A CASE-CONTROL STUDY EXPLORING THE RELATIONSHIPS BETWEEN RISK FACTORS OF DETRUSOR UNDERACTIVITY AND BLADDER OUTLET OBSTRUCTION AND INCOMPLETE BLADDER EMPTYING IN COMMUNITY-DWELLING WOMEN AGED 65 OR OLDER WHO HAVE OVERACTIVE BLADDER SYMPTOMS

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ABSTRACT

JEONGOK PARK: A Case-Control Study Exploring the Relationship between Risk Factors of Detrusor Underactivity and Bladder Outlet Obstruction and Incomplete Bladder Emptying in Community-Dwelling Women Aged 65 or Older Who have Overactive Bladder Symptoms
(Under the direction of Mary H. Palmer, PhD, RNC, FAAN)

Overactive bladder (OAB) is a common health problem in women and tends to increase with age. Although OAB symptoms can occur due to involuntary detruosr contractions and incomplete bladder emptying, incomplete bladder emptying in older women who have OAB symptoms has been given little attention by researchers. Detrusor underactivity (DUA) and bladder outlet obstruction (BOO) have been proposed as causes of incomplete bladder emptying but research about the risk factors related to incomplete bladder emptying in exclusively older women is still scant. Therefore, the purpose of this study was to examine the relationship between risk factors of DUA and BOO and incomplete bladder emptying in women aged 65 or older who have OAB symptoms.

A total of 203 medical records were reviewed and 170 met the inclusion criteria. Model selection was conducted to determine the best model for analyzing the data. Logistic regression and a receiver operator characteristics (ROC) curve were performed to answer the research questions. Sixty-six (39%) of the women had incomplete bladder emptying. The result revealed a significant relationship between the presence of diabetes mellitus and increased bladder capacity (≥500ml) and incomplete bladder emptying. Another significant but unexpected relationship was found between anterior vaginal prolapse and incomplete

bladder emptying: an increase in the degree of anterior vaginal prolapse decreased the risk of incomplete bladder emptying. However, the relationship between incomplete bladder emptying and urinary frequency was not significant. Among urodynamic parameters, a maximal urine flow rate (Q_{max}) and voiding patterns were significantly related to incomplete bladder emptying: a greater maximal urine flow rate (Q_{max}) and interrupted voiding pattern were associated with an increased risk of incomplete bladder emptying.

The current study raises awareness of incomplete bladder emptying in older women with OAB symptoms. In addition, the findings may help nurse researchers and health care professionals understand what risk factors are related to incomplete bladder emptying in older women who have OAB symptoms.

DEDICATION

To my husband, Wonhee Yang, whom I dearly love,

To my parents and parents-in-law, whom I always respect and love.

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ABBREVIATIONS

BOO	Bladder Outlet Obstruction
BMI	Body Mass Index
CI	Confidence Interval
DM	Diabetes Mellitus
DUA	Detrusor Underactivity
OAB	Overactive Bladder
OR	Odd Ratio
PVR	Post Void Residual Urine
POP-Q	Pelvic Organ Prolapse Quantification
ROC	Receiver Operating Characteristic
SCI	Spinal Cord Injury
SCS	Spinal Cord Surgery
UI	Urinary Incontinence

CHAPTER 1

INTRODUCTION

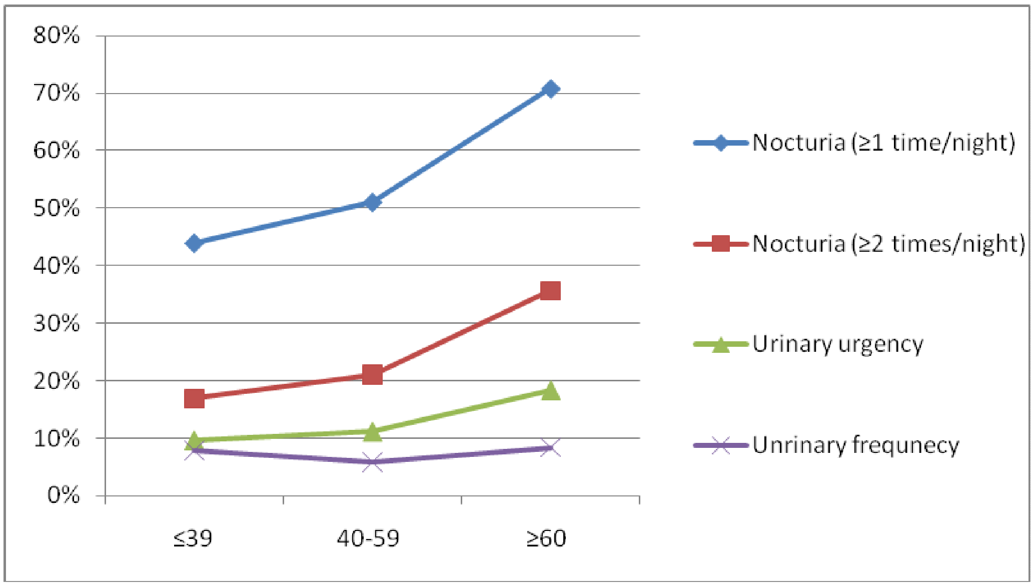
Background and Significance of the Study

Overactive bladder (OAB), defined by the International Continence Society as (Abrams et al., 2003) “urgency with or without urgency incontinence usually with frequency and nocturia in the absence of an underlying metabolic or pathological condition,” is a common health problem that affects approximately 16.9% of American women (Stewart et al., 2003).

Several population-based studies have reported an increasing trend with age in the prevalence of urinary urgency with or without urge urinary incontinence, urinary frequency, and nocturia, all of which are lower urinary tract symptoms of OAB (Irwin et al., 2006; Melville, Katon, Delaney, & Newton, 2005; Minassian, Stewart, & Wood, 2008; Stewart, et al., 2003). Stewart et al. (2003) reported that the age group of 65 to 74 years had about 30% prevalence of OAB, which was the highest prevalence among women aged 18 years and older. Irwin et al. (2006) found that nocturia was the most prevalent lower urinary tract symptom in both men and women. Most significantly, they found a 71% prevalence of nocturia, defined as one or more voiding incidents at night, but even if defined more narrowly as two or more voiding incidents at night, it would included 36% in women aged 60 or older (Figure 1.1).

Figure 1.1

Prevalence of Urinary Urgency and Frequency, and Nocturia by Age in Women



Note.

This graph was created based on data from the "Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: Results of the EPIC study" by Irwin, Milsom, Hunskaar, Reilly, Kopp, Herschorn, et al. (2006). *European Urology, 50*(6), 1306-1314.

OAB symptoms adversely affect women's quality of life and are associated with other health problems (Booth, Lawrence, O'Neill, & McMillan, 2010; Irwin, Abrams, Milsom, Kopp, & Reilly, 2008; Stewart, et al., 2003; Tikikinen et al., 2010). Stewart et al. (2003) found that women, who had OAB with or without urge incontinence, had significantly poorer scores on health related quality of life (HRQOL), mental health, and quality of sleep when compared with a control group. Irwin et al. (2008) also found that the daytime urinary frequency, defined as complaints by patients who thought that they void too often during the day, was reported as bothersome by 152 (66%) women with OAB symptoms. Tikkinen et al. (2010) reported that the degree they were bothered increased with frequency of nocturia in women and specifically two nightly voiding incidents adversely affected their health related quality of life. In a qualitative study, Booth et al. (2010) also noted that nocturia impacted sleep patterns and the quality of personal relationships and increased the fear of falling among people aged 60 or older.

For the initial treatment of OAB symptoms, antimuscarinic agents affect the nerve and muscle function of the detrusor (or bladder) muscle causing the detrusor muscle to relax, and thus reduce the frequency and intensity of contractions of the bladder. Based on these results, they have been widely used by health care providers. A recent study reported that the drug therapy cost for OAB was 1.8 billion dollars (U.S) a year (Onukwugha et al., 2009). However, 25.5% of people using OAB medicines reported discontinuing their use, and the most common reason (46%) was ineffectiveness of the medicine (Benner et al., 2009).

According to the Agency for Health Care Policy and Research (AHCPR), measuring post-void residual urine (PVR) is required prior to administration of antimuscarinic agents (Fantl et al., 1996) because patients who have OAB symptoms and elevated PVR are unlikely to have an improvement in their OAB symptoms using antimuscarinic medication, and it may even progress to complete bladder retention. However, it is unclear whether healthcare practicioners, especially primary health care providers, measured the PVR before prescribing medication therapy for OAB. Moreover measuring the PVR for all patients who have overactive symptoms is practically and economically infeasible. Therefore, understanding the risk factors related to elevated PVR (incomplete bladder emptying) is important for developing clinical guidelines to screen patients who have incomplete bladder emptying.

OAB symptoms (urinary urgency and frequency, and nocturia with/with out urinary incontinence) can occur from involuntary detrusor contractions and/or incomplete bladder emptying. Incomplete bladder emptying can increase the number of voiding incidents a day or a night because the bladder capacity is functionally decreased due to retained urine (Milleman, Langenstroer, & Guralnick, 2004). In other words, the larger the volume of retained urine, the less time is needed for the bladder to achieve the capacity at which the person feels the need to urinate. In previous studies, the prevalence of incomplete bladder emptying in women with OAB symptoms was 8% to 19% (Digesu, Khullar, Cardozo, & Salvatore, 2003; Fitzgerald, Jaffar, & Brubaker, 2001; Milleman, et al., 2004). Milleman et al. (2004) found that 38 (19%) of the women complaining of OAB symptoms aged 20 to 90 (mean age 55) had a PVR of 100ml or greater (mean 211ml, range 100 to 997ml). Digesu et al. (2003) reported that 68 (8.1%) of the women aged 22 to 73 years with OAB symptoms without involuntary detrusor contractions had a PVR greater than 100ml. Fitzgerald et al. (2001) also found 36 (9%) of the women aged 17 to 94 (mean age 60.6) had a PVR of greater than 100ml.

Proposed risk factors related to incomplete bladder emptying in previous studies were associated with detrusor underactivity (DUA) and/or bladder outlet obstructions (BOO) (Yoshimura & Chancellor, 2004). DUA refers to inadequate bladder contractile function which can result from damage of nerves that innervate the bladder, detusor muscle damage, or sensory deficit. Associated factors with bladder nerve damage are neurologic disease such as multiple sclerosis (MS), Parkinson’s disease and stroke, history of spinal cord injury and pelvic surgery, herniated disc, and pelvic and sacral fractures (Yoshimura & Chancellor, 2004). Chronic over-distension of the bladder and advanced aging have been addressed by researchers as factors for detrusor muscle damage (Meyer-Siegler, Iczkowski, & Vera, 2006; Michel & Barendrecht, 2007; Taylor III & Kuchel, 2006; Yoshimura & Chancellor, 2004). Diabetes mellitus (DM) and increased bladder capacity have also been associated with sensory deficit (Lee, Wu, Tai, Yu, & Chiang, 2009; Taylor III & Kuchel, 2006; Yoshimura & Chancellor, 2004), which could be related to incomplete bladder emptying. Common factors related to anatomic bladder outlet obstruction (BOO) in women are advanced pelvic organ prolapse or anti-incontinence surgery (Groutz, Blaivas, & Chaikin, 2000; McCrery & Appell, 2006; Yoshimura & Chancellor, 2004).

Unfortunately, few studies have examined the relationship between risk factors of DUA and BOO and incomplete bladder emptying in older women and moreover their findings have been inconsistent. One of reasons for the inconsistent findings could be from the lack of standardization of voiding parameters in women, such as detrusor pressure and urine flow rates, which could result in mixed results about the effect of neurologic diseases, DM, and anti- incontinence surgery for women’s voiding function (Abarbanel & Marcus, 2007; Fitzgerald, et al., 2001; Lee, Wu, Wu, & Tai, 2007; Lee, et al., 2009; Milleman, et al., 2004). Unlike men, women can void normally with low detrusor pressure (less than 10 cm H_2O), and they are able to empty the bladder completely with a good urinary flow rate using pelvic floor relaxation or abdominal straining (by habit) without needing to generate significant detrusor pressure (Nitti, Tu, & Gitlin, 1999). Thus, urodynamic parameters such as detrusor pressure and urine flow rates are carefully applied when conducting a voiding study in women; furthermore, studies for defining normal voiding parameters in women are needed to produce accurate studies.

In summary, OAB is a common health problem in women, especially older women, and healthcare providers have administered antimuscarinic agents for initial treatment. Before medication therapy for OAB, the Agency for Health Care Policy and Research (AHCPR) recommends measuring the patient's PVR to decrease or avoid adverse effects such as urinary retention. However, measuring PVR for all of women with OAB symptoms is practically and economically infeasible in the primary care settings. Detrusor underactivity (DUA) and bladder outlet obstruction (BOO) can cause incomplete bladder emptying or increased PVR in women who have OAB symptoms but there are limited studies on the risk factors of DUA and BOO related to incomplete bladder emptying. In addition, some of the potential risk factors such as neurologic disease, DM, and anti-incontinence surgery still remain controversial. Furthermore, although incomplete bladder emptying could cause urinary frequency, the relationship between these variables has not been examined. Therefore, investigation of the relationship between risk factors of DUA and BOO and incomplete bladder emptying will help researchers understand the voiding dysfunction in women with OAB symptoms and could produce clinical guidelines for screening women who have incomplete bladder emptying.

Purpose of the Study

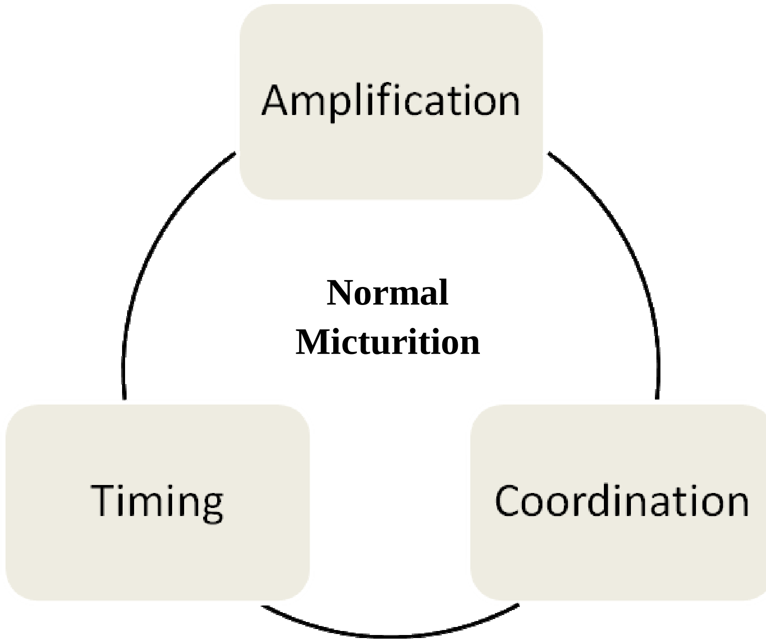
The purpose of this study is to explore the relationship between risk factors of DUA and BOO and incomplete bladder emptying in community-dwelling women aged 65 or older who have OAB symptoms. This is accomplished by examining the relationships 1) between risk factors of DUA and BOO and incomplete bladder emptying, 2) between urinary frequency and incomplete bladder emptying, and 3) between urodynamic parameters and incomplete bladder emptying.

