Ultrasound of the Female Urethra

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Declaration

I, Roopali Karmarkar, confirm that the work presented in this thesis is entirely my own. Where information is derived from other sources, it is clearly indicated in the thesis.

The studies included in this thesis had full approval from the Research Ethics Committee and all participants in the study gave informed consent.

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Abstract

Background: Many theories have been put forward to explain the urinary continence mechanism. Though they seem logical, there is insufficient evidence to support them. Ultrasound has been implemented by researchers to investigate these theories. There is considerable difference in their methodologies and their conclusions. Most of the research on urethral ultrasound is related to stress incontinence; there is a lack of studies on other urodynamic diagnoses.

Aim: To compare the measurements of the female urethra by 2 and 3 dimensional transperineal ultrasound in women with different urodynamic diagnoses and different vaginal parities.

Methodology: 150 women had urodynamic studies and 2 and 3 dimensional transperineal ultrasound. They were divided into 4 groups according to their urodynamic diagnosis as nondiagnostic urodynamics(NU), pure detrusor overactivity(PureDO), pure urodynamic stress incontinence(PureUSI) and mixed urinary incontinence(MUI) and also according to their vaginal parity. New methods of measuring urethral position, bladder neck position and urethral dimension are developed and used for measurement. Multiple regression analysis was performed using a model of urethral sphincter volume(USV), bladder neck position(BNP) and pubourethral distance.

Key findings: USV was smallest in PUSI group. BNP at rest was lower in all incontinent groups than NU. Women with MUI had normal sphincter size but lower BNP. There was no difference in the bladder neck mobility or urethral mobility. Urethral compression was evident in all groups. The statistical model correctly classified 68.2% women with urodynamic stress incontinence and 69.8% women with detrusor overactivity. The urethral sphincter was smaller in women who had a vaginal delivery but there was no difference in the sphincter size of primiparous and multiparous women.

Conclusion: Urethral sphincter volume and bladder neck position are the most differentiating factors for the types of urinary incontinence. Subsequent vaginal delivery in primiparous women may not increase their risk of having urinary incontinence.

“Measure what is measurable and make measurable what is not so”

- Galileo Galilei (1564 – 1642)

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Abbreviations

2D	2 Dimensional
3D	3 Dimensional
4D	4 Dimensional
ATFP	Arcus Tendinus Fascia Pelvis
BMI	Body Mass Index
BNM	Bladder Neck Mobility
BWT	Bladder Wall Thickness
CLPP	Cough Leak Point Pressure
CS	Caesarean Section
DO	Detrusor Overactivity
FUL	Functional Urethral Length
ICS	International Continence Society
IUGA	International Urogynaecology Association
KHQ	King’s Health Questionnaire
LUTS	Lower Urinary Tract Symptoms
MUCP	Maximum Urethral Closure Pressure
MUI	Mixed Urinary Incontinence
MRI	Magnetic Resonance Imaging
NU	Nondiagnostic Urodynamics
OAB	Overactive Bladder
OASI	Obstetric anal sphincter Injury

POP	Pelvic organ Prolapse
PTR	Pressure Transmission Ratio
PureDO	Pure Detrusor Overactivity
PureUSI	Pure Urodynamic Stress Incontinence
PUVA	Posterior Urethro-Vesical Angle
REC	Research Ethics Committee
SUI	Stress Urinary Incontinence
TPU	Trans Perineal Ultrasound
TVU	Trans Vaginal Ultrasound
UD	Urodynamic Diagnosis
UDS	Urodynamic studies
UI	Urinary Incontinence
UIA	Urethral Inclination Angle
UM	Urethral Mobility
UPP	Urethral Pressure Profile
USI	Urodynamic Stress Incontinence
USV	Urethral Sphincter Volume
VCU	Video Cystourethrography
VD	Vaginal Delivery
VLPP	Valsalva Leak Point Pressure

Acknowledgement

I would like to thank Professor Vikram Khullar for the opportunity to conduct this research and for guiding me throughout the process leading to this thesis. I also want to thank Mr Ruwan Fernando for supervising me in other research projects. Recruiting women for projects needs the support of the entire team. I am grateful to the urogynaecology team at the St Mary’s Hospital for helping me in this task.

I dedicate this thesis to my wonderful children, Ajinkya and Tanmayi, and to my husband, Ranjit. Without their enormous help and support, this thesis would not have been possible.

Presentations and publications

No.	References	Type
1.	**Karmarkar R**, Fernando R, Regan L and Khullar V. **Urethral sphincter volume and urodynamic diagnoses.** Neurourology urodynamics 2016;35:S213 Oral presentation at ICS conference in Tokyo, September 2016	O, A
2.	**Karmarkar R**, Fernando R, Regan L and Khullar V. **Is the urethral more mobile in women with stress urinary incontinence.** Neurourology urodynamics 2016;35:S368 Oral presentation at ICS conference in Tokyo, September 2016	O, A
3.	**Karmarkar R**, Fernando R, Regan L and Khullar V. **Should we offer caesarean section to women who develop stress urinary incontinence after first vaginal delivery?** ICS 2016;353 Oral presentation at ICS conference in Tokyo, September 2016	O
4.	**Karmarkar R**, Gargasole C, Digesu A, Fernando R, Khullar V. Noninvasive **Diagnostic Measure of Pure Stress Urinary Incontinence**. ICS 2015;661	P
5.	**Karmarkar R**, Gargasole C, Louca O, Digesu A, Fernando R, Khullar V. **Is the 24 hour pad test an accurate assessment tool for success of continence surgery?** ICS 2015;91 Oral presentation at ICS conference in Montreal, October 2015	O
6.	Gargasole C, **Karmarkar R**, Digesu A, Fernando R, Pifarotti P, Khullar V. **Asymptomatic patients with pelvic organ prolapse: Is urodynamics necessary before surgery?** Int Urogynecol J, 2015; 26:S19 Oral presentation at IUGA conference in Paris, June 2015	O, A
7.	**Karmarkar R**, Khullar V. **Emerging drugs for overactive bladder.** Expert Opin. Emerging Drugs 2015;20:613-624	R

O = Oral presentation, A = Abstract, P = Poster, R = review article

Aim of the thesis

To compare the measurements of female urethra using 2 and 3 dimensional transperineal ultrasound in women with different urodynamic diagnoses and different vaginal parity.

1: Settings

The studies contained in this thesis were undertaken in the Department of Urogynaecology at the St Mary's Hospital, Imperial College Healthcare NHS Trust, London from October 2013 to September 2015.

The Department of Urogynaecology at St Mary's Hospital is a tertiary referral centre led by Professor Vikram Khullar. The department accepts referrals from various parts of the UK and often from overseas. When the research was conducted, the Urogynaecology team consisted of three Consultant Urogynaecologists, one subspecialty trainee in Urogynaecology, three clinical research fellows (of which I was one), a specialist nurse and 2 trained nurses. Many visiting fellows from overseas come to learn management of urinary incontinence and conduct research in Urogynaecology.

A comprehensive service is offered to the women referred to the department. About 1700 new patients are referred to the department each year, mainly from the Northwest London area. The symptoms are assessed at clinical consultation and also by filling in generic and symptom-specific validated questionnaires. The Pelvic Organ Prolapse Quantification (POP-Q) system is used according to the joint report published by the International Urogynaecology Association and International Continence Society to assess the degree of uterovaginal prolapse (Haylen et al. 2010). A range of investigations such as uroflowmetry, conventional cystometrogram and urethral pressure profile are carried out every day for indications such as stress urinary incontinence needing surgical treatment, refractory urgency incontinence, mixed incontinence and complex symptoms.

Video-urodynamics are offered to women with complex disorders and to those with previous continence surgery. Two dimensional ultrasound is used to assess cases with voiding dysfunction or when structural pathologies such as urethral diverticulum are suspected. Magnetic resonance imaging (MRI) is requested for women with pelvic pain or complex defaecatory symptoms.

A weekly pelvic floor clinic is also run by the department. It offers a one-stop assessment of women with bowel symptoms mainly after obstetric anal sphincter injury or prolapse repair surgery. Women are asked to complete the validated questionnaire and then investigated with anal manometry and endoanal ultrasound.

The urogynaecology teams works closely with other medical specialties and healthcare professionals. Multidisciplinary team meetings are held every week in the department with the physiotherapist and specialist in the care of elderly. Complex cases are discussed in these meetings to make management plans. Input from pain management specialists, neurologists, urologists and colorectal surgeons is requested whenever necessary.

Research is integrated into the routine activities of the department. Many clinical trials for drugs as well as treatment equipment are conducted by the urogynaecology team. Clinical fellows conduct studies for postgraduate research qualifications. Visiting international fellows and medical students doing their BSc year are also involved in the research activities. The department is well known for their numerous publications in peer reviewed journals and presentations at national and international meetings.

2. Anatomy of the Female Lower Urinary Tract

The lower urinary tract is composed of the bladder and the urethra which lie in the retropubic space. The bladder acts as a hollow reservoir of urine and the urethra provides tubular passage for urine during voiding.

2.1 The Structure of Bladder

The wall of the bladder is formed by the inner mucosal layer, the middle layer formed by the detrusor muscle and the outer adventitial layer. The innermost lining of transitional epithelium and the subepithelial connective tissue form the mucosal layer. The smooth muscle fibres of the detrusor are arranged in 3 layers. The inner and outer layers are longitudinal and the middle layers is circular. The muscle fibres in these layers form bundles which branch out and interconnect forming a crisscross pattern. The right and the left ureters enter the posterior wall of the bladder, run a course of 1.5 to 2 cm antero-medially in the wall of the bladder and open into the base. The triangular area between the ureteric orifices and the urethral opening is called the trigon of the bladder. At the bladder neck, the fibres of the detrusor muscle surround the intramural portion of the urethra and continue distally up to the 15th percentile. Particular arrangement of the muscle fibres depicting sphincteric structure seen at the bladder neck in males is not identified in females (Booth et al. 1983; Gosling 1996; Li et al. 2015). The adventitious layer is attached to the pelvic peritoneum on the superior aspect.

2.2 The Structure of Urethra

The urethra is the tubular outlet of the bladder. It begins at the internal urethral meatus of the bladder which lies posterior to the pubic symphysis. It runs antero-inferiorly embedded in the anterior vaginal wall and opens into the external urethral meatus which is about 2.5 cm behind the clitoris and anterior to the vaginal opening. An average female urethra is 2.5 to 5 cm long.

The urethra has a complex multi-layered structure which has been extensively studied by cadaveric dissection and various imaging modalities (Gosling et al. 1981; Carlile et al. 1987; Haderer et al. 2002). The innermost layer is the mucosal layer. It has mainly columnar or transitional epithelium near the proximal end and stratified squamous near the distal end of the urethra (Carlile et al. 1987). The submucosal layer contains a dense vascular network with elastic fibres and smooth muscle cells. The vascularity is denser than is required by the tissues (Berkow 1953). This vascularity is considered to be responsible for the closure of urethral lumen with vascular tension preventing leakage of urine (Caine 1986). The mechanism behind successful vaginal oestrogen therapy for stress incontinence in postmenopausal women is thought to be by increasing vascularity in this region (Martan et al. 1999).

The smooth muscle layer of urethra is present throughout its length and is continuous with the detrusor muscle at the cranial end of urethra. It is composed of inner longitudinal and outer circular fibres. An outer longitudinal layer can exist in some women. The striated urethral sphincter surrounds the smooth muscle layer in the mid-urethra. It is spread over the proximal 18th to 64th percentile of urethral length (DeLancey 1986, 1988). It is composed of circular muscles which completely surround the urethra in the shape of a horseshoe in some women, and are deficient on vaginal aspect in others. These muscle fibres are slow twitch fibres responsible for maintaining the resting muscle tone over a prolonged period (Gosling et al. 1981). Beyond the 54th percentile of the urethra, some muscle fibres in the urogenital diaphragm encircle the urethra and vagina forming the urethrovaginal sphincter. Some other fibres pass anteriorly and are attached to the pubic rami forming the compressor urethrae muscle (DeLancey 1990). The different layers of the urethral wall are clearly seen on MRI studies (Strohbehn et al. 1996).

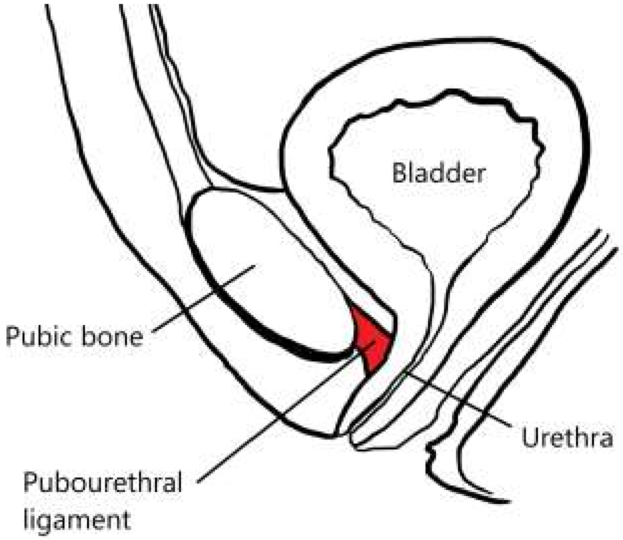
2.3 Supports of the bladder and urethra

The lower urinary tract is supported by the ligaments formed by condensation of the endopelvic fascia (Haderer et al. 2002). Pubovesical ligaments are described by some authors as extending from the bladder neck to the pubic bone on either side. The bladder neck is separated from the anterior vaginal wall by vesico-vaginal space filled with smooth muscle fibres, loose connective tissue and areolar tissue allowing necessary mobility. The urethra lies in a close relationship with the anterior vaginal wall. Both these structures are suspended in the pelvis by their fascial attachment to the arcus tendinous fascia pelvis (ATFP). ATFP is a tendinous band of pelvic fascia which extends from the posterior surface of the pubic symphysis to the ischial spines on either side. Its posterior end is broad and less defined (DeLancey 1990). It is attached to the inner aspect of the levator ani fascia (Haderer et al. 2002). The suspension of the anterior vaginal wall by the ATFP forms a hammock in which lie the urethra and the bladder (DeLancey 1994). During episodes of raised intraabdominal pressure, the urethra is compressed against the firm support of the anterior vaginal wall which prevents the leakage of urine. The muscular attachment to the levator ani muscle provides active support to these structures. The paraurethral fibres of the levator ani are formed of a combination of slow twitch and fast twitch fibres which maintain constant tone and also provide rapid support during sudden stressful activities like coughing (DeLancey 1990; Haderer et al. 2002).

The fibrous tissues around the urethra form the urethral support. They are traditionally called pubourethral ligaments. Zacharin described them in detail as two posterior, an intermediate and an anterior ligament (Zacharin 1977). According to his description, the posterior ligaments are the most important supporting structures. The two ligaments form a pyramidal structure. The apical attachment is to the posterior surface of the pubic bone at the junction of upper four fifths and lower fifth just lateral to the pubic symphysis. The bulky base is attached to the upper paraurethral tissue at the junction of upper third and lower two thirds of the urethra. The ligament fuses at this level with the muscle and fascial sheath of the upper urethra. A flat expansion from the lateral margin of the ligament is seen running laterally across the levator muscle and fascia and fusing with the fascia at a distance. Zacharin thought that it was the only connection the ligaments had with the levator muscle. Another expansion of the ligament is seen extending beneath the subpubic arch and fusing with similar tissue extending from the anterior pubourethral ligament. This junctional tissue was termed the intermediate pubourethral ligament. The anterior pubourethral ligament is the deep extension of the suspensory ligament of the clitoris supporting the external urethral meatus.

Zacharin described the ligaments as completely separate structure from the muscles (Zacharin 1977). These ligaments are responsible for maintaining the position of the urethra (Cruikshank and Kovac 1997). Petros performed studies on cadavers and women undergoing sling procedures and confirmed the presence of these ligaments (Petros 1998). The biopsies of these ligaments showed the presence of smooth muscles along with elastin and collagen, and striated muscles were found to be present in 25% of cases. The variations in the description of the supporting ligaments by different authors have led to doubts about their true structure (Gosling 1996).

Figure 2.1: Pubourethral ligaments



2.4 Blood supply

The blood supply to the bladder is by the superior and inferior vesical arteries, branches of the internal iliac artery. The vascular supply of the urethra is by vaginal, inferior vesical and pudendal vessels (DeLancey 1986). These vessels form the paraurethral vascular plexus underneath the pubovesical ligaments.

2.5 Nerve supply

The bladder and the urethra have autonomic and somatic innervation (Fowler, Griffiths, and de Groat 2008). The posterior and proximal urethra receives more innervation than the anterior (Mazloomdoost et al. 2017). Sympathetic fibres originate in the T11–L2 segments in the spinal cord. They pass through the inferior mesenteric ganglia and the hypogastric nerve and reach the bladder. Alternatively, they travel through the paravertebral chain and enter the pelvic nerves at the bladder base and the urethra. Parasympathetic preganglionic fibres arise from the S2–S4 spinal segments. They travel in sacral roots and pelvic nerves to reach ganglia in the pelvic plexus and in the bladder wall. The postganglionic nerves then supply the bladder and the urethra. The somatic nerves supplying the striated sphincter arise from S2–S4 motor neurons and pass through the pudendal nerves (Fowler, Griffiths, and de Groat 2008). They enter the muscle at 3 o’clock and 9 o’clock positions (Shafik and Doss 1999; Karam et al. 2005). Additionally, numerous nerve bundles follow an intrapelvic course beneath the endopelvic fascia to supply the levator ani and urethral sphincter (Borirakchanyavat et al. 1997). Denervation of the urethra can cause incontinence of urine. It is seen on electromyography studies in a third of cases of stress urinary incontinence (Tawadros et al. 2015).

3. Physiology of Micturition

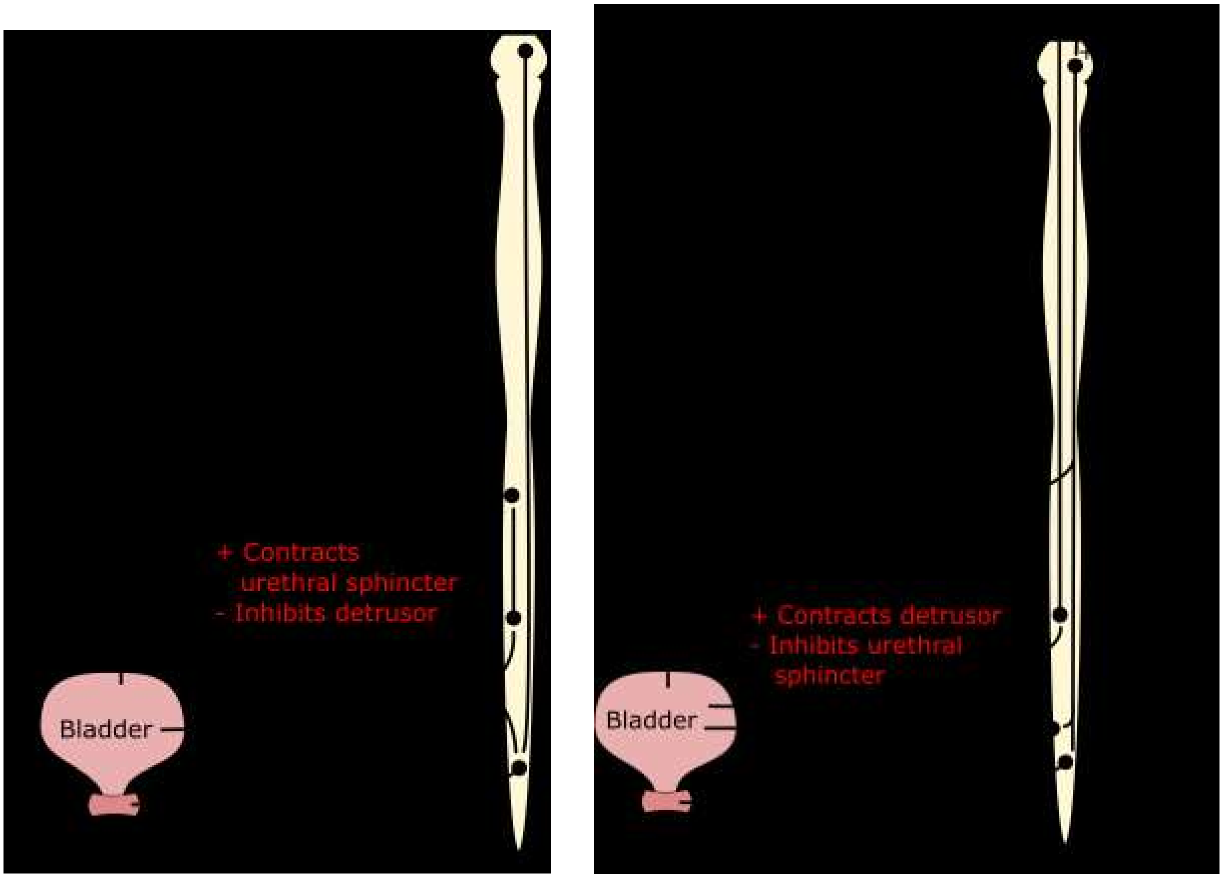
Urine produced by the kidneys is delivered to the bladder through the ureters in the form of intermittent spurts. The bladder acts as a low pressure reservoir for the urine. It is emptied voluntarily at an appropriate time and place by the individual. The urethra acts as an outlet for the urine. It remains closed at all times except during micturition. Any abnormality of this function can have significant impact on the quality of life.

3.1 Micturition cycle

The bladder and urethra are organs involved in the micturition cycle. Their anatomy and nerve supply is discussed in detail in the chapter on ‘Anatomy of Female Lower Urinary Tract’. The micturition cycle is divided into the storage phase and the voiding phase, which are under neurological control. The central neuronal pathways controlling the cycle are organised as simple on-off circuits as shown in figure 3.1.

During the storage phase, the detrusor muscle is relaxed and the urethral sphincter contracted. This is achieved through a spinal reflex by activation of the sympathetic system, deactivation of the parasympathetic system and voluntary contraction of the striated sphincter. With the urine entering the bladder, afferent neurons in the bladder wall are stimulated, either directly or through the activation of various receptors in the urothelium (Andersson and Arner 2004; Birder and Wyndaele 2013; Ochodnicky et al. 2013). These neurons send low level visceral afferent stimuli to the spinal cord through

Figure 3.1: The micturition cycle



Storage phase

Voiding phase

the pelvic nerves. This results in reflex sympathetic stimulation causing relaxation of the bladder and contraction of the smooth muscle sphincter. It also results in contraction of the striated sphincter through stimulation of the pudendal nerve (de Groat 1993; Griffiths 2015). With increasing bladder volume, high level visceral afferent signals are sent through the pelvic nerves which eventually reach the brain.

During the voiding phase, the bulbospinal micturition reflex is activated through the pontine micturition centre. This centre is modulated by excitatory and inhibitory impulses from the cerebral cortex, diencephalon and other areas of the brain stem (Dokita et al. 1994; Burnett 1995). Switching the centre to activation mode results in inhibition of the sympathetic and external sphincter activity and stimulation of the parasympathetic outflow to the bladder. With relaxation of the urethral sphincter and contraction of the detrusor, urine is eliminated from the bladder (de Groat 1993).

3.2 Mechanism of urinary continence

Urinary continence is the ability to hold back urine during the storage phase. Attempts were made to link various anatomical features of the urethra and the bladder to urinary incontinence; funnelling (English, Amundsen, and McGuire 1999), flattening of the posterior vesicourethral angle (Jeffcoate and Roberts 1952), short urethra (Lapides et al. 1960) and lower position of the bladder base Hodgkinson 1953 (Hodgkinson and Doub 1953),to name a few. However, these links could not be proven conclusively by clinical evidence and these parameters were shown to be similar in continent and incontinent women. They are discussed in detail in chapter 5 on ultrasound of urethra. The most significant theories of urinary incontinence are as follows.

3.2.1 Intra-abdominal pressure transmission theory

Enhorning measured the intravesical and urethral pressures simultaneously with a dual channel catheter (Enhorning 1961). He observed that there was leakage of urine when the difference between these two pressures, which was termed the ‘closure pressure’, was lowered to 0 on coughing. He proposed a theory that the rise in intra-abdominal pressure on physical stress is readily transmitted to the bladder and the upper urethra when positioned above the pelvic floor, maintaining higher urethral closure pressures. In a lower urethral position, the increase in the intra-abdominal pressure does not reach the urethra. The bladder pressure is then much higher than the urethral pressure resulting in urinary leakage (Enhorning 1961).

However, there was significant overlap of pressure transmission ratios between the stress incontinent and continent women (Versi, Cardozo, and Cooper 1991; Summitt et al. 1994; Swift, Rust, and Ostergard 1996; Cucchi et al. 2004). The pressure transmission theory also could not explain stress incontinence in a normally placed upper urethra. It was demonstrated by a study on temporal and special distribution of urethral pressures that the distal urethral pressure was magnified 1.5 to 1.7 times the vesical pressure just before the cough impulse (Constantinou and Govan 1982). This reflexly supported the pressure rise in the upper urethra in maintaining incontinence.

3.2.2 Integral theory

Petros and Ulmsten proposed the integral theory for incontinence (Petros and Ulmsten 1990c). According to this theory, stress and urge symptoms may both result from the same anatomical defect of a lax vagina or some defect in the surrounding structures. Active contraction of the pubococcygeus muscle with the supporting pubourethral ligament results in tension in the vaginal wall supporting the urethra. This theory was based on cadaveric dissection, radiological investigations, dynamic urethral pressure measurements, EMG and digital palpation. The ‘sling and tuck’ procedure to correct the laxity in the supporting structure could cure urge as well as stress incontinence (Petros and Ulmsten 1990a, 1990b). It was also curative for insensible urinary leakage though the number of cases studied were small (Petros and Ulmsten 1990d). There is no clinical evidence to prove or disprove this theory.

3.2.3 Hammock hypothesis

Delancey proposed a theory that the increased pressure in the urethra during a cough is due to its compression against the supportive layer of endopelvic fascia and the anterior vaginal wall which acts like a hammock (DeLancey 1994). MRI studies in supine position support this hypothesis (Klutke et al. 1990). Defects in these supporting structures should be seen on imaging in erect position. Recent studies have found this mechanism less important in maintaining continence (DeLancey et al. 2008), suggesting that another mechanism may be important.

It is possible that incontinence can result from major disruption to any one of the continence mechanisms or minor defects in multiple supporting systems.

3.3 Factors affecting urinary continence

3.3.1 Age

The overall incidence of urinary incontinence was estimated to be 25% in the Norwegian EPINCONT study (Hannestad et al. 2000). The incidence was below 20% in women less than 35 years of age. It gradually increased to 40% in women over 90 years. Stress incontinence was predominant in women between 35 to 50 years old, accounting for 60% of the cases. This higher incidence in women of reproductive age could be explained by its association with childbirth (Hannestad et al. 2000). The number of women undergoing surgery for stress incontinence peaked at the perimenopausal age (Shah et al. 2008). Urge incontinence was seen more in the older age group and this effect was independent of vaginal parity. In a large study on nulliparous women, the incidence of all types of urinary incontinence increased with age. (Al-Mukhtar Othman et al. 2017). A similar distribution of incidence was seen in Australian women though the reported incontinence rate of the population was 41% (Botlero et al. 2009).

There is a 0.37% reduction in muscle mass per year in women with increasing age (Mitchell et al 2012). Urogenital tissues also undergo atrophic changes with age (Ulmsten 1994). Postmenopausal status resulting in a lack of oestrogen and reduced vascularity to the urogenital system can explain these changes to some extent. Oestrogen treatment resulted in an increase in the urethral pressure but progesterone treatment did not show this effect (Rud 1980b). Increased vascularity of the urethral mucosa after the vaginal oestrogen treatment was thought to be responsible for this effect (Martan et al. 1999). In a study of cadaveric specimens, the density of the circular smooth muscle fibres was 25% to 50% higher in women under 40 years of age when compared with women over 70 years of age (Clobes, DeLancey, and Morgan 2008).

3.3.2 Pregnancy

The incidence of urinary incontinence increases significantly in pregnancy along with all other lower urinary tract symptoms (Burgio et al. 2003; Huebner, Antolic, and Tunn 2010; Fritel et al. 2012) The high level of oestrogen and progesterone can cause changes in the connective tissues (Buckingham, Selden, and Danforth 1962; Blakeman, Hilton, and Bulmer 2000) Mechanical pressure from the growing uterus and raised intra-abdominal pressure can contribute to this effect. The rate of urgency incontinence increases to 12% at the end of pregnancy and over 30% of pregnant women experience stress incontinence. There is an improvement of symptoms in the majority of the women following delivery (Viktrup and Lose 2000; Hansen et al. 2012).

3.3.3 Childbirth

Vaginal delivery results in significant stretching of the genital hiatus by the foetal head. It also puts enormous strain on the pelvic and pudendal nerves. The neuromuscular damage results in increased incidence of stress incontinence in parous women (Foldspang et al. 1992; Rortveit et al. 2001). The incidence of postpartum urgency incontinence is lower as compared to stress incontinence (Fritel et al. 2012; Tahtinen et al. 2016) The mode of delivery can affect the urinary symptoms after delivery. Though higher than the nulligravid women, the incidence of lower urinary tract symptoms is lower after caesarean delivery than after vaginal birth (Rortveit et al. 2003; Hantoushzadeh et al. 2011).

3.3.4 Body mass index

All types of urinary incontinence have higher incidence with increasing body mass index (BMI) (Townsend et al. 2008; Khullar et al. 2014) Obese (BMI>30) women are at higher risk of developing stress incontinence (Osborn et al. 2013). Increased cough pressure putting more stress on the pelvic floor can be among the main reasons (Swenson et al. 2017). At the same time, the proportion of obese women among the women with mixed incontinence can reach almost 50%. However, the cause and effect relationship between incontinence and obesity could be bidirectional. A study was conducted on women who were undergoing surgically induced weight loss. Out of 12 women who complained of urinary incontinence before the surgery, only 3 women were incontinent at the time of one year after surgery. There was significant reduction seen in vesical pressure, magnitude of rise in bladder pressure on coughing and incontinence episodes. There was evidence of an increase in the abdominal pressure transmission to the urethra (Bump et al. 1992). High BMI is associated with increased failure rate of surgery for stress incontinence (Brennand et al. 2017).

3.3.5 Ethnicity

Ethnicity can influence the risk of having specific type of incontinence. Women of African and Asian origin are found to be at less risk of having stress incontinence than Caucasian women (Novielli et al. 2003; Thom et al. 2006; Townsend et al. 2010) The incidence of urgency incontinence can be higher in women of African origin than of Caucasian ethnicity (Duong and Korn 2001; Townsend et al. 2010)

3.3.7 Pelvic organ prolapse

The majority of women with prolapse symptoms also suffer from urinary incontinence due to the common aetiological cause of loss of support for both problems (Mouritsen and Larsen 2003; Burrows et al. 2004; Lowder et al. 2010). More than a quarter of women undergoing surgery for pelvic organ prolapse without bothersome urinary symptoms can have demonstrable stress incontinence (Schierlitz et al. 2014; van der Ploeg et al. 2017) Mechanical compression or stretching of urethra by the prolapse can mask the incontinence which becomes evident after surgical repair.

3.3.8 Hysterectomy

Evidence regarding the effect of hysterectomy on continence status is controversial. The WHI study showed that the risk of urinary incontinence was higher in postmenopausal women who had undergone hysterectomy in the past (Kudish et al. 2014). This finding is also supported by the results of other studies (Altman, Granath, et al. 2007; Forsgren et al. 2012). Some researchers found that hysterectomy increased the risk of de novo incontinence, especially in those with other risk factors (Lakeman et al. 2011; Bohlin et al. 2017). However, it is not considered to be a risk factor for urinary incontinence in a few other studies (Miller, Botros, et al. 2008; Christiansen, Hansen, and Lauszus 2017). Some found that it did not have consistent effect on continence status (Kruse et al. 2017).

3.3.9 Neurological disorder

Functioning of the lower urinary tract is under complex neurological control. Integrity of the central and autonomic nervous systems as well as the peripheral nerves is of paramount importance for maintaining this function. Urological symptoms manifest in various ways depending on the level of neurological lesion (Agarwal and Rosenberg 2003; Drake et al. 2016). Urinary incontinence is seen in 35% to 55% of patients diagnosed with multiple sclerosis (Murphy et al. 2012; Zecca et al. 2016). 45% of patients with Parkinsonism report some degree of urinary incontinence (Buchman et al. 2017). Urinary incontinence is a common presentation for other neurological disorders such as multiple system atrophy (Mashidori et al. 2007), myelopathy (Mochida, Shinomiya, and Andou 1996), cauda equine lesion (Podnar and Vodusek 2015)or peripheral neuropathy (Bansal et al. 2011). Biopsy of the urethral sphincter shows less skeletal muscle content and neurological activity in women with stress incontinence than continent women (Hale et al. 1999). This indicates neuromuscular damage as the cause of this problem. Hypertrophy of the sphincter is seen in cases of Fowler’s syndrome characterised by chronic painless urinary retention. Relaxing the muscle by injecting onabotulinum toxin A into it relieves the symptoms (Panicker et al. 2016). This underlines the role of the urethral sphincter and the neurological control of micturition.

3.3.10 Lifestyle

Incontinence episodes are common with larger bladder volumes (Seo et al. 2016). Controlling urine output is a common practice to avoid such episodes. Alteration of fluid intake is recommended as part of the conservative management of urinary incontinence. Reduction of caffeine intake is also a recommended measure. However, systematic reviews have not confirmed the effectiveness of these strategies (Townsend et al. 2011; Sun, Liu, and Jiao 2016). The incidence of urinary incontinence is reduced with regular physical activity. (Townsend et al. 2008). This, in part, can be a result of the weight loss achieved by exercise. There is also an association with current or previous smoking (Bump and McClish 1992; Hannestad et al. 2003). Evidence for these associations is poor due to the lack of randomised controlled trials (Imamura et al. 2015).

4. Urodynamic studies

The urodynamic investigations performed at St Mary’s Hospital are according to the standards set by the International Urogynecological Association (IUGA) / International Continence Society (ICS) (Schafer et al. 2002; Haylen et al. 2010). The different urodynamic diagnostic criteria used are as follows –

Detrusor overactivity – The occurrence of involuntary detrusor contractions during filling cystometry. These contractions, which may be spontaneous or provoked, produce an increase in detrusor pressure on the cystometrogram, of variable duration and amplitude. Symptoms of urgency and/or urgency incontinence may or may not occur.

Urodynamic stress incontinence - Involuntary leakage during filling cystometry, associated with increased intra-abdominal pressure, in the absence of a detrusor contraction.

Mixed urinary incontinence – Evidence of urodynamic stress incontinence and detrusor overactivity during filling cystometry.

Bladder oversensitivity – An increased perceived bladder sensation during bladder filling with specific cystometric findings of an early first desire to void, an early strong desire to void which occurs at low bladder volume, a low maximum cystometric bladder capacity and no abnormal increases in detrusor pressure.

Voiding dysfunction - Women with low peak flow rate and post void residual of more than 100 ml, measured within 10 minutes of voiding, are considered to have voiding dysfunction.

Table 4.1 outlines the basic differences in different types of urinary incontinence according to the urodynamic studies. This chapter provides an overview of the procedures performed for this thesis.

Table 4.1: Differences between the urodynamic diagnoses

Parameter	Nondiagnostic urodynamics	Detrusor overactivity	Urodynamic stress incontinence	Mixed urinary incontinence	Bladder oversensitivity
Urgency	-	+	-	+	+
Increase in detrusor pressure	-	+	-	+	-
Leakage on raised intra-abdominal pressure	-	-	+	+	-

4.1 Pretest assessment

A detailed clinical assessment of the patient is necessary to understand the pathology and to individualise treatment (Kalejaiye, Vij, and Drake 2015; Rosier et al. 2017). The following questionnaire and symptoms were recorded.

4.1.1 Quality of life questionnaire

The King’s Health Questionnaire was used to assess urinary symptoms. It is proven to be a valid and reliable instrument in assessing the quality of life in women with urinary symptoms (Kelleher et al. 1997; Reese et al. 2003; Okamura, Nojiri, and Osuga 2009). Part 3 of the questionnaire reports severity of individual urinary symptoms, graded into mild, moderate and severe. Though most of the terms are self-explanatory, they were discussed with the women and their responses confirmed. A copy of this questionnaire is added to the appendix 1 at the end of the thesis.

4.1.2 Clinical history

Associated bowel symptoms and pelvic organ prolapse (POP) symptoms were recorded. The IUGA/ICS Joint Report on the Terminology for Female Pelvic Floor Dysfunction was referred to while recording these symptoms (Haylen et al. 2010). Previous conservative management in the form of fluid management, bladder retraining and pelvic floor muscle training, and benefits achieved from such treatment were recorded. Knowledge of the modifications of lifestyle in response to the symptoms is important in understanding their impact on the quality of life. Women’s parity and their wishes for future pregnancies were discussed with them. Symptoms of neurological diseases were explored and details of other medical conditions and their treatment were also noted. An abdominal or pelvic surgery can affect the continence mechanism. Knowledge of previous surgeries for POP or urinary incontinence and their results is important in understanding the problem and planning further management.

4.1.3 Bladder diary

Women were asked to maintain a bladder diary for 3 days covering working and non-working days before coming for the test (Haylen et al. 2010). A bladder diary shows the details of times of fluid consumption with type and quantity of fluid. It also shows the timing and amount of urine passed. Any urgency symptoms and incontinence episodes were also noted by the patient. Change of pads if used for incontinence were recorded. Bladder diaries can provide valuable information about patient symptoms, patterns of fluid consumption and voiding and bladder capacity (Bright et al. 2014; Salvatore and Leone Roberti Maggiore 2014; Jimenez-Cidre et al. 2015). It can sometimes reveal the root cause of the problem such as excessive fluid consumption in the evening causing nocturia and help find simple solutions by fluid management. The details of the diary were reviewed before the urodynamic studies and maximum voided volumes were taken into account while conducting cystometry.

4.1.4 Pad test

The pad test is useful in quantification of urine loss (O'Sullivan et al. 2004; Nitti et al. 2014; Ferreira and Bo 2015). A dry, clean pad is worn by the patient and routine activities are carried out over a certain period of time. This time can vary from 1 to 24 hours. All the pads used over the time period are weighed before and after use to calculate the amount of urine leaked. It is used as an objective test for urinary incontinence in research studies. One hour pad test was performed during the work for this thesis as necessary.

4.1.5 Physical examination

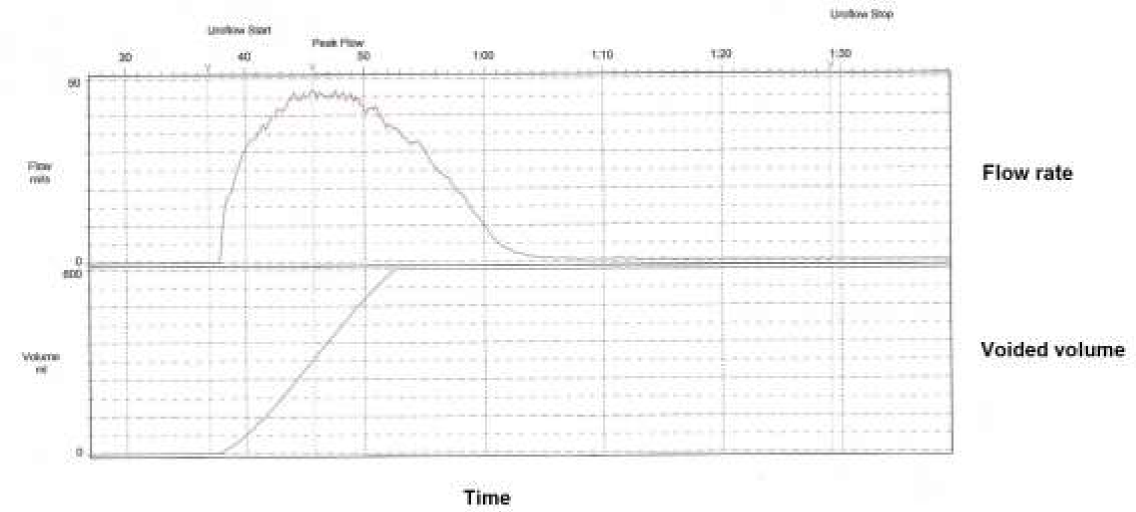
Patient’s posture, gait, mobility and physical abilities were observed to check neuromuscular disorder. Abdominal examination revealed scars from previous surgeries or a mass that could affect bladder capacity and function. Assessment of perineal and sacral sensation and reflexes was a part of the routine examination. Vaginal examination was carried out to assess prolapse, vaginal atrophy, pelvic masses, pelvic floor muscle tone and its contractility. Prolapse could be of the anterior vaginal wall (cystocoele), posterior vaginal wall (rectocoele, enterocoele), uterus, vaginal vault in case of hysterectomy or a combination of these. If the most distal part of the prolapse was in the lower half of vagina but 1 cm or above the hymenal plane, it was considered to be stage 1 prolapse. If it was within 1 cm of the hymenal plane it was stage 2 and if it was lying more than 1 cm caudal to the hymenal plane it was termed as stage 3 prolapse (Haylen et al. 2010; Swift et al. 2006). Insertion of vaginal pessary was considered in women with more than stage 1 prolapse. Reduction of prolapse was helpful in revealing occult urinary incontinence and influence clinical management (Jha et al. 2008).

4.2 Urodynamic tests

4.2.1 Uroflowmetry

Uroflowmetry is a physiological and non-invasive test to assess the flow of urine. It was performed before any invasive urodynamic studies. The important parameters recorded from the test were peak flow rate, acceleration, flow time, voided volume and voiding pattern (Sorel et al. 2017). Post void residual volume was measured using transabdominal ultrasound or by catheterising the bladder for cystometry. The normality of the flow rate can be assessed by plotting it on the nomograms (Haylen et al. 1989). Voiding dysfunction was suspected in the presence of low flow rate, interrupted voiding or high post void residual. Urinalysis was performed before invasive testing to check for haematuria and to rule out the presence of urinary infection. An example of a uroflowmetry trace is shown in figure 4.1.

Figure 4.1: Uroflowmetry



4.2.2 Cystometry

Cystometry involves continuous measurement of pressures and volume during bladder filling in order to understand the lower urinary tract function (D'Ancona, Gomes, and Rosier 2017; Rosier et al. 2016). The test was performed by using a size 12 urethral catheter for filling and 2 size 7F catheters for measuring vesical and abdominal pressure. A dual channel catheter can be used instead of these 2 catheters. The catheter with a flaccid filled balloon with a slit, as shown in the figure 4.2 was used per vaginally or per rectally to measure the abdominal pressure. A balloon prevents blockage of the catheter hole by faecal matter and flaccidity of the balloon allows accurate transmission of the

Figure 4.2: Image of the catheter used to measure abdominal pressure

rectal pressure. After inserting the catheters, they were flushed with normal saline and taped as close to their exit as possible. The pressure transducers were placed at the level of the upper border of pubic symphysis and this level was maintained throughout the test. The pressure was set to zero at the atmospheric pressure. The normal initial abdominal and vesical pressures should be between 5 and 50 cm of water. The detrusor pressure was calculated by the machine by subtracting abdominal pressure from the vesical pressure. The normal baseline detrusor pressure ranges from -5 to +5 cm of water. The correct position of the catheters was confirmed by positive increases in abdominal and vesical pressures with coughing or Valsalva and an absent or symmetrical biphasic cough impulse in detrusor pressure recording. Bladder filling was performed in the sitting position. The initial filling was done at 20 to 30 ml/min. The rate was increased to 50 and then to 100ml/min if tolerated by the woman. The filling rate was started at 10ml/min in women with neurological problems. The detrusor pressure shows minimal rise during the filling phase. An increase in detrusor pressure of more than 1 cm of water for every 40 ml of infusion means compliance of less than 40ml/cm of water and indicates poor compliance of the bladder (Wyndaele et al. 2011). The bladder filling rate was lowered by half in such cases. The position of the catheter was checked after every 100ml of bladder infusion by checking the transmission of cough impulse as done before the start of bladder filling. Women were asked to report 'first sensation of filling' in bladder, 'first desire to void' and 'strong desire to void' during the filling phase. The first sensation of filling is normally experienced at the bladder volume of 150 to 250ml. These sensations were annotated on the trace while conducting the test. Women were also instructed to report urgency, fear of leakage, pain, leakage or any other sensation immediately. These sensations were also annotated on the cystogram. The normal maximum cystometric capacity is 400 to 600ml. The filling was discontinued at the strong desire to void before the woman feels uncomfortable. The filling catheter was then removed leaving the pressure sensing catheters in situ.

Provocation tests were carried out in standing position as this increases the detection rate for detrusor overactivity by 21% (Arunkalaivanan, Mahomoud, and Howell 2004; Al-Hayek, Belal, and Abrams 2008). To test for stress incontinence, the women were asked to cough with a strong force once, three times and five times. Incontinence in women who leaked after single cough was termed as severe, after 3 coughs as moderate and after 5 coughs as mild (Grigoriadis et al. 2016). Repeated coughing can cause fatigue of periurethral muscles and decrease in urethral pressure, causing leakage of urine (Deffieux et al. 2007).The pressure readings were checked each time to rule out cough provoked detrusor overactivity. In addition, on the spot jogging, star jumps and other possible physical activities were performed to demonstrate stress incontinence of urine.

Detrusor overactivity is triggered by opening taps and wetting hands. Any leakage of urine during the test was recorded. Measurements such as ‘maximum detrusor pressure’, ‘detrusor pressure at the end of filling phase’ and ‘maximum cystometric capacity’ were also noted.

4.2.3 Pressure flow study

The pressure flow study begins with the ‘permission to void’ and ends with completion of voiding. It is carried out with the woman in a comfortable sitting down position. She is asked to void when there is no detrusor activity. Privacy is afforded to the woman during this study. Both the catheters are removed after voiding is complete. The post void residual volume was measured by transabdominal ultrasound. The parameters recorded from the pressure flow study were ‘opening detrusor pressure’, ‘peak flow rate’, ‘detrusor pressure at peak flow’ and ‘post void residual’. There is a delay from opening of the urethra at the opening detrusor pressure to the recording of the flow by the flowmeter. This delay is considered as to be of 1 second. The ‘opening detrusor pressure’ was measured as the detrusor pressure recorded 1 second before the start of flow recording. The post void residual was measured immediately after the pressure flow study by transabdominal ultrasound. A normal urodynamic trace is shown in the figure 4.3, Urodynamic stress incontinence is marked on the trace as leakage on coughing in figure 4.4. The detrusor pressure is stable and low during the filling phase. Figure 4.5 shows detrusor overactivity by increased detrusor pressure during the filling phase.

Figure 4.3: Normal urodynamic trace

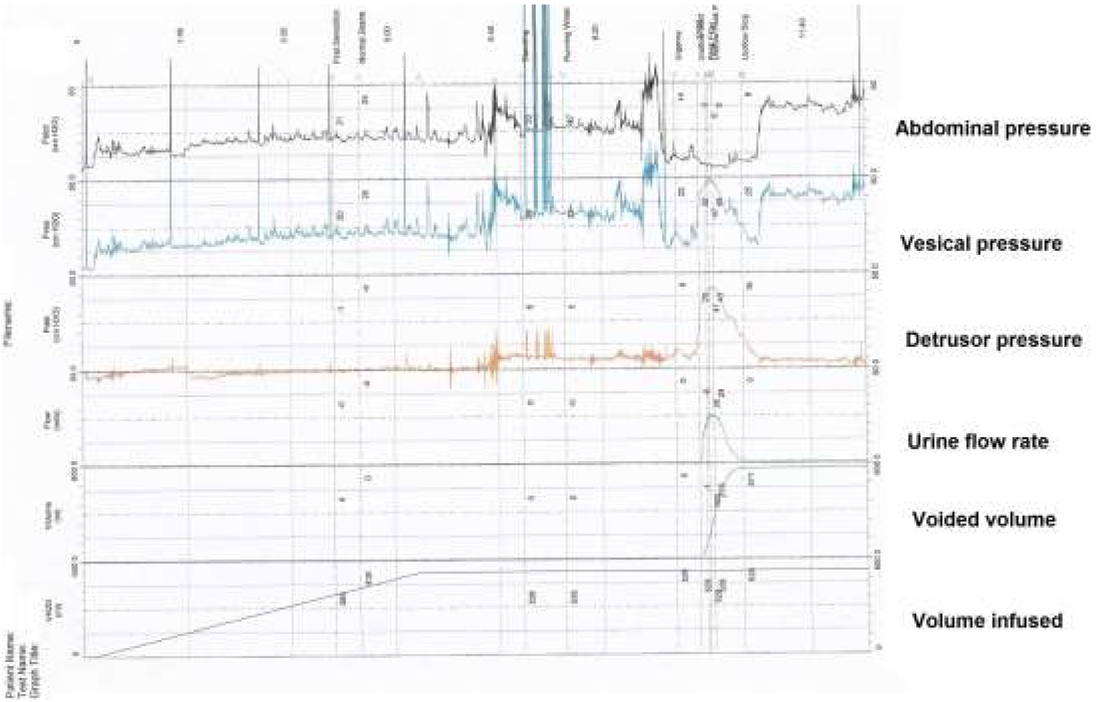


Figure 4.4: Urodynamic stress incontinence with leakage on cough (circled)

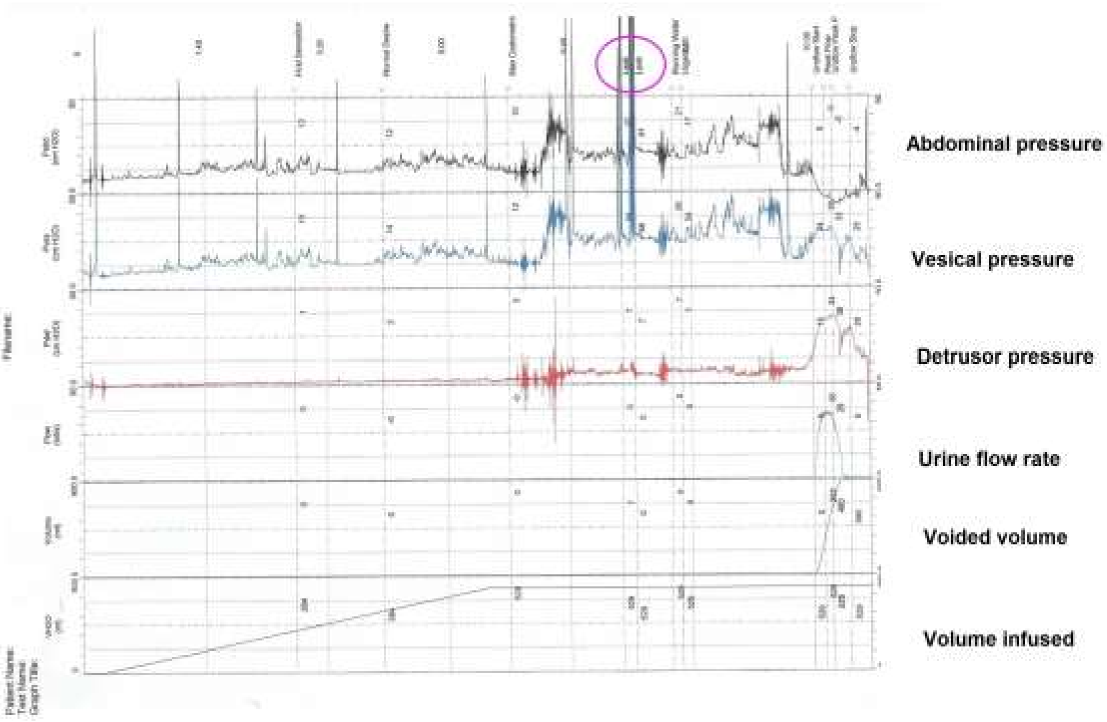
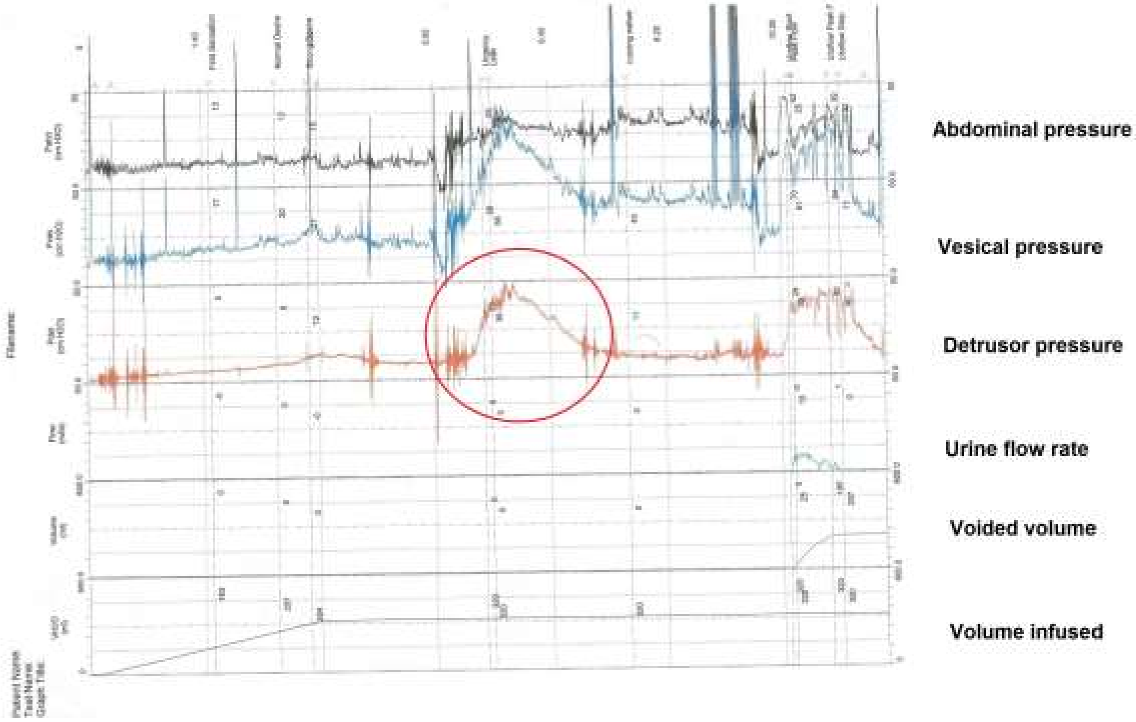


Figure 4.5: Detrusor overactivity with increase in detrusor pressure (circled)



4.2.4 Video cystourethrography

These investigations use radiological contrast media for bladder filling and fluoroscopy to screen simultaneously with cystometry. They were performed on women who complained about lower urinary tract symptoms after surgical treatment of stress incontinence, had complex symptoms and those with neurological diseases (McGuire et al. 1996; Chuang and Kuo 2009; Peng, Chen, and Kuo 2017). These studies are not suitable for pregnant women due to the use of radiation and also for those who are allergic to iodine. Specific conditions which can be diagnosed with video cystourethrography are bladder or urethral diverticulae, trabeculations, vesico-ureteric reflux, urethral stenosis and different types of urinary fistulae. Detrusor-sphincter dys-synergia is a condition seen in neurological disorders when the co-ordination between the two muscles is lost, resulting in simultaneous contraction of the detrusor and the urethral sphincter. Video cystourethrography can be useful in diagnosing the condition (Marks and Goldman 2014).

