Special Article

Current Management of Function Female Bladder Outlet Obstruction

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We have known for a long time that women can have the same lower urinary tract symptoms (LUTS) as men. Sixty-six point six percent of women and 62.5% of men who are over 40 years old have had lower urinary tract symptoms[1]. Women have more storage symptoms and men more voiding symptoms. For years it was assumed that lower urinary tract symptoms in men were caused by obstructions while the same symptoms in women were the result of bladder dysfunction. Thus, bladder outlet obstruction was less frequently suspected in women with lower urinary tract symptoms. However, bladder outlet obstruction has been increasingly observed in women over the past several years. Recognizing women at risk of having BOO, and understanding how to best diagnose this condition are essential steps in choosing the therapies that will provide long-lasting benefit.

1. Prevalence

Bladder outlet obstruction in women is an uncommon disease. The actual prevalence of female BOO in the general population is unknown. Previous large retrospective reviews of women referred for evaluation of lower urinary tract symptoms reported rates of BOO varying from 2.7% to 34%.[2] Therefore, these studies likely underestimated the prevalence of obstruction in women because they didn't include women who may not have had lower urinary tract symptoms. The most likely reason for this wide variation in reported prevalence is the lack of standard diagnostic definitions for the evaluation of female bladder outlet obstruction.

2. Etiology

The causes of bladder outlet obstruction in women are as numerous and varied as in men (Table 1)[2]. They may be broadly divided into anatomic and functional causes. Causes of anatomic obstruction are more common than functional obstruction. The most common causative factor is obstruction from stress urinary incontinence (SUI) surgery or pelvic organ prolapse (POP).[3] Functional obstruction is less common. Patients with functional

Table 1. Anatomic and functional causes of bladder outlet obstruction in women.

Anatomic obstruction
Inflammatory processes
Bladder neck fibrosis
Urethral stricture
Meatal stenosis
Urethral caruncle
Skene's gland cyst/abscess
Urethral diverticulum
Pelvic prolapse
Uterine prolapse
Cystocele
Enterocele
Rectocele
Neoplastic
Urethral carcinoma
Bladder carcinoma
Gynecologic (extrinsic compression)
Retroverted uterus
Vaginal carcinoma
Cervical carcinoma
Ovarian mass
Iatrogenic obstruction
Anti-incontinence procedures
Multiple urethral dilatations
Urethral excision/reconstruction
Miscellaneous
Urethral valves
Ectopic ureterocele
Bladder calculi
Atrophic vaginitis and urethritis
Functional obstruction
Primary bladder neck obstruction
Dysfuntional voiding
Detrusor-sphincter dyssynergia

obstruction must have no apparent structural or anatomic abnormalities. We can subdivide functional obstruction into neurogenic causes, for example, DESD, and non-neurogenic causes, which include primary bladder outlet obstruction and dysfunctional voiding. This chapter will focus on non-neurogenic causes only.

2.1 Primary bladder neck obstruction in women

Primary bladder neck obstruction (PBNO) is a condition that occurs due to a failure of the bladder neck to open properly in the presence of a detrusor contraction of normal or increased pressure and duration (Figure 1).[2] The true prevalence of PBNO in the female populations is unclear because data on the epidemiology of PBNO in the female population are scant. They vary from 4.6% to 8.7% in women with voiding difficulties.[4,5] The precise cause of PBNO has not been clearly elucidated. Theories as to the etiology of the condition are varied. Initial theories focused on structural changes at the bladder neck, such as: hypertrophic or abnormal arrangement of the detrusor trigonal musculature, fibrous contractures, and inflammatory changes[6] A neurologic etiology for PBNO in the form of sympathetic nervous system dysfunction has also been suggested.[7] Recently some authors demonstrated that primary bladder neck obstruction is actually the result of an abnormal extension of the functional external sphincter to the bladder neck.[8]

2.2 Dysfunctional voiding in women

According to the ICS definition (International Continence Society), dysfunctional voiding (DV) is characterized by an intermittent and/or fluctuating flow rate due to involuntary intermittent contractions of the periurethral striated or levator muscles during voiding in neurologically normal women

