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BPH and Enlarged Prostate Progression: What the Primary Care Physician Needs to Know

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In the strictest sense, benign prostatic hyperplasia (BPH) refers to a growth or hyperplasia of the periurethral glands in the prostate that occurs with increasing frequency with advancing age, starting approximately at the age of 40 years. The prevalence of this condition is extraordinary: it is estimated that 50% of men in their 50s and up to 80% or more of men in their 80s will be found to have this condition when examined with appropriate diagnostic tests. Although commonly used as a clinical term, BPH is not in itself a disease requiring treatment. However, it is the

most common cause for lower urinary tract symptoms (LUTS) in men.

LUTS are divided into irritative or storage vs obstructive or voiding symptoms. Examples of irritative symptoms are urgency of urination, frequency, urge incontinence, frequent nighttime urination, or nocturia. Examples of obstructive voiding symptoms are hesitancy, intermittency, slowing of the stream, and incomplete emptying. The symptoms listed as irritative are often called "overactive bladder" (OAB) in women but in men are called irritative voiding symptoms or part of LUTS. Newer terms such as male LUTS or OAB in men have recently been discussed, and it is likely that these new terms will be followed by renewed thinking regarding therapeutic interventions.

Another important condition to consider is benign prostatic enlargement (BPE), or enlarging prostate (EP), terms that can be used synonymously. These terms are used when there is measurable or noticeable enlargement of the prostate, and although a precise cutoff for what constitutes a significant enlargement has not been defined, the enlarged prostate is usually associated with prostate volume >30 mL or a serum prostate specific antigen (PSA) >1.4 ng/mL. This can also be verified by a digital rectal examination (DRE) when one cannot palpate the posterior lobe of the prostate. Not all men with BPH will develop BPE/EP, and not all men with BPE/EP will develop significant or bothersome LUTS symptoms (Figure 1). Finally, it is important to understand the term *benign prostatic obstruction* (BPO), which is

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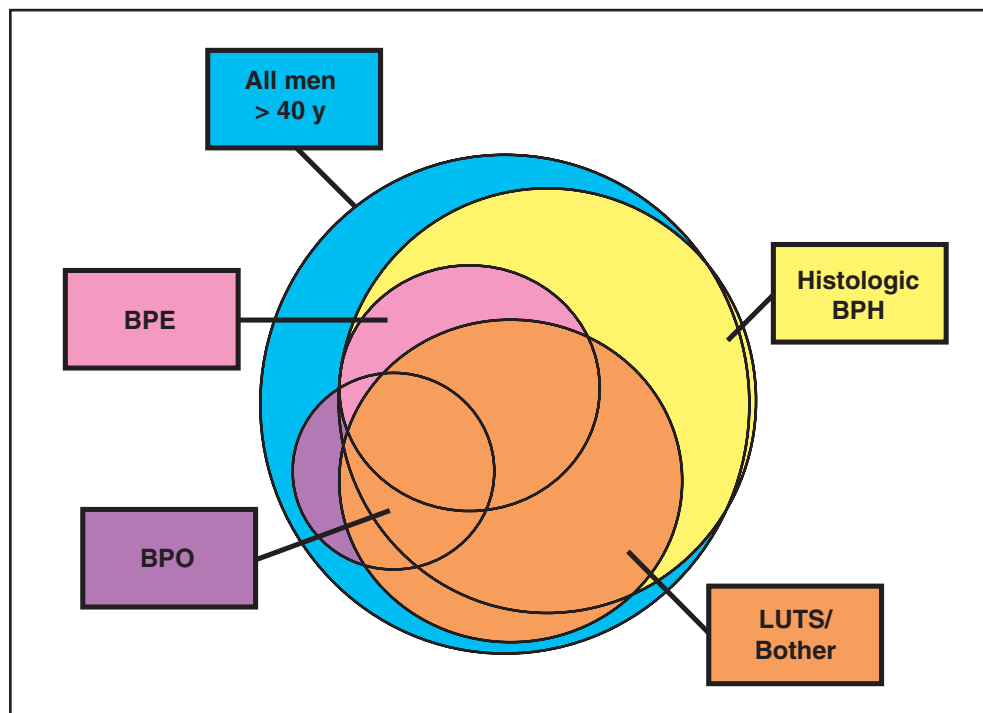


Figure 1: Venn diagram showing the partially overlapping patient populations of men with histologic BPH, lower urinary tract symptoms (LUTS), benign prostatic enlargement (BPE), and benign prostatic obstruction (BPO) (after Roehrborn, personal communication).

used when subvesical obstruction to the urinary flow has either been proven by invasive pressure-flow studies or is highly suspect from urinary flow rate recordings. As Figure 1 demonstrates, BPO is not a necessary consequence of BPE/EP, and there are causes other than BPH or BPE for BPO such as primary bladder neck sclerosis, prostate cancer, urethral stricture disease, or meatal stenosis.

