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Review Article

UROLOGIC PROBLEMS IN THE ELDERLY POPULATION

Abstract

Urological problems are observed commonly in elderly people, and taking care of geriatric patients represents a large portion of the daily routine in the practice of an urologist. Urinary incontinence and voiding dysfunction, nocturia, benign prostatic hyperplasia, prostate cancer, urinary tract infections and late on-set hypogonadism are the most common urologic problems seen in the geriatric age group. Most of these conditions are managed by medications that can affect cognitive functions, blood pressure, heart rate and rhytm, as well as balance, and these medications may interact with the other medications used daily for other conditions. Urinary pathologic conditions, such as incontinence and nocturia, can lead to significant morbidity in the frail elderly, often leading to falls and hip fractures. Surgical intervention is common for urologic diseases, especially for prostatic conditions, but must be carefully evaluated before initiation in geriatric patients.

Key Words: Urinary Incontinence; Nocturia; Prostate; Urinary Tract Infection; Aged.

Derleme

YAŞLI TOPLUMDA ÜROLOJİK SORUNLAR

Öz

Ürolojik sorunlar daha çok yaşlı hastalarda gözlenir ve ürologların günlük rutin pratiklerinin önemli bir kısmını geriatrik hastalar oluşturur. Geriatrik yaş grubunda en sık karşılaşılan ürolojik sorunlar; üriner inkontinans ve işeme disfonksiyonu, noktüri,benign prostate hiperplazisi, prostate kanseri, üriner enfeksiyonlar ve geç başlayan hipogonadizmdir. Bu durumların birçoğu , bilişsel fonksiyonlar,kan basıncı, kalp hızı ve ritminin yanısıra dengeyi de etkileyebilen ilaçlarla tedavi edilebilirler, bu ilaçlar diğer hastalıklar için günlük olarak kullanılan ilaçlarla etkileşim gösterebilirler. İnkontinans ve noktüri gibi üriner patolojik durumlar, kırılgan yaşlılarda sıklıkla düşmeler ve kalça kırıklarına neden olarak ciddi morbiditeye yol açabilirler. Ürolojik hastalıklar , özellikle de prostat hastalıkları için cerrahi gişim sıklıkla kullanılır , ancak geriatrik hastalarda cerrahiden önce dikkatli bir değerlendirme yapılmalıdır.

Anahtar Sözcükler: Üriner İnkontinans; Noktüri; Prostat; Uriner Sistem Enfeksiyonu; Yaşlı.

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INTRODUCTION

The population of our world is dynamically changing, as the proportion of elderly adults is significantly increasing. Since 1950, the ratio of elderly people has been increasing steadily from 8 per cent in 1950 to 11 per cent in 2009, and is expected to reach 22 per cent in 2050 (1). As long as old-age mortality continues to decline and fertility remains low, the proportion of elderly people will continue to increase. Aging is associated with an increased number of social and medical problems. Urology is one of the specialties in medicine that has been influenced mostly by this situation. Urologic issues are the third most common type of complaints in patients 65 years of age or older; in addition, they account for 46.2% of outpatients' visits by specialty (2).

In this age group, there will be an increase of chronic urologic conditions managed by medications that can affect cognitive functions, blood pressure and balance. These medications may interact with the medications used daily for other conditions. Therefore, integration and planning of medications need a thorough evaluation before iniation. Many of the urologic diseases are treated surgically. Operative procedures and the anesthesia administered must be tailored to provide greater margins of safety.

In this article, common urologic conditions of the elderly; mainly geriatric incontinence and voiding dysfunction, nocturia, benign prostatic hyperplasia, prostate cancer, urinary tract infections and late on-set hypogonadism are reviewed.

