



Evidence-based guidelines in lower urinary tract symptoms secondary to benign prostatic hyperplasia and variation in care

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Purpose of review

Guidelines have been developed to assist physicians in the diagnosis and management of patients with lower urinary tract symptoms. These guidelines vary in the level of evidence used and the strength of their recommendations. With variations in guidelines, multiple variations in clinical practice may also be seen.

Recent findings

Although examinations of physician compliance with benign prostatic hyperplasia (BPH) guidelines date back to the 1980s, researchers have become more interested in closer examination of guideline compliance. Furthermore, guidelines themselves are becoming more robust documents, with the American Urological Association and European Association of Urology guidelines updated in 2014 and 2015, respectively. This review examines both the evidence base behind these BPH guidelines and the variations in clinical care related to the guidelines.

Summary

Despite over 40 years of study, variations continue to occur in the work up and treatment of men with BPH. With the proliferation of medications and surgical procedures available for symptomatic lower urinary tract symptoms (LUTS) due to BPH, we will continue to see this variation in care. Our current guidelines can help mitigate this variation by providing a baseline set of assessments and algorithms for routine patients. However, only through continued refinement will the guidelines meet their full potential. The prior review shows how the evidence base is limited for the diagnostic work up for LUTS, provides limited information on comparative effectiveness of therapies in LUTS and BPH, and has not led to consistency between guidelines.

Keywords

benign prostatic hyperplasia, medical treatment, quality assessment, surgery

INTRODUCTION

Guidelines have been developed to assist physicians in the diagnosis and management of patients with lower urinary tract symptoms. These guidelines vary in the level of evidence used and the strength of their recommendations. The guidelines also change over time. Sometimes, these changes reflect new medical knowledge and breakthroughs, whereas other changes result from poor evidence base and differences of opinion among guideline members. In this review, we compare the evidence base of current and past guidelines on lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH), and examine the variations in BPH care related to these guidelines.

CURRENT GUIDELINES

American Urological Association

The American Urological Association (AUA) guidelines on BPH were revised in 2010 [1]. The content was reapproved in 2014, and a new revision is in progress at the time of this review. The 2010 update made extensive updates to the 2003 diagnostic section [2]. The panel used a 2009 article by Abrams

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KEY POINTS

- The two main BPH guidelines have significant difference in methodology, emphasis and scope.
- Justification for most BPH practice styles can be found within the guidelines.
- The evidence base for the guidelines does not lead to consolidation of practice to a single best practice.
- Variations in care can be seen even within group practices.

et al. [3] as the basis for its diagnostic recommendations. Although the 2003 guidelines separated care in recommend, not recommend and optional, the 2010 guidelines followed a simpler metric. There were standards, recommendations and options. A guideline statement was considered a standard when,

'(1) the health outcomes of the alternative interventions are sufficiently well known to permit meaningful decisions and (2) there is virtual unanimity about which intervention is preferred.'

The recommendation level applied when,

'(1) the health outcomes of the alternative intervention are sufficiently well known to permit meaningful decisions, and (2) an appreciable but not unanimous majority agrees on which intervention is preferred.'

The guidelines panel considered care at the option level when,

'(1) the health outcomes of the interventions are not sufficiently well known to permit meaningful decisions, or (2) preferences are unknown or equivocal. Options can exist because of insufficient evidence or because patient preferences are divided and may/should influence choices made.'

Almost all care in the guidelines fell into the option category for the purposes of the AUA guidelines. Exceptions included the use of validated questionnaires and frequency volume charts, considered recommendations in Figure 1.2 of the guidelines. A further recommendation from the figure on detailed management of LUTS was to check the flow rate prior to surgical or minimally invasive surgical therapy. If the flow rate was more than 10 ml/s, then pressure flow studies should be performed. Similarly, prostate specific antigen (PSA) testing and post

void residual (PVR) urine measurement tests were not explicitly endorsed in the guidelines. However, both tests were used in Figure 1.2 to help guide therapy choices. Other aspects of management that rose to the level of recommendations included checking a frequency volume chart for at least 2 days in patients with nocturia, treating nocturia first with fluid restriction and following patients for symptomatic improvement after starting pharmacologic intervention (specifically 2–4 weeks for α blocker therapy and 3 months for 5-alpha reductase inhibitor (5-ARIs)).