Equally important as defining the condition is defining the progression. In the medical literature specifically relating to BPH and LUTS, *progression* and *outcomes* are often used synonymously. Strictly speaking, progression is a transition within the same state of health toward worsening or increase in severity. For example, a patient who scores 12 points on a quantitative symptom severity score but during follow-up scores 17 points can be said to have progressed along the continuum of the symptom score. On the other hand, an outcome is defined as a transition from one state of health to another. An example would be a patient who can urinate normally, but after an inguinal hernia repair, develops acute urinary retention (ie, the inability to void at all). This patient has transitioned from the health state of normal urination to the disease state of urinary retention. Progression and outcomes are used synonymously although methodologically, it is important to distinguish between these two states of disease worsening.

The concept and prevention of progression/outcomes represent new thought in the management of patients with BPH/BPE/BPO. While they have become more familiar to urologists, there is still a significant knowledge gap between urologists and primary care providers and patients. A recent survey suggested that most urologists are aware of the effect of various medical interventions on the treatment of symptoms vs the prevention of progression. In the same survey, however, primary care providers were much less able to distinguish what medical interventions have an effect only on symptoms vs an effect on progression.¹ The overwhelming majority of patients queried in a similar survey said that they were very concerned about long-term outcomes of BPH and LUTS, even more so than about acute symptom relief. Nearly three out of four queried men were willing to take at least one tablet daily to reduce the long-term risk of surgery for this condition.

A survey conducted among 472 European urologists revealed that from a urologist's viewpoint, symptom relief was the most important consideration in treating men with LUTS/BPH/BPE/BPO, with prevention of long-term complications being rated somewhat lower. When the same urologists were asked what they thought was significantly related to the likelihood of progression, the two parameters that have been found to be predictive in

controlled, randomized clinical trials, (ie, an increase in prostate volume and an elevation in serum PSA levels) were given importance ratings of only 5.5 and 3.5. An increase in age was rated even lower in importance despite the fact that the Olmsted County Study of Urinary Symptoms in Men documented that progression of BPH is strongly related to age.²

These observations suggest the critical need for broader education of specialists, primary care physicians, and any other health-care providers caring for men with LUTS/BPH/BPE/BPO, as well as the need to educate patients about the condition itself as well as disease progression and its prevention.

Looking for Evidence for Progression

A multitude of methods exists for finding evidence for progression and outcomes. Each of them has distinct advantages and disadvantages.

Population-based longitudinal studies have no defined selection criteria and are an excellent method for study of the natural history of the condition. They have few biases except for the Hawthorne effect, by which a population may behave differently when observed compared to when it is not observed.

Registries and other databases apply only limited selection criteria and permit the study of natural history as well as of the effect of an intervention on a disease and its natural history. They also have relatively few biases, except for the Hawthorne effect.

Clinical practice studies apply selection criteria because the study necessarily takes place in a physician's or health-care provider's office. Therefore, the clinician's ability to study the natural history is somewhat reduced and biases are more common.

By far the most significant biases are associated with the gold standard—a placebo-controlled clinical trial. All such trials apply strong selection criteria to the study population and limit the ability to use the placebo arm of the trial to study the natural history of the disease. Nonetheless, placebo-controlled, randomized trials are our best tools to study the effect of an intervention, although the choice of patients and the selection criteria applied diminish the generalizability of the data.

Outcome Measures in BPH/LUTS/BPE/BPO

Equally as important as the definition of terms is a review of the outcome measures used to describe BPH/LUTS/BPE/BPO.

BPH (histologic hyperplasia) has no outcome measure for determining progression. The disease is either present or absent, and a biopsy is usually required to verify its presence. Outcome measures and evidence of progression are therefore absent and generally not verifiable.

Progression of LUTS, however, is perhaps the most common and most important outcome measure used when evaluating and treating men presenting with suspected BPH. Several validated symptom score questionnaires are available that assess symptom frequency as well as severity, and in addition assess the bother the symptoms cause as well as the interference with daily activities and the impact on quality of life. The best-known example is the International Prostate Symptom Score (IPSS), a self-administered, seven-item questionnaire that lists the seven most common irritative and obstructive voiding symptoms. Patients are asked about the frequency of these symptoms during the last month, and each question is scored from 0 to 5 for a total score from 0 to 35.^{3,4} Those patients scoring seven points or fewer are considered mildly symptomatic; those scoring 8 to 18 are considered moderately symptomatic; and those scoring 19 to 35 are considered severely symptomatic. In addition to the IPSS score, a so-called BPH Impact Index (BPH-II) has also become very popular. It consists of five questions, and the total score ranges from 0 to 13. This questionnaire attempts to quantify the interference that the condition causes with daily activity.⁵

One disease-specific, quality-of-life question has become very popular and is often added to the seven-item IPSS questionnaire. This question asks "if you were to spend the rest of your life with urinary symptoms the way they are right now, how would you feel?" The answer spectrum ranges from "delighted" to "terrible" on a score from 0 to 6. This question has proven to be most effective in predicting which patients might seek active treatment vs which might be satisfied with their current symptom status.⁶ Many additional questionnaires are available that address symptom severity, frequency, bother, and quality of life, and many of these are excellent and validated. They often also have validated translations into other languages. However, none of them is as widely used, popular, or prevalent in the urologic literature as the IPSS score.

