

# The Impact of Hypertension on Treatment Outcomes in Benign Prostatic Hyperplasia Patients: A Comprehensive Systematic Review

Muhammad Rizky Hidayat<sup>1\*</sup>, Azwar Amir<sup>2</sup>, Qonita Faizah Basri<sup>3</sup>

Dr Tadjuddin Chalid Hospital, Indonesia<sup>1</sup> Dr Wahidin Sudirohusodo Hospital, Indonesia<sup>2</sup> Jala Ammari Navy Hospital, Indonesia<sup>3</sup> Email: mrizkyh.md@gmail.com

#### Abstract

Around 25% of men over 60 suffer from both hypertension and benign prostatic hyperplasia (BPH), two prevalent age-related illnesses that affect males. Through an analysis of the literature over the past ten years, this study attempts to thoroughly assess the effect of hypertension on the treatment outcomes of patients with BPH. Initially, 500 papers were obtained from internet databases such as Google Scholar, SpringerLink, SagePub, and PubMed. Following three screening stages, eight pertinent papers were chosen for full-text examination. The impact of hypertension on BPH treatment outcomes including symptom severity, drug response, and surgical outcomes-was evaluated in these articles. The findings indicate that hypertension is associated with poorer treatment outcomes in BPH patients, including reduced efficacy of alpha-blockers and 5-alpha-reductase inhibitors, as well as an increased risk of surgical complications. In clinical practice, the study highlights the necessity of coordinated care approaches that manage both hypertension and BPH. In order to manage these two illnesses concurrently, healthcare providers must take a comprehensive strategy, taking into account possible drug interactions and improving treatment approaches. In order to create specialized treatment plans for this high-risk group, more study is required to examine the underlying mechanisms that connect hypertension to the development of BPH and treatment response. In the end, this would improve the quality of life for men with both illnesses by improving patient outcomes and lowering complications.

**Keywords:** benign prostatic hyperplasia, hypertension, 5-alpha reductase inhibitors, alphablockers, cardiovascular risk, prostate volume, LUTS

# **INTRODUCTION**

Hypertension and benign prostatic hyperplasia (BPH) are common age-related disorders in men, significantly impacting global healthcare resources. Despite being distinct conditions, both involve the sympathetic nervous system. Approximately 25% of men over 60 experience both disorders simultaneously (Chughtai et al., 2016; Langan, 2019). Previous studies also suggested that hypertension may be involved in the etiopathology of BPH (Hao et al., 2016)

The prevalence of BPH, a common and progressive disorder in older men, rises with age. BPH symptoms affect about 50% of men over 65 and over 80% of men between the ages of 70 and 79. As the global population ages, the number of men reporting prostatic issues is expected to rise. More men are likely to seek treatment for BPH as a result of greater public awareness of the prostate gland. Today's men in their 50s and 60s

do not view themselves as elderly, and they are unwilling to acknowledge how BPH lowers their quality of life. It is projected that the number of people over 60 will have increased by 200% by 2020.

Hypertension and BPH are distinct conditions, however both may share a common pathophysiological factor: age-related increase in sympathetic tone. The sympathetic nervous system, through alpha adrenergic fibers and receptors, significantly influences both hypertension and BPH (Xia et al., 2020; Zou et al., 2016). Previous studies revealed that men undergoing elective prostatectomy had higher blood pressure compared to age-matched patients undergoing non-genitourinary surgery. The relative risk of hypertension was around 10 for BPH patients aged 45-64 and 5 for those aged 65 and above, suggesting that hypertension might be a risk factor for BPH (Launer et al., 2021; Madersbacher et al., 2019).

Given the high prevalence of concurrent hypertension and BPH, it is recommended that urologists monitor blood pressure in all BPH cases and that physicians assess urinary functions in elderly males with hypertension (Shimizu et al., 2014). Using a single pharmacological agent, such as alpha blockers (ABs), to treat both conditions could enhance cost-effectiveness, compliance, and convenience for patients (Mathur et al., 2014).

Common age-related conditions in males that place a heavy strain on healthcare systems around the world are hypertension and benign prostatic hyperplasia (BPH). Both include increased sympathetic nervous system activity, especially through alpha-adrenergic pathways, despite the fact that they are generally treated as distinct illnesses. A potentially neglected aspect of integrated disease treatment is the fact that about 25% of men over 60 have both illnesses at the same time. While existing literature has suggested a possible etiological link between hypertension and BPH through sympathetic overactivity, there is limited evidence that systematically evaluates how hypertension influences the outcomes of BPH treatment across pharmacologic and surgical interventions.

