Chapter

Diagnostic Potential of Imaging Modalities in the Assessment of Lower Urinary Tract Dysfunctions

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Abstract

Lower urinary tract dysfunction (LUTD) is common in both men and women, and the incidence and prevalence increases as people age. Commonly observed symptoms of LUTD include nocturia, urgency, urinary incontinence and frequency of voiding. Recognizing the key role accurate monitoring and evaluation of LUTD play in the day-to-day assessment of the condition, this chapter will explore the diagnostic capabilities of imaging modalities including MRI, ultrasound and fluoroscopy in assessing bladder wall thickness (BWT), detrusor wall thickness (DWT) and estimation of bladder weight both in real-time and static positions, and finally analyze their suitability as surrogates for bladder outlet obstruction (BOO) or detrusor overactivity (DO).

Keywords: lower urinary tract dysfunction, bladder, MRI, ultrasound, PET

1. Introduction

The lower urinary tract (LUT), consisting of the urinary bladder and urethra, functions to store and expel urine in a controlled and coordinated manner [1, 2]. This key function is dependent upon neural circuits located in the central and peripheral nervous system (CNS) (brain, peripheral ganglia, spinal cord and brain) [1], thus distinguishing LUT from other visceral structures such as cardiovascular system and gastrointestinal tract, that are able to sustain a certain level of activity even after elimination of extrinsic neural input [3]. Considering the fact that control over urine storage and voiding is somehow complex and also dependent on neurological elements widely distributed in anatomical terms, the function of LUT can be affected by a myriad of neurological diseases and disorders of the peripheral organs [4].

Lower urinary tract dysfunctions (LUTD) may thus result from lesions affecting the brain, suprasacral spinal cord and sacral spinal cord or peripheral nerve [5]. Lesions affecting the suprasacral or spinal pathways affect the storage phase, leading to reduced bladder capacity and detrusor overactivity, which is characterized by varying degrees of urinary frequency, urgency, incontinence and nocturia, while lesions of the sacral spinal cord pathways result in voiding dysfunction, associated with non-relaxing sphincter and/or absent or poorly sustained detrusor contractions [6]. As a result, functional disorders such as bladder outlet obstruction secondary to prostatic enlargement, overactive bladder and urinary incontinence are common, as are prostate and bladder carcinoma [7].

Clinical assessment of LUDT may include tests such as post-void residual volume measurement, renal ultrasound, uroflowmetry, urethrocystoscopy, neurophysiology and urodynamics depending on the indication [6]. Furthermore, urodynamic tests including filling cystometry and pressure flow study are considered as the gold standard methods for diagnosing detrusor overactivity (DO) and bladder outlet obstruction (BOO) respectively. The key issue with the urodynamic techniques is that, they are invasive and hence are associated with potential patient morbidity [8]. Therefore, there have been efforts over the years toward developing non-invasive techniques such as ultrasound, magnetic resonance imaging (MRI), fluoroscopy and near-infrared spectroscopy, with the potential of serving as suitable surrogates for diagnosing BOO and DO. Recognizing the key role these imaging modalities play in accurate monitoring and evaluation of LUTD, this chapter set out to explore their diagnostic potential in LUTD and finally examine their suitability as surrogates for the urodynamic tests.

2. The lower urinary tract

The lower urinary tract (LUT) consists of urinary bladder and urethra, and also includes the prostate in males. These organs are actively involved in the involuntary storage of urine formed in the upper urinary tract and the voluntary expulsion of urine at a suitable place and time [7]. The effectiveness of these functions depend on the activity of striated and smooth muscles in the bladder, urethra and external urethral sphincter, which is in turn controlled by neural circuits in the spinal cord, peripheral ganglia and brain [4]. Owning to the differences in sexual function and pelvic anatomy, there are considerable differences in the anatomy of LUT in males and females.

The bladder is a hollow organ located within the pelvis. Its wall consists of five layers from inside out, and the muscle of the bladder, the detrusor, is composed of smooth muscle fibers [9]. The wall thickness of the bladder decreases from 2 cm to 2 mm during expansion. The principal function of the bladder is that of a reservoir, storing urine at lower pressures, even with large filling volumes. The normal bladder holds 200–500 ml urine, and for imaging assessment, a full bladder is preferred for visualization. Due to the visco-elastic properties of the bladder wall and the inhibition of the filling phase detrusor contractions, the bladder is compliant and the pressure inside usually remain low [10]. In the clinical assessment of images of the LUT, it is important to note the close relation between the anterior vaginal wall and the urethra in women and between seminal vesicles and prostate and posterior urethra and the bladder base in men [11].

