Pathophysiology of Incontinence in Ageing Men

Shang-Jen Chang, M.D., Hong-Jeng Yu, M.D.[1]

Department of Urology, Buddhist Tzu Chi General Hospital, Taipei Branch, Taipei Taiwan; Department of Urology[1], National Taiwan University Hospital, Taipei, Taiwan

THE MECHANISM OF CONTINENCE IN MEN

For the purpose of understanding the pathophysiology of urinary incontinence, we should be familiar with the micturition cycle and the physiology of bladder storage and emptying. Normal storage of urine depends on: (1) spinal reflex mechanisms that activate sympathetic and somatic pathways to the urethral outlet, and (2) tonic inhibitory systems in the brain that suppress the parasympathetic excitatory outflow to the urinary bladder [1]. The micturition cycle is organized in the pontine micturition center, which is illustrated in Fig. 1. Parasympathetic and somatic components of the sacral spinal cord and sympathetic components of the thoracolumbar spinal cord also help to integrate and modulate the micturition cycle [2]. During the filling phase of the micturition cycle, the bladder accommodates increasing volume and maintains low intra-vesical pressure. The composition of smooth muscle, collagen and elastin in the bladder wall make the bladder highly compliant. Stretch receptors in the detrusor muscle transmit the sensory impulses to the central nervous system (CNS) through sympathetic nerves. Distension of the bladder wall during bladder filling activates a "guarding reflex", which stimulates the sympathetic nerves of the bladder outlet smooth muscle and external urethral sphincter that promote continence [3]. Sympathetic stimulation also inhibits the detrusor muscle and the detrusor remains silent until the patient wishes to void. Initiation of voiding is accompanied by complete relaxation of the striated urethral sphincter, followed by a rise in detrusor pressure and concomitant fall in urethral pressure [4].

FUNCTIONAL ANATOMY OF THE SPHINCTER IN MEN

Normal functions of the urethral sphincter require integrated interaction of the following factors: (1) watertight apposition of the urethral lumen, (2) compression of the wall around the lumen, (3) structure support to keep the proximal urethra from moving during increases in intravesical pressure, (4) a means of compensating for abdominal pressure changes, and (5) neural control [5]. The sphincter mechanism in men has two distinct but related parts, including the bladder neck (internal sphincter) and the distal sphincter (external sphincter). The internal sphincter consists of smooth muscle fibers derived from those in the trigone arranged in a circular sphincter-like fashion [6]. It is innervated by autonomic parasympathetic fibers from the pelvic nerve. During the filling phase, the bladder neck remains closed and leakproof. The bladder neck opens in response to bladder contraction during the voiding phase. It opens in response to abnormal detrusor activity, such as detrusor instability or hyperreflexia. The response of the bladder neck to detrusor contraction may be due to the anatomic arrangement of smooth muscle in the bladder neck.

The external sphincter is composed of intrinsic and extrinsic components. The intrinsic component is composed of periurethral smooth muscle and striated muscle (fatigue-resistant, slow twitch) with variable proximal margins near the verumontanum. It is also called the rhabdosphincter due to its striated muscle component. The extrinsic part of the external sphincter is called the urogenital diaphragm. As the membranous urethra passes through the urogenital diaphragm, the extrinsic muscle forms a ring around the urethra and supports the prostate superiorly. The extrinsic component also contains striated muscle that increases urethral resistance during coughing or abdominal straining, which causes increased intra-abdominal pressure [7]. Unlike its female counterparts whose urethral support may be compromised during childbirth and ageing, injury to the male rhabdosphincter usually occurs after the trauma of surgery.

ETIOLOGY

The International Continence Society's (ICS) definition of urinary incontinence is "the complaint of any involuntary leakage of urine" [8]. In ageing men, urinary incontinence not only results from discoordination between bladder storage and urethral resistance but also from non-genitourinary origins.