Recently, it has been recognized that LUTS symptoms correlate strongly with sexual dysfunction, so it is worthwhile to mention the most commonly used questionnaire in the

assessment of erectile dysfunction in men, the International Index of Erectile Function (IIEF). This is also self-administered, with a score ranging from 0 to 30. A higher score indicates better sexual functioning.^{7,8}

Another important outcome measure is the urinary flow rate. Patients are asked to come to the physician's office with a full bladder and void into a special device that records the intensity of the stream and the voided volume, and then calculates the average urinary flow rate. By far the most common and most important parameter is the maximum or peak urinary flow rate. It is estimated that a peak flow rate of >15 mL/sec represents normal status with obstruction being unlikely, while a maximum flow rate of <10 mL/sec likely represents obstruction. Flow rates between 10 mL/sec and 15 mL/sec represent an indeterminate status.

Measurement of postvoid residual urine (PVR) is also a common tool for urologists to assess the status of the patient with BPH/LUTS/BPE/BPO. This can be done by in-and-out catheterization following an attempt by the patient to empty his bladder completely, or by abdominal ultrasonography (which allows the clinician to estimate residual urine with reasonable precision).⁹

The gold standard of assessing BPO in men with BPH, LUTS, or BPE is invasive pressure-flow studies. These studies are performed by inserting a rectal balloon and an intravesical pressure sensor, then filling the bladder and recording the pressure in the bladder and abdomen during both filling and voiding. The relationship between the pressure in the bladder during voiding and the maximum urinary flow rate is the most pivotal parameter in assessing whether the patient's bladder neck is obstructed. This investigation is akin to hard catheterization where pressure gradients across valves are assessed. A graphic representation of this relationship is the so-called Abrams-Griffiths nomogram, which has been described in the literature and been widely used in clinical trials.¹⁰

Prostate size as a marker for BPE can be assessed by a variety of imaging technologies. Clearly, digital rectal examination is inaccurate in estimating the size of the prostate or a change in size over time.¹¹ More accurate are transrectal ultrasound imaging or magnetic resonance imaging (MRI) to assess the size or weight of the prostate. Because the specific gravity of the prostate is close to 1.0, size in milliliters and weight in grams are nearly interchangeable.

It has been shown that PSA is closely correlated with prostate volume in men with BPH.¹² This allows the physician to use serum PSA in men without prostate cancer as a proxy marker for prostate size.¹³

While most of the above-described outcome measures are measures of progression of PSA, prostate size or weight, symptom severity or frequency, etc, at least two outcomes should be discussed in some detail. These are acute urinary retention (AUR) or the total inability to urinate, and the referral of the patient for prostate surgery. When comparing these two outcomes, it is evident that AUR is a more objective outcome than referral for surgery, because the decision for or against surgery is usually the result of a discussion between the patient and his health-care provider, but neither the patient nor the health-care provider can predict or influence AUR.

What Represents Progression?

An obvious question is what in all these outcome parameters represents progression? The answer is relatively easy when considering outcomes such as AUR or surgery—the very fact that the outcome occurred is evidence for progression. However, there is no clear definition for what constitutes progression in terms of prostate size or weight, serum PSA increases, worsening of urodynamic parameters, worsening of urinary flow rate, or even increase in postvoid residual urine.

The best study topic is worsening of the IPSS score. Evidence suggests that an average increase in the symptom score of three points represents worsening that the patient would equate with an actual deterioration of his health status. Patients participating in a randomized, placebo-controlled trial were asked during the trial whether they thought that their urinary symptoms were markedly, moderately, or slightly improved, not improved, or actually worse. Table 1 suggests that depending on baseline severity, marked improvement was associated with a -7.4 to -15.3-point improvement, while slight improvement was associated with a -1.9 to -6.1-point improvement. For patients to feel worse than before the treatment, a three-point worsening was required for the moderately symptomatic, but only a -1.2-point worsening was required for the severely symptomatic patients.¹⁴ Based on this and other evidence, it is commonly accepted that a worsening by three points represents a deterioration or progression in urinary symptoms and associated health status.