When considering treatments of LUTS, the guidelines have two standards: benefits and harms of therapy should be explained to patients and patients with mild LUTS or moderate or severe LUTS who are not bothered should be offered watchful waiting. The guidelines use the American Urological Association Symptom Index (AUA-SI) to define the severity of the LUTS. Other treatment choices fell into the option category, with exceptions for recommendations related to specific instances. A recommendation to avoid the use of pazosin and phenoxybenzamine was continued from the 2003 guidelines. α Blocker use should be avoided in men who have planned cataract surgery. However, the presence of a cataract is not a contraindication to starting α blocker medication. 5-ARI use should be limited to men who have prostatic enlargement. Finally, no complementary or alternative medications, including saw palmetto and *Urtica dioica*, have evidence to support their use. All of the recommendations were based on panel consensus, and levels of evidence were not provided.

Overall, the current AUA guidelines provide a framework for the evaluation and treatment of LUTS. Using the figures, primary care doctors or urologists can evaluate and treat most men with BPH. Following these algorithms would allow for standardization of care. However, few of the guideline statements rise to the level of standards, and there are no guidelines on best approaches to medical or surgical therapy. The current medical evidence does not support statements that can reach the level of standards.

European Association for Urology

The European Association of Urology (EAU) guidelines from 2015 approach the recommendations provided differently from the 2014 AUA guidelines. The EAU guidelines state the level of evidence and grade for each of the statements in the guideline. These guidelines do not explicitly make statements regarding if tests, medications or procedures should be used. The level of evidence and grade for each

statement can be used to infer the strength of the recommendation.

There were very few instances where the guidelines provided for the diagnostic evaluation of LUTS are informed by randomized trial evidence. Only the recommendation regarding using PSA where the diagnosis of prostate cancer impacts care or the PSA can assist in the determination of risk of progression of BPE received a level of evidence of 1b [4–8]. Otherwise, the list of diagnostic procedures is supported by limited evidence, but all are listed as options for care.

In regards to disease management, there is a stronger set of evidence. Per the guidelines, behavioral and dietary interventions have randomized data to support their use [9]. Furthermore, the guidelines reference 16 randomized controlled studies supporting the use of α blockers in the treatment of LUTS. Similarly, the guidelines reference 10 studies supporting the use of 5- α reductase inhibitors in the treatment of moderate-to-severe LUTS. Use of antimuscarinic medications is supported in the guidelines by seven randomized studies. Phosphodiesterase type 5 inhibitors can also reduce symptomatic LUTS, and the guidelines reference 8 randomized trials and one meta-analysis for this recommendation. Vasopressin for the specific indication of nocturia due to nocturnal polyuria was supported by 12 randomized studies. β -3 agonist therapy was supported by four randomized studies. Combination of α blocker and 5ARI was supported by six randomized studies. Combination of α blockers with antimuscarinic therapy was supported by nine clinical trials.

The guidelines also have excellent support for surgical intervention in LUTS. Eight studies support monopolar or bipolar transurethral resection of the prostate (TURP) in the treatment of LUTS using short-term follow up (up to 12 months). Six studies support TURP with follow up beyond 12 months.

The EAU guidelines also provide a template for the work up and treatment of men with LUTS. Again, the evidence base for diagnostic and evaluative testing is weak. Although there is robust evidence for surgical and medical management of LUTS, there is limited comparative effectiveness literature to help guide therapeutic choices.

DIFFERENCES BETWEEN THE GUIDELINES

The major difference between the guidelines comes in the use of diagnostic testing for the work up of LUTS. Comparing the diagnostic testing algorithm in the EAU guideline to diagnostic testing algorithm in the AUA guideline, more testing is explicitly recommended in the EAU guidelines. For example,

measurement of PVR is recommended, with a follow up renal bladder ultrasound for men with an elevated PVR. If a man has bothersome symptoms, ultrasound of the prostate is recommended in the EAU algorithm, but not mentioned in the AUA algorithm. Overall, the EAU guidelines provide recommendations for a higher volume of diagnostic evaluation testing for men with LUTS while acknowledging a low evidence base for this testing. Differences in the methodology of the guidelines may contribute to differences in the uptake of the guidelines [10].