1. Age: Diokno interviewed 1,955 senior citizens who were 60 or more years old in Michigan in 1985. The overall prevalence of urinary incontinence was 18.9% in men and the prevalence of urinary incontinence increased with age [9]. However, multiple comorbidities in ageing men made it difficult to determine the independent effect of age. Indeed, urodynamic parameters in men change with age. Madersbacher et al. evaluated 253 men in 1998 [10]. They found that as men get older there is an increase in bladder capacity and post-void residual urine, while a decrease in maximal urinary flow rate was noted in urodynamic studies. There were no age-related changes in maximum detrusor pressure and detrusor pressure at peak flow rate. Also, the prevalence of detrusor instability increased with age, which may be associated with outlet obstruction associated with increasing prostate volume.
2. Dementia: Previously, urinary incontinence has been thought to be related to dementia [11]. However, many patients with dementia do not have urinary incontinence. On multivariate analysis, impaired mobility had a stronger relation to incontinence than impaired cognitive function [12].
3. Environment, impaired mobility and dexterity: Mobility and access to a bathroom affect the ability of ageing men to get to the bathroom in time to void. Manual dexterity affects the ability to undress in time to void, as may occur in persons with conditions such as severe

Received: June 11, 2007 Accepted: July 9, 2007
Address correspondence to: Dr. Hong-Jeng Yu, Department of Urology, National Taiwan University Hospital, 7, Chung Shan South Road, Taipei, Taiwan
E-mail: yhj5251@ntu.edu.tw

arthritis.

4. Previous pelvic extirpative surgery or radiation therapy: Patients with previous pelvic extirpative surgery for colon-rectal cancer, or radiation therapy involving the pelvis may have poor bladder compliance, lack of reflex and urethral dysfunction.
5. Neurological disease: Cerebrovascular disease, Parkinson's disease, multiple system atrophy, multiple sclerosis, spinal cord injury and spinal lesions are associated with urinary incontinence. Stroke is one of the neurological disorders that causes detrusor hyperreflexia, which is generally manifested clinically as urge incontinence. Impairment of bladder contractility can accompany urge incontinence in frail elderly patients. Such patients have involuntary detrusor contractions yet must strain to empty their bladders, either incompletely or completely. These patients have symptoms of obstruction and stress incontinence in addition to elevated post-void residual volume. In addition, chronic impairments of physical and cognitive functioning may cause functional incontinence [13,14]. Bladder dysfunction was noticed in patients with Parkinson's disease and multiple system atrophy. In patients with multiple system atrophy, urinary symptoms result from a combination of detrusor hyperreflexia and urethral sphincter weakness [15]. Urethral or anal sphincter electromyograms (EMGs) often disclose denervation resulting from the degeneration of Onuf's nucleus in the sacral cord [16]. In Parkinson's disease, urinary frequency and urgency resulting from detrusor hyperreflexia are common. However, urethral sphincter function is preserved [17].
6. Diabetes: In patients with diabetes, the prevalence of urinary incontinence may be up to 20% [12]. The associated polyuria due to osmotic diuresis may precipitate incontinence. In advanced stages of diabetes, neuropathy that causes detrusor overactivity and/or diabetic cystopathy may lead to incontinence. Kebapci et al evaluated 27 male patients with type II diabetes and lower urinary tract symptoms. Bladder dysfunction was present in 74.07% of the men [18].
7. Congestive heart failure: Heart failure occurs principally in the geriatric population and often is associated with severe comorbidity. Comorbid conditions that occur in the geriatric population, at a prevalence equal to or greater than that of heart failure itself, include urinary incontinence.
8. Psychiatric disorder: Depressive mood may be associated with urinary incontinence. Evidence indicates that urge incontinence may be related to altered levels of serotonin, a neurotransmitter important in depression.
9. Concurrent medications: With multiple comorbidities, ageing men take several kinds of medicine concurrently and this may lead to urinary incontinence.
   (1) Alpha antagonist: Alpha antagonists reduce bladder neck and urethral pressure in men.
   (2) Angiotensin-converting enzyme inhibitors (ACEIs): The side effects of ACEIs may exacerbate stress urinary incontinence.
   (3) Anticholinergics, calcium channel blockers and opiates cause impaired bladder contractility.
   (4) Diuretics: Potent diuretics produce overwhelming urine output beyond the ability of patients to forestall voiding.
10. Urinary tract infection: Urinary incontinence was more common among patients with asymptomatic bacteriuria [19].