Conceptual Framework

The neural pathways in the central nervous system that control micturition perform three major functions: amplification, coordination, and timing (Yoshimura & Chancellor, 2004) (Figure 1.2). The nervous control of the lower urinary tract must be able to amplify weak smooth muscle activity to provide a sustained increase in intravesical pressure that is sufficient to empty the bladder (amplification). The bladder and urethral sphincter function must be coordinated to allow the sphincter to open during micturition but remain closed at all other times (coordination). Timing represents the voluntary control of voiding in normal adults and the ability to initiate voiding over a wide range of bladder volumes.

Figure 1.2

Three Functions of Neural Pathways for Normal Micturition



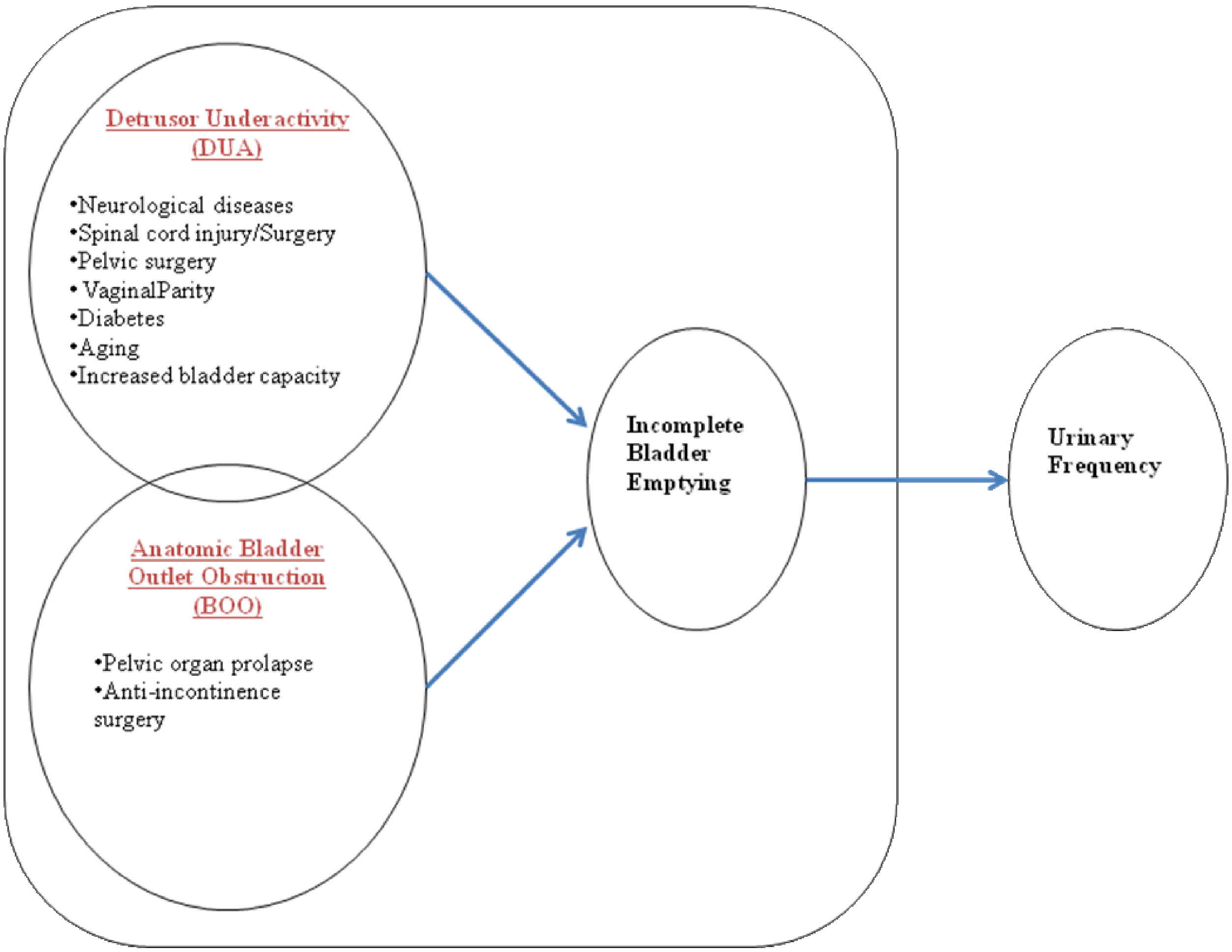
Damaged/altered neural pathways associated with these three functions can result in incomplete bladder emptying due to a reduced strength of detrusor contractions. Damaged nerves that innervate the bladder, detrusor muscle damage, and bladder sensory deficit (Yoshimura & Chancellor, 2004) are related to DUA causing incomplete bladder emptying. Specifically, risk factors for damaged nerves include the presence of neurological disease such as multiple sclerosis (MS), Parkinson’s disease and stroke, history of pelvic surgery, herniated disc, and pelvic and sacral fractures, and those for detrusor muscle damage include chronic over-distension of the bladder and advanced aging (Meyer-Siegler, et al., 2006; Michel & Barendrecht, 2007; Taylor III & Kuchel, 2006; Yoshimura & Chancellor, 2004). DM and increased bladder capacity are also risk factors for sensory deficit associated with incomplete bladder emptying due to DUA (Lee, et al., 2009; Taylor III & Kuchel, 2006; Yoshimura & Chancellor, 2004).

Another risk factor related to incomplete bladder emptying is anatomic bladder outlet obstruction (BOO). The most common causes of anatomic BOO in women are post-operative BOO (e.g., anti-incontinence surgery) and advanced pelvic organ prolapse (Groutz, et al., 2000; McCrery & Appell, 2006; Yoshimura & Chancellor, 2004).

Incomplete bladder emptying resulting from DUA and BOO can increase the frequency of urination because the bladder capacity is functionally decreased due to retained urine (Milleman, et al., 2004). That is, the larger the volume of retained urine, the less time is needed for the bladder to achieve the capacity at which the patient feels the need to urinate. Therefore, a conceptual model was developed to examine the relationships between risk factors of DUA and BOO and incomplete bladder emptying, and between urinary frequency and incomplete bladder emptying (Figure1.3).

Figure 1.3

Conceptual Model for the Relationships between Risk Factors of Detrusor Underactivity and Bladder Outlet Obstruction and Incomplete Bladder Emptying



Research Questions

1. The relationship between risk factors of DUA and BOO and incomplete bladder emptying

1) What are the relationship between risk factors of DUA (presence of neurologic disease, history of spinal cord injury and pelvic surgery, vaginal parity, DM, age, or bladder capacity) and between incomplete bladder emptying?

2) What are the relationship between risk factors of DUA and incomplete bladder emptying, when adding risk factors of BOO (pelvic organ prolapse and history of anti-incontinence surgery)?

2. The relationship between incomplete bladder emptying and urinary frequency

1) What are the sensitivity and specificity of daily voiding incidents to confirm incomplete bladder emptying?

2) What are the sensitivity and specificity of night time voiding incidents to confirm incomplete bladder emptying?

3. The relationship between urodynamic parameters and incomplete bladder emptying

What are the relationships between urodynamic parameters (opening detrusor pressure at voiding ($P_{det.}Open$), detrusor pressure at the maximal urine flow ($P_{det.} Q_{max}$), maximum urine flow rate (Q_{max}), and voiding patterns) and incomplete bladder emptying?

CHAPTER 2

LITERATURE REVIEW

Causes of Incomplete Bladder Emptying:

Detrusor Underactivity and Bladder Outlet Obstruction

Incomplete bladder emptying can result from the detrusor underactivity (DUA) and/or bladder outlet obstruction (BOO). According to the International Continence Society (ICS), DUA is defined as “a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying with a normal time span,” and acontractile detrusor is defined as “ one that cannot be demonstrated to contract during urodynamic studies” (Abrams, et al., 2003). BOO is defined by ICS as “the generic term for obstruction during voiding and is characterized by increased detrusor pressure and reduced urine flow rate.”

In previous studies, the prevalence of DUA and BOO in women vary from 12% to 39% and from 7% to 13%, respectively, because there are no standard definitions for urodynamic parameters (Abarbanel & Marcus, 2007; Groutz, et al., 2000; Groutz et al., 1999; N.M. Resnick, Brandeis, Baumann, DuBeau, & Yalla, 1996). The prevalence of DUA, defined as a maximal flow rate (Q_{max}) of less than 10 ml/second combined with a detrusor pressure at the maximal urine flow rate ($P_{det}.Q_{max}$) of less than 30cm H_2O, was 12% in 99 community dwelling elderly women (mean age 75.1±4.6 years) (Abarbanel & Marcus, 2007).

Lee et al. (2009) reported that the prevalence of DUA and BOO in type 2 diabetic women (mean age 66.9±10.4) was 35% and 13%, respectively. Groutz et al. (2000) reported that the prevalence of BOO, defined as the maximum urine flow rate (Q_{max}) of less than 12 ml/second in non- invasive uroflow studies combined with detrusor pressure at the maximal urine flow rate ($P_{det}.Q_{max}$) of greater than 20cm H_2O during pressure-flow studies, was 7% in 587 women (mean age 63.9±17.5 years) (Groutz, et al., 2000). Groutz et al. (1999) also reported that 40 (19.4%) women showed voiding difficulties, defined as a maximum urine flow rate (Q_{max}) of less than 12ml/s or a PVR greater than 150 ml. Among these 40 women, 98% and 2% of these women's voiding difficulties were caused by DUA and BOO, respectively.

Discrepancy between Lower Urinary Tract Symptoms and Functions

Previous studies have shown that significant numbers of women having DUA or BOO were asymptomatic or that a discrepancy exists between their symptoms and voiding functions (Groutz, et al., 1999; Ueda, Yoshimura, & Yoshida, 1997; Yu et al., 2004). However, studies on the correlation between their lower urinary tract symptoms (LUTS) and urodynamic diagnosis in women are still scarce. Groutz et al. (1999) reported that 13 (33%) women, who were diagnosed as incomplete bladder emptying using urodynamic tests, did not have any voiding related symptoms. Yu et al. (2004) and Ueda et al. (1997) also found, respectively, 22% and 40 % asymptomatic DUA in type 2 diabetic women. Digesu et al. (2003) reported that 68 (8.1%) of women with OAB symptoms such as urinary frequency and urgency without voiding symptoms had a urodynamic diagnosis of voiding dysfunctions.

Effect of Asymptomatic Incomplete Bladder Emptying on Treatments

The presence of only storage symptoms such as urinary urgency, frequency, and nocturia without voiding symptoms such as a feeling of incomplete emptying, slow stream, or hesitancy in women may result in inappropriate treatments. For example, for women with OAB symptoms with normal voiding, antimuscarinic agents might be beneficial for managing their symptoms. However, for women with OAB symptoms and voiding problems, these medicines may not improve their symptoms or may exacerbate their voiding problems so that they could experience bladder emptying or urinary retention.

DUA may also complicate the surgical management of female stress incontinence. That is, the presence of DUA before anti-incontinent surgery can increase the risk of urinary retention after surgery (Lose, Jorgensen, Mortensen, Molsted-Pedersen, & Kristensen, 1987). Lose et al. (1987) reported that 20 (25%) women who had colposuspension developed severe incomplete bladder emptying in the immediate postoperative course. In addition, low detrusor pressure during voiding (less than 15 cm H_2O) preoperatively was found to significantly predispose them to immediate postoperative incomplete bladder emptying.

Problems with Defining Normal Voiding in Women

Normal voiding occurs voluntarily when there is relaxation of the external sphincter followed by a sustained contraction of the bladder, opening of the bladder neck, and flow of urine, which should result in complete or near complete emptying of the bladder (Nitti, et al., 1999). The voiding phase can be altered when there is DUA or BOO and these two conditions are not mutually exclusive. DUA can be defined by low pressure and low flow voiding, and BOO is defined by high pressure and low flow voiding.

To date, these urodynamic parameters (detrusor pressure and flow rate) have been used in most voiding studies on women (Abarbanel & Marcus, 2007; Defreitas, Zimmern, Lemack, & Shariat, 2004; Digesu, et al., 2003; Kuo, 2004; Romanzi, Chaikin, & Blaivas, 1999; Tanaka et al., 2009). However, previous studies used and proposed different criteria to define DUA and BOO because of the absence of standard definitions of urodynamic parameters (Table 2.1 & 2.2). At least two studies also reported that neither the urodynamic parameters nor lower urinary tract symptoms alone may be sufficient for diagnosing obstruction in women (Lemack & Zimmern, 2000; Nitti, et al., 1999). Specifically, Nitti et al. (1999) reported that DUA and BOO defined by the urodynamic parameters (detrusor pressure and flow rate) would include many women with normal bladder function and missed in other women who could void normally with low detrusor pressure (less than 10 cm H_2O). That is, women able to empty their bladders completely with a good urinary flow rate using pelvic floor relaxation or abdominal straining (by habit) without needing to generate significant detrusor pressure.

Pfisterer et al. (2007) recently reported the urodyanmic parameters of bladder function in pre-, peri- and post- menopausal continent women without detrusor overactivity. The median maximum urine flow rate (Q_{max}) and detrusor pressure at maximum flow rate (P_{det}. Q_{max}) were 22ml/s and 27cmH_2O, respectively, for 24 women aged 22 to 80 years (Pfisterer, Griffiths, Rosenberg, Schaefer, & Resnick, 2007). These parameters among the post-menopausal women aged 55 to 80 were 18ml/s and 24 cmH_2O and those values were not significantly different from pre- and peri-menopausal groups (p= .13, p= .07, respectively). However, the small number of subjects limits these findings. Thus, more research based on larger samples is needed to define normal voiding in women.

Table 2.1

Criteria of Urodyamic Parameters Used for Defining BOO

Study	Year	$P_{det}.Q_{max}$	Q_{max}	Other
Chassagne et al.	(1998)	> 20 cmH_2O	≤ 15ml/s	
Nitti et al.	(1999)			Radiologic evidence between the bladder neck and distal urethra
Groutz et al.	(2000)	> 20 cmH_2O	< 12ml/s	
Lemack et al.	(2000)	> 21 cmH_2O	< 11ml/s	
Kuo et al.	(2004)	≥ 35 cmH_2O	≤ 15ml/s	
Defreitas et al.	(2004)	≥ 25 cmH_2O	< 12ml/s	
Cucchi et al.	(2008)	> 50 cmH_2O	< 12ml/s	

Note.

$P_{det}.Q_{max}$: Detrusor pressure at a maximal urine flow rate during pressure flow study

Q_{max}: Maximmal urine flow rate during pressure flow study

Table 2.2

Criteria of Urodyamic Parameters Used for Defining DUA

Study	Year	$P_{det}.Q_{max}$	Q_{max}	Other
Kaplan et al.	(1995)	< 30 cmH_2O	< 12ml/s	
Abarbanel et al.	(2007)	< 30 cmH_2O	< 10ml/s	
Cucchi et al.	(2008)	< 20 cmH_2O		PVR > 50ml, Qmax-below the lower limits of normal in the Liverpool nomograms
Lee et al.	(2009)			Schafer and ICS nomograms
Ho et al.	(2009)	< 20 cmH_2O	< 15ml/s	

Note.