VARIATIONS IN CARE

Variations in care occur between urologists and primary care doctors in the diagnosis and treatment of men with LUTS. These variations also occur among urologists. Given the gaps in the evidence base outlined in our review of the AUA and EAU guidelines, it is not surprising that individual providers have differing practice styles in their care of men with LUTS. However, these differences in care can be associated with measurable consequences in outcomes of men with LUTS.

Primary care versus urology management

Urologists have a more intensive approach to LUTS evaluation and management compared to primary care doctors. From a review of claims from a Michigan HMO, Hollingsworth *et al.* [11] found that most patients with LUTS (more than two thirds) received initial care from a primary care doctor. Urinalysis and transrectal ultrasound were performed more frequently by urologists during the initial patient work up. In an analysis from a large observational, longitudinal cohort of patients, Wei *et al.* [12] found that urologists performed urinalysis, PSA, postvoid residual urine measurement, uroflowmetry, prostate ultrasound, biopsy, renal ultrasound and cystoscopy significantly more often than primary care doctors. Similar to Hollingsworth study, urologists were more likely to prescribe medical therapy for LUTS. In an analysis based on Medicare data, Rensing *et al.* [13] found that nearly 75% of men who were started on LUTS-related medications were under the care of a primary care physician. Although the most common change in medical therapy among all men was discontinuation of medications, men who started care with a primary care doctor were more likely to discontinue care compared to men who started care with a urologist.

The differences in management between primary care providers and urologists have impacts in both costs of care and outcomes for treatment.

In data presented at the AUA meeting in 2016, men with initial medical treatment by urologists had 40% higher expenditures on medication, 5.1% higher expenditures on surgery and 178% higher expenditures on evaluative work up compared to men initially treated by primary care doctors [14]. The overall premium for men who saw a urologist for first-line therapy was 10.1% in direct medical expenditures and 10.6% for nonpatient expenditures at 1 year. However, the long-term impact of this care is unknown as urologists were more likely to use 5-ARIs, in isolation and combination therapy, which are associated with decreased progression of BPH and long-term surgical interventions.

Variations among urologists

Individual practice styles exist in all types of medical care, with BPH care being no exception. BPH surgery was one of the initial procedures investigated when variations among surgical procedure rates were first reported [15]. Rates of TURP varied considerably from community to community, reflecting differences of opinions on indications for surgical intervention [16]. Early epidemiological studies showed declining rates of TURP over time [17]. Further work on these variations in care found poor adherence to joint AUA and Healthcare Cost and Utilization Project guidelines for BPH care [18]. Interestingly, the guidelines at that time recommended documentation of a Digital Rectal Exam, creatinine level and urinalysis prior to surgery. These were documented in only 26% of cases. Altogether, by the late 1990s, BPH care had been shown to be variable based on the urologist seen, changing because of unclear reasons and not consistent with the established guidelines.

This variability in care was further explored through the Urologic Diseases in America Project. This National Institute of Diabetes and Digestive and Kidney Diseases-funded initiative, based at University of California Los Angeles and the RAND corporation, examined the epidemiology of benign urologic disease. The initial compendium expanded earlier studies to show the scope of urologic problems, both financially and for patient morbidity. As the project continued, additional work sought to explore the quality and outcomes of care. One study showed a decreasing use of upper tract imaging for BPH patients [19]. A subsequent BPH study from this collaborative examined the practice styles of urologists in the initial evaluation of men with BPH [20]. This work was based on a 5% sample of Medicare patients from 1999 through 2007. The median urologist per-patient expenditure on diagnostic evaluations was \$92 per month, with a range from \$35 to \$527 per month. Both patient and provider factors

explained the variation in expenditure, and the practice style differences were related to care the guidelines (2003 AUA guidelines) considered optional or not-recommended testing. Finally, having lower expenditures was also associated with lower guideline compliance, suggesting that the lower intensity of practice style was providing less diagnostic testing overall and not necessarily better care.