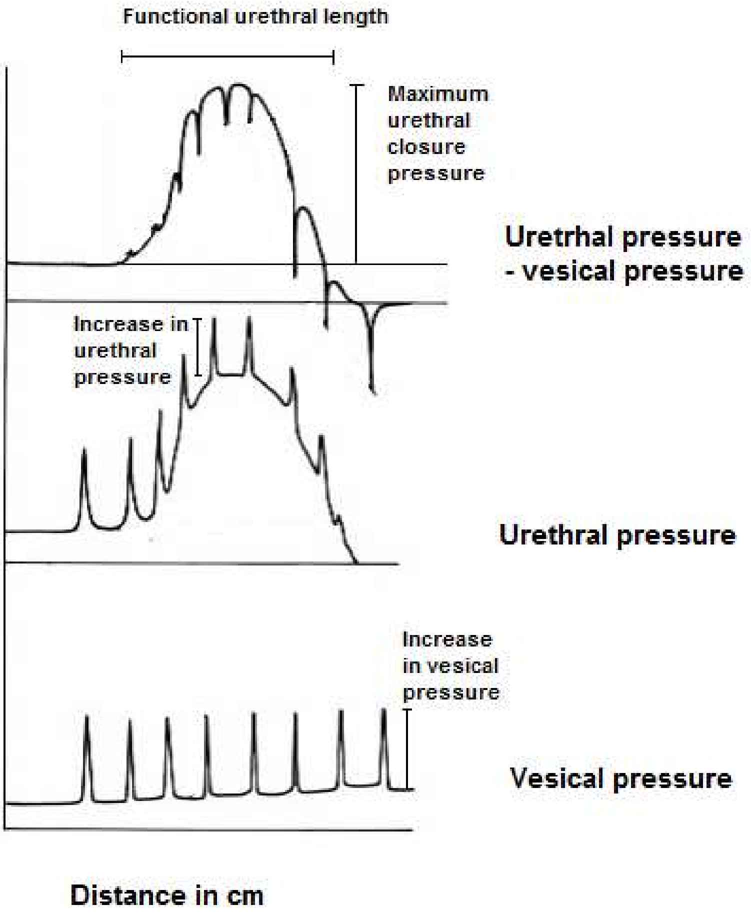
4.2.5 Ambulatory urodynamic

These studies were carried out if conventional filling cystometry did not provide clear explanation for the woman's symptoms (Pannek and Pieper 2008). They were performed outside the clinical setting and allowed physiological filling instead of infusion through the urethral catheter. Routine activities of the women were used as provocative stimuli to test for incontinence. This technique has higher detection rate for detrusor overactivity than conventional urodynamics (Dokmeci, Seval, and Gok 2010; Chester, Toozs-Hobson, and Israfil-Bayli 2016).

4.2.6 Urethral pressure profile

Urethral pressure should be higher than the bladder pressure during the storage phase to maintain continence. Graphical representation of the measurement of urethral luminal pressure along the length of the urethra, at rest and on cough is called urethral pressure profilometry. Figure 4.6 shows the graph obtained on stress urethral pressure profile. The method used in this department is as described by Hilton and Stanton in 1983 (Hilton and Stanton 1983). A silicon catheter with 2 microchip transducers, 1 at the tip and the other at 6 cm from the tip, is used to measure the intravesical and intraurethral pressure simultaneously. The pressure is set as 0 at the atmospheric pressure. The women lies in supine position with her thighs flexed and abducted. The bladder is filled with 250ml of saline. The catheter is introduced with both the transducers positioned inside the bladder.

Figure 4.6: Stress urethral pressure profile



It is then mounted over the mechanic arm positioned at the level of the urethra. The arm withdraws the catheter at a constant slow speed and the pressures measured by the transducers are plotted as the 'rest profile'. The woman is asked to cough strongly at a second's intervals when the proximal transducer traverses the urethra. This creates sharp spikes in the urethral pressure initially and sharp dips as the transducer moves close to the urethral opening. This is called the 'stress profile'. The measurements made during the investigation are mainly the 'functional urethral length' (FUL) which is the length of the urethra with pressure higher than the vesical pressure and the ‘maximum urethral closure pressure’ (MUCP) which is the maximum observed difference between the vesical and urethral pressure readings. The ‘pressure transmission ratio’ (PTR) is the change in the urethral pressure as a percentage of change in the vesical pressure. The value of this investigation is controversial. The MUCP is found to be strongly related to the stress incontinence by some researchers (DeLancey et al. 2008; Pizzoferrato et al. 2017) but others find it a less reliable investigation (Schick et al. 2004). The value of MUCP in predicting failure of midurethral sling surgery is also unequivocal (Wadie and El-Hefnawy 2009; Harris et al. 2011; Vij, Dua, and Freeman 2016). Its reproducibility is found to be low in cases of urodynamic stress incontinence (Rahmanou and Khullar 2011).

Urodynamic studies are able to diagnose the urological condition in most of the women. More complex cases were discussed at the weekly multidisciplinary meetings to confirm the diagnosis, plan additional tests or make multidisciplinary management plans. Women who were diagnosed with bladder oversensitivity experienced urinary urgency but did not demonstrate any abnormality in the detrusor pressure on urodynamic investigation. There was no objective evidence of their condition on the urodynamic trace. The majority of the women with voiding dysfunction suffered from external urethral obstruction or complex neurological problems which are more functional problems than structural. For these reasons, women with these two urodynamic diagnoses were excluded from this study.

5. Ultrasound of female urethra

5.1 Introduction

Ultrasound was first used in the field of medicine by John Wild in 1950 which led to the development of the first 2 dimensional ultrasound scanner (Wild and Reid 1952). The application of this technique in the field of obstetrics and gynaecology was introduced by Professor Ian Donald (Donald 1974). B mode or brightness mode ultrasound shows a 2 dimensional cross sectional image of the tissue. 3 dimensional ultrasound acquires a series of 2 dimensional images to build a 3 dimensional image. The machine displays 3 images which are in three orthogonal planes and a 3D/4D image (Fig 5.1). Ultrasound has now become an important research tool in urogynaecology to assess women with lower urinary tract symptoms (LUTS) and pelvic organ prolapse (POP) symptoms. It is also used to investigate urethral pain and sexual disorders.

Ultrasound gives more information about the structure and function of pelvic organs than can be obtained during a routine clinical examination. It allows us to visualise the internal structures and measure their dimensions and volumes. Real time examination allows us to see their movements and measure their displacement in various directions and angles.

The ultrasound imaging technique uses high frequency sound waves of 1 to 18 MHz in short pulses. When the waves pass through various tissues they undergo refraction and reflection at each tissue interphase. The transit time of the waves is easily measured and a pulse-echo method is used to create an image of the organ. The propagation speed of the waves is fast enough to create an image in a few milliseconds making it possible to create quick successive images and visualise movement of the organs. The ultrasound image of a tissue depends on its echogenicity. Highly echogenic tissues appear white on the ultrasound and the low echogenic tissues appear black. The higher the ultrasound frequency, the better the resolution of images. However, waves of higher frequency have poor penetrability. For this reason, frequencies used for imaging the pelvic organs are in the range of 3.5 to 6 MHz. The image appearance also depends on the orientation of the structures with respect to the direction of travel of the ultrasound waves. Therefore, a tissue can have different echogenicity when viewed from different angles. This is especially important while imaging striated muscles. When the ultrasound waves pass in the direction of muscle fibres, there is minimal reflection of the waves and the muscle appears hypoechogenic. Conversely, when the waves pass perpendicular to the muscle fibres, most of the waves are reflected and the muscle appears hyperechogenic. This is of particular importance when interpreting images of the urethral sphincter complex. The striated urethral sphincter fibres are circularly arranged around the urethra and the smooth muscle sphincter fibres are longitudinal. The echogenicity of these two components is different when scanned externally or internally.

5.2 Procedural variations

5.2.1 Probe position

Transabdominal ultrasound is preferred to urethral catheterisation for measuring the bladder volume. Same approach was used by White to assess the mobility of the urethrovesical junction in patients with stress urinary incontinence (SUI) (White et al. 1980). However, it was difficult to visualise the pelvic organs by this approach due to shadowing by the pubic symphysis. Imaging was difficult in obese patients and also in those with significant descent of bladder neck. Transrectal ultrasound was then employed to evaluate the bladder neck. This technique was used to demonstrate movement of the urethrovesical junction and assess the cause of urinary incontinence (Perkash and Friedland 1986; Richmond and Sutherst 1989). Transvaginal approach was more suitable in women due to greater proximity to the structures and improved quality of images. It was better tolerated and well received by them (Quinn et al. 1988). It was used extensively in urogynaecological research since then. Introital ultrasound was performed by placing the transvaginal probe against the external urethral meatus (Tunn et al. 2005; Mouracade et al. 2010; Kociszewski and Viereck 2013). Some researchers used an endourethral ultrasound probe to measure the dimensions of the urethral sphincter (Schaer et al. 1998; Strasser et al. 1998; Heit 2000). It was evident from various studies that the internal ultrasound probes could restrict the movement of organs resulting in inaccurate dynamic measurement. They could also distort the shape of the organs affecting measurement (Wise et al. 1992; Beco, Leonard, and Lambotte 1994). The transvaginal probe compressed the urethra under the pubic symphysis making it look wider (Umek et al. 2001). The transperineal ultrasound (TPU), on the other hand, allowed free movement of pelvic organs and was comparable to other imaging techniques or clinical tests at diagnosing urethral movement (Kohorn et al. 1986; Caputo and Benson 1993; Di Pietto et al. 2008). It was simple, non-invasive and could be used to image the whole pelvis including the pelvic floor. With the advent of three dimensional (3D) ultrasound in urogynaecology, it became possible to visualise pelvic structures and measure them accurately in various planes (Khullar et al. 1994; Athanasiou et al. 1999; Toozs-Hobson et al. 2008; Cassado Garriga et al. 2017).

5.2.2 Patient position

The ultrasound examination is mostly carried out with the women in a supine lithotomy or recumbent position. These are the most suitable positions for transvaginal and transperineal probe placements which are commonly used in urogynaecology. Measurement of bladder volume is a very common application of ultrasound. Patient position does not affect this measurement (Massagli, Cardenas, and Kelly 1989). However, position of the pelvic organs is affected by gravity. Patient posture is an important aspect while studying the position of an organ in the body (Barber et al. 2000). When measured by ultrasound imaging, the bladder neck is at a lower level in erect position than in supine position (Mouritsen and Bach 1994; Lin et al. 1999). When mobility of the bladder neck is assessed on straining, it is more mobile in supine than in a standing position (Handa, Jensen, and Ostergard 1995). The effect of posture is eliminated when maximum Valsalva or straining force is applied (Bader et al. 1995; Rodriguez-Mias et al. 2017). A standing position is used by some researchers using introital or transperineal approach though maintaining probe position is difficult in this position (Tunn and Petri 2003; Braekken et al. 2008).

5.2.3 Stress induction techniques

SUI is a common presenting symptom in urogynaecology. While investigating these women, intra-abdominal pressure is artificially raised either by strong cough or by straining or Valsalva. There is fundamental difference between straining and Valsalva. Reduced pelvic floor muscle activity during straining results in significantly more descent of the pelvic organs (Baessler, Metz, and Junginger 2017). The women have to voluntarily relax the pelvic floor to achieve maximum descent of the bladder neck which they may find difficult. Pelvic floor muscle activity can still be seen on electromyography when women are asked to relax the pelvic floor during Valsalva (Giannantoni et al. 2003). Persistence of the muscle activity is also seen when the woman is trying to relax the muscle (Orno and Dietz 2007).

A study was conducted to compare the bladder neck movement on cough and Valsalva in women. The bladder neck movement was more in continent women on Valsalva than on cough. However, the movement was similar in women with SUI (Howard, Miller, et al. 2000).

Valsalva and cough techniques were compared in another study. The mobility of the urethrovesical junction was assessed by ultrasound in pregnant women and the test was repeated at 6 weeks and at 6 months after delivery. Hypermobility seen on Valsalva at 6 weeks disappeared by 6 months but the hypermobility on coughing was found to be persistent after 6 months (Wijma et al. 2003). This indicated that cough technique was more consistent and effective than Valsalva. Voluntary pelvic floor muscle contraction or difficulty in relaxing them voluntarily during Valsalva may have been responsible for these results. A sudden reflex relaxation of the pelvic floor occurs on coughing which can show persistent hypermobility of the urethra.

An experiment was conducted to find out the difference between cough leak point pressure (CLPP) and Valsalva leak point pressure (VLPP). SUI was demonstrated more effectively by cough than at VLPP of 60 cm of water. All the women with SUI leaked on coughing but only 33% of them leaked on Valsalva (Sinha, Nallaswamy, and

Arunkalaivanan 2006). Leak point pressures were more frequently induced by cough than Valsalva in another study (Seo et al. 2016).

Cough technique is not suitable for stress induction in studies using 3D ultrasound as instantaneous nature of cough does not allow for time to capture the image.

5.2.4 Reference values for pressure measurements

The force applied during stress manoeuvres can be measured by measuring abdominal pressure as CLPP or VLPP. However, researchers use different reference values ranging from 30 to 60 cm of water (Hol, van Bolhuis, and Vierhout 1995; Petrou and Wan 1999; Kim et al. 2011). These methods are in need of standardisation.

5.2.5 Technical details

Other technical factors such as catheter size, method to confirm urine loss and type of pressure sensor can have effect on the measurements and need to be specified while reporting the studies on urodynamics and ultrasound (Bump et al. 1995; Rosier et al. 2017).

5.3 Ultrasound measurements of urethra

5.3.1 Urethral sphincter measurement

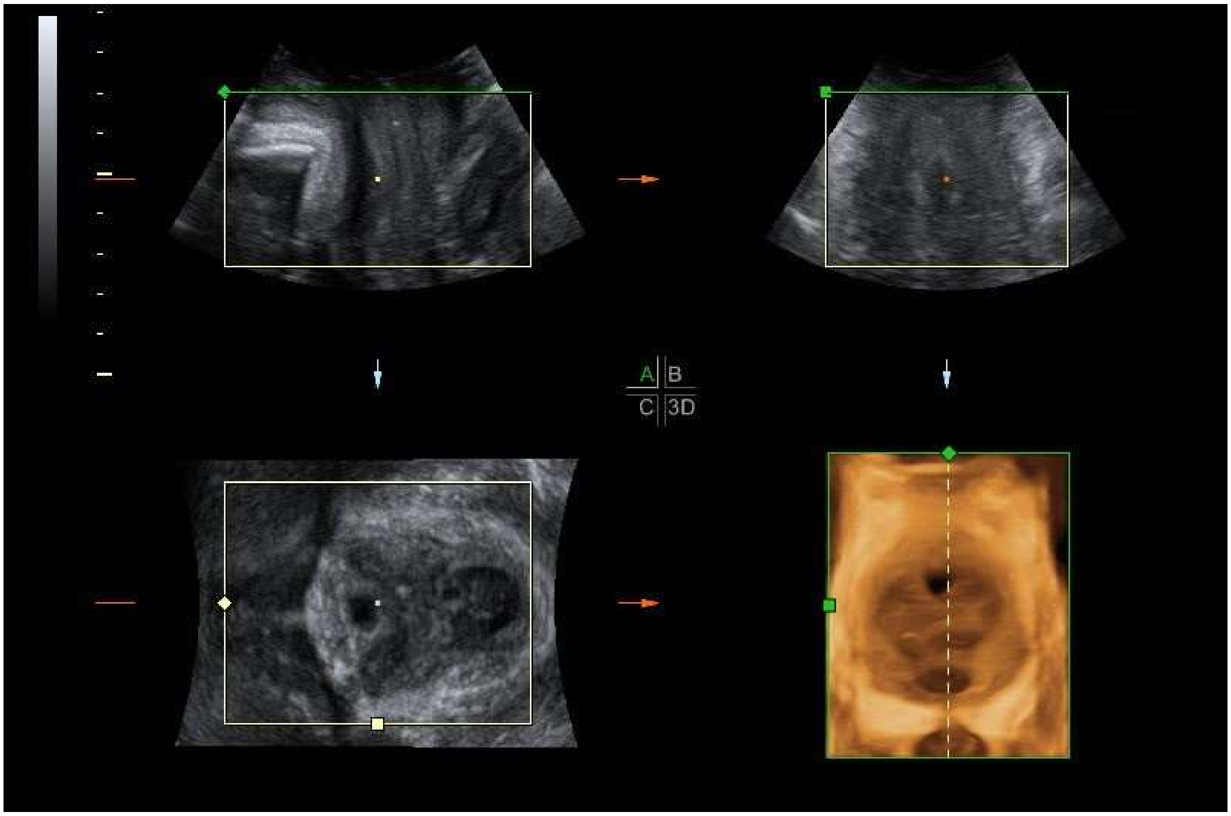
As the name suggests, the urethral sphincter controls the urinary outlet. It is logical that the strength of the sphincter is the main determinant of the continence status of a person. An interesting study was conducted to assess the effect of sphincter relaxation on the urethral closure pressure and continence status. After paralysing the sphincter by spinal anaesthesia, the urethral closure pressure was measured and stress test was conducted.

The maximum urethral pressure decreased under the anaesthesia, resulting in SUI (Haeusler et al. 1998).

The sphincter complex can be measured on ultrasound imaging. Figure 5.1 shows the image of the urethra obtained by the transperineal 3 dimensional ultrasound.

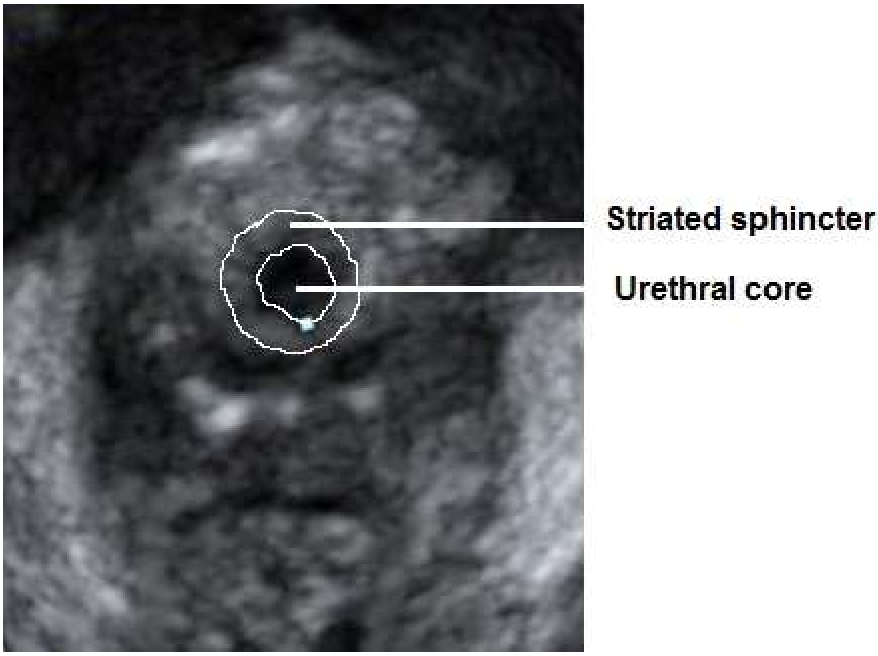
Figure 5.1: Images of the urethra by 3D transperineal ultrasound.

Image A shows the urethra in sagittal section, image B in coronal section, image C in transverse section and image D shows the 3D or 4D image.



The sphincter is visible as two distinct components on the trans-sectional image. The central hypoechogenic core seen on TPU consists of the mucosa, submucosal tissue and the smooth muscle sphincter (Figure 5.2). This central area is surrounded by an area of increased echogenicity which is caused by the striated sphincter. The central core looks hyperechogenic and the striated muscle looks hypoechogenic on TVU due to different direction of the ultrasound waves. The correlation between the histological components of the sphincter and its imaging is established through cadaveric study (Khullar et al 1996). The length and width of the sphincter complex can be measured in various planes by using 2 dimensional image. 3D ultrasound can measure the volume of different components of the complex.

Figure 5.2: Image of the urethral sphincter on transperineal ultrasound.



Age related reduction in the sphincter thickness was noticed in women on intra-urethral ultrasound (Klauser et al. 2004). A larger sphincter size was seen in nulliparous continent women of black ethnicity than white, when the sphincter was measured on 3D TPU. (Derpapas, Ahmed, et al. 2012).

The sphincter size was measured in women with urinary incontinence using intraurethral, TVU and TPU. Many studies have shown that the sphincter volume was smaller in women with SUI than incontinent women (Khullar et al. 1994; Frauscher et al. 1998; Athanasiou et al. 1999). The relationship between the sphincter length and SUI was supported by a recent study by TPU (Cassado Garriga et al. 2017). Women with detrusor overactivity (DO) were found to have larger sphincters (Khullar et al. 1994; Kondo et al. 2001). This could be the result of voluntary contraction and strengthening of the sphincter during the episodes of detrusor overactivity (DO) in these women.

Chronic isolated urinary retention is characterised by overactivity of the urethral sphincter and its failure to relax resulting in hypertrophy of the sphincter. When measured by TVU, the sphincter volume was significantly more in women with this condition (Wiseman et al. 2002).

The effect of childbirth on the sphincter volume was assessed by using 3D TVU in the third trimester and postpartum. The sphincter was smaller after delivery and the difference was not related to the mode of delivery (Toozs-Hobson et al. 2008). The sphincter looked larger during pregnancy, probably due to increased vascularity and hormonal effect, and the reduction in size after delivery was seen as these effects wore off. Levator ani injuries were seen after vaginal delivery especially with forceps (Kearney et al. 2010). However, the size of the urethral sphincter was not related to the levator ani deficiency (Santiago et al. 2015).

The change in the sphincter volume following incontinence treatment was studied by many researchers. Duloxetine treatment for 4 to 8 weeks caused alteration in the smooth muscle component and resulted in increased sphincter core width in successful cases (Duckett, Patil, and Aggarwal 2008). Pelvic floor muscle training caused compression of urethra by the contracting levator ani (Umek et al. 2002). It also resulted in sphincter hypertrophy in women providing relief from SUI (Madill et al. 2015). Injection of myoblasts into the urethral sphincter was carried out in women with deficient sphincter under transurethral ultrasound guidance. When the women were followed after a year with ultrasound examination, the striated sphincter thickness and its contractility were increased with cure of incontinence (Mitterberger et al. 2008).

The size of the sphincter was also found to have implications for success of the treatment. The risk of failure of colposuspension surgery was higher in women with smaller sphincters (Digesu et al. 2009). Such findings are useful in treatment planning and counselling women preoperatively. A recent systematic review provided evidence that the retropubic tape procedures were more effective than transobturator procedures in cases with intrinsic sphincter deficiencies (Ford and Ogah 2016).

Khullar and co-workers tried to determine the structural and functional relationship of the urethra and paraurethral tissue by measuring urethral pressure profiles and the sphincter length by transperineal 3D ultrasound (Khullar et al. 1994). They found significant correlation between functional urethral length and sphincter length by ultrasound. Moreover, the length of the urethra before the peak pressure and the distance from the cranial end of the sphincter to the maximal cross-sectional area were also significantly related. Similar relationship between sphincter measurement and urethral pressures was observed by other researchers (Kirschner-Hermanns et al. 1994; Toozs-Hobson et al. 2008; Kondo et al. 2001; Umek et al. 2001). Researchers of the ROSE project concluded that low MUCP and not the urethral support was the main causal factor in cases of SUI (DeLancey et al. 2008).

Ultrasound measurement of the sphincter gives us the unique opportunity of understanding the pathophysiology of urinary incontinence. It might be helpful in planning surgical treatment of the condition.

5.3.2 Urethral mobility

Urethral hypermobility is considered to be a major causative factor for SUI. However, this term is used as a measure of cranio-caudal or rotational movement of the bladder neck around the pubic symphysis on stress in many studies. This section relates to the changes in the position of the whole urethra with stress.

According to the Hammock hypothesis, the urethra is compressed against the firm hammock of the anterior vaginal wall during stress and this mechanism prevents SUI (DeLancey 1994). Loss of tension in the vaginal wall results in ineffective compression and leads to escape of the urine. For this hypothesis to be true, the urethral mobility (UM) should be less in continent women.

The UM can be measured by various methods. Measuring the angle between proximal and distal urethra is one such method. In a study based on this method, the angle was smaller at rest and further decreased on straining in women with SUI (Pregazzi et al.

2002). Measurement of this angle was found to be a better indicator of stress incontinence than the bladder neck mobility.

Another method of measuring UM is by making 2 measurements. One of them is the distance between the posterior border of the pubic bone and the midurethra. The other measurement is of the angle of inclination between urethral axis and axis of the pubic bone. A significant degree of mobility was observed in asymptomatic women of different ages and parity using this method (Di Pietto et al. 2008). Larger angles were seen on stress in women with SUI (Al-Saadi 2016).

Massata and co-workers developed another method of measuring urethral mobility at 6 different points along the urethra and the bladder base (Masata et al. 2006). The x axis was along the long axis of the pubic symphysis and the y axis was through the inferior border of the symphysis according to the guidelines by the German Urogynaecology Working Group (Schaer et al. 1996). They measured the co-ordinates of the points on the urethra at rest and on straining and calculated the vectoral displacement. Shek and Dietz described similar method with the x axis represented by a horizontal line from the inferoposterior border of the pubic symphysis (Shek and Dietz 2008).

Midurethral tape procedure is currently the most commonly performed surgery for SUI (Kurkijarvi et al. 2016; Tincello et al. 2017). Ultrasound studies showed that the UM at the tape was reduced on Valsalva (Masata et al. 2006). It was described as the ‘iris’ effect (Dietz and Wilson 2004). A urethral knee angulation was observed in cured and improved cases on straining (Lo et al. 2001). The angulation was greater in cases with voiding dysfunction.

The different methods to measure the urethral mobility are developed and used by individual teams. There is a lack of multicentric studies using the same technique. The link between urethral mobility and urinary incontinence is still unestablished.

5.3.3 Bladder neck position and mobility

The pelvic outlet is guarded by a fibromuscular floor consisting of the levator ani muscle. It has deficiencies which allow the passage of urogenital structures and anal canal. Therefore, there is some degree of physiological dorsocaudal movement of pelvic organs. The bladder neck is suspended in the pelvis by various ligaments and surrounding structures, mainly the anterior vaginal wall (DeLancey 1988). The bladder volume affects its position and mobility (Dietz and Wilson 1999).

Bladder neck mobility (BNM) can be assessed by its vertical and transverse displacement or its rotation around the pubic symphysis. Before routine use of imaging in urogynaecology, the Q-tip test was used to assess BNM. However it had very low sensitivity and predictive value for diagnosing hypermobility when compared with the TPU (Caputo and Benson 1993). The ultrasound method for measurement of position of the bladder neck at rest and on valsalva and measurement of its mobility in 2 perpendicular dimensions - parallel and perpendicular to the axis of pubic symphysis was first described in 1995 (Schaer et al. 1995).

The extent of BNM was measured in nulliparous continent women. There was 4 mm to 33 mm displacement noticed on cough or valsalva on TPU (Peschers et al. 2001). In addition to significant linear movement, angular rotation was also observed on ultrasound scan (Reed et al. 2004). The bladder neck was found to be at a lower position and hypermobile after vaginal delivery but it did not always translate into SUI (Wijma et al.

2003). Morphological and functional differences in the urethral sphincter and its support system were also observed in nulliparous women of black and white ethnicity (Howard, Delancey, et al. 2000).

It was concluded from many TPU studies that the bladder neck was at a lower level at rest and on straining with increased descent on straining in women with SUI (Chen, Su, and Lin 1997; Minardi et al. 2007; Naranjo-Ortiz et al. 2016). Bladder neck position at straining was found to be significantly more dorsal and caudal in women with SUI in another study but the mobility was found to be similar (van Veelen, Schweitzer, and van der Vaart 2014). BNM in the antenatal period was predictive of postpartum stress incontinence in a study (King and Freeman 1998). Half the number of women with antepartum BNM in this study experienced postpartum incontinence.

Many studies were performed to assess the effect of continence treatments on BNM, in order to understand their mechanisms of action and improve the results. Pelvic floor physiotherapy strengthened the levator ani muscle which had an independent action of maintaining continence (Kenton and Brubaker 2002). It could elevate the bladder neck more on pelvic floor contraction but it did not restrict the mobility on stress after a responsive therapy (Hung et al. 2011; Reilly et al. 2014). Active contraction of the pelvic floor in preparation for and during cough could elevate the proximal urethra and prevent stress incontinence (Miller et al. 2001; Miller, Botros, et al. 2008).

The BNM was seen to be lower after a successful transobturator tape procedure than after a failed procedure (Torella et al. 2014). The linear movement and angular rotations were significantly lower after a continence surgery; more so after colposuspension than after midurethral tape insertion (Atherton and Stanton 2000). Excessive mobility of the bladder neck evident on ultrasound after the colposuspension was associated with high recurrence rate for stress incontinence (Viereck et al. 2006). Women with urinary urgency after colposuspension had over-elevation of the bladder neck with reduced mobility (Martan et al. 2001).

Considering various claims about usefulness of ultrasound in diagnosing SUI, a study was conducted to assess predictability of the condition. Five experts were shown ultrasound images of single cough in women with and without stress incontinence. They were able to predict stress incontinence correctly in only 57% of cases (Lewicky-Gaupp et al. 2009). This has raised questions regarding the validity of current ultrasound methodologies in diagnosing stress incontinence.

5.3.4 Bladder neck funnelling

Funnelling of the bladder neck or open bladder neck is a common finding on ultrasound. It is found in continent women as well as in women with incontinence. It was seen in 24% of nulliparous asymptomatic women in a study (Chapple et al. 1989). It is possible that, in these cases, the closure of urethra was achieved mainly by the striated sphincter which was absent near the bladder neck allowing funnelling. In a large study, 70% of the women with stress incontinence were found to have open bladder neck compared to 27% with detrusor overactivity and 9% asymptomatic women (Digesu, Khullar, et al. 2004). Though it had low specificity for diagnosing stress incontinence, funnelling was found to have 92.8% negative predictive value for low leak point pressures (Huang and Yang 2003). Funnelling before retropubic tape procedures and its persistence after the procedure indicated increased risk of persistence or recurrence of incontinence (Harms et al. 2007). Significant reduction in funnelling from 55% to 11% was seen after colposuspension procedure which was successful in 90% of cases (Viereck et al. 2004). Persistent bladder neck funnelling after colposuspension was associated with higher failure rate of over 40% and risk of complications such as urinary urgency and a new symptom of urge incontinence after 6 months (Skala et al. 2004).

Though funnelling is observed on various imaging modalities over decades, its value in diagnosing stress incontinence is doubtful.

5.3.5 Posterior urethrovesical angle

The posterior urethrovesical angle (PUVA) was considered as the diagnostic feature of SUI on cystourethrogram before the use of other imaging techniques (Green 1957). It could be easily measured with ultrasound. There was a significant increase in the measurement on Valsalva in women with SUI but the range of the measurements was very wide and the method was thought to be unsuitable as a diagnostic test (Alper et al. 2001). The measurement of posterior urethrovesical angle increased significantly after anterior vaginal repair but it was not related to change in urinary incontinence (Sumi et al. 2000; Duckett and Chakani 2013). The measurement of the angle was not different in women with and without stress incontinence in a recent study (Cosimato et al. 2015). Measuring the angle is not included in current management of stress urinary incontinence.

5.3.6 Bladder wall thickness

The bladder wall thickness (BWT) was found to be significantly more in women with DO than with USI (Khullar et al. 1994). 94% of women with BWT of 5mm or more were diagnosed with DO on video cystourethrography and ambulatory urodynamics (Khullar et al 1996). Similar findings were reported by other groups of researchers (Kuhn et al. 2011; Abou-Gamrah et al. 2014; Otsuki et al. 2014). Higher BWT was found to be a negative predictor for the success of anticholinergic therapy in cases of DO (Serati et al. 2011)). However, a recent multicentre trial found the measurement of low sensitivity of 43%, specificity of 62% and likelihood ratio of 1.11 (Latthe et al. 2017). Increased BWT is also an indicator of bladder outlet obstruction (Manieri et al. 1998; Oelke et al. 2007). It was a more reliable predictor than uroflowmetry. Automated machines were used to estimate bladder weight and BWT (Chalana et al. 2005; Al-Shaikh and Al-Mandeel 2012; Bright, Pearcy, and Abrams 2012). The reproducibility of BWT by this method was moderate (Al-Shaikh and Al-Mandeel 2012). The change in BWT after successful treatment of either condition was not significant (Akselim et al. 2017; Robinson et al. 2016; Bray et al. 2018; Lee, Lee, et al. 2017) Further studies are needed to assess the value of this measurement in clinical practice.

5.3.7 Surgeries for stress incontinence

When described originally in 1996, the midurethral tape was placed at 0.5 cm from the external urethral meatus (Ulmsten et al. 1996). There was some modification at a later date with the tape being placed at 1 cm from the external meatus (Ulmsten, Johnson, and Rezapour 1999). Individual variation in the urethral length was not taken into consideration at that stage.

There is an unequivocal evidence regarding position of the tape and success of midurethral tape surgery. Some researchers concluded that the tape position was not related to the success of the procedure (Dietz and Wilson 2004; Ng, Lee, and Han 2005; Rodriguez-Mias et al. 2017). However, there was some evidence that the tape location affects the outcome of the surgery. It was concluded in some studies that tape placements in upper and lower quarters of urethra were associated with more failure rates (Kociszewski et al. 2008; Flock et al. 2011). High rate of persistent or recurrent SUI was also seen in women with tape position at the bladder neck (Jiang et al. 2013; Bogusiewicz et al. 2014; Kociszewski et al. 2017). Efforts are made to achieve placement in the midurethral region to increase the success rate (Pirtea et al. 2015).

Voiding dysfunction is a known complication of the midurethral tape surgery. A smaller distance between the tape and the smooth muscle layer of the urethra was seen in women with complications such as overactive bladder, urinary retention and recurrent urinary infection (Flock et al. 2011; Kociszewski et al. 2017). Ultrasound guided management was tried in such cases. Loosening of tape restored normal voiding in 96% of patients with postoperative voiding dysfunction (Rautenberg et al. 2014). TPU was useful in selecting women for postoperative tape lysis for lower urinary tract symptoms. Women with tape placement in the upper or lower third of the urethra and/or urethral distortion were considered to have abnormalities on ultrasound in a study (Mouracade et al. 2010). Most of the women with overactive bladder symptoms and ultrasound abnormality were relieved of their symptoms after tape excision. However, 4 out of 5 women with normal ultrasound remained symptomatic post excision. Though the failure rate of the midurethral tape was low (Ford et al. 2015), the reasons for failure, other than the position of the tape were also investigated using ultrasound. Reduced postoperative mobility of the urethra was found to be one of them (Viereck et al. 2006).

Repair of the cystocoele was performed at the same time as tape insertion in many cases (Khullar et al. 2017; van der Ploeg et al. 2017). This reduced the risk of postoperative stress incontinence but increased the risk of serious adverse events (Van der (van der Ploeg et al. 2017; Wu et al. 2017).

Intraoperative ultrasound assessment was used to measure the bladder neck elevation during colposuspension procedure. It was useful in optimising the elevation to 10mm and avoiding overactive bladder symptoms due to excessive elevation (Viereck et al. 2004; Viereck et al. 2005).

Periurethral injection of bulking agent is used to treat SUI (Schulz et al. 2004; Siddiqui et al. 2017; Zivanovic et al. 2017). Synthetic agents such as Macroplastique looked hyperechogenic and collagen looked hypoechogenic on scanning. It was common to find the bulking agent on ultrasound at different location in relation to the urethra from where it was intended to be. It was found to be tracking towards the bladder neck or distal urethra instead of forming a sphere in 41% of women immediately after injection (Yune et al. 2016). Proximal location and circumferential distribution of the agent gave best short term results after the treatment (Elia and Bergman 1996; Hegde et al. 2013). Ultrasound studies were useful to investigate the cases with failed treatment or for planning repeat injections (Poon and Zimmern 2004; Bacsu et al. 2015).

Ultrasound assessment has proved to be useful in investigating complication of treatment to improve the efficiency of that intervention.

5.3.8 Other applications of urethral ultrasound

Various paraurethral and paravaginal structures can be clearly diagnosed with ultrasound (Eppel et al. 2000; Shobeiri et al. 2013; Rios et al. 2016). Paraurethral cystic structures could be seen in 1% to 6% of asymptomatic women on transvaginal ultrasound (Cross et al. 2001). Urethral diverticulae had varied clinical presentations and need a high level of suspicion to be diagnosed (Lee, Lim, et al. 2017). Transvaginal ultrasound was superior to cystourethrography and cystoscopy in diagnosing urethral diverticula (Gerrard et al. 2003). TPU was efficient in diagnosing simple as well as complex urethral diverticulae such as multiloculated, septate and U shaped (Gugliotta et al. 2015). Rare structures such as paraurethral leiomyomas could be diagnosed by ultrasound examination though other imaging techniques are used more often for their assessment (Bruschini et al. 2006; Migliari, Buffardi, and Mosso 2015). The variations in urethral vascularity could be studied by Doppler ultrasound (Yang, Yang, and Huang 2006). The vascularity around the bladder neck increased with improvement in SUI after 3 months of hormone replacement therapy (Tsai et al. 2001). Such a difference was not seen after pelvic floor muscle training or surgical treatment of SUI (Lone et al. 2016).

5.4 Other imaging techniques

5.4.1 X ray

Cystourethrogram with bead chain was important in evaluation and treatment planning for stress incontinence for many years before other imaging techniques were available (Nilsen 1958; Green 1962). Video cystourethrogram was combined with urodynamic studies to investigate selective complex cases as described in the chapter on urodynamic studies. TPU correlated well with this investigation and it was quick, cheap, readily available and more acceptable to the women (Kohorn et al. 1986; Kolbl, Bernaschek, and Wolf 1988). It gave similar information about the PUVA, angle of urethral inclination and

SUI status. The choice of investigation currently depends on the availability of facilities and the expertise.

5.4.2 Magnetic resonance imaging (MRI)

MRI can be used to study the pathophysiology of urinary incontinence (Klutke et al. 1990; Howard, Miller, et al. 2000; Tunn et al. 2005; Morgan et al. 2009). It is an excellent modality for investigating cases of suspected urethral pathology (Dwarkasing et al. 2011; Pathi et al. 2013). It can diagnosed the diverticulae and other paraurethral pathologies undiagnosed by cystourethroscopy. However, it has limited role in management of urinary incontinence (Haylen et al. 2010).

5.5 Conclusion

When compared with urodynamic studies which are the current gold standard tests, ultrasound has many advantages. It is very informative when in trained hands. It is inexpensive, widely available and does not take more than a few minutes. Portable ultrasound machines have increased the accessibility further. As the examination is non-invasive or minimally invasive, it is painless and well accepted by women. There is no risk of infection or trauma. It can be used efficiently in women with communication problems, physical disabilities and cognitive dysfunction. Urodynamic studies diagnose detrusor overactivity in only 44% of women with urinary urgency without incontinence and in 58% of women with urgency incontinence (Hashim and Abrams 2006). Ultrasound measurements may have better sensitivity for these conditions.

There have been a large number of ultrasound studies on urinary incontinence. There are various methods and techniques used for measuring the UM by different groups of researchers. However, studies from other institutes using the same technique and duplicating their results are yet to be published. The normal values of many measurements in asymptomatic individuals are not available. At the same time, there is a contradictory evidence from different studies regarding predictive value of some ultrasound measurements such as BNM. Most of the measurements are compared in women with or without a single urodynamic diagnosis, mainly SUI. However, such measurements are not compared in women with different urodynamic diagnoses. The ultrasonographic characteristics of different types of urinary incontinence are not available. Ultrasound studies of the urethra are not able to diagnose voiding dysfunction. However, a combination of ultrasound measurement of post void residual volume and non-invasive free flowmetry may be able to diagnose the condition in most cases.

Ultrasound has not been able to replace the urodynamic testing, however, it can be useful in cases where urodynamics is contraindicated or not acceptable to the patient.

It has a major advantage over other imaging modalities such as X ray and MRI. It does not use ionising radiation and therefore has no radiation risks for the patient or the examiner. Similarly, it does not use the electromagnetic fields, hence, can be carried out in patients with metallic implants. The examination can be performed over a prolonged period and can be repeated many times. Modern ultrasound machines are compact and can be easily accommodated in rooms of small size. Portable machines allow examinations to be performed in any location, which is a great advantage. The ultrasound equipment is inexpensive compared to other imaging machines and the installation cost is also very low. The operating cost of the ultrasound is much lower than other imaging techniques. It has a potential of becoming part of routine clinical assessment in urogynaecology.

6. Urethral Sphincter Volume

6.1 Introduction

Urinary continence is maintained as long as the pressure in the urethra remains higher than the pressure in the bladder. The urethral pressure is generated partially by the action of the urethral sphincter and also by the vascular and surface tension (Rud 1980a). The sphincter is made up of smooth and striated sphincter muscles. The internal smooth muscle has inner longitudinal fibres along the entire length surrounded by an outer thin layer of circular muscle (DeLancey 1988). The striated external muscle surrounds the smooth muscles in the middle two-thirds of the urethra. It is found to be thinner on dorsal aspect in women (DeLancey 1986; Masumoto et al. 2012).

Khullar et al performed a study to show correlation between the ultrasound images of the urethral sphincter and its histology (Khullar et al 1996). They performed transperineal ultrasound (TPU) on cadaveric specimens. The specimens were dissected longitudinally in the sagittal plane and then transversely. There was significant correlation between the measurements of the internal and striated urethral sphincters on dissection and their measurements by ultrasound. The striated sphincter looked hyperechoic and the smooth muscle sphincter looked hypoechoic on this approach. In contrast, the smooth muscle sphincter looked hyperechoic and the striated sphincter looked hypoechoic on transvaginal ultrasound (TVU) (Athanasiou et al. 1999).

Different probe positions were used to measure the sphincter. A transabdominal approach was used by White in cases of stress urinary incontinence (SUI) (White et al. 1980). Using this approach, the urethra could be visualised as a ‘bull’s eye’ structure (Hennigan and DuBose 1985). However this approach was unreliable as the distance between the probe and urethra was too long to define the sphincter accurately. The sphincter could not be visualised in women with high body mass index (BMI) or significant prolapse. It was sometimes difficult to differentiate it from other pelvic tissues. Urethral catheters could make it easier to identify the sphincter but they could change its dimensions. Size 6 to 9 french catheters were used to perform intraurethral ultrasound (IUUS) by some researchers. They were able to provide 360^0 view to measure the dimensions of the sphincter (Kirschner-Hermanns et al. 1994). A three dimensional (3D) rendering and calculation of the urethral sphincter volume (USV) was possible by this approach, however that data was not published. A transrectal approach was used by Noble to measure the USV in women with obstructive voiding (Noble et al. 1995). The sphincter volume was less than 2 cc in women with normal voiding. In their opinion, transrectal approach was easier than transvaginal approach and it gave better images. 3D TVU was used to calculate the USV in women with urodynamic stress incontinence (USI) and continent counterparts (Athanasiou et al. 1999). It showed that the USV was reduced in women USI than their continent counterparts.

Robinson and co-workers have performed 3D TPU studies which confirmed the close relationship between urethral pressure profile (UPP) and size of the sphincter (Robinson et al. 2004). Nineteen women were included in their study. It showed that area under curve on UPP and the USV were significantly related. Similarly, the urethral length before the peak urethral pressure and the distance from the proximal edge of the sphincter to the maximal cross-sectional area were also shown to be related (Khullar et al. 1994).

The relationship of sphincter size with the incontinence status has been studied by many researchers. They found it to be shorter, thinner and smaller in women with USI compared to continent women on 3D TVU (Athanasiou et al. 1999). When measured on IUUS, the average cross sectional area of the sphincter was smaller in incontinent women than the continent (Kirschner-Hermanns et al. 1994). Similar findings were obtained by studies with IUUS where the sphincter volume was smaller with increasing grades of SUI (Frauscher et al. 1998).

The probe could be placed close to the urethra transvaginally to visualise the sphincter more clearly but lateral imaging of the sphincter was impaired due to the direction of the ultrasound waves passing through the tissue. TVU and IUUS had the advantage of proximity to the urethral sphincter allowing high frequency ultrasound to be used for better images but then there was a risk of tissue distortion due to compression (Beco, Leonard, and Lambotte 1994). An invasive approach also increased the patient discomfort and risk of infection.

Though many studies compared the USV in women with SUI and continent women, these studies did not comment on associated overactive bladder (OAB) symptoms or DO seen on urodynamic studies. They also did not compare the USV in women with urodynamically confirmed continence, DO or mixed urinary incontinence (Urodynamic stress incontinence and detrusor overactivity) (MUI).

6.2 Aim

To compare the urethral sphincter measurements in women with different urodynamic diagnoses using 3 dimensional transperineal ultrasound.

6.3 Methodology

6.3.1 The Recruitment for the study

Ethical approval for the study was obtained from the Queen Square Research Ethics Committee (REC reference number 15/LO/0264). Women above 18 years of age undergoing urodynamic investigations for lower urinary tract symptoms (LUTS) or pelvic organ prolapse (POP) were recruited for the study. Women who had pelvic malignancy or radiotherapy were excluded. Women who could not communicate in English or unable to consent were also excluded. All women had received an information leaflet about the study and written consent was obtained before recruitment. Detailed clinical history was taken and physical examination was performed. Pre-test assessment and urodynamic studies were performed as part of their clinical management as described in the chapter on urodynamic studies. I performed the TPU of urethra as part of the study procedure.

6.3.2 TPU procedure

TPU was performed with woman lying in supine recumbent position with the legs abducted and bladder volume of less than 100ml. A GE Voluson-I machine (G E Healthcare, Tiefenbach 15, 4871 Zipf, Austria) with a 4-8 MHz transperineal 3D/4D ultrasound transducer (RIC 4-8 RS) was used for the study. Ultrasound conducting gel was applied over the probe, and the probe was covered with a non-latex glove. The gel was applied over the glove and it was placed over the external urethral meatus in the sagittal plane. The probe was adjusted to obtain a clear image of the urethra with the sphincter in B-mode. Figure 6.1 shows the position of the probe for transperineal ultrasound imaging.

A 3D image was taken using a slow scan time to obtain high intensity images. The whole scanning process took approximately 4-6 seconds. After the scanning was complete, three perpendicular sectional planes and a 3D/4D image were displayed on the screen of the ultrasound machine as shown in figure 5.1. If there was any probe movement during the scanning, the images were distorted and movement artefacts were seen. The scanning was therefore repeated if such artefacts were detected. The images were stored and measurements were taken at a later date after anonymising the data.

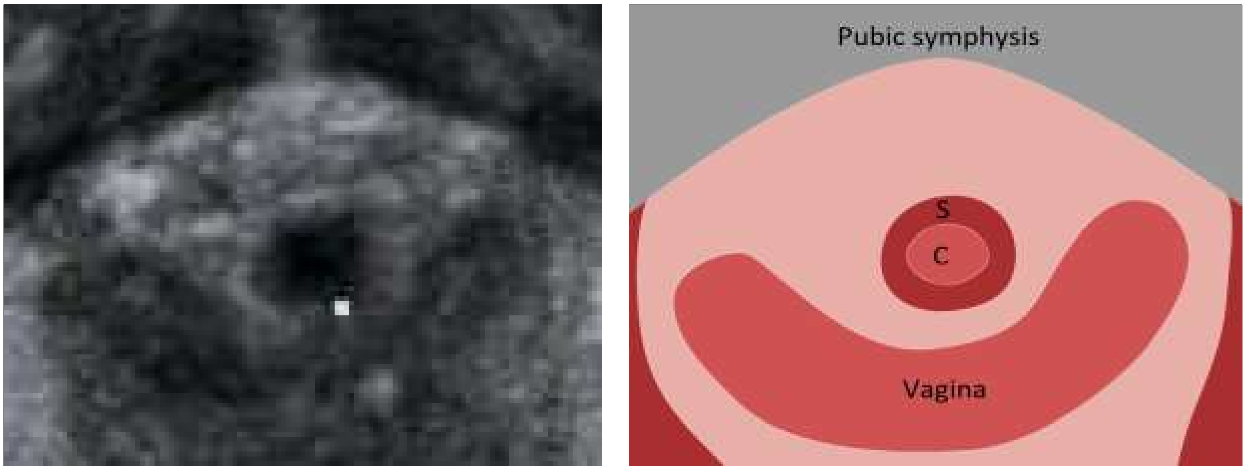
While taking measurements of the sphincter, the striated sphincter was identified in the sagittal plane and transectional plane. The outer margin of this sphincter was traced using a rollerball in transectional planes along the entire length of the sphincter with 1mm slice gaps between the planes. The marking was done as shown in figure 6.2.