Table 1: Mean Absolute Changes in IPSS and BPH-II for Levels of Self-rated GSA¹⁴

	IPSS		BPH II	
	8-19	20-35	0-5	6-13
Marked	-7.4	-15.3	-1.4	-4.6
Moderate	-4.0	-8.7	-0.7	-2.4
Slight	-1.9	-6.1	+0.1	-1.6
None	-0.2	-2.0	+0.4	-0.7
Worse	+3.3	+1.2	+1.8	+2.2

Table 2: Key Studies Supporting BPH as a Progressive Condition**Population-Based Cohort Studies**

- Olmsted County Study (USA, N = 7,000)
- Baltimore Longitudinal Study of Aging (USA)
- Forth Valley Study (Scotland)
- Krimpen Study (Netherlands)
- Health Professionals Study (USA)
- Urology Practice Study (USA)

Placebo Groups and Practice Studies

- Veterans Affairs COOP Study Surgery vs Watchful Waiting (US)
- 2-Year Combined Finasteride (Worldwide)
- The Proscar Long Term Efficacy and Safety Study (PLESS Study, USA)
- Medical Therapy of Prostate Symptoms (MTOPS Study, USA)
- Dutasteride Phase III Studies (Worldwide)
- Vienna Study of Patients with Mild Symptoms (Austria)
- Practice Cohort Study de la Rosette (Netherlands)

Evidence for Progression

The key studies supporting LUTS and BPH/BPE/BPO as progressive conditions are listed in Table 2. Several population-based cohort studies have longitudinal follow-up over variable periods of time, and in addition, a substantial number of placebo-controlled groups and practice studies allow certain types of progression events to be studied with the caveats listed above.

A prospective community-based study from Forth Valley, Scotland, is a good example demonstrating the progressive nature of LUTS and associated bother.^{15,16} Figure 2 shows the changes in urinary symptoms and bother status between baseline and 3 years of follow-up, demonstrating that there are significant increases in symptom and bother levels for most typical LUTS symptoms, although with a significant degree of variability. Another population-based study, the Olmsted County Study of Urinary Symptoms

in Men, provides a numerical estimate for the annual increase in the IPSS score. Based on data from the Olmsted County Study, it has been suggested that there might be up to a five-point increase in symptoms for each decade of a man's life.¹⁷

Regarding maximum urinary flow rate, a decrease in maximum flow rate of approximately 2% per year across all age groups was demonstrated in the Olmsted County Study of Urinary Symptoms in Men. The actual decrease varies by decade of life, with men in their 70s having a greater decrease per annum compared to men in their 40s and 50s.¹⁸ The same study also analyzed the increase in prostate volume with increasing age and found a 0.6% increase in prostate volume per year in cross-sectional studies and 1.6% per year in longitudinal studies. Cross-sectional studies have assessed prostate volume and transition zone volume by either transrectal ultrasound or MRI and give an idea of volume

increase over time. These studies show the linear increase in prostate size with advancing patient age.¹⁹

A variety of population-based studies is available from which the overall prevalence and the annualized incidence rate of AUR episodes can be calculated. Similarly, data from several long-term, placebo-controlled studies permit us to calculate the probability for an individual patient to experience urinary retention and the need for surgery. Generally, the literature on this topic uses analyses of baseline risk factors, and a more detailed discussion of the predictors of progression can be found in the relevant section. A number of watchful waiting studies have been performed comparing TURP vs watchful waiting, as well as other studies, that permit calculation of incidence rates. The incidence rate is expressed as AUR episodes/1,000 patient years of follow-up, and ranges from 3.7 to 130. In the most carefully conducted study of this type—the Olmsted County study—the incidence rate is 6.8/1,000 patient years, with a 95% confidence interval of 5.2 to 8.9.

When assessing the overall risk of progression and adverse outcomes, it should be stressed that in most studies, the risk for AUR or surgery increased in a linear fashion over time. An example of this trend is shown in Figure 3 from the 4-year Proscar Long Term Efficacy and Safety Study (PLESS study).²⁰ The probability of either surgery or AUR as an outcome is shown to increase in a linear fashion in the placebo group, beginning at the start of the study to the end point at 4 years (Figure 4). Similar observations can be made from the dutasteride phase III trials.²¹⁻²³

Based on findings in the Olmsted County Community study, it does not appear that symptomatic worsening or prostate growth occurs in a linear fashion over time. However, certain conclusions regarding the likelihood of progression and developing certain clinical outcomes over time can be drawn.

Consider a 60-year-old man with no prior diagnosis of LUTS or BPE/BPO, who presents to a health-care provider with a prostate size of 30 mL, a 10-point baseline score on the IPSS, an annual risk of progression of 1 mL volume increase of his prostate, and a 0.2-point increase in his symptom score. The annual risk of AUR for this individual is approximately 1%, the annual risk of requiring any form of treatment is 3%, and the risk for surgery is 1%. Assuming a linear risk, this same patient at the age of 80 years might have a prostate size increased by 20 mL to 50 mL, and have

a symptom score from 10 to 14 points. The cumulative risk of AUR would be 20%, with a cumulative risk for overall treatment of 60% and the risk for surgery 20%. In contrast, a 60-year-old man already diagnosed with LUTS or BPH might be assumed to start out with an already enlarged prostate gland of 50 g and a higher symptom score of 15 points. The annual increase in prostate size might be 2 mL for a total volume increase of 40 mL to an end volume of 90 mL at the age of 80 years. Similarly, the symptom score might worsen from 15 to 19 points, although the overall risk of AUR and surgery appears to be higher in patients diagnosed with BPE, leading to a cumulative risk of 40% for AUR, and 60% for surgery.