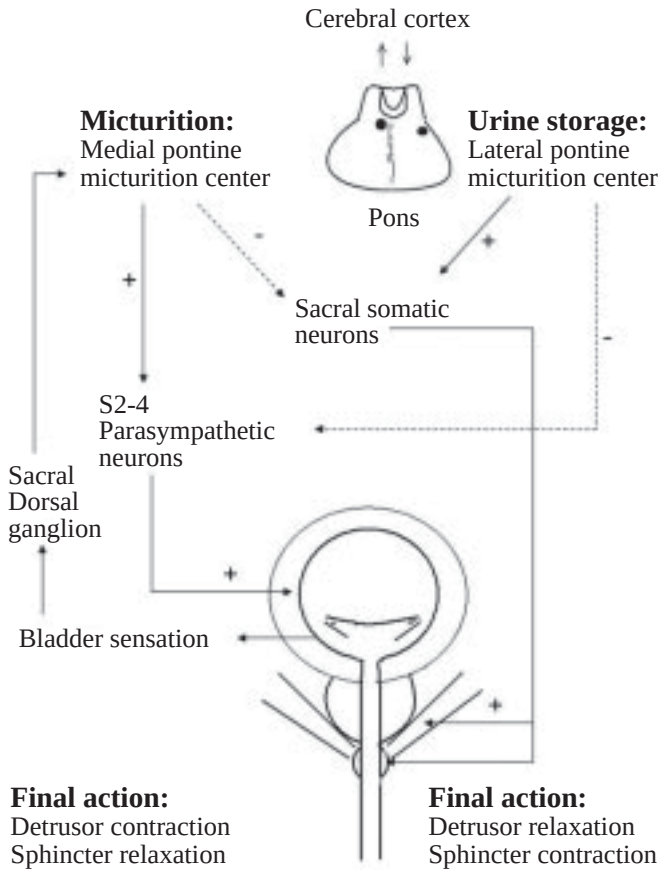

Fig. 1. Afferent and efferent pathways of micturition and urine storage. The lateral pontine micturition center stimulates the sacral somatic neurons and inhibits the parasympathetic neurons, with the final result of detrusor relaxation and sphincter contraction. In contrast, the medial pontine micturition center stimulates the parasympathetic neurons and inhibits the somatic neurons, with the final action of detrusor contraction and sphincter relaxation. (+) Stimulatory effect, (-) Inhibitory effect.

PATHOPHYSIOLOGY

The pathophysiology of urinary incontinence in ageing men can be classified into overflow incontinence, stress incontinence, urge incontinence or mixed type incontinence.

Urge incontinence

The ICS defines urge incontinence as the complaint of involuntary leakage accompanied by or immediately preceded by urgency, while urgency is defined as a sudden compelling desire to void that is difficult to defer. Urgency is the key symptom in the definition of overactive bladder (OAB). About one third of patients with OAB had urge urinary incontinence [20]. Urge incontinence can occur because an involuntary bladder contraction (motor urge incontinence) or urge to urinate (sensory urge incontinence) occurs at a volume less than the capacity. Motor urgency is seen in detrusor instability and detrusor hyperreflexia. Sensory urgency is associated with increased bladder sensation without obvious bladder contraction.

Bladder factors

(1)Detrusor instability (replaced by "idiopathic detrusor overactivity" in

ICS definition)[8].

The definition of detrusor instability is detrusor contraction occurring during the filling phase of the micturition cycle. This term is used when the patient has no overt neurological disorder. In male patients with bladder outlet obstruction, detrusor instability occurs in 75% of patients [21]. Detrusor instability, in some conditions, occurs in the absence of bladder outlet obstruction, which might be due to ischemia or other hormone change. In patients with bladder outlet obstruction, an increase in intravesical pressure results in partial denervation of bladder smooth muscle. There is an increase in the number of spontaneous action potentials in the bladder smooth muscle. The spontaneous action potential causes micromotion of the smooth muscle rather than effective bladder contraction and bladder emptying. Increased intra-vesical pressure stimulates the mechanoreceptors in the detrusor muscle, which in turn transmit the message to the CNS through A-delta nerves and cause the sensation of urgency [5]. With detrusor instability, patients have irritative symptoms such as frequency, urgency and nocturia, which might then give rise to urge incontinence.

(2)Detrusor hyperreflexia (replaced by "neurogenic detrusor overactivity" in ICS definition) [8].

Detrusor hyperreflexia is neuropathic in origin. Detrusor hyperreflexia is associated with spinal cord injury, cerebral vascular accident, Parkinsonism, multiple sclerosis, prolapsed intervertebral discs or degenerative spine disease. When suprapontine inhibition of the micturition reflex occurs, detrusor hyperreflexia develops. Other examples of neurogenic causes of urgency are axon injury in the spinal cord, loss of peripheral inhibition and enhancement of excitatory neuro-transmission in the micturition pathway [1].