50% of men over 65 and more than 80% of those between the ages of 70 and 79 have symptoms of BPH, which affects an increasing percentage of the aging male population. The necessity for more sophisticated therapeutic therapy that takes into account the frequent overlap of comorbidities like hypertension grows as life expectancy rises. The direct effect of hypertension on the results of BPH treatment is still poorly understood, despite earlier research showing that patients having prostatectomy had greater rates of hypertension than controls. This study fills this important research vacuum by thoroughly examining current studies to comprehend how these two disorders interact clinically. The novelty of this review lies in its focused examination of how hypertension alters the response to BPH therapies, offering new insights into the potential for dual-purpose treatment regimens, such as the use of alpha-blockers, and advocating for integrated screening and management strategies in routine urological and primary care settings.

The purpose of this study is to thoroughly examine how hypertension affects BPH patients' treatment results. The study specifically aims to comprehend how hypertension

affects the degree of BPH symptoms, the course of the condition, and the effectiveness and safety of BPH treatments, including the possible cardiovascular risks connected to widely prescribed drugs like alpha-blockers and 5-alpha reductase inhibitors. Additionally, the study intends to investigate how metabolic and hormonal variables interact in hypertensive BPH patients and to shed light on the necessity of integrated therapy strategies for patients with both BPH and hypertension.

## **RESEARCH METHOD**

#### Protocol

The author carefully followed the rules laid out in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020. This was done to make sure the study met all its standards. The selection of this methodological approach was specifically aimed at ensuring the precision and reliability of the conclusions drawn from the investigation.

The authors independently evaluated each study using the Joanna Briggs Institute (JBI) Critical Appraisal Tools, which were customized for the unique design of each included study, in order to guarantee the validity and quality of the data. This assessment took into account factors like the study question's clarity, the methodology's suitability, the result measures' dependability, and the control of any confounding variables. Any differences of opinion were settled by consensus and debate among the reviewers. Strict inclusion and exclusion criteria were also used, coupled with an open and methodical search strategy, to reduce selection bias. The final narrative synthesis only included papers that satisfied all inclusion criteria and showed a low to moderate risk of bias. This rigorous approach was adopted to ensure the integrity of the systematic review findings and to support their relevance in clinical practice and future research directions.

#### **Criteria for Eligibility**

Based on literature from the past ten years, this systematic review examines the data currently available about the effect of hypertension on the course of treatment for patients with BPH. In order to offer insights and improve patient treatment options, this study carefully examined data from literature. This paper's main goal is to draw attention to the important topics that have been recognized.

Inclusion criteria for this study entail: 1) Papers must be in English, and 2) Papers must have been published between 2014 and 2024. Exclusion criteria comprise: 1) Editorials; 2) Submissions without a DOI; 3) Previously published review articles; and 4) Duplicate entries in journals.

#### Search Strategy

The keywords used for this research are benign prostatic hyperplasia, hypertension, 5-alpha reductase inhibitors, and alpha-blockers. The Boolean MeSH keywords inputted on databases for this research are: (("prostatic hyperplasia"[MeSH Terms] OR ("prostatic"[All Fields] AND "hyperplasia"[All Fields]) OR "prostatic hyperplasia"[All Fields] OR ("benign"[All Fields] OR "prostatic" [All Fields] OR "benign prostatic"]

