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ORIGINAL RESEARCH

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Is there a relationship between benign prostatic hyperplasia and symptomatic lumbar spinal stenosis in men? A retrospective comparative study

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Abstract

Despite extensive research into the pathophysiology of lumbar spinal stenosis (LSS), the precise reasons behind its increased symptomatic nature in women remain elusive. Notably, the physiological disparities between males and females, particularly concerning organ structures, such as the prostate, play a significant role. This study sought to explore potential correlations between symptomatic LSS and benign prostatic hyperplasia (BPH) exclusively in men. Conducted as a retrospective comparative analysis, the study encompassed individuals over the age of 60 with severe lumbar spinal stenosis seeking treatment for lower back and leg discomfort and undergoing lumbar magnetic resonance imaging (MRI) scans at relevant medical facilities. The assessment involved evaluating the functional status of the participants through the Oswestry disability index (ODI) and Visual Analog Scale (VAS), alongside determining the presence of BPH, and examining any history of medication utilization. A cohort of 49 patients were included in the study, with an average age of 70.7 $\pm$ 6.2 years. The median VAS pain score was 5 (25–75%: 3–8), while the mean ODI score stood at 43.5 $\pm$ 18.1. Notably, the ODI scores were worse in the BPH group (mean, 46.1 *vs.* 41.4). However, no statistically significant difference was observed between VAS and ODI scores (p = 0.834, p = 0.360) between patients with and without BPH. Similarly, no significant differences were noted in clinical scores between drug users and non-users (p = 0.868, p = 0.346). Statistically, the presence of BPH did not exhibit any discernible impact on the clinical prognosis of LSS. However, further comprehensive studies are imperative to elucidate the symptomatic variances between men with and without BPH.

Keywords

Lumbar stenosis; Benign prostatic hyperplasia; Neurosteroids; Pain sensitivity; Allopregnanolone; Gender differences

1. Introduction

Lumbar spinal stenosis (LSS) is widely recognized as the leading cause of spinal surgery, with a prevalence estimated to be between 6% and 47%, yet its pathophysiology remains incompletely understood [1]. This painful, progressive, and degenerative condition is strongly linked to neurogenic claudication (NC), which significantly hinders daily activities. A complex interaction may exist between NC and mechanical compression, cerebrospinal fluid (CSF) dynamics, genetics, biomechanics, and spinal alignment [2, 3]. From a biomechanical perspective, vascular insufficiency may also be present alongside mechanical compression, leading to a substantial reduction in the affected region. The Monro-Kellie doctrine [4], a theory proposed to elucidate the pathophysiology of symptoms, suggests that rather than the compression theory resulting from a narrowed lumbar canal, clinical issues arise due to decreased compliance disrupting the CSF pulsation.

Gender differences in sensory transmission and perception have been examined, contrasting with compression or compromised CSF dynamics that cause leg pain in LSS. In a study by Kim H-J *et al.* [5], the Oswestry Disability Index (ODI) significantly varied between males and females despite similar age and radiological lumbar spinal stenosis severity, possibly due to differences in pain sensitivity. Another study on topographical pain analysis evaluated anthropometric and demographic characteristics, spinal mobility, and pain archaea measurements in patients with axial spondyloarthritis, indicating a greater prevalence of peripheral pain and overall disease activity in women [6]. Furthermore, a separate study on gender differences found that women generally report higher pain scores than men across all scales, except for walking, and that the intensity of pain in women is often accompanied by a tendency towards depression [7].