(Figure 2).[9] Two well-known abnormal voiding disorders are included in the cause of obstruction. One is the Hinman syndrome that is most commonly found in children and adolescents. The other is the Fowler syndrome that is commonly found in women younger than 35 years presenting with urinary retention. Like PBNO, the true prevalence of DV in the general adult female population is not known. A wide variation from 2-37% has been reported depending on the definition used and the methodology adopted to define the dysfunctional voiding. Carlson et al reported this abnormality is the most common abnormality of the voiding phase in women presenting with LUTS.[9] Kavia et al also reported that the Fowler syndrome is the most common cause of urinary retention in women[10] At present it is recognized that DV in children may represent a developmental abnormality, in which the transitional phase persists between infantile reflexogenic voiding and the normal volitional voiding of adulthood, or as a response to psychogenic problems. However, the etiology of DV in adults is still unclear. There are several theories concerning why dysfunctional voiding occurs in adults. The most plausible theory is that it represents learned behavior in response to an adverse event or condition, such as inflammation, irritation, infection (cystitis, urethritis or vaginitis), urethral diverticulum, pelvic inflammatory disease, anorectal disease or trauma.[11,12] Bellina et al suggested that dysfunctional voiding may result from the voluntary withholding of urination in individuals who work long hours.[13] McGuire and Savastano attributed that this abnormality is a habitual dyssynergic sphincter response to a primary abnormality of detrusor instability. This hypothesis is based on evidence that showed detrusor instability and sensory urgency are common urodynamic findings in dysfunctional voiding.[14]

Some studies showed that about 4-19% of initially diagnosed DV by videourodynamic study were reclassified to true external sphincter dyssynergia, due to the subsequent neurologic evaluation that found some occult neurologic conditions in these patients.[9,25] Compared with patients without neurological disease, those with true external detrusor-sphincter dyssynergia had a statistically significantly higher incidence of urge incontinence and involuntary contractions[9]; they were also and younger.[25] Based on this evidence these authors recommend that women with increased sphincter activity during voiding and detrusor instability, with associated urge incontinence, be candidates for neurological evaluation, especially when younger than 40 years.

3. Symptoms and signs

Female bladder outlet obstruction may present with the same variety of lower urinary tract symptoms as men. Data from a large retrospective study shows that 69% of female patients had mixed non-specific obstructive and irritative symptoms. Twenty-nine percent of patients had isolated storage symptoms. Only 8% of patients had isolated voiding symptoms. The most common voiding symptom was weak stream, followed by feelings of incomplete emptying and straining of voiding.[15] These data showed that even if patients complain predominantly of storage symptoms, obstruction should not be overlooked. The same authors also found that mean the AUA symptom score and the most obstructive question sub-scores were