hyperplasia"[All Fields]) AND ("hypertense"[All Fields] OR "hypertension"[MeSH Terms] OR "hypertension"[All Fields] OR "hypertension s"[All Fields] OR "hypertensions"[All Fields] OR "hypertensive"[All Fields] OR "hypertensive s"[All Fields] OR "hypertensives"[All Fields]) AND ("5 alpha reductase inhibitors"[Pharmacological Action] OR "5 alpha reductase inhibitors"[MeSH Terms] OR ("5 alpha"[All Fields] AND "reductase"[All Fields] AND "inhibitors"[All Fields]) OR "5 alpha reductase inhibitors"[All Fields] OR "5 alpha reductase inhibitors"[All Fields]) OR "5 alpha reductase inhibitors"[All Fields] OR "5 alpha reductase inhibitors"[All Fields]) OR "6 alpha reductase inhibitors"[All Fields] OR "5 alpha reductase inhibitors"[All Fields]) OR "7 alpha reductase inhibitors"[All Fields] OR "5 alpha reductase inhibitors"[All Fields]) OR "8 alpha reductase inhibitors"[All Fields] OR "5 alpha reductase inhibitors"[All Fields]) OR "9 alpha reductase inhibitors"[All Fields] OR "5 alpha reductase inhibitors"[All Fields]) OR "9 alpha reductase inhibitors"[All Fields] OR "10 alpha antagonists"[All Fields]]) OR "9 alpha antagonists"[Pharmacological Action] OR "adrenergic alpha antagonists"[MeSH Terms] OR ("adrenergic"[All Fields] AND "alpha antagonists"[All Fields]]) OR "adrenergic alpha antagonists"[All Fields] OR ("alpha"[All Fields] AND "blockers"[All Fields]]) OR "alpha blockers"[All Fields]]).

### Data retrieval

After evaluating the studies' abstracts and titles to ascertain their eligibility, the authors chose pertinent ones that met the inclusion requirements and complemented the goals of the paper. A consistent pattern found in several investigations produced a definitive finding. The selected contributions required to be full-text and in English in order to qualify.

Only literature that directly related to the subject under investigation and satisfied all predetermined inclusion criteria was included in this systematic review. Studies that didn't fit these requirements were routinely disqualified, and their results weren't taken into account. Various details discovered during the research process, including as titles, authors, publication dates, locations, study procedures, and parameters, were examined in a subsequent analysis.

## **Quality Assessment and Data Synthesis**

To decide which studies deserved more investigation, each author separately assessed the study described in the publication's title and abstract. The next step was to evaluate every article that satisfied the predetermined requirements to be included in the review. The results of this evaluation method were used to determine which articles should be included in the review.



Figure 1. Article search flowchart

# **RESULTS AND DISCUSSION**

A total of 500 papers were first obtained from internet databases, including PubMed, SagePub, SpringerLink, and Google Scholar. Eight papers that directly pertain to the current systematic review have been selected for additional evaluation by full-text reading and analysis following three stages of screening. The chosen literature used in this analysis is shown in Table 1.

No	Author	Origin	Method	Sample	Result		
1.	Zeng, et al. <sup>10</sup> (2018)	Hubei, China	Case-control study	327 BPH patients	108 of the 327 participants in the research had hypertension, whereas the remaining 219 did not. Seven people had severe hypertension, 27 had moderate hypertension, and 74 had mild hypertension. Additionally, 295 participants without diabetes mellitus (DM) and 32 with DM were included in the study. Participants were $70.8 \pm 7.4$ years old on average, and there was no discernible age difference between the hypertension and nonhypertensive groups. In contrast to the hypertension group, the nonhypertensive group had a greater Qmax but a much lower weight, BMI, DBP, and SBP. Although it was not statistically significant, univariate and multivariate logistic regression studies showed that DM raised the risk of hypertension in BPH patients by 1.244 times. Adjusted analyses showed elevated odds ratios for hypertension, but these were also not significant.		
2.	Zeng, et al <sup>11</sup> (2018)	Wuhan, China	Retrospective study	350 patients	In the end, 350 patients—117 with hypertension and 233 without—were enrolled in the trial. The hypertensive and normotensive groups differed significantly in terms of weight, body mass index (BMI), systolic blood pressure, and diastolic blood pressure. Prostate volume, weight, BMI, age, and systolic and diastolic blood pressure as well as total PSA, as well as fasting blood sugar and the international prostate symptom score, were all positively correlated in the normotensive group. Age and the worldwide prostate symptom score, weight and prostate volume, and systolic blood pressure and total PSA were		