When the sphincter was traced completely along the entire length, the volume of the sphincter complex was calculated by the software programme embedded in the system. The inner core volume was calculated by a similar process. The inner core volume was then subtracted from the volume of the sphincter complex to obtain the striated sphincter volume. Sphincter length was calculated in the sagittal plane and maximum transectional

Figure 6.1: Image of probe position for transperineal ultrasound of urethra

Figure 6.2: Image of urethral sphincter in transverse plane by 3D transperineal ultrasound

C = Urethral core, S = Striated sphincter



area was calculated using rollerball in the transectional plane. This method of measurement has been validated by Digesu et al (Digesu et al. 2012).

Statistical analysis was performed using SPSS software package version 25 published by the IBM company. Kruskal-Wallis test was used to find the relationship between the UD and urethral sphincter measurements. Chi Square test was used to test the association between the sphincter measurements and various demographic characteristics. Mann-Whittney U test was used to during the subgroup analysis.

6.4 Results

One hundred and fifty women were included in the study. The predominant symptoms of these women and their UD were as shown in table 6.1.

They had UD as nondiagnostic urodynamics (NU) in 37 women, DO in 53, USI in 22 and MUI in 38 women. The group of women with UD as USI was named as pure USI (PureUSI) for the purpose of analysis. Similarly the group of women with UD of DO were named as pure DO (PureDO). There was no relationship between UD and age or BMI of the women or the POP in this group. All 4 groups included women with different vaginal parities which were divided into groups as 0, 1, 2 and 3 or more. The distribution of vaginal parity among different UD groups was not statistically significant. The demographic information for different groups was as shown in table 6.2.

Table 6.1: Predominant urinary symptom and urodynamic diagnosis

Urinary symptom	Urodynamic diagnosis				
	Nondiagnostic urodynamics	Detrusor overactivity	Urodynamic stress incontinence	Mixed incontinence	Total
None	7	4	0	0	11
Pure overactive bladder	11	22	1	5	39
Pure stress incontinence	0	1	5	1	7
Mixed incontinence	19	26	16	32	93
Total	37	53	22	38	150

Table 6.2: Demographics of all women

Parameter	Nondiagnostic urodynamics (n=37)	Detrusor overactivity (n=53)	Urodynamic stress incontinence (n=22)	Mixed incontinence (n=38)	P value
Age	52	52	54	53	0.960
Body mass index	28	28	25	29	0.125
Cystocoele	16	16	7	17	0.206
Rectocoele	11	24	9	18	0.141

The measurement of total USV, striated sphincter volume, core volume, maximum cross-sectional area of the urethral sphincter and the striated sphincter length were as shown in table 6.2. The mean and standard deviation of the sphincter measurements for various UD were as shown in figures 6.3 to 6.7. All the dimensions and volumes were significantly different amongst the groups (P<0.05). They were maximum in women with PureDO and minimum in women with PureUSI. Measurements in women with MUI were larger than in women with NU.

Table 6.3: Urethral sphincter measurements and urodynamic diagnoses

Measurement	Nondiagnostic urodynamics Mean (SD) (n=37)	Detrusor overactivity Mean (SD) (n=53)	Urodynamic stress incontinence Mean (SD) (n=22)	Mixed incontinence Mean (SD) (n=38)	P value	Total Mean (SD) (n=150)
Total sphincter volume cm^3	2.3 (0.99)	2.71 (1.07)	1.68 (0.73)	2.62 (1.19)	0.001	2.44 (1.09)
Striated sphincter volume cm^3	1.84(0.77)	2.24 (0.88)	1.32 (0.5)	1.98 (0.89)	0.000	1.94 (0.86)
Core volume cm^3	0.45 (0.25)	0.47 (0.23)	0.29 (0.15)	0.53 (0.32)	0.008	0.45 (0.26)
Sphincter length cm	1.37 (0.42)	1.49 (0.38)	1.15 (0.36)	1.44 (0.35)	0.005	1.40 (0.39)
Maximum cross-sectional area cm^2	2.10 (0.53)	2.38 (0.66)	1.94 (0.73)	2.32 (0.73)	0.037	2.23 (0.68)

Figure 6.3: Total sphincter volume (cc) and urodynamic diagnosis

NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence.

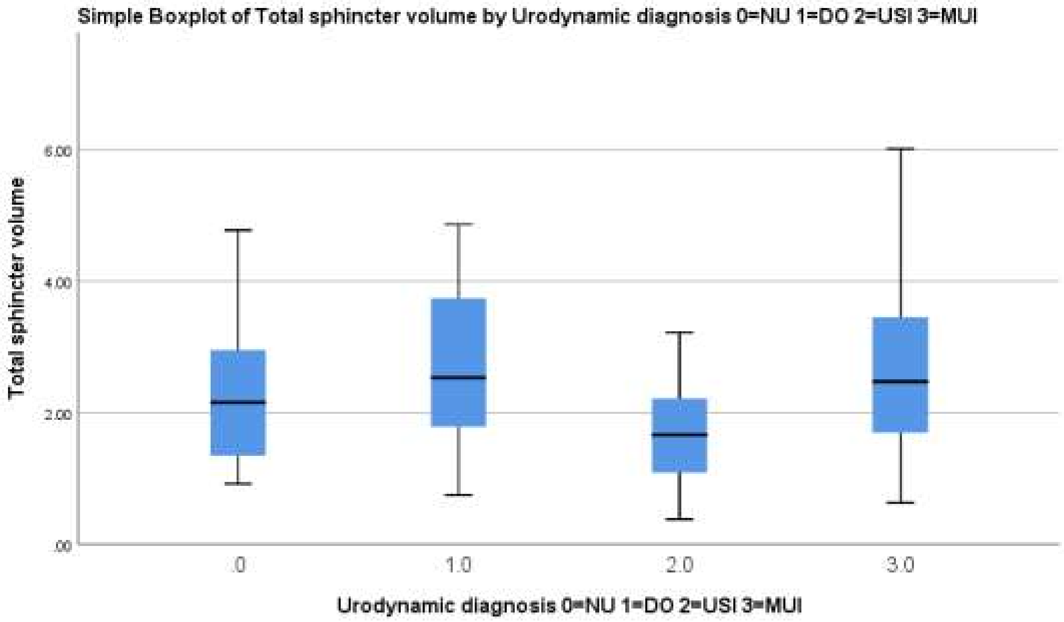


Figure 6.4: Striated sphincter volume (cc) and urodynamic diagnosis

NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence.

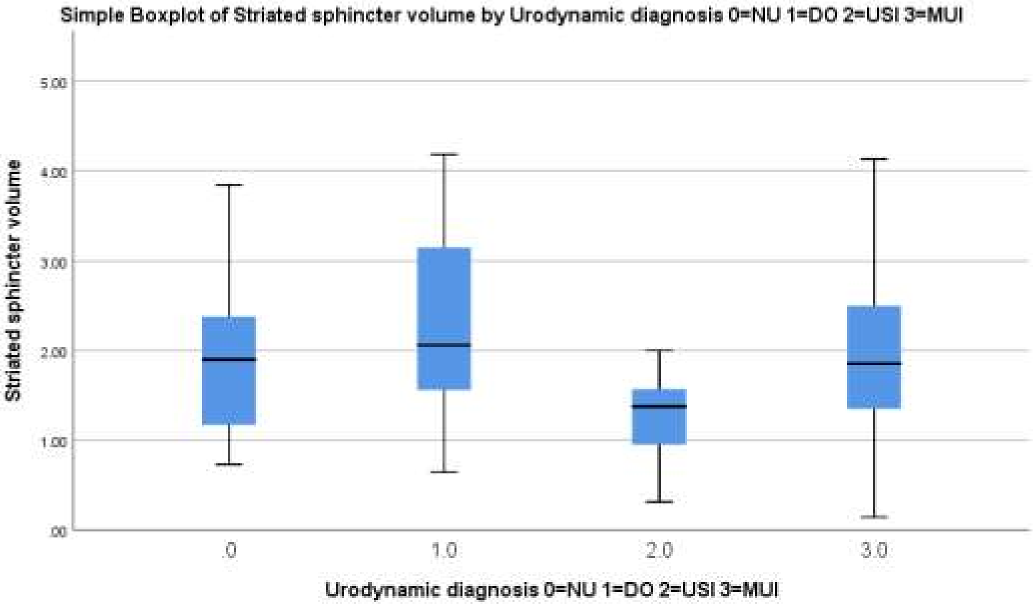


Figure 6.5: Core volume (cc) and urodynamic diagnosis

NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence.

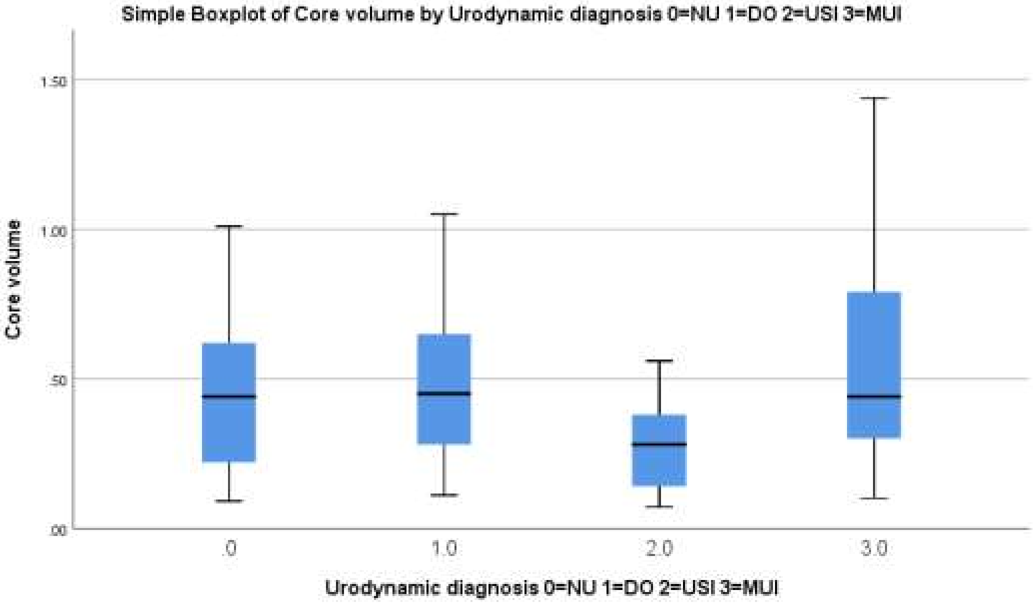


Figure 6.6: Maximum sphincter cross-sectional area (sq cm) and urodynamic diagnosis

NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= stress incontinence, MUI= mixed urinary incontinence.

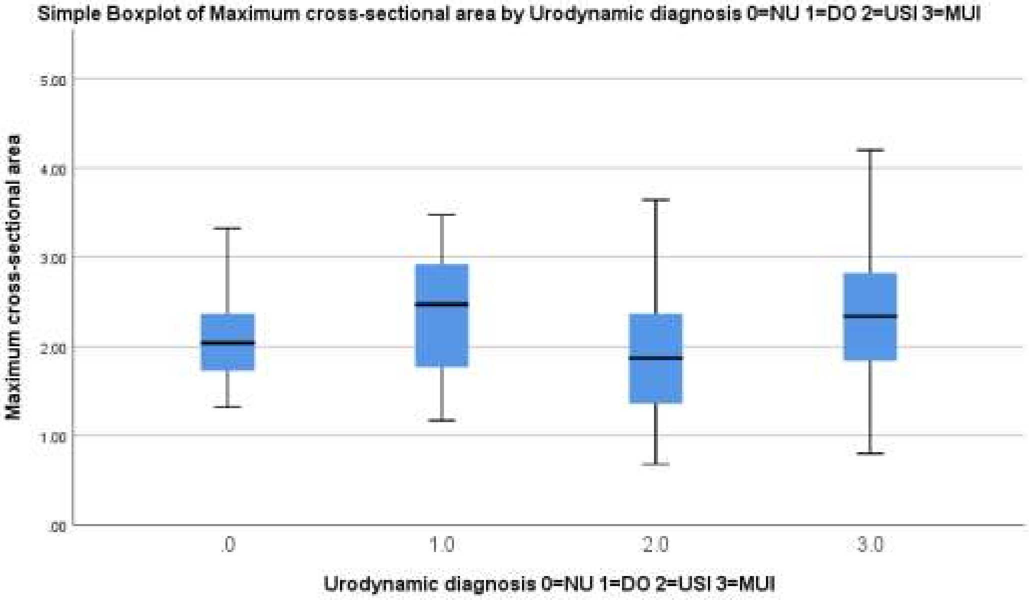
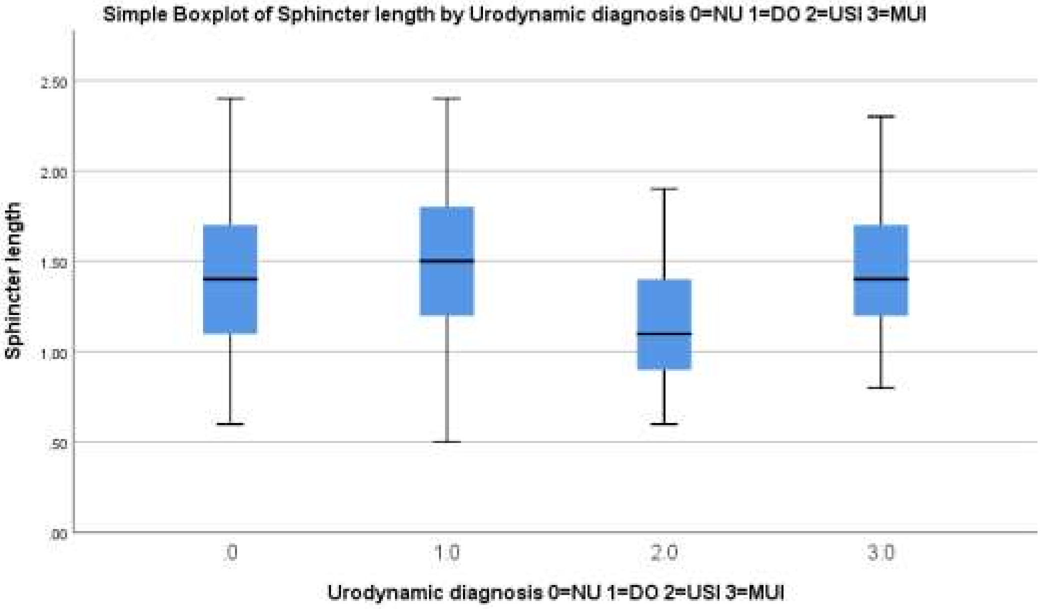


Figure 6.7: Striated sphincter length (cm) and urodynamic diagnosis

NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence.

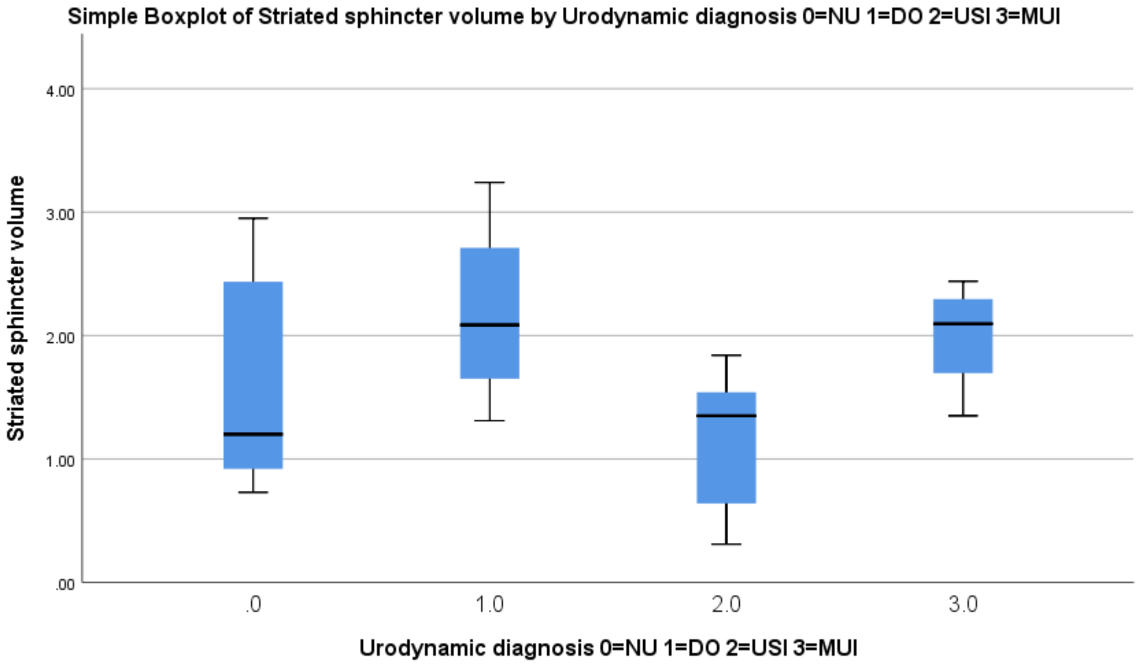


On subgroup analysis, all the measurements were significantly lower in women with PureUSI than women with PureDO or MUI. They were significantly lower in women with PureUSI when compared with NU group. None of the measurements were significantly different when NU group was compared with the PureDO group or the MUI group.

There were 20 women who had undergone midurethral tape surgery. Out of those, 8 women had NU, 4 women had PureDO, 5 women had PureUSI and 3 women were diagnosed with MUI. Their mean striated sphincter volumes were 1.60, 2.18, 1.14 and 1.85 cc respectively as shown in figure 6.8.

Figure 6.8: Mean striated sphincter volume (cc) and urodynamic diagnosis in women with previous midurethral tape surgery.

NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence.



Power of the study

Assuming a standardised difference of 1.03 cc which assumes a clinically relevant difference of 0.9 cc, a power of 0.8 and sig level of 0.05, each group should have 15 patients (Altman, 1980). The significance levels and power of individual measurement by post-hoc analysis using SPSS were as shown in the table 6.4. A power of 87.24% was achieved for this study while using 5% significance level. The alpha value was set at 5%. A maximum power of 97.5% was achieved for striated sphincter volume.

Table 6.4: Post-hoc power calculations for urethral sphincter measurements.

Measurement	P value	Power percent
Striated sphincter volume	0.000	97.5
Total sphincter volume	0.001	94.3
Core volume	0.005	86.6
Sphincter length	0.005	86.8
maximum cross-sectional area	0.030	71.0

6.5 Discussion

This study gave us the comparative values of sphincter measurements and volumes in women with nondiagnostic urodynamics and different UD for the first time, which were measured by the non-invasive transperineal approach. There was an overlap of measurements in different groups but the mean measurements were significantly different amongst the groups. It confirmed the previous finding that the sphincter measurements in women with PureUSI were smaller than in the continent women. More importantly, it pointed out the difference between the PureUSI and MUI for the first time. All the sphincter measurements were significantly larger in women with MUI than in PureUSI.

6.5.1 Sphincter volume

A larger USV can be hypothesised to have a larger volume of muscles which can close the urethra with greater force to be able to withstand the rising intra-abdominal pressures and maintain continence. UPP studies have shown that the USV is related to urethral pressure (Robinson et al. 2004).

This study showed a significant relationship between the USV and UD. A smaller and weaker sphincter would be unable to resist the rising pressures on raised intra-abdominal pressure resulting in stress incontinence. The sphincter was largest in women with PureDO. These women contract the sphincter during episodes of detrusor contraction to prevent urgency incontinence. Repeated powerful and prolonged contraction could have caused hypertrophy of the sphincter and hence increased muscle volume was obtained on measurement. Women with MUI had similar sphincter measurements as women with NU. However, the urethral sphincter in these women was unable to withstand the pressure during stress. There is a possibility of other factors causing stress incontinence in these women. The sphincter measurements between the PureDO and MUI groups were also similar. Other factors responsible for stress incontinence in these women are assessed in the following chapters.

Athanasiou had measured USV in women with USI and continent women by 3D TVU (Athanasiou et al. 1999). The sphincter was shorter, thinner and smaller in women with stress incontinence. Though women with stress incontinence had their diagnosis confirmed by urodynamic studies, the women from the continent group did not undergo urodynamic studies to confirm NU. The study also lacked a group of women with OAB or DO for comparison. Heit used IUUS to measure the sphincter in women with and without USI (Heit 2000). The findings of the study were similar to the previous study and women with DO were also not included in that study.

6.5.2 Core volume

The hypoechogenic core of the urethra seen on TPU is made up of urethral epithelium, subepithelial tissue and smooth muscle layer (Khullar et al 1996). The core volume was smallest in women with PureUSI. The reduced vascularity and atrophy of the smooth muscle layer may be contributing to the weakness of urethral closure mechanism. Duloxetine is a serotonine and noradrenaline reuptake inhibitor which is effective in treating stress urinary incontinence (Li et al. 2013). A study has shown that its action increases the MUCP (Yono et al. 2015). Another study has shown that the drug increases the width of the urethral core after four to eight weeks of effective treatment (Duckett, Patil, and Aggarwal 2008). The vascularity of the urethral core at the bladder neck and the urethral pressure increase after vaginal oestrogen treatment, resulting in better urinary continence (Rud 1980a). These studies support my finding of smaller core volume in women with SUI.

6.5.3 Urethral sphincter length

The striated sphincter surrounds approximately the middle two-thirds of the urethra. The mean length of the sphincter was significantly different in different groups in this study. The sphincter was shortest in women with PureUSI and was longest in women with PureDO. Similar findings were obtained in women with SUI in another study (Cassado Garriga et al. 2017).

Versi studied UPP in 70 women with USI and 102 women with NU as control group (Versi 1990). The functional urethral length was smaller in the USI group than the control group but it did not reach a statistical significance. This study did not include women with DO so it was not possible to compare the lengths in women with different UD. Khullar et al had compared 3D TPU measurement of the sphincter and the UPP in 34 women with different UD (Khullar et al. 1994). The functional urethral length was significantly related to the sphincter length measured by ultrasound. Bump et al measured functional urethral length and MUCP in women before, during and after narcotic analgesia (Bump et al 1991). The pressures decreased significantly with anaesthesia and paralysis in continent women. However, such a fall in pressure was not significant in women with stress incontinence suggesting pre-existing neuromuscular dysfunction in these women. Reduction in all parameters of UPP was seen after spinal anaesthesia (Haeusler et al. 1998). These studies iindicate the role of the striated sphincter in maintaining increased urethral pressure and therefore urinary continence.

6.5.4 Maximum cross-sectional area

The MUCP was seen to be related to the maximum cross-sectional area measured by TPU (Khullar et al. 1994). The length of urethra before the peak and the distance from the cranial end of the sphincter to the maximal cross-sectional area were also significantly related. This shows that the greater the number of muscle fibres surrounding the urethra at a point, the higher the pressure the muscle can create inside the urethra and hence better the continence. Positive correlation was seen by Heit between the maximum urethral sphincter thickness and MUCP (Heit 2000). A link between MUCP and stress incontinence has been already established (DeLancey et al. 2008). All these studies support the relationship between the USI and maximum cross-sectional area of the sphincter observed in this study.

Urethral sphincter dysfunction and urethral hypermobility are considered to be the two most important causative factors for stress incontinence (DeLancey et al. 2008). The pathophysiology of incontinence in the group with PureUSI could be explained on the basis of sphincter dysfunction in this study. However, it was not sufficient to explain the stress incontinence in case of the MUI group. It was important to explore urethral mobility and other factors responsible for incontinence in these women.

100 women out of the 150 included in this study complained of stress incontinence. However, only 54 (54%) of them demonstrated stress incontinence on UDS. Similarly, out of 132 women who complained of overactive bladder symptoms, 85 (64%) demonstrated DO. 4 (36%) of the 11 asymptomatic women also showed DO on UDS. These results were similar to those reported in the published literature (Digesu et al. 2003; Hashim and

Abrams 2006; Caruso et al. 2010; Guralnick et al. 2010; Chung et al. 2011; Chen et al. 2017) Artificial nature of the study can be responsible for these results. Irregularity of the symptoms experienced by the patient and low repeatability of the urodynamic studies may also contribute (Rahmanou and Khullar 2011).

The risk of urinary incontinence increases with age (Hannestad et al. 2000). It can result from generalised weakening of skeletal muscles with age (Mitchell et al. 2012). The resting tone of the striated sphincter may get reduced with age along with reduced support from the levator ani. Increasing weight and BMI increase the risk of urinary incontinence (Townsend et al. 2007). Women with BMI of 30 or above were 4 times more likely to have frequent or severe urinary incontinence than women with BMI of 21 or less. It is postulated that these women have increased abdominal pressure at rest and they also increase the pressure to greater extent on stress or strain. The groups in our study were not significantly different with respect to their BMI.

The striated sphincter volume was measured to be 1.2 cc by 3D TVU in continent women (Athanasiou et al. 1999). By transrectal ultrasound, the sphincter volume was 1.3 cc (Noble et al. 1995). The mean striated sphincter volume on MRI study on raised intra-abdominal pressure in continent women was 1.2 cc (Madill et al. 2015). The corresponding measurement in my study was 1.8 cc which was comparable to above mentioned studies. The differences in measurement were probably due to different approaches and techniques of measurement.

There is no evidence available regarding effect of the MUT on the USV. 20 women with previous MUT surgery were included in this study. The USV in women with persistent USI was smaller than other groups. Urethral pressure is closely related to the USV so a study which showed low MUCP in cases of failed MUT supports my finding (Vij, Dua, and Freeman 2016). Analysis of the groups showed similar pattern of mean sphincter measurements with respect to the UD as the entire study population of 150 women.

6.6 Conclusion

The size of the urethral sphincter measured by TPU varies significantly in different UD. The sphincter size is smaller in women with PureUSI than women in all other groups. The sphincter volume is larger in women with PureDO when compared to women with NU and PureUSI. The measurements in women with MUI were similar to the measurements in the PureDO and NU groups. The sphincter size alone is unable to explain the cause of stress incontinence in these women.

7. Reliability study for ultrasound of urethra

7.1 Introduction

The urethra is embedded in the anterior vaginal wall and is also supported by various ligaments. The pubourethral ligaments connect the urethra and the anterior vaginal wall to the lower part of the pubic bone (Zacharin 1977). The vagina is also supported by its lateral attachment to the levator ani muscle and its fascia (DeLancey 1988). Urethral Hypermobility is considered to be a major cause of stress urinary incontinence (SUI). The most successful surgical treatments of the condition are based on the principle of elevation of the bladder neck or restricting the mobility of urethra by a sling. The commonest treatment of SUI at present is by insertion of a midurethral sling. This treatment is based on the concept of recreating the pubourethral ligament (Petros and Ulmsten 1990a). However, there is insufficient evidence to prove the causative association of a defect in the pubourethral ligaments with SUI. Such a defect is likely to result in an altered position and movement of these structures on stress. To test the theory, measuring the distance between the points of its attachment, namely the pubic symphysis and the urethra and comparing such measurements in women with and without stress incontinence is important.

A review of different methods of measuring the urethral mobility was conducted as described in the chapter on ‘Ultrasound of Female Urethra’. The methods of measuring the angle between the proximal and distal urethra, or the angle of urethral inclination did not measure the pubourethral distance. The vector based methods were complex and did not measure the pubourethral distance directly. Perineal bulging on stress can cause rotation of the image and if the axes of measurement are related to the image frame, their rotation can cause errors in measurement. It was therefore necessary to develop a method of measuring the mobility of urethra using a simple, quick, accurate and reproducible technique.

I developed a novel technique to measure the female urethral complex and to assess the changes it undergoes on raised intra-abdominal pressure, using transperineal ultrasound imaging. I used the inferior margin of the pubic symphysis as the reference line to measure bladder neck mobility. The perpendicular distance of the bladder neck from this line was measured as the bladder neck position. The posteroinferior point of the pubic symphysis was used as the reference point for the measurement of urethral position. Urethral diameters were measured at 5 equidistant points along the urethra. These methods are described in more detail in the methodology section of this chapter.

7.2 Aim

To assess the intraobserver and interobserver reliability of a novel method of measuring bladder neck mobility, urethral mobility and urethral dimensions, using 2 dimensional transperineal ultrasound.

7.3 Methodology

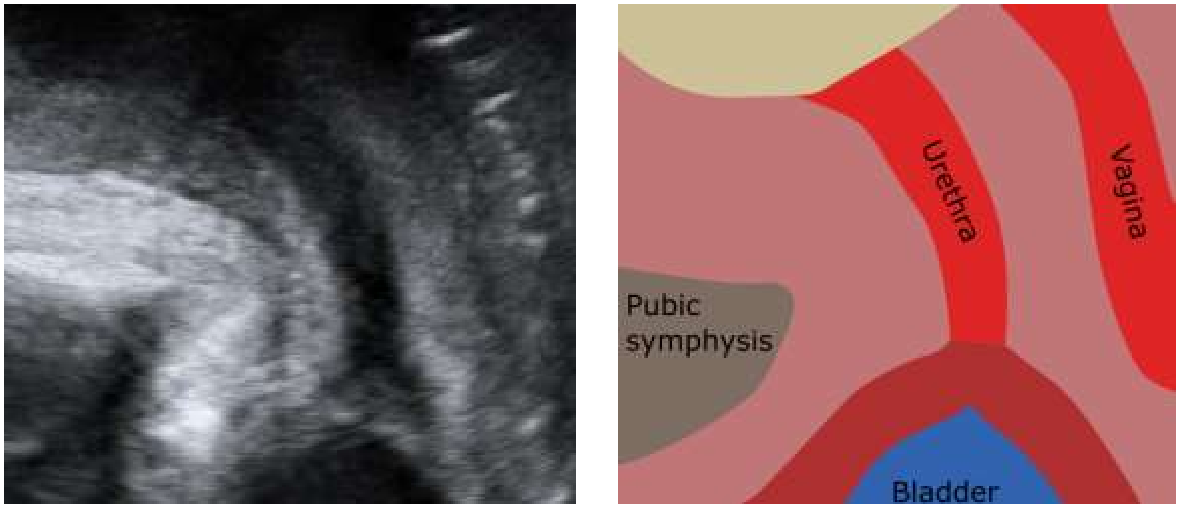
The Recruitment for the study, pretest assessment and urodynamic studies were performed as explained in the chapter on urodynamic studies.

The women were positioned and the preparations were made for the ultrasound as described in the chapter on ‘Urethral Sphincter Volume’.

During transperineal ultrasound (TPU) of the urethra, the probe was placed in the sagittal plane over the external urethral meatus and an image was obtained as shown in figure 7.1. The urethral core was seen as a long hypoechogenic vertical area in the middle of the screen. It consisted of urethral epithelium, subepithelial tissue and internal urethral sphincter (Khullar et al 1996). It was surrounded by an area of slightly increased echogenicity which was the striated sphincter (Khullar et al 1996) present around the middle two thirds of the urethra. The connective tissue around the urethra was of increased echogenicity and it was important to identify the demarcation to get accurate measurements.

The probe was so positioned as to get the urethral image in the middle of the screen perpendicular to the probe. The depth was adjusted to include the urethrovesical junction, periurethral tissue and the pubic symphysis.

Figure 7.1: Image of the urethra and surrounding structures on transperineal ultrasound.

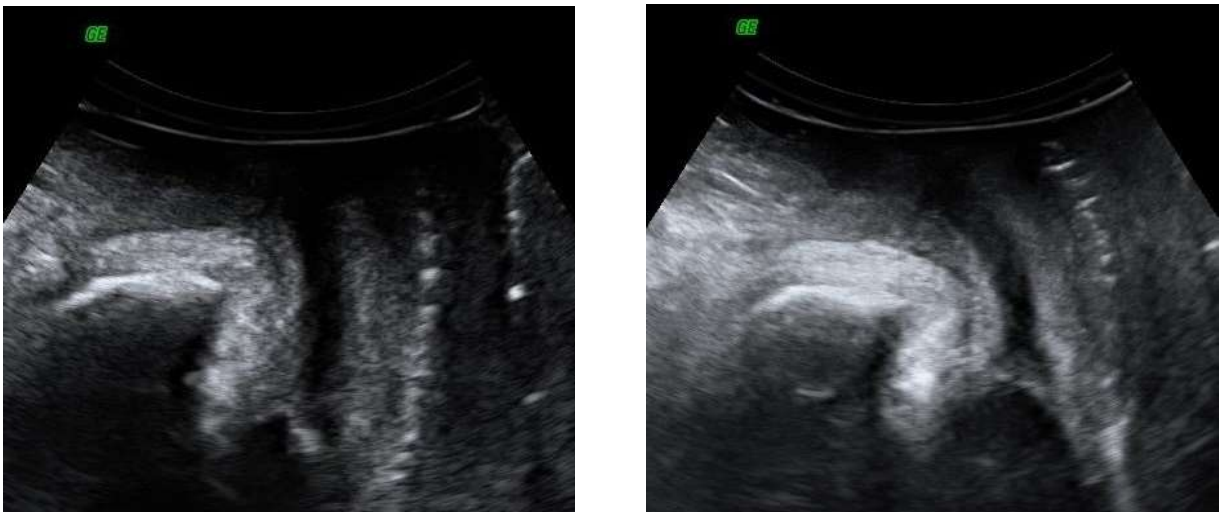

Ultrasound image **Structural diagram**

7.3.1 Imaging at rest and on stress

The probe was applied against urethral meatus without any pressure and adjusted to obtain a clear image in B-mode. An image at rest was stored as ‘rest image’. The patient was then asked to cough with maximum force. Any pressure by the probe over the perineum was avoided allowing free movement of the perineum. The image with maximum displacement of the bladder neck from its original position was saved. Coughing was repeated three times and the images were compared to select the image with maximum displacement as the ‘stress image’. Figure 7.2 shows these 2 images.

As the probe was positioned against the urethral opening, perineal descent on cough caused movement of probe, resulting in a rotation of the pubic symphysis on the ultrasound image. Such a rotation was evident from the two images below. The stress image used hence forward in this chapter is so rotated that the images of the pubic symphysis are at the same position in order to appreciate the changes in urethral position and dimensions on cough.

Figure 7.2: The 'Rest' and 'Stress' images



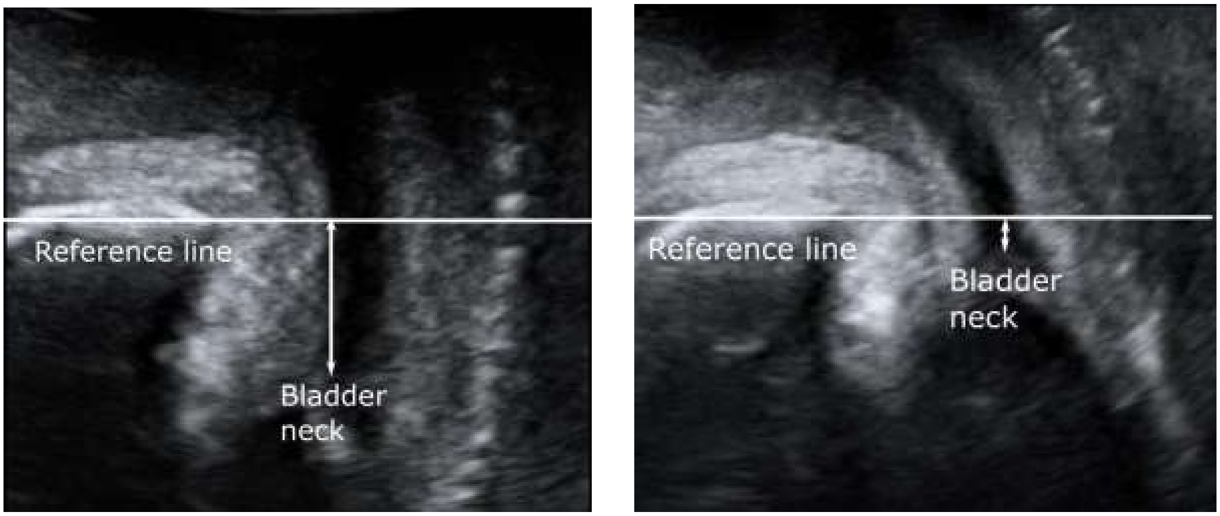
Rest image

Stress image

7.3.2 Bladder neck position and movement

The bladder neck was identified on ultrasound in sagittal plane by the midpoint of the urethrovesical junction. Its position was assessed by measuring its perpendicular distance from the reference line along the caudal border of the pubic symphysis. Distances measured cranial to the reference line were considered as negative. Conversely, distance of bladder neck lying below the plane of pubic symphysis was positive. The measurements were carried out on the resting image and the stress image. Figure 7.3 shows the measurement of the bladder neck position. The bladder neck movement was calculated by subtracting the distance at rest from the distance on cough.

Figure 7.3: Measurement of bladder neck position



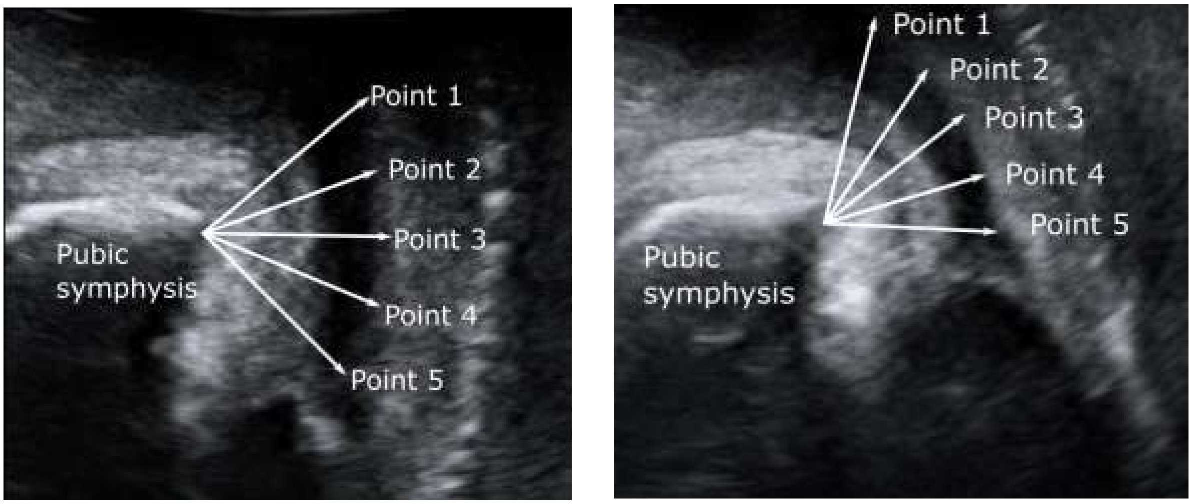
Bladder neck position at rest **Bladder neck position on cough**

7.3.3 Urethral mobility

To measure the urethral mobility, the urethra was divided into four equal segments by five equidistant points. The point on the posterior margin of the urethra at the external urethral meatus was named as point 1. The points were then numbered serially with the point on the posterior margin of the urethra at the urethrovesical junction numbered as point 5. The posteroinferior point of the pubic symphysis was considered to be the reference point. The distances of the 5 points along urethra were measured from this point at rest and on cough. Measurement of the urethral mobility is shown in figure 7.4. The movement of each point was calculated by subtracting distance at rest from the distance on cough.

Figure 7.4: Measurement of pubourethral distance

Point 1: At external urethral meatus, Point 2: Midway between midurethra and external urethral meatus, Point 3: At midurethra, Point 4: Midway between bladder neck and midurethra, Point 5: At the bladder neck



Urethral position at rest **Urethral position on cough**

7.3.4 Urethral dimensions

The length of the urethra was measured by tracing the urethral lumen along its length as shown in figure 7.5. The measurement was done on the resting image and the stress image. The antero-posterior urethral diameter was measured at 5 equidistant points along the urethra. Point 1 was at external urethral meatus and point 5 was at the urethrovesical junction. It was observed in the majority of the women that the external and internal urethral openings were at an angle and not perpendicular to the mucosal surfaces at the vestibule and the bladder. The diameters at points 1 and 5 are measured between the end points of the anterior and posterior urethral margins. At the points 2, 3 and 4, the perpendicular distance between the outer margins of the urethral sphincter complex is measured as the urethral diameter as shown in figure 7.6.

Figure 7.5: Urethral length measurement

The arrow indicates the length of the urethra from external meatus at the upper end to the urethra-vesical junction at the lower end.

Urethral length at rest **Urethral length on cough**

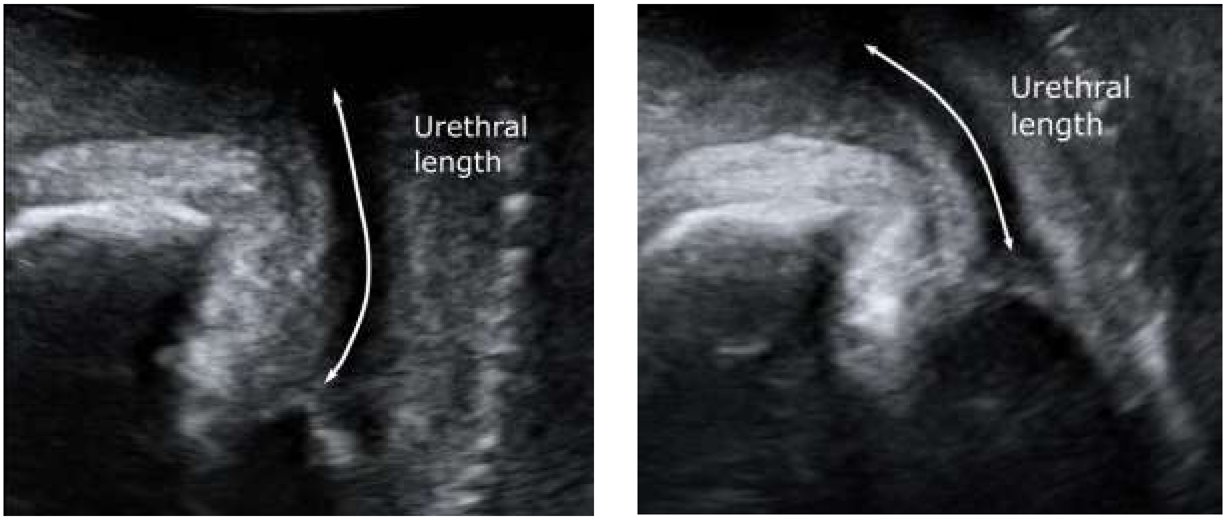
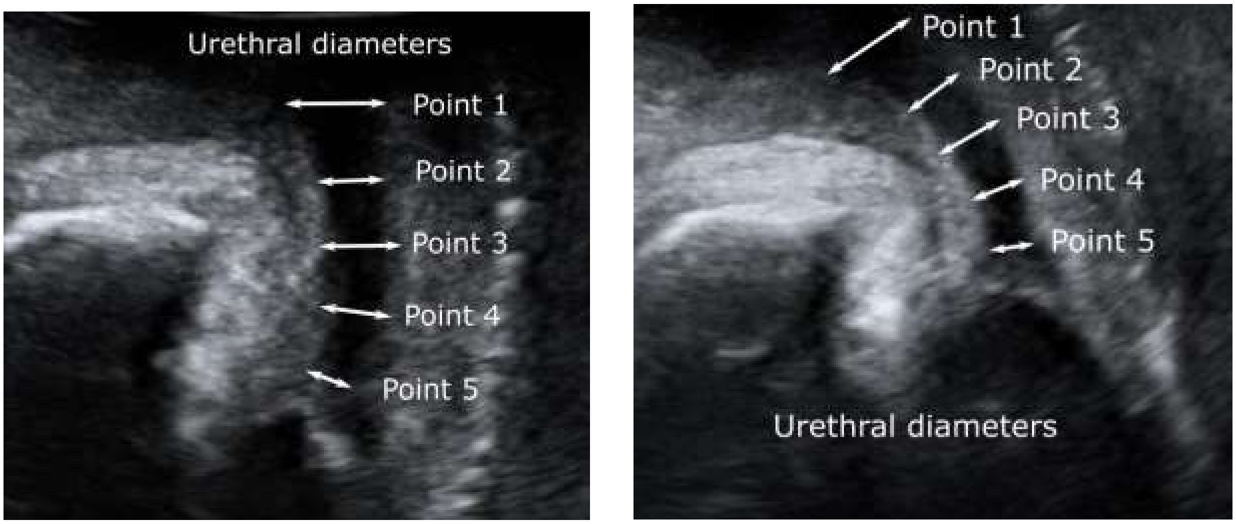


Figure 7.6: Urethral diameter measurement

Point 1: At external urethral meatus, Point 2: Midway between midurethra and external urethral meatus, Point 3: At midurethra, Point 4: Midway between bladder neck and midurethra, Point 5: At the bladder neck



Urethral diameter at rest **Urethral diameter on cough**

I performed the scanning twice as the first investigator. I made measurements on the 2 sets of images. This data was used to calculate the intraobserver variability. The scanning and measurements were performed on the same women independently by Professor Vikram Khullar as the other investigator. The measurements made by the two investigators were compared to calculate the interobserver variability. The data was analysed by using SPSS software version 25.

7.4 Results

The scanning was completed in less than 5 minutes. The women tolerated the examination very well. They did not experience any pain or discomfort. Good quality images were obtained and measurements were possible in all cases.

The demographics were as shown in table 7.1. The mean values of the measurements were as in table 7.3, 7.4 and 7.5. The results of the analysis were as shown in table 6.

Table 7.1: Demographics of women in validation study

Characteristic		Measurement
Mean age years(range)		54 (38-71)
Lower urinary tract symptoms	None	2
	Overactive bladder	2
	Stress incontinence	2
	Mixed incontinence	9
Urodynamic diagnosis	Nondiagnostic	4
	Detrusor overactivity	2
	Urodynamic stress incontinence	6
	Mixed urinary incontinence	3

Table 7.2: Measurement of bladder neck position

Bladder neck position in cm	Investigator 1, measurement 1 mean (SD)	Investigator 1, measurement 2 mean (SD)	Investigator 2 mean (SD)
At rest	-1.54 (0.62)	-1.52 (0.58)	-1.52 (0.6)
On cough	-0.45 (0.82)	-0.44 (0.85)	-0.47 (0.83)

Table 7.3: Measurement of pubourethral distance

Mean Measurement in cm		Investigator 1, measurement 1 mean (SD)	Investigator 1, measurement 2 mean (SD)	Investigator 2 mean (SD)
Resting distance	Point 1	1.74 (5.2)	1.74(5.4)	1.74(5.3)
	Point 2	1.68 (0.58)	1.68 (0.6)	1.67 (0.59)
	Point 3	1.87 (0.52)	1.88 (0.5)	1.86 (0.46)
	Point 4	2.1 (0.44)	2.1 (0.44)	2.11 (0.46)
	Point 5	2.42 (0.5)	2.43 (0.49)	2.42 (0.51)
Distance on cough	Point 1	1.71 (0.48)	1.72 (0.48)	1.68 (0.47)
	Point 2	1.71 (0.56)	1.72 (0.53)	1.72 (0.55)
	Point 3	1.8 (0.54)	1.8 (0.54)	1.78 (0.55)
	Point 4	1.94 (0.52)	1.94 (0.52)	1.93 (0.53)
	Point 5	2.21 (0.59)	2.19 (0.58)	2.2 (0.61)

Table 7.4: Measurement of urethral dimensions at rest and on cough.

Mean Measurement in cm		Investigator 1, measurement 1 mean (SD)	Investigator 1, measurement 2 mean (SD)	Investigator 2 mean (SD)
Urethral diameter at rest	Point 1	0.69 (0.2)	0.72 (0.21)	0.72 (0.2)
	Point 2	0.66 (0.19)	0.68 (0.17)	0.67 (0.17)
	Point 3	0.73 (0.18)	0.72 (0.18)	0.72 (0.16)
	Point 4	0.69 (0.13)	0.69 (0.14)	0.7 (0.13)
	Point 5	0.64 (0.1)	0.63 (0.1)	0.63 (0.11)
Urethral diameter on cough	Point 1	0.61 (0.23)	0.62 (0.24)	0.62 (0.25)
	Point 2	0.63 (0.19)	0.64 (0.18)	0.63 (0.21)
	Point 3	0.66 (0.16)	0.65 (0.15)	0.67 (0.16)
	Point 4	0.63 (0.15)	0.63 (0.15)	0.62 (0.13)
	Point 5	0.58 (0.17)	0.59 (0.18)	0.59 (0.17)
Urethral length at rest		2.24 (0.60)	2.4 (0.59)	2.23 (0.64)
Urethral length on cough		2.07 (0.84)	2.08 (0.83)	2.09 (0.85)

Table 6: Results of variability study

Test	Interclass Correlation Coefficient		95% confidence interval
Intraobserver relability	Single measures	0.996	0.995-0.997
	Average measures	0.998	0.998-0.998
Interobserver reliability	Single measures	0.997	0.984-0.990
	Average measures	0.994	0.992-0.995

All the values of the Interclass Correlation Coefficient were above 0.9 indicating the excellent interobserver and intraobserver correlation for this method of measuring bladder neck position and mobility, urethral mobility and urethral dimensions.

Figures 7.7 to 7.8 show the Bland- Altman plot of the pubourethral distance measurements in the intraobserver and interobserver studies. Similarly, figures 7.9 and 7.10 show the urethral diameter measurements and figure 7.11 and 7.12 show the bladder neck position measurements. The red lines in the figures indicate the limits of agreement. Over 99% of measurements were within the 95% CI from the mean.

