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MINI-REVIEW

Natural history and epidemiology of benign prostatic hyperplasia

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Summary Benign prostatic hyperplasia (BPH) is a common benign tumor that develops in men and is bothersome in elderly patients. The prevalence of lower urinary tract symptoms in the general population increases with aging. The normal prostate weighs 20 ± 6 g in men aged 21–30 years. The prevalence of pathological BPH is only 8% at the 4th decade of life; however, 50% of the male population develop pathological BPH at age 51–60 years. The average weight of a prostate that is recognized at autopsy as having BPH is 33 ± 16 g. Men aged 70–79 years are 4.6 times more likely (95% confidence interval, 2.1–10.1) than those aged 40–49 years to have sought health care because of urinary symptoms. Health care-seeking behavior is influenced by BPH-related symptoms severity, particularly if the symptoms are bothersome and interfere with a patient's daily activities. The progression of BPH is observed in terms of increased prostate volume and decreased maximal urinary flow rate. In addition, disease progression increase the risk of acute urinary retention and surgery. On average, the international prostate symptom score increases 0.18 points/yr, maximal urinary flow rate decreases by 2%/yr, and median prostate growth increases 1.9%/yr for BPH. In addition, the accumulative incidence of acute urinary retention is 2.7%. BPH itself is associated with a deteriorated clinical and symptomatic natural history, and early treatment may benefit patients with bothersome symptoms of BPH.

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1. Natural history of benign prostatic hyperplasia prior to diagnosis

Benign prostatic hyperplasia (BPH) is the most common nonmalignant condition of the prostate developing in aging men. BPH is a major public health concern, causing high morbidity and substantial worsening of men's quality of life (QOL).[1] The prevalence rates of BPH mostly depend on the parameters used in a case definition.[2] In Japan, these rates have been estimated on the basis of the results of community-based studies.[3] Six percent and 12% of Japanese men in their 60s and 70s, respectively, met all of the following criteria for BPH: (1) an international prostate symptom score (IPSS) >7 points; (2) prostate volume (PV) >20 mL; and (3) peak urinary flow rate (Q_{max}) <10 mL/s. Only 2% of men in their 40s and 50s met the aforementioned criteria.

The principal risk factors for BPH are aging and the hormone produced from normally functioning testes. Although no definitive genes responsible for BPH have been identified, a family history of BPH and molecular abnormalities may increase the likelihood of the development of BPH. Dietary factors, such as isoflavonoids and lignans in vegetables, grains, and soy, may negatively affect the development of BPH.[1] Furthermore, recent studies have claimed a relationship between metabolic syndrome and BPH.[4,5] A normal prostate weighs 20 ± 6 g in men aged 21–30 years, and this weight remains essentially constant with increasing age unless BPH develops. The prevalence of pathological BPH is 8% in the 4th decade of life; however, 50% of men develop pathological BPH at age 51–60 years. The average weight of a prostate identified at autopsy as having BPH is 33 ± 16 g. Only 4% of the prostates in men older than 70 years weigh >100 g. An analysis of a logistic growth curve of BPH lesions removed at prostatectomy indicates that the growth of BPH is initiated probably before the patient is 30 years. The early phase of BPH growth (in men aged 31–50 years) is characterized by a doubling time for the tumor weight of 4.5 years. In the mid-phase of BPH growth (in men aged 51–70 years), the doubling time is 10 years and increases to >100 years in patients older than 70 years.[6] BPH is a physiological process that occurs with aging, regardless of race, ethnicity, or region.[6,7] Estimated rates of prostate growth increased with increasing age. However, the estimated average annual change was 1.6% across all age groups. Estimated rates of prostate growth are high, depending on the baseline PV, with higher growth rates for men with larger prostates.[8]

BPH is a progressive disease in a certain proportion of men older than 50 years. Men showing prostate growth are at a greater risk of symptomatic deterioration. Men with no prostate growth are significantly more likely to improve symptomatically.[9] The prevalence of lower urinary tract symptoms (LUTS) in the general population is age-related.[10,11] Longitudinal studies have shown an increase in the IPSS with aging as a whole[9,12] but with simultaneous decreases in the IPSS in certain subgroups.[12,13] Q_{max} decreases with aging,[3] and this may be attributable to benign prostatic obstruction and detrusor underactivity. In addition, longitudinal studies have confirmed age-related increases in prostate volume (PV),[8,9] although PV decreased with aging in a small proportion of men.[14] Recent studies have indicated that PV may increase in men in whom the prostate has a visible transition zone with a clear border[15] and those in whom transrectal ultrasound shows a large transition zone volume at baseline.[16] In general, the relationship among LUTS, urinary flow rate, and PV is poor in men presenting at hospitals, but the relationship is modest in the general population. Prostate enlargement may be involved in the progression of symptoms of BPH.[9]