The reasons behind why men's quality of life is less impacted, despite having comparable radiological stenosis sever-

ity, remain unclear. The factors outlined above and extensively studied in literature have yet to fully explain the intensity of pain experienced by women. One notable gender-specific characteristic is physical differences, which play a role in pain sensitivity. In men, Benign prostatic hyperplasia (BPH) is a prevalent urological condition that becomes more common with age. Research on BPH and its medication-related complications has suggested that alterations in spinal neuroactive steroid levels may influence peripheral pain sensitivity, unlike in women [8]. Joksimović SL. *et al*. [9] demonstrated the active production of neurosteroids with potent analgesic activities, such as progesterone and the neuroprotective derivate of progesterone by 5α-reductase, allopregnanolone, in the dorsal horn of the spinal cord, which plays a crucial role in transmitting painful stimuli from the peripheral nociceptors.

This study postulates that medications used to treat BPH in men reduce the production of protective neurosteroids, particularly allopregnanolone in the dorsal spinal horn, thereby increasing the likelihood of symptomatic presentation in individuals with severe lumbar spinal stenosis. Therefore, in this retrospective comparative analysis, we investigated the correlation between activity-limiting symptoms and the presence of BPH and BPH medications in men with severe lumbar spinal stenosis.

2. Materials and methods

This retrospective cohort study was conducted in adherence to the principles outlined in the Declaration of Helsinki. The medical facility from which the data was collected serves as the sole tertiary care hospital in a district with an estimated population of 1.5 million individuals. Male patients who had not yet scheduled a surgical appointment with either the neurosurgery or orthopedics department, but presented with symptoms of low back-leg pain, numbness, or leg weakness between March 2021 and January 2022, and underwent lumbar Magnetic Resonance Imaging (MRI), were included in this study. The MRI findings of these patients were initially categorized based on age (>60 years or younger) and subsequently searched using specific keywords such as “absolute stenosis”, “narrow canal”, “lateral recess stenosis” and “foraminal stenosis”. Inclusion criteria were determined following a thorough review of the lumbar spinal MRI reports and images, which included patients over 60 years of age, Schizas grade C/D, and male patients with or without BPH history.

As per Schizas P *et al*. [10], the qualitative assessment of the axial images was conducted by a certified Orthopedic Spine surgeon with fellowship training and a trained neurosurgeon, each independently analyzing every axial MRI. All measurements were repeated after a washout period of more than 6 weeks.

The assessments encompassed a detailed medical history, physical examination, and completion of questionnaires, including walking distance in a single trial without interruption, ODI, and VAS for back pain. The ODI is a self-administered questionnaire evaluating “back-specific function” on a 10-item scale with six response categories for each item, scored from 0 to 5, and then transformed to a scale of 0–100. The VAS for back pain/leg pain was gauged using a bar with “none” at one end (zero) of a 100-mm line and “disabling pain” at the other end. Patients with Lumbar Spinal Stenosis (LSS) were specifically asked to indicate the VAS for leg pain at the onset of claudication while walking, marking the 100-mm line, with the distance (mm) from the zero point considered as the score.

The data was analyzed using the SPSS (IBM, Armonk, NY, USA) 22 program. Mean $\pm$ standard deviation (SD) and median (minimum–maximum) were used as descriptors for quantitative variables, while the number of patients (percentage) was employed for qualitative variables. The *t*-test was employed to assess the presence of a difference between the categories of qualitative variables with two categories concerning a quantitative variable, contingent on the fulfillment of normal distribution assumptions, and the Mann-Whitney U test was used in cases where these assumptions were not met. In instances where there was a difference between the categories of a qualitative variable with more than two categories in relation to a quantitative variable, the One-Way ANOVA (analysis of variance) test was utilized if normal distribution assumptions were met, and the Kruskal Wallis H test is used if they were not. The chi-square test was employed to explore the relationship between two qualitative variables. Statistical significance was established at $p < 0.05$.

3. Results

In this retrospective comparative analysis, the hospital registry system acquired lumbar MR images of 2026 patients who presented to physical therapy, neurosurgery, neurology, or orthopedics outpatient clinics with complaints of low back or leg pain. Among these patients, 81 patients with severe lumbar spinal stenosis were identified (Fig. 1). However, a total of 32 patients who declined to participate in the study, those who were unreachable, and those who were lost due to mortality were excluded from the analysis. All data from the remaining 49 patients were included in the final evaluation.

