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Mini Review

Pathological Characteristics and Clinical Significance of High-Volume Benign Prostatic Hyperplasia

Tag Keun Yoo*

Department of Urology, Nowon Eulji University Hospital, Eulji University, Korea

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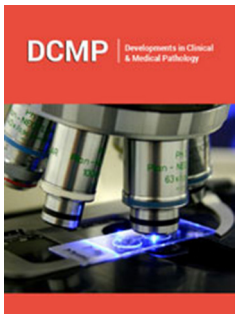

***Corresponding author:** Tag Keun Yoo, Department of Urology, Nowon Eulji University Hospital, Eulji University, Korea

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Abstract

High-volume benign prostatic hyperplasia (BPH, prostate>80g) typically requires invasive surgical intervention per current guidelines. This mini-review explores the pathological characteristics and clinical significance of high-volume BPH, highlighting its inherent heterogeneity. BPH involves epithelial and stromal proliferation. While stromal-dominated hyperplasia (SDH) causes early, severe LUTS in smaller prostates, high-volume BPH often features epithelial-dominated hyperplasia (EDH), leading to significant gland growth but delaying symptom recognition due to less dynamic obstruction. This pathological diversity suggests high-volume BPH is not a uniform condition. Understanding this heterogeneity and identifying its precise drivers are crucial for developing personalized molecular treatments and preventive strategies, potentially reducing invasive surgery for high-volume BPH patients.

Keywords: Benign Prostatic Hyperplasia (BPH); High-volume BPH; Pathological Heterogeneity; Epithelial-dominated hyperplasia (EDH)

Introduction

High-volume benign prostatic hyperplasia (BPH) refers to a condition where the prostate gland exceeds 80g in size, typically warranting highly invasive surgical interventions such as open prostatectomy or robotic-assisted laparoscopic surgery as primary recommendations in major urologic society guidelines [1]. This mini-review aims to summarize the pathological characteristics of high-volume BPH. Specifically, it focuses on the heterogeneity of high-volume BPH beyond the limitations of existing BPH classifications. Based on this, we anticipate that future molecular-based research will pave the way for more appropriate treatments or preventive strategies for these patients, including for high-volume BPH.

Pathology of Benign Prostatic Hyperplasia

BPH is a chronic disease that afflicts patients by obstructing urine outflow due to the proliferation of periurethral/transitional zone prostatic tissue, compressing the urethra. Despite its high prevalence, there is still no complete consensus on whether the main element involved in prostate growth is epithelial in origin (ducts or prostatic alveoli) or due to stromal cell proliferation [2]. The generally accepted morphological progression in BPH is characterized by diffuse growth initially, followed by the emergence of small epithelial and stromal nodules in prostates over 50g, and eventually the formation of dilated cystic glands with very little stroma in high-volume prostates [3, 4]. Thus, the pathological characteristic of high-volume BPH patients can primarily be considered epithelial-dominated hyperplasia.

BPH tissues from individual patients who undergo surgery are classified into subtypes based on the predominant proliferation of either epithelial or stromal cells [5]. Specifically, in cases where stromal-dominated hyperplasia (SDH) (involving smooth muscle cells and

fibroblasts) is predominant, even if the prostate size is relatively small, it can directly compress the urethra and increase urethral smooth muscle tone, causing functional obstruction. This leads to early and severe lower urinary tract symptoms (LUTS). These patients often seek early treatment, and when smooth muscle proliferation is dominant within the stroma, they tend to respond well to alpha-blocker therapy [6]. Excessive accumulation of fibrosis and extracellular matrix (ECM) also increases tissue stiffness and can act as a factor aggravating LUTS, particularly in SDH patients [5].

Conversely, epithelial-dominated hyperplasia (EDH) is a form of benign proliferation that significantly contributes to the overall prostate volume increase. Since high-volume BPH predominantly consists of epithelial-dominated hyperplasia, even if the prostate grows considerably, dynamic urethral obstruction due to the stromal component is relatively less severe, which can lead to delayed symptom recognition or milder perception of symptoms. This delay in symptom manifestation often results in patients seeking medical attention only when the prostate has become high-volume. Of course, whether high-volume BPH is primarily associated with genetic alteration from the outset, or if it arises from an initial stromal hyperplasia phase with relatively mild symptoms that then rapidly transforms into epithelial-dominated hyperplasia due to an aggravating factor, remains a subject for future research [7].

Conclusion

High-volume BPH patients with prostates over 80g often require more invasive surgical approaches such as open prostatectomy or robotic-assisted simple prostatectomy (RASP), as minimally invasive surgeries like TURP are difficult or incomplete [8]. Although there is still insufficient research on the factors contributing to the development of high-volume BPH, histological heterogeneity of the phenotype has challenged a clear understanding. However, future comprehensive efforts to meticulously understand the pathological characteristics at a microscopic level and identify the factors involved in the genesis and progression of high-volume BPH are crucial for establishing personalized treatment strategies for patients.

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