Predictors of Progression or Outcomes

Practically, it is equally or even more important to understand what baseline factors might predict the likelihood of a given patient to progress or experience outcomes than to understand the overall risks of such events. In fact, it would be ideal if a health-care provider could, during the first visit with a patient, determine his individual risks of progression or outcomes, and based on this assessment, initiate a policy of either watchful waiting or active surveillance if the risk is low, or appropriate treatment if the risk is high. Extensive study has been done regarding the predictors of outcomes in both population-based studies and placebo-controlled groups from randomized

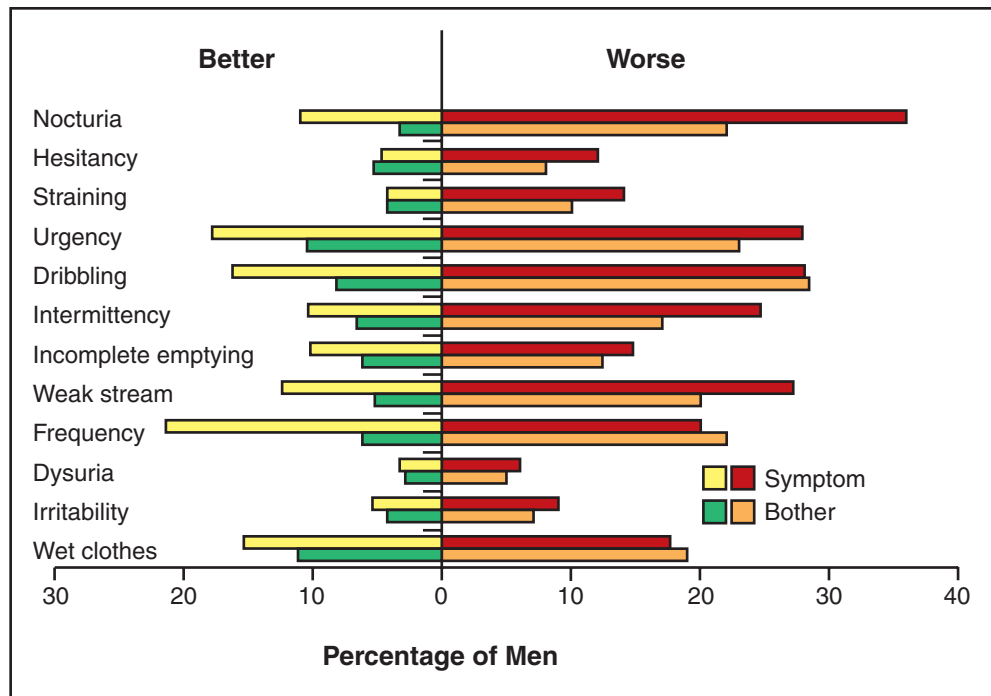


Figure 2: Changes in urinary symptoms and bother status between baseline and 3 years in a Scottish community-based study.

trials. Efforts have been made to understand what triggers the risk for symptoms, bother, quality of life deterioration, further growth in prostate volume, or PSA increases, and most importantly, the risk of acute urinary retention and surgery.

As a rule, the risk of deterioration of symptom severity and frequency, bother, and quality of life are linked to the symptom severity score at baseline as well as to the patient's age. The

FLINT Men's Health Study demonstrates that symptom worsening is clearly more likely in men in their 70s compared to men in their 40s.²⁴ In addition to age, the authors also found prostate size to be a significant predictor of symptomatic worsening. The odds ratio for progression on the AUA Symptom Score over time with a prostate volume of >30 mL was 1.52 compared to men with a prostate volume of <30 mL.