The demographic variables, such as age, BMI (Body Mass Index), and gender, did not show any statistically significant differences between the two groups ($p > 0.05$). The average age of the patients was 70.7 $\pm$ 6.2. The median VAS score of the patients was 5 (25–75%: 3–8), and the mean ODI score was 43.5 $\pm$ 18.1 (ODI and age demonstrated normal distribution; Fig. 2).

The patients’ BMI was 27.2 $\pm$ 4.8. A comparison of the clinical outcomes between patients with and without benign prostatic hyperplasia (BPH) revealed no statistically significant differences in VAS and ODI scores ($p = 0.834$, $p = 0.360$) (Table 1).

The clinical outcomes of patients with BPH who used medications and those who did not were assessed, showing no statistically significant differences in VAS and ODI scores ($p = 0.471$, $p = 0.150$) (Table 2).

There were no statistically significant differences in VAS and ODI scores when comparing patients with drug use and those without, as well as between patients with and without BPH ($p = 0.868$, $p = 0.346$) (Table 3).

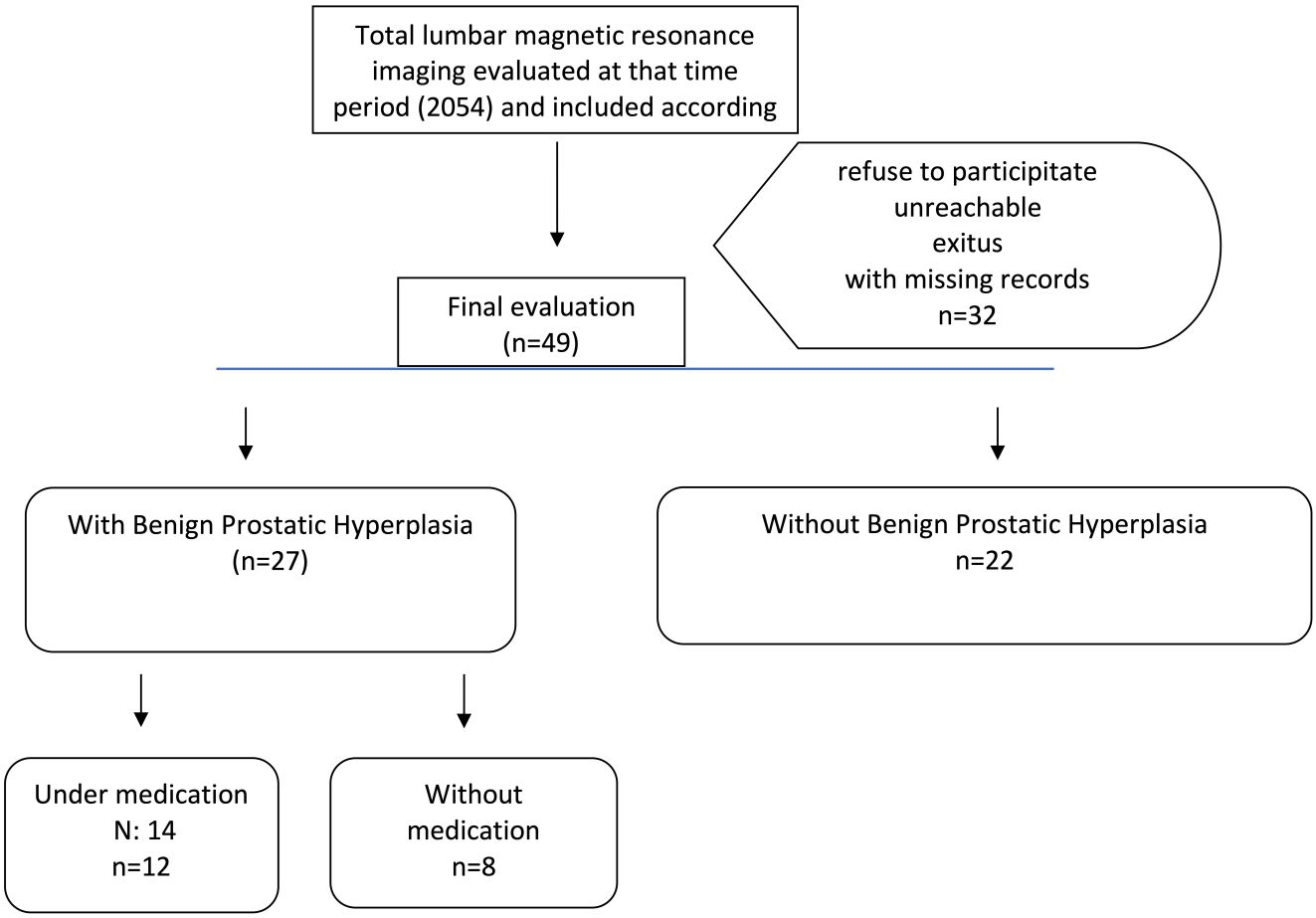

FIGURE 1. Flowchart of the study.