Figure 7.7: Bland Altman plot of intra-observer variation for pubourethral distance measurements (Mean 0.0013, SD 0.0614, 95% CI -0.12 to 0.12)

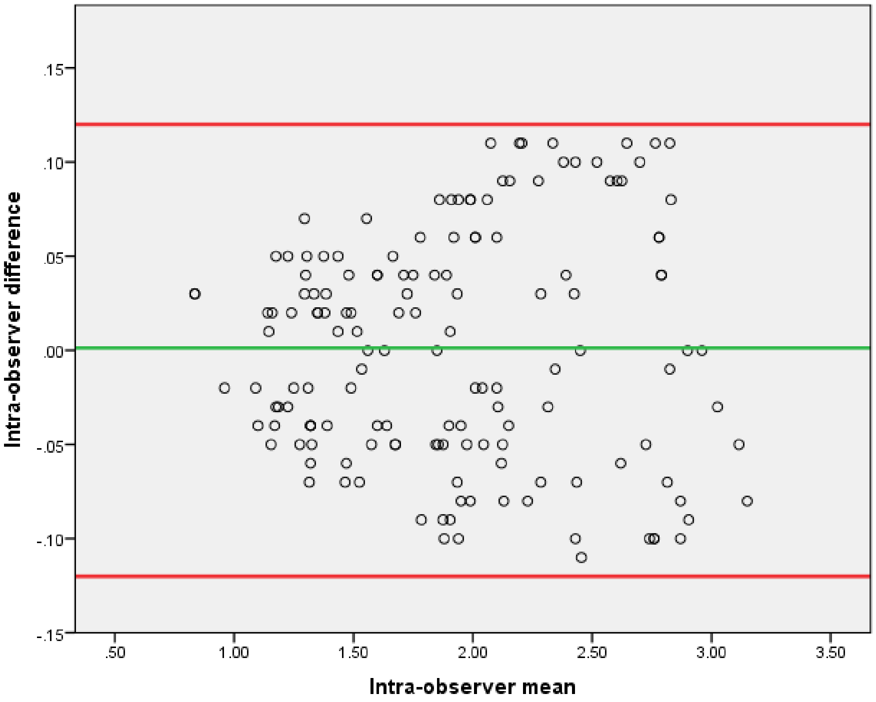


Figure 7.8: Bland Altman plot of inter-observer variation for pubourethral distance measurements (Mean 0.0069, SD 0.0674, 95% CI -0.13 to 0.14)

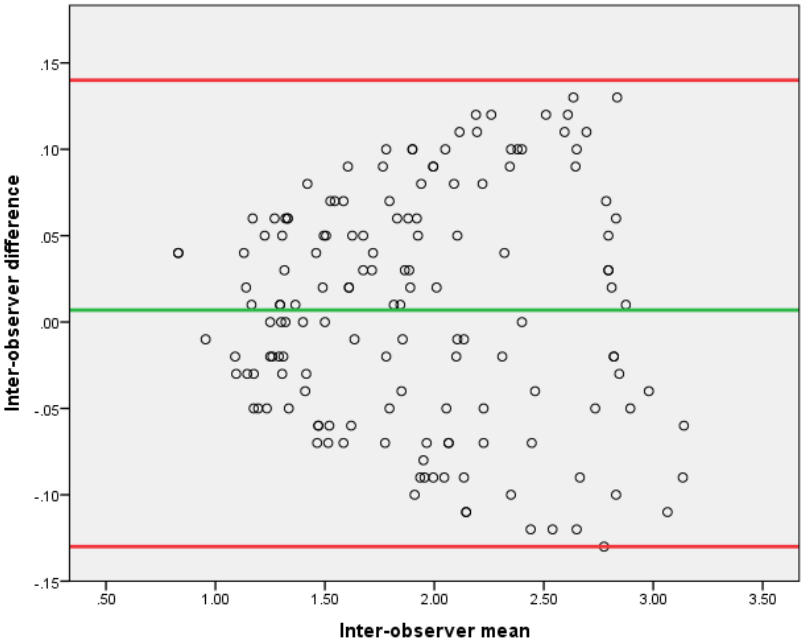


Figure 7.9: Bland Altman plot of intra-observer variation for urethral diameter measurements (Mean 0.0014, SD 0.0251, 95% CI -0.05 to 0.05)

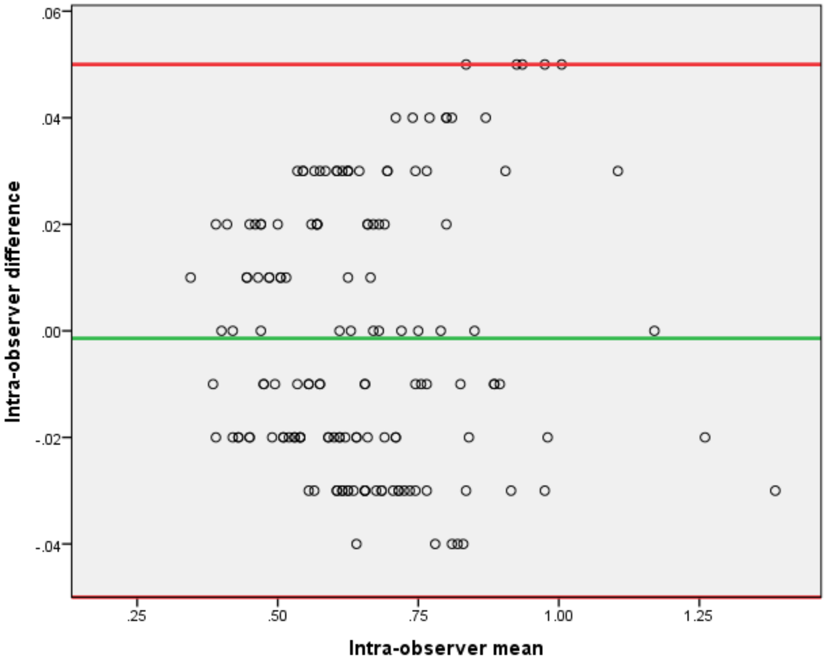


Figure 7.10: Bland Altman plot of inter-observer variation for urethral diameter measurements (Mean 0.0014, SD 0.0251, 95% CI -0.05 to 0.05)

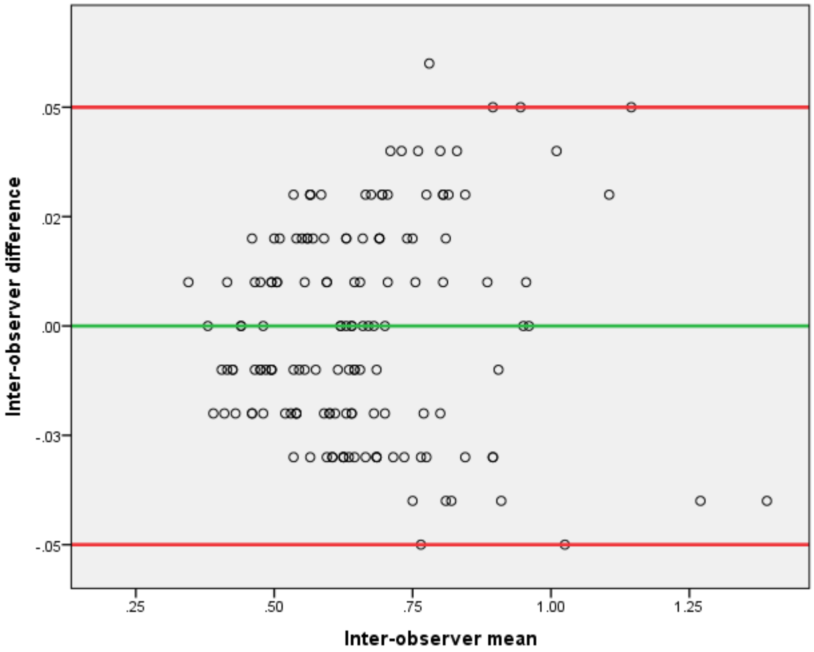


Figure 7.11: Bland Altman plot of intra-observer variation for bladder neck position measurements (Mean -0.0025, SD 0.0524, 95% CI -0.10 to 0.11)

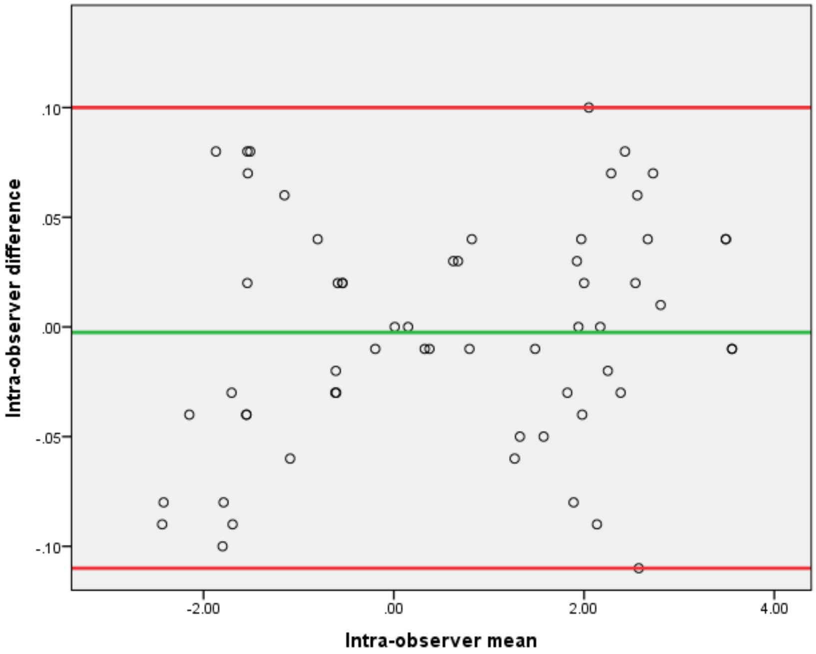
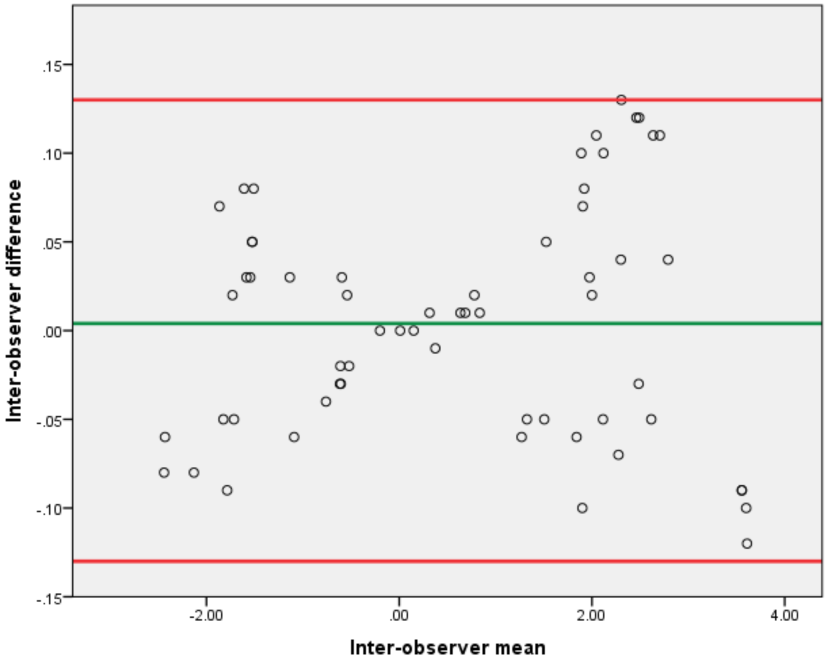


Figure 7.12: Bland Altman plot of inter-observer variation for bladder neck position measurements (Mean 0.0040, SD 0.0617, 95% CI -0.11 to 0.13)



7.5 Discussion

Transperineal ultrasound of urethra provides good quality of images necessary for identification of pubic symphysis and margins of urethra. The scanning and measurements had good reproducibility. The intraobserver and interobserver correlation was good and the variability was low. This method of measuring the urethral and bladder neck mobility was found to be reliable by this study. Supine recumbent position was chosen for this study. This was the commonest position used for scanning. The women found it comfortable and they were able to perform the stress manoeuvres in this position. The imaging was quick and the images obtained were of good quality.

Cough was used as the stress induction manoeuvre as it is the natural event when women complained of incontinence most of the times. It was an easy technique for the women to follow. The bladder neck movement was comparable to Valsalva and it was easily reproducible. A detailed comparison of these techniques is given in the chapter on 'Ultrasound of Female Urethra'.

Women with voiding dysfunction were excluded from the study. The scanning was performed with the bladder volume of less than 100ml. Higher bladder volumes could have affected the mobility of the bladder neck (Dietz and Wilson 1999).

Over the years, researchers have used different reference lines to measure the position of the bladder neck. Schaer et al used the line between the superior and inferior borders of the pubic symphysis (Schaer et al. 1995). I found that the cranial margin of the pubic symphysis was not always visible in the image chosen to measure the distances with utmost accuracy. Shek and Dietz used inferior border of the pubic symphysis as the reference point and drew lines from this point which were parallel and perpendicular to the ultrasound image (Shek and Dietz 2008). Their method used a single fixed point and measurements may not be reproducible as slight rotation of the probe from perineal bulging could change the direction of the 'x' and 'y' axes. Hennemann et al proposed a line between the two hyperechoic contours of the interpubic disc (Hennemann et al. 2014).

I decided to draw the reference line along the inferior surface of the pubic symphysis. This landmark was clearly visible in the scan of every woman. As the line was along a bony margin of the pubis, rotation of the pubis, perineal descent or movement of the probe did not have any effect on the measurement. Measurements above this line were considered as negative and those below this line were considered to be positive.

7.6 Conclusion

This study tested a new method of measuring the position of the urethra on 2 dimensional transperineal ultrasound. A reference line along the inferior surface of pubic symphysis was used to measure the bladder neck position. The posteroinferior point of the pubic symphysis was used as the reference point to measure the pubourethral distance. This method of measurement proved to be reliable and reproducible. It was then used for the purpose of this thesis.

8. Bladder Neck Position and Movement

8.1 Introduction

Any weakness in the supporting structure of the pelvic floor results in excessive movement of the pelvic organs through the levator hiatus. Raised intra-abdominal pressure adds to the gravitational force when upright and during physical activities such as coughing, sneezing and straining, resulting in displacement of the bladder neck below the level of the pelvic floor. The urethra, in this case, lacks the support of the intra-abdominal pressure in maintaining high urethral pressure. At the same time, there is substantial increase in the intravesical pressure which easily overcomes the reduced urethral pressure resulting in leakage. The urethral pressure profile in such cases shows a reduction in the pressure transmission ratio. This observation was the basis of the 'Pressure Transmission Theory' proposed by Enhorning in 1961 (Enhorning 1961). The reflex contraction of the urethral sphincter before a cough adds to the continence mechanism. According to Delancey's 'Hammock Hypothesis', the urethra is compressed against the firm hammock of anterior vaginal wall during raised intra-abdominal pressure and this mechanism maintains urinary continence (DeLancey 1994). These theories of SUI are discussed in the chapter on 'Physiology of Micturition'.

The relationship between bladder neck mobility (BNM) and stress urinary incontinence (SUI) has been studied for many decades. Various techniques have been used by researchers to measure the position of the bladder neck and its mobility. Bead chain cystography, Q tip testing, video cystourethrography (VCU), MRI and ultrasonography are a few of these techniques. These techniques and their relevance to the current practice is as follows.

8.1.1 Measurement techniques

X Ray

Metallic bead chain cystourethrography was designed to understand the relationship of the bladder and urethra at rest and on cough and was recommended as the pre-operative investigation for SUI (Hodgkinson and Doub 1953). A metallic bead chain was introduced into the bladder through the urethra and a lateral X ray imaging of the pelvis was performed. It was thought that incontinence occurred when the posterior urethrovesical angle (PUVA) was flattened and the bladder neck lost its support. The PUVA and urethral inclination angle (UIA) to the vertical line were measured by this investigation. In type I SUI there was increased PUVA but the UIA was less than 45^0. Both the angles were increases in type II SUI. The treatment of incontinence was based on the principle of reducing the PUVA in both types and fixing the bladder neck by retropubic procedures only for type II SUI. Success rate of 90% could be achieved by this management (Green 1962, 1968). However, these radiological criteria were unable to distinguish between SUI and detrusor overactivity (DO) (Fantl et al. 1981). An ultrasound study showed that the urethral inclination was increased in cases of SUI but the PUVA was not different (Costantini et al. 2005).

Q-tip test

This test was accidently invented while performing lateral bead chain cystography in 1971 (Crystle, Charme, and Copeland 1971). Angular rotation of the Q-tip inserted in the urethra was used to differentiate between type I and type II stress urinary incontinence. It became a common practice for many years to use this test for urinary incontinence without validation. However, the test lacked sensitivity and specificity for diagnosis (Montz and Stanton 1986). A study showed that the visual assessment of urethral mobility was more relevant and better acceptable to the patients than the Q-tip test (Robinson et al. 2012).

Videourodynamics

This technique was developed in the sixties by performing fluoroscopy at the same time as urodynamic studies (Bates and Corney 1971). The degree of bladder neck descent seen was more on VCU than observed during saline urodynamics (Barnick et al 1989). The position of the bladder neck at rest and its descent on increased abdominal pressure can be clearly assessed by this technique. It is valuable especially in women with complex conditions or neurological disease or after failed continence surgery. However, surrounding soft tissue structures including urethra are not visible by this technique so it is not possible to measure these structures. There is exposure to radiation and specialised scanning suite is needed which is not commonly available.

Magnetic resonance imaging (MRI)

MRI continues to be an important research technique to assess the bladder neck movement (BNM) (Pontbriand-Drolet et al. 2016). It can delineate the lower urinary tract and the use of contrast can enhance the views. It is expensive for routine use and the image can be distorted if internal coils are used.

Ultrasound

Ultrasound has been used in urogynaecology for more than 3 decades and it has become the most common imaging modality used to study urinary incontinence. It is a quick and relatively easy technique, needs a small set up and gives excellent tissue information without use of radiation or magnetic field.

Current evidence

There are a number of ultrasound studies aimed at finding out the relationship of BNM with SUI, however, their results were not consistent. Some authors noted that the bladder neck was at a lower position in women with SUI and it descended more on increased intra-abdominal pressure (Chen, Su, and Lin 1997; Cassado et al. 2006). Other authors noted that the bladder neck was at a more dorsal and caudal position in women with urodynamic stress incontinence (USI) but its movement was not significantly different from continent women (van Veelen, Schweitzer, and van der Vaart 2014). Some researchers described an increased BNM in USI but did not comment on the position at rest or on cough (Cassado Garriga et al. 2017). These studies grouped the women according to the stress continence status. By doing so, the women with mixed incontinence were included in the USI group and women with DO were included in the continent group. It was necessary to differentiate between these categories for better understanding of the pathophysiology of each condition. To my knowledge, none of the studies have measured the BNM and estimated its relationship with different types of incontinence. The women were divided into continent, stress incontinent and mixed incontinent groups in a recent study using MRI. There was no difference noted in the position of their bladder neck on cough (Pontbriand-Drolet et al. 2016).

8.2 Aim

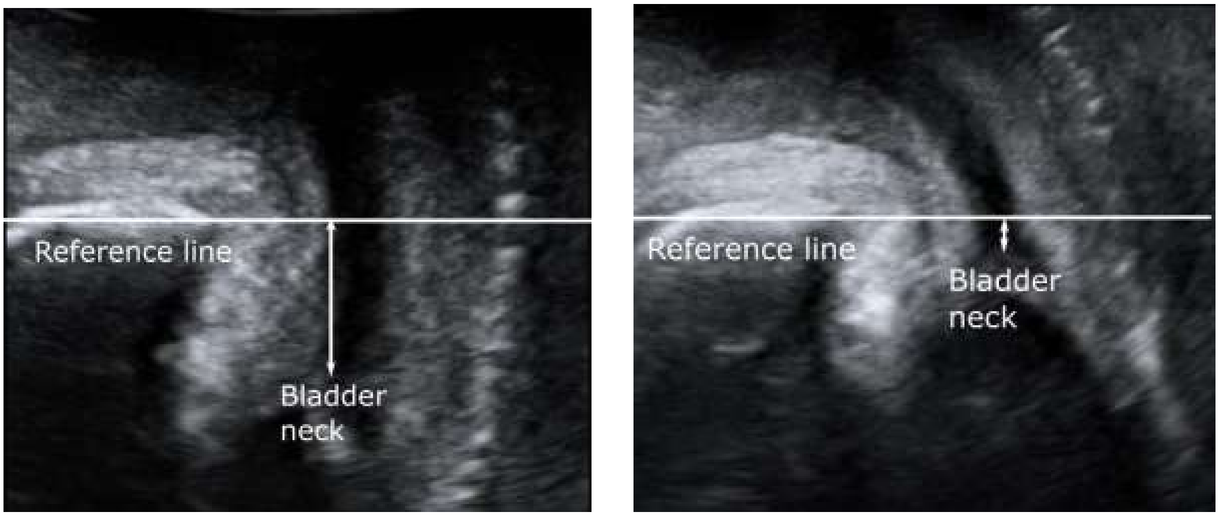
To find the difference in the position and mobility of bladder neck in relation to the pubic symphysis in women with different urodynamic diagnoses (UD).

8.3 Methodology

Women attending urogynaecology department for urodynamic studies were recruited for the study. The demographic data and urodynamic study data was collected as described in chapter on ‘Urodynamic Studies’ and I performed the scanning on all the women in the study group as described in the methodology section of chapter on ‘The Validation Study for Ultrasound of Urethra’. Ethical approval for the study was obtained from the Queen Square Research Ethics Committee (REC reference number 15/LO/0264).

The bladder neck position at rest and on cough were measured from the reference line along the inferior border of pubic symphysis (Figure 8.2). The distances above the reference line and plane were marked negative while those below the level were marked positive. The BNM was calculated by subtracting the distance at rest from the distance on maximum cough.

Figure 8.2: Measurement of bladder neck position



Bladder neck position at rest

Bladder neck position on cough

The data was analysed using SPSS software version 25 by IBM Compamy. Kruskal Wallis test and Chi square test were used for analysing data for 4 groups of urodynamic diagnoses. Data was divided into 2 groups and it was analysed using Mann Whitney U test. The difference is considered to be significant if the probability is less than 5%.

8.4 Results

One hundred and fifty women were recruited for the study. The UD of these women were nondiagnostic urodynamics (NU) in 37 women, DO in 53 women, USI in 22 women and MUI in 38 women. The group with a UD of USI (without DO) was termed as pure USI (PureUSI). Similarly the group with UD of DO (without USI) was termed as pure DO (PureDO). There was no relationship between the UD and age, body mass index or pelvic organ prolapse in this group. The mean values and standard deviation of the resting position, stress position and BNM in women with different UD were as shown in table 8.1.

Out of the 150 women, 129 women did not undergo any continence procedure. They were divided into 4 groups according to the UD. 29 women had NU, 49 had PureDO, 17 had PureUSI and 34 were diagnosed with MUI. Table 8.2 shows the results for these women. Figures 8.1, 8.2 and 8.3 show the bladder neck position at rest and on cough and its movement in women with different UD who had not undergone any continence surgery.

The mean bladder neck position at rest was above the plane of pubic symphysis in all groups. It was significantly different in 4 UD and it was lowest in women with PureUSI. The bladder neck position on cough in women with PureUSI showed similar results. However, BNM was not different in any of the groups.

On subgroup analysis of all UD, the mean BNM was similar amongst all groups. The bladder neck positions at rest was significantly higher in women with NU than any other group. The bladder neck position at rest was significantly higher in PureDO group than the MUI. The position on cough, but not at rest, was significantly lower in PureUSI group than PureDO group. There was no difference in bladder neck positions between the women with PureUSI and MUI.

Table 8.1: Bladder neck position and urodynamic diagnoses of all women

Bladder neck	Urodynamic diagnosis								P value	Total (N=150)	
	Nondiagnostic urodynamics (N=37)		Detrusor overactivity (N=53)		Urodynamic stress incontinence (N=22)		Mixed urinary incontinence (N=38)				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		Mean	SD
Position at rest in cm	-1.56	0.59	-1.31	0.58	-1.17	0.55	-1.16	0.6	0.024	-1.32	0.6
Position on cough in cm	-0.45	0.86	-0.22	0.78	0.29	0.81	-0.56	0.92	0.005	-0.16	0.86
Movement in cm	1.12	0.61	1.11	0.82	1.47	1.05	1.15	0.95	0.385	1.17	0.85

Table 8.1: Bladder neck position and urodynamic diagnoses for women without previous continence procedure

Bladder neck	Urodynamic diagnosis								P value	Total (N=129)	
	Nondiagnostic urodynamics (N=29)		Detrusor overactivity (N=49)		Stress urinary incontinence (N=17)		Mixed urinary incontinence (N=34)				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		Mean	SD
Position at rest in cm	-1.65	0.54	-1.34	0.58	-1.2	0.59	-1.08	0.57	0.002	-1.32	0.60
Position on cough in cm	-0.54	0.78	-0.21	0.79	0.26	0.63	-0.02	0.93	0.008	-0.17	0.84
Movement in cm	1.12	0.61	1.14	0.83	1.46	1.02	1.10	0.95	0.502	1.17	0.85

Figure 8.2: Bladder neck position (cm) at rest and urodynamic diagnoses for women without previous continence surgery.
NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence.

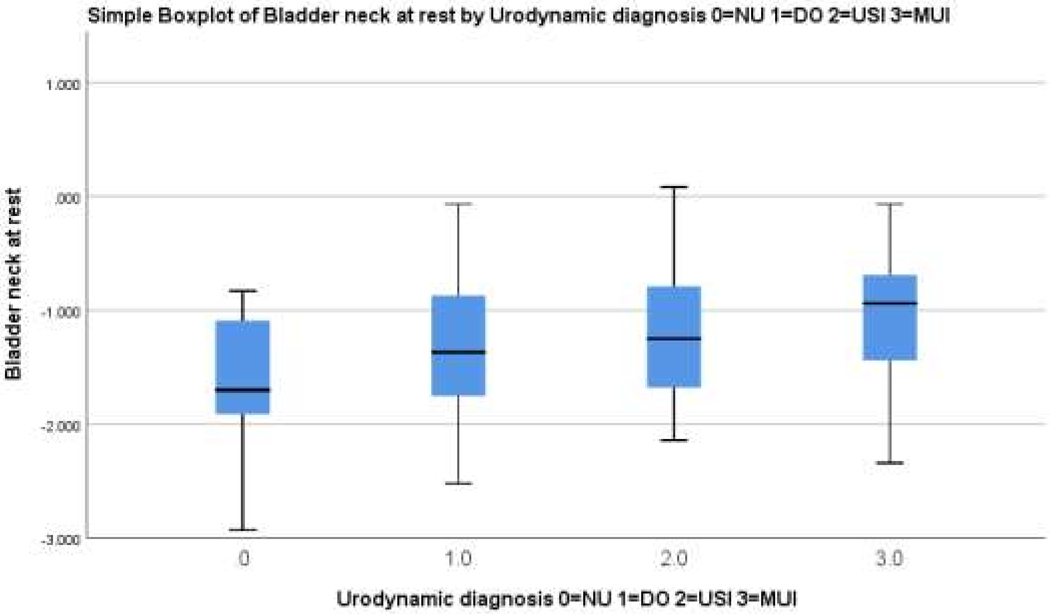


Figure 8.3: Bladder neck position (cm) on cough and urodynamic diagnoses for women without previous continence surgery.
(NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence).

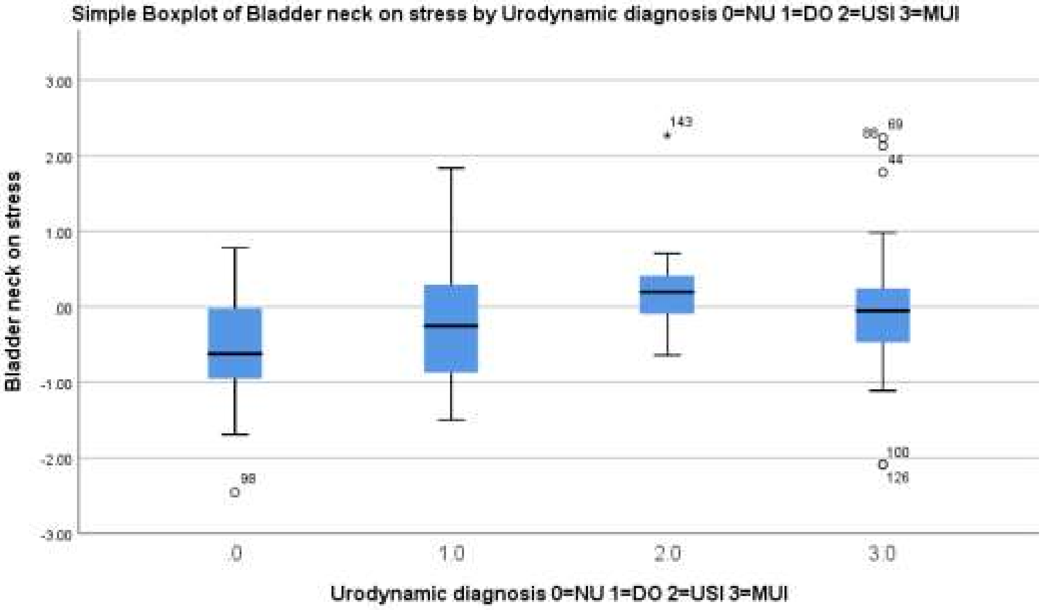
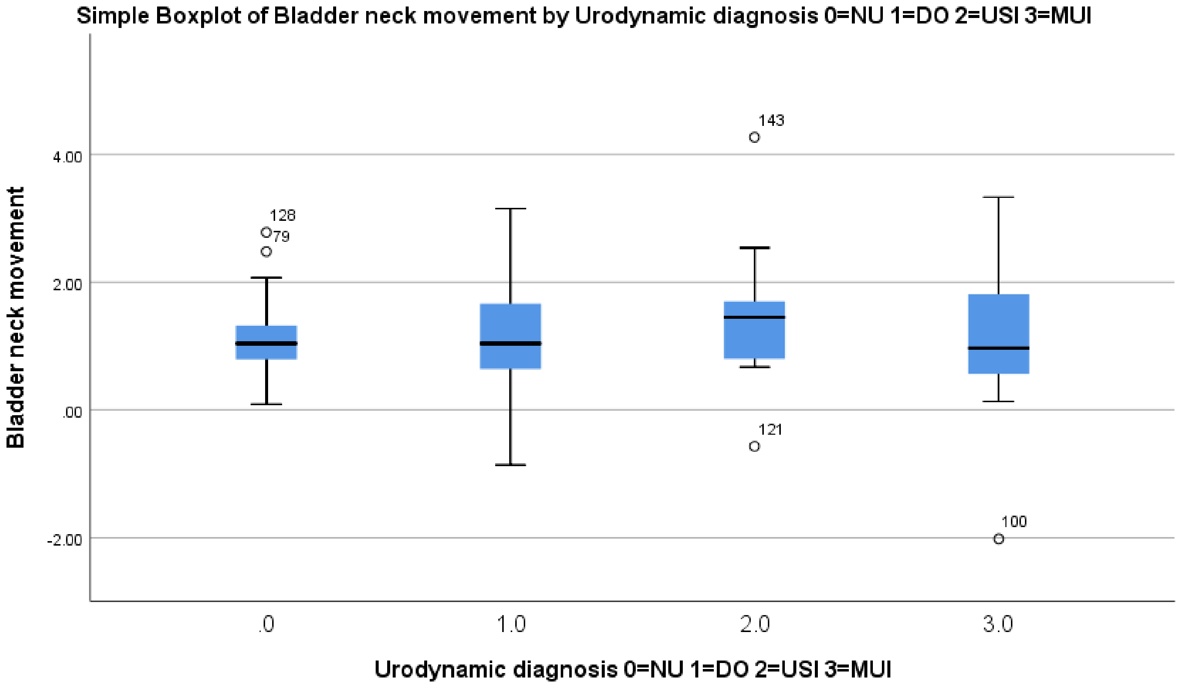


Figure 8.4: Bladder neck movement (cm) and urodynamic diagnoses for women without previous continence surgery.
NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence.



When the women without previous continence surgery were divided into 2 groups as incontinent and continent on stress, the mean bladder neck position at rest and on cough were significantly lower. However, the BNM remained insignificant. The mean values with standard deviation are shown in table 8.3. Figures 8.4, 8.5 and 8.6 show graphical presentation of this data.

Table 8.3: Bladder neck and stress incontinence for women without previous continence surgery

Bladder neck	Urodynamic stress incontinence				P value	Total (N=129)	
	Absent (N=78)		Present (N=51)				
	Mean	SD	Mean	SD		Mean	SD
Position at rest in cm	-1.45	0.58	-1.12	0.58	0.002	-1.32	0.60
Position on cough in cm	-0.33	0.80	0.07	0.85	0.006	-0.17	0.84
Movement in cm	1.13	0.75	1.22	0.98	0.618	1.17	0.85

Figure 8.5: Bladder neck position (cm) at rest and urodynamic stress incontinence for women without previous continence surgery

(0= stress continent, 2=stress incontinent)

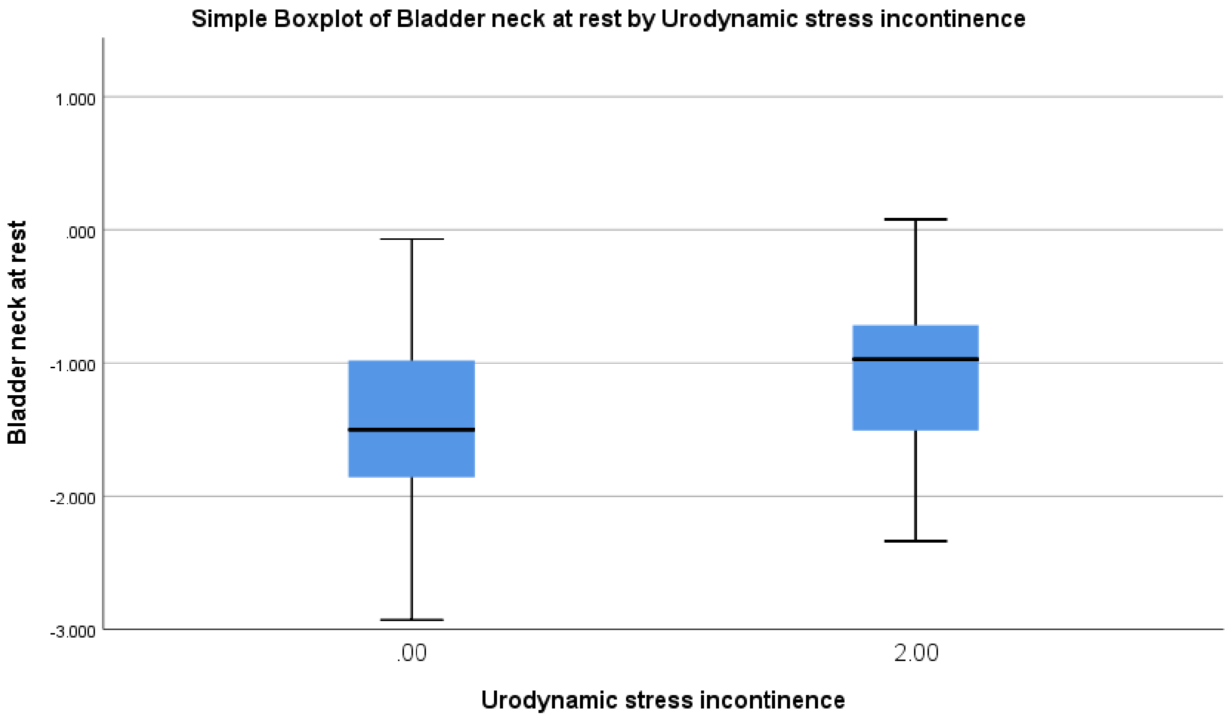


Figure 8.6: Bladder neck position (cm) on cough and urodynamic stress incontinence for women without previous continence surgery. (0= stress continent, 2=stress incontinent)

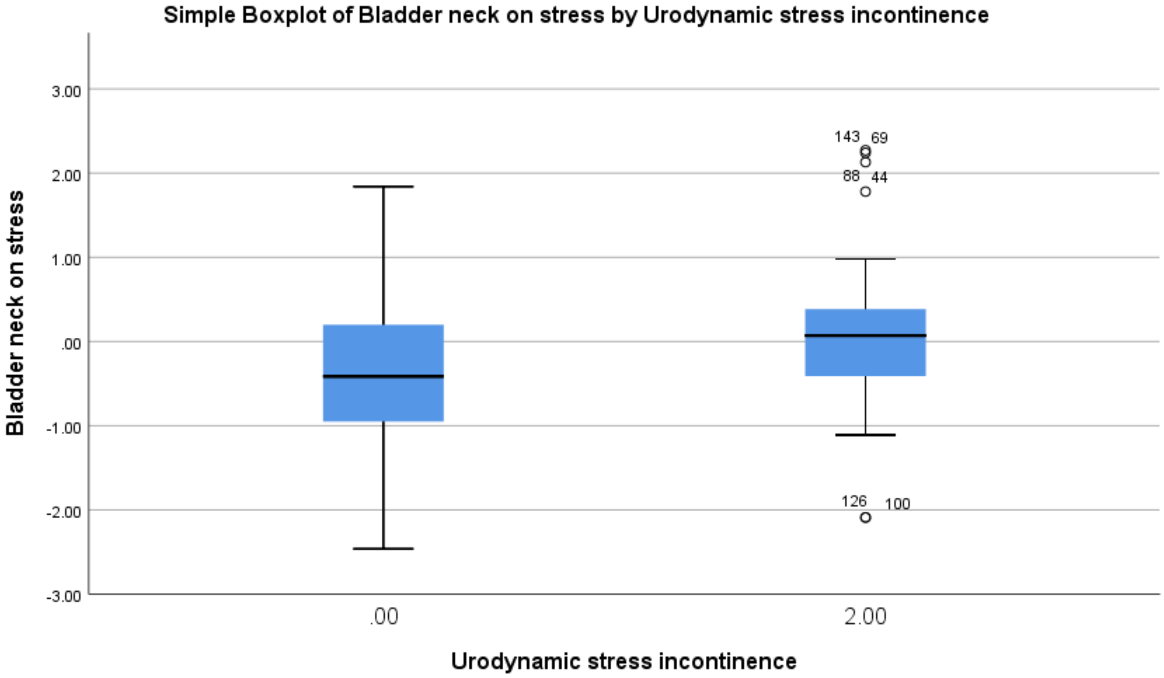
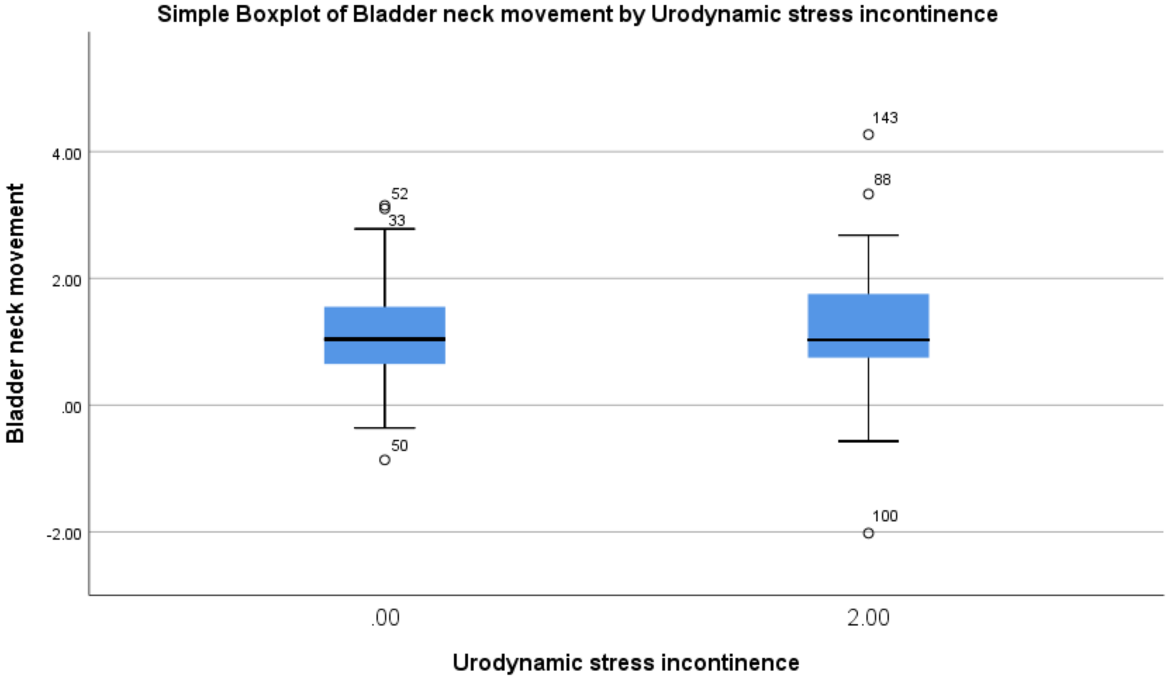


Figure 8.7: Bladder neck movement (cm) and urodynamic stress incontinence for women without previous continence surgery. (0= stress continent, 2=stress incontinent)



The data was analysed after dividing the women with respect to DO. Women with the UD of DO and MUI were included in the DO group and women with the UD of NU and USI were put together in the control group. Women with this UD had the bladder neck at a lower level at rest. The other 2 measurements were similar in the 2 groups as shown in the table 8.4. Figures 8.7, 8.8 and 8.9 shows these measurements.

Table 8.4: Bladder neck and detrusor overactivity for women without previous continence surgery

Bladder neck	Detrusor overactivity				P
	Absent (46)		Present (83)		
	Mean	SD	Mean	SD	
Position at rest in cm	-1.48	0.60	-1.23	0.59	0.021
Position on cough in cm	-0.24	0.82	-0.14	0.85	0.694
Movement in cm	1.25	0.79	1.13	0.88	0.396

Figure 8.8: Bladder neck position (cm) at rest and detrusor overactivity for women without previous continence surgery. (0= stable detrusor, 1=detrusor overactivity)

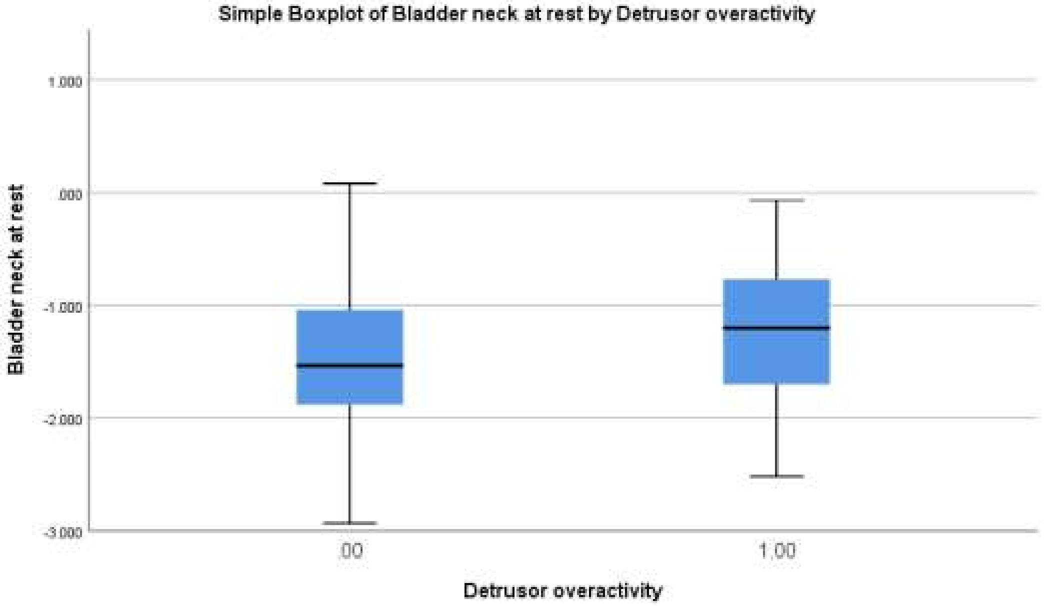


Figure 8.9: Bladder neck position (cm) on cough and detrusor overactivity for women without previous continence surgery. (0= stable detrusor, 1=detrusor overactivity)

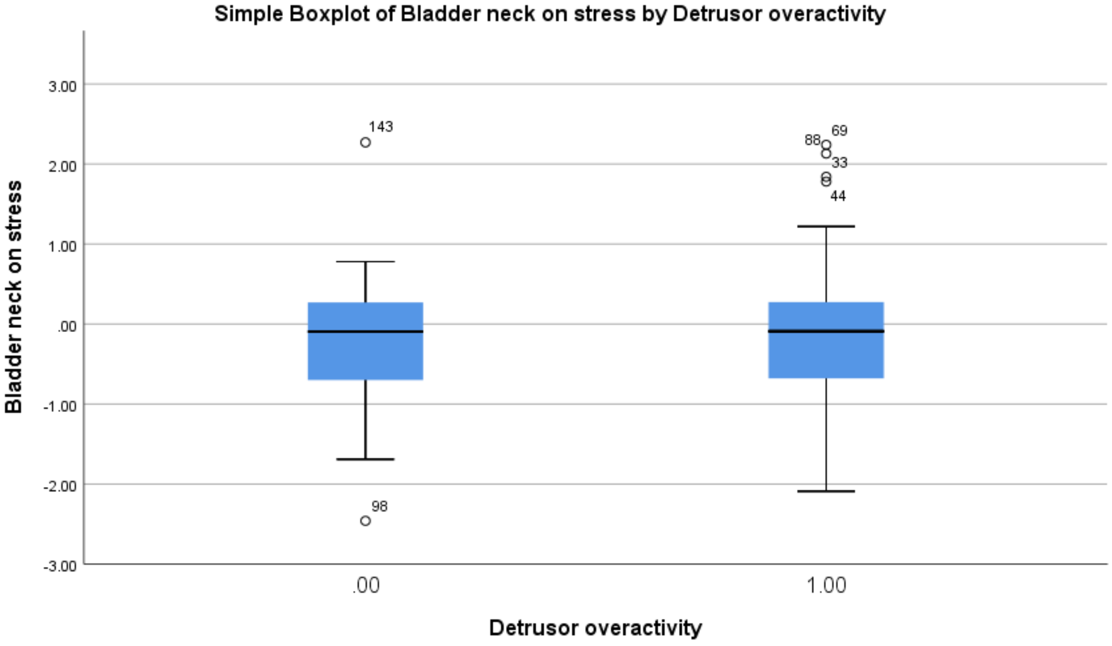
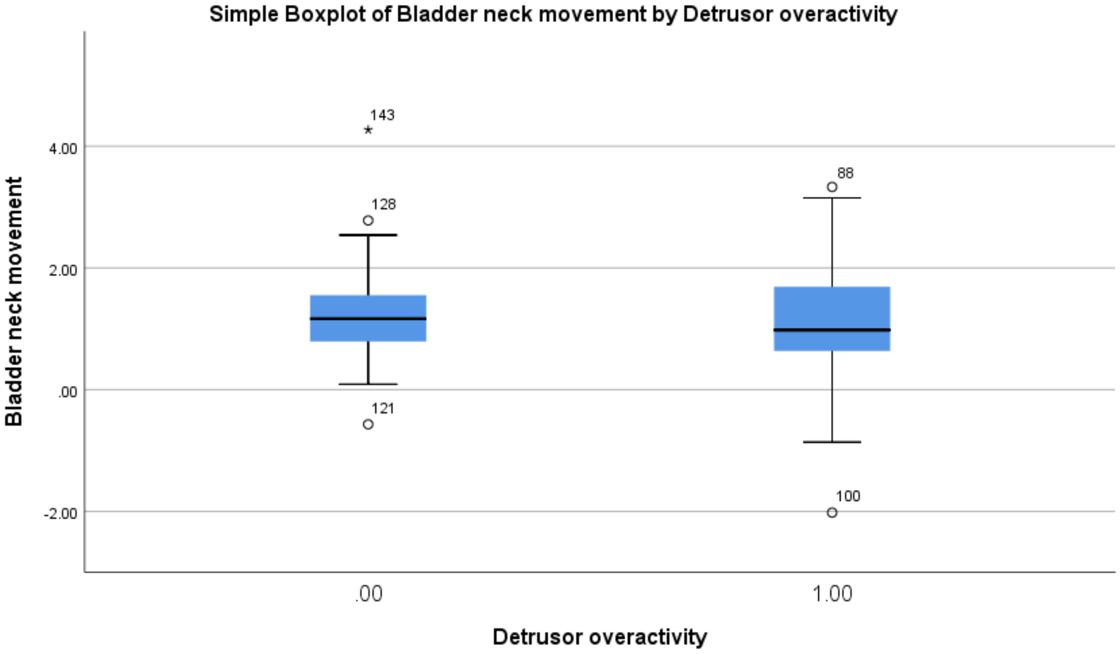


Figure 8.10: Bladder neck movement (cm) and detrusor overactivity for women without previous continence surgery. (0= stable detrusor, 1=detrusor overactivity)



On comparing the group with MUI to the other groups, the bladder neck was at a significantly lower level at rest than the NU group and PureDO group. It was also at a significantly lower position on cough than that of the PureDO group. Both the positions were similar to those of the PureUSI group.

Power calculation

A post-hoc power calculation showed that a power of 88.25% was achieved for this study with sample size of 129 after excluding women with previous continence surgery using a 5% significance level. The alpha value was set at 5%. The significance levels and power for individual measurement were as shown in the table 8.5.

Table 8.5: Post-hoc power calculation for bladder neck position

Measurement	P value	Power percent
Bladder neck position at rest	0.001	93.5
Bladder neck position on raised intra-abdominal pressure	0.009	83.0

8.5 Discussion

Many researchers have studied the BNM as a measure of urethral movement. While most of the studies have compared the measurements in women with and without stress incontinence, this study has compared these parameters in women with NU and 3 most common types of UD.

This study pointed out the important difference between women with NU and all incontinent women. There was statistically significant difference in bladder neck position at rest and also on cough in these 2 categories. The difference between continent women and women with USI was evident from many studies but none of these studies compared DO with NU, to my knowledge. My study also showed that the bladder neck position is significantly lower at rest in women with DO possibly indicating failure of supporting structure in all types of urinary incontinence. Ulmsten and Petros had proposed ‘Integral Theory’ in 1990 (Petros and Ulmsten 1990c). According to this theory, the urgency incontinence and USI are caused by the same anatomical defect of laxity of vagina or its supporting ligaments, or altered connective tissue. The findings of my study can be explained by this hypothesis. The resting position, but not the stress position, of bladder neck was lower in MUI group than PureDO group. It can be hypothesized from this finding that structural defect could be the predominant cause of USI in women with MUI. In contrast, the stress position, but not the resting position, was significantly lower in case of PureUSI group than PureDO group indicating the possibility of increased elasticity.

The bladder neck was at significantly lower resting position in women with MUI than those with PureDO. It is possible that this lower position might prevent compensatory abdominal pressure transmission resulting in leakage of urine. Through my previous study on measurement of urethral sphincter, the urethral sphincter volume was found to be similar in women with PureDO and MUI. This difference in urethral position might be sufficient to cause leakage on raised intra-abdominal pressure in MUI group. A study on UPP showed that the pressure transmission ratio in women with SUI and MUI was significantly lower than women with urgency incontinence (Sharipova et al. 2016).

The pressure transmission theory is based on the position of proximal urethra with respect to the pelvic floor. However, most studies measure the movement of urethra in relation to a reference line drawn through the fixed bony landmark of the pubic symphysis. These methods do not consider the position of the pelvic floor, its curvature or the elasticity. The urethra, being a midline structure, is scanned in the midsagittal plane and is within the genital hiatus. The levator ani is not visible in this plane to assess its position or influence on urethral mobility. 3D ultrasound, which is frequently used by researchers, can visualise the puborectalis part of the muscle and the urethra in the same plane. Transperineal approach for scanning can avoid distortion and allow maximum mobility of the structures. However, cough is an instantaneous process and 3 dimensional imaging during cough does not capture images of sufficient details. Straining has been employed in research studies which require voluntary relaxation of the pelvic floor by the subject. But straining is not the same as the physiological cough or sneeze which is when most women complain of leakage of urine. Moreover, straining or Valsalva has to be described carefully to ensure correct movement (Bump et al. 1995). Therefore new modalities of investigation need to be invented to completely understand the pathophysiology of incontinence.

Many factors affect urethral supports. The bladder neck lies at a lower level with higher bladder volume and the higher volume increases the risk of SUI (Theofrastous et al. 1996; Dietz and Wilson 1999). Effect of pregnancy on the connective tissues and mechanical trauma during childbirth is considered to be the commonest cause of laxity in urethral supporting structures. Research related to this topic is discussed in detail in the chapter on ‘Parity and urethral ultrasound’. There was no significant difference in the groups in this study with respect to the parity.

BNM is a common finding in nulliparous continent women (Peschers et al. 2001; Reed et al. 2004). Some degree of movement in response to raised intra-abdominal pressure is not only natural but also essential to keep the pressure under control. Such mobility was also observed in this study.

Cassado et al. performed introital ultrasound examination on 245 continent and 138 stress incontinent women (Cassado et al. 2006). They found that bladder neck position at rest and on straining and bladder neck descent on straining were the most significant measurements differentiating the groups. The continent group was asymptomatic and did not undergo urodynamic studies. A descent of 8 mm has sensitivity of 92% and specificity of 76.8%. The mean descent in all groups in my study, including NU was more than a centimetre. A cut-off of 13 mm was proposed by Chen et al (Chen, Su, and Lin 1997). The study included 2 groups of women, stress incontinent and continent. This value is more than the mean value of both such groups in my study. Since there is no significant difference in the BNM in different groups in my study, it is not possible to predict USI from this measurement. USI can be easily demonstrated by the clinical stress test (Berild and Kulseng-Hanssen 2012). Ultrasound prediction of the condition is of doubtful clinical significance.

Electromyelography studies have shown that the action of the levator ani muscle is independent of the sphincter (Kenton and Brubaker 2002). Pelvic floor muscle physiotherapy is commonly employed as first line management for USI. It is effective in improving mild to moderate incontinence in majority of women. It has shown to elevate the bladder neck position at rest and on pelvic floor contraction. However, it did not change the movement on cough or Valsalva. It was concluded that the exercises improved the ability of women to elevate the bladder neck voluntarily but did not improve its stiffness. This improved ability can be used to control leakage during coughing or sneezing by almost 80% (Miller, Sampselle, et al. 2008).