2. Factors affecting health care-seeking behavior

A cross-sectional, population-based cohort study in Olmsted County, MN, USA, revealed that health care-seeking behavior is influenced by symptom severity, particularly if the symptoms are bothersome and interfere with a patient's daily activities. While symptom severity is a vital determinant of health care-seeking behavior in men with urinary symptoms, age-related factors may drive men to seek care for urinary symptoms. Men aged 70–79 years were 4.6 times more likely (95% confidence interval, 2.1–10.1) than those aged 40–49 years to have sought health care because of urinary symptoms.[17] Seventy-six percent of men who had sought medical care had prostate enlargement, depressed peak urine flow rates, and moderate-to-severe symptoms of BPH (sensitivity). By contrast, only 55% of men who did not seek health care for urinary symptoms had mild symptoms of BPH, normal prostatic volume, and normal peak urine flow rates (specificity). Clinical, physiological, and anatomic measures of prostatism do not adequately distinguish the men who seek medical care for their urinary symptoms from those who do not.[18]

Voiding symptoms may influence health care-seeking behavior through QOL impairment in Japanese men. The QOL score revealed more pronounced differences between men admitted to clinics and community settings than did the IPSS category.[19] The Core Lower Urinary Tract Symptom Score questionnaire is more comprehensive than the IPSS questionnaire for symptom assessment in men with various diseases/conditions, although both questionnaires can capture LUTS with a potential negative impact on QOL.[20]

3. Prediction of symptomatic progression

A systematic review of the placebo arm of clinical trials related to BPH revealed that disease progression was relative to increased PV and decreased Q_{max}. In addition, disease progression increased the risk of acute urinary retention (AUR) and surgery.[21]

Progression may be associated with a higher IPSS, lower Q_{max}, increased postvoid residual urine (PVR), and enlarged PV. According to the Medical Therapy of Prostatic Symptoms study (MTOPS), the clinical progression of the placebo arm ($n = 737$) was 17%, AUR was 2%, and invasive therapy for BPH was 5%.[22] The results from this study suggested that the risk factors for clinical progression may include age ≥62 years, prostate volume ≥31 mL, prostate specific antigen ≥1.6 ng/mL, Q_{max} <10.6 mL/s, and PVR ≥39 mL.[23] However, medical

practitioners often encounter patients with several unfavorable conditions and not with a single risk factor. In a comprehensive analysis of expert opinions, considerable PVR (>150 mL), poor Q_{max} (<10 mL/s), and severe symptoms (total IPSS = 20–35 points) were the most dominant factors predicting an elevated risk of disease progression.[24] Enlarged prostate and high prostate specific antigen value were good clinical predictors of AUR and BPH-related surgery. In addition, high PVR should be reconsidered as a predictor of BPH progression because of evidence from the results of population-based, longitudinal studies and analysis of the placebo arm of controlled studies.[25]

4. Natural history of BPH after diagnosis

The best method to evaluate the natural history of BPH after diagnosis is to understand the fate of a watchful–waiting or placebo treatment group. In a community-based, longitudinal study followed for 12 years, an average increase in the IPSS of 0.18 points/yr (0.05 points for men in their 50s to 0.44 points for men in their 70s) was observed. Q_{max} decreased 2%/yr, and median prostate growth decreased 1.9%/yr. In addition, the accumulative incidence of AUR was 2.7% when monitored for over 4 years.[26] In the placebo-controlled arm of the MTOPS study, evidence revealed that symptom deterioration (IPSS $\geq$ 4 points) was the most prevalent progression event (79.5%), with an accumulative incidence of 14% over a mean follow-up period of 4.5 years.[22]

After diagnosis of BPH, self-management intervention, including lifestyle modification and specific behavioral changes, such as decreasing fluid intake at bedtime and avoiding consumption of caffeine and alcohol, may be the most suitable management strategies that offer an enhanced clinical response. However, the failure rate at 3 months, 6 months, and 12 months is higher in watchful–waiting patients (40.3% vs. 9.6%; 58.2% vs. 17.8%; and 65.7% vs. 24.6%, respectively) than in patients receiving active management.[27] This evidence indicates that BPH results in a deteriorated clinical or symptomatic natural progression, and early treatment may benefit the patients with bothersome symptoms of BPH.

The Prowess Study revealed that patients with moderate symptoms of BPH show a significantly greater improvement with finasteride therapy than those in the placebo group. The PV decreased 15.3% in the treatment group compared with that in the placebo group, in which PV increased approximately 8.9% after 24 months.[28] A nationally representative database study reported that in addition to α-blocker therapy, each 30-day delay in the treatment with 5-α-reductase inhibitors may increase overall clinical progression (21.1%), AUR (18.6%), and likelihood of prostate-related surgery (26.7%) within 6 months of follow-up.[29] This result indicates that even after receiving early treatment with α-blockers, patients have an elevated risk of symptomatic progression if they cannot reduce the prostate size. In the Veterans Affairs Cooperative Study, 24% watchful–waiting patients underwent surgery within 3 years of waiting for assignment.[30] Based on the natural history after diagnosis of BPH with or without medical treatment, monitoring clinical progression should help raise awareness among clinicians and patients, who should also remain informed, particularly those receiving watchful–waiting treatment.

5. Comments

The prevalence of LUTS in the general population is related to age. Health care-seeking behavior is influenced by age-related factors and symptom severity, particularly if they are bothersome. The disease progression of BPH may be associated with a higher IPSS, lower Q_{max}, increased PVR, and enlarged PV. BPH is associated with a deteriorated clinical or symptomatic natural progression. Thus, early treatment may benefit patients with bothersome symptoms.

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