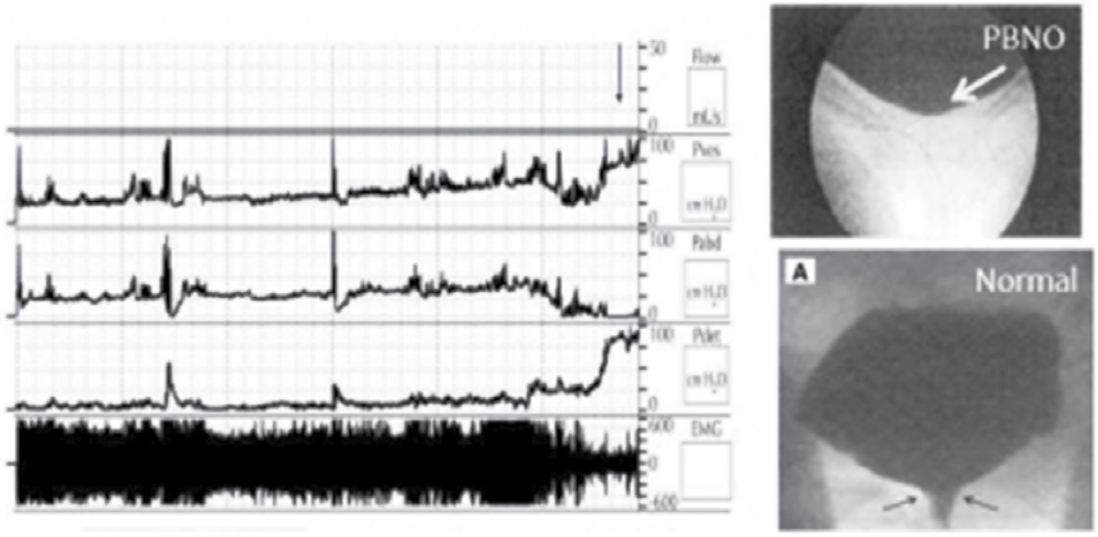

Figure 1. Videourodynamics show the bladder neck completely closed (above) compared to the normal bladder neck funneling (below) during voiding phase. Pressure flow studies show increased bladder contraction with reduction of urinary flow and relaxed sphincter signals. The normal bladder necking configuration was demonstrated in comparison with the normal micturition; the funnel opening of the bladder neck during voiding.

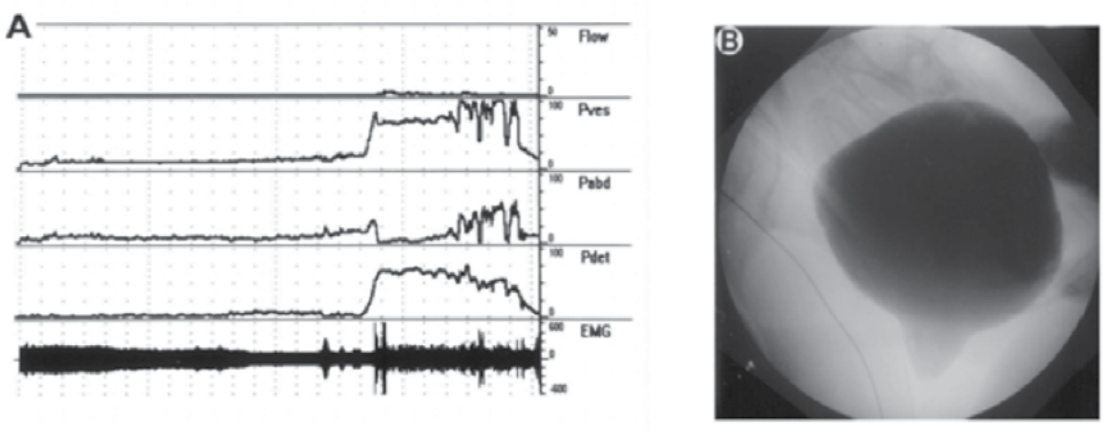

Figure 2. Video urodynamics in a 33-year-old woman with dysfunctional voiding. A, high pressure, low flow voiding dynamics associated with increased electromyography (EMG) activity. Pves, vesical pressure. Pabd, abdominal pressure. Pdet, detrusor pressure. B, fluoroscopy during voiding shows dilated proximal urethra with the point of obstruction at external sphincter.

significantly higher in women with obstruction than in those with stress incontinence. They also found that the cutoff point of 20 or greater for the AUA symptoms score had a 34.2% sensitivity, 92.6% specificity, 86.7% positive predictive value, and 50% negative predictive value for the presence of bladder outlet obstruction in women. But lack of correlation of the AUA symptom scores with objective urodynamic parameters was found, and post-void residual urine weakly correlated with symptom severity. Thus, they concluded that the AUA symptom index score may be useful as a bothersomeness index in women with bladder outlet obstruction. However, this index should not be relied on as an indicator of clinical severity. Higher scores, especially with respect to voiding symptoms, may increase suspicion for voiding abnormalities and prompt urodynamic investigation[16] Besides lower urinary tract symptoms, some patients may present with recurrent urinary tract infection, acute or chronic urinary retention. Patients with severe obstruction may develop renal failure. Complete physical examination is crucial for uncovering some obvious causes of bladder outlet obstruction or lower urinary tract symptoms. Non-urodyanamic studies, including cystoscopy, ultrasonography or voiding cystourethrography (VCUG), may be useful in the evaluation of bladder anatomy and for ruling out urethral anomalies and detecting the signs of lower and upper tract deterioration, such as bladder diverticulum and hydronephrosis. However, the exact cause of non-neurogenic functional obstruction cannot be discovered by physical examination and non-urodynamic testing. Urodynamic evaluation is essential for making the diagnosis.