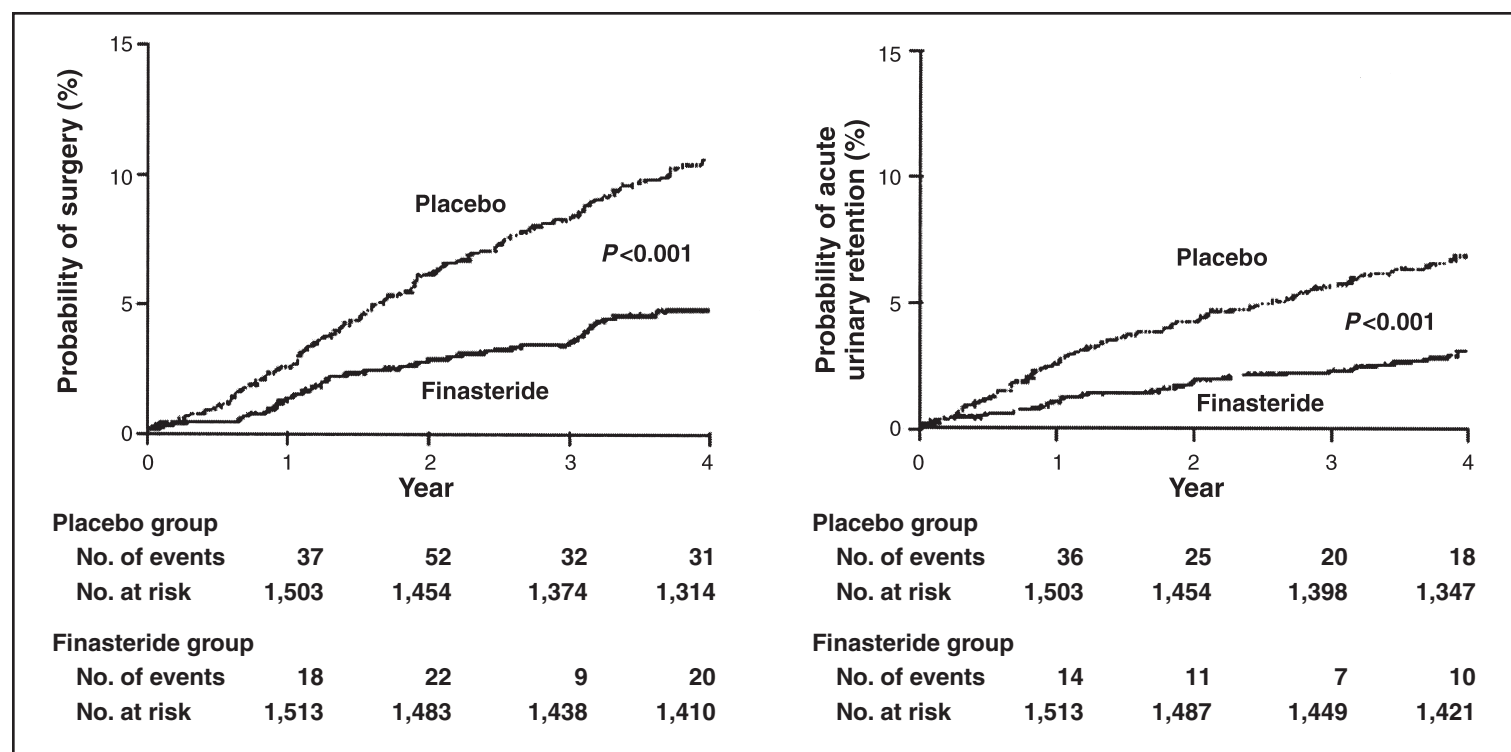


Figure 3: The risk of AUR and surgery is linear in placebo-treated patients in the 4-year PLESS study.²⁰

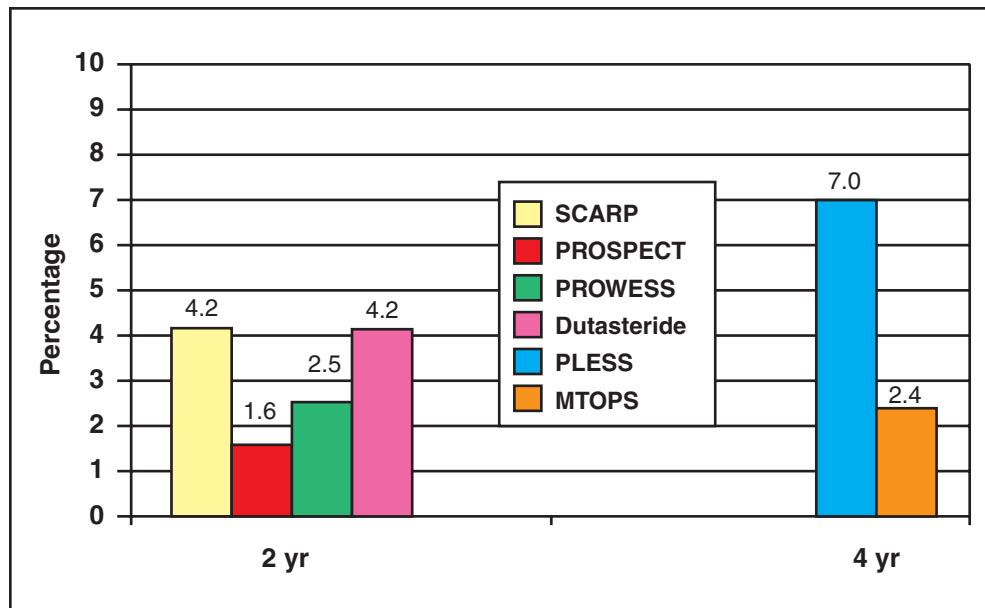


Figure 4: Cumulative incidence of acute urinary retention in placebo arms of controlled BPH trials of 2 and 4 years' duration.

