

# A CRITICAL REVIEW ON THE DIAGNOSIS OF PRIMARY BLADDER NECK OBSTRUCTION

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## ABSTRACT

### Introduction.

Lower urinary tract symptoms are extremely frequent in the male population independently from age. Among these, primary bladder neck obstruction (PBNO) accounts for a significant proportion of the cases in men younger than fifty. This disorder is difficult to be diagnosed, mostly due to other interference factors (e.g.: benign prostatic obstruction) and because of the lack of knowledge from urologists.

### Objective.

To review current national and international Guidelines and scientific publications on the diagnosis of PBNO and lower urinary tract symptoms (LUTS) in male patients, and to define an optimal diagnostic schedule for the everyday clinical practice.

### Methods.

All the available publications on PBNO and all the current national and international Guidelines on lower urinary tract symptoms were evaluated. A comparison among recommendations from different publications was done.

### Results.

Some variability was observed among different Guidelines and publications. The most appropriate and shared recommendations for the diagnosis of PBNO were identified. Each diagnostic procedure was analysed in detail; advantages and limitations were described.

### Conclusions.

PBNO is a heterogeneous disease, with a great variability in symptoms at first presentation. The initial suspect is based on clinical data, while diagnosis is only confirmed with invasive diagnostic procedures. Unfortunately, a unique diagnostic workflow is not possible due to the lack of actual knowledge on the precise aetiology of the disease. A better understanding of the cause/effect sequence may contribute to the identification of a more precise diagnostic approach.

### Keywords.

primary bladder neck obstruction, functional urology, voiding symptoms, storage symptoms, bladder outlet obstruction diagnosis, pelvic floor muscles hypertonicity

## INTRODUCTION

Primary bladder neck obstruction (PBNO) is a voiding disorder of the male which consists of an inadequate relaxation of the bladder neck during micturition; an external urethral sphincter hypercontraction may be associated [1]. As a consequence, urinary flow is obstructed in the absence of any clear urologic disease (e.g.: benign prostatic enlargement or urethral stricture). At first presentation, patients usually report a wide variety of symptoms, both attributable to storage and voiding phase; urgency is the most prevalent symptom [2-4]. PBNO was traditionally considered an infrequent disorder. On the contrary, few reports identified this condition in up to 47-54% of male patients aged 18-45 years with chronic voiding dysfunction symptoms [5,6]. Its definitive aetiology has not been already identified, although numerous hypotheses have been proposed. A proper diagnosis is usually difficult: on one side symptoms are non-specific, on the other hand patients develop a mechanism of adaptation due to the chronic nature of the disease. Therefore, we decided to review the diagnostic workflow to the correct identification of PBNO in males.

## MATERIALS AND METHODS

An extensive bibliographic research (PubMed/Medline, Web of Science, and Cochrane databases) was performed. All the publications we were able to find on PBNO were evaluated. Moreover, current International Guidelines for non-neurogenic lower urinary tract symptoms [7-13] and urinary incontinence [14-16] were taken into consideration; in case of multiple editions, only the latest versions were analysed.

## RESULTS

Being PBNO a heterogeneous disease, different diagnostic work-flow has been presented in the past. In this section we will discuss all the diagnostic procedures proposed in scientific publications specifically focused on PBNO. Moreover, Guidelines from the European Association of Urology, the American Urological Association, the International Consultation on Incontinence, the National Institute for Health and Care Excellence were included.

A variable degree of diagnostic procedures and tests were suggested for the proper characterization of male lower urinary tract symptoms. All the considered publications strongly suggest the execution of a deep

investigation of general and medical history; many factors (such as drugs, other diseases, previous surgery, lifestyle, etc.) may influence the normal urinary and faecal continence. Moreover, a careful characterization of the reported symptoms should always be done. Patients may in fact only focus on a predominant symptom, neglecting the complexity of the micturition discomfort or of other eventually associated disorders (e.g.: bowel or penile sensitivity alteration, pelvic/perineal pain or dysesthesia). An in-depth physical examination with digital rectal examination is required for the evaluation of abdominal, flank and pelvic objectivity. The more accurate is this initial assessment, the more probable is the precise identification of the pathogenic mechanism and the setting of a correct therapy.

Patient reported outcome measures (validated questionnaires) may help in assessing the degree of storage and voiding symptoms. Questionnaires are more useful when the reported symptoms are vague, when the physician suspects an unreliable or uncompliant patient, or to monitor disease course during therapy. The most used questionnaires are International Prostatic Symptoms Score to define LUTS [17] and International Consultation on Incontinence Modular Questionnaire to exclude urinary leakage [18,19].