4. Urodynamic evaluation

Urodynamic testing is an important part of the evaluation of female voiding dysfunction. Non-invasive uroflowmetry and post-voided residual (PVR) are generally accepted as “screening tests” for female lower urinary tract abnormalities. Farrar et al used only flow rates to diagnose obstruction as they believed that low flow in the presence of normal or low detrusor pressures might be an indication of “relative” obstruction. It defined as a maximum flow rate of <15 mL/sand voided volume of 200 mL or more.[17] Bass and Leach have stated that a peak flow of >15 mL/sec with a voided volume of >100 mL, a normal uroflow curve configuration, and no significant postvoid residual usually excludes outlet obstruction18. However, these measurements provide only data on emptying ability. They are unable to define the causes of abnormality. Pressure–flow studies should be considered to differentiate hypocontractility from obstruction.

Unfortunately, the pressure-flow urodynamic criteria of obstructions in women, unlike in men, are not yet standardized. High pressure low flow is generally accepted as the hallmark for diagnosing BOO in men. But this concept cannot be applied to the diagnosis of BOO in all women. It is clear that bladder outlet obstruction can be defined in women by high pressure and low-flow voiding, which is also the case in men. However, many cases of obstruction would be missed in women if the same pressure and flow values were used to define obstruction as in men. The reason is that the micturition of women is more complicated than men. A woman might void by pelvic floor relaxation without generating a detrusor contraction. Recently, a number of authors have attempted to provide a

urodynamic definition of obstruction applicable to women. At least 6 urodynamic diagnostic criteria for bladder outlet obstruction in women have been published in the past years (Table 2). Some criteria have been evaluated using the sensitivity and specificity in diagnosing female bladder outlet obstruction. In 1998 Chassagne et al suggested Qmax <15 mL/sec and Pdet >20 cm/H_2O as a cutoff point of obstruction after comparing the urodynamic parameters of the obstructed female patients with stress incontinence patients in a control group. This criteria provide 74.3% sensitivity and 91.1% specificity for diagnosing bladder outlet obstruction in women.[19] In 2004 Defreitas et al compared the urodynamics parameters of women with BOO to normal women in a control group. They define the obstruction as Qmax <12 and Pdet >25 cm/ H_2O.[20]

Blaivas and Groutz created a nomogram for bladder outlet obstruction in women in 2000. BOO was defined as Qmax <12 mL/sec in free flow measurements combined with a Pdet Qmax > 20 cm H_2O or Pdet Qmax >20 cm H_2O with obvious radiographic obstruction or urinary retention or the inability to void with a transurethral catheter in place. This nomogram also classified the severity of obstruction in women into mild, moderate, and severe as in men.[21]

Nitti et al found that, it is difficult to define outlet obstruction in women by pressure flow criteria in terms of detrusor pressure or urinary flow rate either independently or together. They reported the use of videourodynamics to help make the diagnosis of obstruction in women. The authors defined BOO as radiologic evidence of obstruction between the bladder neck and distal urethra in the presence of a sustained detrusor contraction without the application of strict pressure-flow criteria.[5]

Table 2. Diagnostic Criteria for Bladder Outlet Obstruction

Author	Parameters			Sens	Spec
	Q_{max} (ml/sec)	$P_{det}Q_{max}$ (cmH_2O)	Other		
Axelrod and Blavivas	<12	>20	-	NR	NR
Massey and Abrams	<12	>50	urethra resistance coefficient >0.2 or Significant PVR	NR	NR
Chassagne et al.	<15	>20	-	74.3%	91.1%
Kim et al.	<12	>30	Max urethral obstruction pressure >80 cmH_2O	NR	NR
Lemack et al.	<11	>21	-	91.5%	73.6%
Defreitas et al.	<12	>25	-	NR	NR

Modified from Pressure Flow Urodynamic Studies: The Gold Standard for Diagnosing Bladder Outlet Obstruction. REVIEWS IN UROLOGY; VOL. 7 SUPPL. 6 2005.