(3)Low compliant bladder

Inability to accommodate increasing volumes of urine, which results in a steep increase in intravesical pressure, may be caused by anatomic or neuropathic factors. Anatomic factors affecting the viscoelastic properties of the bladder are seen in contracted bladder states. Low compliance of the bladder with abnormal elastic and vesicoelastic properties may be due to changes in the extracellular matrix. The extracellular matrix is composed of collagen, elastin, proteoglycans and glycoproteins. Collagen and elastin account for the structural support of bladder tissue. In the non-compliant bladder, the ratio of Type III collagen to Type I collagen increases, while elastin in the bladder decreases [5]. Irradiation, tuberculosis infection, multiple surgical interventions or multiple resections may all cause this problem.

The most common neuropathic cause of poor compliance in the male patient is pelvic plexus injury [22]. Although it would be expected that this lesion would cause an acontractile, low-pressure bladder, in reality it produces an acontractile, low-compliant bladder. This may be seen as a result of traumatic causes, namely pelvic fracture, but it is most common in patients who have undergone low anterior or abdominoperineal resection of the colon and rectum. Patients will often present with voiding dysfunction following these procedures, and prostatectomy should only be contemplated if the bladder remains contractile and outlet obstruction can be definitely confirmed urodynamically. The causes of incontinence in this situation are complex. The abnormal bladder pressures may overcome outlet resistance, which in itself may be compromised neurologically or by previous prostatectomy. The acontractility will exacerbate the situation by causing inefficient emptying with overflow.

(4)The role of muscarinic receptors and the urothelium in bladder function.

Muscarinic receptors also play a role in the function of detrusor muscle [23]. Of the 5 subtypes of muscarinic receptors, M2 and M3 are located in smooth muscle, indicating they are potential targets for the treatment of OAB. Human bladder smooth muscle contains primarily M2 receptors (70% to 80%), along with M3 receptors (20% to 30%). M3 receptors have been demonstrated to evoke smooth muscle contraction, which is the primary stimulus for bladder contraction. It has been postulated that M2 and M3 receptors are involved not only in motor (efferent) activation but also in sensory (afferent) activation as well. The activation of M2 receptors may reverse sympathetically mediated smooth muscle relaxation during the filling/storage phase of micturition; there are additional mechanisms by which M2 receptors may cause smooth muscle contraction [24].

Additional to neurogenic and myogenic origins, more and more studies support the idea that the urothelium is an active participant in the modulation of bladder function. Previously, the urothelium was thought to be a passive barrier to toxins in the urine. Actually, the urothelium actively participates in sensory functions, expressing various receptors and ion channels, as well as releasing neurotransmitters in response to stimuli [25]. Vanilloid receptors, $P2X_3$ purinergic receptors, adenosine triphosphate, nitric oxide and acetylcholine have been implicated in urothelial-neuronal interactions. Evidence suggests that the involvement of the muscarinic receptor in bladder function extends beyond detrusor contractility and into afferent sensory functioning. Substances released from urothelial cells can alter the excitability of bladder afferent nerves acutely and chronically; these observations appear to be of particular importance in chronic bladder conditions and in the aging bladder.

Urethral factors

The male sphincter system is generally able to withstand the pressures in daily life. Schaefer evaluated 78 patient with OAB and detrusor overactivity, and showed that a decline in urethral pressure was noted when detrusor overactivity and urge incontinence was reproduced [26].

Overflow incontinence

Older men may have impaired bladder contractility due to detrusor underactivity or an acontractile bladder, and this may cause decreased flow rate and an increase in post-void residual urine. With overt post-void residual urine, overflow incontinence may occur.

The cause of acontractility of the bladder may be chronic retention due to bladder outlet obstruction, diabetic cystopathy, pelvic plexus injury during surgery for rectal or colon cancer, or spinal disease.

Detrusor underactivity 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 within a normal time span. Detrusor underactivity can be a consequence of ageing, hormonal change, neurological disease and bladder ischemia. Recent studies have indicated that detrusor underactivity is a very prevalent, yet under-diagnosed, condition in men, particularly in the frail older population and in patients with chronic retention [27].

In frail older men, the bladder may have both weak contractility and detrusor hyperreflexia, a condition called detrusor hyperreflexia with impaired contractility (DHIC). In institutionalized elderly people, DHIC is the second leading cause of urinary incontinence [12].