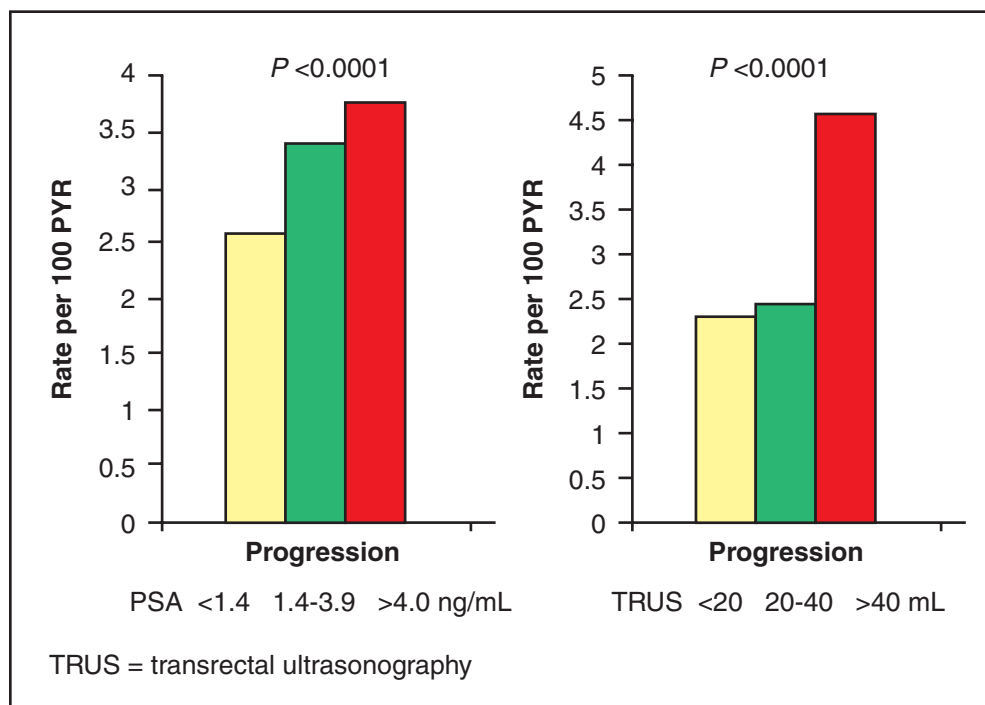


Figure 5: Association of baseline PSA and prostate volume in convenience tertiles in the MTOPS trial and symptomatic progression (ie, greater than 4-point worsening). A significant difference exists between men with prostate volumes <40 and >40 mL.²⁶

A study from Vienna also demonstrated that prostate volume, baseline symptom score, and serum PSA were predictive factors for the progression from mild to moderate or severe symptoms.²⁵

The only controlled trial that truly assesses the risk of symptom progression, based on a priori definition, is the Medical Therapy of Prostatic Symptoms or MTOPS study.²⁶ In this study, progression was defined as an increase in four or more IPSS points from

baseline, as verified twice within a 2-week window, or the development of urinary retention, recurrent UTIs with an infection-free interval, development of socially unacceptable incontinence, or development of renal failure secondary to BPO. Progression to a surgical intervention for BPO was not defined as integral to the primary outcome. When stratifying the risk of symptomatic worsening by four or more points in the placebo group, Figure 5 demonstrates that the risk of symp-

tomatic progression decreases significantly for men with baseline PSAs of <1.4 ng/mL compared to those with a PSA in the intermediate or higher range. Similarly, the risk of symptomatic progression nearly doubles for those men with baseline prostate volumes by transrectal ultrasound of >40 mL, vs those with baseline values <40 mL. Regarding the deterioration of maximum urinary flow rate, the Olmsted County Study established that there is a greater decrease in urinary flow rate in men in their 70s compared to younger men. The placebo group in the PLESS study demonstrated that men with higher serum PSA levels at baseline were more likely to experience a deterioration of their maximum urinary flow rate compared to those with lower PSA values <1.4 ng/mL.²⁷

The placebo group of the 4-year PLESS study also permitted an analysis of predictors of prostate growth over time, with the usual caveats.²⁸ Men in the lowest PSA tertile showed a volume growth of 7.4% during 4 years for an annualized growth of 1.9%, compared to those in the intermediate PSA category of 16.2% (for an annualized growth of 4.1%), and those in the highest PSA category of 22%, resulting in an annualized growth of 5.5 points. The stratification by age in the placebo group yielded considerably smaller differences, ie, age did not play as much of a role in men already diagnosed with BPE in predicting future prostate volume increases, compared to the baseline PSA score. Similar findings were obtained from the placebo group of the 2-year dutasteride studies as well as from the MTOPS study.²⁶

In reviewing predictors for AUR and surgical intervention for LUTS and presumed or proven BPO, significant and well-analyzed data are available from population-based studies, as well as from cohort designs and placebo-controlled studies.