Cormier et al also looked at other, less traditional, pressure-flow values to differentiate obstructed women from non-obstructed women. They found that the area under the detrusor-pressure curve obtained during voiding, adjusted for voided volume was the best parameter for determining obstructed women from non-obstructed women .The cutoff value for obstruction is >5.83 cmH_2O /sec/ mL and <2.56 cm H_2O/sec/mL for unobstructed. However, these values need special software in order to be calculated, and further study is needed to prove their accuracy before gaining widespread applicability.[22]

An alternative to the urodynamic technique to defining obstruction is the micturition urethral pressure uroflowmetry (MUPP). This technique has been used more commonly in men but has also been reported in women.[23] A urethral pressure catheter is slowly withdrawn in the urethra, and should a significant pressure drop be found, obstruction is suspected. In males, a pressure disparity of greater than 5 cm H_2O in the urethra is considered suspicious for obstruction. A specific pressure disparity in females has not been absolutely established, and this pressure drop is difficult to measure because of the short segment between the pressure drop and the meatus. Because the technique of MUPP is somewhat labor intensive and requires specific expertise, as well as fluoroscopic monitoring to accurately observe the position of the catheter, this criteria are not generally used in clinical practice.

As mentioned above, there is no universally accepted definition of bladder outlet obstruction in women. One article compared 5 contemporary urodynamic definitions and determined how well they correlated with each other and with the clinical suspicion of bladder outlet obstruction. These criteria included Videourodynamics, 1998 cut points (Qmax < 15 mL/sec with Pdet > 20 cm H_2O), 2000 cut points (Qmax < 11 mL/sec with Pdet > 21 cm H2O), 2004 cut points: (Qmax < 12 mL/sec with Pdet > 25 cm H_2O) and Blaivas-Groutz normogram. The authors concluded that each urodynamic definition of female bladder outlet obstruction has merit. VUDS criteria had the highest concordance with the clinically obstructed group, followed by the 1998 and 2000 cutpoint criteria. Cut points in the 2004 criteria tended to underestimate obstruction and the Blaivas-Groutz nomogram tended to overestimate obstruction. Among these urodynamic criteria, videourodynamics and the 1998 cut point have the highest concordance.[24] Thus, recent data supported that videourodynamics with EMG is the “gold standard” investigation for the diagnosis of functional bladder neck obstruction, because it is able to make an accurate diagnosis of BOO, identify the location of the obstruction in women, and detect complications from high pressure storage, such as hydronephrosis and bladder diverticulum. If videourodynamic studies are unavailable, multichannel urodynamics in conjunction with subsequent voiding cystourethrogram (VCUG) may be utilized to evaluate for radiographic evidence of any abnormality between the bladder and urethral opening.

5. Treatment

Various treatments have been developed for non-neurogenic functional BOO in women. Treatment options include watchful waiting, pharmacotherapy, and surgical intervention. Treatment options depend on the etiology of the obstruction. Although some treatments differ

between primary bladder neck obstruction and dysfunctional voiding, there is an overlap of treatment between these two conditions. Most treatment options for female bladder outlet obstruction are based on "expert opinion" with only a few small series available for review. Furthermore, many studies enrolled the subjects as BOO and didn't divide them into primary bladder neck obstruction or dysfunctional voiding. Therefore, this literature reviewed the treatment in terms of only bladder outlet obstruction.

5.1 Watchful waiting

Watchful waiting is an option for patients who are not bothered much by their symptoms and for whom there is no clinical or urodynamic evidence of upper and/or lower urinary tract decompensation. This treatment can apply to PBNO and dysfunctional voiding. There is one question concerning this treatment option: How many women who elect watchful waiting have progressive symptoms, and develop decompensation?