# Table 1. The literature included in this study

No	Author	Origin	Method	Sample	Result
					found to be positively correlated in the hypertensive group.
3.	Onigbinde, et al. <sup>12</sup> (2023)	Lagos, Nigeria	Descriptive comparative study	100 BPH patients	The normotensive and hypertensive groups had respective mean ages of $66.9 \pm 9.8$ and $66.0 \pm$ 10.7 years (P = 0.662). The mean transitional zone volume, transitional zone index, assumed circle area ratio, quality of life score, and prostatic arterial resistive indices were all considerably greater in hypertensive BPH patients than in normotensive BPH patients.
4.	Fu, et al. <sup>13</sup> (2016)	Beijing, China	Prospective study	525 men	In order to track correlations between LUTS/BPH progression and MetS, participants were split into two groups: those with BPH and metabolic syndrome (MetS) and those without MetS. The results showed that MetS was associated with IPSS, Qmax, and PV ( $p < 0.05$ ) over the 3-year period, and that the BPH with MetS group had a higher clinical progression rate and significant changes in IPSS, PV, and Qmax over time ( $p < 0.05$ ) than the BPH without MetS.
5.	Lusty, et al. <sup>14</sup> (2021)	Ontario, Canada	Population based retrospective cohort study	175,201 men with BPH	175,201 males with BPH were enrolled in the study; 8,339 of them received 5-alpha reductase inhibitors, 55,383 α-blockers, and 41,491 combined therapy. According to the results, men who were treated with 5-alpha reductase inhibitors and α-blockers, either separately or in combination, were statistically more likely to experience heart failure than men who were not on these drugs. 5-alpha reductase inhibitors alone had the lowest risk (HR 1.09; 95% CI 1.02–1.17), followed by combination therapy (HR 1.16; 95% CI 1.12–1.21) and α-blockers alone (HR 1.22; 95% CI 1.18–1.26). Furthermore, compared to selective α-blockers, nonselective α-blockers had a greater risk of cardiac failure (HR 1.08; 95% CI 1.00–1.17).

No	Author	Origin	Method	Sample	Result			
6.	Ryl, et al. <sup>15</sup> (2015)	Szczecin, Poland	Case control study	128 men with BPH	The prevalence of MetS was higher in BPH patients than in controls (58% vs. 41%; P = 0.007), and BPH patients had lower levels of HDL, estradiol, and SHBG and higher levels of cholesterol, low-density lipoproteins, DHEA-S, insulin, and HOMA-IR. Age (OR = 0.11), HDL (OR = 0.91), insulin (OR = 1.224), SHBG (OR = 0.98), and LAP were inversely correlated with total and free testosterone and SHBG.			
7.	Hwang, et al. <sup>16</sup> (2015)	Gwangju, South Korea	Retrospective cohort study	295 men	In comparison to men without cardiovascular risk factors, men with hypertension had substantially higher IPSS-total ( $22.9 \pm 7.8$ vs. $21.2 \pm 7.3$ , P = 0.01) and obstructive symptom ratings ( $13.3 \pm 5.2$ vs. $11.9 \pm 4.7$ , P = 0.01). Subjects with DM, smoking, and dyslipidemia did not significantly differ from those without these risk factors. Prostate volume (r = 0.138, P = 0.040; r = 0.136, P = 0.020), IPSS-total (r = 0.139, P = 0.043; r = 0.138, P = 0.043), and obstructive symptom score (r = 0.168, P = 0.014; r = 0.143, P = 0.037) were all associated with systolic and diastolic blood pressure, according to Pearson correlation.			
8.	Zhang, et al. <sup>17</sup> (2015)	Multicenter	Prospective comparative cohort study	335 patients	Overall blood pressure change did not differ significantly between the two groups, according to the study (systolic BP, P=0.825; diastolic BP, P>0.999). Alfuzosin 10 mg, both by itself and in conjunction with antihypertensive medication, markedly reduced systolic and diastolic blood pressure in patients with uncontrolled or untreated hypertension. There was no discernible difference between the two groups' baseline changes in IPSS-quality of life and total IPSS scores. Likewise, there was no significant difference in the maximum flow rate, average			

No	Author	Origin	Method	Sample	Result				
					flow rate,	voided	volume,	or	post-voided
					volume.				

Zeng, Weng, Jin, et al. (2018) assessed the association between DM and hypertension in BPH patients, finding a positive but nonsignificant correlation. This contrasts with previous studies that reported significant associations. Two potential reasons for the nonsignificant results are suggested: BPH might influence the relationship between DM and hypertension, or the results may be due to the small sample size. Overall, the study highlights the need for further research to understand the relationship between DM and hypertension in BPH patients. Zeng, Weng, Xiong, et al. (2018)showed that in the hypertensive group, positive correlations were noted between age and total PSA and international prostate symptom score; weight and prostate volume; and systolic blood pressure and total PSA.