2.1 Lower urinary tract dysfunction (LUTD)

The primary physiological functions of the LUT are the storage of urine (at relatively low pressure) and its voiding (expulsion) at appropriate time. LUT dysfunction is a common problem, and the prevalence increases with ageing. The term "dysfunction" indicates an abnormality in the physiology of the lower urinary tract, including urinary sphincter, associated nervous system, bladder neck and detrusor muscle. This may result in failure to store urine, failure to empty or a combination of both [12]. Lower urinary tract symptoms can thus be divided into storage phase symptoms, voiding phase symptoms and postmicturition symptoms. These symptoms can be caused by various types of bladder dysfunctions such as overactive bladder, underactive bladder, urinary tract infections and neurogenic disorders [13]. Storage symptoms include increased nocturia, daytime frequency, urgency and incontinence. Voiding symptoms include splitting or spraying, slow stream, intermittency, hesitancy, straining and terminal dribble. Post micturition symptoms include a feeling of incomplete emptying and post micturition dribble [14].

2.1.1 Bladder outlet obstruction (BOO)

Voiding as intended by nature should result in complete emptying of the bladder. This depends on a coordinated contraction of the detrusor smooth muscle with a simultaneous lowering of bladder outlet resistance. Distortion, compression or occlusion of the outlet of the bladder obstructs urine flow during expulsion, with attendant characteristic symptoms of dribbling, poor stream, incomplete emptying and hesitancy. Bladder outlet obstruction (BOO) is an indication of the existence of abnormal tissue which modifies the configuration of the bladder outlet through distortion, compression or occlusion, thus impeding the urine flow at the time of expulsion. Accompanying urine symptoms include slow stream, intermittent stream, hesitancy, straining to void, terminal dribble, post-micturition dribble and feeling of incomplete emptying [15].

These LUT symptoms are caused by a variety of different pathologies. The commonest processes responsible for BOO in men are benign prostatic enlargement (BPE) or urethral stricture disease [15]. For lesser degrees of obstruction, the symptomatic consequences may be slight, owing to compensatory responses, such as enhanced bladder contractility. However, a potential feature of BPE is the progression of obstruction with ageing, which leads to evident expulsion and post-micturition LUT symptoms. Also, the emergence of LUT symptoms point to relative inadequacy in the expulsive capacity of the bladder, which may be a consequence of detrusor underactivity. Detrusor underactivity is characterized by a contraction of reduced duration and/or strength, thus resulting in failure to achieve complete bladder emptying within regular time span and/or prolonged bladder emptying. The variables of detrusor contraction strength, contraction duration and outlet obstruction severity leads to varied clinical features of BOO. The basis of obstruction in females may be bladder neck distortion, urethral compression or luminal occlusion and functional issues [16]. However, in women, due to difficulty in assessing bladder contractility, there is difficulty in arriving at decisions on issues regarding diagnosis of BOO [15]. Diagnosis of BOO can be made based on invasive urodynamic study, such as videourodynamic study or pressure flow study. Also, a noninvasive method to diagnose BOO is needed for more accurate treatment [17].

2.1.2 Overactive bladder (OAB) and detrusor overactivity (DO)

According to the International Continence Society (ICS), overactive bladder (OAB) is defined as a complex of urgency, usually with increased daytime frequency and nocturia, with (OAB wet) or without (OAB dry) urinary incontinence. Urgency is the key symptom of OAB, and it is a sudden compelling desire to pass urine, which is difficult to defer [18]. In diagnosing OAB, it is assumed that conflicting issues such as, urinary tract infections are excluded. OAB might be because of increased bladder sensation or detrusor overactivity (DO). Confusion usually exists between these two disease states because patients usually cannot differentiate the sensation of urgency from the urge to void [19].

DO is an urodynamic observation characterized by involuntary detrusor contractions during the filling phase that may be provoked or spontaneous. The ICS

2002 report categorizes DO into two types: (1) terminal, which is a single involuntary detrusor contraction that often results in complete bladder emptying; and (2) phasic, which may or may not lead to urinary incontinence. Therefore, OAB is a symptom-based diagnosis, while DO is an urodynamic diagnosis. A research on OAB and DOO showed that 64% of patients with OAB symptoms had DO on urodynamic investigation, while 30% of the patients with DO did not have AOB [18].