Predictors of AUR/Surgery

Arrighi et al reported in 1990 that the need for surgery was strongly dependent on baseline factors such as change in size and force of stream, sensation of incomplete emptying, and prostate enlargement as noted on digital rectal examination.²⁹ In population-based studies, it has been known for some time that age is a strong predictor of the incidence of AUR³⁰ as data analyzed from the Physicians' Health Study clearly demonstrate.

In the Olmsted County study, the relative risk of AUR increased significantly for men in their 70s compared to younger men, for men with moderate-to-severe symptoms compared

to those with mild symptoms, and for men with a reduced maximum urinary flow rate of <12 mL/sec.³¹

An informative analysis of the role of baseline variables in predicting the risk for medical or surgical treatment overall, or for needing a transurethral resection of the prostate (TURP), can be seen again in findings from the well-known Olmsted County study. The risk for treatment in this study was increased for men in their 50s, 60s, and 70s compared to those in their 40s, and for those with moderate-to-severe symptoms, compared to those with mild symptoms. Furthermore, a reduced urinary flow rate, prostate volume >30 mL, and a PSA of >1.4 predict an increased risk for treatment compared to normal flow rate, small prostate volume, and a low serum PSA.³¹ Age plays a major role. It is noteworthy that the risk of overall treatment as well as the risk for surgical treatment appears to be linear, ie, predictable over time.

Extensive information regarding baseline predictors of the risk for retention or surgery comes from three placebo-controlled arms of the dutasteride phase III studies, the PLESS study, and the MTOPS study. In dutasteride phase III studies, patients who had a baseline prostate volume >30 mL and a baseline serum PSA of >1.5 ng/mL were enrolled. The incidence rate of AUR increased from 1.6% to 9%, while the proportion of subjects requiring BPH-related surgery increased from 2.9% to 7.5% stratified in quartiles of serum PSA.^{22,32}

In the PLESS study, prostate volume was measured by MRI only in a subset of 10% of patients. The risk of spontaneous retention, precipitated retention, or the combined spontaneous plus precipitated or total AUR rate, as well as the risk of surgery increased with both increasing prostate volume as well as increasing serum PSA tertiles. The overall risk of surgery or AUR reached 22% in the highest prostate volume group, and 20% in the highest PSA tertile, while it was only 11% and 8% in the lowest volume and PSA tertile groups, respectively.

Additional information regarding the risk of AUR stratified by baseline prostate volume and serum PSA comes from the MTOPS study.²⁶ The risk of AUR increases with increasing serum PSA and specifically, doubled with a PSA of >4.0 ng/mL compared to those with a lower PSA. The risk of AUR increased although much less noticeably, with an increase in prostate volume from <20 to >20 mL.

Conclusion

Extensive data support the progressive nature of enlarged prostate, with risks that include worsening of urinary symptoms, acute urinary retention, and prostate-related surgery. Physicians in the primary-care setting should intervene for patients presenting with a PSA >1.4, a prostate volume >30 mL, or an AUA-IPSS score >7.

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Self Test

This self-assessment test is presented as an educational adjunct to the monograph. Completion of this brief test will help reinforce the material you have read. Answers are elsewhere on this page.

1. Which is *not* part of the typical LUTS symptom complex and is *not* assessed in the IPSS questionnaire?
 - a. frequency
 - b. urgency
 - c. dysuria
 - d. nocturia
 - e. incomplete emptying
2. Which type of study is *not* suitable to evaluate natural history of LUTS and BPH?
 - a. population-based studies
 - b. placebo-controlled groups of long-term studies
 - c. sham-control groups of long-term studies
 - d. short-term medical treatment studies
 - e. disease registries
3. Which is the best-studied criterion for LUTS and BPH progression?
 - a. prostate size
 - b. symptom severity questionnaires
 - c. serum PSA
 - d. flow-rate parameters
 - e. serum creatinine
4. The overall risk of acute urinary retention in placebo-controlled groups followed for 2 years is:
 - a. 0%
 - b. 10%-20%
 - c. 5%-10%
 - d. >20%
 - e. 1.5%-4.5%
5. Which statement is correct regarding predictors of progression of LUTS and BPH?
 - a. Serum PSA and prostate volume do not predict progression.
 - b. Serum PSA predicts progression but prostate volume does not.
 - c. Prostate volume predicts progression but serum PSA does not.
 - d. PSA is much better at predicting progression compared to volume.
 - e. Serum PSA and prostate volume both predict progression.

Self Test Answers for This Issue:
1. c 2. d 3. b 4. e 5. e

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