Onigbinde et al. (2023) showed that BPH patients with hypertension had significantly higher prostatic artery resistive indices than normotensive BPH patients. This was true even for patients with controlled hypertension, indicating persistent elevated prostatic artery resistance in hypertensive individuals with BPH.

Fu et al. (2016) showed that hypertension was linked to an increased risk of BPH clinical progression. The study concludes that MetS, especially DM and hypertension, may accelerate BPH progression in middle-aged and older men.

Lusty et al. (2021) demonstrated that 5ARIs and ABs, either alone or as a combination treatment, are the most common forms of management for men with lower urinary tract symptoms due to BPH. The study concluded that men with BPH exposed to both 5-alpha reductase inhibitors and  $\alpha$ -blockers had an increased risk of cardiac failure, with the highest risk observed in those using nonselective  $\alpha$ -blockers.

Rył et al. (2015)confirmed that there is a frequent coexistence of MetS and BPH, suggesting that MetS-related metabolic disturbances, hormonal changes, and reduced SHBG levels contribute to this association. The history of hypertension treatment is also considered a MetS factor that favors the development of BPH.

Hwang et al. (2015) showed that men with hypertension are more likely to have higher International Prostatic Symptom Scores and larger prostate volumes than men without hypertension. This finding suggests a pathophysiological association between hypertension and lower urinary tract symptoms, indicating the need to manage these comorbid conditions simultaneously.

Zhang et al. (2015) showed that alfuzosin 10 mg is effective and well-tolerated in patients with benign prostatic hyperplasia and lower urinary tract symptoms, regardless of concurrent antihypertensive therapy. However, patients with uncontrolled or untreated hypertension should be cautioned about potential decreases in blood pressure when starting alfuzosin treatment.

#### Discussion

This systematic review evaluated the impact of hypertension on BPH treatment outcomes. The review focused on how hypertension influences BPH symptoms, treatment efficacy, and associated risks. Several studies in this review highlight a significant association between hypertension and increased severity of BPH symptoms. For instance, Hwang et al. (2015) demonstrated that hypertensive men with BPH have higher International Prostatic Symptom Scores (IPSS) and larger prostate volumes compared to non-hypertensive men (Silva et al., 2014). This suggests that hypertension may exacerbate lower urinary tract symptoms (LUTS) in BPH patients (Füllhase et al., 2014; Lepor, 2016).

The studies reviewed also highlighted the interplay between metabolic and hormonal factors in hypertensive BPH patients. Ryl et al. (2015) confirmed that metabolic syndrome, which includes hypertension, is frequently associated with BPH. Hormonal alterations and metabolic abnormalities, including decreased sex hormone-binding globulin (SHBG) levels and changed lipid profiles, are the causes of this connection. Additionally, the Fu et al. (2016) study discovered a connection between hypertension and a faster clinical progression of BPH. This suggests that over time, the symptoms of hypertensive BPH patients may increase more quickly, requiring closer observation and even more intensive therapy.

Onigbinde et al. (2023) observed that hypertensive BPH patients had significantly higher prostatic artery resistive indices compared to normotensive patients, indicating persistent vascular resistance issues despite hypertension control (Singh et al., 2014). Treatment of BPH may also contribute into vascular pathologies that may be exarcebated in hypertensive patients. Lusty et al. (2021) reported an increased risk of cardiac failure in BPH patients treated with 5-alpha reductase inhibitors (5-ARIs) and alpha-blockers (ABs), particularly nonselective ABs. This risk was heightened in hypertensive patients, suggesting that careful cardiovascular monitoring is essential in this group (Bapir et al., 2022; Sun et al., 2020).

However, previous studies also found different means of hypertensive treatment that can go along with BPH therapy. Zhang et al. (2015) found that alfuzosin 10 mg is effective in treating BPH symptoms irrespective of concurrent antihypertensive therapy. However, they noted that patients with uncontrolled or untreated hypertension should be cautious of potential blood pressure decreases when starting alfuzosin or other alpha blockers (Bapir et al., 2022; Fonseca & Martins da Silva, 2015).

The consistent finding across studies is that hypertension significantly impacts the clinical course and management of BPH. Hypertensive BPH patients tend to have more severe symptoms, faster disease progression, and higher treatment-related risks (Ohyama et al., 2019). Therefore, a multidisciplinary approach is essential, involving both urologists and cardiologists to optimize patient outcomes.