$P_{det}.Q_{max}$: Detrusor pressure at a maximal urine flow rate during pressure flow study

Q_{max}: Maximal urine flow rate during pressure flow study

Risk Factors of Detrusor Underactivity Influencing Incomplete Bladder Emptying

Nervous Control of Bladder

The bladder is controlled by efferent and afferent innervations (Fry, 2005). In terms of efferent innervations, the lower urinary tract receives dual autonomic innervations: a parasympathetic supply from S2-S4 and a sympathetic supply from T10-L2. There is also a dual somatic supply which runs in the nervi erigentes. Typical motor neurons in levels S2-S4 provide axons in the pudendal nerve to innervate the pelvic floor musculature and part of the urethra. A second component provides fibers to the intrinsic rhabdosphincter. Regarding afferent innervations, afferent fibers originate in the suburothelial layer, the urothelium, and detrusor layers. Distension of the urinary bladder by increasing urine volume elicits afferent signals to the central nervous system. Although the molecular identity of the distension sensors has not been fully elucidated, recent data suggest that the urothelium plays a key role in this process (Brider & De Groat, 2007). The afferent signals from the bladder are sent to the brain where they are processed in the pontine storage and mictutition centers (Michel, Oelke, & Peters, 2005). Low frequency stimulation of the afferent nerves, which occurs with low filling volumes, initially triggers the activation of descending pathways which activates sympathetic outflow via sympathetic hypogastric nerves and also somatic nervous outflow via the pudendal nerve (Michel & Barendrecht, 2007). If bladder filling increases further, greater afferent stimulation occurs. When the cerebral cortex determines that it is socially acceptable to void, efferent signaling switches from the pontine storage to the pontine micturition center. This stops the sympathetic outflow to the bladder and instead activates parasympathetic outflow via the pelvic nerves. They release acetylcholine to stimulate muscarinic receptors in the detrusor (Michel & Barendrecht, 2007).

Nerve Damage

Neurological damage to the peripheral nerves of the bladder or the lower spinal cord may cause the sensation of bladder filling to be absent or reduced, and adequate bladder emptying fails (Rigby, 2005). The most common conditions or events damaging nerves and nerve pathways related to bladder function are spinal cord injury, multiple sclerosis, stroke, diabetes, and vaginal childbirth. Since normal voiding relies on the synergy between bladder contraction and the bladder neck opening, patients with spinal cord lesions may present with a lack of detrusor-sphincter synergy which is a particular feature of voiding dysfunction in patients following a cerebrovascular accident (CVA). In particular, suprapontine lesions from a stroke and Parkinson's disease usually result in voiding dysfunction.

Voiding problems such as severe hesitancy and an elevated PVR in stroke patients were reported in a recent study (Natsume, 2008). Natsume (2008) found that 10 of 23 (43%) women had DUA and 8 (80%) of those 10 showed concurrent OAB symptoms. As a possible etiology, the voiding reflex pathway after CVA may be modulated by a variety of transmitter mechanisms in the suprapontine area (Yoshimura & de Groat, 1997). It is also conceivable that a mechanism that promotes complete bladder emptying acts ineffectively, being linked to less sustained detrusor contractility power and fading contraction (Pfisterer, Griffiths, Schaefer, & Resnick, 2006; Resnick & Yalla, 1987).

Aging

Normal aging is known as a strong factor associated with DUA because impaired sensory function and morphological changes in the bladder have been found in normal aging (Kenton, Simmons, FitzGerald, Lowenstein, & Brubaker, 2007; Pfisterer, et al., 2007; Pfisterer, Griffiths, Schaefer, et al., 2006).

Impaired sensory functions with normal aging

Previous studies have demonstrated that age-induced changes in sensory transduction and afferent function of the urethra and bladder could affect detrusor contractility (Kenton, et al., 2007; Pfisterer, et al., 2007; Pfisterer, Griffiths, Schaefer, et al., 2006). Because activation and maintenance of the micturition response depends on normal sensory transduction relative to bladder volume and urethral stimulation during flow (Gustafson, Creasey, & Grill, 2004), sensory dysfunctions may contribute to voiding dysfunctions, including DUA.

Aging has also been associated with degradation of bladder and urethral sensations. In an animal model, aging was associated with increased volume and pressure thresholds for voiding, and diminished response to intravesical capsaicin instillation (Chai, Andersson, Tuttle, & Steers, 2000). Aging in urodynamically normal women was found to be associated with higher mean/median volume thresholds for desire to void and strong desire to void (Pfisterer, et al., 2007; Pfisterer, Griffiths, Rosenberg, Schaefer, & Resnick, 2006). Specifically, the means of desire to void were, respectively, 115ml, 168, and 223ml for the women's groups aged 20 to 39, 40 to 59, and 60 years or older, and these volumes were significantly different by group ($p < .001$) (Pfisterer, Griffiths, Schaefer, et al., 2006). Similarly, in the same report, the mean volumes for strong desire to void increased with age (232ml, 328ml, and 351ml for each group) and these volumes were significantly different ($p = .002$). Likewise, Kenton et al. (2007) found that the bladder and urethra sensory threshold measured objectively with current perception testing (CPT) increased (i.e., was less sensitive) with increased age in 48 women aged 23 to 67 years ($p < .0005$).

Morphological changes

Age-induced morphologic changes include a decrease in the ratio of detrusor muscle to collagen, changes in collagen and muscle quantity, and a decrease in axonal content (Elbadawi, Yalla, & Resnick, 1993; Lepor, Sunaryadi, Hartanto, & Shapiro, 1992). Lepor et al. (1992) found that aging was associated with a decrease in the area density of smooth muscle to connective tissue ratio in both males and females aged 65 to 75 years, and these morphometirc changes were associated with a relative increase in detrusor fibrosis. Elbadwi et al. (1993) also found that aging was associated with a so-called dense-band pattern including widening of the spaces between muscle cells and depleted caveolae in elderly men and women without DUA, and these structural changes were consistent with impaired detrusor contractility.

Diabetes Mellitus

Voiding dysfunctions in diabetic patients have been classically known as “diabetic cystopathy” which can be characterized as decreased bladder sensitivity, increased bladder capacity, and impaired detrusor contractility (Frimodt-Moller, 1980). Diabetes-induced autonomic neuropathy (Vinik, Maser, Mitchell, & Freeman, 2003) and changes in the physical properties of the bladder such as bladder hypertrophy and increased bladder capacity resulting from increased fluid intake and urine output by virtue of hyperosmolar status (Kudlacz, Gerald, & Wallace, 1989) were proposed as the pathophysiology of DUA in type 2 diabetic patients.

Based on disease progression and urodynamic findings, bladder dysfunction in DM can be stratified into incipient (compensated) and advanced (decompensated) stages, and the fundamental differentiating factor between these two stages is residual urine (Ellenberg, 1980). The early detection of bladder dysfunction is important because poor emptying of the bladder can impair renal function. However, it is difficult to diagnose diabetic cystopathy at an early stage because the onset of diabetic cystopathy is insidious and may not be recognized until it has reached an advanced stage (Goldman & Appell, 1999). Early signs and symptoms may be overlooked by the patients, but impaired bladder sensation is usually the first manifestation of lower urinary tract involvement. Symptoms may begin as infrequent voiding, reduced stream, hesitancy in initiating the urinary flow, dribbling due to overflow incontinence, and the sensation of incomplete emptying.

Yu et al. (2004) found that type 2 diabetic women (mean age 62 years) had a high prevalence (22%) of unrecognized bladder dysfunction in clinical settings, compared with only 5.6% of non-diabetic women (OR= 4.8, 95% CI: 2.3-10.4) (Yu, et al., 2004). Notably, 13.6% of diabetic women had high PVR volume (≥100ml) in the study. Thus, on careful evaluation, a considerable number of women with DM, even when asymptomatic, will be diagnosed with voiding dysfunction.

Risk Factors of Bladder Outlet Obstruction Influencing Impaired Bladder Emptying

Bladder outlet obstruction (BOO) results from a variety of etiologies, which may be functional or anatomic. Functional obstruction may be caused by detrusor-sphincter dysnergia (DSD), either at the level of the smooth muscle or rhabdo-sphincter or it may be due to dysfunctional voiding associated with learned voiding disorders or pelvic floor dysfunctions associated with pain syndrome (Dmochowski, 2005). Anatomical obstruction in women results most commonly from pelvic organ prolapse and anti-incontinence procedures (Dmochowski, 2005; Groutz, et al., 2000; Kuuva & Nilsson, 2002; Massey & Abrams, 1988; Nitti, et al., 1999; Romanzi, et al., 1999).

Pelvic Organ Prolapse

Pelvic organ prolapse refers to loss of support of the uterus, bladder, colon, or rectum leading to prolapse of one or more of these organs in the vagina (Abrams, Cardozo, Khoury, & Wein, 2009). Pelvic organ prolapse quantification (POP-Q) developed by the International Continence Society in 1996 defines prolapse by measuring the descent of one or more of the anterior vaginal wall, posterior vaginal wall, and apex of the vagina (cervix/uterus) or vault after a hysterectomy during valsalva strain relative to a fixed point, the hymen.

Although different cut-off values of the PVR have been used to define incomplete bladder emptying in previous studies, the results have confirmed the association of incomplete bladder emptying and the severity of pelvic organ prolapse (Ellerkmann et al., 2001; Fitzgerald, et al., 2001; Haylen et al., 2007; Haylen et al., 2008; Lukacz, DuHamel, Menefee, & Luber, 2007; Romanzi, et al., 1999). A large anterior vaginal prolapse (cystocele) may impair outflow by creating an angle at the bladder outlet, and dissipating the detrusor pressure into the prolapse (Chassagne et al., 1998). Haylen et al. (2008) noted that the prevalence of incomplete bladder emptying (a PVR of 30ml or greater) increased with increasing stages of prolapse. In their study, the prevalence of an elevated PVR were 9% (prolapse grade 0), 11% (prolapse grade 1), 24% (prolapse grade 2), and 55% (prolapse grade 3 or 4) ($p < .001$). Lukacz et al. (2007) also found that the presence of anterior or apical prolapse at or beyond the hymen was associated with 2.6 times increased odds of having an elevated PVR (100ml or greater). Romanzi et al. (1999) also found that among 60 women, 58% of the women with a grade 3 or 4 cystocele (anterior vaginal prolapse) had BOO compared with only 4% with a grade 1 or 2 cystocele.

Few studies, however, have examined the relationship between the location of pelvic organ prolapsed and incomplete bladder emptying and of those studies, the results have been inconsistent (Ellerkmann, et al., 2001; Haylen, et al., 2007). Haylen et al. (2007) reported that a significant relationship of incomplete bladder emptying (a PVR of 30ml or greater) to increased grades of all types of prolapse (anterior, posterior and apex prolapse) was found ($p < .001$). In contrast, Ellerkmann et a1. (2001) reported that voiding dysfunction characterized by urinary frequency, prolonged or intermittent flow, and a need to change positions was associated with increasing severity of anterior and apical pelvic organ prolapse. However, defecatory dysfunction was associated with worsening posterior compartment pelvic organ prolapse.

Anti-Incontinence Surgery

Another common cause of BOO in women is a complication of anti-incontinence surgery (Groutz, et al., 2000; Kuuva & Nilsson, 2002; Massey & Abrams, 1988; Nitti, et al., 1999; Stanton, Ozsoy, & Hilton, 1983). Stanton (1983) found that anterior colporrhaphy was the most common previous pelvic operation among women having voiding difficulty. Groutz (2000) found that 10 of 38 (26%) urodynamically obstructed women had had previous anti-incontinence surgery. Nitti (1999) also reported that the cause of 11(14%) women having BOO was incontinence surgery.

Summary

Incomplete bladder emptying can be caused by DUA and/or BOO in women. Several risk factors of DUA related to neurologic damage to the peripheral nerves of the bladder or the lower spinal cord have been examined, including spinal cord injury/surgery, multiple sclerosis, stroke, Parkinson’s disease, DM, vaginal child birth, and pelvic surgery. Risk factors of anatomical BOO related to a distortional or kinking effect on the urethra include pelvic organ prolapse, especially anterior vaginal prolapse, and anti- incontinence surgery. To date, these risk factors related to incomplete bladder emptying are limited to older women with OAB symptoms. In addition, previous studies reveal controversy about these risk factors including diabetes, age, and pelvic organ prolapse. To better understand voiding dysfunction in women with OAB symptoms, it is important to examine the relationship between risk factors of DUA and BOO and incomplete bladder emptying in women with OAB symptoms.

CHAPTER 3

METHODOLOGY

This chapter includes the study design, sample and setting, protection of human subjects, data collection procedure, measurements, data management, and method of data analyses.

Study Design

A case-control study was used to explore the association of impaired bladder emptying with factors of DUA and BOO in women aged 65 or older with OAB symptoms. A case-control study is an investigation that compares a group of people with a disease or condition (incomplete bladder emptying) to a group of people without the disease or condition. This study compares the odds of past exposure to a suspected risk factor between cases and controls (Szklo & Nieto, 2000).

The strengths of a case-control study are that they can be used to study infrequent (rare) diseases (Szklo & Nieto, 2000). In addition, they are relatively inexpensive because no follow-up is necessary, thus optimizing speed and efficiency. In this study, a case-control study is appropriate because incomplete bladder emptying is a dependent variable that requires an expensive diagnostic test (urodynamics or measurement of PVR) and is a relatively infrequent problem compared with UI or OAB in women.

The limitations of case-control studies are that they cannot be used to compute incidence rates and that they are often affected by selection bias (Kaelin & Bayona, 2004; Szklo & Nieto, 2000). Selection bias may be present if the control group does not come from the same population as the cases. Information bias is another common problem of case-control studies (Kaelin & Bayona, 2004). One type of information bias is recall bias which may arise when individuals with a disease (cases) remember past exposures more completely (or less completely) than the individuals in a control group.

Sample and Setting

Sample

A thorough medical chart review of women who had completed urodynamic tests at the Urophysiology Laboratory at the University of North Carolina Hospitals at Chapel Hill was conducted. The inclusion criteria were as follows; females who were 1) aged 65 years or older, and 2) completed urodynamic tests. The criteria for exclusion included 1) a documented history of pelvic irradiation, radical hysterectomy, or bladder cancer, 2) a documented history of suspected Alzheimer's disease, 3) a foley catheter, 4) a sacral nerve stimulator (interstim), or 5) taking anticholinergic medications.