Geriatric Incontinence and Voiding Dysfunction

Incontinence

Urinary incontinence (UI) is defined as the complaint of any involuntary leakage of urine and it is one of the most bothersome and common conditions in the geriatric population. It is estimated that 25% to 35% of all adults will experience incontinence during their lifetime (3). While it is not considered as a normal part of aging, UI is more prevalent in the elderly. It affects 15% to 30% of those living in their homes and 60% of those in nursing home residents (3, 4). Although the prevalence of UI is higher in older patients compared to the young age group, UI should not be considered as a normal part of aging. It is abnormal at any age. At no age does incontinence affect the majority of people, even people over the age of 85 (5). Its increased prevalence relates mostly to functional impairment and to diseases occuring at elderly ages.

Urinary incontinence may cause many adverse effects. The condition may lead to social isolation and inability to participate in social activities, often causing depression and functional disability (6). Several studies have shown that elderly patients with UI have a higher risk for falls and fractures (7). The aim of assessing elderly patients with urinary incontinence is to identify temporary or reversible causes, and carefully select those who need to be refferred to a specialist.

Transient incontinence is a sudden onset incontinence usually related to an acute illness, specific medical situation or medication, and most of the time is temporary or reversible. One –third of the cases of incontinent elderly living in the community and half of those in the hospitals have this type of incontinence. The transient causes of incontinence are recalled using the mnemonic DIAPPERS (**D**elirium or confussion; **I**nfection, **A**trophic vaginitis/urethritis; **P**sychological disease, **P**harmaceuticals, **E**xcess fluid and endocrine diseases, **R**estricted mobility, **S**tool impaction) (8).

Most UI experienced by elderly adults is chronicand the symptoms are persistent. A fast and complete evaluation of UI can be done in an office setting allowing the identification of the type and the cause of UI. A detailed history is the first step towards diagnosis. Important information that can be elucidated includes onset and severity, medications and the type of the symptoms. If there are cognitive disorders, an accurate history is often diffucult to obtain. Under these circumstances, relatives of the patient must be considered for history. Chronic UI can be divided into five categories: stress, urge, mixed, overflow, and functional.

Stress incontinence is associated with the pelvic floor support weakness and a hypermobile urethra. Leakage of urine occurs with the increase of intra-abdominal pressure such as when coughing, lifting, laughing or sneezing. In men, stress incontinence is usually due to sphincteric damage following radical prostatectomy.

Urge incontinence is the most common type of UI in the elderly. It is characterized by an abrupt onset of a sensation of needing to void, with the loss of urine occuring before the patient is able to reach the toilet. Urge incontinence can be associated with frequency and nocturia, which is called overactive bladder syndrome (OAB). Frequent causative factors include neurologic diseases such as stroke, multiple sclerosis, Parkinson's disease and spinal cord injury. Other urologic conditions that may cause urgency include benign prostatic hyperplasia (BPH), infections, stones and tumor. OAB can also be caused by age related bladder changes (9).

Overflow incontinence is usually due to impaired detrusor contractility, severe bladder outlet obstruction, or both (3). In men, the reason is mostly benign prostatic hyperplasia and

urethral stricture. Diabetic neuropathy causing bladder contractility dysfunction may also lead to overflow incontinence. UI in presence of large postvoid residual and low voided volume is suggestive of overflow UI. Patients may experience frequent loss of small volumes of urine, dribbling, weak urinary stream and nocturia. The use of anticholinergics, narcotics and alpha-adrenergic agonists may also contribute to this type of UI.

Mixed incontinence is a combination of urge and stress incontinence, commonly seen in elderly women. Treatment may be planned according to the predominant symptoms.

Functional incontinence is associated with the inability or lack of motivation to reach the toilet on time. Inaccessible toilets, mobility disorders such as severe rheumatoid arthritis, cognitive impairment, and psychological disorders may contribute to functional UI. The condition may be transient or chronic. A patient who has experienced a hip fracture, and therefore unable to transfer him or herself to the toilet, is an example of a transient cause. Dementia is an example of a chronic condition that may result in functional UI.

Most of the older patients having UI do not volunteer to share information about their symptoms. This may be due to the feeling of embarrassment or acceptance of UI as a fact of normal aging. Obtaining a thorough history and physical examination are the most important steps in the clinical evaluation of elderly with UI.