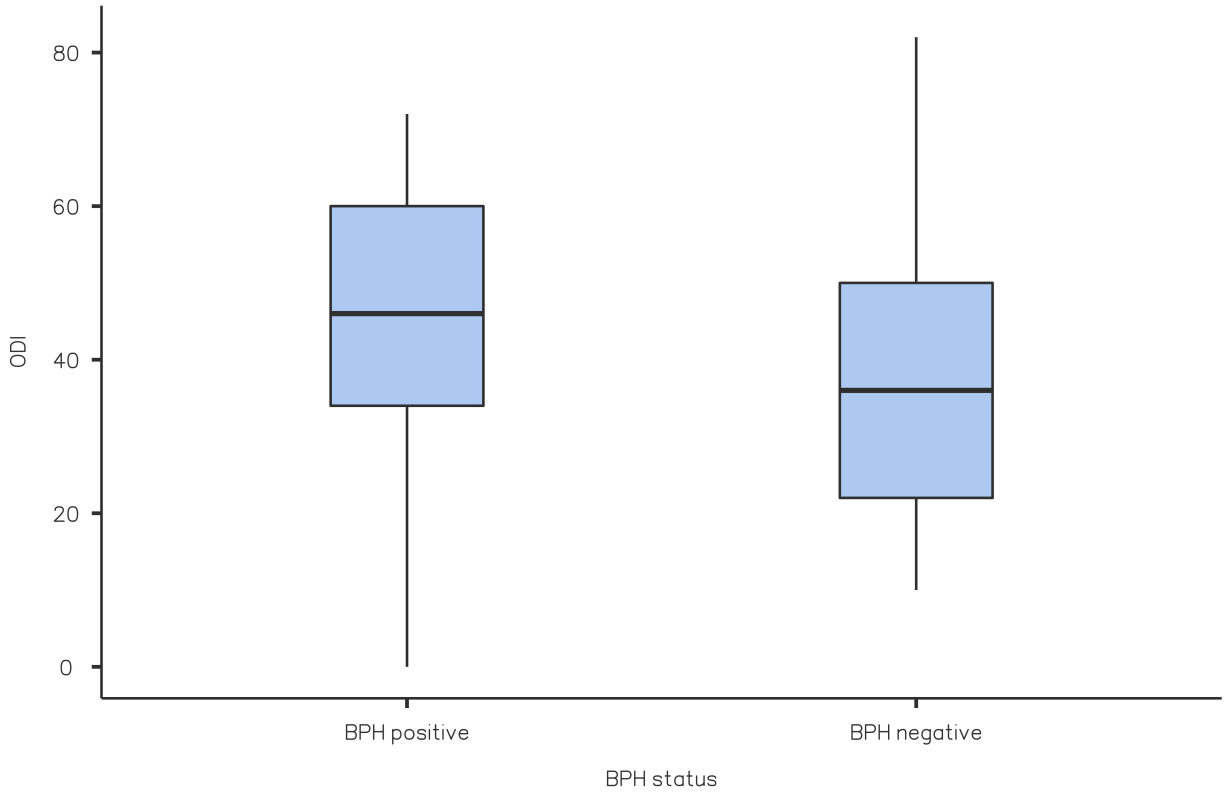

FIGURE 2. Box plot graphic of ODI. ODI: Oswestry disability index; BPH: benign prostatic hyperplasia.

TABLE 1. Comparison of VAS and ODI scores between patients with or without BPH.

	BPH+		BPH−		*p*
	Median	25–75%	Median	25–75%	
VAS	5.5	2.5–8.0	5.0	3.0–7.0	0.834
	Mean	SD	Mean	SD	
ODI	46.1	18.0	41.4	18.2	0.360

Abbreviations: VAS: Visual analog scale; ODI: Oswestry disability index; BPH: benign prostatic hyperplasia; SD: standard deviation.

TABLE 2. Comparison of clinical scores of patients with and without BPH drug use.

	BPH medication (n = 14)		Without medication (n = 35)		*p*
	Median	25–75%	Median	25–75%	
VAS	5.5	4.25–7.0	5.0	2.0–8.0	0.471
	Mean	SD	Mean	SD	
ODI	49.3	14.4	41.2	19.1	0.150

Abbreviations: VAS: Visual analog scale; ODI: Oswestry disability index; BPH: benign prostatic hyperplasia; SD: standard deviation.

TABLE 3. Comparison of clinical scores of BPH patients with and without BPH drug use and patients without BPH.

	With medication (n = 14)		Without medication (n = 8)		Without BPH (n = 27)		*p*
	Median	25–75%	Median	25–75%	Median	25–75%	
VAS	5.5	4.2–7.0	5.0	0–8.0	5.0	3.0–7.0	0.868
	Mean	SD	Mean	SD	Mean	SD	
ODI	49.3	14.4	40.5	23.1	41.4	18.2	0.346

Abbreviations: VAS: Visual analog scale; ODI: Oswestry disability index; BPH: benign prostatic hyperplasia; SD: standard deviation.

4. Discussion

Pain perception and discomfort in humans are influenced by various factors such as genetic, educational, cultural, environmental, and gender disparities; however, limited studies have focused on gender differences in pain related to neuro claudication, especially in cases of lumbar spinal stenosis [5, 11]. This study aims to investigate the impact of BPH on pain intensity in middle-aged to older men with severe lumbar stenosis, which could be a potentially explanatory structural variation. Our hypothesis is that BPH, as a possible structural difference, could be linked to reduced pain intensity in men with high-grade lumbar stenosis, an aspect that has not been extensively explored before. The key finding of this study is that although patients taking BPH medication showed slightly worse ODI scores, there was no statistically significant difference observed in both groups. Ultimately, there is no functional difference between BPH patients using medication and those who are not, as well as LSS patients without BPH.

This study acknowledges both limitations and strengths. Recall bias is a significant limitation to consider, commonly observed in retrospective studies, especially when internally validating the study. This type of bias can lead to differential misclassification of ODI and VAS scores among study participants. However, the presence of specific and easily remembered symptoms, such as neurogenic claudication in LSS and the relatively straightforward ODI scoring, helps minimize this bias. A notable strength of the study is the examination of the potential correlation between lumbar spinal stenosis symptom severity and the presence or use of BPH medication, particularly in men. However, the limited sample size due to the rarity of these two conditions poses a challenge. Additionally, mechanical factors such as spinal alignment disorders accompanying LSS were not evaluated.

