

Review of the European Association of Urology and American Urological Association Diagnostic and Treatment Guidelines for Male Lower Urinary Tract Symptoms

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ABSTRACT

Objective: We reviewed the diagnostic and treatment guidelines for male lower urinary tract symptoms (LUTS) produced by the European Association of Urology (EAU) and American Urological Association (AUA). The purpose of this review was to create a consensus for the construction of treatment guidelines for Taiwanese male LUTS patients. **Materials and Methods:** We searched the Medline database based on three key words, guidelines, LUTS and male. Combined searching was conducted, and finally the male category was used as the limiting one for our purposes. **Results:** A total of 78002 guidelines and 649 articles on the topic of LUTS were collected. Eventually, only 23 articles were retrieved focusing on the issue of male LUTS. **Conclusions:** There was little information in the way of diagnostic and treatment guidelines for male LUTS available. In actuality, there were no specific treatment guidelines for male LUTS except for one report from the British Association of Urological Surgeons, Oxford and London, UK. This was a guideline specific for general practitioners. This mini review focuses on the guidelines available for male LUTS suggestive of benign prostate hyperplasia (BPH) and carries out a comparison of EAU and AUA guidelines in addition to other literature available from Medline.

Key words: guideline, LUTS, BPH, male

INTRODUCTION

The American Urological Association (AUA) has developed evidence-based guidelines since 1989 and acknowledges their importance. As a result, there has been a reinvigoration of these guidelines and this has resulted in an expansion and enhancement of the AUA Clinical Guidelines Program. One question that is important is how one develops a set of treatment guidelines with scientific rigor and integrity. A multidisciplinary expert panel should be involved in the development of the guidelines. Development involves an extensive review of the literature, as well as peer review and a Board approval process. Recommendations should be analyzed in a consensus-based manner that depends on the panel process and the available data. However, in Taiwan, we lack a set of up-to-date scientific and consensus-based diagnostic and treatment guidelines for male LUTS/BPH.

Therefore, the treatment guidelines committee of the Taiwanese Continence Society intends to carry out the task of creating these over the next three years. The first year of the process is 2007 and the process of producing the guidelines has started. In the near future, there will be five scientific symposiums focusing on the issues surrounding male LUTS/BPH. A set of guidelines has many advantages and these include use by urologists, clinicians, general practitioners and patients. They also establish the scope of medical practice, help with reimbursement including pay for performance initiatives and are very useful in the medico-legal field. Guidelines are thus able to promote the highest standards of medical care for patients.

THE IMPORTANCE OF DIAGNOSTIC AND TREATMENT GUIDELINES

A 50 years old lady is a clerk in a bank. She suffered from a day time urination frequency of more than 10 times, urgency and nocturia (2 times per night). She also has to wear an incontinence pad due to fear of urine leakage. There is no leakage during coughing and sneezing. The neurological, abdominal and pelvic examination results are normal. The urinalysis is normal also. What is the diagnosis priority? The possible diagnoses include an overactive bladder, interstitial cystitis and urinary tract infection. In contrast, a 50 years old man is also a manager in a bank and suffers from exactly the same symptoms as the lady. He also has no significant medical history associated with his complaints. The urinalysis, physical and neurological examination results are also normal. The prostate-specific antigen (PSA) is 2 ng/mL. What are the possible diagnoses? The diagnosis priority for male LUTS is suggestive of BPH, an overactive bladder or prostate cancer. The patients with the same clinical symptoms have totally different clinical diagnosis priorities. Based on these scenarios, it is clear that a set of diagnostic guidelines is very important. According to the definition of overactive bladder (OAB) at the 2002 International Continence Society (ICS), this involves urgency with or without urge incontinence and is usually associated with frequency and nocturia. The lady had the correct symptoms for a diagnosis of OAB. However, lower urinary tract symptoms may cover more complicated presentations. Basically, a voiding dysfunction can be classified into three major categories including neurogenic bladder, interstitial cystitis and overactive bladder. While we should take the prostate into consideration, many conditions will be more bizarre. Therefore, benign prostate enlargement (BPE) or benign prostate obstruction (BPO) secondary to BPH, are diagnosed clinically on the basis of lower urinary tract symptoms. We will use the abbreviation LUTS/BPH for LUTS presumed to be secondary to BPH,