Of the 187 medical records after the initial exclusions, 19 met the inclusion criteria for defining normal values of urodynamic parameters. The inclusion criteria were 1) no history of neurologic diseases (stroke, Parkinson's disease, multiple sclerosis), 2) no history of spinal cord injury/surgery, 3) no history of anti-incontinence surgery, 4) no evidence of pelvic organ prolapse defined by 0 or less than POP-Q values, 5) greater than 20 cmH_2O of maximal urethral closure pressure (MUCP) to exclude possible intrinsic sphincter deficiency

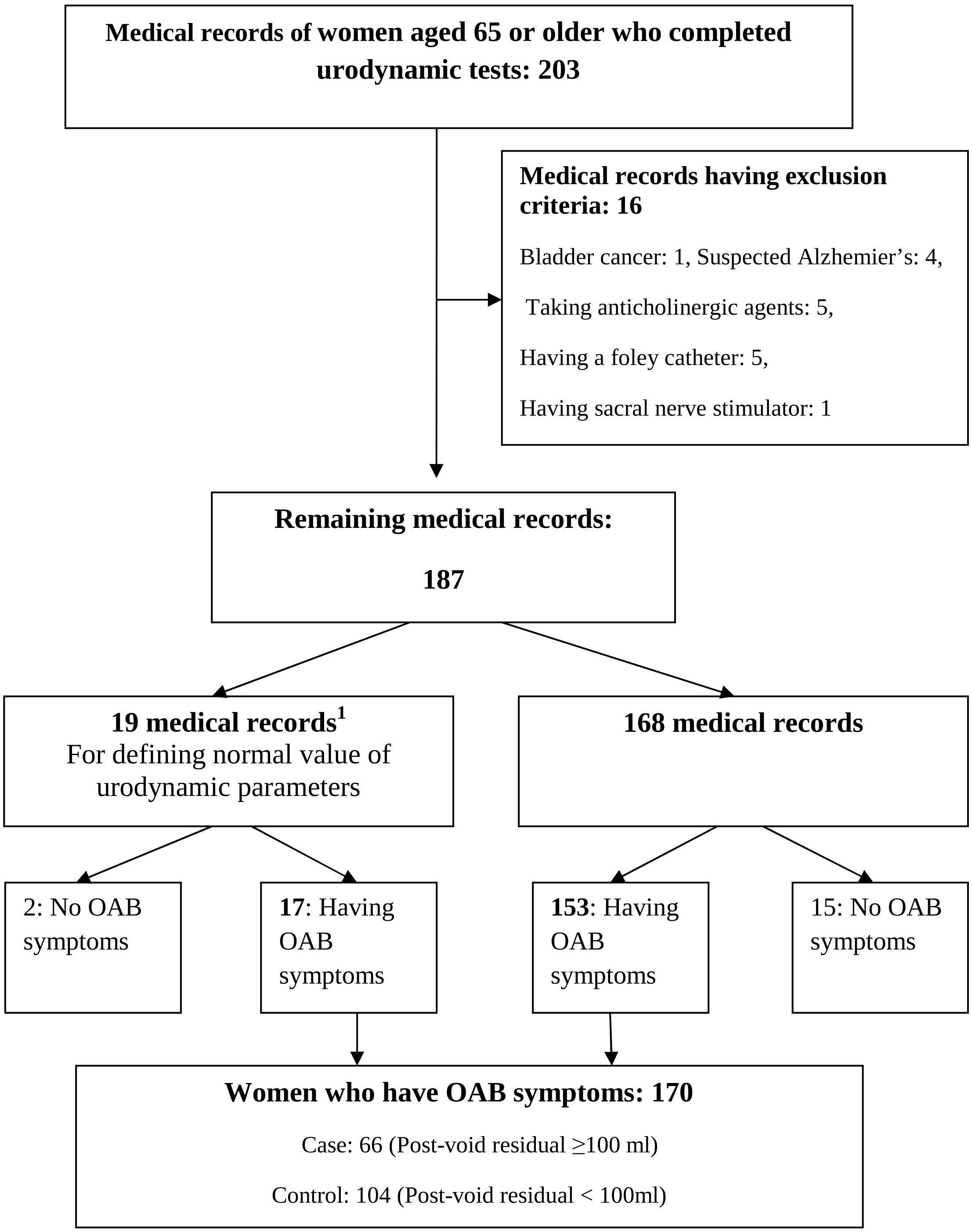
(ISD), 6) 50ml or less of post-void residual urine, and 7) a normal voiding pattern on the urodynamic results interpreted by a medical doctor.

Of the 19 medical records, 17 had and 2 medical records did not have OAB symptoms. Of remaining 168 medical cords which did not meet the inclusion criteria for defining normal values of urodynamic parameters, 153 had OAB symptoms. Therefore, a total of 170 medical records, which had OAB symptoms (15 +153), were used for answering research questions. Among 170 medical records of women, the case group included women having OAB symptoms (symptoms of urinary urgency with/without urinary incontinence or frequent urination) and a post-void residual (PVR) of 100ml or greater (incomplete bladder emptying). The control group included women having OAB symptoms and a PVR of less than 100ml (Figure 3.1).

Purposive sampling, a type of nonprobability sampling, was used to find medical records of eligible women during the study. Purposive sampling is appropriate under the following condictions: 1) when researchers specifically want to limit their research to unique cases, 2) when researchers want to focus on specific cases for further in-depth examination, and 3) when population members are difficult to reach (Wolfer, 2007). In this study, purposive sampling was suitable because women having incomplete bladder emptying (dependent variable) were the specific cases the investigator intended to examine and they were difficult to recruit. A limitation of this sampling method is that the findings cannot be generalized to a broader population because these samples do not have an equal or known probability of selection.

Figure 3.1

Process for Screening Medical Records of 2009-2010



Note.

[1] 19 medical records met the inclusion criteria which were for defining normal values of urodynamic parameters

Sample Size

Power analysis is one way to estimate the sample size. Four parameters are involved in a power analysis: effect size, alpha, power, and sample size (McDonald, 2009). The significance level of the test known as alpha is the probability of rejecting the null hypothesis, if it is true (a false positive). The usual value of alpha is 0.05. The beta is the probability of accepting the null hypothesis, if it is false (a false negative), when the real difference is equal to the minimum effect size. The power of a test is the probability of rejecting the null hypothesis when the real difference is equal to the minimum effect size, or 1-beta. A power of 80% (equivalent to a beta of 20%) is the most common.

In terms of the effect size, although several methods could be used to estimate the effect sizes such as an inductive method, deductive method, and effect size conventions, the estimates of the effect sizes on the association of incomplete bladder emptying with DUA and BOO has not been reported in published literature. Therefore, Cohen (1988) widely accepted effect size conventions was used in this study. According to Cohen (1988), effect sizes are different according to the statistical method used such as a t-test on means, t-test on correlations, F-test ANOVA, F-test regression, and chi-square test (Cohen, 1988). The small-, medium-, and large-effect sizes for the chi-square test are 0.1, 0.3, and 0.5, respectively.

A software program, the G*Power program (3.1.0) was used to determine the sample size for this study. Power analysis calculation were conducted for the proposed statistical model including the following variables: history of neurologic diseases, history of spinal cord injury/surgery, history of pelvic surgery, vaginal parity, diabetes, age, bladder capacity, pelvic organ prolapse, and history of anti-urinary incontinence surgery. Using the G-power program with Chi-square test, power of 0.80, an alpha level of .05, and a medium effect size (0.3), a sample size of 143 was sufficient to answer the research questions. In reality, a chi-square test gives a good estimate of the power of logistic regression with few predictors and the medium effect size is widely used for determining sample size. Considering a 30% missing data rate, a total of 203 medical records were reviewed.

Of the 203 medical records, 170 medical records were used to answer the research questions. Therefore, achieved statistical power was 86%.

Setting

For reviewing medical records, WebCis (electronic medical record system) at the University of North Carolina Hospitals at Chapel Hill was used after this study was approved by the Institutional Review Board (IRB) for the Protection of Human Subjects at the University of North Carolina at Chapel Hill.

Protection of Human Subjects Protocol

The protocol for this study was approved on October 11, 2010 by the Institutional Review Board (IRB) for the Protection of Human Subjects at the University of North Carolina at Chapel Hill (study # : 10-1852).

Confidentiality

The confidentiality procedure was implemented throughout the study. The investigator assigned a confidential and sequential study identification number to each medical record of the subjects. These identification numbers were written on the front page of the form for chart audits. All forms for data collection were kept in a locked file cabinet.

In addition, all data were entered and kept in a password-protected computer. Once this study is complete and no more publication for this study is anticipated, the identified data will be destroyed.

Procedure of Data Collection

After receiving the approval of this study from the Institutional Review Board (IRB) for the Protection of Human Subjects, the form for access to protected health information for research purpose was submitted to the University of North Carolina Health Care System Medical Information Management, and the request was approved.

The data collection procedure started with a review of the medical records of eligible women who had completed urodynamic tests at the Urophysiology Laboratory. These medical records were reviewed and collected by the investigator. All data that were collected during the medical records review were written on a form developed by the investigator (Appendix A). For a pilot test of this form, five eligible medical records were tested and minor revisions were made to the form such as coding changes for data entry and adding subcategories of variables.

Description of Urodynamics

The urodynamics had been conducted in the Urophysiology Laboratory at the University of North Carolina Hospitals at Chapel Hill. All urodynamics tests were conducted by three registered nurses, who used the same instructions to prepare patients (related to inter-rater reliability) and one urodynamic machine (Urovision/Urolab System IV) (Laborie Medical Technologies, Canada) for the urodynamic tests. The result of urodynamic tests was interpreted and reported by medical doctors in urogynecology, who used the same report form and had the same training.

The urodynmaic tests included free uroflowmetry, filling cystometry, and pressure-flow studies. All patients were instructed to go to the laboratory with a comfortably full bladder. The urodynamic tests started with free uroflowmetry and the patients were instructed to sit on the end of a bed and void to test free uroflowmentry. During free uroflowmetry, the peak flow rate, mean flow rate and voided volume were recorded on the computer. Then, a 14 French (Fr) urethreal catheter was used to empty the bladder completely and to measure the PVR volume simultaneously after completing voiding.

The position for the filling cystometry test was semi-sitting on the bed. For the filling cystometry test, an air-charged 7 Fr dual lumen urethral catheter (T-DOC Dual Sensor Catheter, Wilmington, Delaware, U.S.A) was used for simultaneous bladder infusion and an intravasical pressure measurement, and another air-charged 7 Fr single lumen catheter (T-DOC Abdominal Catheter, Wilmington, Delaware, U.S.A) was inserted into the vagina for an abdominal pressure measurement. Two surface electrodes were placed on the perineum for the electromyography. The bladder was infused with normal saline at room temperature at a filling rate of 50ml/minute. During filling for the cystomety test, assessments included bladder sensations, urethral pressure profilometry (UPP), and straining and coughing to assess urinary leakage. In terms of bladder sensations, several numbers were recorded: 1) volumes at first sensation (“a feeling of first fullness of the bladder and not enough to void yet”), 2) first urge (“a feeling of a comfortable trip to the bathroom to void”), 3) strong urge (“a feeling of a strong urge to void to stop favorite activities”), and 4) capacity (final voided volume combined with the PVR). UPP is a test carried out in some centers and measures the urethra's ability to act as a value to contain urine within the bladder. When a T-DOC dual catheter, which was placed into the bladder, was withdrawn along the urethra by a mechanical puller attached to a urodynamic machine, the pressure along the length of the urethra was measured. The maximum pressure measured in the urethra gives an indication of the closure function of the urethra. Leak point pressure was measured from the intravesical pressure, while patients were asked to increase their abdominal pressure by valsalva or by coughing. The greater the pressure required to produce leakage, the better the closure function of the urethra.

The urodynamic tests were continued with pressure-flow studies while the infusion reached the maximal capacity and the patients were instructed to initiate voiding without pushing the abdomen in a sitting position. Voided volume, maximum urine flow rate, and detrusor pressure at initiation of voiding, and the maximal flow rate were recorded ($P_{det.}$Open, $P_{det.}Q_{max}$, respectively). The patient was alone in a room when voiding during both free uroflowmetry and pressure-flow studies. After finishing the pressure-flow studies, the PVR volume was measured using a syringe that was attached into the infusion connecter of a dual lumen catheter and then aspirated.

Measurements

To define incomplete bladder emptying, post-void residual volume (PVR) was used base on pressure-flow studies. A review of the literature does not show an evidence-based specific maximum PVR that is considered normal, nor is there a minimal PVR that is considered abnormal. Since less than 100ml of PVR has been considered normal for women in several studies (Kebapci, Yenilmez, Efe, Entok, & Demirustu, 2007; Lee, et al., 2007; Yu, et al., 2004), a PVR of 100mL or greater during the pressure-flow study was considered as incomplete bladder emptying in this study. Thus, medical records of women with PVR of 100ml or greater were determined as the cases and those of women with less than 100ml of PVR were determined as the controls.

Table 3.1 presents the variables, operational definitions, levels of measurement, and location of medical records.

Table 3.1

Measurements and Definitions of Variables

Variables	**Operational Definition**	**Levels of Variable**	**Location of Medical Record**
Incomplete Bladder Emptying	a PVR of 100ml or greater	Categorical	Urodynamic report-pressure flow study
Risk Factors of DUA			
Age	Age when subjects had a urodynamics	Continuous	Demographics
Vaginal Parity	Number of vaginal parity	Continuous	Obstetrics history
DM	Documentation of DM (yes/no)	Categorical	Past medical history
Parkinson's Diseases	Documentation of Parkinson's disease (yes/no)	Categorical	Past medical history
Stroke	Documentation of Stroke (yes/no)	Categorical	Past medical history
Multiple Sclerosis	Documentation of Multiple Sclerosis (yes/no)	Categorical	Past medical history

Spinal Cord Injury/Surgery	Documentation of spinal cord injury/surgery (yes/no)	Categorical	Past medical & surgical history
Pelvic Surgery	Documentation of pelvic surgery (yes/no)	Categorical	Past surgery history
Bladder Capacity	Sum of voiding volume and PVR	Continuous	Urodynamic report-pressure flow study
Risk Factors of BOO			
Anti UI surgery	Documentation of anti-incontinence surgery (yes/no)	Categorical	Past surgery history
Pelvic Organ Prolapse Quantification			
Aa	Anterior wall 3cm proximal to the hymen (3 to +3cm)	Continuous	Physical examination
Ba	Most distal position of the remaining upper anterior vaginal wall (-3 to ± total vaginal length)	Continuous	Physical examination
C	Most distal edge of cervix or vaginal cuff scar	Continuous	Physical examination
D	Posterior fornix	Continuous	Physical examination
Ap	Posterior vaginal 3cm proximal to the hymen (3 to +3cm)	Continuous	Physical examination
Bp	Most distal position of the remaining	Continuous	Physical

	upper posterior vaginal wall (-3 to ± total vaginal length)		examination
Urodynamic Parameters			
Maximal urine flow rate (Q_{max})	Maximal urine flow rate	Continuous	Urodynamic report-pressure flow study
Opennig detrusor pressure (P_{det}.Open)	Opening detrusor pressure	Continuous	Urodynamic report-pressure flow study
Detrusor pressure at Qmax (P_{det}.Q_{max})	Detrusor pressure at maximal urine flow rate	Continuous	Urodynamic report-pressure flow study
Voiding patterns	Documentation of normal or interrupted pattern interpreted by a physician	Categorical	Urodynamic report-pressure flow study
Urinary Frequency			
No. of voiding Incidents/day	Average number of voiding incidents a day	Continuous	Voiding diary report
No. of voiding incidents /night	Average number of nocturnal voiding incidents a night	Continuous	Voiding diary report
Demographics			
Body mass index (BMI)	BMI at the visit of urodynamics BMI= weight (kg)/ height $(m)^2$	Continuous	Vital sign
Race	White, African American, Asian, or other/unknown	Categorical	Demographics

Data Management

Data Entry

All data collected by the investigator was entered independently into Microsoft Excel (version 2007) by the investigator and a research assistant. To increase the accuracy of the data, double data entry was performed. These data were stored on the investigator's password protected computer and then were compared to check accuracy of data entry using the Visual Basic Macro program in Microsoft Excel (version 2007). Among the total 12180 cells in each data set (60 cells per one medical record multiply a total 203 medical records), 53 different cells (0.44%) were found in these two data sets. These differences were resolved by comparing them with the raw data. After the correction of 53 cells, these data sets were compared again and no difference was found.

Preparation of Data Analysis

Data cleaning was conducted before data analysis. All data were reviewed through SAS programs for accuracy of data entry, outliers, and missing values. SAS MEANS and UNIVARIATE were conducted to ensure accuracy of the data file. To ensure the accuracy of the data file, descriptive statistics were also examined with SAS. For the continuous variables such as age, vaginal parity, bladder capacity, and urodynamic parameters, the means, standard deviations, and ranges of these variables were found. For the categorical variables such as race, and past medical/surgery history, frequencies, and percentages of these variables were determined. There were no out-of range numbers of these variables. No subject had a history of multiple sclerosis as a neurologic disease and therefore, this variable was dropped from the analysis.