Bladder neck suspension has been used to treat SUI for many years (Keane, Eckford, and Abrams 1992). Midurethral tape and colposuspension are the most commonly performed surgeries for USI. The effect of these surgeries and use of BNM to predict failure of the procedure is investigated by many researchers. Digesu demonstrated elevation of the bladder neck and its increased apposition to the levator ani played a role in restoration of continence after colposuspension (Digesu, Bombieri, et al. 2004). Vierek achieved 82% success rate at 4 years' follow up after Burch colposuspension with 7mm elevation of bladder neck demonstrated on scan (Viereck et al. 2004). Koelle showed objectively measured success rate of 86% after tension free vaginal tape surgery (Koelle et al. 2006). The BNM reduced from 23 mm to 17 mm after the surgery. Another study measured BNM after both procedures. The linear movement reduced from an average of 15.3 mm to 11.7 mm after tension free vaginal tape surgery and from 15.6 mm to 2.3 mm after colposuspension (Atherton and Stanton 2000). This showed that the colposuspension mainly has its effect on BNM but the mechanism of action of the tape does not depend on bladder neck elevation.

8.6 Conclusion

The bladder neck position at rest was significantly higher in women with NU than any other group. This may indicate loss of urethral support as a common pathology for different types of urinary incontinence. The position of the bladder neck was significantly higher in the PureDO group than the MUI suggesting the possibility that loss of abdominal pressure transmission is the cause of stress incontinence in the MUI group. The bladder neck positions were significantly lower in women with USI. There was no difference in the mean BNM amongst different groups of urodynamic diagnoses.

9. Urethral movement

9.1 Introduction

Urethra is a tubular structure suspended in the pelvis and is closely related to the anterior vaginal wall. Pubourethral ligaments are thought to be responsible for holding the urethra in place (Zacharin 1977; Petros 1998). Zacharin has described them as 2 posterior, an intermediate and an anterior pubourethral ligament (Zacharin 1977). The most important of them, the posterior pubourethral ligament is a pyramidal structure with an apical attachment to the lower part of the pubic bone on the posterior aspect. The bulky base is attached to paraurethral tissue of the upper urethra fusing with the fascia and muscle of the urethra. The lateral extension of the ligament extends across the levator ani muscle and fuses with the levator fascia providing the only muscular attachment of the urethra. It was suggested that a defect in the pubourethral ligament or support from the anterior vaginal wall results in hypermobility of the urethra and incontinence of urine on stress (Ulmsten 1994).

The urethra is also supported by its connections with the pubic bone through the pubovaginal part of levator ani and arcus tendinous fascia pelvis (Delancey and Ashton-Miller 2004). This supporting system provides a firm backdrop of vaginal hammock against which the urethra is compressed when abdominal pressure is raised (DeLancey 1994). Any disruption in this supporting system changes the resting position and mobility of the urethra.

Sling procedures to support the bladder neck and proximal urethra in stress incontinent patients were practised since early 1900s (Lobel, Manunta, and Rodriguez 2001). The discovery of midurethral tape started with a simple observation that a haemostat applied immediately behind the pubic symphysis at the level of midurethra stopped urinary leakage on coughing. Ulmsten and Petros developed an intravaginal sling in 1990 to create an artificial pubourethral ligament to treat stress urinary incontinence (Petros and Ulmsten 1990a). The sling was removed 4 to 8 weeks after insertion. The success rate of the procedure was maintained in 50% of the patients at the end of 1 year. An additional vaginal tuck surgery increased this success rate after 1 year by 32%. This study led to the invention of 'tension free vaginal tape' (Ulmsten et al. 1996). The midurethral sling surgery soon became mainstay of treatment for SUI (Secco et al. 2012; Fusco et al. 2017). It is most commonly performed surgery for recurrent stress incontinence (Nadeau and Herschorn 2014). These surgeries are successful in about 62% to 98% of cases and majority of women remain continent after 5 years (Ford et al. 2015).

Most of the studies regarding mobility of urethra have assessed the mobility of the bladder neck. Very few studies have assessed the mobility of the entire urethra and the urinary incontinence. Pirpiris et al studied segmental mobility in 198 women with urodynamic studies and four dimensional transperineal ultrasound (Pirpiris, Shek, and Dietz 2010). They measured vector based mobility of six equidistant points along the urethra from resting position to position on straining. They found that the midurethral mobility was significantly more in women with stress urinary incontinence (SUI) and urodynamic stress incontinence (USI) than detrusor overactivity (DO) or voiding dysfunction. They did not find mobility at the bladder neck or external urethral meatus significantly different between the groups. This finding questions the role of the posterior and anterior pubourethral ligaments in pathophysiology of SUI. The pubourethral distance was not compared in the study. Midurethral mobility was also found to be higher in women with SUI than in continent women on dynamic MRI studies (Rinne et al. 2010).

It was important to find the association of the length of the pubourethral ligaments and their elasticity with the urinary incontinence.

9.2 Aim

To find the difference in the position and mobility of urethra in relation to the pubic symphysis in women with different urodynamic diagnoses (UD).

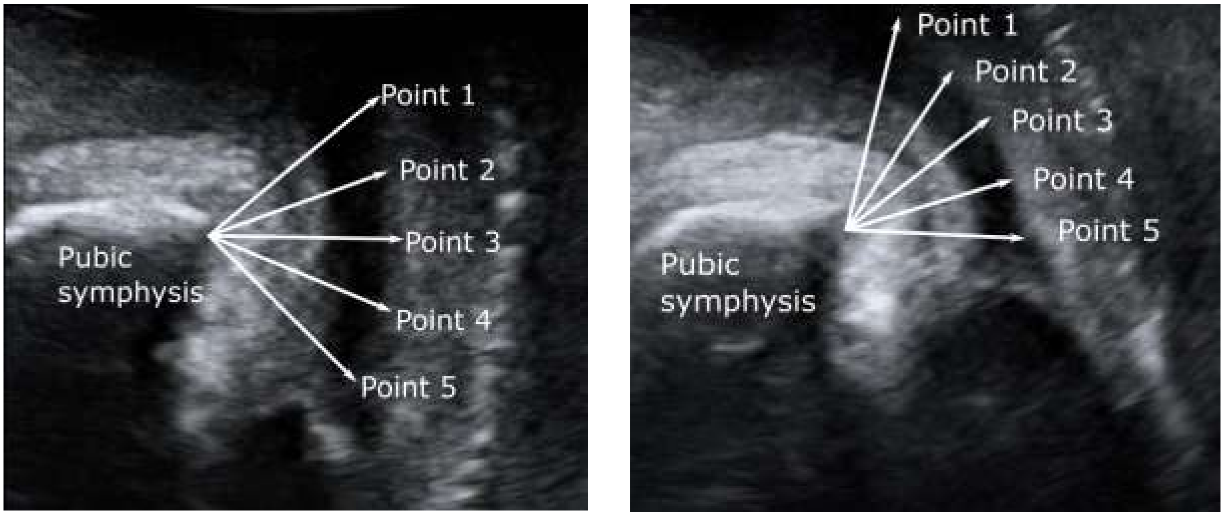
9.3 Methodology

Women attending urogynaecology department for urodynamic studies were recruited for the study. The demographic data and urodynamic study data was collected as described in chapter on ‘Urodynamic Studies’ and I performed the TPU of urethra as part of the study procedure as described in the methodology section of chapter on ‘The Validation Study for Ultrasound Measurement of Urethral Dimensions and Mobility’. Ethical approval for the study was obtained from the Queen Square Research Ethics Committee (REC reference number 15/LO/0264).

To measure the urethral mobility, the urethra was divided into four equal segments by five equidistant points. The point on the posterior margin of the urethra at the external urethral meatus was named as point 1. The points were then numbered serially with the point on the posterior margin of the urethra at the urethrovesical junction numbered as point 5. The posteroinferior point of the pubic symphysis was fixed and considered as the reference point. The distances of the 5 points along urethra were measured from this point at rest and on cough as shown in figure 9.1. The movement of each point was calculated by subtracting distance at rest from the distance on cough.

Figure 9.1: Measurement of distance between posterior margin of urethra and postero-inferior border of the pubic symphysis

Point 1: At external urethral meatus, Point 2: Midway between midurethra and external urethral meatus, Point 3: At midurethra, Point 4: Midway between bladder neck and midurethra, Point 5: At the bladder neck



Urethral position at rest **Urethral position on cough**

The data was analysed using SPSS software version 25 by IBM Compamy. Kruskal Wallis test and Chi square test were used for analysing data for 4 groups of urodynamic diagnoses. Data divided into 2 groups was analysed using Mann Whitney U test. The difference is considered to be significant if the probability is less than 5%.

9.4 Results

One hundred and fifty women were included in the study. They were grouped according to their UD as nondiagnostic urodynamics (NU) in 37 women, pure DO (PureDO) in 53, pure USI (PureUSI) in 22 women and mixed urinary incontinence (MUI) in 38 women. There was no relationship between UD and age or body mass index of the women or the pelvic organ prolapse in this group.

The mean values and standard deviation of the resting position, stress position and urethral movement in women with different UD were as shown in table 9.1. Out of the 150 women, 21 had undergone a continence surgery in the past which could affect the urethral mobility. They were excluded from further analysis. Data was then analysed for the remaining 129 women. These women were divided in 4 groups according to their UD of NU in 29, PureDO in 49, PureUSI in 17 and MUI in 34. The mean pubourethral distances in these groups are as shown in table 2. The mean distance at rest between the pubic symphysis and external urethral meatus and the point a quarter of urethral length cranial to it are significantly related to the UD. There was no difference in the mean distance of points 3, 4 and 5 at rest or any point on cough amongst the groups of women with different

UD. There was no difference in the average mobility of any point on cough in relation to the pubic symphysis. Figures 9.2 and 9.3 show the graphs representing the lengths at rest and on straining and the mobility of 5 points in women with different UD.

Table 9.1: Urethral distance and mobility and urodynamic diagnoses for all women

NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence

Measurement		NU (N=37)		DO (N=53)		USI (N=22)		MUI (N=38)		P value	Total (N=150)	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD		Mean	SD
Distance in cm at rest from point	1	1.42	0.37	1.45	0.29	1.52	0.26	1.53	0.36	0.139	1.47	0.33
	2	1.44	0.39	1.38	0.32	1.49	0.36	1.48	0.31	0.186	1.43	0.34
	3	1.68	0.40	1.54	0.35	1.66	0.42	1.62	0.35	0.302	1.62	0.37
	4	2.02	0.40	1.85	0.36	1.93	0.46	1.89	0.41	0.313	1.91	0.40
	5	2.41	0.41	2.23	0.46	2.28	0.53	2.24	0.47	0.217	2.28	0.46
Distance in cm on cough from point	1	1.60	0.41	1.57	0.32	1.68	0.42	1.62	0.41	0.874	1.60	0.38
	2	1.56	0.44	1.50	0.38	1.63	0.51	1.59	0.41	0.788	1.56	0.42
	3	1.66	0.46	1.57	0.40	1.67	0.59	1.66	0.42	0.647	1.63	0.45
	4	1.83	0.51	1.75	0.41	1.78	0.60	1.80	0.44	0.834	1.79	0.47
	5	2.08	0.56	2.01	0.42	1.96	0.64	2.00	0.47	0.877	2.02	0.50
Mobility of urethra in cm at point	1	0.18	0.33	0.11	0.33	0.16	0.40	0.09	0.34	0.653	0.13	0.34
	2	0.12	0.32	0.12	0.32	0.14	0.41	0.12	0.36	0.971	0.12	0.34
	3	-0.03	0.30	0.03	0.35	0.00	0.37	0.04	0.43	0.834	0.01	0.36
	4	-0.19	0.36	-0.10	0.42	-0.15	0.32	-0.09	0.51	0.587	-0.13	0.41
	5	-0.33	0.43	-0.22	0.46	-0.32	0.32	-0.24	0.56	0.667	-0.27	0.46

Table 9.2: Urethral distance and mobility and urodynamic diagnoses for women without previous continence surgery

NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence

Measurement		NU (N=29)		DO (N=49)		USI (N=17)		MUI (N=34)		P value	Total (N=129)	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD		Mean	SD
Distance in cm at rest from point	1	1.46	0.38	1.43	0.28	1.56	0.22	1.57	0.31	0.043	1.49	0.31
	2	1.44	0.40	1.36	0.31	1.58	0.30	1.50	0.28	0.017	1.44	0.33
	3	1.67	0.41	1.53	0.34	1.79	0.35	1.63	0.33	0.051	1.62	0.36
	4	2.00	0.43	1.85	0.37	2.06	0.39	1.88	0.40	0.156	1.92	0.40
	5	2.41	0.44	2.23	0.47	2.41	0.42	2.19	0.46	0.112	2.28	0.46
Distance in cm on cough from point	1	1.60	0.41	1.56	0.30	1.74	0.44	1.65	0.40	0.580	1.62	0.38
	2	1.54	0.41	1.48	0.37	1.71	0.54	1.62	0.42	0.482	1.56	0.42
	3	1.62	0.44	1.55	0.39	1.78	0.61	1.68	0.43	0.487	1.63	0.45
	4	1.77	0.49	1.73	0.41	1.89	0.61	1.81	0.46	0.708	1.78	0.47
	5	2.02	0.53	1.99	0.42	2.03	0.60	2.01	0.48	1	2.01	0.48
Mobility of urethra in cm at point	1	0.15	0.34	0.13	0.28	0.18	0.44	0.08	0.35	0.674	0.13	0.33
	2	0.10	0.33	0.12	0.28	0.13	0.46	0.12	0.37	0.958	0.12	0.34
	3	-0.05	0.31	0.02	0.33	-0.01	0.42	0.05	0.44	0.634	0.01	0.36
	4	-0.23	0.33	-0.12	0.41	-0.17	0.36	-0.07	0.51	0.354	-0.14	0.42
	5	-0.38	0.34	-0.24	0.46	-0.38	0.32	-0.18	0.55	0.220	-0.28	0.45

Figure 9.2: Mean resting length (cm) at point 1 and urodynamic diagnoses.

(NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence).

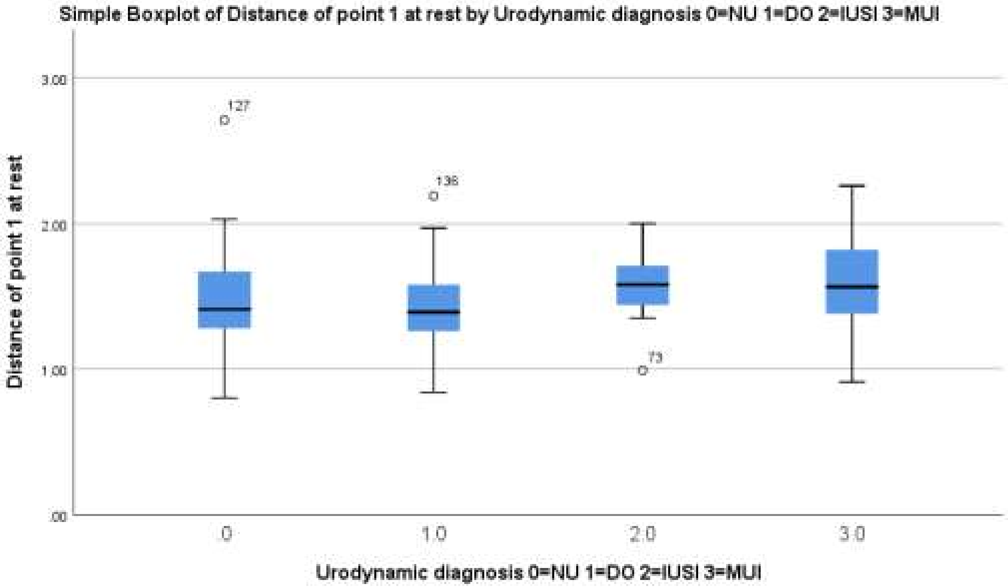
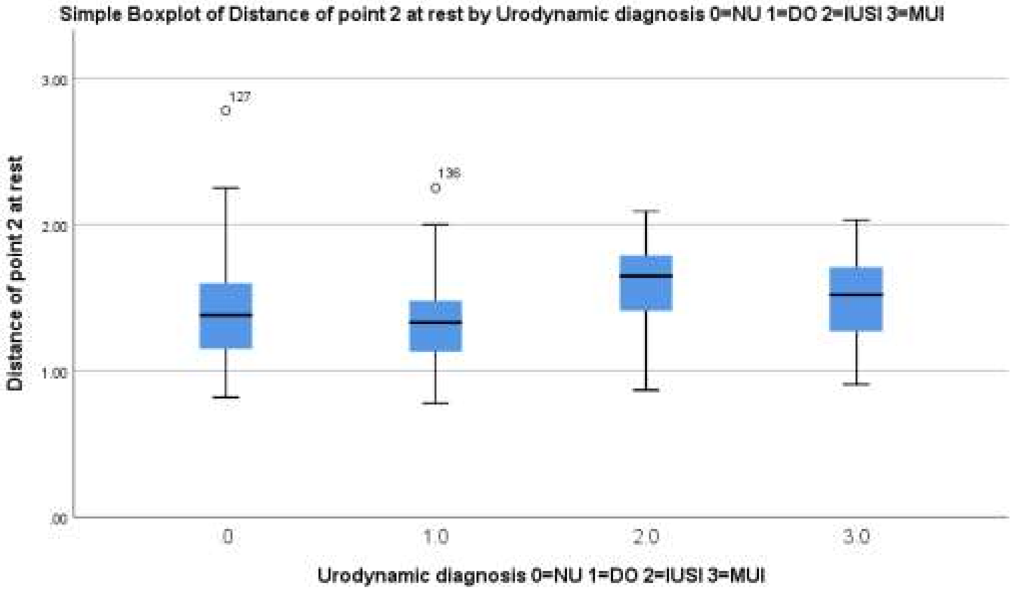


Figure 9.3: Mean resting length (cm) at point 2 and urodynamic diagnoses.

(NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence).



After dividing the women according to their stress incontinence status, those with USI had significantly longer mean pubourethral distance at points 1 and 2. There was no difference in other readings as shown in table 9.3. The urethral mobility on cough was same in both the groups. Figures 9.4 and 9.5 show the resting length at point 1 and 2 in the 2 groups.

Table 9.3: Urethral distance and mobility and urodynamic stress incontinence for women without previous continence surgery

Measurement		Stress continent (N=78)		Stress incontinent (N=51)		P value	Total (N=129)	
		Mean	Standard Deviation	Mean	Standard Deviation		Mean	Standard deviation
Distance in cm from pubic symphysis at rest of point	1	1.44	0.32	1.56	0.28	0.005	1.49	0.31
	2	1.39	0.35	1.52	0.29	0.004	1.44	0.33
	3	1.58	0.37	1.68	0.34	0.055	1.62	0.36
	4	1.91	0.40	1.94	0.40	0.560	1.92	0.40
	5	2.30	0.46	2.26	0.45	0.583	2.28	0.46
Distance in cm from pubic symphysis on cough of point	1	1.57	0.34	1.68	0.41	0.201	1.62	0.38
	2	1.50	0.38	1.65	0.46	0.146	1.56	0.42
	3	1.57	0.41	1.71	0.50	0.147	1.63	0.45
	4	1.74	0.44	1.84	0.51	0.256	1.78	0.47
	5	2.00	0.46	2.02	0.52	0.998	2.01	0.48
Mobility of urethra in cm at point	1	0.13	0.30	0.11	0.38	0.476	0.13	0.33
	2	0.11	0.30	0.12	0.40	0.761	0.12	0.34
	3	-0.01	0.32	0.03	0.43	0.666	0.01	0.36
	4	-0.16	0.38	-0.10	0.46	0.291	-0.14	0.42
	5	-0.30	0.42	-0.25	0.49	0.398	-0.28	0.45

Figure 9.4: Resting length (cm) at point 1 in women with and without Urodynamic stress incontinence (0= stress continent, 2=stress incontinent)

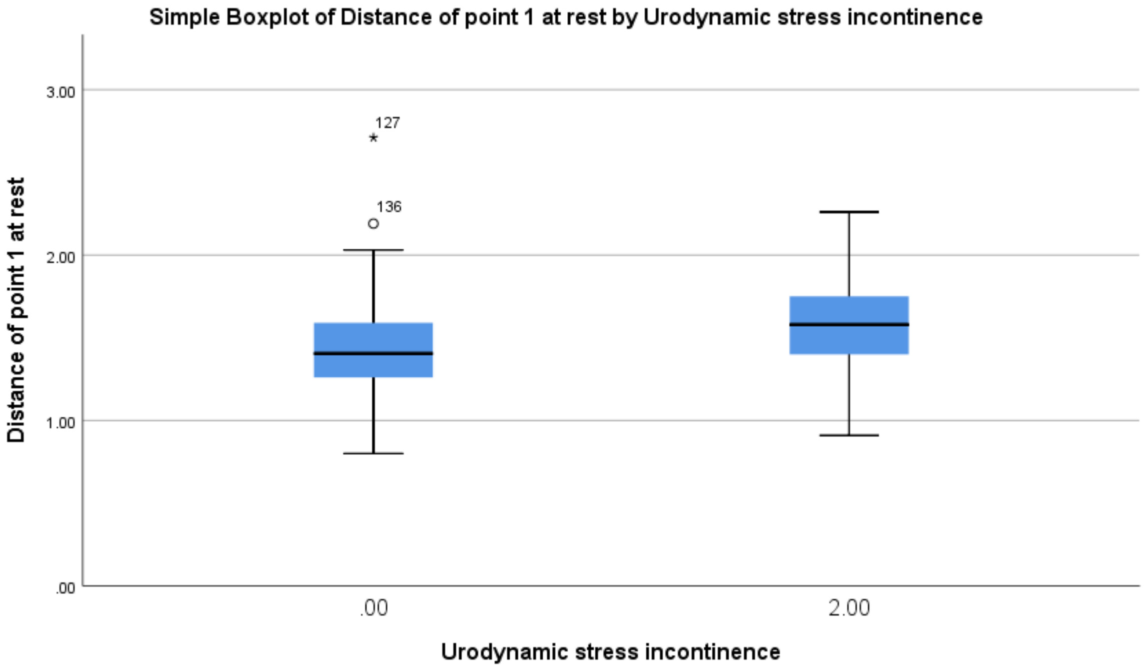
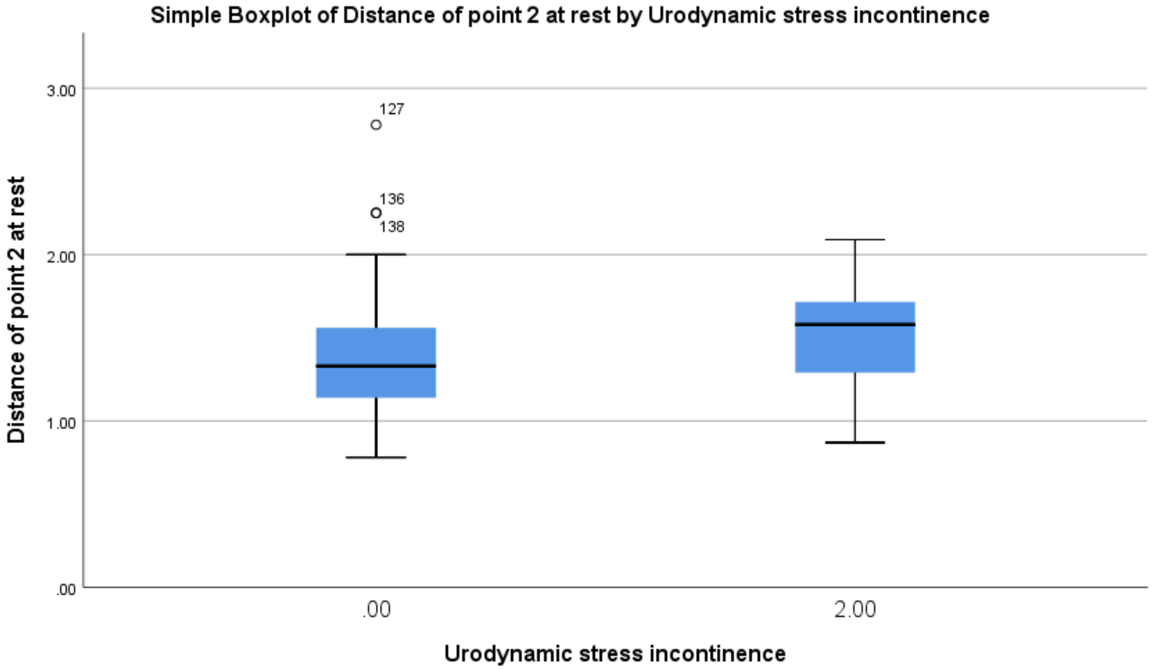


Figure 9.5: Resting length at point 2 (cm) in women with and without Urodynamic stress incontinence (0= stress continent, 2=stress incontinent)



The women were grouped into those with DO and with normal detrusor activity. Those with the diagnosis of DO and MUI were included in the DO group and women with the UD of NU and USI were put together in the group with normal detrusor activity. Women with DO had shorter mean resting distance at points 4 and 5. The mobility at these points was also less though these differences did not reach statistical significance. The mean values were as shown in table 9.4. Figures 9.6 and 9.7 denote the resting length at point 4 and 5 in these groups.

Table 9.3: Urethral distance and mobility and detrusor overactivity for women without previous continence surgery

Measurement		Normal detrusor activity (N=46)		Detrusor overactivity (N=83)		P value	Total (N=129)	
		Mean	Standard Deviation	Mean	Standard Deviation		Mean	Standard deviation
Distance in cm from pubic symphysis at rest of point	1	1.49	0.34	1.49	0.30	0.777	1.49	0.31
	2	1.49	0.37	1.41	0.31	0.234	1.44	0.33
	3	1.71	0.39	1.57	0.34	0.053	1.62	0.36
	4	2.02	0.41	1.86	0.38	0.030	1.92	0.40
	5	2.41	0.43	2.22	0.46	0.017	2.28	0.46
Distance in cm from pubic symphysis on cough of point	1	1.65	0.42	1.59	0.35	0.740	1.62	0.38
	2	1.60	0.46	1.53	0.39	0.618	1.56	0.42
	3	1.68	0.51	1.60	0.41	0.742	1.63	0.45
	4	1.82	0.54	1.76	0.43	0.920	1.78	0.47
	5	2.02	0.55	2.00	0.44	0.961	2.01	0.48
Mobility of urethra in cm at point	1	0.16	0.37	0.11	0.31	0.590	0.13	0.33
	2	0.11	0.38	0.12	0.32	0.858	0.12	0.34
	3	-0.04	0.35	0.03	0.37	0.211	0.01	0.36
	4	-0.21	0.34	-0.10	0.45	0.132	-0.14	0.42
	5	-0.38	0.33	-0.22	0.50	0.058	-0.28	0.45

Figure 9.6: Resting length at point 4 (cm) in women with and without detrusor overactivity (0= stable detrusor, 1=detrusor overactivity)

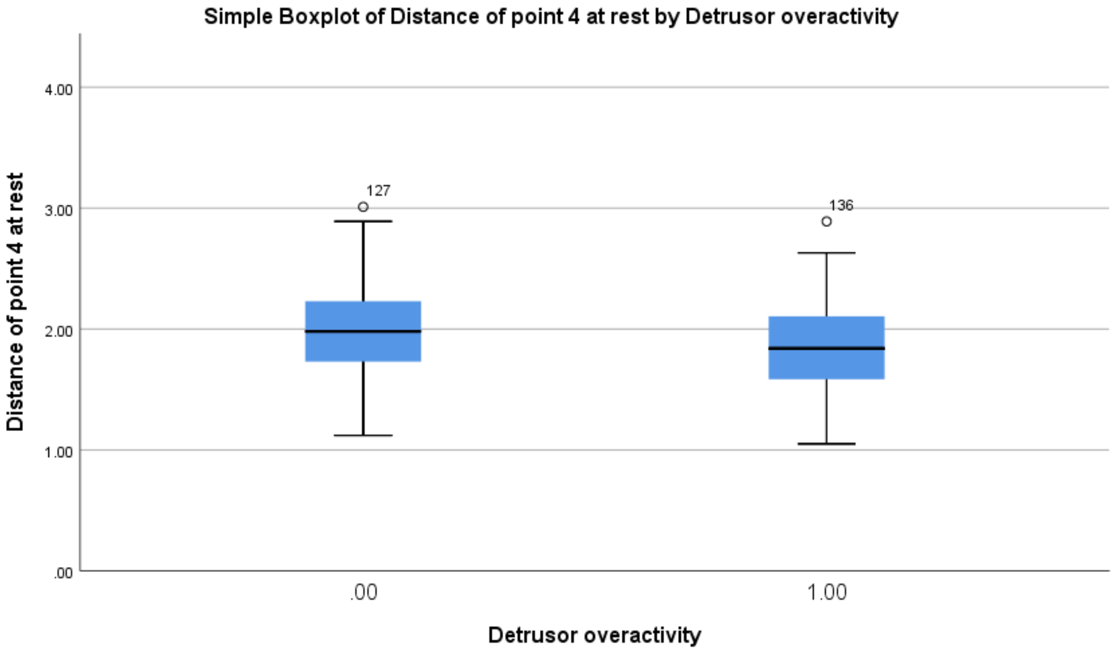
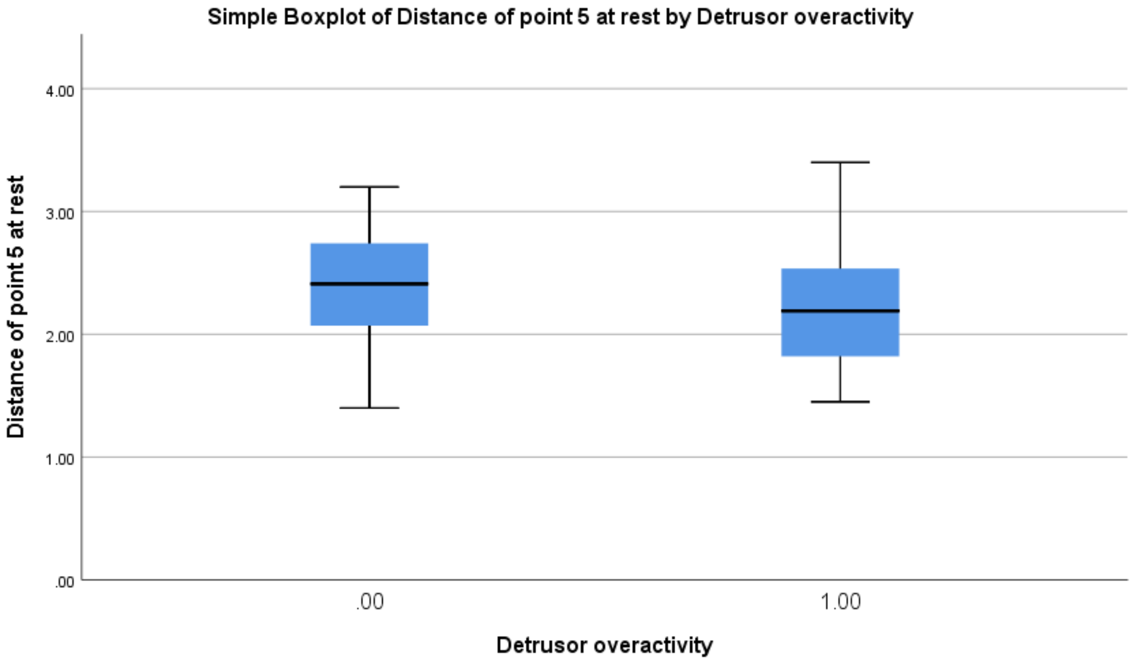


Figure 9.7: Resting length (cm) at point 5 in women with and without detrusor overactivity (0= stable detrusor, 1=detrusor overactivity)



9.5 Discussion

The lower urethra was positioned at a longer mean distance from the pubic symphysis in women with USI but there was no difference in the position of upper urethra with respect to the UD. The study failed to show any difference in urethral mobility among women with and without PureUSI. The upper urethra was lying closer to the pubic symphysis in women with DO. This part of the urethra was less mobile in women with DO than without, however, the difference did not reach statistical significance.

The midurethral point was at similar distance in all the groups of women. Its distance from the pubis symphysis did not show much change on cough. This study did not confirm increased midurethral mobility in cases of SUI and USI observed by other researchers (Pirpiris 2010). This difference can be because of the variation in methodology. Pirpiris et al calculated the vector based mobility by measuring the movement along the x and y axes which were the horizontal and perpendicular lines on the ultrasound image, passing through the posteroinferior border of the pubic symphysis. This movement was not necessarily towards or away from the pubic symphysis so was not a measure of laxity or flexibility of the pubourethral ligaments.

The pubourethral ligaments were considered to be responsible to maintaining the position of the upper urethra and continence on stress (Zacharin 1977; DeLancey 1990; Petros 1998). The causative association of laxity of the pubourethral ligaments with stress incontinence in women could not be proven by this study. Moreover, the distance of the midurethral point did not change on cough. It does not support the hypothesis that the midurethral tape replaces the pubourethral ligament and prevents stress incontinence.

Midurethral tape insertion has become the primary surgery for urinary incontinence for over a decade (Ford and Ogah 2016; Serati et al. 2017). Ultrasound studies are conducted to understand its mechanism of action. Sarlos et al studied 40 patients with transperineal ultrasound before and after tension free vaginal tape surgery (Sarlos, Kuronen, and Schaer 2003). They observed kinking of urethra during stress with movement of the tape closer to the symphysis after the surgery. Mobility of the bladder neck is unaffected by the single tension-free vaginal tape procedure.

Masata conducted transperineal and introital ultrasound examination on 52 women before and after insertion of tension free vaginal tape (Masata et al. 2006). They used a vector based system to assess the mobility of 4 points along the urethra. There was no change in the resting position of the urethra after the surgery. However, there was significant reduction in mobility after the tape insertion. The data regarding distance of midurethra from the pubic symphysis was not discussed in the article though there was significant reduction in the pubourethral distance on stress in the graphical representation.

3D introital ultrasound was used to measure the effect of the tape on the urethra (Yang et al. 2011). The study sample consisted of 31 women who underwent midurethral tape surgery. It showed that the distance between the tape and urethral mucosa decreased on straining and on strong coughs. It also showed that there was narrowing of the central hypoechoic area of the urethra in these patients on stress. Another study with similar results was published by the same researchers which included 128 women (Yang et al. 2013). These studies provided evidence that there was compression of urethra after the surgery. However, the pubourethral distance was not considered by the researchers.

These studies prove that the midurethral tape prevent leakage of urine on stress by reducing the pubourethral distance and compressing the urethra on stress but increased urethral mobility in relation to the pubic symphysis as the cause of stress incontinence remains to be proven.

It is possible that physical stress has more effect on lateral stretching of the urethra and anterior vaginal wall. Defect in the lateral attachment of the vaginal wall to the levator ani muscle can result in loss of tension in the anterior vaginal wall and deficiency in the support mechanism resulting in stress incontinence. The lateral stretch of the vagina can be explained by widening of the levator hiatus seen on straining (Derpapas, Digesu, et al. 2012). My experiment measured the pubourethral distances only in the midsagittal plane, hence, unable to comment on this mechanism.

The distal urethra was located away from the pubic symphysis in women with USI. This may indicated reduced support to this part of urethra in these women. However, the mechanism of incontinence cannot be explained by this finding on the basis of the anatomy.

The upper urethra was held closer to the pubic symphysis in women with DO. This portion also showed less mobility on stress. The significance of this finding in these women is not known.

The study shows differences in position of the upper and the lower urethra in women with USI and DO. The upper urethral position in closer to the symphysis in DO but not different in women with USI. Similarly, the lower urethra is at a longer distance from the symphysis in women with USI but there is no difference when women with DO are considered. The upper urethral movement is very much less in women with DO. These findings contradict the integral theory of common basis of vaginal laxity for USI and DO (Petros and Ulmsten 1990c).

9.6 Conclusion

There was no difference in urethral mobility in women with different UD. The causative association of laxity of the pubourethral ligaments with stress incontinence in women could not be proven. The resting position of distal urethra was further away from the pubic symphysis in women with urodynamic stress incontinence. The proximal urethra was closer to the symphysis at rest in women with detrusor overactivity.

10. Urethral dimensions

10.1 Introduction

The basic principle behind maintaining continence is to maintain the urethral pressure greater than the vesical pressure. The urethra is a fibromuscular tube in the pelvis. It is affected by external pressures from surrounding organs, especially during physical stress. There is a rise in the vesical pressure during stress and in order to maintain continence, the urethral pressure should increase and be greater than the vesical pressure. According to the Hammock hypothesis, the urethra is compressed against the anterior vaginal wall by an increase in the abdominal pressure, thus providing support and increasing the closure pressure (DeLancey 1994).

Urethral pressure profilometry (UPP) has been performed in women to understand the physiology of continence for different groups (Enhorning 1961; Brown and Wickham 1969; Harrison and Constable 1970; Pizzoferrato et al. 2017). There is contradictory evidence regarding the value of this investigation in diagnosing stress urinary incontinence (SUI). The area under curve on rest UPP was shown to be significantly related to the urethral sphincter volume (Robinson et al. 2004). The pressure changes on stress were considered to be the differentiating factor for stress urinary incontinence by some researchers. The test was shown to have a high specificity for diagnosing the condition (Enhorning 1961; Bump et al. 1988; Hanzal, Berger, and Koelbl 1991). However, there was considerable overlap of measured urethral pressures in women with and without SUI so this test was considered less useful as a diagnostic test (Versi 1990;

Summitt et al. 1994). The reduction in the urethral closure pressure was thought to be an artefact by some, or due to urethral mobility (Richardson 1986). Recent research regenerated interest in this investigation as the most specific biomarker (Pizzoferrato et al. 2017). Urethral closure pressure was shown to be a discriminatory factor for sphincter competence and assessing the supporting structures of the urethra. The magnitude of the urethral closure pressure was inversely related to the severity of the SUI. The rise in intraurethral pressure results from transmission of the intra-abdominal pressure to the urethra as well as from reflex contraction of the urethral sphincter which occurs a few milliseconds before the increase in abdominal pressure (Constantinou and Govan 1982). Though the pressure changes in the urethra are studied by the UPP, there are no studies published on changes in urethral dimensions with increases in intra-abdominal pressure..

10.2 Aim

To find the difference in urethral dimensions in relation to the pubic symphysis in women with different urodynamic diagnoses (UD).

10.3 Methodology

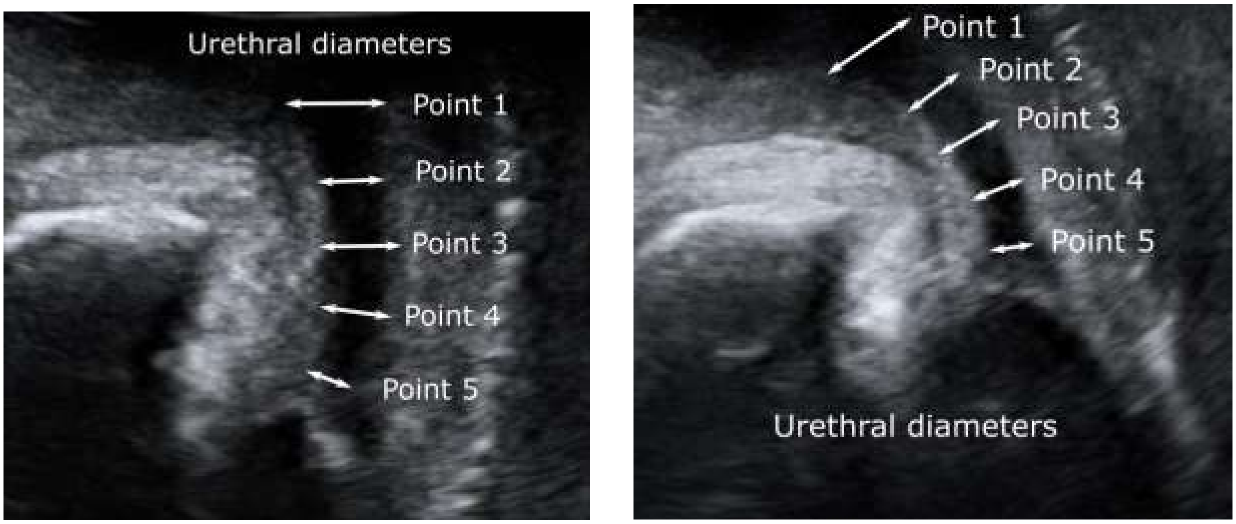
Women attending the urogynaecology department for urodynamic studies were recruited for the study. Data was collected and I performed the TPU of urethra as part of the study procedure as described in the methodology section of the chapter on ‘The Validation

Study for Ultrasound Measurement of Urethral Dimensions and Mobility'. Ethical approval for the study was obtained from the Queen Square Research Ethics Committee (REC reference number 15/LO/0264).

The measurement was done on the resting image and on the stress image. The urethral diameter was measured at 5 equidistant points along the urethra. Point 1 was at external urethral meatus and point 5 was at the urethrovesical junction. The diameters at points 1 and 5 are measured between the end points of the anterior and posterior urethral margins. At the points 2, 3 and 4, the distance between the outer margins of the urethral sphincter complex perpendicular to the urethral length is measured as urethral diameter as shown in figure 10.1. The length of the urethra was measured along the urethral lumen as shown in figure 10.2.

Figure 10.1: Urethral diameter measurement

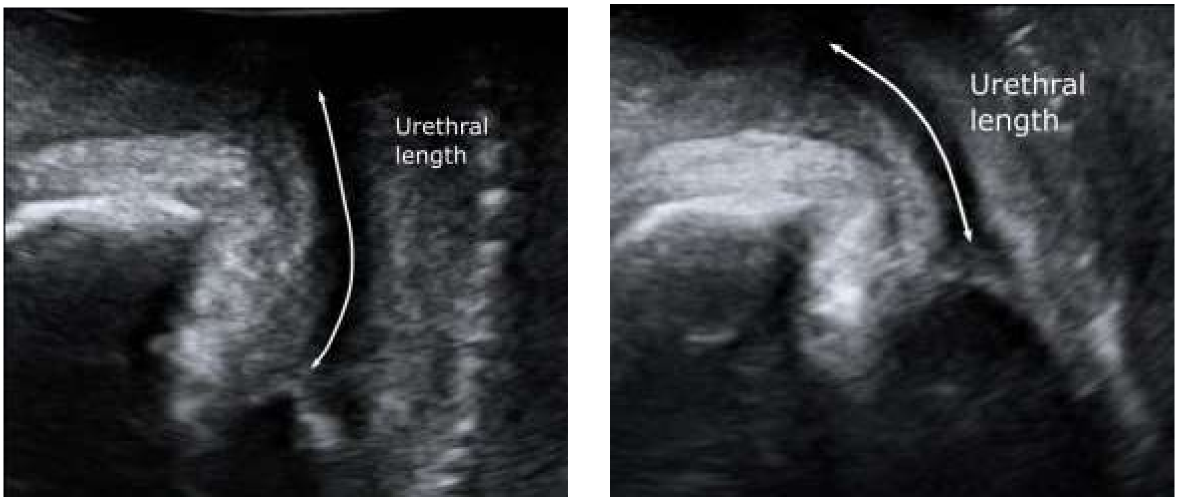
Point 1: At external urethral meatus, Point 2: Midway between midurethra and external urethral meatus, Point 3: At midurethra, Point 4: Midway between bladder neck and midurethra, Point 5: At the bladder neck



Urethral diameter at rest **Urethral diameter on cough**

Figure 10.2: Urethral length measurement

The arrow indicates the length of the urethra from the external meatus at the upper end to the vesico-urethral junction at the lower end.



Urethral length at rest **Urethral length on cough**

The data was analysed using SPSS software version 25 by IBM Compamy. Kruskal Wallis test and Chi square test were used for analysing data for 4 groups of urodynamic diagnoses. The data divided into 2 groups was analysed using Mann Whitney U test. The difference is considered to be significant if the probability is less than 5%.

10.4 Results

One hundred and fifty women were recruited for the study. 21 of these women had undergone continence procedure which could affect the urethral diameter on cough. 129

women did not have any previous continence procedure and they were included in this analysis. The UD of these women were as nondiagnostic urodynamics (NU) in 29 women, pure detrusor overactivity (PureDO) in 49 women, pure urodynamic stress incontinence (PureUSI) in 17 women and mixed incontinence (MUI) (DO and USI) in 34 women. There was no difference between age, body mass index or pelvic organ prolapse of women in these groups.

There was narrowing of the urethra at all 5 points in all the groups. Maximum mean narrowing of 17% was seen at the point 4. The mean urethral length was 2.55 cm. There was shortening of the urethra on cough by 15%. The mean diameter at different points at rest, on cough and the change in diameter at the 5 points along the urethra and the urethral length measurements were as shown in table 10.1.

The values in women with and without urodynamic stress incontinence were as shown in table 10.2. There was no significant difference in the mean urethral diameters at any point in women with different UD. Figure 10.3 represents changes in urethral dimension at point 4 and figure 10.4 shows urethral length on cough.

Table 10.2 shows analysis of the data according to the stress incontinence status. There was no major difference in the urethral diameters in the 2 groups. The urethra was shorter on cough in women with stress incontinence but the difference was not statistically significant. Figures 10.5 and 10.6 represent the data from this analysis.

Table 10.1: Urethral dimensions and urodynamic diagnoses

NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence

Measurement (cm)		NU (N=29)		DO (N=49)		USI (N=17)		MUI (N=34)		P value	Total (N=129)	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD		Mean	SD
Urethral diameter at rest of points -	1	0.57	0.19	0.54	0.15	0.53	0.11	0.58	0.25	0.756	0.56	0.18
	2	0.63	0.17	0.57	0.15	0.62	0.15	0.60	0.16	0.420	0.61	0.16
	3	0.70	0.17	0.70	0.21	0.70	0.19	0.70	0.17	0.965	0.70	0.19
	4	0.74	0.15	0.78	0.21	0.74	0.17	0.80	0.18	0.529	0.77	0.18
	5	0.65	0.18	0.64	0.20	0.66	0.17	0.70	0.20	0.432	0.66	0.19
Urethral diameter on cough at points -	1	0.51	0.21	0.48	0.18	0.54	0.20	0.47	0.15	0.777	0.49	0.17
	2	0.55	0.20	0.53	0.17	0.56	0.22	0.53	0.14	0.992	0.54	0.17
	3	0.63	0.24	0.59	0.19	0.60	0.20	0.59	0.14	0.954	0.60	0.18
	4	0.67	0.24	0.63	0.17	0.61	0.21	0.63	0.14	0.751	0.64	0.18
	5	0.63	0.23	0.57	0.18	0.55	0.17	0.64	0.21	0.381	0.61	0.20
Decrease in diameter at points-	1	0.07	0.12	0.05	0.13	0.01	0.19	0.11	0.27	0.349	0.08	0.18
	2	0.08	0.17	0.04	0.14	0.06	0.20	0.06	0.17	0.605	0.07	0.17
	3	0.07	0.22	0.10	0.19	0.10	0.17	0.11	0.19	0.971	0.10	0.20
	4	0.07	0.24	0.15	0.22	0.13	0.18	0.18	0.18	0.500	0.13	0.21
	5	0.03	0.17	0.06	0.21	0.10	0.15	0.06	0.27	0.620	0.05	0.22
Urethral length at rest		2.65	0.74	2.60	0.52	2.44	0.39	2.51	0.43	0.720	2.55	0.53
Urethral length on cough		2.34	0.61	2.24	0.57	2.01	0.64	2.09	0.58	0.285	2.18	0.59
Decrease in urethral length		0.31	0.81	0.37	0.62	0.43	0.65	0.42	0.49	0.632	0.37	0.63

Figure 10.3: Change in urethral diameter (cm) at point 4 and urodynamic diagnose

(median, IQR and range of measurements) NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence

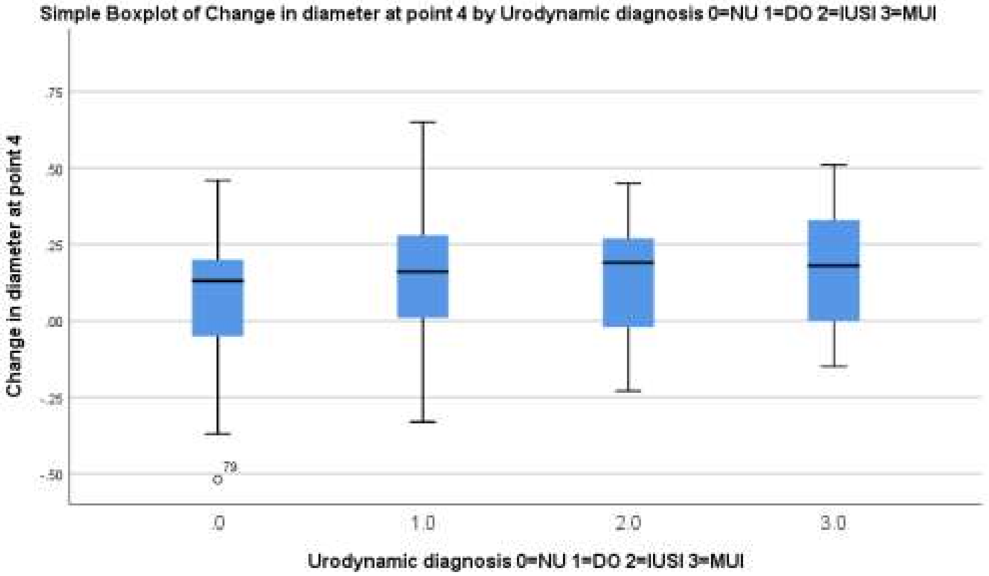


Figure 10.4: Urethral length (cm) on cough and urodynamic diagnoses.