Physical examination includes a pelvic or genital, and rectal examination in both men and women. Physical examination must focus on prostatic diseases, pelvic floor support, urethral mobility, bladder fullness and pelvic organ prolapse. Urinalysis and urine culture, voided volume and postvoid residual volume measurements all may be performed in office settings.

Treatment

Most patients prefer to initiate with less invasive therapies before considering medications or surgery to treat their UI. Dietary modifications, weight loss and behavioral interventions are the first steps in treatment. These treatments can yield significant improvements in UI symptoms. Pelvic-floor exercises, bladder retraining and biofeedback are useful as first-line management of incontinence. These are all well studied in the geriatric population and are recommended by most guidelines as an initial approach to therapy. However, they require good cognitive function and motivation as the success of the treatment depends on the active participation of the patient (10).

Antimuscarinic drugs are the most commonly used drugs for the treatment of urgency incontinence (11). These drugs target bladder smooth muscle and show their effect by blocking cholinergic receptors in the bladder, which leads to a decrease in bladder contractility. Patients should be started at lower doses of antimuscarinics due to their side effects. Most common side effects are dry mouth, constipation, reduction in cognition, tachycardia, dry eye and blurred vision.

Glaucoma, bronchitis, chronic airway disease, diabetes mellitus, dementia, constipation and congestive heart failure can be exacerbated by anticholinergic therapy (12). Overall success in the control of urge incontinence in clinical studies is in the range of 60% to 80% (13).

Surgery should be considered in selected patients. Older age should not be considered as a contraindication if the patient is fit enough (14). Preoperative optimization of comorbid conditions such as hypertension, diabetes, cardiovascular and pulmoner diseases can help to enhance surgical outcomes and improve safety. Recent advances in minimally invasive surgical procedures mostly in urethral slings make surgery for stress UI a good option for a larger number of geriatric patients than in the past. Carr and colleagues (15) reported a 100% succcess with pubovaginal sling procedure in the geriatric age group. Sacral nevre stimulation and botulinum toxin injection are minimally invasive surgical interventions for refractory urge UI (14).

Nocturia

Nocturia is defined as the complaint that an individual has to wake at night one or more times to void (16). Each void must be preceded and followed by sleep. It is an underreported, understudied, infrequently recognized problem in adults (17). The incidence of nocturia is similar for men and women, and increases significantly with age (14). The incidence in men is 29-59%, whereas it is 28-62% for women in the geriatric age group (18). Nocturia may cause a range of detrimental effects because of the associated sleep disturbances experienced by patients on a regular basis. These effects include: reduced quality of life, cognitive disturbances, exacerbation of medical illness and increased falls and fractures (18).

Nocturia in its nature is multifactorial and is caused by factors that increase urine production and others that decrease the bladder storage. Potential causes of nocturia can be categorized as arising from: nocturnal polyuria (NP), diurnal polyuria, bladder storage problems, and sleep disturbance or combination of these factors (18). The most common causes of nocturia in men found in the population-based FINNO study

were: urinary urgency, BPH, and sleep disruption. Other causes were obesity and the use of anti-depressants (19).

Nocturnal urine volume is defined as the total volume of urine passed between the time the person goes to bed with the intention of sleeping and the time of waking with the intention of rising (20). It excludes the last void before going to bed, but includes the first void in the morning. Nocturnal polyuria signifies that an increased proportion of the 24-h output occurs at night. Thus, if the ratio of nocturnal urine volume to 24-h output is >20% in younger adults, or > 33% in the older population, NP is present (20). Although the pathophysiology of NP is not clear, some of the investigators believe that low levels of antidiuretic hormone (ADH) at night and mobilization of fluids in patients with edema are mostly involved (21,22).

Nocturia can be an early feature of potentially serious underlying pathology that may not be previously diagnosed. The first priority in treating nocturia is to identify and treat these underlying conditions, such as diabetes mellitus, congestive heart failure, diabetes insipidus, urinary tract infections, hypercalcemia, and hypokalemia. After such contributing conditions have been searched for and treated, behavioral therapy can then be instituted. Avoiding nighttime fluid intake, wearing compression stockings and elevating the legs in the afternoon, ceasing consumption of coffee, tea and alcohol late at night are among the behavioral modifications that may provide help. Pharmacotherapy of nocturia includes desmopressin to manage nocturnal polyuria and antimuscarinic agents to manage the patient's decreased ability to store urine.