5.2 Behavior therapy with biofeedback

Behavior therapy with biofeedback may be useful in adult women with DV. Behavioral therapy is based on the presumption that the disorder is a learned one and hence potentially reversible. Biofeedback can be performed using uroflowmetry biofeedback, biofeedback for re-training the pelvic floor or by combinations of these techniques. Some centers report upwards of 80% of patients will experience improvement marked by a reduction in incontinence and recurrent urinary infection25. However, biofeedback has been shown to be useful in suggesting a strong center-specific response factor.

5.3 Pharmacotherapy

Alpha-blockers have been the mainstay of treatment for PBNO. The therapeutic rationale of using alpha-blockers for functional BOO in women is based on certain data. The bladder neck and proximal urethra receive noradrenergic excitatory impulses from the sympathetic nervous system. Thus, alpha-blockers may decrease the dynamic component of obstruction through the blockage of alpha-adrenergic receptors on the urethral smooth muscle, and by decreasing the activity of the sympathetic nerve fibers innervating the bladder neck and urethra. In addition, alpha-blockers have an inhibiting effect on detrusor function, as well as bladder outlet. Consequently, symptomatic improvement in storage symptoms and a urodynamic decrease in detrusor pressure occurs in patients with BOO treated with alpha-blockers. Most of the alpha-blockers were evaluated and show statistically significant improvements in the symptoms and some urodynamic parameters (Table 3). Urinary retention seems to be the only negative predictive factor of efficacy. However, most studies have been small, nonrandomized, and non placebo-controlled.

In contrast to the usefulness of alpha-blockers in the treatment of PBNO in women, these agents would not be expected to improve voiding in patients with DV, which is a condition that affects the striated sphincter rather than the bladder neck, although Danuser et al suggested that non-selective alpha-blockers may decrease somatic neural activity to the external urethral sphincter[26] A study form Kessler et al demonstrated that terazosin didn't change EMG activity and radiographic obstruction in all of two dysfunctional voiding patients. This

may imply that alpha-blockers does not work in dysfunctional voiding patients.[27] Anecdotal studies have been reported successful results with amitriptyline and diazepam in the treatment of DV.

Bethanecol, a parasympathomimetic drug for bladder contraction, has been used for a long time in the treatment of urinary retention. However, there are no studies confirming that parasympathomimetics can induce or reinforce detrusor contractions. Nevertheless, they might have the clinical effect of the sensation of bladder fullness being recognized earlier due to an increase in the muscle tone of the bladder, therefore, benefit some patients.[28]

5.4 Surgical therapy

Currently, surgical intervention for bladder outlet obstruction in women includes the transurethral incision of the bladder neck (TUI-BN), transurethral resection of the bladder (TUR-BN), botulinum toxin injection, sacral neuromodulation, and urinary diversion. Treatment options may differ for different patients, depending on the causes and severity of the disease. Surgery is reserved for those patients who didn't respond to conservative or pharmacologic therapy.

Transurethral urethral incision or resection of the bladder neck usually provides a definitive treatment for a patient with PBNO. TUI-BN in women can be performed using several modified techniques. There is no consensus on the optimal location for the bladder neck incision in women. Turner-Warwick et al first described the concept of bladder neck incision in 1973. They made a single anterior midline incision to avoid the risk of subsequent fistula into the vaginal vault[29]. For the same reason, Kumar et al chose the 12-o'clock position for the incision. They found that the pediatric resectoscope, compared with the standard resectoscope, is useful for making a well-controlled incision safely in the female urethra[30]. Gravias et al also reported the efficacy of Otis Urethrotomy combined with six weeks of 40 Fr urethral dilations