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which sometimes is called symptomatic BPH. It is not easy for us to separate LUTS and OAB. LUTS is a constellation of storage symptoms (frequency, urgency, nocturia, urge incontinence) and voiding symptoms (hesitancy, poor flow, terminal dribbling, abdominal straining and intermittency) in addition to the post micturition symptoms such as a sensation of incompletely emptying. The symptoms of OAB are mainly confined to the storage symptoms category [1]. If we look at the different conditions associated with OAB and LUTS, we will see they are totally different problems. LUTS/BPH is usually associated with hypertension, while OAB is associated with irritable bowel syndrome, smoking, high caffeine intake, depression/anxiety and attention deficit hyperactivity disorder [2]. Furthermore, LUTS/BPH is caused by a bladder outlet obstruction induced detrusor response [3], while OAB is usually associated with urothelium and neuronal growth factor (NGF) [2]. The former can be proved by showing increased bladder weight and a thickened bladder wall after bladder outlet obstruction [4]. Since differentiation between OAB and LUTS/BPH is very important and will change the treatment strategy, we need to pay significant attention to the diagnostic and treatment guidelines for these disorders.

THE ADVANTAGES OF GUIDELINES AND THE REALITY

From the EPIC study, we can see an overall prevalence of male LUTS over 18 years old of about 61.3%. Storage symptoms involve 49.7% of patients, voiding symptoms involve 25.7% of patients and post micturition symptoms involve 16.5% of patients [5]. The most bothersome problem is storage symptoms, just like OAB. However, LUTS may have the simultaneous problems of bladder outlet obstruction and detrusor overactivity or OAB [6]. Diagnostic and treatment guidelines do have a positive impact on physicians and patients. A randomized controlled trial on the effect of a distance learning program on patient self-management of lower urinary tract symptoms in general practice (GP) revealed that the treatment guidelines seem to help the GP to treat complaints and decrease the symptoms. This can involve telling the patient what he intends to do, explaining the treatment in a clear way, and involving the patient in thinking about the complaint [7]. Furthermore, the patient enablement score filled in directly after a guideline consultation revealed that the patients were able to maintain their independence, cope with their illness better, help themselves with the disease and were more confident about their health [7]. We all know that guidelines may produce a lot of benefits. Unfortunately, many specialists including urologists do not use the guidelines in reality. A survey on complementary investigation request modalities among French urologists showed that almost 60% of urologists gave a prescription on the first visit. However, only 23.3% of urologists kept a record of the patient's international prostate symptom score (IPSS); 65% of urologists ordered uroflowmetry and 89.9% carried out a bladder scan for post voiding residual [8]. Another study involved the diagnostic procedures for Italian GPs in response to male LUTS. Prospectively, it was revealed that less than one third of GPs did a digital rectal examination [9]. These facts tell us that, although diagnostic and treatment guidelines are important, the adherence of the physician and the patient to the guidelines is even more important. A well accepted and easy to use set of guidelines is the most valuable.

WHAT KIND OF DIAGNOSTIC AND TREATMENT GUIDELINES DO WE NEED?

In fact, the treatment of LUTS/BPH has changed. In the past, we focused on etiologies and thus treatment was also dependent on these issues. Therefore, an operation to reduce the obstruction and to increase uroflow rate was carried out. Nowadays, we are outcome oriented. We are concerned about a satisfactory quality of life. Medical treatment is usually carried out prior to surgery. In the short term, we need to relieve LUTS faster and to prevent long term complications [10]. The ideal guidelines should be based on a strategic approach when confronting a patient with LUTS/BPH. Basically, five steps need to be carried out when facing a LUTS/BPH patient [11]. The first step is to identify the cause of LUTS, the second is to assess the risk factors related to progression, the third is to identify the high and low risk patients and the fourth is to protect bladder and reduce or delay progression with minimal morbidity in addition to providing faster and sustained symptom relief as well as an improved quality of life. The last step is to reassess which treatment options may achieve our goals. Therefore, an excellent set of diagnostic and treatment guidelines should be very clear and enable coverage of these five issues. This leads us to the reality of the guidelines available in the literature. We believe that there are still some problems that need to be solved if we are to create a guideline suitable for Taiwanese physicians and patients. In terms of the relationship between patients and physicians in Taiwan, it is not clear whether we should make the diagnostic and treatment guidelines available to patients and what effect such provision would have in terms of a positive influence on the relationship between patient and doctor? We recommend offering patients a concise format version of the guideline. This ought to promote a level practice standard among physicians as well as providing patients with the right to know their problem and will clearly outline where the next step is likely to go.