3. Imaging modalities used for the clinical assessment of LUTD

The lower urinary tract (LUT) requires coordination of the prostate, bladder, pelvic floor, urethra, and specific spinal cord and brain areas. Different imaging modalities can be utilized to visualize these structures and are employed to study its pathophysiology and diagnose voiding dysfunction. Although the bladder and urethra are anatomically distinct structures, they are functionally closely interrelated. Therefore, imaging of the bladder is often needed to confirm clinical examination.

Imaging modalities including ultrasound (US), voiding cystourethrogram X-ray (VCUG), magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) are used to visualize the distinctive structures of the LUT. US is the commonly used technique in daily practice, to evaluate LUTD. The utilization of MRI for voiding dysfunction however remains limited, but several clinical studies have already shown its potential in the benign prostatic hyperplasia (BPH) and diagnosis of stress urinary incontinence. Also, PET and fMRI of the brain have made it possible to study supraspinal control of the LUT, in the light of LUT being subjected to a complex neural control mechanism.

Urodynamic tests have over the years been considered the gold standard method for diagnosing common conditions of the lower urinary tract such detrusor overactivity (DO) and bladder outlet obstruction (BOO). However, with increasing concern about their "invasiveness" and associated potential patient morbidity, there has been a search towards non-invasive techniques such as ultrasound, computed tomography (CT), PET, magnetic resonance imaging (MRI), with the potential of becoming the mainstay diagnostic tools for LUTD. Furthermore, clinical assessment of the urethral symptoms is challenging and often requires further evaluation with imaging.

3.1 Ultrasonography

Ultrasonography (US) has over the years emerged as the most widely used imaging technique for the study of the LUT. In the past, US was identified as a technique of approach and guidance for the evaluation of LUT, but it is now recognized worldwide as the investigation of choice allowing precise diagnosis of many pathological conditions of the LUT, usually obviating the need for further radiological examinations. For instance, Transabdominal US is a cheap and easy modality to evaluate structural abnormalities of the bladder, stone disease of the bladder, post-void residual urine (PVR) or vesico-ureteral junction, neoplasms and inflammatory disorders [20].

The US, although simple to use, safe and acceptable by majority of patients, still remains real-time operator dependent, and in the light of new applications, requires experienced and skilled operator in whose hands often becomes the only exam needed to be able to direct the next phase of the diagnostic algorithm. Recent advances in US, incorporating a high resolution multi frequency transducers allows a meticulous study of the kidneys, its size, location and parenchymal structure, including a thorough assessment of the urinary bladder, perivesical space as well as pelvicalyceal and ureteral dilatation [21]. The use of US requires when possible a full bladder which is not distended to the extent that the individual has pain. This is necessary because, it is only a well-distended bladder that allows true mass abnormalities to be seen, or else, apparent focal wall diverticula or masses can be stimulated by invaginations of the deflated bladder, usually obscuring true bladder lesions such as calculi by the non-distended bladder folds [22].

In the assessment of LUT using US, patients are normally examined in the supine position but sometimes is required when there is the need to differentiate mobile intravesical abnormalities such as foreign bodies or stones from fixed lesions. The use of a 3.5–5-MHz curved array is normally acceptable for most US examinations of the LUT, however, with regards to anterior bladder wall, higher frequency linear probes are sometimes required for better resolution [22].