Stress urinary incontinence

Stress urinary incontinence is the complaint of involuntary leakage on effort or exertion, or on sneezing or coughing. However, stress incontinence is rare in men. Urethral incompetence is generally seen following prostate surgery, neurological injury or trauma. The incidence of post-prostatectomy incontinence (PPI) differs significantly among studies depending on the definition of incontinence used. Many studies also combine urge and stress incontinence, thus the true incidence of sphincter weakness incontinence following prostatectomy is difficult to judge. The incidence of incontinence following transurethral resection of the prostate or simple open prostatectomy ranges from 1% to 5% [28]. The functional length and position of the external urethral sphincter is variable. It is generally located in the area just distal to the verumontanum. The length of the external striated sphincter varies considerably and, therefore, patients with shorter sphincters or close proximity to the verumontanum are at risk of injury during surgery.

(1)Post-radical prostatectomy incontinence

Despite the low incidence of prostate cancer in Taiwan, the incidence and mortalities of prostate cancer have been increasing rapidly for the past 20 years [29]. In Taiwan, the incidence of prostate cancer has increased from 8.07 to 14.27 per 100,000 of the population from the year 1995 to 2003. In the treatment of localized prostate cancer, radical prostatectomy plays a major role. However, the prevalence of PPI was noted in 5%-20% of patients after radical prostatectomy [30]. Strasser et al [31] evaluated PPI patients with transurethral ultrasound. They demonstrated scarring, thinning or complete atrophy of minimal contractions in the rhabdosphincter in these incontinent patients. Tuygun et al [32] evaluated 22 patients with PPI and 14 patients without PPI, and showed the incidence of fibrosis on pelvic magnetic resonance imaging (MRI) was much greater in patients with PPI than in patients without PPI. Thus, fibrosis plays an important role in the development of PPI because it may have a negative effect on external urethral sphincter function. Groutz et al [30] evaluated 83 consecutive men who had PPI. Sphincteric incontinence was identified as the most common etiology of PPI (88%). Detrusor instability occurred in 33.7% of patients but was regarded as the major etiology in only 7.2% patients. Bladder outlet obstruction, related to anastomotic scarring and impaired bladder contractility, was noted in a minority of patients.

CONCLUSIONS

Despite a relatively lower prevalence rate of incontinence in ageing men (7% to 15%) compared with ageing women (15% to 30%) [33], urinary incontinence is associated with negative psychosocial effects and only 25% of men deem urinary incontinence as a negligible problem [34]. The pathophysiology of urinary incontinence may differ from one man to another. Management strategies in dealing with ageing men who have urinary incontinence should be based on the underlying pathophysiology.