Frequency-volume charts (bladder diaries) are written reports of data regarding bladder functioning during normal patient's life. These are semi-objective measurements of the frequency and severity of LUTS. An accurate and precise filling of these forms can provide more information to the urologist than too many investigations asked without a precise focus. They are useful in a better qualification of patient's reported symptoms, and in the identification of eventual discrepancies. Moreover, in many cases they represent a good support to the definition of the underlying pathological mechanism of storage LUTS. Voiding diaries should be filled for at least three consecutive days.

Urinalysis (physical, chemical, and microscopic evaluation of urine sediment) is a useful tool to search for leucocyte esterase or nitrite, pyuria, glycosuria, ketonuria or proteinuria. Frequently LUTS may be elicited by infections, diabetes or stones. This non-invasive inexpensive test may help in defining the subsequent diagnostic workflow, which may vary from patient to patient. In case of haematuria or history of heavy-smoking, urine cytology on three samples should be asked to exclude the presence of a possible – although infrequent in young subjects – transitional carcinoma of the bladder/upper urinary tract.

Blood tests are not routinely asked, and should only be reserved to patients with a suspicious of possible renal impairment (serum creatinine, urea) or prostatitis (total PSA, reactive C protein, procalcitonin).

Uroflowmetry with post-void residual urine is a non-invasive diagnostic investigation used to measure the flow and force of urine stream during micturition.

Uroflowmetry is performed by urinating into a special funnel connected to a measurement device that calculates the voided volume and the rate of flow voided per second. At the end of micturition, post-void residual urine (amount of urine that eventually remains in the bladder after voiding) is measured by bladder ultrasound or by catheterization. Depending on the morphology of the curve, on the flow rate (average and maximum) and on post-void residual urine, this investigation may suggest the diagnosis and influence the following diagnostic workflow [20-22]. In case of doubtful or noncoherent results, it is advisable to repeat the exam at minimum twice.

Abdominal ultrasound might be performed to exclude the presence of urinary stones, hydronephrosis, transitional carcinoma of the bladder, etc.

Outpatient flexible urethroscopy is asked in order to exclude the presence of cicatricial urethral strictures or benign prostatic obstruction causing compression/occlusion to the urethra. It allows to identify bladder neck contracture and external urethral sphincter hypertonicity. The new generation scopes are usually well tolerated by patients, and no anaesthesia is required.

Urodynamics and video-urodynamics are invasive procedures previously shown to be effective in the assessment of LUTS and in the diagnosis of PBNO [5,23-26

]. A urodynamic-based classification of PBNO was also proposed, which recognize three possible conditions: a high vesical pressure with low voiding flow, a normal vesical pressure with low voiding flow, and a delayed opening of the bladder neck [6]. The adoption of videourodynamics made urethroscopy an optional test.

Electromyographic tests were suggested [27], but to date there are no definitive data to support the clinical utility of these procedures.

## DISCUSSION

Voiding symptoms are extremely frequent in the male population, starting from the age of thirty [28]. Usually, they are non-specific and may be not fully perceived by the patient. Benign prostatic obstruction and overactive bladder were traditionally accounted for as the two major causes of bladder voiding dysfunction. Therefore, other voiding disorders could be neglected. In this scenario, urologists are challenged in properly diagnosing voiding diseases which are considered rare.

Among all the possible urological dysfunction, PBNO is one of the most frequent in males; in previous publications, it was diagnosed in up to 47-54% of male patients aged 18-45 years with chronic voiding symptoms [5,6]. PBNO is defined as a delayed and/or incomplete bladder neck opening, resulting in a significant symptoms variability. According to literature, urinary frequency is

the most common symptom [2-4,29]. To date a definitive aetiology leading to PBNO has not been recognized [1], thus various etiopathogenetic hypotheses have been presented. The most reliable scientific theories presented are an incomplete dissolution of mesenchymal tissue or an excessive amount of connective tissue [30], an abnormal morphologic arrangement of the detrusor/trigonal musculature [31], a sympathetic nervous system dysfunction determining an altered control at the bladder neck [32], structural changes at the bladder neck such as fibrous narrowing or hyperplasia [1]. None of these theories was proved. Therefore, a better understanding of the nature and aetiology of PBNO is required. Understanding the cause/effect sequence may contribute to the identification of a most suitable diagnostic schedule, which is essential for the definition of a proper therapeutic approach.