3.1.1 Ultrasonographic methods in the assessment of LUTD

Ultrasonography has proven to be essential in the evaluation of patients with lower urinary tract dysfunction (LUTD). This is based on the premise that LUTD may result in an alteration of the anatomic structures of the lower urinary tract (LUT) and vice versa [23]. In routine practice, US is mostly used to accurately measure the post-void residual urine (PVR) which indicates how completely an individual empties his bladder. Individuals with bladder outlet obstruction (BOO) and/or detrusor underactivity are commonly associated with elevated PVR [24]. The ultrasound measurement of bladder wall thickness (BWT) has also been linked to the diagnosis of overactive bladder (OAB) and BOO, with several studies reporting that increases in BWT can be a valuable biomarker for detrusor overactivity (DO) in subjects with an OAB syndrome [25, 26]. This is based on the assumption that increased BWT in BOO or OAB is secondary to hypertrophy of the detrusor wall, which is associated with increased isometric detrusor contraction against a competent urethral sphincter. These contractions lead to a rise in intravesical pressure, giving the individual a very strong desire to void [27]. Furthermore, it is generally accepted that an increase in mean BWT is unique to DO, with a study recording a statistically significant correlation between DO and BWT [27]. Detrusor wall thickness (DWT) might be a more accurate measure for BOO. A DWT >2 mm has been reported in 94% of men with signs of BOO on urodynamics [28]. In addition, measurement of DWT or BWT with US can used to examine the response to surgical or medical treatment of BOO. For instance, reduced BWT is detected after treatment with α-1 receptor blockers and transvesical prostatectomy [29, 30]. The ultrasonographic sections of the urinary bladder are defined from outside-in as bladder hyperechoic (adventitia), hypoechoic (detrusor muscle) and hyperechoic (bladder mucosa) [31, 32]. DWT measures only the middle layer, while the measurement of BWT involves all the three layers. The only issue with BWT measurement is that, it is volume dependent, and bladder wall thickness decrease with increasing filling volume. Hence, there is the need to measure bladder weight which should remain constant at different bladder volumes. Thus, with the aid of US, bladder weight is calculated from the thickness of the bladder wall and the intravesical volume assuming a spherical bladder (see **Figure 1**).

The benefit of utilizing US to monitor the deformation in the detrusor muscle have been shown by a recent study [33]. This provides insight into the detrusor muscle's dynamic and structural properties related to bladder pressure. In the study, it was demonstrated that US could be used to estimate strain in the detrusor muscle, which was positively correlated with the detrusor pressure. This suggests a possibility of using US in a real time manner to monitor detrusor muscle activity. Also, this