PROSTATE DISEASES

Benign Prostatic Hyperplasia

Prostate diseases are common in men of all ages. The most frequent diseases are benign prostatic hyperplasia (BPH), prostatitis and prostate cancer. Benign prostatic hyperplasia is a histological condition characterized by benign hyperplasia of stromal and /or epithelial prostate tissue. The incidence and prevalence of BPH and prostate cancer increase with age. It is found in a cross-sectional analysis of 1557 men (aging from 40 to 96) that increasing age is an independent risk factor for lower urinary tract symptoms (LUTS) (23). BPH can create an outflow obstruction statically (prostatic enlargement) or dynamically (increased internal sphincteric tone). LUTS are assessed with both subjective and objective studies. The international prostate symptom score (I-PSS) was designed to quantify the severityof BPH- associated LUTS. Patients are asked seven questions regarding their urinary symptoms. A focused physical examination should be performed to assess lower abdomen to rule out globe vesicale. Digital rectal examination (DRE) should be performed to evaluate anal sphincter tonus and the prostate with regard to size and consistency, which may be suggestive of cancer. Urinanalysis and serum prostate spesific antigen (PSA) measurement should be performed as a part of the basic evaluation.

Basically low I-PSS scoring patients are advised to follow behavioral changes, median range patients are given the option of medication, and patients with the highest scores suffering with most of the complaints are offered either medication or surgery.

Surgery may be indicated for patients with recurrent infection, hematuria, bladder stones, hydronephrosis, obstructive nephropathy or urinary retention. Transurethral resection of the prostate (TURP) is well tolerated in the elderly population (24). For the patients who are at significant surgical risk, less invasive transurethral treatment modalities include laser ablation, microwave therapy or neddle ablation.

Medications used for treatment of BPH include phytotherapeutic agents, α1-adrenergic receptor blocking agents, 5α-reductase inhibitors (5ARIs). Medical therapy by using alpha blockers and 5α-reductase inhibitors is now considered first-line treatment for BPH (25). The two major approaches of medical therapy for bladder outlet obstruction related to BPH are decreasing the glandular volume and decreasing the bladder outlet resistance by relaxing prostate smooth muscle tissue. α1-adrenergic blockers cause relaxation of these muscles, thus treating the dynamic component of bladder outlet obstruction. Non-selective α blockade can have significant side effects and in order to overcome this problem α1 selective medications were developed to target the urinary system more specifically. Non-selective agents commonly used include terazosin and doxazosin; selective medications are tamsulosin, alfuzosin and silodosin. The most common side effects are asthenia, dizziness and postural hypotension. These problems may be more pronounced in older men, and a lower target dose should be considered in the very old patients. Attention must especially focus on dizziness and postural hypotension, which may increase the risk of falls in this age group.

5α-reductase inhibitors block the conversion of testosterone to dihydrotestosterone, which is a potent stimulator of prostatic glandular tissue. The inhibition of local androgen stimulation results in reduction of overall prostatic glandular volume over a period of 6 months. The combination of an α1-adrenergic receptor blocker and a 5α-reductase inhibitor may

have synergistic effects to improve LUTS especially in patients with prostatic volume greater than 30 gr. The combination therapy has been shown to decrease the incidence of acute urinary retension and surgery for BPH (26).