(median, IQR and range of measurements) NU= nondiagnostic urodynamics, DO= detrusor overactivity, USI= urodynamic stress incontinence, MUI= mixed urinary incontinence

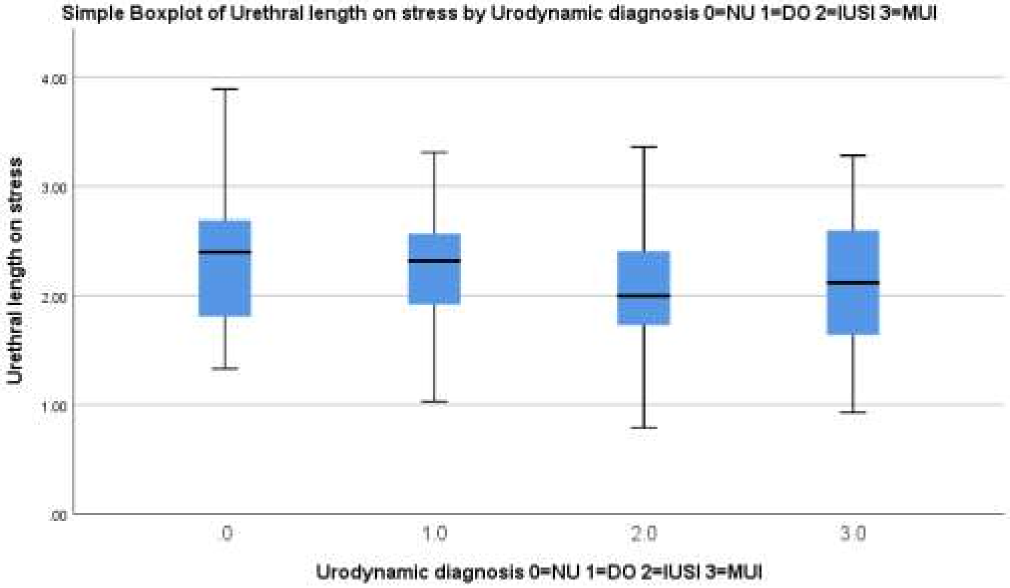


Table 10.2: Urethral dimensions and urodynamic stress incontinence

Measurement (cm)		Stress continence n=78		Urodynamic stress incontinence n=51		P value	Total n=129	
		Mean	SD	Mean	SD		Mean	SD
Urethral diameter at rest of points	1	0.55	0.17	0.57	0.21	0.923	0.56	0.18
	2	0.59	0.16	0.60	0.16	0.847	0.61	0.16
	3	0.70	0.19	0.70	0.17	0.912	0.70	0.19
	4	0.77	0.19	0.78	0.17	0.451	0.77	0.18
	5	0.64	0.19	0.68	0.19	0.197	0.66	0.19
Urethral diameter on cough at points	1	0.49	0.19	0.49	0.17	0.714	0.49	0.17
	2	0.54	0.18	0.54	0.17	0.811	0.54	0.17
	3	0.61	0.21	0.59	0.16	0.883	0.60	0.18
	4	0.65	0.20	0.62	0.17	0.369	0.64	0.18
	5	0.59	0.20	0.61	0.20	0.651	0.61	0.20
Decrease in diameter at points	1	0.06	0.12	0.07	0.25	0.787	0.08	0.18
	2	0.06	0.15	0.06	0.18	0.696	0.07	0.17
	3	0.09	0.20	0.10	0.18	0.994	0.10	0.20
	4	0.12	0.23	0.16	0.18	0.409	0.13	0.21
	5	0.05	0.20	0.07	0.24	0.305	0.05	0.22
Urethral length at rest		2.62	0.61	2.49	0.41	0.364	2.55	0.53
Urethral length on cough		2.27	0.58	2.07	0.59	0.073	2.18	0.59
Difference in urethral length		0.35	0.69	0.42	0.54	0.260	0.37	0.63

Figure 10.5: Resting diameter (cm) at point 4 and urodynamic stress incontinence. (Median, IQR and range) (0= stress continent, 2=stress incontinent)

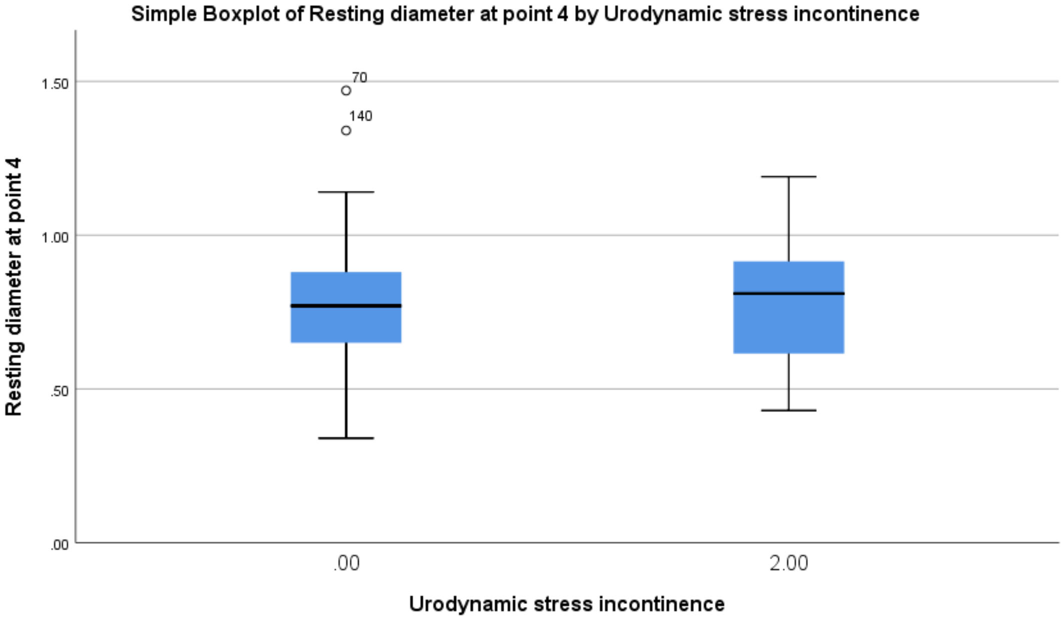
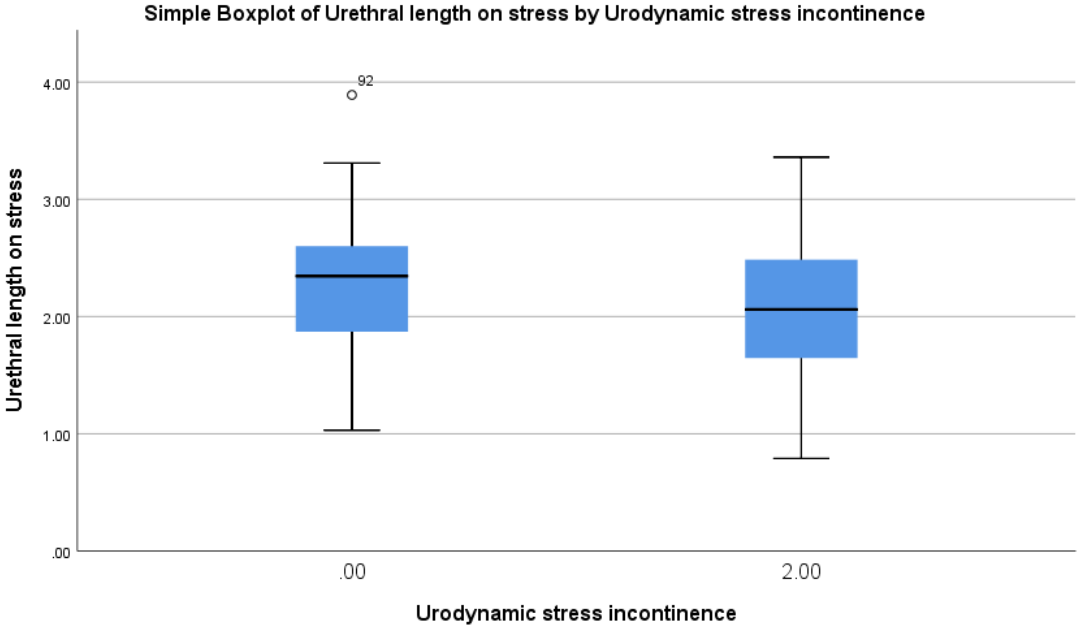


Figure 10.6: Urethral length (cm) on cough and urodynamic stress incontinence. (Median, IQR and range) (0= stress continent, 2=stress incontinent)



Data analysis according to the presence of DO is shown in the table 10.3. Women with the diagnosis of DO and MUI were included in the DO group and women with the UD of NU and PureUSI were put together in the group with normal detrusor activity. None of the measurements were significantly different between the groups.

Table 10.3: Urethral dimensions and detrusor overactivity

Measurement (cm)		Normal detrusor activity n=46		Detrusor overactivity n=83		P value	Total n=129	
		Mean	SD	Mean	SD		Mean	SD
Urethral diameter at rest of points	1	0.56	0.16	0.56	0.20	0.508	0.56	0.19
	2	0.63	0.16	0.58	0.15	0.111	0.60	0.16
	3	0.70	0.17	0.70	0.19	0.672	0.70	0.19
	4	0.74	0.16	0.79	0.20	0.220	0.77	0.19
	5	0.66	0.17	0.66	0.20	0.927	0.66	0.19
Urethral diameter on cough at points	1	0.52	0.20	0.48	0.17	0.384	0.49	0.18
	2	0.55	0.21	0.53	0.16	0.869	0.54	0.18
	3	0.62	0.23	0.59	0.17	0.714	0.60	0.19
	4	0.65	0.23	0.63	0.16	0.992	0.64	0.19
	5	0.60	0.21	0.60	0.19	0.616	0.60	0.20
Decrease in diameter at points	1	0.04	0.15	0.08	0.20	0.557	0.06	0.18
	2	0.07	0.18	0.05	0.15	0.309	0.06	0.16
	3	0.08	0.20	0.11	0.19	0.674	0.10	0.19
	4	0.09	0.22	0.16	0.20	0.192	0.14	0.21
	5	0.06	0.17	0.06	0.24	0.779	0.06	0.21
Urethral length at rest		2.57	0.64	2.57	0.48	0.527	2.57	0.54
Urethral length on cough		2.22	0.64	2.18	0.57	0.766	2.19	0.59
Difference in urethral length		0.36	0.75	0.39	0.57	0.580	0.38	0.64

10.5 Discussion

There was reduction in the mean urethral diameter at all 5 equidistant points along the urethra on coughing. This indicates urethral compression along the entire length of the urethra. Maximum reduction was seen at point 4 which approximately corresponds to the thickest portion of the external urethral sphincter (DeLancey 1988). When the spatial distribution and timing of the rise in urethral pressure was studied, there was pressure transmission in the same area indicating the importance of the activity of the urethral sphincter in maintaining the continence on stress (Constantinou and Govan 1982). This experiment supports the hypothesis that reflex sphincter contraction plays an important role in preventing stress incontinence.

The stress UPP studies indicated transmission of “abdominal pressure” to the proximal urethra. The distal part of urethra did not show an increase in pressure (Versi 1990). However, this study showed compression of the entire urethra, thus supporting the concept of Hammock formed of endopelvic fascia and the anterior vaginal wall being tightened during an increase in intra-abdominal pressure. However, the urethral compression was similar in all groups of women. There was no difference in urethral compression in stress continent and incontinent women. Limited compressibility of the urethral complex may be responsible for this finding. This study does not support the hypothesis that continence depends on the degree of support provided by these underlying structures.

Short urethra was once considered to be responsible for stress incontinence (Lapides et al. 1960). Surgery to elevate bladder neck and lengthen the urethra to 4cm were performed to treat the condition (Lapides et al. 1960). However, no difference in the urethral length was seen in women with and without SUI by other researchers (Low 1964; Hilton and Stanton 1983). This study did not find a significant difference in the urethral length at rest in women with respect to their continence status. The stress incontinent women had a shorter urethra on cough than continent women but the difference did not reach statistical significance (P=0.073).

10.6 Conclusion

Urethral compression on cough was seen in women with all UD and it was similar in women with or without urinary incontinence. The urethra was shorter on cough in women with USI but the difference did not reach statistical significance.

11. Vaginal Parity

11.1 Introduction

Pregnancy and childbirth have major effects on the urinary function due to the proximity of the urinary and genital systems. These effects can be temporary or have long term implications for the quality of life.

Pregnancy affects urinary function in many ways. The urine output is increased by about 25% from early pregnancy. The incidence of nocturia can increase to 53% (Parboosingh and Doig 1973). Stress urinary incontinence (SUI) is present in 3 to 5% of women before pregnancy and the risk increases to 26% to 55% during pregnancy (Al-Mukhtar Othman et al. 2017; Dolan et al. 2003). The incidence of urgency urinary incontinence (UUI) increases similarly from 6 to 15% at pre-pregnancy to 8 to 34% during pregnancy (Dolan et al. 2003; Fritel et al. 2012; Beksac et al. 2017; Dinc 2017). Some of these symptoms can be because of the increased risk of bacteriuria in pregnancy (Gilbert et al. 2013).

The overall incidence of urinary incontinence is 2.5 times in women after delivery (Hansen et al. 2012). A third of the incontinent postpartum women have de novo incontinence after the childbirth (Rocha et al. 2017). The overactive bladder (OAB) symptoms experienced during pregnancy tend to disappear, regardless of the mode of delivery, but the symptoms of SUI tend to persist longer after vaginal delivery (VD) (Botelho et al. 2012). The symptoms of incontinence improve over the 6 to 12 months period after delivery in the majority of the women and the frequency of incontinence episodes gradually decreases (Burgio et al. 2003; Viktrup and Lose 2008; Hansen et al. 2012)

Though the overall risk of urinary incontinence is higher after childbirth, women who have VD are at a higher risk than those who have elective or emergency caesarean section (CS) (Ekstrom et al. 2008; Chang et al. 2014; Tahtinen et al. 2016; Volloyhaug et al. 2017). Prolonged second stage and delivery with forceps increases this risk further (Gartland et al. 2012). Symptoms of mild and moderate SUI are more common after VD than CS (Altman, Ekstrom, et al. 2007). This difference is persistent at one year after the delivery (Hansen et al. 2012). However, the effect of mode of delivery on urinary symptoms disappears at 5 to 10 years after delivery (Altman, Ekstrom, et al. 2007). 20% to 25% of parous women have severe urinary incontinence symptoms a decade after the delivery irrespective of the mode of delivery (Viktrup and Lose 2008; MacArthur et al. 2011). If SUI was present in early pregnancy, it increased the risk of having the symptoms later, both in the VD as in CS group (van Brummen et al. 2007; Hantoushzadeh et al. 2011). Higher birth weight and head circumference of the baby are also implicated by some in increasing this risk (Wesnes, Hannestad, and Rortveit 2017). Parous women have increased risk of all types of urinary incontinence (UI) till the age of 65 years when the effect of parity is lost (Rortveit et al. 2010).

Pregnancy is characterised by high levels of oestrogen and progesterone. Receptors for these hormones are present abundantly in the lower urinary tract (Blakeman, Hilton, and Bulmer 2000). These hormones alter the biochemical properties of the connective tissue and increase water retention in the matrix (Buckingham, Selden, and Danforth 1962). There is loosening of collagen bundles and clear spaces appear between the fibres. There is reduced tensile strength of tissues during pregnancy and childbirth (Buckingham, Selden, and Danforth 1962). In addition to these changes, the growing uterus puts more pressure on the bladder and urethra, pressing them against the pubic symphysis and reducing the bladder capacity.

The genital hiatus is stretched by the passing foetal head during vaginal delivery. The pelvic floor bears an enormous strain resulting in the maximum stretch ratio of 3.26 over the pubococcygeus part of the pubovisceral muscle (Ashton-Miller and Delancey 2009). The pudendal nerve which supplies the urethral sphincter is stretched with the resulting strain effect of 13% (Lien et al. 2005). The greater the perineal descent, the greater the strain on the nerve. Nerve damage during childbirth is because of stretch as well as due to compression by the foetal head.

Vaginal parity increases the risk of urinary incontinence and the urethral sphincter volume is significantly related to the urodynamic diagnosis. To my knowledge, there are no studies published regarding measurement of urethral sphincter volume in women of different parity.

11.2 Aim

To find the difference in ultrasound measurements of the urethra in women with different vaginal parity.

11.3 Methodology

Women attending the urogynaecology department for urodynamic studies were recruited for the study. The inclusion and exclusion criteria were as described in the chapter on ‘Urethral sphincter measurement by 3D ultrasound’. Pretest assessment and urodynamic studies were performed as described in the chapter on ‘Urodynamic studies’. I performed the TPU of urethra as part of the study procedure as described in the methodology section of the chapters on ‘Urethral sphincter measurement by 3D ultrasound’ and on ‘The Validation Study for Ultrasound of Urethra’. Ethical approval for the study was obtained from the Queen Square Research Ethics Committee (REC reference number 15/LO/0264).

The women were divided into 4 groups according to the number of vaginal deliveries they had as 0, 1, 2 and 3 or more. Statistical analysis was performed using SPSS software version 25 by IBM Company. Kruskal-Wallis test and Chi square test were used to calculate statistical significance. A P-value of less than 0.05 was considered to be statistically significant. Ethical approval was obtained from Queen Square Research Ethics Committee (REC reference number 15/LO/0264).

11.4 Results

One hundred and fifty women were included in the study. The group with 0 parity included 28 women who were nulliparous and 6 women who had delivered by caesarean sections only. The number of women who had 1, 2 and 3 or more VD were 22, 48 and 46 respectively. The mean age of the study group was 52 years. The last childbirth was more than 3 years prior to entering the study. Each group included women of all urodynamic diagnoses (UD). The UD were nondiagnostic urodynamics (NU), pure detrusor overactivity (PureDO), pure urodynamic stress incontinence (PureUSI) and mixed incontinence (MUI) in 37, 53, 22 and 38 women respectively. There was no statistically significant difference in the UD among the groups (P>0.05). The demographics of the groups are shown in table 11.1.

Table 11.1: Demographics of women with different vaginal parity

Parameter	Number of vaginal deliveries				P value
	0 (n=34)	1 (n=22)	2 (n=48)	3 or more (n=46)	
Age	48	48	56	57	0.004
Body mass index	28	28	27	28	0.598
Cystocoele	6	13	16	23	0.004
Rectocoele	5	13	19	26	0.001

Urethral sphincter measurements in all the groups were as shown in table 11.2. The urethral sphincter measurements were significantly related to the number of vaginal deliveries (P<0.05). Figure 11.1 and 11.2 show the measurements of the total sphincter volume and the external sphincter volume in these women.

Table 11.2: Urethral sphincter measurement in women with different vaginal parity

Measurement	Number of vaginal deliveries								P value
	0 N=34		1 N=22		2 N=48		3 or more N=46		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Total sphincter volume in cc	3.01	0.99	1.96	1.32	2.32	1.04	2.37	0.95	0.000
Striated sphincter volume in cc	2.42	0.79	1.37	0.77	1.86	0.85	1.95	0.80	0.000
Core volume in cc	0.59	0.26	0.37	0.34	0.43	0.24	0.42	0.22	0.001
Rhabdo- sphincter length in cm	1.58	0.37	1.23	0.45	1.30	0.37	1.45	0.36	0.001
Maximum cross-sectional area in sq.cm	2.54	0.60	1.93	0.59	2.23	0.67	2.17	0.71	0.004

Figure 11.1: Total sphincter volume (cc) in all women who had vaginal deliveries

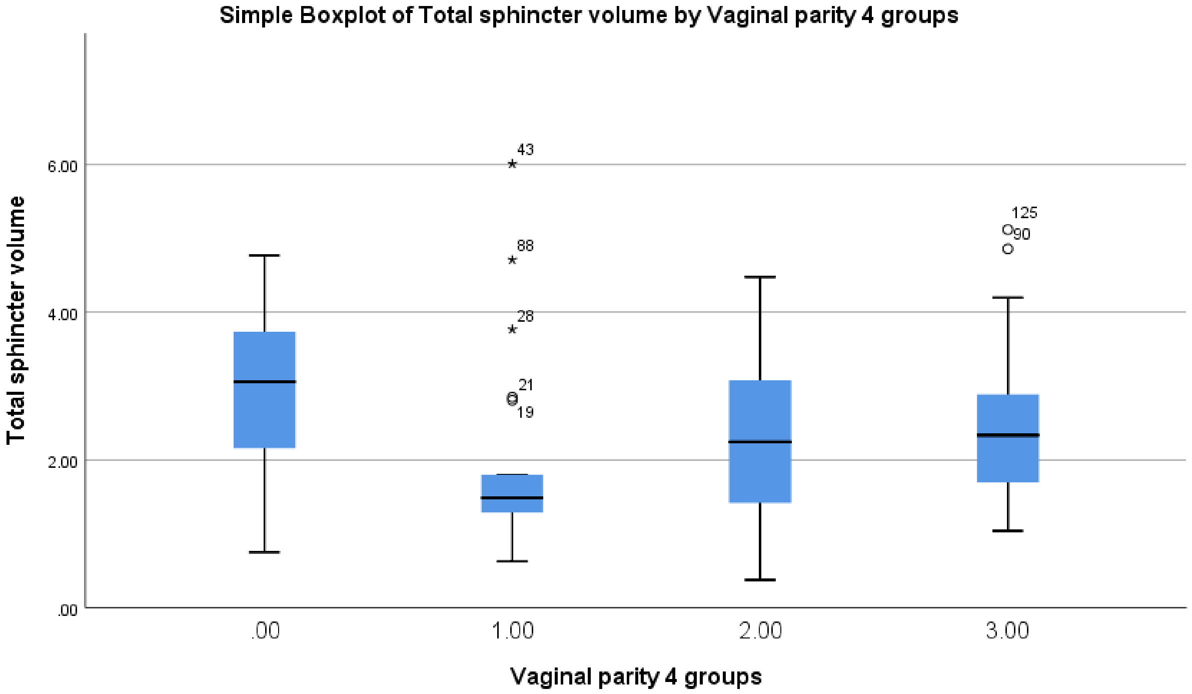
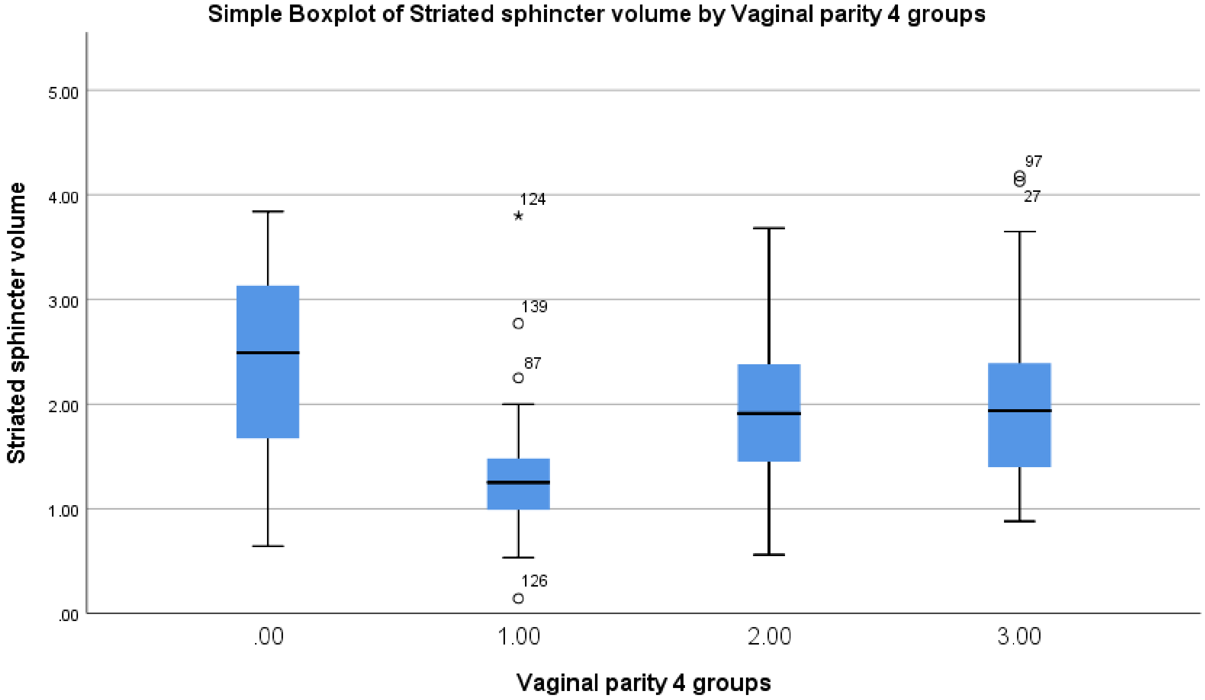


Figure 11.2: Striated sphincter volume (cc) in all women who had vaginal deliveries



The bladder neck measurements were as shown in table 11.3. The bladder neck position at rest was significantly different among the group. The difference in the bladder neck position on cough and the bladder neck movement was not statistically significant. Figure 3 shows the bladder neck position at rest in the 4 groups. Figure 11.4 and 11.5 show the urethral length at rest and on cough in 4 groups according to vaginal parity.

Table 11.3: Bladder neck position and movement in women with different vaginal parity

Measurement	Number of vaginal deliveries								P value	Total (N=150)	
	0 (N=34)		1 (N=22)		2 (N=48)		3 or more (N=46)				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		Mean	SD
Bladder neck											
Position at rest in cm	-1.56	0.55	-1.28	0.58	-1.26	0.58	-1.20	0.64	0.019	-1.32	0.60
Position on cough in cm	-0.30	0.80	0.11	0.81	-0.15	0.95	-0.02	0.83	0.137	-0.17	0.84
Movement in cm	1.26	0.95	1.47	0.75	1.14	0.81	1.01	0.83	0.089	1.17	0.85
Urethral length in cm											
At rest	2.71	0.45	2.32	0.44	2.61	0.59	2.47	0.52	0.010	2.55	0.53
On cough	2.35	0.55	1.83	0.64	2.26	0.59	2.13	0.53	0.007	2.18	0.59
Difference	0.36	0.59	0.49	0.52	0.35	0.72	0.34	0.61	0.432	0.57	0.63

Figure 11.3: Bladder neck position (cm) at rest and vaginal parity

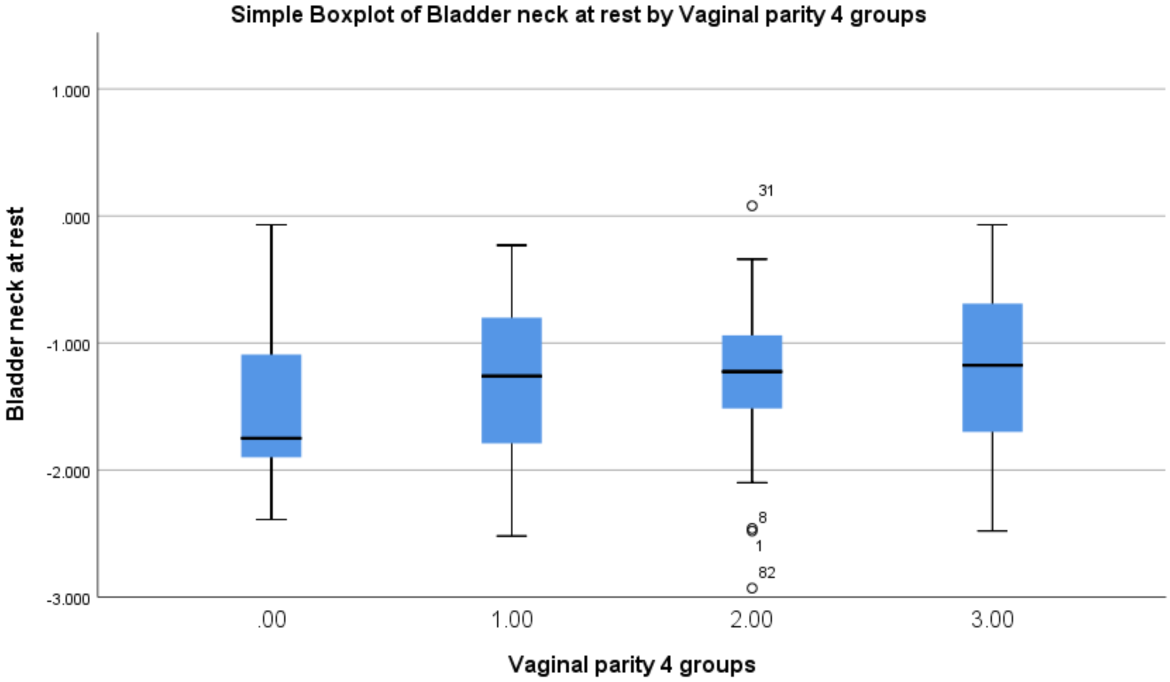


Figure11. 4: Urethral length (cm) at rest and vaginal parity

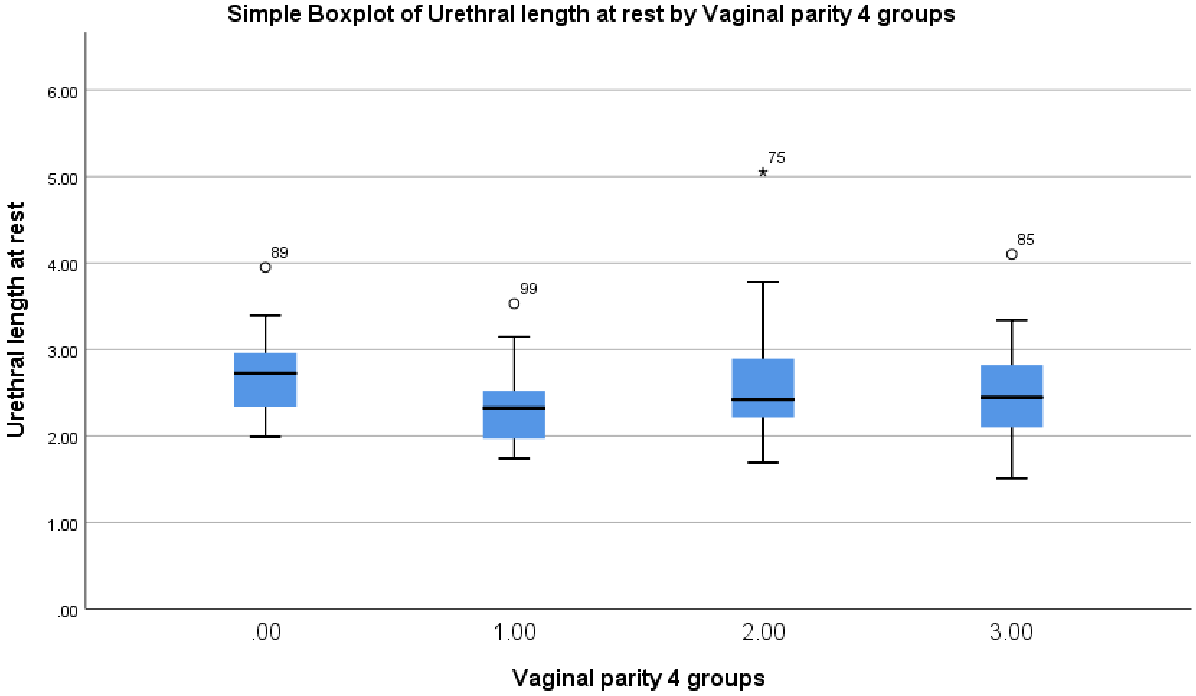
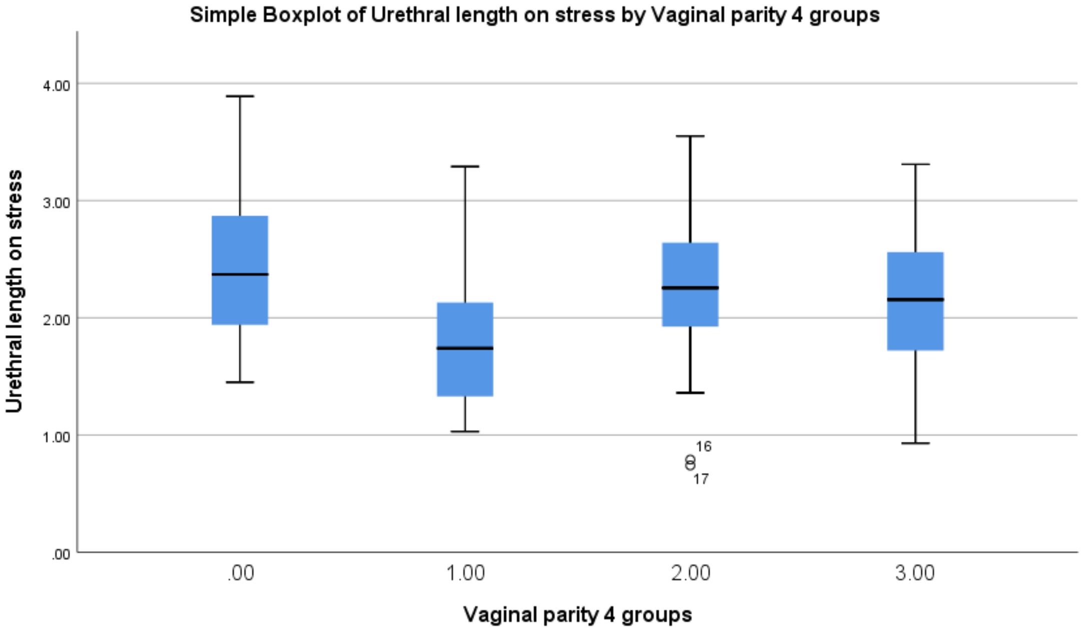


Figure 11.5: Urethral length (cm) on cough and vaginal parity



Continence surgery changes the position and mobility of the urethra. As shown by the studies previously discussed in this thesis, ultrasound measurements of the urethra are different in women with stress incontinence which is more prevalent in parous women. To eliminate this bias, the stress continent women without previous continence surgery were selected and they were divided into 2 groups as with or without VD. The difference in age and presence of major cystocoele and rectocoele remained significant. There was no relationship between the groups with respect to the urodynamic diagnosis (P=0.535). The demographics of these women were as shown in table 11.4 and the ultrasound measurements were as shown in table 11.5. All sphincter measurements remained significantly different in the 2 groups. Figure 11.6 and 11.7 show the sphincter volume measurements in the 2 groups. The difference in other observations did not reach statistical significance. These measurements were as shown in figures 11.8 and 11.9.

Table 11.4: Demographics of women without stress incontinence

Parameter	Number of vaginal deliveries		P value
	0 (n=23)	1 (n=55)	
Age	47	53	0.084
Body mass index	26	28	0.076
Cystocoele	3 (16%)	23 (44%)	0.005
Rectocoele	4 (17%)	28 (51%)	0.003

Table 11.5: Urethral sphincter measurements in stress continent women

Measurement	Number of vaginal deliveries				P value	Total (N=78)	
	0 (N=23)		1 or more (N=55)				
	Mean	SD	Mean	SD		Mean	SD
Total sphincter volume	3.13	1.04	2.36	0.98	0.003	2.59	1.05
Striated sphincter volume	2.53	0.83	1.95	0.81	0.005	2.12	0.86
Core volume	0.60	0.27	0.41	0.21	0.006	0.47	0.24
Sphincter length	1.61	0.36	1.40	0.39	0.024	1.46	0.39
Maximum cross-sectional area	2.51	0.65	2.17	0.61	0.028	2.27	0.63
Bladder neck at rest	-1.57	0.57	-1.40	0.59	0.132	-1.45	0.58
Bladder neck on cough	-0.44	0.72	-0.29	0.83	0.446	-0.33	0.80
Bladder neck movement	1.13	0.79	1.13	0.75	0.857	1.13	0.75
Urethral length at rest	2.69	0.47	2.59	0.66	0.234	2.62	0.61
Urethral length on cough	2.48	0.55	2.19	0.58	0.071	2.27	0.58
Difference in urethral length	0.22	0.56	0.40	0.74	0.343	0.35	0.69

Figure 11.6: Total sphincter volume (cc) and vaginal parity in women without stress incontinence or previous continence surgery

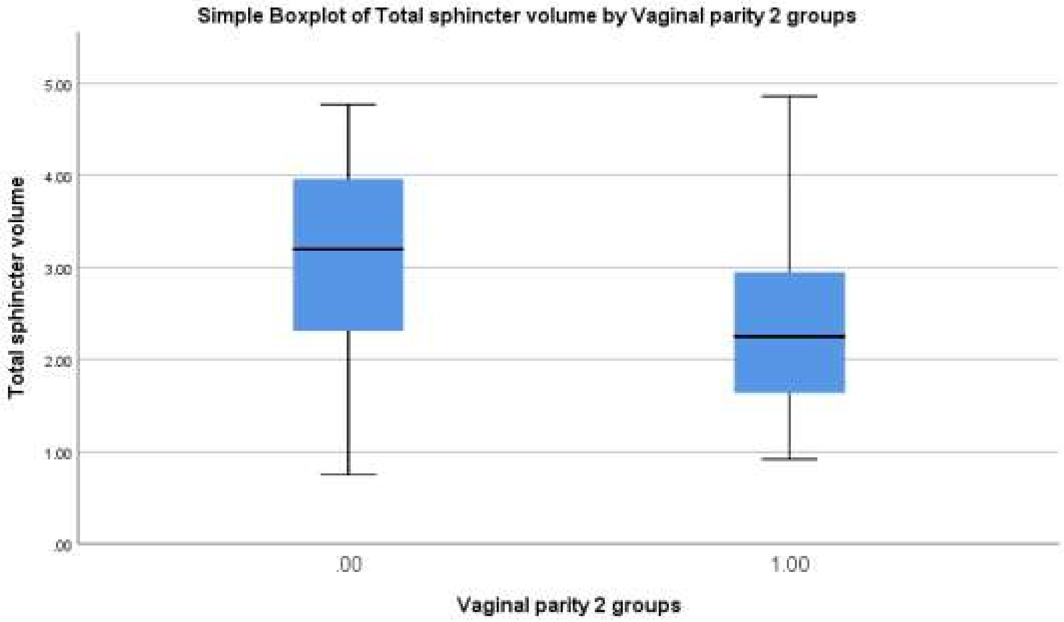


Figure 11.7: Striated sphincter volume (cc) and vaginal parity in women without stress incontinence or previous continence surgery

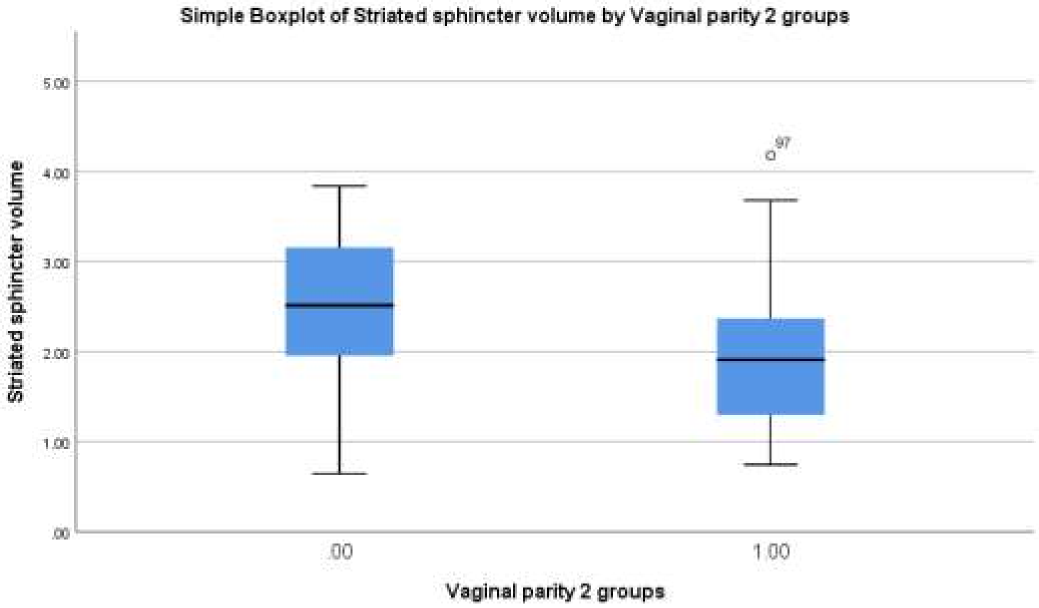


Figure 11.8: Bladder neck position (cm) at rest and vaginal parity in women without stress incontinence or previous continence surgery

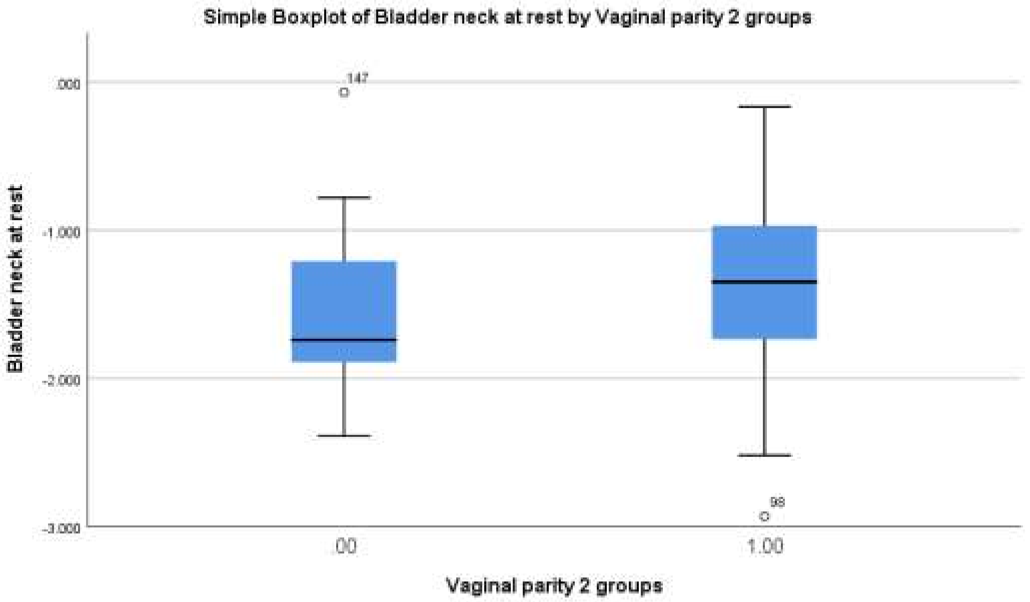


Figure 11.9: Urethral length (cm) at rest and vaginal parity in women without stress incontinence or previous continence surgery

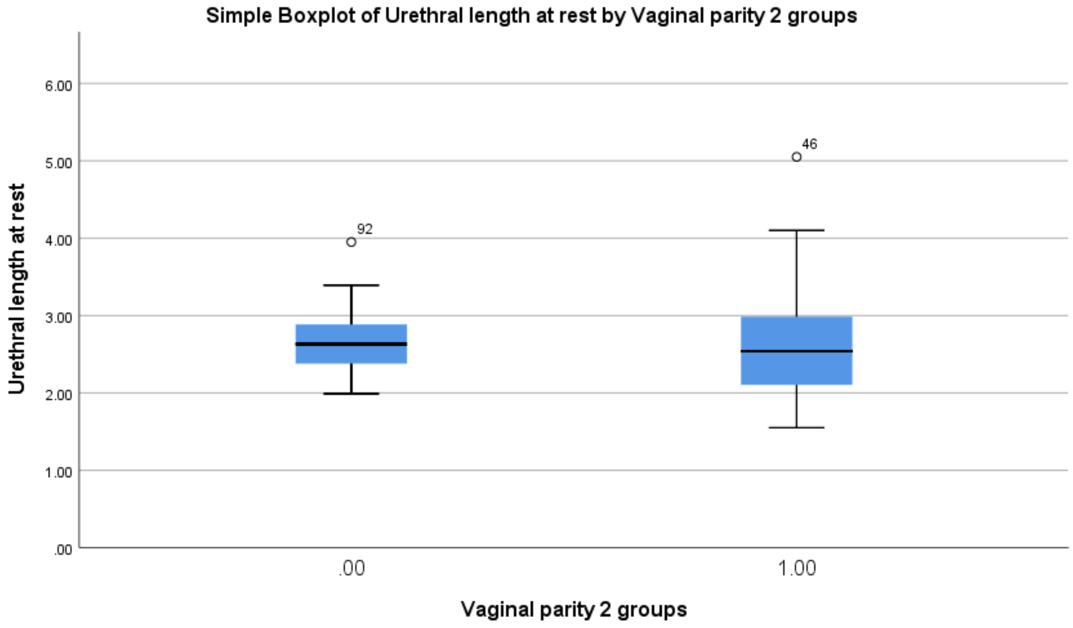
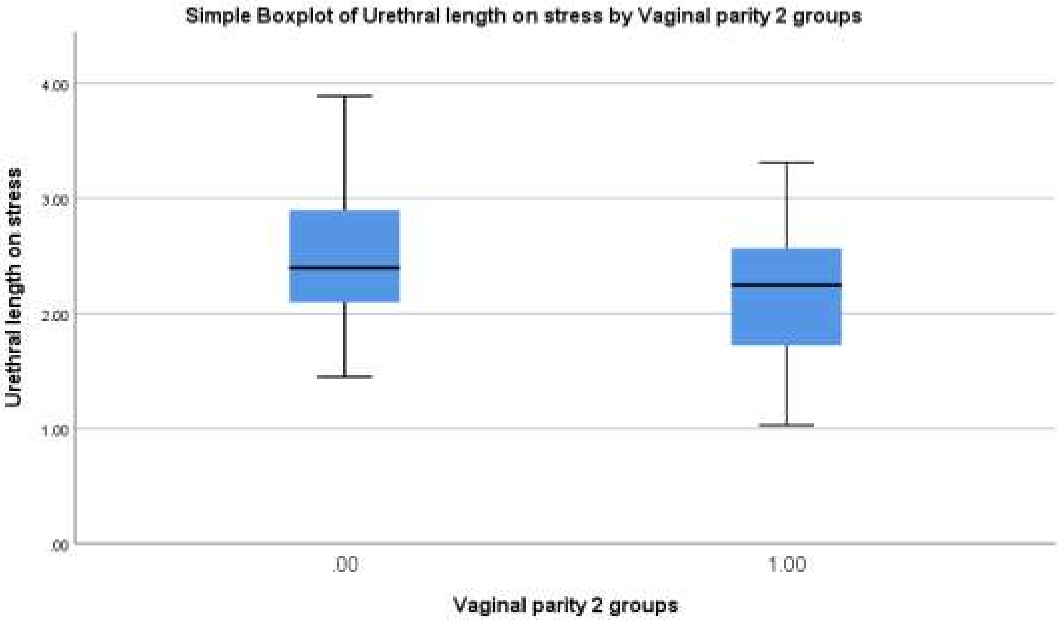


Figure 11.10: Urethral length (cm) on cough and vaginal parity in women without stress incontinence or previous continence surgery



11.5 Discussion

The study showed the differences in the urethral anatomy in women who had vaginal delivery and those who did not. The urethral sphincter was significantly smaller in the vaginally parous groups than vaginally nulliparous group. This difference remained significant when stress continent women without previous continence surgery were selected. The differentiating factor among the groups was the vaginal delivery. The difference in sphincter volume was possibly due to the neuromuscular damage from the vaginal birth. It was unlikely that this difference was related to the short term effect of pregnancy as all the women had their last childbirth more than 3 years before entering the study.

The neuromuscular trauma during delivery may result in lowering of bladder neck position as well as SUI (Demirci et al. 2001; Volloyhaug et al. 2017). Recovery from the neuromuscular damage can take many months and the recovery may be minimal (Weidner et al. 2009; Cosimato et al. 2015). It was observed in this study that the bladder neck was at a lower position at rest in parous women than the nulliparous. However, this difference was not significant when only stress continent women without previous continence surgery were considered. Similarly, the difference in urethral length was eliminated in this second analysis. It can be postulated that though the sphincter is damaged by childbirth, continence is maintained in parous women because of the ligamentous and muscular support maintaining the bladder neck position and urethral length.

This study showed that sphincter volume in primiparous women was significantly lower than the nulliparous women. However, the sphincter volume in multiparous women was similar to primiparous women. It was seen in past studies that the urethral sphincter volume was lower in women with SUI (Frauscher et al. 1998; Athanasiou et al. 1999). About a third of postnatal incontinent women develop the SUI symptom after the vaginal delivery (Rocha et al. 2017). Many of these women request elective CS for their subsequent delivery as they worry about further damage to the urethral sphincter by another VD and worsening of the SUI symptoms. This study shows that the changes in the urethral sphincter occur as a result of first VD, and that subsequent vaginal deliveries may not add to the damage. Women can be reassured by the findings of the study; doing so will help in reducing the elective CS rate after successful VD.

These findings are in contrast with the obstetric anal sphincter injury (OASI). Women with altered faecal continence after first VD are at a higher risk of deterioration after second VD. The risk of mechanical anal sphincter injury is greatest during the first VD (Fynes et al. 1999; Jango et al. 2017). Risk of recurrent OASI is 7% and the risk of anal incontinence increases to 50% in these women against 37% in women who have second delivery without OASI (Jango et al. 2017). Elective CS after OASI for symptomatic women can be justified on this basis.

Defects in levator ani muscle are seen after a VD due to mechanical stretching by the foetal head. However, the changes in urethra associated with SUI may not be related of these defects. 50% primiparous women in a study experienced SUI when the incidence of levator ani defect was 20% (DeLancey et al. 2003). Another study diagnosed levator ani defect in only 20% of women with postpartum SUI (Hegde, Aguilar, and Davila 2017). Neurophysiological studies have assessed the effect of vaginal birth on the pelvic floor (Snooks et al. 1990). Pudendal nerve dysfunction causing weakness in perineal musculature was observed after vaginal birth and was persistent after many years. The symptoms due to this damage may become evident many years after the damage takes place. Continent parous women with reduced sphincter volume may be at a higher risk of developing SUI after many years.

Reduction in urethral sphincter volume was seen after delivery on 3 dimensional transvaginal ultrasound (TVU) (Robinson et al. 2004). However, the relationship seen antenatally between the sphincter volume and urethral pressure was lost at 3 to 6 months after delivery. The changes due to pregnancy persist much longer than 6 months after delivery. Electromyography study of the urethral sphincter has shown persistent changes following VD at 6 months postpartum (Weidner et al. 2009). An extended study is needed to assess the long term relationship between structure and function of the sphincter and childbirth.

Age related changes are seen in the urethral sphincter in cadaveric studies. The thickness of the urethral sphincter decreases by 1.5 to 4.6% every year in older women (Perucchini et al. 2002). 2% of the striated muscle fibres in the urethra are lost each year(Perucchini et al. 2002). A urethral pressure study on continent women has shown that the urethral pressure increases from infancy to 20 to 25 years of age and then gradually decreases (Rud 1980a; Kapoor et al. 2012). The mean ages of the different groups in my study were significantly different. However, there was a major difference between the sphincter volumes of the nulliparous and primiparous groups which had the same mean age. This indicates that this difference in the sphincter volume is unlikely to be because of the age. The urethral pressure diminishes by 1 cm of water per year (Kapoor et al. 2012). This difference may not be clinically significant. Vaginal wall prolapse was seen more commonly in parous women. It was a known consequence of vaginal delivery but it was not related to the stress incontinence status of women in this study.

The drawback of this study is that it is a cross-sectional study. A large number of cases are needed to overcome the effect of individual case. A longitudinal ultrasound study on urethral measurements in nulliparous women and following them up after each vaginal delivery would give us more reliable results.

11.6 Conclusion

Women who had a vaginal delivery had significantly smaller urethral sphincter but it did not always translate into stress incontinence. There was no difference in the mean urethral sphincter volume of primiparous and multiparous women. Incidence of cystocoele and rectocoele was higher in parous women. The urethral dimensions, position and mobility were similar in stress continent women with or without vaginal delivery.

12 Multifactorial Analysis

12.1 Analysis for four urodynamics diagnoses

One hundred and fifty women who had urodynamic studies were divided into four groups according to their urodynamic diagnosis such as nondiagnostic urodynamics (NU), pure urodynamic stress incontinence (PUSI), pure detrusor overactivity (PDO) and mixed urinary incontinence (MUI). Various ultrasound measurements were performed on these women with the urethra at rest and on strong cough. The association of these measurements with the four groups has been discussed thoroughly in the previous chapters. The mean urethral sphincter measurements using 3 dimensional transperineal ultrasound showed that measurements, such as, the total sphincter volume, striated sphincter volume, core volume, sphincter length and maximum cross-sectional diameter, were all significantly different among these four groups. The urethral mobility, on the other hand, was found to be similar in all these groups. The bladder neck positions were different among the groups. But after the Bonferroni correction for multiple comparisons, the bladder neck position on cough, but not at rest, remained significantly different among the groups. The urethral diameter and urethral length though did not differ in these four groups.

12.2 Analysis for stress incontinence

When the women were divided into two groups with respect to their stress incontinence status, it was found that the women with urodynamic stress incontinence (with or without detrusor overactivity) had significantly smaller sphincter measurements compared to other women. These women had a lower position of the bladder neck, at rest and on cough. The distal quartile of their urethra was also at a significantly lower position at rest. One parameter from each category that was significantly different was selected for multiple regression analysis. These 3 measurements were striated sphincter volume, position of bladder neck on cough and position of external urethral meatus at rest. The logistic regression model was found to be statistically significant using Chi square test with P=0.001. The model explained 15.6% (Nagelkerke R^2) of the variance in USI and correctly classified 68.2% of the cases. Increasing striated sphincter volume was associated with a reduction in the likelihood of USI (P=0.038, OR = 0.617), and lower position of bladder neck was associated with an increased likelihood of diagnosing USI (P=0.021, OR=1.730). Position of external urethral meatus at rest did not add to the model significantly.

12.3 Analysis for detrusor overactivity

The women were divided into 2 groups based on whether they demonstrated detrusor overactivity on urodynamic studies or had a stable detrusor. Those with a detrusor overactivity (with or without stress incontinence) had significantly larger urethral sphincter, lower position of the bladder neck at rest and a shorter distance between the pubic symphysis and the upper quartile of the urethra. Striated sphincter volume, position of bladder neck at rest and distance of the bladder neck from the pubic symphysis at rest were used in the logistic regression to find their effect on the likelihood of DO. The logistic regression model was statistically significant using Chi square test with P=0.000. The model explained 18.1% (Nagelkerke R^2) of the variance in USI and correctly classified 69.8% of the cases. Increasing striated sphincter volume was associated with an increased likelihood of DO (P=0.001, OR = 2.294), but position of bladder neck at rest (P=0.164) and distance of the bladder neck from the pubic symphysis at rest (P=0.139) did not add to the model significantly.