The companion piece to this report examined how urologists varied in their compliance with the guidelines. Over 748 urologists were included based on Medicare claims from 1999 to 2007 [21]. A measure of compliance with guidelines was created based on concordance with the urologist's average use of tests considered recommended, optional and not recommended in the 2003 AUA guidelines. With a range of -1 (no compliance) to +1 (complete compliance), actual levels of urologist compliance varied from -0.53 to 0.91. Only certain types of care varied between guideline concordant and nonconcordant urologists. The differing levels of compliance reflected use of PSA testing and urinalysis (recommended), uroflow and PVR urine checks (optional) and cystoscopy and ultrasound studies (not recommended).

A final article from this collaborative examined how the intensity and quality of the evaluative care work up for BPH influenced subsequent surgical therapy [22]. The overall surgery rate within 1 year of an initial visit to a urologist for BPH was 6.7%. However, this varied by guideline compliance (10.9% surgery in lowest compliance urologists to 2.4% for highest compliance urologists). After controlling for patient and physician factors, there was a 91% decrease in the adjusted odds of receiving surgery for high guideline compliance surgeons (odds ratio 0.09; 95% confidence interval 0.05, 0.15). Overall, these results suggested that discretionary use of diagnostic testing was related to use of surgical procedures.

Subsequent to the Urologic Diseases in America studies, groups have examined individual provider adherence to AUA guidelines. Using review of an electronic medical record (EMR), a group from Northwestern University found that baseline adherence rates for the nine recommended measures in the 2003 guidelines ranged from 53 to 92.8% [23]. Optional care, PVR and uroflow were performed in 68.1 and 4.6% of new visits. Of the five not recommended care procedures, the greatest use was 10.2% of encounters. Overall, baseline adherence to AUA guidelines could be assessed through EMR extraction.

A similar review of individual practice was performed in unpublished data from Washington

University in Saint Louis. Using the 2010 revision of the AUA guidelines as the reference, our group examined the individual compliance of eight surgeons with the updated guidelines. Documented AUA-SI scores were found in 62–100% of the urologists' patients charts prior to surgery. The 2010 guidelines recommended a urinary flow rate study prior to surgical intervention. We found this study documented in 3.7–89.7% of patients charts in the preoperative period. Finally, pressure-flow urodynamics are an option, and encouraged in the guidelines when the urine flow rate is greater than 10 ml/s. Individual surgeons in the series used this intervention inconsistently, ranging from 7.4 to 93.1% of patients prior to surgical intervention for LUTS due to BPH. We then assessed the impact of these and other factors on success of surgery in data presented at the AUA meeting in 2017 [24]. We examined two outcomes: achieving an AUA-SI of less than 8 or no use of BPH-related medications at 4 months after surgery. In multivariable logistic regression for each outcome, the individual surgeon was the significant factor in successful outcome from surgery. For diagnostic testing, only performance of PVR urine had an independent impact on the success of surgery achieving an AUA-SI less than 8 by 4 months after surgery. These results suggest the diagnostic work up plays a limited role in success of BPH-related surgery.

CONCLUSION

Despite over 40 years of study, variations continue to occur in the work up and treatment of men with BPH. With the proliferation of medications and surgical procedures available for symptomatic LUTS due to BPH, we will continue to see this variation in care. Our current guidelines can help mitigate this variation by providing a baseline set of assessments and algorithms for routine patients. However, only through continued refinement will the guidelines meet their full potential. The prior review shows how the evidence base is limited for the diagnostic work up for LUTS, provides limited information on comparative effectiveness of therapies in LUTS and BPH and has not led to consistency between guidelines. These limitations lead to an array of choices in care, with justification for multiple practice styles from high-intensity to low-intensity care. These variations in practice can occur even within group practices, with significant impacts on patient outcomes.

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Conflicts of interest

There are no conflicts of interest.

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