Missing Data Management

Several variables had missing values. Of 170 medical records, 17 (10%) records were missing the urinary frequency data such as the number of voiding incidents a day or the number of nocturnal voiding incidents a night. Missing urodynamic parameters included 4 (2.4%) with detrusor pressure at the maximal urine flow rate ($P_{det}.Q_{max}$), 2 (1.2%) with opening detrusor pressure (P_{det}.Open), and 1(0.6%) with a maximal urine flow rate (Q_{max}). In the 6 points of pelvic organ prolpase quantification (POP-Q), the missing rate for Aa, Ba, Ap, Bp and D was 7 (4.1%) and for C was 8 (4.7%).

The missing rates of variables were from 0.6% to 10% and, therefore, as an alternative for handling missing data, listwise deletion (also called casewise) of missing data was used for this study. This method is used to eliminate the subjects having missing data from the analysis. That is, if a subject has missing data on any of the variables used in the analysis, it is dropped completely (De Leeuw, 2001). Advantages of this method are that it can be used for any kind of statistical analysis and no special computational method is required (Alison, 2002). The limitation of this method is that it may result in a substantial reduction in sample size. Furthermore, the results of the analysis may be biased because of the possibility of systematic differences between subjects with and without missing data (De Leeuw, 2001).

Similarly, D (a measurement of the posterior fornix) in pelvic organ prolapse quantification (POPQ) was not included in the analysis. Because D is used only for the identification of women with cervical hyperplasia (Abrams, Cardozo, Khoury, & Wein, 2009), subjects who had a hysterectomy could not have a value of D. Of 170 subjects, 102 (60%) did not have the values of D, so this variable was dropped in the analysis.

Multicollinearity Diagnostic Statistics

To diagnose multicollinearity, which is a result of strong correlations between independent variables, a SAS PROC REG was conducted. The variance inflation factor (VIF) in the regression model was used to determine the muticollinearity of the independent variables. In this statistic, muticollinearity was found in the variables of Aa (anterior wall 3cm proximal to the hymen), Ba (most distal position of the remaining upper anterior vaginal wall), Ap (posterior vaginal wall 3cm proximal to the hymen), and Bp (most distal position of the remaining upper posterior vaginal wall). Based on the concept of pelvic organ prolapse quantification (POPQ), both Aa and Ba are used to quantify anterior vaginal wall prolapse. Similarly, both Ap and Bp represent the degree of posterior vaginal prolapse. However, because Ba and Bp have more widely varying values (range -3 cm to total vaginal length) compared to Aa and Ap (range -3 to +3cm), Aa and Ap were dropped in the model. After eliminating these two variables, the VIFs of the remaining variables were less than 2.65 which is considered to be the absence of multicollinearity.

Method of Analysis

Descriptive Statistics

For descriptive statistics, such as the mean, median, standard deviation and range of continuous variables, the frequency and percentage of categorical variables were used to describe the characteristics of the subjects.

Explanatory Data Analysis

For model constructions for 1-1, 1-2, and 3-1, backward regressions were used for exploratory analyses, where the analyses began with a full model and variables were eliminated from the model in an iterative process. The fit of the model was tested after the elimination of each variable to ensure that the model still adequately fit the data.

Logistic Regression

To answer the relationship between incomplete bladder emptying and factors of DUA (detrusor underactivity) and BOO (bladder outlet obstruction), logistic regression was used. For this analysis, subjects' post-void residual volume (PVR), which was a dependent variable for research question 1, was categorized into normal (less than 100ml of PVR) or incomplete bladder emptying (≥ 100ml of PVR). For independent variables, age, vaginal parity and variables for prolapse were continuous variables and history of neurologic disease, history of spinal cord surgery/injury, and history of pelvic/anti urinary incontinence surgery were binary variables (presence /absence). The bladder capacity variable was categorized into 4 categories: decreased capacity (< 300ml), normal capacity (≥ 300ml and < 500ml), moderately increased (≥ 500ml and < 700ml), and severely increased (700ml >). Because a normal bladder capacity during urodynamic tests in post menopausal women has been reported to be about 300 to 500ml (Pfisterer, et al., 2007; Wakavaiachi et al., 2001), the range of 300 to 500ml was determined as normal capacity.

The logistic equation for answering the research question 1(the relationship between risk factors of DUA and BOO and incomplete bladder emptying) is as follows.

$$Z= b_0 + b_1X_1+ b_2X_2$$

Where z is the log odds of the dependent variable (PVR), where b_0 is the constant, and where there are independent variables (X_1= risk factors of DUA, X_2 =risk factors of BOO).

The logistic equation for answering the research question 3 (the relationship between urodynamic parameters and incomplete bladder emptying) is as follows.

$$Z= b_0 + b_1X_1+ b_2X_2 + b_3X_3+ b_4X_4$$

Where z is the log odds of the dependent variable (PVR), where b_0 is the constant, and where there are independent variables (X_1=maximal urine flow rate, X_2=opening detrusor pressure, X_3=detrusor pressure and the maximal urine flow rate, X_4= voiding pattern).

The odds ratio (OR) and 95% confidence interval (CI) were computed to assess the associations between the multiple independent variables and dependent variable.

Sensitivity, 1- Specificity and Receiver Operating Characteristic (ROC)

To answer research question 2, sensitivity, 1-specificity, and Receiver Operating Characteristic (ROC) curve statistics were used. In a ROC curve, the true positive rate (sensitivity) is plotted in the function of the false positive rate (100-specificity) for different cut-off points. Each point on the ROC plot represents a sensitivity/specificity pair corresponding to a particular decision threshold (Zweig & Campbell, 1993).

A perfect predictor has a single point on its ROC curve (namely, the upper left corner of the unit square) with 100% sensitivity and 100% specificity. In a similar vein, a noninformative maker's ROC curve lies along the diagonal of the unit square. Therefore, to select an optimal threshold, there are two widely used methods: 1) choose the threshold that will make the resulting binary prediction as close to a perfect predictor as possible, and 2) choose the threshold that will make the resulting binary prediction as far way from a noninformative predictor as possible (Gonen, 2007). For this study, method 1 was used to select the optimal threshold because of the convenience of calculation. That is, because a perfect predictor is the point with 100% sensitivity (Y axis) and 0% of 1-specificity (X axis) on the ROC curve, each distance between this perfect point (X =0, Y =1) and each point of the observations (with sensitivity and 1-specificity) was calculated using EXCEL program and the closest point to the perfect point was selected for the optimal threshold.

CHAPTER 4

RESULTS

A total of 203 medical records of women, who was 65 years and completed urodynamic studies, were reviewed and 16 records were excluded. One woman had a documented history of bladder cancer, five women were taking an anticholinergic medication, five women had a foley catheter, one woman had a sacral nerve stimulator, and four women had a documented history of suspected Alzheimer's. After excluding these 16 medical records, 187 medical records remained (Figure 3.1).

Normal Values of Urodynamic Parameters

Of the 187 medical records after applying the initial exclusions, 19 met the inclusion criteria for defining normal values of urodynamic parameters.

Table 4.1 displays the characteristics of the 19 subjects. Among these subjects, the mean of the maximal urine flow rate was 20.37ml/second (SD=6.30). The means of opening detrusor pressure and detrusor pressure at the maximal urine flow rate were 10.95 cmH_2O (SD=10.51), and 18.14 cmH_2O (SD=9.37), respectively. The mean of voiding volume was 369.74ml (SD=127.36) and the mean of post-void residual urine was 9.26 ml (SD=10.86) (Table 4.2).

Table 4.1
Characteristics of the Samples for Defining Normal Urodynamic Parameters (N=19)

		Mean (SD)	Range (min-max)
Age (years)		73.37 (4.95)	65 - 82
BMI[1]		29.90 (5.77)	19.29 – 41.91
Vaginal Parity (number)		2.95 (2.20)	0 -7
			N (%)
Race	White		12 (63.16)
	African American		4 (21.05)
	Asian		1 (5.26)
	Unknown		2 (10.53)

Note.
[1]BMI: Body mass index (kg/m^2)

Table 4. 2
Values of Urodynamic Parameters (N=19)

	Mean	(SD)	Median	Range (min-max)
Q_{max} (ml/sec)	20.37	(6.30)	20.85	7.5 - 29
P_{det}.Open (cmH_2O)	10.95	(10.51)	10.00	0 - 41
$P_{det}.Q_{max}$ (cmH_2O)	18.14	(9.37)	17.00	1.7 - 33
Voiding volume (ml)	369.74	(127.36)	372.00	97 - 686
Post-void residual urine (ml)	9.26	(10.86)	5.00	0 - 40

Note.
Q_{max}: Maximal urine flow rate, P_{det}.Open: Opening detrusor pressure
$P_{det}.Q_{max}$: Detrusor pressure at the maximal urine flow rate

Description of Subjects for Research Questions

Of 187 medical records, 170 which had documentation of OAB symptoms (“urinary frequency,” or/ and “urinary urgency,” with/without urinary incontinence) were eligible to answer the research questions (Figure 3.1).

Table 4.3 displays the characteristics of the sample.

Table 4.3

Characteristics of the Sample (N=170)

		Mean (SD)	Median		Range (min-max)
Age (years)		72.94 (6.25)	72.00		65 - 94
Body Mass Index (kg/m^2)		28.90 (6.08)	27.31		19.29 - 48.26
Vaginal Parity (number)		2.61 (1.49)	2.00		0 - 7
Post-Void residual (ml)		112.72 (136.23)	62.00		0 - 625
					N (%)
Incomplete Bladder Emptying[1]				Yes	66 (38.82)
				No	104 (61.18)
Race	White				125 (73.53)
	African American				21 (12.35)
	Asian				1 (0.59)
	Unknown				23 (13.53)
Documentation of Medical/ Surgical History	Stroke			Yes	13 (7.65)
				No	157 (92.35)
	Parkinson's disease			Yes	3 (1.76)
				No	167 (98.24)
	Multiple Sclerosis			Yes	0 (0.00)
				No	170 (100.0)
	Spinal Cord Injury/Surgery			Yes	13 (7.65)
				No	157 (92.35)
	Diabetes Mellitus			Yes	29 (17.06)
				No	141 (82.94)
	Pelvic Surgery			Yes	115 (67.65)
				No	55 (32.35)
	Anti-Incontinence Surgery			Yes	32 (18.82)
				No	138 (81.18)

Note.

[1] Incomplete bladder emptying indicates post-void residual urine of 100ml or greater

Research Question 1

Research question 1 included 1-1) “What are the relationships between risk factors of DUA (presence of neurologic disease, history of spinal cord injury and pelvic surgery, vaginal parity, DM, age, or bladder capacity) and incomplete bladder emptying?” and 1-2) “What are the relationships between risk factors of DUA and incomplete bladder emptying, when controlling for risk factors of BOO (pelvic organ prolapse and history of anti-incontinence surgery)?”

Relationships between Risk Factors of DUA and Incomplete Bladder Emptying

To answer research question 1-1, 170 eligible medical records were used in the analysis. A logistic regression model was constructed using backward selection. All risk factors for DUA (age, vaginal parity, history of Parkinson’s disease, history of stroke, history of spinal cord injury/surgery, history of pelvic surgery, DM, and bladder capacity) were included in the initial model. In each step, an independent variable, which had the highest *p*-value greater than 0.2, was eliminated. The variables removed from the model were: history of stroke (*P*= .93), history of pelvic surgery (*P*= .77), vaginal parity (*P*= .57), and history of Parkinson’s disease (*P*= .53). The risk factors of age, history of spinal cord injury/surgery, diabetes, and bladder capacity remained in the final model.

Therefore, the logistic equation for the model was

log(p/1-p) = -4.45 + 0.5*age + 0.91*presence of SCI/SCS + 0.83*presence of DM - 1.44*bladder capacity (decreased) + 1.27*bladder capacity (moderately increased) + 1.59*bladder capacity (severely increased) where p is the probability of incomplete bladder emptying. The reference group of bladder capacity was the normal bladder capacity.

Table 4.4 displays the results of logistic regression describing the relationships between age, history of spinal cord injury/surgery, DM, and bladder capacity and incomplete bladder emptying.

Table 4.4

The Relationship between Risk Factors of DUA and Incomplete Bladder Emptying (N=170)

	Univariable		Multivariable			
Factors	Unadjusted OR	*P*	B	Adjusted OR	95% CI	*P*
Age	1.01	.63	.05	1.05	0.99 -1.12	.09
History of SCI/SCS						
No	Reference					
Yes	1.94	.25	0.91	2.47	0.67 - 9.15	.17
Diabetes Mellitus						
No	Reference					
Yes	1.60	.25	0.83	2.30	0.08 - 6.14	.10
Bladder Capacity		<.0001				<.0001
Decreased	0.37	.04	-1.44	0.24	0.08 - 0.66	.01
Normal	Reference					
Moderately increased	3.86	.00	1.27	3.57	1.43 - 8.89	.01
Severely increased	5.03	.01	1.59	4.92	1.40 -17.35	.01

Note.

Probability modeled was dependent variable: incomplete bladder emptying.

SCI: spinal cord injury, SCS: spinal cord surgery

OR: odds ratio, CI: confidence interval

Bladder Capacity: normal (≥ 300 and <500ml), decreased (<300ml), moderately increased (≥ 500 and <700ml), severely increased (≥700ml)

Among the risk factors of DUA, bladder capacity was the only risk factor that was significantly related to incomplete bladder emptying (p < .0001). In particular, women with decreased bladder capacity (< 300ml) had a 76% lower odds of incomplete bladder emptying than women with normal bladder capacity (≥ 300 and <500ml) (Adjusted OR= 0.24, 95% CI: 0.08-0.66). In contrast, women with moderately and severely increased bladder capacity had, respectively, 3.57 and 4.92 times the odds of incomplete bladder emptying as women with normal bladder capacity (Adjusted OR=3.57, 4.92, 95% CI: 1.43-8.89, 1.40-17.35, respectively). Women's age, history of spinal cord injury/surgery, and presence of diabetes were not significantly associated with incomplete bladder emptying.

Relationship between Incomplete Bladder Emptying and Risk Factors of DUA and BOO

Of 170 eligible medical records, 163 medical records were used in the analysis for research question 1-2 because 7 medical records had missing data in the factor of prolapse. To answer research question 1-2, risk factors of bladder outlet obstruction (BOO) were added to the previous model. Three points (Ba, C, Bp) of pelvic organ prolapse quantification (POP-Q) and history of anti-urinary incontinence surgery were added with age, history of spinal cord surgery, diabetes, and bladder capacity. Backward selection was used to define the best model for research question 1-2 and in each step, an independent variable, which had the highest p-value greater than 0.2 was eliminated. The variables removed from the model were: Bp (indicating posterior vaginal prolapse) (*p*= .99), C (*p*= .79), and history of anti-incontinence surgery (p= .35). Therefore, the variable of Ba remained in the final model along with age, history of spinal cord injury/surgery, diabetes, and bladder capacity.

The logistic equation for this model was

log(p/1-p) = -6.65 + 0.5*age + 0.92*presence of SCI/SCS + 1.04*presence of DM - 1.63*bladder capacity (decreased) + 1.24*bladder capacity (moderately increased) + 1.48*bladder capacity (severely increased) – 0.17*anterior vaginal prolapse

where p is the probability of incomplete bladder emptying. The reference group of bladder capacity was the normal bladder capacity.