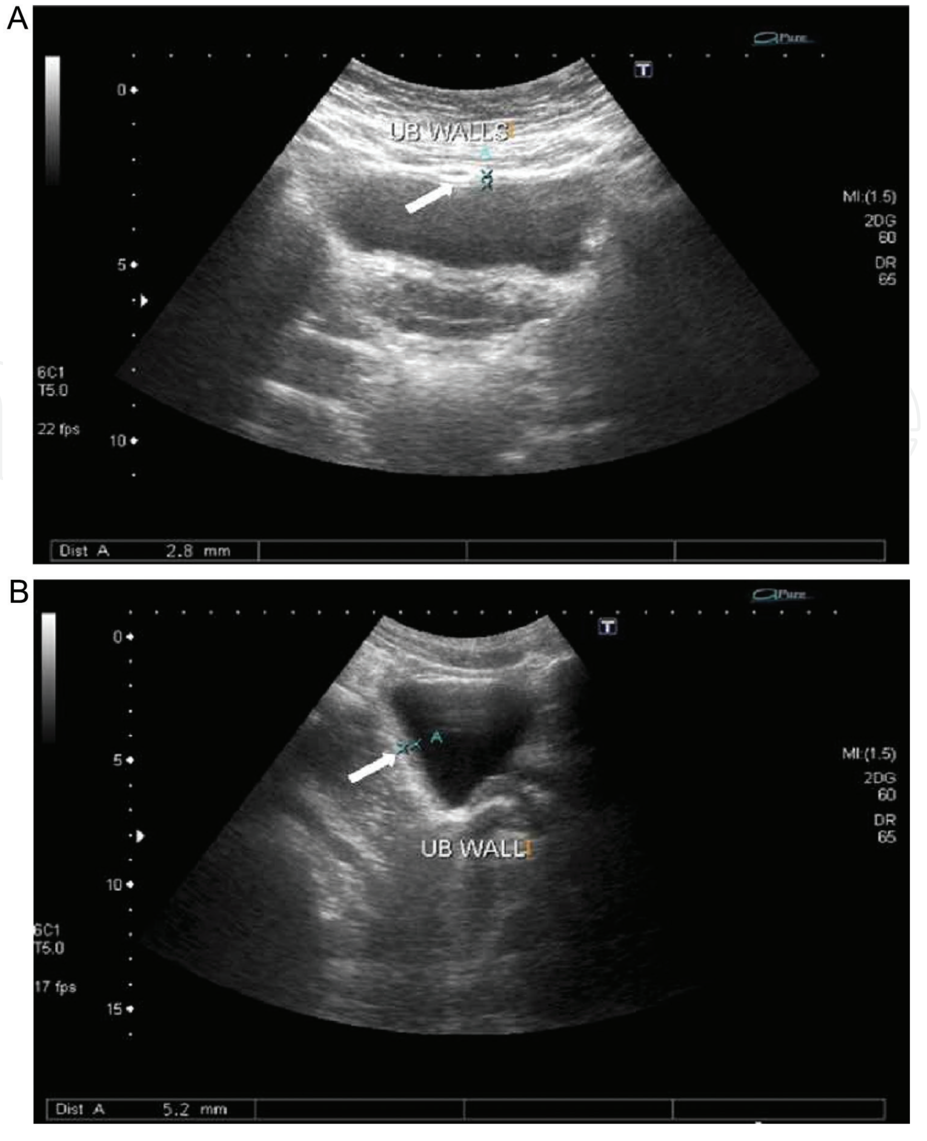

Figure 1.
(A) An ultrasound image of the urinary bladder (transverse scan) showing normal bladder wall thickness (BWT) (a, arrow) in a middle-aged woman with irritative lower urinary tract symptoms (LUTS) and normal filling cystometry (FCM); (B) ultrasound image (longitudinal scan) showing increased BWT (b, arrow) in a middle-aged man with irritative LUTS and detrusor overactivity [26].

finding is important because, it is an indication that US imaging could be used as a non-invasive modality option to replace the pressure flow studies which remain the standard diagnostic urodynamic tests for lower urinary tract symptoms (LUTS).

With recent advances in US imaging of the urethra, imaging of different structural abnormalities such as urethral neoplasms and urethral diverticulae are now possible. The typical symptoms of urethral diverticula are dyspareunia, urethral pain and post-voiding dribbling [34]. In addition, the multiplanar US allows imaging of the size, location, content, and configuration of the diverticulum. Also, in the case of surgical planning, US allows the diverticulum neck can to be evaluated, together with the presence of calculi in sac [20].

3.1.2 Recent innovations in the field of ultrasonography

The recent years have seen an evolution in the field of ultrasonography, with the introduction of applications which have great importance in the assessment of LUT. These new applications include harmonic imaging, motion-mode, transperineal US and 3D and 4D ultrasound.

Harmonic imaging (HI) is based on the harmonic response generated by the tissue or, when used by the contrast medium, rather than on the reflection of the fundamental frequency of the ultrasound beam. This provides a better definition of the profiles, particularly of the fluid structure systems, such as reduces artifacts; improves the representation of the contrast medium; and dilated collectors. Thus, HI removes low frequency sonic artifact which is usually the result of reverberation artifact and help better define the bladder wall. Motion-mode (M-mode) assists in the assessment of movement, and is therefore valuable in providing documentation and semiquantitative evaluation of ureteral peristalsis. Transperineal US, incorporating high-frequency linear probes allows ideal visualization of the vagina, urethra and surrounding structures. 3D and 4D US offer a multiaxial illustration of the entire kidney and bladder, thus improving renal parenchymal volume calculation, mostly in hydronephrosis or irregularly shaped kidneys. This is possible because, the dilated collecting system can be deducted from the overall kidney volume. Also, the potential of creating rendered views will allow the comprehensive demonstration of complex pathology [21, 35].

3.2 Voiding cystourethrogram X-ray (VCUG) of LUTD

VCUG uses a small amount of radiation to make images of an individual's urinary system, and it enables the assessment of the bladder's size and shape and also looks for abnormalities, such as a blockage along the path of the urine [36]. Images from VCUG can also show whether the urine is moving in the right direction. The normal flow of urine is from the kidneys down to the bladder through the ureters. However, in a condition called vesicoureteral (VU) reflux, urine flows backward from the bladder to one or both ureters and sometimes to the kidneys, and it sometimes occurs only at the voiding stage [37]. VU reflux can be detected by VCUG, which also includes taking X-ray images while the bladder is being emptied. This makes VCUG appropriate for diagnosing VU that only occurs while voiding [38].