The performed literature review showed that the diagnostic workflow in case of bladder outlet obstruction remained substantially unchanged over the past decades. Discrepancies are due to the wide variability in symptoms and disorders; therefore, it was not possible to identify a unique diagnostic scheme. When evaluating non-neurogenic LUTS, recommendations and guidelines are only available for men over 40 years-old [12]. Thus, younger patients usually require an individualized and more extensive approach.

A general consensus exists on the administration of patient reported outcome measures, on the collection and the interpretation of bladder diaries, on a deep medical history collection and on an accurate physical examination. According to the current EAU Guidelines on Urinary Incontinence in Adults [16], the anamnestic report should always include details on type, timing, severity and reported symptoms of LUTS or urinary incontinence. This accurate evaluation allows the physician to get a general comprehension on the reported voiding dysfunction and on its possible nature (e.g.: voiding/filling phase, obstructive/non-obstructive, incontinence/retention, etc.). Moreover, it helps in deciding whether the patient should be referred to other specialists to investigate additional symptoms as pain or bowel dysfunction. Urinalysis and abdominal ultrasound are useful to exclude other urological conditions as possible determinants of the voiding disorder reported by the patient. Based on the results of these evaluations, a subsequent panel of diagnostic tests may be activated.

The most important urological procedures to diagnose PBNO are uroflowmetry (showing plateau and/or interrupted urinary flow, and reduced voided volume) and post-void residual urine (with no clear presence of a recurrent pattern). Invasive procedures such as urethrocystoscopy are justified if uroflowmetry shows pathological results in patients with bothersome symptomatology [6]. Endoscopically, not only the internal urinary sphincter (bladder neck) but also the external urethral sphincter (rabdosphincter) appears to

be contracted.

Previous publications reported also the extensive use of urodynamic tests and voiding cystourethrography in men with a long history of urological complains [31]. On the contrary, a survey showed that only 11 % of urologists in the United States routinely use these diagnostic procedures when assessing LUTS in the male [33]. In fact, the use of urodynamics and video-urodynamics is not widespread, due both to its invasiveness and to the limited additional information provided. Moreover, it has been demonstrated that this procedure has low sensitivity, specificity or predictive value as first level test [34]. Therefore, to date it is considered optional when suspecting PBNO.

Transrectal ultrasound is not useful in the assessment of PBNO, as it only provides information on prostatic size and shape which are not determinant in the etiopathogenetic mechanism of the disease. This diagnostic procedure, as well as serum total PSA test, should be avoided because not useful and potentially misleading.

To date there is no consensus on the use of neurophysiological testing such as concentric needle EMG, sacral reflex responses to electrical stimulation of penile nerves, and pudendal nerve latency. Second level imaging (e.g.: pelvic-perineal or lumbosacral spine magnetic resonance imaging) is only indicated in the suspicion of a disease of the peripheral nervous system or of the pelvic floor muscle system.

Not all the subjects reporting voiding dysfunction suggestive for PBNO should undergo all of the described diagnostic procedures. In our experience, judicious selection of the diagnostic workflow is mandatory to avoid procedures which add little information. Clinical presentation, subjectively perceived bother, entity and relevance of reported symptoms (pain, bowel, others) by each patient represent the optimal driver to decide whether it is better to deepen diagnostics or to follow a more clinical approach.

Finally, it was recently proposed that postural and kinematic impairments may directly correlate with PBNO; a pelvic floor muscles hypertonicity due to an adaptation mechanism in the pelvis may be responsible of the internal and external urethral sphincter hypercontraction [35,36]. Recent researches proved that full spine X-ray, magnetic resonance imaging of pelvis/perineum and gait analysis might provide useful information on pathological aspects in PBNO patients [29]. In this setting, neurophysiological testing may add extra information. If these preliminary data will be confirmed by further researches, it seems reasonable to imagine a multidisciplinary approach for disease management.

## CONCLUSIONS

PBNO is a frequent condition in males, leading to altered micturition and significant reduction in quality of life. It is frequently misdiagnosed due to the non-specificity of the reported symptoms at first presentation. According to the available literature, different non-invasive and invasive procedures may be adopted in diagnosing PBNO. The most suitable diagnostic work-flow is still debatable. Patients diagnosed with PBNO are extremely heterogeneous, therefore a unique scheme may not be indicated. Invasive procedures should always be avoided in case they do not add clinical or pathological information useful in the subsequent therapeutic approach. Future researches are needed, as they might provide further insights from new perspectives, which appear to be indispensable for a better understanding of disease mechanisms.

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