Prostate Cancer

Prostate cancer is one of the most common malignancies in men. Delongchamps et al. (27) identified prostate cancer in 45% of men older than 70 years of age in their autopsy study. It is evident in this study that this selected group of men died of diseases other than prostate cancer. Thus, we may conclude that all prostate cancer cases do not need therapy, but also not all tumors require detection if that tumor will not affect the patient. After the PSA era, most of the prostate cancer diagnoses are based on the PSA screening. There is little evidence to support the benefit of PSA screening in elderly populations. Randomized trials were performed to predict a benefial impact of PSA screening on prostate cancer mortality with contradictory results (28, 29). There is still serious controversy regarding PSA screening. In men aged 75 years or older, the US Preventive Services Task Force declared that there is adequate evidence that the incremental benefits of treatment for prostate cancer detected by screening are little to none. For men 75 years or older, there is moderate certainty that the harms of screening for prostate cancer outweigh the benefits (14). The American Cancer Society recommends that asymptomatic men who have at least a 10-year life expectancy have an opportunity to make an informed decision with their health care provider about screening for prostate cancer after receiving information about the uncertainties, risks and potential benefits associated with prostate cancer screening (30).

Age, clinical stage, PSA level, histologic grade, and comorbid conditions should be taken into account before planning a treatment, especially in older men suffering from prostate cancer. There are several forms of effective treatment options offered at present. Curative or definitive treatment is only considered possible if the tumor is confined to the prostate gland. Radical prostatectomy is a curative way of treatment for confined disease and offers long-term palliation for locally advanced cancers even in older men (31). Radiation therapy is another option for curative treatment. It may be delivered by external and interstitial methods with newer technology decreasing complications and increasing effectiveness (32). Incontinence is the main complication after radical prostatectomy and radiotherapy, and it may profoundly decrease quality of life. New modalities have been developed to ablate the cancerous prostate tisue, using freezing (cryotherapy) or heating (high-intensity focused ultrasound) (33-35).

There is still no known curative treatment for advanced prostate cancer that has metastatized. Hormonal ablative therapy is the cornerstone endocrine treatment for advanced prostate cancer. The aim of this therapy is to remove the sources of androgen or testosterone in the body. Bilateral orchidectomy, luteinizing hormone –releasing hormone (LHRH)- and antiandrogens are the options for hormonal ablative therapy (36).

AGING MALE/LATE ON-SET HYPOGONADISM OR PARTIAL ANDROGEN INSUFFICIENCY SYNDROME

As a natural result of aging, gonadal function diminishes as well as several other changes both in men and women (37). This situation is referred as Symptomatic Late On-set Hypogonadism (SLOH) and Partial Androgen Insufficiency Syndrome (38). It is a clinical and biochemical syndrome, and may affect the function of multiple organ systems and result in a significant decline in the quality of life.

The prevalence of SLOH is not exactly known, but it can be predicted that it is on the rise according to the population based studies. In the Massachusetts Male Aging Study (MMAS), a crude incidence rate of 12.3 per 1000 person-years was reported in American men from 40 to 69 years old (39). It is known that serum testosterone level decreases after the age of 31. Therefore, biochemical hypogonadism was observed in 7% of men aged between 40-60 years old, in 21% of those between 60-80 years old, and in 35% of men older than 80 years of age (37,40,41).

Four groups of clinical findings are evaluated:

1. Physical findings: Decrease in muscle mass and strength, fatigue, weakness, abdominal obesity, gynecomastia.
2. Vasomotor findings: Sweating, hot flushing, sleeplessness, oversleeping, palpitation.
3. Psychologic findings: Mental fatigue, decrease in cognitive function, distortion in well-being, uncomfortable feeling, depression, nervousness.
4. Sexual findings: Decrease in sexual function, loss of libido, erectile dysfunction, and decrease in ejaculation.

Some questionnaires have been developed in the clinical evaluation of SLOH: 1) St. Louis University's ADAM; 2) The Aging Male Survey (AMS), and 3) The MMAS (42-46). Interest of the androgen deficiency in aging males (ADAM) questionnaire for the AMS symptom scale is the most commonly

used form of inquiry, and evaluates all of symptom groups with 17 questions. If the total score is greater than 27, a clinical diagnosis of SLOH can be made.