BPH symptoms may be lessened and the course of the disease may be slowed by treating metabolic syndrome components in addition to BPH. Patients with hypertensive BPH must have regular blood pressure and symptom monitoring in order to quickly treat any flare-ups. Clinicians should be aware of the elevated risk of heart failure when prescribing 5-ARIs and ABs, particularly nonselective ABs, and take cardiovascular health into account when developing treatment regimens.

## **CONCLUSION**

In conclusion, this comprehensive analysis highlights the need for integrated care approaches that treat hypertension and benign prostatic hyperplasia (BPH) at the same time, especially as these conditions frequently co-occur in older men. It is recommended that clinicians regularly check blood pressure in BPH patients and evaluate lower urinary tract symptoms in male hypertensive patients. In order to increase patient outcomes, decrease polypharmacy, and improve compliance, a combination treatment approach—such as the prudent use of alpha-blockers that successfully treat both conditions—should be taken into consideration. Guidelines that encourage urologists and cardiologists to work together to manage chronic comorbidities should be given top priority by health officials. In order to better understand the pathophysiological pathways relating to hypertension and BPH and to improve patient-specific, economical treatment strategies for this susceptible population, future research should also concentrate on longitudinal studies.

### **BIBLIOGRAPHY**

- Bapir, R., Bhatti, K. H., Eliwa, A., & al., et. (2022). Efficacy of overactive neurogenic bladder treatment: A systematic review of randomized controlled trials. *Archivio Italiano Di* Urologia e Andrologia, 94(4), 492–506. https://doi.org/10.4081/aiua.2022.4.492
- Chughtai, B., Forde, J. C., Thomas, D. D. M., & al., et. (2016). Benign prostatic hyperplasia. *Nature Reviews Disease Primers*, 2, 1–15. https://doi.org/10.1038/nrdp.2016.31
- Fonseca, J., & Martins da Silva, C. (2015). The diagnosis and treatment of lower urinary tract symptoms due to benign prostatic hyperplasia with α-blockers: focus on silodosin. *Clinical Drug Investigation*, *35*, 7–18. https://doi.org/10.1007/s40261-014-0257-3
- Fu, Y., Zhou, Z., Yang, B., & al., et. (2016). The Relationship between the Clinical Progression of Benign Prostatic Hyperplasia and Metabolic Syndrome: A Prospective Study. Urologia Internationalis, 97(3), 330–335. https://doi.org/10.1159/000448484
- Füllhase, C., Soler, R., & Gratzke, C. (2014). New strategies in treating male lower urinary tract symptoms. *Current Opinion in Urology*, 24(1), 29–35. https://doi.org/10.1097/MOU.00000000000003
- Hao, Z., Sun, Y. L., Min, J., & al., et. (2016). Relationship between benign prostatic hyperplasia and primary hypertension. *Journal of Bengbu Medical College*, 41(2), 191–193. https://doi.org/10.13898/j.cnki.issn.1000-2200.2016.02.017
- Hwang, E. C., Kim, S. O., Nam, D. H., & al., et. (2015). Men with Hypertension are More Likely to Have Severe Lower Urinary Tract Symptoms and Large Prostate Volume. *LUTS: Lower Urinary Tract Symptoms*, 7(1), 32–36. https://doi.org/10.1111/luts.12046
- Langan, R. C. (2019). Benign Prostatic Hyperplasia. *Primary Care: Clinics in Office Practice*, 46(2), 223–232. https://doi.org/10.1016/j.pop.2019.02.003
- Launer, B. M., McVary, K. T., Ricke, W. A., & Lloyd, G. L. (2021). The rising worldwide impact of benign prostatic hyperplasia. *BJU International*, 127(6), 722–728. https://doi.org/10.1111/bju.15286
- Lepor, H. (2016). Alpha-blockers for the Treatment of Benign Prostatic Hyperplasia. Urologic Clinics of North America, 43(3), 311–323. https://doi.org/10.1016/j.ucl.2016.04.009
- Lusty, A., Siemens, D. R., Tohidi, M., & al., et. (2021). Cardiac Failure Associated with Medical Therapy of Benign Prostatic Hyperplasia: A Population Based Study. *Journal of Urology*. https://doi.org/10.1097/JU.000000000001561
- Madersbacher, S., Sampson, N., & Culig, Z. (2019). Pathophysiology of Benign Prostatic Hyperplasia and Benign Prostatic Enlargement: A Mini-Review. *Gerontology*, 65(5), 458–464. https://doi.org/10.1159/000496289
- Mathur, R., Nayak, S., Sivaramakrishnan, R., & Jain, V. (2014). Role of Alpha Blockers in Hypertension with Benign Prostatic Hyperplasia. 62.