REFERENCES

1. De Groat WC: A neurologic basis for the overactive bladder. Urology 1997; **50(6A Suppl)**:36-56.
2 . Noto H, Roppolo JR, Steers WD, de Groat WC: Electrophysiological analysis of the ascending and descending components of the micturition reflex pathway in the rat. Brain Res 1991; **549**:95-105.
3. Yoshimura N, de Groat WC: Neural control of the lower urinary tract. Int J Urol 1997; **4**:111-125.
4. Yalla SV, Sharma GV, Barsamian EM: Micturitional static urethral pressure profile: A method of recording urethral pressure profile during voiding and the implications. J Urol 1980: **124**:649-656.
5 . Wein AJ: Campbell-Walsh Urology. Philadelphia Elsevier Inc, 2007, pp 2046-2078.
6. Caine M, Raz S, Zeigler M: Adrenergic and cholinergic receptors in the human prostate, prostatic capsule and bladder neck. Br J Urol 1975; **47**:193-202.
7. Gosling JA, Dixon JS, Critchley HO, Thompson SA: A comparative study of the human external sphincter and periurethral levator ani muscles. Br J Urol 1981; **53**:35-41.
8. Abrams P, Cardozo L, Fall M, et al: The standardisation of terminology in lower urinary tract function: Report from the standardisation sub-committee of the International Continence Society. Urology 2003; **61**:37-49.
9. Diokno AC, Brock BM, Brown MB, Herzog AR: Prevalence of urinary incontinence and other urological symptoms in the noninstitutionalized elderly. J Urol 1986: **136**:1022-1025.
10. Madersbacher S, Pycha A, Schatzl G, Mian C, Klingler CH, Marberger M: The aging lower urinary tract: A comparative urodynamic study of men and women. Urology 1998: **51**:206-212.
11. Brocklehurst JC: Urinary incontinence in the community--analysis of a MORI poll. BMJ 1993; **306**:832-834.
12 . Dubeau CE: The aging lower urinary tract. J Urol 2006; **175**:S11-S15.
13. Resnick NM, Yalla SV: Detrusor hyperactivity with impaired contractile function. An unrecognized but common cause of incontinence in elderly patients. JAMA 1987; **257**:3076-3081.
14. Williams ME, Pannill FC; Urinary incontinence in the elderly: Physiology, pathophysiology, diagnosis, and treatment. Ann Intern Med 1982; **97**:895-907.
15. Wenning GK, Scherfler C, Granata R, et al: Time course of symptomatic orthostatic hypotension and urinary incontinence in patients with postmortem confirmed parkinsonian syndromes: A clinicopathological study. J Neurol Neurosurg Psychiatry 1999; **67**:620-623.
16 . Pramstaller PP, Wenning GK, Smith SJ, Beck RO, Quinn NP, Fowler CJ: Nerve conduction studies, skeletal muscle EMG, and sphincter EMG in multiple system atrophy. J Neurol Neurosurg Psychiatry 1995; **58**:618-621.
17. Stocchi F, Carbone A, Inghilleri M, et al: Urodynamic and neurophysiological evaluation in Parkinson's disease and multiple system atrophy. J Neurol Neurosurg Psychiatry 1997; **62**:507-511.
18. Kebapci N, Yenilmez A, Efe B, Entok E, Demirustu C: Bladder dysfunction in type 2 diabetic patients. Neurourol Urodyn 2007.
19. Hedin K, Petersson C, Wideback K, Kahlmeter G, Molstad S: Asymptomatic bacteriuria in a population of elderly in municipal institutional care. Scand J Prim Health Care 2002; **20**:166-168.
20 . Wein AJ, Rackley RR: Overactive bladder: A better understanding of pathophysiology, diagnosis and management. J Urol 2006; **175**: S5-10.
21. Turner WH, Brading AF: Smooth muscle of the bladder in the normal and the diseased state: Pathophysiology, diagnosis and treatment. Pharmacol Ther 1997; **75**:77-110.
22. Mundy AR: An anatomical explanation for bladder dysfunction following rectal and uterine surgery. Br J Urol 1982; **54**:501-504.
23. Eglen RM: Muscarinic receptor subtypes in neuronal and non-neuronal cholinergic function. Auton Autacoid Pharmacol 2006; **26**:219-233.
24. Wang P, Luthin GR, Ruggieri MR: Muscarinic acetylcholine receptor subtypes mediating urinary bladder contractility and coupling to GTP binding proteins. J Pharmacol Exp Ther 1995; **273**:959-966.
25. De Groat WC: The urothelium in overactive bladder: Passive bystander or active participant? Urology 2004; **64(6 Suppl 1)**:7-11.

26. Shaefer W, Tadic S, Griffths, Resnick NM: Updates of American Urology Association 2007, pp 1677.
27. Taylor JA, Kuchel GA: Detrusor underactivity: Clinical features and pathogenesis of an underdiagnosed geriatric condition. J Am Geriatr Soc 2006; **54**:1920-1932.
28. Habib NA, Luck RJ: Results of transurethral resection of the benign prostate. Br J Surg 1983; **70**:218-219.
29. Pu YS, Chiang HS, Lin CC, Huang CY, Huang KH, Chen J: Changing trends of prostate cancer in Asia. Aging Male 2004; **7**:120-132.
30 . Groutz A, Blaivas JG, Chaikin DC, Weiss JP, Verhaaren M: The pathophysiology of post-radical prostatectomy incontinence: A clinical and video urodynamic study. J Urol 2000; **163**:1767-1770.
31. Strasser H, Frauscher F, Helweg G, Colleselli K, Reissigl A, Bartsch G: Transurethral ultrasound: Evaluation of anatomy and function of the rhabdosphincter of the male urethra. J Urol 1998; **159**:100-104.
32. Tuygun C, Imamoglu A, Keyik B, Alisir I, Yorubulut M: Significance of fibrosis around and/or at external urinary sphincter on pelvic magnetic resonance imaging in patients with postprostatectomy incontinence. Urology 2006; **68**:1308-1312.
33. Herzog AR, Fultz NH: Prevalence and incidence of urinary incontinence in community-dwelling populations. J Am Geriatr Soc 1990: **38**:273-281.
34. Hunskaar S, Sandvik H: One hundred and fifty men with urinary incontinence. III. Psychosocial consequences. Scand J Prim Health Care 1993; **11**:193-196.