However, these findings should also be supported biochemically. Serum testosterone level should be measured from blood taken between 8.00-11.00 A.M. If testosterone levels are below or at the lower limit of accepted values (<230 ng/dl), the results should be confirmed with a second determination together with measurement of gonadotropins, especially LH, and prolactin. If serum testosterone level is in the normal range (>350 ng/dl) in a patient with clinical findings, other causes of symptoms should be investigated. On the contrary, when serum testosterone levels are found between 230-350 ng/dl, not only testosterone level should be measured, but also the bioavailable testosterone level should be calculated (38,47,48).

The aims of the treatment of SLOH are; 1) Preservation of sexual function, libido and well-being; 2) Prevention of osteoporosis and protection of muscle strength; 3) Maintenance of cognitive function; and 4) Keeping the testosterone and its metabolite levels within normal limits (48).

There are several testosterone preparations in the market. The choice among these preparations depends on availability, safety, tolerability, efficacy, and preference by the patient and the physician. Before the treatment, serum PSA level and bladder outlet obstruction should be evaluated carefully. Androgen replacement treatment is contraindicated in patients having suspected prostate/breast cancer or having severe infravesical obstruction due to benign prostate hyperplasia. Men having significant erytrocytosis, untreated severe congestive heart failure, and untreated severe obstructive sleep apnea should not be initiated androgen replacement therapy before detailed investigation of these co-morbid conditions. Age is not a contraindication to initiate androgen replacement treatment (49,50).

Urinary Tract Infection in Elderly

Urinary tract infections are a common problem in the elderly. Moreover, as the life expectancy increases in the whole world, the morbidity/mortality and the significance of urinary infections seem to be increasing in importance. Foxman et al. reported that urinary tract infections account for nearly 25% of all infections in elderly people (51). Also, in a study from Turkey, urinary tract infection was found as one of the most common causes of hospitalization in elderly (34%) (52).

At least 20% of women and 10% of men older than 65 years have bacteriuria, but most of them are asymptomatic (53). On the contrary, bacteriuria was observed in women living in nursing homes with a range of 17% to 55%, and in men with a range of 15% to 31% (54).

The risk factors of urinary infection in the elderly are considered as age-related changes that include: decline in cell-mediated immunity, neurogenic bladder dysfunction, fecal and urinary incontinence, increased incidence of urethral catheter placement; and in women, changes in the vaginal environment, atrophic vaginitis due to estrogen depletion after menopause and cystocele due to pelvic muscle relaxation; and in men, infravesical obstruction due to benign prostate hyperplasia as well as impaired cognitive function and disability in everyday life (55,56).

Escherichia coli remains the most common uropathogen (75% of all urinary infections). Additionally, there is a significant increase in the incidence of *Proteus, Klebsiella, Enterobacter, Serratia,* and *Pseudomonas* species, enterococci as well as polymicrobial bacteriuria, which are more common among the elderly (55,57).

Urinary tract symptoms are often controversial, and comorbid diseases can mask or mimic infection findings. Diagnosis should depend on carefully obtained urinalysis and culture. The presence of bacteria greater than 10^5 cfu/mL in urine is an important finding. However, counts of 10^2 cfu/mL or more bacteria in catheterized patients are clinically significant (55,56,58).

Asymptomatic patients do not need antimicrobial treatment. However, if lower urinary tract symptoms are present for more than 7 days, antimicrobial therapy is recommended. In addition, in elderly people, these agents should be used carefully and the patients should be followed closely because these agents have the potential to cause more toxic and adverse effects in elderly than young patients due to impaired renal/hepatic function in the elderly and the possible interaction with other systemic drugs. Treatment should be planned according to the results of the urine culture and tailored to the physiologic and pathophysiologic conditions of the elderly.

In summary, geriatric patients require a careful planning when developing a treatment program for various urologic problems. In treating BPH or prostate cancer, quality of life and expected life span become important factors in making treatment decisions. Especially in frail older men with prostate cancer, treatment should be planned to relieve symptoms and maintain the quality of life rather than radical cure. Medications that are used to treat urologic conditions such as in-

continence, erectile dysfunction and BPH might interfere with cardiac function and balance; therefore, they should be titrated appropriately.

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