During VCUG, a patient's bladder is filled with contrast material, followed by an X-ray machine used to send beams of radiation through the abdomen and pelvis, and images are recorded on special film or a computer. These images help physicians see problems in parts of the urinary system, including the bladder, urethra (the tube connecting the bladder with the outside of the body), and the ureters (the tubes connecting the kidneys to the bladder) (LUT), aiding in diagnosing LUTDS [39].

3.3 Magnetic resonance imaging in the assessment of LUTD

Technological advancement in imaging modalities, allowing cross-sectional imaging of the LUT is essential for further functional and/or morphological evaluation. Primary disorders for MRI of the LUT are bladder tumors and congenital abnormalities, and in addition, MRI is usually employed as a secondary imaging modality, particularly for assessing voiding dysfunction in pediatric urology [40]. MRI can also be used in conjunction with US for imaging of the size, content and position of the urethral diverticulae (see **Figure 2**). With regards to urethral neoplasms, MRI can reveal different characteristics of the different types of the neoplasms (see **Figure 2**). These neoplasms of the urethra appear as more heterogeneous lobulated, deeply infiltrating or exophytic lesions [20]. Urethral hypermobility can also be identified on both MR imaging and US, and it has been linked with stress urinary incontinence in women [42].

Currently, MRI is the only imaging modality that provides outstanding functional imaging and anatomical information without the use of ionizing radiation.

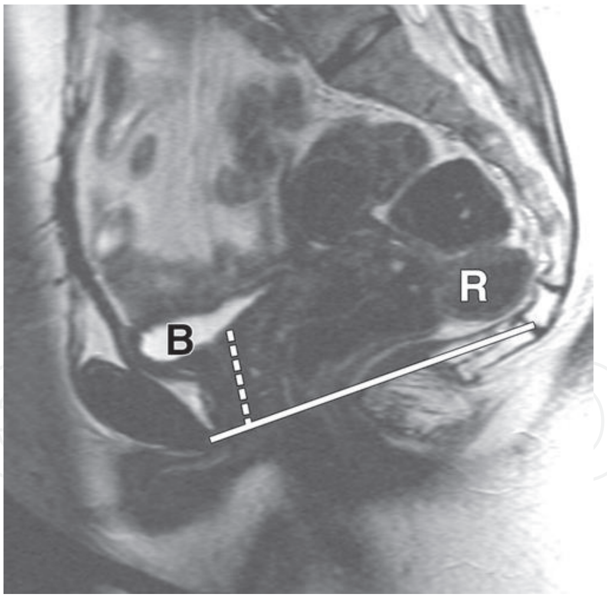

Figure 2.
A woman undergoing MRI evaluation of possible urethral diverticulum. Patient had previously undergone hysterectomy. Midline sagittal T2-weighted TSE image (6000/116, flip angle, 180°) obtained at rest shows no significant prolapse. Solid line represents pubococcygeal line, above which all pelvic organs are located. B = bladder, dotted line = urethra, R = rectum. Adapted from Bennett et al. [41].

MR imaging, in the light of rapid technological changes is now faster with less movement artifact, and therefore improved image quality and resolution. It allows an overall evaluation of the renal parenchyma, excretory cavity, surrounding tissue, together with the main vessels. The dynamic contrast enhancement of MRI is comparable to renal scintigraphy, and thus ensures a higher contrast spatial and temporal resolution. As a result of this inherently superior contrast resolution, MRI of the pelvis provides much better anatomical visualization than CT. Furthermore, heavy T2-weighted MRI is well suited for imaging of the urinary bladder, since the organ is filled with fluid, thus improving bladder visualization. With the advent of diffusion weighted MRI, in which imaging and MRI signals are weighted toward the diffusion characteristics of water, evaluation of LUT neoplasms, particularly bladder cancer has been done [21].

The evident advantages of MRI include the lack of both nephrotoxic contrast media and ionizing radiation required for CT, thus making it particularly suitable for imaging during renal failure and pregnancy. As a result, indications for MRI have been increasing rapidly over the years, and it is currently used as the standard imaging modality for staging pelvic cancers. In fact, it is better than CT for the anatomical depiction of the bladder wall [22].

3.4 Computed tomography in the assessment of LUTD

The combination of contrast studies and US scan have revolutionized imaging of LUT, pinpointing many of the clinical problems originating in the bladder. CT has become a vital complementary tool in the investigation of several disorders, and crucial for staging cancers. Thus, CT imaging is often employed in the staging of bladder cancer, however, its utility in the evaluation of LUTD remains limited. CT is the standard imaging modality for the study of adult urology, with or without contrast medium for the detection of stones [22]. Key advantages of CT are in providing detailed demonstration of overall bladder and pelvic anatomy.