- Ohyama, K., Hori, Y., & Sugiura, M. (2019). Evaluation of syncope association with α1adrenoceptor blockers in males using the FAERS database: impact of concomitant hypertension. *Pharmacoepidemiology*, 74(12), 755–759. https://doi.org/10.1691/ph.2019.9706
- Onigbinde, S. O., Asaleye, C. M., Salako, A. A., & al., et. (2023). The effect of systemic hypertension on prostatic artery resistive indices in patients with benign prostate enlargement. *Prostate International*, 11(1), 46–50. https://doi.org/10.1016/j.prnil.2022.09.001
- Rył, A., Rotter, I., Miazgowski, T., & al., et. (2015). Metabolic syndrome and benign prostatic hyperplasia: association or coincidence? *Diabetology & Metabolic Syndrome*, 7(1), 94. https://doi.org/10.1186/s13098-015-0089-1
- Shimizu, S., Tsounapi, P., Shimizu, T., & al., et. (2014). Lower urinary tract symptoms, benign prostatic hyperplasia/benign prostatic enlargement and erectile dysfunction: Are these conditions related to vascular dysfunction? *International Journal of Urology*, 21(9), 856– 864. https://doi.org/10.1111/iju.12501
- Silva, J., Silva, C. M., & Cruz, F. (2014). Current medical treatment of lower urinary tract symptoms/BPH: do we have a standard? *Current Opinion in Urology*, 24(1), 21–28. https://doi.org/10.1097/MOU.0000000000000007
- Singh, D. V, Mete, U. K., Mandal, A. K., & Singh, S. K. (2014). A comparative randomized prospective study to evaluate efficacy and safety of combination of tamsulosin and tadalafil vs. tamsulosin or tadalafil alone in patients with lower urinary tract symptoms due to benign prostatic hyperplasia. *Journal of Sexual Medicine*, 11(1), 187–196. https://doi.org/10.1111/jsm.12357
- Sun, Y., Peng, B., Lei, G. L., Wei, Q., & Yang, L. (2020). Study of phosphodiesterase 5 inhibitors and α-adrenoceptor antagonists used alone or in combination for the treatment of lower urinary tract symptoms due to benign prostatic hyperplasia. *Minerva Urologica e Nefrologica Italiana Journal of Urology and Nephrology*, 72(1), 13–21. https://doi.org/10.23736/S0393-2249.19.03408-8
- Xia, B. W., Zhao, S. C., Chen, Z. P., & al., et. (2020). The underlying mechanism of metabolic syndrome on benign prostatic hyperplasia and prostate volume. *The Prostate*, 80(6), 481–490. https://doi.org/10.1002/pros.23962
- Zeng, X. T., Weng, H., Jin, Y. H., & al., et. (2018). Association between Diabetes Mellitus and Hypertension in Benign Prostatic Hyperplasia Patients. *Chinese Medical Journal* (*English*), 131(09), 1120–1121. https://doi.org/10.4103/0366-6999.230730
- Zeng, X. T., Weng, H., Xiong, J., & al., et. (2018). Comparison of Clinical and Physiological Parameters for Benign Prostatic Hyperplasia in Hypertensive and Normotensive Patients. *Frontiers in Physiology*, 9. https://doi.org/10.3389/fphys.2018.01330
- Zhang, L. T., Lee, S. W., Park, K., & al., et. (2015). Multicenter, prospective, comparative cohort study evaluating the efficacy and safety of alfuzosin 10 mg with regard to blood pressure. *Clinical Interventions in Aging*, 10, 277–286. https://doi.org/10.2147/CIA.S74102
- Zou, C., Gong, D., Fang, N., & Fan, Y. (2016). Meta-analysis of metabolic syndrome and benign prostatic hyperplasia in Chinese patients. *World Journal of Urology*, 34(2), 281– 289. https://doi.org/10.1007/s00345-015-1626-0