Table 4.5 displays the results of the logistic regression of the relationships between risk factors of DUA and BOO and incomplete bladder emptying. Risk factors of diabetes, bladder capacity and anterior vaginal prolapse were significantly related to incomplete bladder emptying in multivariable analysis. In particular, diabetic women had 2.83 times the odds of incomplete bladder emptying as non-diabetic women (Adjusted OR=2.83, 95% CI: 1.04-7.72). Women with decreased bladder capacity had about 80% lower odds of incomplete bladder emptying than women having normal bladder capacity (Adjusted OR=0.20, 95% CI: 0.07-0.57). Women with moderately and severely increased bladder capacity had respectively 3.48 and 4.39 times the odds of incomplete bladder emptying as women with normal bladder capacity (Adjusted OR=3.48, 4.39, 95% CI: 1.35-8.98, 1.17 - 16.52 , respectively). Anterior vaginal prolapse was also a significant variable related to incomplete bladder emptying. For one unit (1cm) increase in anterior vaginal prolapse (Ba), the odds of incomplete bladder emptying decreased by 16% (Adjusted OR=0.84, 95% CI: 0.71-0.99).

Table 4.5

The Relationships between Risk Factors of Detrusor Underactivity (DUA) and Bladder Outlet Obstruction (BOO) and Incomplete Bladder Emptying (N=163)

	Univariable		Multivariable			
Factors	Unadjusted OR	*P*	B	Adjusted OR	95% CI	*P*
Age	1.01	.63	.05	1.06	0.99 -1.12	.08
History of SCI/SCS						
No	Reference					
Yes	1.94	.25	0.92	2.51	0.66 - 9.53	.17
Diabetes Mellitus						
No	Reference					
Yes	1.60	.25	1.04	2.83	1.04 - 7.72	.04
Bladder Capacity		<.0001				<.0001
Decreased	0.37	.04	-1.63	0.20	0.07 - 0.57	.00
Normal	Reference					
Moderately increased	3.86	.00	1.24	3.48	1.35 - 8.98	.01
Severely increased	5.03	.01	1.48	4.39	1.17 - 16.52	.03
Anterior Vaginal Prolapse	.93	.30	-.17	0.84	0.71 - 0.99	.04

Note.

SCI: spinal cord injury, SCS: spinal cord surgery

Bladder Capacity: normal (≥ 300 and <500ml), decreased (<300ml), moderately increased (≥ 500 and <700ml), severely increased (≥700ml)

OR=odds ratio, CI=confidence interval

Research Question 2

Research question 2 included 2-1) "What are the sensitivity and specificity of number of voiding a day to detect incomplete bladder emptying?" and 2-2) "What are the sensitivity and specificity of the nocturnal voiding a night to detect incomplete bladder emptying?"

Of the 170 eligible medical records, 153 were used in this analysis because 17 records had missing data about urinary frequency. Table 4.6 displays the sensitivity and 1-specificity of number of the voiding incidents a day to detect incomplete bladder emptying.

Table 4.6

Results of Sensitivity and 1-Specificity of the Number of Voiding Incidents a Day to Confirm Incomplete Bladder Emptying (N=153)

Obs	# OF VOID a DAY	PROB	POS	NEG	FALSE POS	FALSE NEG	SENSIT	1 - SPECIF
1	3	0.65985	2	62	0	89	0.02198	0.00000
2	4	0.65037	3	61	1	88	0.03297	0.01613
3	5	0.64077	7	58	4	84	0.07692	0.06452
4	5.5	0.63593	9	58	4	82	0.09890	0.06452
5	6	0.63106	14	55	7	77	0.15385	0.11290
6	6.5	0.62616	19	53	9	72	0.20879	0.14516
7	7	0.62124	25	53	9	66	0.27473	0.14516
8	7.5	0.61629	29	48	14	62	0.31868	0.22581
9	8	0.61131	37	46	16	54	0.40659	0.25806
10	8.5	0.60632	48	42	20	43	0.52747	0.32258
11	9	0.60130	52	34	28	39	0.57143	0.45161

12	9.5	0.59626	58	29	33	33	0.63736	0.53226
13	10	0.59120	67	27	35	24	0.73626	0.56452
14	10.5	0.58612	69	23	39	22	0.75824	0.62903
15	11	0.58102	73	18	44	18	0.80220	0.70968
16	11.5	0.57590	76	17	45	15	0.83516	0.72581
17	12	0.57077	78	14	48	13	0.85714	0.77419
18	12.5	0.56562	82	11	51	9	0.90110	0.82258
19	13	0.56046	83	6	56	8	0.91209	0.90323
20	13.5	0.55529	83	5	57	8	0.91209	0.91935
21	14	0.55010	84	5	57	7	0.92308	0.91935
22	14.5	0.54490	85	4	58	6	0.93407	0.93548
23	15	0.53970	86	2	60	5	0.94505	0.96774
24	15.5	0.53448	87	2	60	4	0.95604	0.96774
25	16.5	0.52403	87	1	61	4	0.95604	0.98387
26	17	0.51879	88	1	61	3	0.96703	0.98387
27	18.5	0.50306	89	0	62	2	0.97802	1.00000
28	21.5	0.47162	90	0	62	1	0.98901	1.00000
29	35	0.33624	91	0	62	0	1.00000	1.00000

Note.

Frequency missing=17

Obs: observations, PROB: probability, POS: true positive, NEG: true negative,

FALSE POS: false positive, FALSE NEG: false negative, SENSIT: sensitivity,

1 –SPECIF: 1-specificity

Figure 4.1 displays the receiver operating characteristic (ROC) curve for the sensitivity (true positive) and 1-specificity (false positive) for the number of voiding incidents a day to detect incomplete bladder emptying. The area under the ROC curve was 0.5946. An optimal threshold, which was the closest point to the point (with 100% sensitivity and 100 % specificity), was with 53% sensitivity and 68% specificity (1-specificity: 32%) on this ROC curve and this threshold was with 8.5 times voiding incidents a day.

Figure 4.1

ROC Curve for the Model of Number of Voiding Incidents a Day to Detect Incomplete Bladder Emptying

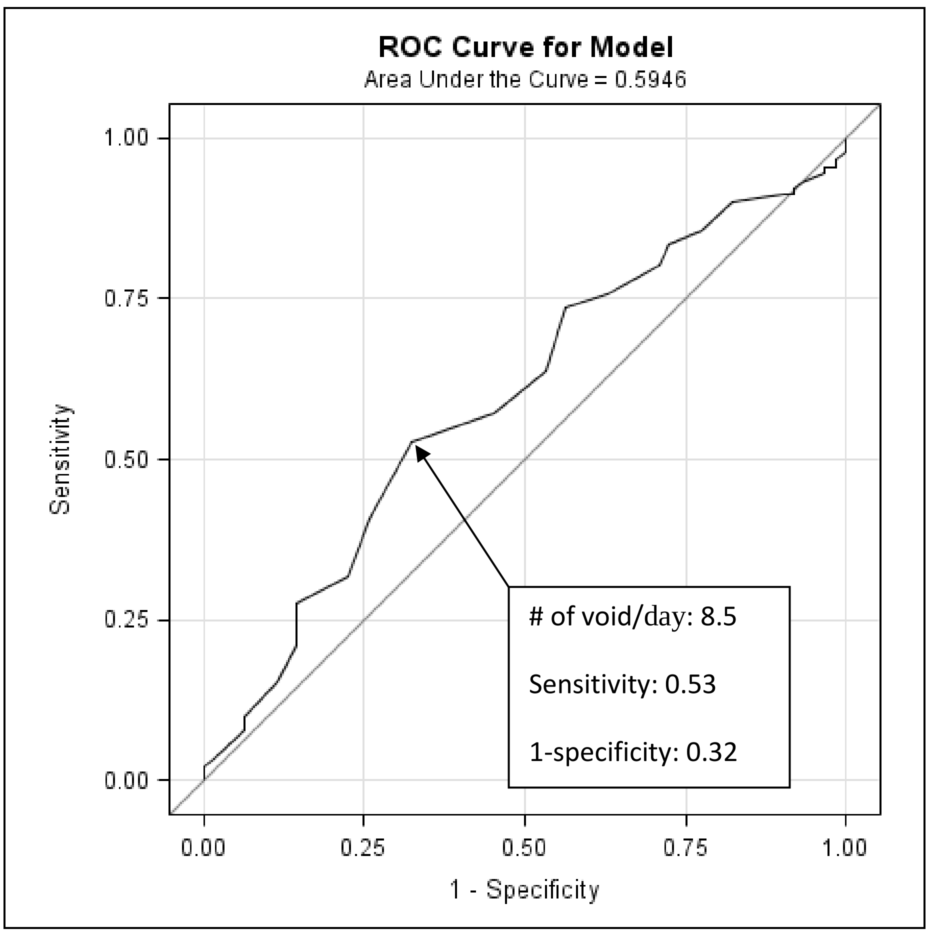


Table 4.7 presents the sensitivity and 1-specificity for the number of nocturnal voiding incidents a night to detect incomplete bladder emptying.

Table 4.7

Results of Sensitivity and 1-Specificity of Number Nocturnal Voiding Incidents a Night to Confirm Incomplete Bladder Emptying (N=153)

Obs	# OF VOID at Night	PROB	POS	NEG	FALSE POS	FALSE NEG	SENSIT	1 - SPECIF
1	0	0.63002	26	44	18	65	0.28571	0.29032
2	0.5	0.61623	32	41	21	59	0.35165	0.33871
3	1	0.60225	57	26	36	34	0.62637	0.58065
4	1.5	0.58810	63	21	41	28	0.69231	0.66129
5	2	0.57381	75	16	46	16	0.82418	0.74194
6	2.5	0.55939	84	8	54	7	0.92308	0.87097
7	3	0.54487	88	4	58	3	0.96703	0.93548
8	3.5	0.53027	89	3	59	2	0.97802	0.95161
9	4	0.51562	90	1	61	1	0.98901	0.98387
10	5	0.48627	91	1	61	0	1.00000	0.98387
11	6	0.45701	91	0	62	0	1.00000	1.00000

Note.

Frequency missing: 17

Obs: observations, PROB: probability, POS: true positive, NEG: true negative,

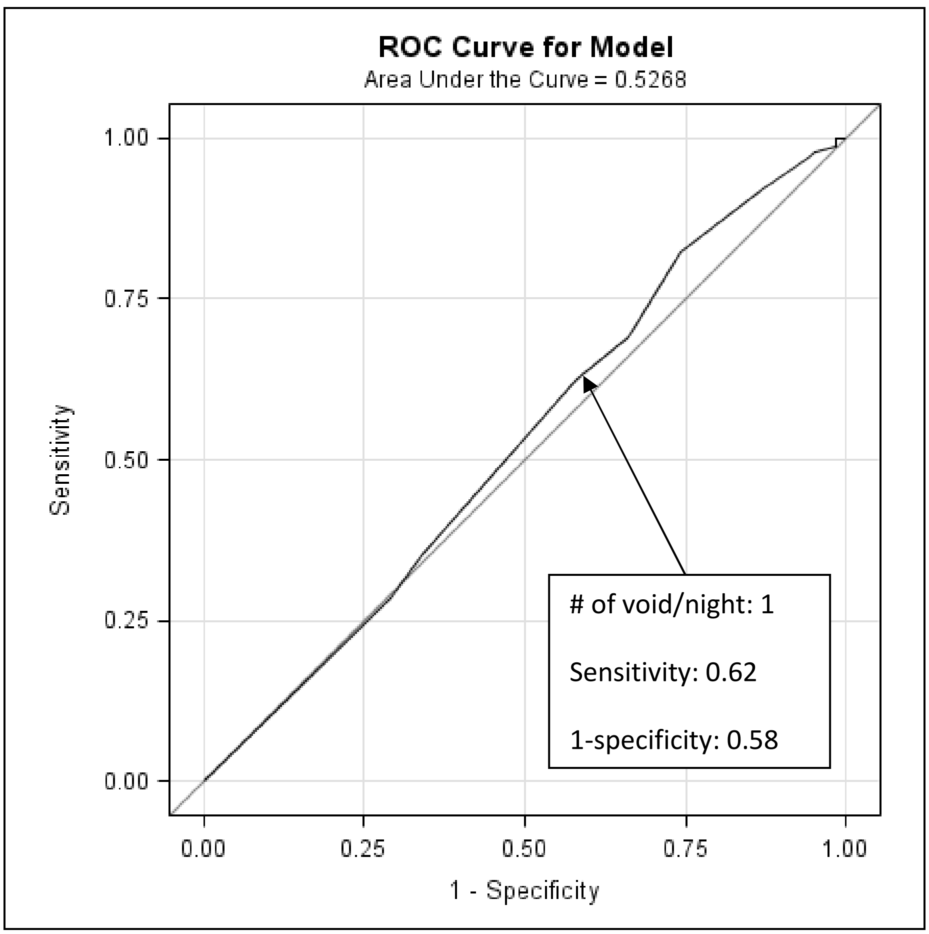
FALSE POS: false positive, FALSE NEG: false negative, SENSIT: sensitivity,

1 –SPECIF: 1-specificity

Figure 4.2 presents the receiver operating characteristic (ROC) curve for the sensitivity and 1-specificity of number of the nocturnal voiding incidents a night to detect incomplete bladder emptying. The area under the ROC curve was 0.568. An optimal threshold, which was the closest point to the point (with 100% sensitivity and 100 % specificity), was with 62% sensitivity and 42% specificity on this ROC curve and this threshold was with 1 nocturnal voiding incident a night.

Figure 4.2

ROC Curve for the Model of Number of Nocturnal Voiding Incidents a Night to Detect Incomplete Bladder Emptying



Research Question 3

Research question 3 was “What are the relationships between urodynamic parameters- opening detrusor pressure at voiding ($P_{det.}$open), detrusor pressure at maximal urine flow ($P_{det.}\ Q_{max}$), maximum urine flow rate (Qmax), and voiding patterns and incomplete bladder emptying? ”

Table 4.8 displays the results of the relationships between urodynamic parameters and incomplete bladder emptying. Of 170 eligible medical records, 166 records were used in this analysis because 4 medical records had missing data in urodynamic parameters.

The logistic equation for this model was

log(p/1-p) = -2.04 - 0.05* (Qmax) -0.02 + 0.92 ($P_{det.}$open) + 0.03*($P_{det.}\ Q_{max}$) + 3.98* voiding pattern (interrupted)

where p is the probability of incomplete bladder emptying. The reference group of the voiding pattern was normal voiding pattern.

The urodynamic parameters of the maximal urine flow rate (Q_{max}) and voiding pattern were significantly associated with incomplete bladder emptying. For one unit (1ml/second) increase in the maximal urine flow rate (Q_{max}), the odds of incomplete bladder emptying decreased by about 5 % (Adjusted OR=0.95, 95% CI: 0.91-0.99). Women who had an interrupted voiding pattern had 3.98 times the odds of incomplete bladder emptying as women with normal voiding pattern (Adjusted OR =3.98, 95% CI: 1.92-8.26).

Table 4.8

The Relationships between Urodynamic Parameters and Incomplete Bladder Emptying

(N=166)

	Univariable		Multivariable			
Factors	Unadjusted OR	*P*	B	Adjusted OR	95% CI	*P*
Q_{max} (ml/second)	0.95	.01	-0.05	0.95	0.91-0.99	.01
P_{det}.Open (cmH_2O)	1.00	.68	-0.02	0.98	0.94-1.02	.23
$P_{det}.Q_{max}$ (cmH_2O)	1.01	.26	0.03	1.03	0.99-1.07	.10
Voiding pattern						
Normal	Reference					
Interrupted	3.60	.00	1.38	3.98	1.92-8.26	.00

Note.