13. Conclusion and Future Studies

13.1 Conclusion

The aim of my research was to understand the pathophysiology of urinary incontinence using transperineal ultrasound and to understand the value of ultrasound in making a urological diagnosis and planning the treatment. To achieve this aim, I measured the urethral sphincter and developed a new method of measuring urethral dimensions and mobility and bladder neck mobility. I conducted variability studies to prove the validity of this method before using this method in my research. The important findings of my research are as shown in the table 13.1.

Table 13.1: Ultrasound measurements for the major incontinence groups as compared to the continent group

Measurement	Detrusor overactivity	Urodynamic stress incontinence
Uretrhal sphincter volume	Larger	Smaller
Bladder neck position at rest	Lower	Lower
Bladder neck position on cough	Similar	Lower
Bladder neck movement	Similar	Similar

The urethral sphincter volume measured smaller in women with urodynamic stress incontinence (USI) as already proven by previous studies. A smaller sphincter may not be able to raise the urethral pressure above the intravesical pressure on stress. Additionally, this study found that the sphincter was significantly larger in women with detrusor overactivity (DO). It was an interesting finding that the women with mixed urinary incontinence (MUI) had mean sphincter volume similar to the women with nondiagnostic urodynamics (NU).

The urethra was found to be mobile in all study groups. I found that the mean urethral mobility measured at five points along its length was not different in women with NU and different types of urinary incontinence. There was no difference in mobility of different segments of the urethra between the groups. These findings of mobility in women with incontinence were contrary to the findings published in literature. This study could not prove the causative effect of urethral hypermobility on stress continence.

The available evidence regarding bladder neck mobility causing stress incontinence was contradictory. This research showed that the bladder neck was considerably mobile in all the groups and its mobility was similar in women with or without urinary incontinence. The mean bladder neck position at rest and on cough was significantly lower in women with USI when compared with the women who were continent on stress. The resting position was lower in women with DO than without.

Urethral diameter measurements confirmed urethral compression on cough but the degree of compression was similar in all study groups. The Hammock hypothesis of reduced support from anterior vaginal wall causing stress incontinence was not supported by this study. The urethral length was smaller on cough in women with USI but this finding did not reach statistical significance at 5%.

This study confirmed the current opinion that women who had vaginal childbirth had higher incidence of vaginal prolapse. Analysis of the data from this study with respect to urethral structure gave some interesting results as shown in table 13.2. Stress continent women with 1 or more vaginal deliveries had smaller urethral sphincter than those who had none but the urethral dimensions and its mobility were similar in the 2 groups. However, the sphincter volume in multiparous women was not smaller than the primiparous women. This information may reassure women regarding progressive deteriorating effect of multiple vaginal deliveries on the urethra and thus help reduce the number of maternal requests for caesarean section for subsequent deliveries.

Findings in women with MUI were interesting and helpful in understanding the condition better. The mean urethral sphincter size in these women was significantly larger than those with isolated USI. It was also similar in size to those with NU. So the sphincter size alone could not explain the cause of stress incontinence in these women. On measuring the bladder neck position, these women had significantly lower positioned bladder neck at rest and on cough than women with NU. This shows that it is not the smaller sphincter but the low location of bladder neck on stress and lack of pressure transmission which might be making these women prone to leakage on stress.

On multiple logistic regression analysis, higher striated sphincter volume was associated with a reduced likelihood of USI (P=0.038, OR = 0.617), and lower bladder neck position was associated with an increased likelihood of diagnosing USI (P=0.021, OR=1.730). Position of external urethral meatus at rest did not add significantly to the model. On the contrary, higher striated sphincter volume was associated with an increased likelihood of DO (P=0.001, OR = 2.294), but position of bladder neck at rest (P=0.164) and distance of the bladder neck from the pubic symphysis at rest (P=0.139) did not add significantly to the model.

13.2 Future studies

The work for this thesis included a pilot study using the new method of measuring urethral and bladder neck mobility and urethral dimensions. More studies using the same method will further validate the method. Studies with larger numbers will confirm the findings of this study.

Studies using the same method but different radiological investigation such as MRI will also be advantageous.

This study included 21 women who had undergone continence procedure. 20 of them had undergone tension free vaginal tape procedure and only 1 woman had undergone colposuspension. Studies involving more women with these procedures will help us understand the mechanism of action of these procedures.

A prospective study on nulliparous women following them after vaginal deliveries will show the effect of vaginal parity on the urethra more clearly though such study would span over many years.

Measuring bladder wall thickness at a specific bladder volume in addition to the parameters used in this study will throw more light on the pathophysiology of overactive bladder and DO.

References

Abou-Gamrah, A., M. Fawzy, H. Sammour, and S. Tadros. 2014. 'Ultrasound assessment of bladder wall thickness as a screening test for detrusor instability', *Arch Gynecol Obstet*, 289: 1023-8.

Agarwal, P., and M. L. Rosenberg. 2003. 'Neurological evaluation of urinary incontinence in the female patient', *Neurologist*, 9: 110-7.

Akselim, B., M. Doganay, N. Ozcan, S. Akselim, and S. Cavkaytar. 2017. 'Correlation of bladder wall thickness and treatment success in types of urinary incontinence', *Int Urogynecol J*, 28: 417-22.

Al-Hayek, S., M. Belal, and P. Abrams. 2008. 'Does the patient's position influence the detection of detrusor overactivity?', *Neurourol Urodyn*, 27: 279-86.

Al-Mukhtar Othman, J., S. Akervall, I. Milsom, and M. Gyhagen. 2017. 'Urinary incontinence in nulliparous women aged 25-64 years: a national survey', *Am J Obstet Gynecol*, 216: 149 e1-49 e11.

Al-Saadi, W. I. 2016. 'Transperineal ultrasonography in stress urinary incontinence: The significance of urethral rotation angles', *Arab J Urol*, 14: 66-71.

Al-Shaikh, G., and H. Al-Mandeel. 2012. 'Ultrasound estimated bladder weight in asymptomatic adult females', *Urol J*, 9: 586-91.

Alper, T., M. Cetinkaya, S. Okutgen, A. Kokcu, and E. Malatyalioglu. 2001. 'Evaluation of urethrovesical angle by ultrasound in women with and without urinary stress incontinence', *Int Urogynecol J Pelvic Floor Dysfunct*, 12: 308-11.

Altman, D., A. Ekstrom, C. Forsgren, J. Nordenstam, and J. Zetterstrom. 2007. 'Symptoms of anal and urinary incontinence following cesarean section or spontaneous vaginal delivery', *Am J Obstet Gynecol*, 197: 512 e1-7.

Altman, D., F. Granath, S. Cnattingius, and C. Falconer. 2007. 'Hysterectomy and risk of stress-urinary-incontinence surgery: nationwide cohort study', *Lancet*, 370: 1494-9.

Andersson, K. E., and A. Arner. 2004. 'Urinary bladder contraction and relaxation: physiology and pathophysiology', *Physiol Rev*, 84: 935-86.

Arunkalaivanan, A. S., S. Mahomoud, and M. Howell. 2004. 'Does posture affect cystometric parameters and diagnoses?', *Int Urogynecol J Pelvic Floor Dysfunct*, 15: 422-4; discussion 24.

Ashton-Miller, J. A., and J. O. Delancey. 2009. 'On the biomechanics of vaginal birth and common sequelae', *Annu Rev Biomed Eng*, 11: 163-76.

Athanasiou, S., V. Khullar, K. Boos, S. Salvatore, and L. Cardozo. 1999. 'Imaging the urethral sphincter with three-dimensional ultrasound', *Obstet Gynecol*, 94: 295-301.

Atherton, M. J., and S. L. Stanton. 2000. 'A comparison of bladder neck movement and elevation after tension-free vaginal tape and colposuspension', *BJOG*, 107: 1366-70.

Bacsu, C. D., C. Cunningham, A. Christie, and P. E. Zimmern. 2015. 'Durability of collagen injection for stress urinary incontinence in women proven by transvaginal 3-dimensional ultrasound', *Female Pelvic Med Reconstr Surg*, 21: 25-9.

Bader, W., F. Degenhardt, W. Kauffels, K. Nehls, and J. Schneider. 1995. '[Ultrasound morphologic parameters of female stress incontinence]', *Ultraschall Med*, 16: 180-5.

Baessler, K., M. Metz, and B. Junginger. 2017. 'Valsalva versus straining: There is a distinct difference in resulting bladder neck and puborectalis muscle position', *Neurourol Urodyn*, 36: 1860-66.

Bansal, R., M. M. Agarwal, M. Modi, A. K. Mandal, and S. K. Singh. 2011. 'Urodynamic profile of diabetic patients with lower urinary tract symptoms: association of diabetic cystopathy with autonomic and peripheral neuropathy', *Urology*, 77: 699-705.

Barber, M. D., A. Lambers, A. G. Visco, and R. C. Bump. 2000. 'Effect of patient position on clinical evaluation of pelvic organ prolapse', *Obstet Gynecol*, 96: 18-22.

Bates, C. P., and C. E. Corney. 1971. 'Synchronous cine-pressure-flow cystography: a method of routine urodynamic investigation', *Br J Radiol*, 44: 44-50.

Beco, J., D. Leonard, and R. Lambotte. 1994. 'Study of the artefacts induced by linear array transvaginal ultrasound scanning in urodynamics', *World J Urol*, 12: 329-32.

Beksac, A. T., E. Aydin, C. Orhan, E. Karaagaoglu, and T. Akbayrak. 2017. 'Gestational Urinary Incontinence in Nulliparous Pregnancy- A Pilot Study', *J Clin Diagn Res*, 11: QC01-QC03.

Berild, G. H., and S. Kulseng-Hanssen. 2012. 'Reproducibility of a cough and jump stress test for the evaluation of urinary incontinence', *Int Urogynecol J*, 23: 1449-53.

Berkow, S. G. 1953. 'The corpus spongeosum of the urethra: its possible role in urinary control and stress incontinence in women', *Am J Obstet Gynecol*, 65: 346-51.

Birder, L., and J. J. Wyndaele. 2013. 'From urothelial signalling to experiencing a sensation related to the urinary bladder', *Acta Physiol (Oxf)*, 207: 34-9.

Blakeman, P. J., P. Hilton, and J. N. Bulmer. 2000. 'Oestrogen and progesterone receptor expression in the female lower urinary tract, with reference to oestrogen status', *BJU Int*, 86: 32-8.

Bogusiewicz, M., M. Monist, K. Galczynski, M. Wozniak, A. P. Wieczorek, and T. Rechberger. 2014. 'Both the middle and distal sections of the urethra may be regarded as optimal targets for 'outside-in' transobturator tape placement', *World J Urol*, 32: 1605-11.

Bohlin, K. S., M. Ankardal, H. Lindkvist, and I. Milsom. 2017. 'Factors influencing the incidence and remission of urinary incontinence after hysterectomy', *Am J Obstet Gynecol*, 216: 53 e1-53 e9.

Booth, C. M., P. J. Shah, E. J. Milroy, S. A. Thompson, and J. A. Gosling. 1983. 'The structure of the bladder neck in male bladder neck obstruction', *Br J Urol*, 55: 279-82.

Borirakchanyavat, S., S. R. Aboseif, P. R. Carroll, E. A. Tanagho, and T. F. Lue. 1997. 'Continence mechanism of the isolated female urethra: an anatomical study of the intrapelvic somatic nerves', *J Urol*, 158: 822-6.

Botelho, S., J. M. Silva, P. Palma, V. Herrmann, and C. Riccetto. 2012. 'Can the delivery method influence lower urinary tract symptoms triggered by the first pregnancy?', *Int Braz J Urol*, 38: 267-76.

Botlero, R., S. R. Davis, D. M. Urquhart, S. Shortreed, and R. J. Bell. 2009. 'Age-specific prevalence of, and factors associated with, different types of urinary incontinence in community-dwelling Australian women assessed with a validated questionnaire', *Maturitas*, 62: 134-9.

Braekken, I. H., M. Majida, M. Ellstrom-Engh, H. P. Dietz, W. Umek, and K. Bo. 2008. 'Test-retest and intra-observer repeatability of two-, three- and four-dimensional perineal ultrasound of pelvic floor muscle anatomy and function', *Int Urogynecol J Pelvic Floor Dysfunct*, 19: 227-35.

Bray, R., R. Cartwright, L. Cardozo, S. Hill, Z. Guan, and V. Khullar. 2018. 'Tolterodine ER reduced increased bladder wall thickness in women with overactive bladder. A randomized, placebo-controlled, double-blind, parallel group study', *Neurourol Urodyn*, 37: 237-43.

Brennand, E. A., S. Tang, C. Birch, M. Murphy, S. Ross, M. Robert, and Group Calgary Women's Pelvic Health Research. 2017. 'Five years after midurethral sling surgery for stress incontinence: obesity continues to have an impact on outcomes', *Int Urogynecol J*, 28: 621-28.

Bright, E., N. Cotterill, M. Drake, and P. Abrams. 2014. 'Developing and validating the International Consultation on Incontinence Questionnaire bladder diary', *Eur Urol*, 66: 294-300.

Bright, E., R. Pearcy, and P. Abrams. 2012. 'Automatic evaluation of ultrasonography-estimated bladder weight and bladder wall thickness in community-dwelling men with presumably normal bladder function', *BJU Int*, 109: 1044-9.

Brown, M., and J. E. Wickham. 1969. 'The urethral pressure profile', *Br J Urol*, 41: 211-7.

Bruschini, H., J. C. Truzzi, R. Simonetti, R. Mesquita, R. Delcelo, J. Szenfeld, and M. Srougi. 2006. 'Paraurethral leiomyoma in a female causing urinary obstruction', *Int Urogynecol J Pelvic Floor Dysfunct*, 17: 286-9.

Buchman, N. M., S. E. Leurgans, R. J. Shah, V. VanderHorst, R. S. Wilson, Y. G. Bachner, D. Tanne, J. A. Schneider, D. A. Bennett, and A. S. Buchman. 2017. 'Urinary Incontinence, Incident Parkinsonism, and Parkinson's Disease Pathology in Older Adults', *J Gerontol A Biol Sci Med Sci*, 72: 1295-301.

Buckingham, J. C., R. Selden, and D. N. Danforth. 1962. 'Connective tissue changes in the cervix during pregnancy and labor', *Ann N Y Acad Sci*, 97: 733-42.

Bump, R. C., W. E. Copeland, Jr., W. G. Hurt, and J. A. Fantl. 1988. 'Dynamic urethral pressure/profilometry pressure transmission ratio determinations in stress-incontinent and stress-continent subjects', *Am J Obstet Gynecol*, 159: 749-55.

Bump, R. C., D. M. Elser, J. P. Theofrastous, and D. K. McClish. 1995. 'Valsalva leak point pressures in women with genuine stress incontinence: reproducibility, effect of catheter caliber, and correlations with other measures of urethral resistance. Continence Program for Women Research Group', *Am J Obstet Gynecol*, 173: 551-7.

Bump, R. C., and D. K. McClish. 1992. 'Cigarette smoking and urinary incontinence in women', *Am J Obstet Gynecol*, 167: 1213-8.

Bump, R. C., H. J. Sugerman, J. A. Fantl, and D. K. McClish. 1992. 'Obesity and lower urinary tract function in women: effect of surgically induced weight loss', *Am J Obstet Gynecol*, 167: 392-7; discussion 97-9.

Burgio, K. L., H. Zyczynski, J. L. Locher, H. E. Richter, D. T. Redden, and K. C. Wright. 2003. 'Urinary incontinence in the 12-month postpartum period', *Obstet Gynecol*, 102: 1291-8.

Burnett, A. L. 1995. 'Nitric oxide control of lower genitourinary tract functions: a review', *Urology*, 45: 1071-83.

Burrows, L. J., L. A. Meyn, M. D. Walters, and A. M. Weber. 2004. 'Pelvic symptoms in women with pelvic organ prolapse', *Obstet Gynecol*, 104: 982-8.

Caine, M. 1986. 'Peripheral factors in urinary continence', *J Urol (Paris)*, 92: 521-30.

Caputo, R. M., and J. T. Benson. 1993. 'The Q-tip test and urethrovesical junction mobility', *Obstet Gynecol*, 82: 892-6.

Carlile, A., I. Davies, E. Faragher, and J. C. Brocklehurst. 1987. 'The epithelium in the female urethra: a quantitative study', *J Urol*, 138: 775-7.

Caruso, D. J., P. Kanagarajah, B. L. Cohen, R. Ayyathurai, C. Gomez, and A. E. Gousse. 2010. 'What is the predictive value of urodynamics to reproduce clinical findings of urinary frequency, urge urinary incontinence, and/or stress urinary incontinence?', *Int Urogynecol J*, 21: 1205-9.

Cassado Garriga, J., A. Pessarrodona Isern, M. Rodriguez Carballeira, M. Pallarols Badia, M. Moya Del Corral, M. Valls Esteve, and E. Huguet Galofre. 2017. 'Three-dimensional translabial ultrasound assessment of urethral supports and the urethral sphincter complex in stress urinary incontinence', *Neurourol Urodyn*, 36: 1839-45.

Cassado, J., A. Pessarrodona, R. Tulleuda, L. Cabero, M. Valls, S. Quintana, and M. Rodriguez-Carballeira. 2006. 'Introital ultrasonography: a comparison of women with stress incontinence due to urethral hypermobility and continent women', *BJU Int*, 98: 822-8.

Chalana, V., S. Dudycha, J. T. Yuk, and G. McMorrow. 2005. 'Automatic Measurement of Ultrasound-Estimated Bladder Weight (UEBW) from Three-Dimensional Ultrasound', *Rev Urol*, 7 Suppl 6: S22-8.

Chang, S. R., K. H. Chen, H. H. Lin, M. I. Lin, T. C. Chang, and W. A. Lin. 2014. 'Association of mode of delivery with urinary incontinence and changes in urinary incontinence over the first year postpartum', *Obstet Gynecol*, 123: 568-77.

Chapple, C. R., C. W. Helm, S. Blease, E. J. Milroy, D. Rickards, and J. L. Osborne. 1989. 'Asymptomatic bladder neck incompetence in nulliparous females', *Br J Urol*, 64: 357-9.

Chen, G. D., T. H. Su, and L. Y. Lin. 1997. 'Applicability of perineal sonography in anatomical evaluation of bladder neck in women with and without genuine stress incontinence', *J Clin Ultrasound*, 25: 189-94.

Chen, S. L., S. C. Ng, Y. H. Huang, and G. D. Chen. 2017. 'Are patients with bladder oversensitivity different from those with urodynamically proven detrusor overactivity in female overactive bladder syndrome?', *J Chin Med Assoc*, 80: 644-50.

Chester, J., P. Toozs-Hobson, and F. Israfil-Bayli. 2016. 'The role of ambulatory urodynamics in investigation of female urinary incontinence', *Int Urogynecol J*, 27: 381-6.

Christiansen, U. J., M. J. Hansen, and F. F. Lauszus. 2017. 'Hysterectomy is not associated with de-novo urinary incontinence: A ten-year cohort study', *Eur J Obstet Gynecol Reprod Biol*, 215: 175-79.

Chuang, F. C., and H. C. Kuo. 2009. 'Videourodynamic evaluation of urge syndrome following pubovaginal sling procedure for stress urinary incontinence in women', *Int Urogynecol J Pelvic Floor Dysfunct*, 20: 1253-8.

Chung, S. D., C. H. Liao, Y. C. Chen, and H. C. Kuo. 2011. 'Urgency severity scale could predict urodynamic detrusor overactivity in patients with overactive bladder syndrome', *Neurourol Urodyn*, 30: 1300-4.

Clobes, A., J. O. DeLancey, and D. M. Morgan. 2008. 'Urethral circular smooth muscle in young and old women', *Am J Obstet Gynecol*, 198: 587 e1-5.

Constantinou, C. E., and D. E. Govan. 1982. 'Spatial distribution and timing of transmitted and reflexly generated urethral pressures in healthy women', *J Urol*, 127: 964-9.

Cosimato, C., L. M. Cipullo, J. Troisi, A. Di Spiezio Sardo, G. A. Tommaselli, R. R. Oro, F. Zullo, V. Altieri, and M. Guida. 2015. 'Ultrasonographic evaluation of urethrovesical junction mobility: correlation with type of delivery and stress urinary incontinence', *Int Urogynecol J*, 26: 1495-502.

Costantini, S., C. Nadalini, F. Esposito, M. M. Valenzano, D. Risso, P. Lantieri, and E. Mistrangelo. 2005. 'Perineal ultrasound evaluation of the urethrovesical junction angle and urethral mobility in nulliparous women and women following vaginal delivery', *Int Urogynecol J Pelvic Floor Dysfunct*, 16: 455-9.

Cross, J. J., M. Fynes, L. Berman, and D. Perera. 2001. 'Prevalence of cystic paraurethral structures in asymptomatic women at endovaginal and perineal sonography', *Clin Radiol*, 56: 575-8.

Cruikshank, S. H., and S. R. Kovac. 1997. 'The functional anatomy of the urethra: role of the pubourethral ligaments', *Am J Obstet Gynecol*, 176: 1200-3; discussion 03-5.

Crystle, C. D., L. S. Charme, and W. E. Copeland. 1971. 'Q-tip test in stress urinary incontinence', *Obstet Gynecol*, 38: 313-5.

Cucchi, A., S. Siracusano, P. Di Benedetto, M. Comelli, and B. Rovereto. 2004. 'Urgency of voiding and abdominal pressure transmission in women with mixed urinary incontinence', *Neurourol Urodyn*, 23: 43-7.

D'Ancona, C. A. L., M. J. Gomes, and Pfwm Rosier. 2017. 'ICS teaching module: Cystometry (basic module)', *Neurourol Urodyn*, 36: 1673-76.

de Groat, W. C. 1993. 'Anatomy and physiology of the lower urinary tract', *Urol Clin North Am*, 20: 383-401.

Deffieux, X., K. Hubeaux, R. Porcher, S. S. Ismael, P. Raibaut, and G. Amarenco. 2007. 'Decrease in urethral pressure following repeated cough efforts: a new concept for pathophysiology of stress urinary incontinence', *Int J Urol*, 14: 1019-24.

DeLancey, J. O. 1986. 'Correlative study of paraurethral anatomy', *Obstet Gynecol*, 68: 91-7.

———. 1988. 'Structural aspects of the extrinsic continence mechanism', *Obstet Gynecol*, 72: 296-301.

———. 1990. 'Functional anatomy of the female lower urinary tract and pelvic floor', *Ciba Found Symp*, 151: 57-69; discussion 69-76.

———. 1994. 'Structural support of the urethra as it relates to stress urinary incontinence: the hammock hypothesis', *Am J Obstet Gynecol*, 170: 1713-20; discussion 20-3.

Delancey, J. O., and J. A. Ashton-Miller. 2004. 'Pathophysiology of adult urinary incontinence', *Gastroenterology*, 126: S23-32.

DeLancey, J. O., R. Kearney, Q. Chou, S. Speights, and S. Binno. 2003. 'The appearance of levator ani muscle abnormalities in magnetic resonance images after vaginal delivery', *Obstet Gynecol*, 101: 46-53.

DeLancey, J. O., E. R. Trowbridge, J. M. Miller, D. M. Morgan, K. Guire, D. E. Fenner, W. J. Weadock, and J. A. Ashton-Miller. 2008. 'Stress urinary incontinence: relative importance of urethral support and urethral closure pressure', *J Urol*, 179: 2286-90; discussion 90.

Demirci, F., S. Ozden, Z. Alpay, E. T. Demirci, and S. Ayas. 2001. 'The effects of vaginal delivery and cesarean section on bladder neck mobility and stress urinary incontinence', *Int Urogynecol J Pelvic Floor Dysfunct*, 12: 129-33.

Derpapas, A., S. Ahmed, G. Vijaya, G. A. Digesu, L. Regan, R. Fernando, and V. Khullar. 2012. 'Racial differences in female urethral morphology and levator hiatal dimensions: an ultrasound study', *Neurourol Urodyn*, 31: 502-7.

Derpapas, A., A. G. Digesu, G. Vijaya, R. Fernando, and V. Khullar. 2012. 'Real-time in vivo assessment of levator ani muscle deformation in women', *Eur J Obstet Gynecol Reprod Biol*, 165: 352-6.

Di Pietto, L., C. Scaffa, M. Torella, A. Lambiase, L. Cobellis, and N. Colacurci. 2008. 'Perineal ultrasound in the study of urethral mobility: proposal of a normal physiological range', *Int Urogynecol J Pelvic Floor Dysfunct*, 19: 1405-9.

Dietz, H. P., and P. D. Wilson. 1999. 'The influence of bladder volume on the position and mobility of the urethrovesical junction', *Int Urogynecol J Pelvic Floor Dysfunct*, 10: 3-6.

———. 2004. 'The 'iris effect': how two-dimensional and three-dimensional ultrasound can help us understand anti-incontinence procedures', *Ultrasound Obstet Gynecol*, 23: 267-71.

Digesu, G. A., L. Bombieri, A. Hutchings, V. Khullar, and R. Freeman. 2004. 'Effects of Burch colposuspension on the relative positions of the bladder neck to the levator ani muscle: An observational study that used magnetic resonance imaging', *Am J Obstet Gynecol*, 190: 614-9.

Digesu, G. A., N. Calandrini, A. Derpapas, P. Gallo, S. Ahmed, and V. Khullar. 2012. 'Intraobserver and interobserver reliability of the three-dimensional ultrasound imaging of female urethral sphincter using a translabial technique', *Int Urogynecol J*, 23: 1063-8.

Digesu, G. A., V. Khullar, L. Cardozo, and S. Salvatore. 2003. 'Overactive bladder symptoms: do we need urodynamics?', *Neurourol Urodyn*, 22: 105-8.

———. 2004. 'The open bladder neck: a significant finding?', *Int Urogynecol J Pelvic Floor Dysfunct*, 15: 336-9.

Digesu, G. A., D. Robinson, L. Cardozo, and V. Khullar. 2009. 'Three-dimensional ultrasound of the urethral sphincter predicts continence surgery outcome', *Neurourol Urodyn*, 28: 90-4.

Dinc, A. 2017. 'Prevalence of Urinary Incontinence During Pregnancy and Associated Risk Factors', *Low Urin Tract Symptoms*.

Dokita, S., S. D. Smith, T. Nishimoto, M. A. Wheeler, and R. M. Weiss. 1994. 'Involvement of nitric oxide and cyclic GMP in rabbit urethral relaxation', *Eur J Pharmacol*, 266: 269-75.

Dokmeci, F., M. Seval, and H. Gok. 2010. 'Comparison of ambulatory versus conventional urodynamics in females with urinary incontinence', *Neurourol Urodyn*, 29: 518-21.

Dolan, L. M., G. L. Hosker, V. T. Mallett, R. E. Allen, and A. R. Smith. 2003. 'Stress incontinence and pelvic floor neurophysiology 15 years after the first delivery', *BJOG*, 110: 1107-14.

Donald, I. 1974. 'Sonar--the story of an experiment', *Ultrasound Med Biol*, 1: 109-17.

Drake, M. J., A. Apostolidis, A. Cocci, A. Emmanuel, J. B. Gajewski, S. C. Harrison, J. P. Heesakkers, G. E. Lemack, H. Madersbacher, J. N. Panicker, P. Radziszewski, R. Sakakibara, and J. J. Wyndaele.

2016. 'Neurogenic lower urinary tract dysfunction: Clinical management recommendations of the Neurologic Incontinence committee of the fifth International Consultation on Incontinence 2013', *Neurourol Urodyn*, 35: 657-65.

Duckett, J., and D. Chakani. 2013. 'The effect of prolapse repair on urinary flow rates and the relationship to changes in the ultrasound appearance of the bladder neck', *Eur J Obstet Gynecol Reprod Biol*, 171: 372-5.

Duckett, J., A. Patil, and I. Aggarwal. 2008. 'The effect of duloxetine on urethral sphincter morphology', *Ultrasound Obstet Gynecol*, 31: 206-9.

Duong, T. H., and A. P. Korn. 2001. 'A comparison of urinary incontinence among African American, Asian, Hispanic, and white women', *Am J Obstet Gynecol*, 184: 1083-6.

Dwarkasing, R. S., W. Dinkelaar, W. C. Hop, A. B. Steensma, G. R. Dohle, and G. P. Krestin. 2011. 'MRI evaluation of urethral diverticula and differential diagnosis in symptomatic women', *AJR Am J Roentgenol*, 197: 676-82.

Ekstrom, A., D. Altman, I. Wiklund, C. Larsson, and E. Andolf. 2008. 'Planned cesarean section versus planned vaginal delivery: comparison of lower urinary tract symptoms', *Int Urogynecol J Pelvic Floor Dysfunct*, 19: 459-65.

Elia, G., and A. Bergman. 1996. 'Periurethral collagen implant: ultrasound assessment and prediction of outcome', *Int Urogynecol J Pelvic Floor Dysfunct*, 7: 335-8.

English, S. F., C. L. Amundsen, and E. J. McGuire. 1999. 'Bladder neck competency at rest in women with incontinence', *J Urol*, 161: 578-80.

Enhorning, G. 1961. 'Simultaneous recording of intravesical and intra-urethral pressure. A study on urethral closure in normal and stress incontinent women', *Acta Chir Scand Suppl*, Suppl 276: 1-68.

Eppel, W., P. Frigo, C. Worda, and D. Bettelheim. 2000. 'Ultrasound imaging of Bartholin's cysts', *Gynecol Obstet Invest*, 49: 179-82.

Fantl, J. A., W. G. Hurt, M. C. Beachley, H. A. Bosch, K. F. Konerding, and P. J. Smith. 1981. 'Bead-chain cystourethrogram: an evaluation', *Obstet Gynecol*, 58: 237-40.

Ferreira, C. H., and K. Bo. 2015. 'The Pad Test for urinary incontinence in women', *J Physiother*, 61: 98.

Flock, F., F. Kohorst, R. Kreienberg, and A. Reich. 2011. 'Ultrasound assessment of tension-free vaginal tape (TVT)', *Ultraschall Med*, 32 Suppl 1: S35-40.

Foldspang, A., S. Mommsen, G. W. Lam, and L. Elving. 1992. 'Parity as a correlate of adult female urinary incontinence prevalence', *J Epidemiol Community Health*, 46: 595-600.

Ford, A. A., and J. A. Ogah. 2016. 'Retropubic or transobturator mid-urethral slings for intrinsic sphincter deficiency-related stress urinary incontinence in women: a systematic review and meta-analysis', *Int Urogynecol J*, 27: 19-28.

Ford, A. A., L. Rogerson, J. D. Cody, and J. Ogah. 2015. 'Mid-urethral sling operations for stress urinary incontinence in women', *Cochrane Database Syst Rev*: CD006375.

Forsgren, C., C. Lundholm, A. L. Johansson, S. Cnattingius, J. Zetterstrom, and D. Altman. 2012. 'Vaginal hysterectomy and risk of pelvic organ prolapse and stress urinary incontinence surgery', *Int Urogynecol J*, 23: 43-8.

Fowler, C. J., D. Griffiths, and W. C. de Groat. 2008. 'The neural control of micturition', *Nat Rev Neurosci*, 9: 453-66.

Frauscher, F., G. Helweg, H. Strasser, B. Enna, A. Klauser, R. Knapp, K. Colleselli, G. Bartsch, and D. Zur Nedden. 1998. 'Intraurethral ultrasound: diagnostic evaluation of the striated urethral sphincter in incontinent females', *Eur Radiol*, 8: 50-3.

Fritel, X., V. Ringa, E. Quiboeuf, and A. Fauconnier. 2012. 'Female urinary incontinence, from pregnancy to menopause: a review of epidemiological and pathophysiological findings', *Acta Obstet Gynecol Scand*, 91: 901-10.

Fusco, F., M. Abdel-Fattah, C. R. Chapple, M. Creta, S. La Falce, D. Waltregny, and G. Novara. 2017. 'Updated Systematic Review and Meta-analysis of the Comparative Data on Colposuspensions, Pubovaginal Slings, and Midurethral Tapes in the Surgical Treatment of Female Stress Urinary Incontinence', *Eur Urol*, 72: 567-91.

Fynes, M., V. Donnelly, M. Behan, P. R. O'Connell, and C. O'Herlihy. 1999. 'Effect of second vaginal delivery on anorectal physiology and faecal continence: a prospective study', *Lancet*, 354: 983-6.

Gartland, D., S. Donath, C. MacArthur, and S. J. Brown. 2012. 'The onset, recurrence and associated obstetric risk factors for urinary incontinence in the first 18 months after a first birth: an Australian nulliparous cohort study', *BJOG*, 119: 1361-9.

Gerrard, E. R., Jr., L. K. Lloyd, W. S. Kubricht, and P. N. Kolettis. 2003. 'Transvaginal ultrasound for the diagnosis of urethral diverticulum', *J Urol*, 169: 1395-7.

Giannantoni, A., S. M. Di Stasi, A. Cucchi, E. Mearini, V. Bini, and M. Porena. 2003. 'Pelvic floor muscle behavior during Valsalva leak point pressure measurement in males and females affected by stress urinary incontinence', *J Urol*, 170: 485-9.

Gilbert, N. M., V. P. O'Brien, S. Hultgren, G. Macones, W. G. Lewis, and A. L. Lewis. 2013. 'Urinary tract infection as a preventable cause of pregnancy complications: opportunities, challenges, and a global call to action', *Glob Adv Health Med*, 2: 59-69.

Gosling, J. A. 1996. 'The structure of the bladder neck, urethra and pelvic floor in relation to female urinary continence', *Int Urogynecol J Pelvic Floor Dysfunct*, 7: 177-8.

Gosling, J. A., J. S. Dixon, H. O. Critchley, and S. A. Thompson. 1981. 'A comparative study of the human external sphincter and periurethral levator ani muscles', *Br J Urol*, 53: 35-41.

Green, T. H., Jr. 1957. 'Urinary stress incontinence in women', *Am J Nurs*, 57: 598-600.

———. 1962. 'Development of a plan for the diagnosis and treatment of urinary stress incontinence', *Am J Obstet Gynecol*, 83: 632-48.

———. 1968. 'The problem of urinary stress incontinence in the female: an appraisa of its current status', *Obstet Gynecol Surv*, 23: 603-34.

Griffiths, D. 2015. 'Neural control of micturition in humans: a working model', *Nat Rev Urol*, 12: 695-705.

Grigoriadis, T., G. Giannoulis, D. Zacharakis, A. Protopapas, L. Cardozo, and S. Athanasiou. 2016. 'The "1-3-5 cough test": comparing the severity of urodynamic stress incontinence with severity measures of subjective perception of stress urinary incontinence', *Int Urogynecol J*, 27: 419-25.

Gugliotta, G., G. Calagna, G. Adile, S. Polito, P. Speciale, A. Perino, and B. Adile. 2015. 'Use of trans-labial ultrasound in the diagnosis of female urethral diverticula: A diagnostic option to be strongly considered', *J Obstet Gynaecol Res*, 41: 1108-14.

Guralnick, M. L., G. Grimsby, M. Liss, A. Szabo, and R. C. O'Connor. 2010. 'Objective differences between overactive bladder patients with and without urodynamically proven detrusor overactivity', *Int Urogynecol J*, 21: 325-9.

Haderer, J. M., H. K. Pannu, R. Genadry, and G. M. Hutchins. 2002. 'Controversies in female urethral anatomy and their significance for understanding urinary continence: observations and literature review', *Int Urogynecol J Pelvic Floor Dysfunct*, 13: 236-52.

Haeusler, G., C. Sam, A. Chiari, C. Tempfer, E. Hanzal, and H. Koelbl. 1998. 'Effect of spinal anaesthesia on the lower urinary tract in continent women', *Br J Obstet Gynaecol*, 105: 103-6.

Hale, D. S., J. T. Benson, L. Brubaker, M. C. Heidkamp, and B. Russell. 1999. 'Histologic analysis of needle biopsy of urethral sphincter from women with normal and stress incontinence with comparison of electromyographic findings', *Am J Obstet Gynecol*, 180: 342-8.

Handa, V. L., J. K. Jensen, and D. R. Ostergard. 1995. 'The effect of patient position on proximal urethral mobility', *Obstet Gynecol*, 86: 273-6.

Hannestad, Y. S., G. Rortveit, A. K. Daltveit, and S. Hunskaar. 2003. 'Are smoking and other lifestyle factors associated with female urinary incontinence? The Norwegian EPINCONT Study', *BJOG*, 110: 247-54.

Hannestad, Y. S., G. Rortveit, H. Sandvik, S. Hunskaar, and Epincont study Epidemiology of Incontinence in the County of Nord-Trondelag Norwegian. 2000. 'A community-based epidemiological survey of female urinary incontinence: the Norwegian EPINCONT study. Epidemiology of Incontinence in the County of Nord-Trondelag', *J Clin Epidemiol*, 53: 1150-7.

Hansen, B. B., J. Svare, L. Viktrup, T. Jorgensen, and G. Lose. 2012. 'Urinary incontinence during pregnancy and 1 year after delivery in primiparous women compared with a control group of nulliparous women', *Neurourol Urodyn*, 31: 475-80.

Hantoushzadeh, S., P. Javadian, M. Shariat, B. Salmanian, S. Ghazizadeh, and M. Aghssa. 2011. 'Stress urinary incontinence: pre-pregnancy history and effects of mode of delivery on its postpartum persistency', *Int Urogynecol J*, 22: 651-5.

Hanzal, E., E. Berger, and H. Koelbl. 1991. 'Reliability of the urethral closure pressure profile during stress in the diagnosis of genuine stress incontinence', *Br J Urol*, 68: 369-71.

Harms, L., G. Emons, W. Bader, R. Lange, R. Hilgers, and V. Viereck. 2007. 'Funneling before and after anti-incontinence surgery--a prognostic indicator? Part 2: tension-free vaginal tape', *Int Urogynecol J Pelvic Floor Dysfunct*, 18: 289-94.

Harris, N., L. Swithinbank, S. A. Hayek, Q. Yang, and P. Abrams. 2011. 'Can maximum urethral closure pressure (MUCP) be used to predict outcome of surgical treatment of stress urinary incontinence?', *Neurourol Urodyn*, 30: 1609-12.

Harrison, N. W., and A. R. Constable. 1970. 'Urethral pressure measurement: a modified technique', *Br J Urol*, 42: 229-33.

Hashim, H., and P. Abrams. 2006. 'Is the bladder a reliable witness for predicting detrusor overactivity?', *J Urol*, 175: 191-4; discussion 94-5.

Haylen, B. T., D. Ashby, J. R. Sutherst, M. I. Frazer, and C. R. West. 1989. 'Maximum and average urine flow rates in normal male and female populations--the Liverpool nomograms', *Br J Urol*, 64: 30-8.

Haylen, B. T., D. de Ridder, R. M. Freeman, S. E. Swift, B. Berghmans, J. Lee, A. Monga, E. Petri, D. E. Rizk, P. K. Sand, and G. N. Schaer. 2010. 'An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction', *Int Urogynecol J*, 21: 5-26.

Hegde, A., V. C. Aguilar, and G. W. Davila. 2017. 'Levator ani defects in patients with stress urinary incontinence: three-dimensional endovaginal ultrasound assessment', *Int Urogynecol J*, 28: 85-93.

Hegde, A., A. L. Smith, V. C. Aguilar, and G. W. Davila. 2013. 'Three-dimensional endovaginal ultrasound examination following injection of Macroplastique for stress urinary incontinence: outcomes based on location and periurethral distribution of the bulking agent', *Int Urogynecol J*, 24: 1151-9.

Heit, M. 2000. 'Intraurethral ultrasonography: correlation of urethral anatomy with functional urodynamic parameters in stress incontinent women', *Int Urogynecol J Pelvic Floor Dysfunct*, 11: 204-11.

Hennemann, J., L. N. Kennes, N. Maass, and L. Najjari. 2014. 'Evaluation of established and new reference lines for the standardization of transperineal ultrasound', *Ultrasound Obstet Gynecol*, 44: 610-6.

Hennigan, H. W., Jr., and T. J. DuBose. 1985. 'Sonography of the normal female urethra', *AJR Am J Roentgenol*, 145: 839-41.

Hilton, P., and S. L. Stanton. 1983. 'Urethral pressure measurement by microtransducer: the results in symptom-free women and in those with genuine stress incontinence', *Br J Obstet Gynaecol*, 90: 919-33.

Hodgkinson, C. P., and H. P. Doub. 1953. 'Roentgen study of urethrovesical relationships in female urinary stress incontinence', *Radiology*, 61: 335-45.

Hol, M., C. van Bolhuis, and M. E. Vierhout. 1995. 'Vaginal ultrasound studies of bladder neck mobility', *Br J Obstet Gynaecol*, 102: 47-53.

Howard, D., J. O. Delancey, R. Tunn, and J. A. Ashton-Miller. 2000. 'Racial differences in the structure and function of the stress urinary continence mechanism', *Obstet Gynecol*, 95: 713-7.

Howard, D., J. M. Miller, J. O. Delancey, and J. A. Ashton-Miller. 2000. 'Differential effects of cough, valsalva, and continence status on vesical neck movement', *Obstet Gynecol*, 95: 535-40.

Huang, W. C., and J. M. Yang. 2003. 'Bladder neck funneling on ultrasound cystourethrography in primary stress urinary incontinence: a sign associated with urethral hypermobility and intrinsic sphincter deficiency', *Urology*, 61: 936-41.

Huebner, M., A. Antolic, and R. Tunn. 2010. 'The impact of pregnancy and vaginal delivery on urinary incontinence', *Int J Gynaecol Obstet*, 110: 249-51.

Hung, H. C., S. M. Hsiao, S. Y. Chih, H. H. Lin, and J. Y. Tsauo. 2011. 'Effect of pelvic-floor muscle strengthening on bladder neck mobility: a clinical trial', *Phys Ther*, 91: 1030-8.

Imamura, M., K. Williams, M. Wells, and C. McGrother. 2015. 'Lifestyle interventions for the treatment of urinary incontinence in adults', *Cochrane Database Syst Rev*: CD003505.

Jango, H., J. Langhoff-Roos, S. Rosthoj, and A. Sakse. 2017. 'Recurrent obstetric anal sphincter injury and the risk of long-term anal incontinence', *Am J Obstet Gynecol*, 216: 610 e1-10 e8.

Jeffcoate, T. N., and H. Roberts. 1952. 'Observations on stress incontinence of urine', *Am J Obstet Gynecol*, 64: 721-38.

Jha, S., P. Toozs-Hobson, M. Parsons, and F. Gull. 2008. 'Does preoperative urodynamics change the management of prolapse?', *J Obstet Gynaecol*, 28: 320-2.

Jiang, Y. H., C. C. Wang, F. C. Chuang, Q. S. Ke, and H. C. Kuo. 2013. 'Positioning of a suburethral sling at the bladder neck is associated with a higher recurrence rate of stress urinary incontinence', *J Ultrasound Med*, 32: 239-45.

Jimenez-Cidre, M. A., L. Lopez-Fando, M. Esteban-Fuertes, L. Prieto-Chaparro, F. J. Llorens-Martinez, J. Salinas-Casado, D. Castro-Diaz, C. Muller-Arteaga, J. M. Adot-Zurbano, F. Rodriguez-Escobar, C. Gutierrez, S. Arlandis-Guzman, M. A. Bonillo-Garcia, B. Madurga-Patuel, M. Leva-Vallejo, A. Franco de Castro, L. Peri-Cusi, J. Conejero-Sugranes, J. Jimenez-Calvo, P. Rebollo, and A. Mora. 2015. 'The 3-day bladder diary is a feasible, reliable and valid tool to evaluate the lower urinary tract symptoms in women', *Neurourol Urodyn*, 34: 128-32.

Kalejaiye, O., M. Vij, and M. J. Drake. 2015. 'Classification of stress urinary incontinence', *World J Urol*, 33: 1215-20.

Kapoor, D. S., F. Housami, P. White, L. Swithinbank, and M. Drake. 2012. 'Maximum urethral closure pressure in women: normative data and evaluation as a diagnostic test', *Int Urogynecol J*, 23: 1613-8.

Karam, I., S. Droupy, I. Abd-Alsamad, J. F. Uhl, G. Benoit, and V. Delmas. 2005. 'Innervation of the female human urethral sphincter: 3D reconstruction of immunohistochemical studies in the fetus', *Eur Urol*, 47: 627-33; discussion 34.

Keane, D. P., S. D. Eckford, and P. Abrams. 1992. 'Surgical treatment and complications of urinary incontinence', *Curr Opin Obstet Gynecol*, 4: 559-64.

Kearney, R., M. Fitzpatrick, S. Brennan, M. Behan, J. Miller, D. Keane, C. O'Herlihy, and J. O. DeLancey. 2010. 'Levator ani injury in primiparous women with forceps delivery for fetal distress, forceps for second stage arrest, and spontaneous delivery', *Int J Gynaecol Obstet*, 111: 19-22.

Kelleher, C. J., L. D. Cardozo, V. Khullar, and S. Salvatore. 1997. 'A new questionnaire to assess the quality of life of urinary incontinent women', *Br J Obstet Gynaecol*, 104: 1374-9.

Kenton, K., and L. Brubaker. 2002. 'Relationship between levator ani contraction and motor unit activation in the urethral sphincter', *Am J Obstet Gynecol*, 187: 403-6.

Khullar, V., R. Anding, D. Robinson, D. Castro-Diaz, R. Dmochowski, and L. Cardozo. 2017. 'Under what circumstances should stress incontinence surgery be performed at the same time as prolapse surgery? ICI-RS 2015', *Neurourol Urodyn*, 36: 909-14.

Khullar, V., S. Athanasiou, L. Cardozo, K. Boos, S. Salvatore and M. Young. 1996. 'Histological correlates of the urethral sphincter and surrounding structures with ultrasound imaging', 21st Annual meeting of International Urogynaecology Association, abstract 47.

Khullar, V., S. Salvatore, L. Cardozo, T. H. Bourne, D. Abbott, and C. Kelleher. 1994. 'A novel technique for measuring bladder wall thickness in women using transvaginal ultrasound', *Ultrasound Obstet Gynecol*, 4: 220-3.

Khullar, V., C. C. Sexton, C. L. Thompson, I. Milsom, C. E. Bitoun, and K. S. Coyne. 2014. 'The relationship between BMI and urinary incontinence subgroups: results from EpiLUTS', *Neurourol Urodyn*, 33: 392-9.

Kim, S. O., Y. J. Kim, D. H. Yoo, I. S. Hwang, E. C. Hwang, S. I. Jung, T. W. Kang, D. Kwon, and K. Park. 2011. 'Clinical factors associated with low valsalva leak point pressure among women with stress urinary incontinence', *Int Neurourol J*, 15: 211-5.

King, J. K., and R. M. Freeman. 1998. 'Is antenatal bladder neck mobility a risk factor for postpartum stress incontinence?', *Br J Obstet Gynaecol*, 105: 1300-7.

Kirschner-Hermanns, R., H. M. Klein, U. Muller, W. Schafer, and G. Jakse. 1994. 'Intra-urethral ultrasound in women with stress incontinence', *Br J Urol*, 74: 315-8.

Klauser, A., F. Frauscher, H. Strasser, G. Helweg, D. Kolle, D. Strohmeyer, A. Stenzl, and D. zur Nedden. 2004. 'Age-related rhabdosphincter function in female urinary stress incontinence: assessment of intraurethral sonography', *J Ultrasound Med*, 23: 631-7; quiz 38-9.

Klutke, C., J. Golomb, Z. Barbaric, and S. Raz. 1990. 'The anatomy of stress incontinence: magnetic resonance imaging of the female bladder neck and urethra', *J Urol*, 143: 563-6.

Kociszewski, J., G. Fabian, S. Grothey, A. Kuszka, A. Zwierzchowska, W. Majkusiak, and E. Barcz. 2017. 'Are complications of stress urinary incontinence surgery procedures associated with the position of the sling?', *Int J Urol*, 24: 145-50.

Kociszewski, J., O. Rautenberg, D. Perucchini, J. Eberhard, V. Geissbuhler, R. Hilgers, and V. Viereck. 2008. 'Tape functionality: sonographic tape characteristics and outcome after TVT incontinence surgery', *Neurourol Urodyn*, 27: 485-90.

Kociszewski, J., and V. Viereck. 2013. 'Introital ultrasound in the diagnosis of occult abscesses following a tape procedure: a case report', *Arch Gynecol Obstet*, 288: 577-9.

Koelle, D., J. Windisch, D. Doerfler, C. Marth, and S. Kropshofer. 2006. 'Effect of tension-free vaginal tape operation on urethral closure function', *Urology*, 67: 524-8; discussion 28-9.

Kohorn, E. I., A. L. Scioscia, P. Jeanty, and J. C. Hobbins. 1986. 'Ultrasound cystourethrography by perineal scanning for the assessment of female stress urinary incontinence', *Obstet Gynecol*, 68: 269-72.

Kolbl, H., G. Bernaschek, and G. Wolf. 1988. 'A comparative study of perineal ultrasound scanning and urethrocystography in patients with genuine stress incontinence', *Arch Gynecol Obstet*, 244: 39-45.

Kondo, Y., Y. Homma, S. Takahashi, T. Kitamura, and K. Kawabe. 2001. 'Transvaginal ultrasound of urethral sphincter at the mid urethra in continent and incontinent women', *J Urol*, 165: 149-52.

Kruse, A. R., T. D. Jensen, F. F. Lauszus, E. Kallfa, and M. R. Madsen. 2017. 'Changes in incontinence after hysterectomy', *Arch Gynecol Obstet*.

Kudish, B. I., D. Shveiky, R. E. Gutman, V. Jacoby, A. I. Sokol, R. Rodabough, B. V. Howard, P. Blanchette, and C. B. Iglesia. 2014. 'Hysterectomy and urinary incontinence in postmenopausal women', *Int Urogynecol J*, 25: 1523-31.

Kuhn, A., S. Genoud, D. Robinson, G. Herrmann, A. Gunthert, S. Brandner, and L. Raio. 2011. 'Sonographic transvaginal bladder wall thickness: does the measurement discriminate between urodynamic diagnoses?', *Neurourol Urodyn*, 30: 325-8.

Kurkijarvi, K., R. Aaltonen, M. Gissler, and J. Makinen. 2016. 'Surgery for stress urinary incontinence in Finland 1987-2009', *Int Urogynecol J*, 27: 1021-7.

Lakeman, M. M., C. H. Van Der Vaart, J. W. Van Der Steeg, J. P. Roovers, and V. A. study group Hys. 2011. 'Predicting the development of stress urinary incontinence 3 years after hysterectomy', *Int Urogynecol J*, 22: 1179-84.

Lapides, J., E. P. Ajemian, B. H. Stewart, J. R. Lichtwardt, and B. A. Breakey. 1960. 'Physiopathology of stress incontinence', *Surg Gynecol Obstet*, 111: 224-31.

Latthe, P., L. Middleton, S. Rachaneni, S. McCooty, J. Daniels, A. Coomarasamy, M. Balogun, J. Duckett, R. Thakar, I. Goranitis, T. Roberts, J. Deeks, and B. U. S. Collaborative Group. 2017. 'Ultrasound bladder wall thickness and detrusor overactivity: a multicentre test accuracy study', *BJOG*, 124: 1422-29.

Lee, H. N., Y. S. Lee, D. H. Han, and K. S. Lee. 2017. 'Change of Ultrasound Estimated Bladder Weight and Bladder Wall Thickness After Treatment of Bladder Outlet Obstruction With Dutasteride', *Low Urin Tract Symptoms*, 9: 67-74.

Lee, S. R., Y. M. Lim, J. H. Jeon, and M. H. Park. 2017. 'Diagnosis of urethral diverticulum mimicking pelvic organ prolapse with translabial ultrasonography', *Am J Obstet Gynecol*, 217: 482.

Lewicky-Gaupp, C., J. Blaivas, A. Clark, E. J. McGuire, G. Schaer, J. Tumbarello, R. Tunn, and J. O. DeLancey. 2009. '"The cough game": are there characteristic urethrovesical movement patterns associated with stress incontinence?', *Int Urogynecol J Pelvic Floor Dysfunct*, 20: 171-5.