The prostate gland, responsible for semen fluid formation, is located just below the bladder and surrounds the area through which urine passes from the bladder to the penis. Changes in the prostate gland typically begin in one's forties, with volume enlargement occurring in the fifties. The use of alpha-blockers and 5α-reductase inhibitors (5ARI) in pharmacological treatment may lead to adverse side effects. Notably, sexual dysfunction has been associated with decreased neuroactive steroid production. A study revealed lower total testosterone and dihydrotestosterone levels, along with elevated CSF-E2 (Cerebrospinal Fluid-Estrogen 2) levels, in patients using a combination of drugs [8]. This study's premise is based on the reduced levels of these potent neurosteroids in actively medicated BPH patients, known for their strong analgesic effects in the posterior spinal column. However, with mean ODI scores exceeding 40 in both groups, indicating that pa-

tients with severe lumbar spinal stenosis symptoms are not seeking surgical intervention, it highlights the need to carefully examine data related to the limited sample size and other prognostic factors.

The narrowing of intervertebral disc height, hypertrophy of facet joints, and calcification or thickening of the ligamentum flavum collectively lead to spinal nerve compression and reduced epidural venous return, thereby increasing vascular pressure. Additionally, factors such as spinal nerve edema ratio on magnetic resonance myelography, motor unit number index, altered CSF dynamics, and vascular narrowing or obstruction have been implicated in the development of intermittent neurogenic claudication and radicular pain [3, 12–15]. Coronel and Schumacher, in their research on the pathophysiology of this condition, demonstrated that allopregnanolone, a derivative of progesterone synthesized through an enzymatic cycle starting from cholesterol in the spinal cord with 5ARI, shows analgesic and specific neuroprotective effects [15, 16]. It is hypothesized that the use of 5ARI does not diminish the analgesic effect but rather compromises its neuroprotective properties, leading to an increase in the analgesic activities of neuroactive steroids with GABA (Gamma-Aminobutyric Acid)-mediated transmission promotion, while decreasing the neuroprotective effect in in patients using combined drugs for BPH [17].

We observed that patients using BPH medications had slightly worse ODI scores compared to non-users or those without BPH, although this difference did not reach statistical significance. Based on the available data, this could be attributed to the inhibition of 5α-reductase and the subsequent decrease in neural protective efficacy. 5ARIs may also contribute to the impairment of ODI scores through their systemic effects. In addition to known side effects such as erectile dysfunction, gynecomastia, cardiac failure, depression, prostate cancer, metabolic syndrome with altered metabolic function, lower testosterone levels, increased A1c, and altered lipid profiles could particularly impact functional capacity in these patients [18].

5. Conclusions

Our initial hypothesis, suggesting a higher incidence of complaints associated with lumbar spinal stenosis (LSS) in male LSS patients undergoing treatment for benign prostatic hyperplasia (BPH) due to a reduction in intrathecal levels of neuroprotective steroids resulting from BPH treatment, did not hold true based on statistical analysis. We observed that functional limitations were comparable in BPH patients using medication and those who were not. Future Phase 4 clinical trials or experimental studies involving a large number of patients and interdisciplinary collaboration between urology and neurology to explore the neurosteroid content of cerebrospinal fluid (CSF) and CSF dynamics will offer a more precise elucidation of the relationship between these two conditions.

ABBREVIATIONS

LSS, lumbar spinal stenosis; BPH, benign prostatic hyperplasia; ODI, Oswestry disability index; MRI, Magnetic Resonance imaging; VAS, Visual analog scale; CSF, Cerebrospinal fluid; BMI, Body mass index; 5ARI, 5α-reductase inhibitors.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

ÖNK and İD—Conceptualization; Formal Analysis. AT and FG—Investigation; Methodology. ÖNK—Project Administration. FG—Writing-Original Draft. AT and İD—Writing-Review & Editing.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This research has been approved by Toros University (Mersin-Turkey) ethics committee (Protocol no: 104). Informed consent was obtained from all individual participants included in the study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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