Q_{max}: Maximum urine flow rate

P_{det}.Open: Opening detrusor pressure at voiding

$P_{det}.Q_{max}$: Detrusor pressure at the maximal urine flow rate

Summary

The findings of this current study provided evidence for the relationship between bladder capacity and incomplete bladder emptying. In specific, women who had a decreased bladder capacity (< 300ml) had a 76% lower odds of incomplete bladder emptying (OR=0.24) than women with normal bladder capacity (≥ 300ml and < 500ml). On the other hand, women having increased bladder capacity (moderately increased: ≥ 500ml and < 700ml, severely increased: ≥ 700ml) had increased risk of incomplete bladder emptying as women having normal bladder capacity (OR=3.57, 4.92, respectively).

After adding factors of BOO in the previous model, bladder capacity was still significantly related to incomplete bladder emptying (OR=0.20, 3.48, 4.39, decreased, moderately increased, severely increased bladder capacity, respectively). Interestingly, presence of DM was significantly related to incomplete bladder emptying after adding a factor of anterior vaginal prolapse in the model. That is, having DM increased risk of incomplete bladder emptying (OR=2.3). One unexpected finding was the significant relationship between degree of anterior vaginal prolapse measured by POP-Q (Ba) and incomplete bladder emptying (OR=0.84). Greater degree of anterior vaginal prolapse decreased the odd of incomplete bladder emptying.

Regarding the relationship between urinary frequency and incomplete bladder emptying, the area under the ROC curve for model of number of voiding a day to incomplete bladder emptying was 0.59 and optimal threshold was 8.5 times voiding a day (with 53% sensitivity and 68% specificity). The area under the ROC curve for model of number of voiding a night to incomplete bladder emptying was 0.52 and optimal threshold was 1 void a night (with 62% sensitivity and 58% specificity). That is, neither number of voiding a day nor number of voiding a night seem to become a good tool to detect incomplete bladder emptying in women because the areas under the ROC curve were close to 0.5 (the worst case value).

Urodynamic parameters of maximal urine flow rate and voiding pattern were significantly related to incomplete bladder emptying; for increasing in maximal urine flow rate (Q_{max}), the odds of incomplete bladder emptying decreased (OR=0.95) and having interrupted voiding pattern increased the odds of incomplete bladder emptying (OR=3.98).There were no significant relationships between any detrusor pressures such as opening detrusor pressure (P_{det}.open) or detrusor pressure at maximal urine flow rate (P_{det}.Q_{max}) and incomplete bladder emptying.

CHAPTER 5

DISCUSSION

This study defined normal values of urodynamic parameters in women aged 65 or older and examined several relationships: 1) the relationship between risk factors of detrusor underactivity (DUA) and bladder outlet obstruction (BOO) and incomplete bladder emptying, 2) the relationship between urinary frequency and incomplete bladder emptying, and 3) the relationship between urodynamic parameters and incomplete bladder emptying in women aged 65 or older who had OAB symptoms. A logistic regression and receiver operating characteristic (ROC) curve were employed for analyses in order to examine these relationships. This chapter compares the results with previous studies and presents limitations, recommendations for future nursing studies, and nursing and clinical implications.

Defining Normal Values of Urodynamic Parameters

To define normal values of urodynamic parameters, 19 medical records were selected from 187 (Figure 3.1). The median (mean) of the maximal urine flow rate (Q_{max}) was 20.85 (20.37) ml/second. The median (mean) of detrusor pressure at the maximal urine flow rate (P_{det}. Q_{max}) was 17.00 (18.14) cmH_2O. These results showed a slightly higher value of the maximal urine flow rate (Q_{max}) and a slightly lower value of detrusor pressure at the maximal urine flow rate (P_{det}. Q_{max}) compared to previous studies (Defreitas, et al., 2004; Pfisterer, et al., 2007). Pfisterer et al. (2007) reported that the median of the maximal urine flow rate

(Q_{max}) was 18ml/second and the median of detrusor pressure at the maximal urine flow rate (P_{det}. Q_{max}) was 24 cm H_2O among 10 women aged 55 to 80 without any OAB symptoms and urinary incontinence. Defreitas et al. (2004) reported 16ml/second maximal urine flow rate (Q_{max}) and 24cmH_2O detrusor pressure at Q_{max} (P_{det}. Q_{max}) in 20 women without any lower urinary tract symptoms assessed by the Urogenital Distress Inventory (UDI-6) questionnaire and any history of bladder or urethral surgery.

These differences in the maximal urine flow rate (Q_{max}) and detrusor pressure at the maximal urine flow rate (P_{det}. Q_{max}) between this current study and Defreitas' study could be explained by age differences of the sample. For instance, the mean age of this study was 73.37 (SD=5) years, while the mean age in Defreitas' study (2004) was 42 (SD=7) years. That is, the subjects in this study were older than in the previous study. It has been well established that the urethral pressure profile (UPP) in women changes with age. A study of 25 women, ages 20 to 77 years, without detrusor overactivity, neuropathy, or pelvic or urinary incontinence surgery, confirmed that the maximal urethral closure pressure (MUCP) was negatively associated with age ($r = -0.489$, $p < .0001$) (Schick, Tessier, Bertrand, Dupont, & Jolivet-Tremblay, 2003). Similarly, Pfisterer et al. (2007) found that the median of the maximal urethral closure pressure (cmH_2O) in postmenopausal women was significantly lower than in premenopausal women ($p < .01$). That is, older women (as in this study) could have lower urethral pressure compared to younger women (as in previous studies), and thus they with lower urethral pressure could void faster and more strongly. Furthermore, they needed lower detrusor pressure to void because of lower resistance on the urethra (indicating low urethral pressure).

Another possible explanation for these differences could be the differences in the characteristics of the samples between the current and previous studies. The subjects in previous studies did not have any urologic complaints such as OAB symptoms and urinary incontinence (Defreitas, et al., 2004; Pfisterer, et al., 2007). In contrast, only medical records having OAB symptoms with/without urinary incontinence were used for this study. Significantly, previous studies reported a higher rate of maximal urine flow (Q_{max}) and lower detrusor pressure at the maximal urine flow rate (P_{det}. Q_{max}) in the urinary incontinent women than in continent women (Lemack, Baseman, & Zimmern, 2002; Teleman et al., 2002). Teleman et al. (2002) reported that the mean of the maximum urine flow rate (Q_{max}) was significantly higher in urinary incontinent women, 22ml, than in continent women, 16ml ($p < .01$). Similarly, Lemack et al (2002) found that the mean of the maximal urine flow rate (Q_{max}) in urinary incontinent and continent women was 22 ml and 17ml, respectively, and this difference was statistically significant ($p = .04$). Furthermore, they found that the mean of detursor pressure at the maximal urine flow rate (P_{det}. Q_{max}) was 16cmH_2O and 24 cmH_2O, respectively, in urinary incontinent and continent women ($p = .02$).

Relationship between Risk Factors of DUA and BOO and Incomplete Bladder Emptying

Of the 170 medical records, 66 (38.8%) had incomplete bladder emptying defined as post-void residual (PVR) of 100ml or greater. The risk factors of age, spinal cord injury/surgery, bladder capacity, DM, and anterior vaginal prolapse remained in the final model to analyze the relationship between risk factors of DUA and BOO and incomplete bladder emptying. In the multivariable analysis, the risk factors of bladder capacity, diabetes, and anterior vaginal prolapse were significantly associated with incomplete bladder emptying in women having OAB symptoms (Table 4.5). Specifically, increased bladder capacity and the presence DM increased the risk of incomplete bladder emptying. In contrast, decreased bladder capacity (<300ml) and anterior vaginal prolapse decreased the risk of incomplete bladder emptying. Other risk factors of age and history of spinal cord injury/surgery were not significantly related to incomplete bladder emptying.

Increased Bladder Capacity

In previous studies, the relationship between increased bladder capacity and incomplete bladder emptying in older women has not been explored. This relationship has been examined in men and animal models in previous studies. In men, one possible explanation about this relationship might be related to decreased in bladder blood flow at bladder capacity (Kershen, Azadzoi, & Siroky, 2002). Kershen et al. (2002) found that as bladder volume and pressure increased with filling, blood flow increased but at capacity (mean capacity=450ml, SD=64.4ml), defined as the volume at which detrusor contractions occurred or further filling could not be tolerated, bladder blood flow significantly decreased in 17 healthy male subjects. Similar results were reported in the animal models with bladder outlet obstruction (Buttyan, Chen, & Levin, 1997; Gabella & Uvelius, 1999; Gosling et al., 2000; Greenland & Brading, 2001). These studies reported that prolonged bladder over-distension following bladder outlet obstruction induced smooth muscle damage, muscle loss, and fibrosis in animal models, resulting in reduced contractility of the detrusor muscle. That is, detrusor ischemia caused by bladder over distension, which may increase bladder capacity, may be a factor in impaired detrusor contractility, resulting in incomplete bladder emptying. It is difficult to apply or compare this explanation to/with this study because voiding for women is quite different than for men. Unlike men, women can void normally with low detrusor pressure (less than 10cm H_2O) and are able to empty the bladder completely with a good urinary flow rate using pelvic floor relaxation or abdominal straining without needing to generate significant detrusor pressure (Nitti, et al., 1999).

Diabetes Mellitus

This study found a significant relationship between the presence of DM and incomplete bladder emptying after adding the factor of anterior vaginal prolapse (Table 4.5). Similarly, Lee et al. (2007) reported that incomplete bladder emptying defined as greater than 100ml of PVR was significantly associated with DM in women (mean age 63±10 years) (OR=12.5, 95% CI: 3.4-41.9). More specifically, they found that 27(15%) of diabetic and 3 (2%) of non-diabetic women had greater than 100ml of PVR. Yu et al. (2004) also found that 24 (14%) of diabetic women (mean age 62±9 years) and 3(2%) of non-diabetic women (mean age 61±10 years) had incomplete bladder emptying defined as PVR of 100ml or greater and this difference between these groups was statistically significant ($p < .00$).

Possible explanations for the relationship between the presence of DM and incomplete bladder emptying could be decreased bladder sensation and/or sensory impairment of the bladder in older diabetic women. For instance, Lee et al. (2009) found a decreased first bladder sensation on urodynamic tests (defined by the feeling the patient has when she first becomes aware of the bladder feeling) and sensory impairment of the bladder (measured by intravesical current perception threshold testing) in diabetic women (mean age 67±10 years). The median volume of the first sensation during urodynamic tests in diabetic women was significantly higher than in the control group (198m, 150ml respectively). The mean value of the current perception threshold (CPT) in diabetic women was significantly greater than in the control group at frequencies of 5 and 250 Hz ($p < .001$). In addition, they found that a decrease in the maximal urine flow rate (Q_{max}) was associated with an increase in the intravesical CPT values at 5Hz (p=.03). This could mean that sensory impairments of the bladder can attenuate detrusor contractions and result in incomplete bladder emptying (elevated PVR) in diabetic women. However, a causal relationship between sensory impairments of the bladder and incomplete bladder emptying is still unclear.

In contrast, Melleman et al. (2004) and Fitzgerlad (2001) did not find a relationship between the presence of DM and incomplete bladder emptying in middle aged and older women having OAB symptoms. A possible explanation of this discrepancy could be that not the presence of diabetes but concommittant chronic complications of DM such as peripheral neuropathy or diabetic retinopathy may be related to incomplete bladder emptying (Kebapci, et al., 2007; Lee, et al., 2007). For instance, Lee et al. (2007) found that diabetic women having a PVR greater than 100ml had a significantly higher prevalence of peripheral neuropathy, which was assessed by questioning subjects about symptoms of paresthesia, dulled sensation, and pain as well as by measuring the sensory threshold using vibratory and thermal on the feet, as compared to diabetic women having a PVR of 100ml or less (p=.045). More specifically, 18 (38%) diabetic women with a PVR greater than 100ml and 31 (23%) diabetic women having a PVR of 100ml or less had peripheral neuropathy. In a similar vein, Kebapci et al. (2007) found that abnormal vibration sensation (OR=1.29, 95%CI: 0.14-11.54) and diabetic retinopathy (OR=1.8, 95% CI: 0.15-21.47), which was assessed by an ophalmologist, were significantly associated with increased bladder emptying defined by a PVR of 100ml or greater in diabetic women (mean age 62±9 years).

Anterior Vaginal Prolapse

Significantly but unexpected relationship between anterior vaginal prolapse and incomplete bladder emptying was found in this study (Adjusted OR=0.84, 95% CI: 0.711-0.995). That is, for one centimeter increase in the most distal position of the remaining upper anterior vaginal wall (point of Bp among POPQ) indicating the degree of anterior vaginal prolapse, the odds of incomplete bladder empting decreased by 16%. This result was inconsistent with previous studies and moreover showed an opposite direction of a relationship between the degree of pelvic organ prolapse and incomplete bladder emptying.

In previous studies, an advanced stage of anterior vaginal prolapse was significantly associated with incomplete bladder emptying (Fitzgerald, Jaffar, & Brubaker, 2001; Haylen, et al., 2008; Lukacz, DuHamel, Menefee, & Luber, 2007). Specifically, Lukacz et al. (2007) reported that incomplete bladder emptying, defined as greater than 100ml, was significantly associated with pelvic organ prolapse, defined as at least one vaginal point descending at least to within 1cm of the hymen with straining, in women with symptoms of urinary urgency, frequency and urge incontinence ($p < .001$). Fitzgerald et al. (2001) also found that incomplete bladder emptying, defined as greater than 100ml, was quite common in women with pelvic organ prolapse stage II or greater for 19 (50 %) women, compared to women with pelvic organ prolapse stage I or less for 44 (27%) women ($p < .001$). Similarly, Haylen et al. (2008) reported that stages II and III of vaginal prolapse were significantly associated with increased PVR (> 30ml) in multivariable analysis ($p < .001$). The significant positive relationship between vaginal prolapse and increased PVR might imply a distortional or kinking effect of the prolapse on the urethra to create bladder outlet obstruction.

In contrast, this study showed that increases in the most distal position of the anterior vaginal wall (Ba) decreased the odds of incomplete bladder emptying (Adjusted OR=0.84).

There are several possible explanations for the discrepancy between this study and previous studies. First, the current study had a high prevalence of absence of anterior vaginal prolapse compared to the previous studies. For instance, 100 (61%) women in this study had -1 centimeter or less of Ba, which can be considered as an absence of anterior vaginal prolapse. In contrast, the studies of Hylen (2008) and Lukacz (2007) had only 40 (10%) and 122 (40%) women who were considered as having an absence of prolapse. In addition, these previous studies included all types of pelvic organ prolapses such as anterior, apex, posterior of vaginal wall prolapses and categorized the variable of prolapse into less than stage II or stage II or greater.

Another possible explanation is that there may have been less of a prolapse effect on the urethra to create a bladder outlet obstruction in this study. In previous studies, the subjects' pelvic organ prolapse and PVR were both measured at the same visit. However, in this study the subjects' pelvic organ prolapse was measured at the clinic visit and their PVRs were measured when they had urodynamic tests, and these visits were not the same day. Moreover, while conducting the urodyamic tests for women who had pelvic organ prolapse, a practitioner intentionally reduced their prolapse using an 8-inch cotton swab to find the occult/masked urinary incontinence and/or to assess the presence of detrusor contractions during the pressure-flow study. Therefore, the subjects' degree of prolapse at the visit for urodynmic tests especially during voiding might have been different (more likely less severe) than at the clinic visit. That is, reducing the prolapse during the urodynamic tests could have decreased the kinking effect of the prolapse on the urethra, and thus, this might have made the subjects with prolapse urinate efficiently resulting in less than 100ml of PVR.