Considering the fact that CT examination is highly radiant, its diagnostic potential cannot be transferred carelessly to children, since they have a higher radio sensitivity, smaller structures, lesser representation of adipose tissue, different tissue composition and different diseases, contrary to that of adults. Also, CT is not suitable for imaging of the urethra, penis and prostate, which are better assessed with MRI. That is, CT has limitations when applied to the urinary tract beyond the bladder.

Nevertheless, recent technological advancement in CT, incorporating multi-slice scanning with the possibility of isotropic imaging have further enhanced the precision of CT. In isotropic imaging, the block (or voxel) of imaging is acquired as a perfect cube, and is thus as dimensionally accurate as possible. Therefore, the 3D reconstruction of the contrast-filled bladder is rendered precisely, and virtual cystoscopy is possible. Thus, CT urography is being touted as one-stop imaging of the entire urinary tract, with the potential to replace conventional contrast studies and ultrasound, but this however requires further technical developments.

3.5 Positron emission tomography and functional MRI in the assessment of LUTD

Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) are powerful non-invasive tools utilized in the study of the supra-spinal control of the LUT directly through imaging of the brain. fMRI measures the changing proportion of deoxygenated and oxygenated hemoglobin in activated brain centers, while PET needs the injection of a radioactive isotope that will accumulate in a metabolically active brain region [20]. fMRI has a superb spatial and temporal resolution but needs multiple runs of the same event to increase signal-to-noise ratio, while PET is very sensitive for small changes in neural activity but not able to detect rapid changes in brain metabolism [42, 43].

Near infrared spectroscopy (NIRS) is occasionally utilized in the study of supraspinal control of the bladder. NIRS takes advantage of the varying concentrations of hemoglobin in the cerebral cortex, but its key disadvantage is the very limited resolution for deeper brain structures since it can only accurately measure to a depth of 1 cm beneath the skull [44].

In recent years, these different brain imaging techniques have been widely spread and optimized, providing a vast amount of literature about nearly every human cortical function. Unfortunately, the number of studies that have looked into brain control of bladder function is until now still relatively small, but nevertheless these studies have provided us with valuable new insights into LUT pathophysiology.

3.6 Imaging modalities as surrogates to urodynamic tests for the clinical assessment of BOO and DO

Lower urinary tract symptoms alone are usually not sufficient in diagnosing common complications of the LUT such as BOO, DO and BPE. Hence, in most cases, other investigations are required.

Uroflowmetry, though cheaper and easy to perform in clinical setting, is limited by its lack of specificity and inability to differentiate between BOO and detrusor underactivity. In much the same way, pressure-flow studies which serve as gold standard for diagnosing BOO are able to provide key information on the presence of obstruction as well as detrusor contractility. But this come at a cost, as urodynamic tests are invasive and require specialist equipment and training to perform tests and interpreted results, coupled with associated potential patient morbidity.

Therefore, the search for non-invasive diagnostic tests as potential replacement for these urodynamic tests, especially for the diagnosis of BOO, has been ongoing for many years. As such, parameters such as PVR, free uroflowmetry and quantification of prostate volume has been investigated. However, over the past two decades, the interest has been on BWT, DWT and bladder wall weight, owing to the rationale that BOO and DO are associated with an increase in bladder wall thickness and detrusor hypertrophy. These parameters (BWT, DWT) has been shown by several studies to be diagnostic of BOO and DO. Ultrasonography has thus emerged as the easiest and non-invasive option capable of measuring BWT, DWT and bladder wall weight, thus potentially obviating the need to resort to cumbersome and invasive urodynamic tests to diagnose BOO and DO (see **Figure 1**).

4. Conclusion

Imaging techniques can contribute prominently to our current understanding of lower urinary tract dysfunction. A variety of imaging modalities is available to visualize the urethra, bladder, prostate and pelvic floor. These techniques can be used to enhance our current knowledge of LUT pathophysiology and confirm clinical diagnosis, as an alternative diagnostic method to replace invasive urodynamic studies.

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Conflict of interest

The authors declare no conflict of interest.

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