THE VALIDITY OF GUIDELINE FOR LUTS/BPH

In 1995, the National Health and Medical Research Council (NHMRC) of Australia announced its commitment to developing evidence-based clinical practice guidelines "to promote best practice linked to outcomes and effective cost management". The first clinical practice guidelines for the management of men with lower urinary tract symptoms (LUTS) were launched in 1997 and published in 2000 [12]. The only known set of diagnosis and treatment guidelines for LUTS was created for GP referral by the British Association of Urological Surgeons (BAUS) from Oxford and London, UK. They committed themselves to this set of guidelines because LUTS attributed to benign prostatic obstruction (BPO) is a very common problem affecting older men in United Kingdom. The prevalence of LUTS in Europe varies with age and ranges from 14% for men in their fourth decade to >40% in their sixth decade. Assuming an overall prevalence of LUTS of 30%, this would mean that 4 million men aged > 40 years have LUTS in the UK [13]. Nocturia and the assessment of risk factors are important items in the BAUS's diagnostic algorithm. In actuality, there are more than six common diagnostic and treatment guidelines for LUTS/BPH. A comparison between these guidelines was carried out by Novara et al [14]. In addition to history taking, physical examination, digital rectal examination and urinalysis, a symptom score is recommended by all guidelines. Uroflowmetry, post voiding residual (PVR), prostate specific antigen (PSA) and serum creatinine are recommended by the EAU

guideline only [15]. These tests are regarded as the optional choices by the rest of guidelines. However, serum creatinine was not recommended in the latest AUA guideline. The measurement of serum PSA was suggested for patients with at least 10 years life expectancy and for whom knowledge of the prostate cancer would change management or where PSA measurement may change the management of their voiding symptoms [16]. A pressure-flow study, cysto-urethroscopy, prostate ultrasound and upper urinary tract imaging are not recommended or just regarded as an option by almost all the guidelines. Therefore, the fully recommended or mandatory procedures include between three and seven items. However, this leaves open the question as to whether more tests have increased value when assessing patients with LUTS/BPH. An analysis according to the validity, reproducibility, cost-efficacy, being representative, multi-disciplinarity, clinical applicability, flexibility, clearness, reviewability and amenability to clinical audit of the tests revealed that the overall scores for the AUA and EAU guidelines were 72 versus 56 respectively. However, the highest score is the Australian NHMRC diagnostic and treatment guideline with a score of 86. The recommended routine tests are 3, 7 and 3 items, respectively, for these guidelines. It is not clear what this means but the guidelines do need to be concise and easy to carry out. The greater is the number of recommended routine tests, the harder it will be for physicians and patients to follow the guidelines.

THE DIFFERENT MANagements OF LUTS/BPH UNDER THE EAU AND AUA GUIDELINES

According to these two treatment guidelines, the medical treatment of LUTS/BPH may be classified into dynamic and static portions. Four alpha1-adrenoceptor antagonists including Alfuzosin, Doxazosin, Tamsulosin and Terazosin are recommended for dynamic problems. They have almost equal clinical benefits, although there are trivial differences, especially the adverse effects. However, Prazosin and non-selective α -blockers such as Phenoxybenzamine do have no sufficient supportive evidence to be recommended for patients. This is important for us since health reimbursement is limited in Taiwan and this may induce some physicians to choose an older and cheaper drug. The 5- α reductase inhibitors including Finasteride (type-2) and Dutasteride (type I and II) show basically the same effectiveness on static prostate problems. In addition, 5- α reductase inhibitors are beneficial for hematuria associated with the BPH, but their long term effects on the sexual functioning means they should be used with caution. Based on the serial results from the MTOPS research group, it is clear that a combination therapy of 5- α reductase inhibitors and α -blockers give a better response in terms of IPSS, uroflow rate, reduced acute urine retention and surgery than any single use [17]. However, the effectiveness and safety of simultaneous therapy with anti-muscarinics in addition to the treatment with 5- α reductase inhibitors and/or α -blockers is not discussed by either the EAU or AUA guidelines.