Age

Age was not a significant risk factor related to incomplete bladder emptying in this study. In the literature, the relationship between age and incomplete bladder emptying in women aged 65 or older is not clear. Although several previous studies found that age was significantly related to incomplete bladder emptying, their studies examined women aged 18 or older, not exclusively older women (Fitzgerald, Jaffar, & Brubaker, 2001; Haylen, et al., 2008; Milleman, et al., 2004). For instance, Milleman et al. (2004) found that women aged 55 or older were more like to have incomplete bladder emptying than women aged less than 55 (Adjusted OR=3.71, *P*=.007). That is, it is not clear how age was associated with incomplete bladder emptying for women aged 55 or older and therefore, it is difficult to compare these findings with the current study.

Comparing with the Conceptual Model

Of the risk factors in the conceptual model, which was proposed for this study (Figure 1.3), many risk factors including neurological diseases such as Parkinson's disease and multiple sclerosis, history of stroke, history of pelvic surgery, vaginal parity, history of anti-incontinence surgery were eliminated while determining the best model for the analysis. Among the remaining risk factors, DM, bladder capacity, and anterior vaginal prolaspe were significantly associated with incomplete bladder emptying in this study and there was no significant relationship between risk factors of age and history of spinal cord injury/surgery and incomplete bladder emptying in multivariable analysis (Table 4.5).

Although many risk factors were eliminated and did not have a significant relationship, this conceptual model needs to be tested more in the future because the findings in previous studies were inconsistent and little evidence about these relationships exist in older women. Several previous studies, which were similar to this study, proposed and examined similar risk factors associated with incomplete bladder emptying in women aged 18 or older (Fitzgerald, et al., 2001; Lukacz, et al., 2007; Milleman, et al., 2004). Advanced stage of vaginal prolaspe (stage 2 or greater) was only the significant risk factor which was found in all of these studies. In Milleman et al. (2004), risk factors of age, history of anti-incontinence surgery, and history of multiple sclerosis were significantly related to incomplete bladder emptying, while other studies did not find these relationships. Therefore, to clarify the relationship between these risk factors and incomplete bladder emptying, this conceptual model needs to be examined more closely in the future in women aged 65 or older who have OAB symptoms.

Relationship between Urinary Frequency and Incomplete Bladder Emptying

For research question 2, examining whether urinary frequency could be used to detect incomplete bladder emptying, 153 medical records (17 medical records had missing data) were used for the ROC analysis. This study found that the area under the curve for the models of number of voiding incidents a day was 0.5946 and that for the model of number of voiding incidents a night was 0.5268. None of them had a good value to detect incomplete bladder emptying because the values were close to the worst value (0.5).

There are two possible explanations about the insignificant relationship between incomplete bladder emptying and urinary frequency. Firstly, this result could be the variation in healthcare practitioners, who interpreted the patients’ voiding diaries, which were used for measuring their urinary frequency and/or measurement errors. Specifically, subjects’ urinary frequency measured by the number of voiding incidents a day and a night based on their 3-

day voiding diary (interpreted by the physician) might be underestimated because patients often neglect to record the nocturnal voiding times in the diary because they forget or it is inconvenient. During urodynamic tests at the Urophysiology Laboratory, a practitioner who interprets a voiding diary usually asks a patient how many times she voids at night because there is often no record of nocturnal voiding in the voiding diary. Thus, it is unclear whether the practitioner always asked patients about their nocturnal voiding and if their verbal report of nocturnal voiding was added to the total number of voiding incidents a day on the medical report. Therefore, the relationship between urinary frequency and incomplete bladder emptying in this study might be contaminated by this variation and/ or measurement error.

Another explanation is that, there are other causes of urinary frequency such as sensory urgency and diabetic incipidus. In sensory urgency, the affected patients experience urinary frequency and urgency even though the bladder is behaving normally. In addition, patients with diabetes incipidus, which occurs when the kidneys are unable to conserve water as they perform their function of filtering blood, have the symptom of urinary frequency because the patient has excessive thirst and excessive urine volume.

Therefore, it might be inappropriate to use the symptoms of urinary frequency alone to detect incomplete bladder emptying in older women with OAB symptoms.

Relationship between Incomplete Bladder Emptying and Urodynamic Parameters

For research question 3, about the relationship between urodynamic parameters and incomplete bladder emptying, 166 medical records were used for logistic regression analysis. This study found a significant relationship between the maximal urine flow rate (Q_{max}) and voiding patterns and incomplete bladder emptying. For 1 ml/second increase in maximal urine flow rate, the odds of incomplete bladder emptying decreased by about 5% (Adjusted OR=0.95, 95% CI: 0.91-0.99). That is, a decrease in the maximal urine flow rate (Q_{max}) increases the risk of incomplete bladder emptying. In addition, women having an interrupted voiding pattern are more likely have incomplete bladder emptying than women having a normal voiding pattern (Adjusted OR=3.98, 95% CI; 1.92-8.26). However, opening detrusor pressure (P_{det}.Open) and detrusor pressure at the maximal urine flow rate (P_{det}. Q_{max}) were not significantly related to incomplete bladder emptying.

The significant relationships between the maximal urine flow rate (Q_{max}) and interrupted voiding pattern and incomplete bladder emptying were similar to the findings in Groutz et al. (1999). They found that the maximal flow rate in 40 women (mean age 62.5 ± 15.8) with voiding difficulty defined as a maximal urine flow rate (Q_{max}) less than 12ml/second or PVR greater than 150 ml was significantly lower than in 166 women (mean age 57.2 ± 12.2) without voiding difficulty ($P <.000$). Also, they reported that the interrupted voiding pattern was significantly prevalent in women with voiding difficulty ($P < .04$).

The insignificant relationship between the opening detrusor pressure (P_{det}.Open) and detrusor pressure at the maximal urine flow rate (P_{det}. Q_{max}) and incomplete bladder emptying in women could be that women can void normally with low detrusor pressure (less than 10 cm H_2O) and are able to empty the bladder completely with a good urinary flow rate using pelvic floor relaxation without needing to generate significant detrusor pressures (Nitti, et al., 1999).

Limitations

This study has several limitations. First, because this was a retrospective study design, that used existing data recorded for reasons other than research, accuracy of the written medical records might be uncertain. That is, reporting bias may exist in the medical records such as the subjects' past medical and surgical histories. Selection of the variables was also limited because of the retrospective design. For instance, functional obstruction such as detrusor-sphincter dysnergia (DSD)(Dmochowski, 2005), detrusor hyperactivity with impaired contractility (DHIC) (Resnick & Yalla, 1987), and the symptom of voiding difficulty (Fitzgerald, et al., 2001; Lee, et al., 2007) have been reported as significant variables associated with incomplete bladder emptying, but this information was not included in this study.

Measurement errors might be another limitation related to the reliability in this study. As explained earlier, because the subjects' pelvic organ prolapse and PVR were measured on different days and the subjects' prolapse was reduced by a practitioner during the urodynamic tests, it is unclear if the degrees of the subjects' pelvic organ prolapse were the same between these two visits. Therefore, the result of the relationship between anterior vaginal prolapse and incomplete bladder emptying in this study may be contaminated by this measurement error.

Lastly, generalization of these findings, which is related to external validity, may be restricted. The sample for this study included only women who were referred to the Urophysiology Laboratory to conduct urodynamic tests. That is, it is not a representative sample of all U.S. older women with OAB symptoms. Hence, it is not suitable for generalization to all older women who have OAB symptoms.

Recommendations for Further Research

From the results of the current study, several recommendations for future studies can be suggested. First, it is recommended that future replication studies use a prospective design including more variables, which can be associated with incomplete bladder emptying and were not included in this study. In addition, a larger sample is needed, especially with women who have a history of multiple sclerosis, history of stroke, Parkinson's disease, or spinal cord injury/surgery. Although this study contributes knowledge about the relationship between the risk factors of DUA and BOO and incomplete bladder emptying, few studies have examined these relationships.

Another suggestion is to conduct a longitudinal study to examine the etiology of incomplete bladder emptying in older diabetic women. This study supports the independent and significant relationships between the presence of diabetes and increased bladder capacity and incomplete bladder emptying in women aged 65 or older who have OAB symptoms. It is, however, still unclear how diabetes affects incomplete bladder emptying and what is the causal relationship between sensory impairment and increased bladder capacity in older women.

Finally, a study examining the threshold of post-void residual volume (PVR) in older women is needed. In this study, incomplete bladder emptying was defined as a PVR of 100ml or greater since many previous studies have used this definition (Digesu, et al., 2003; Fitzgerald, et al., 2001; Gotoh, Yoshikawa, & Ohshima, 2006; Milleman, et al., 2004). However, there is no standardized PVR indicating normal or abnormal. Therefore, the relationship between lower urinary symptoms such as urinary frequency, urgency, and urinary incontinence and PVR, and the relationship between urinary tract infection and PVR need further explanation in older women.

Nursing and Clinical Implications

Sixty-six (39%) women with OAB symptoms had incomplete bladder emptying (PVR of 100ml or greater) in this study. Increased bladder capacity, the presence of DM, and anterior vaginal prolapse were factors that were significantly related to incomplete bladder emptying in multivariable analysis. In addition, a low maximal urine flow rate (Q_{max}) and an interrupted voiding pattern in urodynamic parameters were significantly associated with incomplete bladder emptying in multivariable analysis.

These findings have two implications. First, health care providers may use these findings when screening women aged 65 or older who have OAB symptoms and who have incomplete bladder emptying. For instance, before administering an anti-muscarinic agent to women, a healthcare provider evaluates the PVR when a patient has DM and/or an interrupted voiding pattern, by asking such as “Have you been diagnosed as a DM?” and “When you empty your bladder, does the urine start, stop and start again?” These women are unlikely to have improvement in their OAB symptoms using an anti-muscarinic medication, and may even progress to complete bladder retention. Therefore, applying the two screening criteria of the presence of DM and an interrupted voiding pattern would be useful to identify older women who have incomplete bladder emptying.

Second, this study supported an assumption that a bladder capacity of 500ml or greater was related to incomplete bladder emptying in older women with OAB symptoms. Increased bladder capacity may be caused by ignoring urge sensations from the bladder and/or by impaired bladder sensations. Regarding the former, nurses and teachers have been reported to suppress and ignore the desire to void during working hours (Bendtsen, Andersen, & Andersen, 1991; Crutchlow, Dudac, MacAvoy, & Madara, 2002), so they tend to hold large amounts of urine. Older women who have infrequent voiding could be related to the latter. Therefore, healthcare providers need to be aware of the importance of proper response to the urge to urinate to avoid bladder over distension, and they may encourage older women who urinate infrequently to use scheduled voiding for adequate bladder emptying.

Conclusions

This is the first study to examine the relationship between risk factors of DUA and BOO and incomplete bladder emptying and the relationship between urinary frequency and incomplete bladder emptying in women aged 65 or older who have OAB symptoms. Sixty-six (39%) women had incomplete bladder emptying. This study supports the relationship between the presence of DM and increased bladder capacity (≥500ml) and incomplete bladder emptying. Interestingly, another significant but unexpected finding was the opposite direction of a relationship between anterior vaginal prolapse and incomplete bladder emptying, which means that an increase in the degree of anterior vaginal prolapse decreases the risk of incomplete bladder emptying. However, this study did not support the relationships between other risk factors related to detrusor underactivity (such as a history of neurological disease, history of spinal cord injury/surgery, and history of pelvic surgery, age, and number of vaginal delivery) and related to anatomical bladder outlet obstruction (such as a history of anti-incontinence surgery) and incomplete bladder emptying.

As for urinary frequency, this study did not find a significant relationship between urinary frequency and incomplete bladder emptying, and imply that the number of voiding incidents alone might not be a clinical indicator to detect incomplete bladder emptying.

The current study raises awareness of incomplete bladder emptying in older women with OAB symptoms. In addition, the findings may help nurse researchers and health care professionals understand what risk factors are related to incomplete bladder emptying in older women who have OAB symptoms. However, little evidence still exists about incomplete bladder emptying in older women which indicates the need for a replication study with a larger sample.

Appendix A: Form for Data Collection

MR: ***date of UDS:*** ***data collector:***

	Variables	**Data Source**	**Sub items**			**Variable name for SAS**
1	Age	Medical chart				age
2	OAB symptoms	subjective	Urgency Urge UI frequency Nocturia	No =0 No =0 No =0 #/night	Yes=1 Yes=1 Yes=1	OAB_urge OAB-UUI OAB-Fre OAB-Noc
			SUI	No =0	Yes=1	SUI_Sym
			# of UTI /year			UTI
Exclusion criteria checking						
3	Bladder ca Bladder irradiation Taking anticholinergic Having a foley cath Having an interstim			No =0 No =0 No =0 No =0 No =0	Yes=1 Yes=1 Yes=1 Yes=1 Yes=1	
If a subject has one of above criteria of exclusion→ stop here						
4 5 6	Height Weight BMI	Medical chart Medical chart Medical chart			inch lb kg/m^2	Hei Wei BMI
7	Smoking status	Medical chart	Current smoker=1 Previous smoker=2 never smoker=3			SMO
8	Race	Medical chart	White= 1 African American=2			Race

		Ethnicity	Asian=3 Others=4 Unknown=5 Hispanic	No =0	Yes=1	Hisp
9	Vaginal parity	Medical chart				Pari
10	Type of living	Medical chart	Home=1 Assistant Facility=2 Nursing home=3			Type_live
11	Hx of Neurologic disease	Medical chart	MS	No =0	Yes=1	Neu_MS
			Stroke	No =0	Yes=1	Neu_Stro
			Parkinson’s disease	No =0	Yes=1	Neu_Park
			TIA	No =0	Yes=1	Neu_TIA
			Neuropathy	No =0	Yes=1	Neu_pathy
			Alzheimer	No =0	Yes=1	Alz
12	Spinal cord injury/surgery	Medical chart		No =0	Yes=1	SCI
13	DM	Medical chart		No =0	Yes=1	DM
			Type2	No =0	Yes=1	DM2
			Type1	No =0	Yes=1	DM1
14	Pelvic surgery	Medical chart		No =0	Yes=1	Sx_Pel
15	Hx of anti-incontinence surgery	Medical chart		No =0	Yes=1	Sx_AntiUI
16	prolapse	Medical chart at gyn visit	Anterior prolapse	Aa		Pro_Aa

			Anterior prolapse apex apex Posterior prolapse Posterior prolapse	Ba C D Ap Bp		Pro_Ba Pro_C Pro_D Pro_Ap Pro_Bp
Voiding diary						
17	# of voids/day # of voids/night # of voids/daytime	Subtraction line 5 to 7				Void_tot Void_Noc Void_Day
Cystometrogram						
18	Detrusor overactivity		Presence of DO UI with DO Max pdet at DO	No =0 No =0	Yes=1 Yes=1	DO DO_UI DO_Max
19	SUI		Leak with stress 150ml (< 100cmH2O) Leak with stress 300ml (< 100cmH2O)	No =0 No =0	Yes=1 Yes=1	SUI_150 SUI_300
20	UPP	Without reduction	MUCP FUL			UPP_MUCP UPP_FUL
Pressure flow study						
21	Pdet.opening					Pdet_Open

	Qmax						Qmax
	Pdet.Qmax						Pdet_Qmax
	Voiding volume						Vol_Void
	PVR						PVR
	Bladder capacity						Capa
	Voiding pattern		Normal=1 Interrupted=2				Void_Pat
	Pelvic floor muscle activity		Normal=1 Non-relaxing=2 Dysnergia=3				EMG

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