Table 3. Efficacy of alpha-blockers in treatment of female BOO

	Design	No	Duration	Drug	Symptoms improvement (% No.patients)	Urodynamics Improvement	Side effect
Kumar el at; 1999	retrospect	24	6 wks	Phenoxybenzamine Prazosin, terazosin	50%	Qmax, PVR	NR
Pischedda et al; 2005	retrospect	18	4 wks	Tamsulozin 0.4 mg	56%	Qmax, PVR	NR
Kessler et al; 2005	prospect	15	4 wks	Terazosin 5 mg	66%	Qmax, PVR, Pdet Voided volume, MUCP	NR
Athanasopoulos et al; 2008	prospect	25	8 wks	Alfuzosin 10 mg	64% 24% severity	Qmax, PVR, Pdet urethral resistence	16%

in the treatment of BOO in a small series of women. All studies showed the dramatic improvement of symptoms and urodynamic parameters after surgery. However, several studies reported some patients underwent a repeated incision 12 months later because the symptoms recurred30. It implied that the single incision at the 12-o'clock position could not relieve the bladder neck obstruction thoroughly. Hence, modified multiple bladder neck incisions and resection techniques, in order to decrease the recurrence rate, were evaluated. Blaivas et al and Peng et al all chose the 5- and7-o'clock positions as the incision site.[31,32] Zhang et al preferred to make the incision at the 2 and 10 o'clock position of the bladder in order to prevent VV fistula.[33] Jonas et al reported that they made 3 incisions at the 5-, 7-, and 12-o'clock positions of the bladder neck.[34] Jin et al et al performed transurethral incisions of the bladder neck with modifications of the incisions at 4 different sites on the bladder neck (the 3-, 6-, 9-, and 12-o'clock positions), and followed the incisions with regular urethral dilations. They suggested that this modified technique is effective in the long term (>5 years) in relieving voiding difficulties without recurrent obstruction and severe stress urinary incontinence.[35] Blaivas et al have reported successful TURBN for female PBNO in a small series. Incisions are made at the 5 and 7o'clock positions with a Collings knife, extending from just inside the vesical neck through the proximal third of the urethra. Using a resectoscope, small segments of the interposing tissue within the proximal third of the urethra are resected.[36] Six of seven patients considered themselves cured, and 1 improved. Urodynamic parameters including Qmax, voided volume, and post voided residual (PVR) were significantly improved. Nevertheless, several complications were identified after these transurethral surgeries, including hemorrhage, repeated surgery, vesicovaginal fistula (VVF), stress urinary incontinence (SUI), and urethral stricture.

Small case series show the benefits of botulinum toxin injection into the external sphincter for the treatment of DV. Various authors have used between 50-100 units diluted into 1-8 mL and injected submucosally in each quadrant at the level of the most prominent narrowing of the urethra.[37]

Sacral neuromodulation (SNM) is the only treatment that can restore voiding function in women with urinary retention, although the exact mechanism of action of SNM is still not well understood. After SNM, up to72% of women could void spontaneously, with a mean PVR of 100 mL, and half no longer needed CIC.[38] However, the method sand data reported vary widely. Randomised controlled trials are needed.

In long-lasting cases with irreversible bladder damage, self-catheterization cannot be performed. Urinary diversion is the last treatment option.

Urethral dilatation, which is a less invasive procedure than is generally applied to patients with true urethral stricture, is not accepted currently as an effective treatment for functional bladder outlet obstruction because the literature in this regard is sparse. In a series of women undergoing urethral dilatation for a voiding dysfunction, there was a small increase in flow rates. The benefits of dilatation were sustained at six months in only 19% and there was a new onset of stress incontinence in 13%.[39] Yee et al also compared urodynamic parameters before and six months after urethral dilatation in women with primary bladder outlet obstruction. Decreased Pdet Qmax was the only

significantly improved parameters. There was no significant change in Qmax and post-void residual urine after urethral calibration. Durability of urethral dilatation is uncertain.[40]

6. Conclusion

Women with functional bladder outlet obstruction may have storage symptoms, voiding symptoms, or a combination of both. None of the symptoms are specific to BOO. A high index of suspicion is important for the obstructed female. When obstruction is suspected, a number of tests should be conducted. Urodynamics and imaging studies are crucial for the appropriate diagnosis and in order to determine the proper management. Unfortunately, it must be emphasized that no general urodynamic definition of obstruction is currently accepted. A combination of clinical and urodynamic findings is the best way to diagnose an obstruction in women. Obstructions in women result from a variety of etiologies. Treatment options are different for each individual patients, and usually aimed atrelieving the obstruction and symptoms.

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