence no widely accepted definition for fBOO. Clinical history, pelvic ultrasound scan, and flow rates provide guidance to decide on more invasive investigations such as endoscopy or (V)UDS. TPUS is as an alternative noninvasive method in diagnosing fBNO [24,25], and the use of TVUS to assess the BN [20] may be more appropriate as adjuncts rather than primary diagnostic modalities.

3.5.3. How the review compares with previous reviews/guidelines

We have highlighted the difficulties in establishing appropriate and accepted criteria to define fBOO. The complexity of the diagnosis of fBOO was highlighted in a meeting of experts, which concluded that the diagnosis should be multifactorial and should include a detailed history, neurological and urogynaecological examination, pressure-flow studies, voiding phase fluoroscopy, urethral pressure profile, ultrasound, and cystoscopy [2].

3.5.4. Strengths and limitations

A major strength of this review is the systematic approach taken to examine the evidence base, including the use of Cochrane methodology, RoB assessment using QUADAS-2 tool, and adherence to the PRISMA checklist.

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There are limitations at a review level. Firstly, we included only studies with a minimum sample size (including ten or more patients), potentially limiting the inclusion of promising studies on other diagnostic techniques. However, such smaller series are deemed unlikely to influence practice due to a lack of power and potential for selection bias. Secondly, we intentionally excluded from the final qualitative analysis the studies that included female patients with LUTS for whom a clear aetiological diagnosis was established *before* undergoing any diagnostic test for suspected BOO. While following this criterion has allowed us to homogenise the final qualitative analysis by focusing only on studies including women with *suspected* BOO of (predominantly) unknown cause, this choice might have led us to exclude potentially relevant papers describing useful diagnostic tests for fBOO. Thus, our findings should be interpreted carefully in light of the specific research question framework defined for this review.

There are limitations at a study level, including the heterogeneity amongst studies with regard to both definitions and the use of index tests and reference standards, as shown by our RoB assessment (Fig. 2 and 3).

We assumed, based on current guidelines [1] and consensus publications [2], that pressure-flow studies with fluoroscopy was the definitive diagnostic test and reference standard. However, a lot of studies omitted this, or the criteria for index UDS, such as Q_{max} and $P_{det.Qmax}$, varied. Therefore, for over half of the studies included, test accuracy was either not reported or not possible to calculate. A second key limitation was the heterogeneity across included studies regarding the study design and the patient inclusion/exclusion criteria (Supplementary Table 2), which partly limit the generalisability of this review's findings. Finally, the extent to which the different time periods in which the included studies were performed might have contributed to differences in the diagnostic criteria for fBOO (in light of the changing paradigms to evaluate female patients with LUTS over time) is unknown.

3.5.5. Future research

Larger studies with more stringent methodological standards are required urgently. Future researchers in this topic area are encouraged to study better-defined cohorts and, as a minimum, separate fBOO into its anatomical and functional entities. The evaluation of diagnostic methods should include precise detail of diagnostic parameters, conventional measures of accuracy, assessment of prediction of treatment outcome, and sensitivity to change following treatment. In addition, future research/guidelines should focus on a standardised reporting system for fBOO that may enable a meta-analysis of individual trials, which was not possible in this review.

4. Conclusions

The available evidence on diagnostic tests and definition criteria for fBOO is limited and heterogeneous. Nomograms using pressure-flow measurements have also been proposed, but variation exists between them. Clearly in contemporary practice, appropriate management of patients and diagnosis of fBOO should be based on a careful history, clinical examination, and VUDS, which remains the recommended standard evaluation as it provides objective functional and anatomical data, but agreement regarding diagnostic criteria is needed urgently.

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Study concept and design: Omar, Harding.
Acquisition of data: Pang, Campi, Omar, Harding.
Analysis and interpretation of data: Pang, Campi, Omar, Harding.
Drafting of the manuscript: Pang, Campi.
Critical revision of the manuscript for important intellectual content: Omar, Harding, Arlandis, Bo, Chapple, Costantini, Farag, Groen, Karavitakis, Lapitan, Manso, Arteaga, Nambiar, Nic An Ríogh, O'Connor, Osman, Peyronnet, Phé, Sakalis, Sihra, Tzelves, van der vaart, Yuan.
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Appendix A. Supplementary data

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