Li, J., L. Yang, C. Pu, Y. Tang, H. Yun, and P. Han. 2013. 'The role of duloxetine in stress urinary incontinence: a systematic review and meta-analysis', *Int Urol Nephrol*, 45: 679-86.

Li, X. M., H. Yang, D. Q. Li, P. Zhang, Q. T. Ma, and L. D. Zhai. 2015. 'Muscular structure at the male bladder outlet examined with successive celloidin-embedded slices', *Urology*, 85: 629-35.

Lien, K. C., D. M. Morgan, J. O. Delancey, and J. A. Ashton-Miller. 2005. 'Pudendal nerve stretch during vaginal birth: a 3D computer simulation', *Am J Obstet Gynecol*, 192: 1669-76.

Lin, L. Y., S. Y. Chen, H. S. Lee, S. L. Chung, T. H. Ying, and G. D. Chen. 1999. 'Female bladder neck changes with position', *Int Urogynecol J Pelvic Floor Dysfunct*, 10: 277-82.

Lo, T. S., A. C. Wang, S. G. Horng, C. C. Liang, and Y. K. Soong. 2001. 'Ultrasonographic and urodynamic evaluation after tension free vagina tape procedure (TVT)', *Acta Obstet Gynecol Scand*, 80: 65-70.

Lobel, B., A. Manunta, and A. Rodriguez. 2001. 'The management of female stress urinary incontinence using the sling procedure', *BJU Int*, 88: 832-9.

Lone, F., R. Thakar, A. P. Wieczorek, A. H. Sultan, and A. Stankiewicz. 2016. 'Assessment of urethral vascularity using 2D colour Doppler high-frequency endovaginal ultrasonography in women treated for symptomatic stress urinary incontinence: 1-year prospective follow-up study', *Int Urogynecol J*, 27: 85-92.

Low, J. A. 1964. 'Clinical Characteristics of Patients with Demonstrable Urinary Incontinence', *Am J Obstet Gynecol*, 88: 322-35.

Lowder, J. L., E. A. Frankman, C. Ghetti, L. J. Burrows, M. A. Krohn, P. Moalli, and H. Zyczynski. 2010. 'Lower urinary tract symptoms in women with pelvic organ prolapse', *Int Urogynecol J*, 21: 665-72.

MacArthur, C., C. Glazener, R. Lancashire, P. Herbison, D. Wilson, and group ProLong study. 2011. 'Exclusive caesarean section delivery and subsequent urinary and faecal incontinence: a 12-year longitudinal study', *BJOG*, 118: 1001-7.

Madill, S. J., S. Pontbriand-Drolet, A. Tang, and C. Dumoulin. 2015. 'Changes in urethral sphincter size following rehabilitation in older women with stress urinary incontinence', *Int Urogynecol J*, 26: 277-83.

Manieri, C., S. S. Carter, G. Romano, A. Trucchi, M. Valenti, and A. Tubaro. 1998. 'The diagnosis of bladder outlet obstruction in men by ultrasound measurement of bladder wall thickness', *J Urol*, 159: 761-5.

Marks, B. K., and H. B. Goldman. 2014. 'Videourodynamics: indications and technique', *Urol Clin North Am*, 41: 383-91, vii-viii.

Martan, A., J. Masata, M. Halaska, and R. Voigt. 1999. '[Ultrasound imaging of the lower urinary tract in post-menopausal women with urinary stress or combined type of incontinence before and after intravaginal administration of estriol]', *Ceska Gynekol*, 64: 6-9.

———. 2001. 'Ultrasound imaging of the lower urinary system in women after Burch colposuspension', *Ultrasound Obstet Gynecol*, 17: 58-64.

Masata, J., A. Martan, K. Svabik, P. Drahoradova, and M. Pavlikova. 2006. 'Ultrasound imaging of the lower urinary tract after successful tension-free vaginal tape (TVT) procedure', *Ultrasound Obstet Gynecol*, 28: 221-8.

Mashidori, T., T. Yamanishi, K. Yoshida, R. Sakakibara, K. Sakurai, and K. Hirata. 2007. 'Continuous urinary incontinence presenting as the initial symptoms demonstrating acontractile detrusor and intrinsic sphincter deficiency in multiple system atrophy', *Int J Urol*, 14: 972-4.

Massagli, T. L., D. D. Cardenas, and E. W. Kelly. 1989. 'Experience with portable ultrasound equipment and measurement of urine volumes: inter-user reliability and factors of patient position', *J Urol*, 142: 969-71.

Masumoto, H., A. Takenaka, J. F. Rodriguez-Vazquez, G. Murakami, and A. Matsubara. 2012. 'Reappraisal of intergender differences in the urethral striated sphincter explains why a completely circular arrangement is difficult in females: a histological study using human fetuses', *Anat Cell Biol*, 45: 79-85.

Mazloomdoost, D., L. B. Westermann, G. Mutema, C. C. Crisp, S. D. Kleeman, and R. N. Pauls. 2017. 'Histologic Anatomy of the Anterior Vagina and Urethra', *Female Pelvic Med Reconstr Surg*, 23: 329-35.

McGuire, E. J., R. D. Cespedes, C. A. Cross, and H. E. O'Connell. 1996. 'Videourodynamic studies', *Urol Clin North Am*, 23: 309-21.

Migliari, R., A. Buffardi, and L. Mosso. 2015. 'Female paraurethral leiomyoma: treatment and long-term follow-up', *Int Urogynecol J*, 26: 1821-5.

Miller, J. J., S. M. Botros, J. L. Beaumont, S. O. Aschkenazi, T. Gamble, P. K. Sand, and R. P. Goldberg. 2008. 'Impact of hysterectomy on stress urinary incontinence: an identical twin study', *Am J Obstet Gynecol*, 198: 565 e1-4.

Miller, J. M., D. Perucchini, L. T. Carchidi, J. O. DeLancey, and J. Ashton-Miller. 2001. 'Pelvic floor muscle contraction during a cough and decreased vesical neck mobility', *Obstet Gynecol*, 97: 255-60.

Miller, J. M., C. Sampselle, J. Ashton-Miller, G. R. Hong, and J. O. DeLancey. 2008. 'Clarification and confirmation of the Knack maneuver: the effect of volitional pelvic floor muscle contraction to preempt expected stress incontinence', *Int Urogynecol J Pelvic Floor Dysfunct*, 19: 773-82.

Minardi, D., V. Piloni, A. Amadi, Z. El Asmar, G. Milanese, and G. Muzzonigro. 2007. 'Correlation between urodynamics and perineal ultrasound in female patients with urinary incontinence', *Neurourol Urodyn*, 26: 176-82; discussion 83-4.

Mitchell, W. K., J. Williams, P. Atherton, M. Larvin, J. Lund, and M. Narici. 2012. 'Sarcopenia, dynapenia, and the impact of advancing age on human skeletal muscle size and strength; a quantitative review', *Front Physiol*, 3: 260.

Mitterberger, M., G. M. Pinggera, R. Marksteiner, E. Margreiter, M. Fussenegger, F. Frauscher, H. Ulmer, S. Hering, G. Bartsch, and H. Strasser. 2008. 'Adult stem cell therapy of female stress urinary incontinence', *Eur Urol*, 53: 169-75.

Mochida, K., K. Shinomiya, and M. Andou. 1996. 'Urodynamic and electrophysiologic study of the urinary disturbances caused by cervical myelopathy', *J Spinal Disord*, 9: 141-5.

Montz, F. J., and S. L. Stanton. 1986. 'Q-Tip test in female urinary incontinence', *Obstet Gynecol*, 67: 258-60.

Morgan, D. M., W. Umek, K. Guire, H. K. Morgan, A. Garabrant, and J. O. DeLancey. 2009. 'Urethral sphincter morphology and function with and without stress incontinence', *J Urol*, 182: 203-9.

Mouracade, P., S. El Abiad, C. Roy, H. Lang, D. Jacqmin, and C. Saussine. 2010. 'Correlation of introital ultrasound with LUTS after sling surgery', *Int Urogynecol J*, 21: 1261-4.

Mouritsen, L., and P. Bach. 1994. 'Ultrasonic evaluation of bladder neck position and mobility: the influence of urethral catheter, bladder volume, and body position', *Neurourol Urodyn*, 13: 637-46.

Mouritsen, L., and J. P. Larsen. 2003. 'Symptoms, bother and POPQ in women referred with pelvic organ prolapse', *Int Urogynecol J Pelvic Floor Dysfunct*, 14: 122-7.

Murphy, A. M., F. Bethoux, D. Stough, and H. B. Goldman. 2012. 'Prevalence of stress urinary incontinence in women with multiple sclerosis', *Int Neurourol J*, 16: 86-90.

Nadeau, G., and S. Herschorn. 2014. 'Management of recurrent stress incontinence following a sling', *Curr Urol Rep*, 15: 427.

Naranjo-Ortiz, C., K. L. Shek, A. J. Martin, and H. P. Dietz. 2016. 'What is normal bladder neck anatomy?', *Int Urogynecol J*, 27: 945-50.

Ng, C. C., L. C. Lee, and W. H. Han. 2005. 'Use of three-dimensional ultrasound scan to assess the clinical importance of midurethral placement of the tension-free vaginal tape (TVT) for treatment of incontinence', *Int Urogynecol J Pelvic Floor Dysfunct*, 16: 220-5.

Nilsen, P. A. 1958. 'Cystourethrography in stress incontinence', *Acta Obstet Gynecol Scand*, 37: 269-85.

Nitti, V. W., A. Mourtzinos, B. M. Brucker, and Sufu Pad Test Study Group. 2014. 'Correlation of patient perception of pad use with objective degree of incontinence measured by pad test in men with post-prostatectomy incontinence: the SUFU Pad Test Study', *J Urol*, 192: 836-42.

Noble, J. G., P. J. Dixon, D. Rickards, and C. J. Fowler. 1995. 'Urethral sphincter volumes in women with obstructed voiding and abnormal sphincter electromyographic activity', *Br J Urol*, 76: 741-6.

Novielli, K. D., Z. Simpson, G. Hua, J. J. Diamond, C. Sultana, and N. Paynter. 2003. 'Urinary incontinence in primary care: a comparison of older African-American and Caucasian women', *Int Urol Nephrol*, 35: 423-8.

O'Sullivan, R., E. Karantanis, T. L. Stevermuer, W. Allen, and K. H. Moore. 2004. 'Definition of mild, moderate and severe incontinence on the 24-hour pad test', *BJOG*, 111: 859-62.

Ochodnicky, P., B. Uvelius, K. E. Andersson, and M. C. Michel. 2013. 'Autonomic nervous control of the urinary bladder', *Acta Physiol (Oxf)*, 207: 16-33.

Oelke, M., K. Hofner, U. Jonas, J. J. de la Rosette, D. T. Ubbink, and H. Wijkstra. 2007. 'Diagnostic accuracy of noninvasive tests to evaluate bladder outlet obstruction in men: detrusor wall thickness, uroflowmetry, postvoid residual urine, and prostate volume', *Eur Urol*, 52: 827-34.

Okamura, K., Y. Nojiri, and Y. Osuga. 2009. 'Reliability and validity of the King's Health Questionnaire for lower urinary tract symptoms in both genders', *BJU Int*, 103: 1673-8.

Orno, A. K., and H. P. Dietz. 2007. 'Levator co-activation is a significant confounder of pelvic organ descent on Valsalva maneuver', *Ultrasound Obstet Gynecol*, 30: 346-50.

Osborn, D. J., M. Strain, A. Gomelsky, J. Rothschild, and R. Dmochowski. 2013. 'Obesity and female stress urinary incontinence', *Urology*, 82: 759-63.

Otsuki, E. N., E. Araujo Junior, E. Oliveira, M. G. Sartori, M. J. Girao, and Z. I. Jarmy-Di Bella. 2014. 'Ultrasound thickness of bladder wall in continent and incontinent women and its correlation with cystometry', *ScientificWorldJournal*, 2014: 684671.

Panicker, J. N., J. H. Seth, S. Khan, G. Gonzales, C. Haslam, T. M. Kessler, and C. J. Fowler. 2016. 'Open-label study evaluating outpatient urethral sphincter injections of onabotulinumtoxinA to treat women with urinary retention due to a primary disorder of sphincter relaxation (Fowler's syndrome)', *BJU Int*, 117: 809-13.

Pannek, J., and P. Pieper. 2008. 'Clinical usefulness of ambulatory urodynamics in the diagnosis and treatment of lower urinary tract dysfunction', *Scand J Urol Nephrol*, 42: 428-32.

Parboosingh, J., and A. Doig. 1973. 'Studies of nocturia in normal pregnancy', *J Obstet Gynaecol Br Commonw*, 80: 888-95.

Pathi, S. D., D. D. Rahn, J. L. Sailors, V. A. Graziano, R. D. Sims, R. J. Stone, D. D. McIntire, and C. Y. Wai. 2013. 'Utility of clinical parameters, cystourethroscopy, and magnetic resonance imaging in the preoperative diagnosis of urethral diverticula', *Int Urogynecol J*, 24: 319-23.

Peng, C. H., S. F. Chen, and H. C. Kuo. 2017. 'Videourodynamic analysis of the urethral sphincter overactivity and the poor relaxing pelvic floor muscles in women with voiding dysfunction', *Neurourol Urodyn*.

Perkash, I., and G. W. Friedland. 1986. 'Posterior ledge at the bladder neck: crucial diagnostic role of ultrasonography', *Urol Radiol*, 8: 175-83.

Perucchini, D., J. O. DeLancey, J. A. Ashton-Miller, A. Galecki, and G. N. Schaer. 2002. 'Age effects on urethral striated muscle. II. Anatomic location of muscle loss', *Am J Obstet Gynecol*, 186: 356-60.

Peschers, U. M., G. Fanger, G. N. Schaer, D. B. Vodusek, J. O. DeLancey, and B. Schuessler. 2001. 'Bladder neck mobility in continent nulliparous women', *BJOG*, 108: 320-4.

Petros, P. E. 1998. 'The pubourethral ligaments--an anatomical and histological study in the live patient', *Int Urogynecol J Pelvic Floor Dysfunct*, 9: 154-7.

Petros, P. E., and U. I. Ulmsten. 1990a. 'The combined intravaginal sling and tuck operation. An ambulatory procedure for cure of stress and urge incontinence', *Acta Obstet Gynecol Scand Suppl*, 153: 53-9.

———. 1990b. 'Cure of urge incontinence by the combined intravaginal sling and tuck operation', *Acta Obstet Gynecol Scand Suppl*, 153: 61-2.

———. 1990c. 'An integral theory of female urinary incontinence. Experimental and clinical considerations', *Acta Obstet Gynecol Scand Suppl*, 153: 7-31.

———. 1990d. 'Non stress non urge female urinary incontinence--diagnosis and cure: a preliminary report', *Acta Obstet Gynecol Scand Suppl*, 153: 69-70.

Petrou, S. P., and J. Wan. 1999. 'VLPP in the evaluation of the female with stress urinary incontinence', *Int Urogynecol J Pelvic Floor Dysfunct*, 10: 254-9.

Pirpiris, A., K. L. Shek, and H. P. Dietz. 2010. 'Urethral mobility and urinary incontinence', *Ultrasound Obstet Gynecol*, 36: 507-11.

Pirtea, L., I. Sas, R. Ilina, D. Grigoras, and O. Mazilu. 2015. 'Transversal incision of the vagina favors the remaining of the tape in the middle-third urethra compared to longitudinal incision during transobturator sling procedures for stress urinary incontinence', *BMC Surg*, 15: 84.

Pizzoferrato, A. C., A. Fauconnier, X. Fritel, G. Bader, and P. Dompeyre. 2017. 'Urethral Closure Pressure at Stress: A Predictive Measure for the Diagnosis and Severity of Urinary Incontinence in Women', *Int Neurourol J*, 21: 121-27.

Podnar, S., and D. B. Vodusek. 2015. 'Lower urinary tract dysfunction in patients with peripheral nervous system lesions', *Handb Clin Neurol*, 130: 203-24.

Pontbriand-Drolet, S., A. Tang, S. J. Madill, C. Tannenbaum, M. C. Lemieux, J. Corcos, and C. Dumoulin. 2016. 'Differences in pelvic floor morphology between continent, stress urinary incontinent, and mixed urinary incontinent elderly women: An MRI study', *Neurourol Urodyn*, 35: 515-21.

Poon, C. I., and P. E. Zimmern. 2004. 'Role of three-dimensional ultrasound in assessment of women undergoing urethral bulking agent therapy', *Curr Opin Obstet Gynecol*, 16: 411-7.

Pregazzi, R., A. Sartore, P. Bortoli, E. Grimaldi, L. Troiano, and S. Guaschino. 2002. 'Perineal ultrasound evaluation of urethral angle and bladder neck mobility in women with stress urinary incontinence', *BJOG*, 109: 821-7.

Quinn, M. J., J. Beynon, N. J. Mortensen, and P. J. Smith. 1988. 'Transvaginal endosonography: a new method to study the anatomy of the lower urinary tract in urinary stress incontinence', *Br J Urol*, 62: 414-8.

Rahmanou, P., and V. Khullar. 2011. 'Short-term test-retest reproducibility of urethral pressure profilometry in women with urodynamic stress incontinence with and without detrusor overactivity', *Neurourol Urodyn*, 30: 1356-60.

Rautenberg, O., J. Kociszewski, J. Welter, A. Kuszka, J. Eberhard, and V. Viereck. 2014. 'Ultrasound and early tape mobilization--a practical solution for treating postoperative voiding dysfunction', *Neurourol Urodyn*, 33: 1147-51.

Reed, H., R. M. Freeman, A. Waterfield, and O. Adekanmi. 2004. 'Prevalence of bladder neck mobility in asymptomatic non-pregnant nulliparous volunteers', *BJOG*, 111: 172-5.

Reese, P. R., A. M. Pleil, G. J. Okano, and C. J. Kelleher. 2003. 'Multinational study of reliability and validity of the King's Health Questionnaire in patients with overactive bladder', *Qual Life Res*, 12: 427-42.

Reilly, E. T., R. M. Freeman, M. R. Waterfield, A. E. Waterfield, P. Steggles, and F. Pedlar. 2014. 'Prevention of postpartum stress incontinence in primigravidae with increased bladder neck mobility: a randomised controlled trial of antenatal pelvic floor exercises', *BJOG*, 121 Suppl 7: 58-66.

Richardson, D. A. 1986. 'Reduction of urethral pressure in response to stress: relationship to urethral mobility', *Am J Obstet Gynecol*, 155: 20-5.

Richmond, D. H., and J. R. Sutherst. 1989. 'Burch colposuspension or sling for stress incontinence? A prospective study using transrectal ultrasound', *Br J Urol*, 64: 600-3.

Rinne, K. M., S. Kainulainen, S. Aukee, S. Heinonen, and C. G. Nilsson. 2010. 'Dynamic magnetic resonance imaging of the behavior of the mid-urethra in healthy and stress incontinent women', *Acta Obstet Gynecol Scand*, 89: 373-9.

Rios, S. S., L. C. Pereira, C. B. Santos, A. C. Chen, J. R. Chen, and B. Vogt M. de Fatima. 2016. 'Conservative treatment and follow-up of vaginal Gartner's duct cysts: a case series', *J Med Case Rep*, 10: 147.

Robinson, B. L., E. J. Geller, B. A. Parnell, A. K. Crane, M. L. Jannelli, E. C. Wells, A. Connolly, and C. A. Matthews. 2012. 'Diagnostic accuracy of visual urethral mobility exam versus Q-Tip test: a randomized crossover trial', *Am J Obstet Gynecol*, 206: 528 e1-6.

Robinson, D., M. Oelke, V. Khullar, H. Wijkstra, R. Tretter, B. Stow, G. Compion, and A. Tubaro. 2016. 'Bladder wall thickness in women with symptoms of overactive bladder and detrusor overactivity: Results from the randomised, placebo-controlled shrink study', *Neurourol Urodyn*, 35: 819-25.

Robinson, D., P. Toozs-Hobson, L. Cardozo, and A. Digesu. 2004. 'Correlating structure and function: three-dimensional ultrasound of the urethral sphincter', *Ultrasound Obstet Gynecol*, 23: 272-6.

Rocha, J., P. Brandao, A. Melo, S. Torres, L. Mota, and F. Costa. 2017. '[Assessment of Urinary Incontinence in Pregnancy and Postpartum: Observational Study]', *Acta Med Port*, 30: 568-72.

Rodriguez-Mias, N. L., N. Subramaniam, T. Friedman, K. L. Shek, and H. P. Dietz. 2017. 'Prolapse assessment supine and standing: do we need different cutoffs for "significant prolapse"?', *Int Urogynecol J*.

Rortveit, G., A. K. Daltveit, Y. S. Hannestad, S. Hunskaar, and Epincont Study Norwegian. 2003. 'Urinary incontinence after vaginal delivery or cesarean section', *N Engl J Med*, 348: 900-7.

Rortveit, G., Y. S. Hannestad, A. K. Daltveit, and S. Hunskaar. 2001. 'Age- and type-dependent effects of parity on urinary incontinence: the Norwegian EPINCONT study', *Obstet Gynecol*, 98: 1004-10.

Rortveit, G., L. L. Subak, D. H. Thom, J. M. Creasman, E. Vittinghoff, S. K. Van Den Eeden, and J. S. Brown. 2010. 'Urinary incontinence, fecal incontinence and pelvic organ prolapse in a population-based, racially diverse cohort: prevalence and risk factors', *Female Pelvic Med Reconstr Surg*, 16: 278-83.

Rosier, P. F., R. Kirschner-Hermanns, J. Svihra, Y. Homma, and A. J. Wein. 2016. 'ICS teaching module: Analysis of voiding, pressure flow analysis (basic module)', *Neurourol Urodyn*, 35: 36-8.

Rosier, Pfwm, W. Schaefer, G. Lose, H. B. Goldman, M. Guralnick, S. Eustice, T. Dickinson, and H. Hashim. 2017. 'International Continence Society Good Urodynamic Practices and Terms 2016: Urodynamics, uroflowmetry, cystometry, and pressure-flow study', *Neurourol Urodyn*, 36: 1243-60.

Rud, T. 1980a. 'The effects of estrogens and gestagens on the urethral pressure profile in urinary continent and stress incontinent women', *Acta Obstet Gynecol Scand*, 59: 265-70.

———. 1980b. 'Urethral pressure profile in continent women from childhood to old age', *Acta Obstet Gynecol Scand*, 59: 331-5.

Salvatore, S., and U. Leone Roberti Maggiore. 2014. 'Incontinence: a novel, psychometrically validated bladder diary for LUTS', *Nat Rev Urol*, 11: 314-5.

Santiago, A. C., D. E. O'Leary, L. H. Quiroz, and S. A. Shobeiri. 2015. 'Is there a correlation between levator ani and urethral sphincter complex status on 3D ultrasonography?', *Int Urogynecol J*, 26: 699-705.

Sarlos, D., M. Kuronen, and G. N. Schaer. 2003. 'How does tension-free vaginal tape correct stress incontinence? investigation by perineal ultrasound', *Int Urogynecol J Pelvic Floor Dysfunct*, 14: 395-8.

Schaer, G. N., O. R. Koechli, B. Schuessler, and U. Haller. 1995. 'Perineal ultrasound for evaluating the bladder neck in urinary stress incontinence', *Obstet Gynecol*, 85: 220-4.

———. 1996. 'Perineal ultrasound: determination of reliable examination procedures', *Ultrasound Obstet Gynecol*, 7: 347-52.

Schaer, G. N., T. Schmid, U. Peschers, and J. O. Delancey. 1998. 'Intraurethral ultrasound correlated with urethral histology', *Obstet Gynecol*, 91: 60-4.

Schafer, W., P. Abrams, L. Liao, A. Mattiasson, F. Pesce, A. Spangberg, A. M. Sterling, N. R. Zinner, P. van Kerrebroeck, and Society International Continence. 2002. 'Good urodynamic practices: uroflowmetry, filling cystometry, and pressure-flow studies', *Neurourol Urodyn*, 21: 261-74.

Schick, E., C. Dupont, P. E. Bertrand, M. Jolivet-Tremblay, and J. Tessier. 2004. 'Predictive value of maximum urethral closure pressure, urethral hypermobility and urethral incompetence in the diagnosis of clinically significant female genuine stress incontinence', *J Urol*, 171: 1871-5.

Schierlitz, L., P. L. Dwyer, A. Rosamilia, A. De Souza, C. Murray, E. Thomas, R. Hiscock, and C. Achtari. 2014. 'Pelvic organ prolapse surgery with and without tension-free vaginal tape in women with occult or asymptomatic urodynamic stress incontinence: a randomised controlled trial', *Int Urogynecol J*, 25: 33-40.

Schulz, J. A., C. W. Nager, S. L. Stanton, and K. Baessler. 2004. 'Bulking agents for stress urinary incontinence: short-term results and complications in a randomized comparison of periurethral and transurethral injections', *Int Urogynecol J Pelvic Floor Dysfunct*, 15: 261-5.

Secco, S., A. Crestani, F. Cattaneo, V. Ficarra, F. Zattoni, and G. Novara. 2012. 'Slings in surgery of genuine stress incontinence', *World J Urol*, 30: 465-70.

Seo, Y. H., S. O. Kim, H. S. Yu, and D. Kwon. 2016. 'Leak point pressure at different bladder volumes in stress urinary incontinence in women: Comparison between Valsalva and cough-induced leak point pressure', *Can Urol Assoc J*, 10: E23-7.

Serati, M., S. Salvatore, E. Cattoni, G. Siesto, M. Soligo, A. Braga, P. Sorice, A. Cromi, F. Ghezzi, L. Cardozo, and P. Bolis. 2011. 'Female urinary incontinence at orgasm: a possible marker of a more severe form of detrusor overactivity. Can ultrasound measurement of bladder wall thickness explain it?', *J Sex Med*, 8: 1710-6.

Serati, M., P. Sorice, G. Bogani, A. Braga, S. Cantaluppi, S. Uccella, G. Caccia, S. Salvatore, and F. Ghezzi. 2017. 'TVT for the treatment of urodynamic stress incontinence: Efficacy and adverse effects at 13-year follow-up', *Neurourol Urodyn*, 36: 192-97.

Shafik, A., and S. Doss. 1999. 'Surgical anatomy of the somatic terminal innervation to the anal and urethral sphincters: role in anal and urethral surgery', *J Urol*, 161: 85-9.

Shah, A. D., N. Kohli, S. S. Rajan, and L. Hoyte. 2008. 'The age distribution, rates, and types of surgery for stress urinary incontinence in the USA', *Int Urogynecol J Pelvic Floor Dysfunct*, 19: 89-96.

Sharipova, K., Z. Pilsetniece, Y. Bekmukhambetov, and E. Vjaters. 2016. 'The Correlation of Urethral Pressure Profilometry Data in Women with Different Types of Urinary Incontinence', *Urol Int*, 97: 218-23.

Shek, K. L., and H. P. Dietz. 2008. 'The urethral motion profile: a novel method to evaluate urethral support and mobility', *Aust N Z J Obstet Gynaecol*, 48: 337-42.

Shobeiri, S. A., G. Rostaminia, D. White, L. H. Quiroz, and M. A. Nihira. 2013. 'Evaluation of vaginal cysts and masses by 3-dimensional endovaginal and endoanal sonography', *J Ultrasound Med*, 32: 1499-507.

Siddiqui, Z. A., H. Abboudi, R. Crawford, and S. Shah. 2017. 'Intraurethral bulking agents for the management of female stress urinary incontinence: a systematic review', *Int Urogynecol J*, 28: 1275-84.

Sinha, D., V. Nallaswamy, and A. S. Arunkalaivanan. 2006. 'Value of leak point pressure study in women with incontinence', *J Urol*, 176: 186-8; discussion 88.

Skala, C., G. Emons, T. Krauss, R. Hilgers, A. Gauruder-Burmester, R. Lange, W. Bader, and V. Viereck. 2004. 'Postoperative funneling after anti-incontinence surgery--a prognostic indicator?--Part 1: colposuspension', *Neurourol Urodyn*, 23: 636-42.

Snooks, S. J., M. Swash, S. E. Mathers, and M. M. Henry. 1990. 'Effect of vaginal delivery on the pelvic floor: a 5-year follow-up', *Br J Surg*, 77: 1358-60.

Sorel, M. R., H. J. B. Reitsma, Pfwm Rosier, Rjlhr Bosch, and L. M. O. de Kort. 2017. 'Uroflowmetry in healthy women: A systematic review', *Neurourol Urodyn*, 36: 953-59.

Strasser, H., F. Frauscher, G. Helweg, K. Colleselli, A. Reissigl, and G. Bartsch. 1998. 'Transurethral ultrasound: evaluation of anatomy and function of the rhabdosphincter of the male urethra', *J Urol*, 159: 100-4; discussion 04-5.

Strohbehn, K., L. E. Quint, M. R. Prince, K. J. Wojno, and J. O. Delancey. 1996. 'Magnetic resonance imaging anatomy of the female urethra: a direct histologic comparison', *Obstet Gynecol*, 88: 750-6.

Sumi, T., O. Ishiko, K. Hirai, H. Yoshida, and S. Ogita. 2000. 'Is measuring the posterior urethrovesical angle of clinical value for controlling pelvic organ Prolapse?. Retrospective analysis of 107 postoperative cases', *Gynecol Obstet Invest*, 49: 183-6.

Summitt, R. L., Jr., D. R. Sipes, 2nd, A. E. Bent, and D. R. Ostergard. 1994. 'Evaluation of pressure transmission ratios in women with genuine stress incontinence and low urethral pressure: a comparative study', *Obstet Gynecol*, 83: 984-8.

Sun, S., D. Liu, and Z. Jiao. 2016. 'Coffee and caffeine intake and risk of urinary incontinence: a meta-analysis of observational studies', *BMC Urol*, 16: 61.

Swenson, C. W., G. E. Kolenic, E. R. Trowbridge, M. B. Berger, C. Lewicky-Gaupp, R. U. Margulies, D. M. Morgan, D. E. Fenner, and J. O. DeLancey. 2017. 'Obesity and stress urinary incontinence in women: compromised continence mechanism or excess bladder pressure during cough?', *Int Urogynecol J*.

Swift, S. E., P. F. Rust, and D. R. Ostergard. 1996. 'Intrasubject variability of the pressure-transmission ratio in patients with genuine stress incontinence', *Int Urogynecol J Pelvic Floor Dysfunct*, 7: 312-6.

Swift, S., S. Morris, V. McKinnie, R. Freeman, E. Petri, R. J. Scotti, and P. Dwyer. 2006. 'Validation of a simplified technique for using the POPQ pelvic organ prolapse classification system', *Int Urogynecol J Pelvic Floor Dysfunct*, 17: 615-20.

Tahtinen, R. M., R. Cartwright, J. F. Tsui, R. L. Aaltonen, Y. Aoki, J. L. Cardenas, R. El Dib, K. M. Joronen, S. Al Juaid, S. Kalantan, M. Kochana, M. Kopec, L. C. Lopes, E. Mirza, S. M. Oksjoki, J. S. Pesonen, A. Valpas, L. Wang, Y. Zhang, D. Heels-Ansdell, G. H. Guyatt, and K. A. O. Tikkinen. 2016. 'Long-term Impact of Mode of Delivery on Stress Urinary Incontinence and Urgency Urinary Incontinence: A Systematic Review and Meta-analysis', *Eur Urol*, 70: 148-58.

Tawadros, C., K. Burnett, L. F. Derbyshire, T. Tawadros, N. W. Clarke, and C. D. Betts. 2015. 'External urethral sphincter electromyography in asymptomatic women and the influence of the menstrual cycle', *BJU Int*, 116: 423-31.

Theofrastous, J. P., G. W. Cundiff, R. L. Harris, and R. C. Bump. 1996. 'The effect of vesical volume on Valsalva leak-point pressures in women with genuine stress urinary incontinence', *Obstet Gynecol*, 87: 711-4.

Thom, D. H., S. K. van den Eeden, A. I. Ragins, C. Wassel-Fyr, E. Vittinghof, L. L. Subak, and J. S. Brown. 2006. 'Differences in prevalence of urinary incontinence by race/ethnicity', *J Urol*, 175: 259-64.

Tincello, D. G., N. Armstrong, P. Hilton, B. Buckley, and C. Mayne. 2017. 'Surgery for recurrent stress urinary incontinence: the views of surgeons and women', *Int Urogynecol J*.

Toozs-Hobson, P., J. Balmforth, L. Cardozo, V. Khullar, and S. Athanasiou. 2008. 'The effect of mode of delivery on pelvic floor functional anatomy', *Int Urogynecol J Pelvic Floor Dysfunct*, 19: 407-16.

Torella, M., P. De Franciscis, C. Russo, P. Gallo, A. Grimaldi, D. Ambrosio, N. Colacurci, and M. T. Schettino. 2014. 'Stress urinary incontinence: usefulness of perineal ultrasound', *Radiol Med*, 119: 189-94.

Townsend, M. K., G. C. Curhan, N. M. Resnick, and F. Grodstein. 2010. 'The incidence of urinary incontinence across Asian, black, and white women in the United States', *Am J Obstet Gynecol*, 202: 378 e1-7.

Townsend, M. K., K. N. Danforth, B. Rosner, G. C. Curhan, N. M. Resnick, and F. Grodstein. 2007. 'Body mass index, weight gain, and incident urinary incontinence in middle-aged women', *Obstet Gynecol*, 110: 346-53.

———. 2008. 'Physical activity and incident urinary incontinence in middle-aged women', *J Urol*, 179: 1012-6; discussion 16-7.

Townsend, M. K., Y. H. Jura, G. C. Curhan, N. M. Resnick, and F. Grodstein. 2011. 'Fluid intake and risk of stress, urgency, and mixed urinary incontinence', *Am J Obstet Gynecol*, 205: 73 e1-6.

Tsai, E., C. Yang, H. Chen, C. Wu, and J. Lee. 2001. 'Bladder neck circulation by Doppler ultrasonography in postmenopausal women with urinary stress incontinence', *Obstet Gynecol*, 98: 52-6.

Tunn, R., and E. Petri. 2003. 'Introital and transvaginal ultrasound as the main tool in the assessment of urogenital and pelvic floor dysfunction: an imaging panel and practical approach', *Ultrasound Obstet Gynecol*, 22: 205-13.

Tunn, R., M. Rieprich, O. Kaufmann, A. Gauruder-Burmester, and D. Beyersdorff. 2005. 'Morphology of the suburethral pubocervical fascia in women with stress urinary incontinence: a comparison of histologic and MRI findings', *Int Urogynecol J Pelvic Floor Dysfunct*, 16: 480-6.

Ulmsten, U. 1994. 'Urogenital ageing', *Gerontology*, 40 Suppl 3: 6-8.

Ulmsten, U., L. Henriksson, P. Johnson, and G. Varhos. 1996. 'An ambulatory surgical procedure under local anesthesia for treatment of female urinary incontinence', *Int Urogynecol J Pelvic Floor Dysfunct*, 7: 81-5; discussion 85-6.

Ulmsten, U., P. Johnson, and M. Rezapour. 1999. 'A three-year follow up of tension free vaginal tape for surgical treatment of female stress urinary incontinence', *Br J Obstet Gynaecol*, 106: 345-50.

Umek, W. H., T. Laml, D. Stutterecker, A. Obermair, S. Leodolter, and E. Hanzal. 2002. 'The urethra during pelvic floor contraction: observations on three-dimensional ultrasound', *Obstet Gynecol*, 100: 796-800.

Umek, W. H., A. Obermair, D. Stutterecker, G. Hausler, S. Leodolter, and E. Hanzal. 2001. 'Three-dimensional ultrasound of the female urethra: comparing transvaginal and transrectal scanning', *Ultrasound Obstet Gynecol*, 17: 425-30.

van Brummen, H. J., H. W. Bruinse, G. van de Pol, A. P. Heintz, and C. H. van der Vaart. 2007. 'The effect of vaginal and cesarean delivery on lower urinary tract symptoms: what makes the difference?', *Int Urogynecol J Pelvic Floor Dysfunct*, 18: 133-9.

van der Ploeg, J. M., A. van der Steen, S. Zwolsman, C. H. van der Vaart, and J. W. R. Roovers. 2017. 'Prolapse surgery with or without incontinence procedure; a systematic review and meta-analysis', *BJOG*.

van Veelen, A., K. Schweitzer, and H. van der Vaart. 2014. 'Ultrasound assessment of urethral support in women with stress urinary incontinence during and after first pregnancy', *Obstet Gynecol*, 124: 249-56.

Versi, E. 1990. 'Discriminant analysis of urethral pressure profilometry data for the diagnosis of genuine stress incontinence', *Br J Obstet Gynaecol*, 97: 251-9.

Versi, E., L. Cardozo, and D. J. Cooper. 1991. 'Urethral pressures: analysis of transmission pressure ratios', *Br J Urol*, 68: 266-70.

Viereck, V., W. Bader, T. Krauss, M. Oppermann, A. Gauruder-Burmester, R. Hilgers, R. Hackenberg, W. Hatzmann, and G. Emons. 2005. 'Intra-operative introital ultrasound in Burch colposuspension reduces post-operative complications', *BJOG*, 112: 791-6.

Viereck, V., H. U. Pauer, W. Bader, M. Oppermann, R. Hilgers, A. Gauruder-Burmester, R. Lange, G. Emons, R. Hackenberg, and T. Krauss. 2004. 'Introital ultrasound of the lower genital tract before and after colposuspension: a 4-year objective follow-up', *Ultrasound Obstet Gynecol*, 23: 277-83.

Viereck, V., H. U. Pauer, O. Hesse, W. Bader, R. Tunn, R. Lange, R. Hilgers, and G. Emons. 2006. 'Urethral hypermobility after anti-incontinence surgery - a prognostic indicator?', *Int Urogynecol J Pelvic Floor Dysfunct*, 17: 586-92.

Vij, M., A. Dua, and R. M. Freeman. 2016. 'Should maximal urethral closure pressure be performed before midurethral sling surgery for stress incontinence? A time to revisit', *Int Urogynecol J*, 27: 1491-5.

Viktrup, L., and G. Lose. 2000. 'Lower urinary tract symptoms 5 years after the first delivery', *Int Urogynecol J Pelvic Floor Dysfunct*, 11: 336-40.

———. 2008. 'Incidence and remission of lower urinary tract symptoms during 12 years after the first delivery: a cohort study', *J Urol*, 180: 992-7.

Volloyhaug, I., I. van Gruting, K. van Delft, A. H. Sultan, and R. Thakar. 2017. 'Is bladder neck and urethral mobility associated with urinary incontinence and mode of delivery 4 years after childbirth?', *Neurourol Urodyn*, 36: 1403-10.

Wadie, B. S., and A. S. El-Hefnawy. 2009. 'Urethral pressure measurement in stress incontinence: does it help?', *Int Urol Nephrol*, 41: 491-5.

Weidner, A. C., M. M. South, D. B. Sanders, and S. S. Stinnett. 2009. 'Change in urethral sphincter neuromuscular function during pregnancy persists after delivery', *Am J Obstet Gynecol*, 201: 529 e1-6.

Wesnes, S. L., Y. Hannestad, and G. Rortveit. 2017. 'Delivery parameters, neonatal parameters and incidence of urinary incontinence six months postpartum: a cohort study', *Acta Obstet Gynecol Scand*, 96: 1214-22.

White, R. D., D. McQuown, T. A. McCarthy, and D. R. Ostergard. 1980. 'Real-time ultrasonography in the evaluation of urinary stress incontinence', *Am J Obstet Gynecol*, 138: 235-7.

Wijma, J., A. E. Potters, B. T. de Wolf, D. J. Tinga, and J. G. Aarnoudse. 2003. 'Anatomical and functional changes in the lower urinary tract following spontaneous vaginal delivery', *BJOG*, 110: 658-63.

Wild, J. J., and J. M. Reid. 1952. 'Application of echo-ranging techniques to the determination of structure of biological tissues', *Science*, 115: 226-30.

Wise, B. G., G. Burton, A. Cutner, and L. D. Cardozo. 1992. 'Effect of vaginal ultrasound probe on lower urinary tract function', *Br J Urol*, 70: 12-6.

Wiseman, O. J., M. J. Swinn, C. M. Brady, and C. J. Fowler. 2002. 'Maximum urethral closure pressure and sphincter volume in women with urinary retention', *J Urol*, 167: 1348-51; discussion 51-2.

Wu, J. M., A. A. Dieter, V. Pate, and M. Jonsson Funk. 2017. 'Cumulative Incidence of a Subsequent Surgery After Stress Urinary Incontinence and Pelvic Organ Prolapse Procedure', *Obstet Gynecol*, 129: 1124-30.

Wyndaele, J. J., A. Gammie, H. Bruschini, S. De Wachter, C. H. Fry, R. I. Jabr, R. Kirschner-Hermanns, and H. Madersbacher. 2011. 'Bladder compliance what does it represent: can we measure it, and is it clinically relevant?', *Neurourol Urodyn*, 30: 714-22.

Yang, J. M., S. H. Yang, and W. C. Huang. 2006. 'Functional correlates of Doppler flow study of the female urethral vasculature', *Ultrasound Obstet Gynecol*, 28: 96-102.

Yang, J. M., S. H. Yang, W. C. Huang, and C. R. Tzeng. 2011. 'Reliability of a new method for assessing urethral compression following midurethral tape procedures using four-dimensional ultrasound', *Ultrasound Obstet Gynecol*, 38: 210-6.

———. 2013. 'Matched-pair analyses of resting and dynamic morphology between Monarc and TVT-O procedures by ultrasound', *Eur J Obstet Gynecol Reprod Biol*, 169: 402-7.

Yono, M., M. Otani, K. Ito, Y. Inoue, K. Furukawa, M. Hori, S. Tsuji, T. Tanaka, Y. Sakata, and S. Irie. 2015. 'Effect of Duloxetine on Urethral Resting Pressure and on Sphincter Contractility in Response to Coughing and Magnetic Stimulation in Healthy Women', *Low Urin Tract Symptoms*, 7: 93-8.

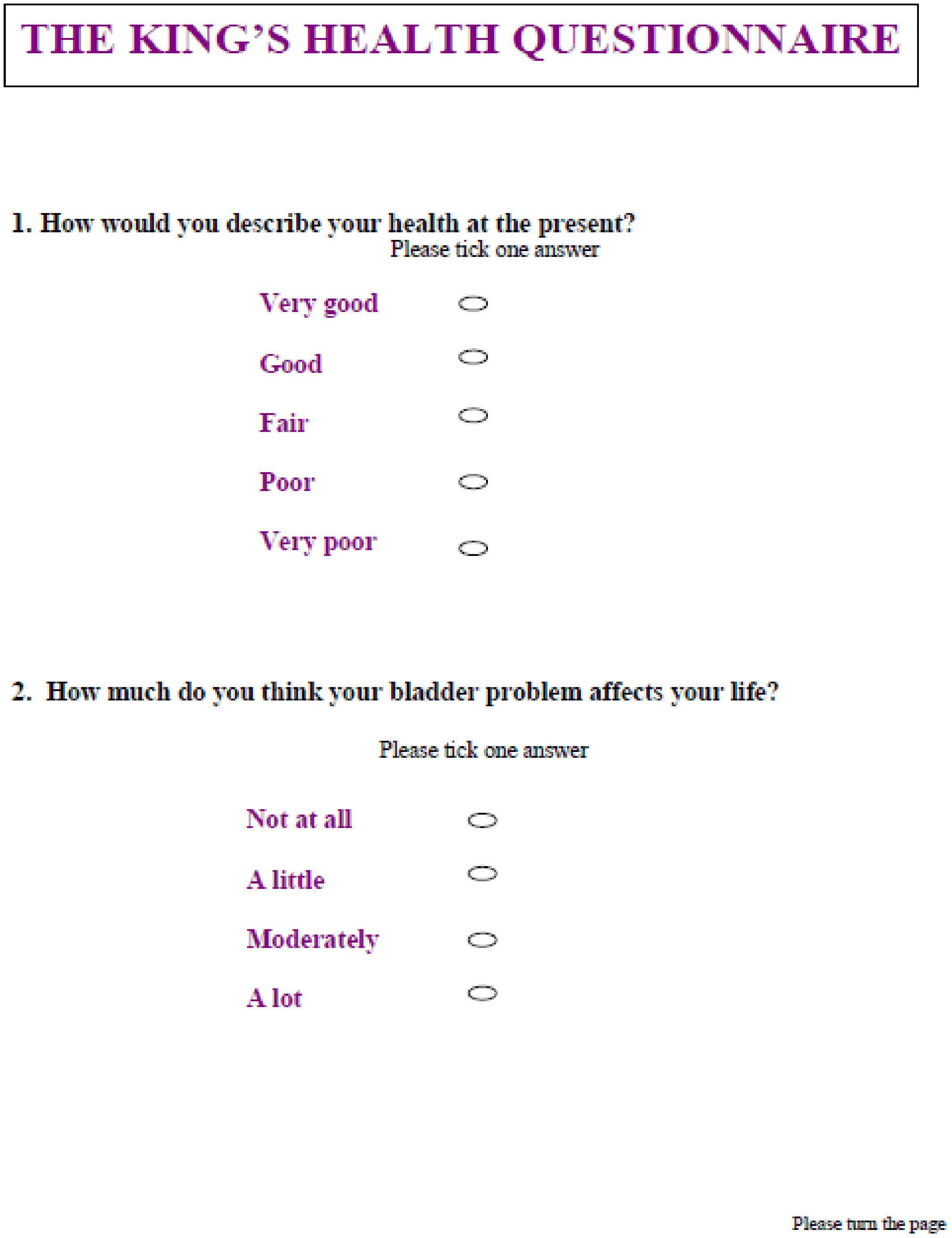
Yune, J. J., L. Quiroz, M. A. Nihira, S. Siddighi, D. E. O'Leary, A. Santiago, and S. A. Shobeiri. 2016. 'The Location and Distribution of Transurethral Bulking Agent: 3-Dimensional Ultrasound Study', *Female Pelvic Med Reconstr Surg*, 22: 98-102.

Zacharin, R. F. 1977. 'Abdominoperineal urethral suspension: a ten-year experience in the management of recurrent stress incontinence of urine', *Obstet Gynecol*, 50: 1-8.

Zecca, C., G. C. Riccitelli, G. Disanto, A. Singh, G. A. Digesu, L. Panicari, F. Puccini, M. Mattioli, A. Tubaro, and C. Gobbi. 2016. 'Urinary incontinence in multiple sclerosis: prevalence, severity and impact on patients' quality of life', *Eur J Neurol*, 23: 1228-34.

Zivanovic, I., O. Rautenberg, K. Lobodasch, G. von Bunau, C. Walser, and V. Viereck. 2017. 'Urethral bulking for recurrent stress urinary incontinence after midurethral sling failure', *Neurourol Urodyn*, 36: 722-26.

Appendix 1



THE KING'S HEALTH QUESTIONNAIRE

1. How would you describe your health at the present?

Please tick one answer

Very good	○
Good	○
Fair	○
Poor	○
Very poor	○

2. How much do you think your bladder problem affects your life?

Please tick one answer

Not at all	○
A little	○
Moderately	○
A lot	○

Please turn the page

**Below are some daily activities that can be affected by bladder problems.
How much does your bladder problem affect you?**

We would like you to answer every question. Simply tick the box that applies to you

	1	2	3	4
3. ROLE LIMITATIONS	Not at all	Slightly	Moderately	A lot
A. Does your bladder problem affect your household tasks? (cleaning, shopping etc)	○	○	○	○
B. Does your bladder problem affect your job, or your normal daily activities outside the home?	○	○	○	○

	1	2	3	4
4. PHYSICAL/SOCIAL LIMITATION	Not at all	Slightly	Moderately	A lot
A Does your bladder problem affect your physical activities (e.g. going for a walk, running, sport, gym etc)?	○	○	○	○
B. Does your bladder problem affect your ability to travel?	○	○	○	○
C. Does your bladder problem limit your social life?	○	○	○	○
D. Does your bladder problem limit your ability to see and visit friends?	○	○	○	○

	0	1	2	3	4
5. PERSONAL RELATIONSHIPS	Not Applicable	Not at all	Slightly	Moderately	A lot
A. Does your bladder problem affect your relationship with your partner?	○	○	○	○	○
B. Does your bladder problem affect your sex life?	○	○	○	○	○
C. Does your bladder problem affect your family life?	○	○	○	○	○

6. EMOTIONS	**1** **Not at all**	**2** **Slightly**	**3** **Moderately**	**4** **Very much**
A. Does your bladder problem make you feel depressed?	○	○	○	○
B. Does your bladder problem make you feel anxious or nervous?	○	○	○	○
C. Does your bladder problem make you feel bad about yourself?	○	○	○	○

7.SLEEP/ENERGY	**1** **Never**	**2** **Sometimes**	**3** **Often**	**4** **All the time**
A. Does your bladder problem affect your sleep?	○	○	○	○
B. Does your bladder problem make you feel worn out and tired ?	○	○	○	○

8.Do you do any of the following?	**If so how much?**			
	1 **Never**	**2** **Sometimes**	**3** **Often**	**4** **All the time**
A. Wear pads to keep dry?	○	○	○	○
B. Be careful how much fluid you drink ?	○	○	○	○
C. Change your underclothes because they get wet?	○	○	○	○
D. Worry in case you smell?	○	○	○	○

We would like to know what your bladder problems are and how much they affect you ? From the list below choose only those problems that you have at present. Leave out those that don't apply to you.

How much do they affect you?

FREQUENCY: going to the toilet very often

1. A little ○ **2.Moderately** ○ **3. A lot** ○

NOCTURIA: getting up at night to pass urine

1. A little ○ **2.Moderately** ○ **3. A lot** ○

URGENCY: a strong and difficult to control desire to pass urine

1. A little ○ **2.Moderately** ○ **3. A lot** ○

URGE INCONTINENCE: urinary leakage associated with a strong desire to pass urine

1. A little ○ **2.Moderately** ○ **3. A lot** ○

STRESS INCONTINENCE: urinary leakage with physical activity eg. coughing, running

1. A little ○ **2.Moderately** ○ **3. A lot** ○

NOCTURNAL ENURESIS: wetting the bed at night

1. A little ○ **2.Moderately** ○ **3. A lot** ○

INTERCOURSE INCONTINENCE: urinary leakage with sexual intercourse

1. A little ○ **2.Moderately** ○ **3. A lot** ○

WATERWORKS INFECTIONS

1. A little ○ **2.Moderately** ○ **3. A lot** ○

BLADDER PAIN

1. A little ○ **2.Moderately** ○ **3. A lot** ○

Thank You For Your Time

To Calculate Scores

PART 1

1) General Health Perceptions

Very good	1
Good	2
Fair	3
Poor	4
Very poor	5

Score = ((Score to Q1 – 1)/4) x 100

2) Incontinence Impact

Not at all	1
A little	2
Moderately	3
A lot	4

Score =((Score to Q2 – 1)/3) x 100

PART 2

Individual scores as recorded at the top of each column of possible responses

3) Role limitations

Score =(((Scores to Q 3A + 3B) – 2)/6) x 100

4) Physical limitations

Score =(((Scores to Q 4A + 4B) – 2)/6) x 100

5) Social limitations

[If 5C >/= 1] Score =(((Score to Q 4C + 4D + 5C) – 3)/9) X 100

[If 5C = 0] Score =(((Score to Q 4C + 4D) – 2)/6) x 100

6) Personal relationships

[If 5A+5B >=2]Score =(((Scores to Q 5A + 5B) – 2)/6) x 100

[If 5A+5B =1] Score =(((Scores to Q 5A + 5B) – 1)/3) x 100

[If 5A+5B =0] Treat as missing value

7) Emotions

Score =(((Score to Q 6A + 6B + 6C) – 3)/9) X 100

8) Sleep / energy

Score =(((Scores to Q 7A + 7B) – 2)/6) x 100

9) Severity measures

Score =(((Scores to Q 8A + 8B + 8C + 8D) – 4)/12) x 100

PART 3

Scale	*score*
Omitted	0
A little	1
Moderately	2
A lot	3