In the AUA treatment guidelines, the uroflow and PVR tests are options for patients with IPPP \geq 8. The AUA guideline was first proposed in 2003, however, treatment combined with anti-muscarinics for LUTS with BPH and/or OAB was still not discussed in 2006 update. Neither is there a discussion in the EAU guidelines. Currently, the use of anti-cholinergic agents as the primary therapy for BPH/LUTS or in combination with blockers cannot be recommended for routine use in the absence of an adequate published evidence base; this is the

review's opinion in 2004 [18]. A Korean study revealed that combination therapy consisting of an alpha1-adrenoceptor antagonist with anti-muscarinics represents an effective and relatively safe treatment modality for selected patients with OAB coexisting with benign prostate obstruction [19]. A randomized controlled trial using Tolterodine and Tamsulosin as treatment of men with lower urinary tract symptoms and an overactive bladder was reported in JAMA 2006 [20]. These results suggest that treatment with Tolterodine ER plus Tamsulosin for 12 weeks provides benefit for men with moderate to severe lower urinary tract symptoms including OAB and BPH. In addition, the incidence of acute urinary retention requiring catheterization was low (Tolterodine ER plus Tamsulosin, 0.4%; Tolterodine ER, 0.5%; Tamsulosin, 0%; and placebo, 0%). Treatment with Detrusitol together with Doxazosin in an α -blocker failed study revealed that the antimuscarinics are able to provide further improvement from 37.5% to 73% in patients with BOO vs BOO with detrusor overactivity when the patient failed a three month α -blocker treatment [21]. The result of antimuscarinics in addition to α -blockers shows that an accurate diagnosis and combined treatment may be safe and effective. The question is how to make an accurate diagnosis between LUTS/BPH and LUTS/OAB. From the literature, we know that an urodynamic study is not necessary for the diagnosis of OAB. One possibility is a simple uroflow and PVR study to distinguish between these two entities. If this helps to differentiate between them, the EAU guidelines are probably the more valuable set for us to use at present.

Phytotherapy is an emerging therapy in the AUA treatment guidelines. However, it has been popular in treating LUTS/BPH in Europe for many years. These agents are composed of various plant extracts and, therefore, it is always difficult to identify the major biological activity of the treatment. Some randomized trials and meta-analyses have shown clinical efficacy without major side effects for compounds such as *Pygeum africanum* and *Serenoa repens*, and these treatments seem to be equivalent to Finasteride and α -blockers [15]. The composition, extraction and mechanism of action of these phytotherapeutic agents still remain an unknown factor.

The use of different minimal invasive treatments basically shows no major differences. Prostatron[®], transurethral needle ablation (TUNA), UroLume endoprosthesis stent and water induced thermotherapy including transurethral microwave therapy (TUMT) are the possible choices. However, prostate ethanol injection and high-intensity focused ultrasound (HIFU) are now not recommended in the AUA guidelines [16].

The transurethral resection/incision of prostate (TUR-P/TUIP) is still the operation of choice for BPH. Four type of laser treatment are mentioned in the EAU guidelines including Nd:YAG, Hol:YAG, KTP:YAG and diode laser [15]. Visual laser ablation of the prostate (VLAP) and interstitial laser coagulation (ILC) use the Nd:YAG laser. The indication for laser prostatectomy is that the patient is receiving anticoagulant medication or the patient is unfit for TURP and wants to maintain ejaculation (side-fire or ILC). The green light KTP laser is now gradually becoming more popular, but it is too early to reach any conclusion about its efficacy.

CONCLUSION

In Taiwan, we do not have a set of diagnostic and treatment guidelines for male LUTS/BPH as yet. At present, the PRC including Hong Kong are trying to construct a set of guidelines for BPH in the greater

China area, which they propose includes Taiwan. Thus it is important that we fulfill our obligations and commitments and create our own diagnostic and treatment guidelines for LUTS/BPH.

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