

Association of Lower Urinary Tract Symptoms and Benign Prostatic Enlargement in Patients with Hypertension

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Abstract

Development of hyperplastic nodules in the transition zone of the prostate is the characteristic of Benign prostatic enlargement (BPE). Men with hypertension have a high risk of severe lower urinary tract syndrome (LUTS). This retrospective cohort analytic study investigated the association between LUTS and BPE in hypertension patients. Subjects were BPE patients with primary hypertension who visited the urology clinic of Dr. Hasan Sadikin General Hospital Bandung that were sampled consecutively from 2017 to 2020. Three hundred and twenty-four patients from the urology department participated in the study. These patients were categorized into mild LUTS (IPSS 1-7) (n=37, 11.4%), moderate LUTS (IPSS 8-19) (n=169, 52.2%), and severe LUTS (IPSS 20-35) (n=118, 36.4%). A positive correlation ($r=0.761$, $p=0.000$) and weak positive correlation ($r=0.152$, $p=0.006$) were found between systolic blood pressure and prostate volume and between LUTS and systolic blood pressure, respectively. In addition, there was also a weak positive correlation between diastolic blood pressure and prostate volume ($r=0.065$, $p=0.245$) and LUTS ($r=0.015$, $p=0.784$). Thus, there is an association between hypertension and prostate enlargement and the severity of lower urinary tract symptoms.

Keywords: Benign prostate enlargement, hypertension, lower urinary tract symptoms

Introduction

The characteristic of benign prostatic enlargement (BPE) is the development of hyperplastic nodules in the transition zone of the prostate, which is also described as an enlargement of the whole prostate. BPE is a prevalent benign tumor among the middle-aged and elderly.¹ The prevalence of BPE at the age of 90 years ranges from 8 to 60%, increasing after the age of 40.² The exact incidence of BPE in Indonesia has not been studied; however, as an illustration, hospital prevalence from 1994 to 2013 was found to be 3,804 cases with an average patient age of 66.61 years at Dr. Cipto Mangunkusumo Hospital (RSCM). A similar average age of patients was obtained from the statistical results of Dr. Hasan Sadikin General Hospital Bandung, Bandung, which was 67.9 years old with a total of 718 cases from 2012-2016.³

Although BPE is not life-threatening, it could cause significant public health problems. The rapid growth of prostate tissue around the urethra will cause constriction or obstruction in the orifice of the urethra, which causes urinary tract-related symptoms, known as lower urinary tract symptoms (LUTS).⁴ This condition is commonly found in the elderly and often worsens their quality of life. LUTS is often becoming the outcome of BPE.^{5,6} LUTS is a likely diagnosed condition in the elderly population. In the United States, LUTS ranks as the fourth most common condition for elderly patients, after coronary artery disease (CAD), hyperlipidemia, and type 2 diabetes.⁶

Most treated LUTS patients (89% of patients in the UK and 79% in several other European countries) were admitted because of troubling symptoms.⁷ Moreover, LUTS also has serious complications, including acute urinary retention, urinary tract infections, acute renal insufficiency, and even kidney failure, which is very dangerous for the patient's life.⁸

LUTS is associated with various risk factors, including age, obesity, metabolic syndrome, race, diet, and cardiovascular disease.⁸ Hypertension or high blood pressure is a problem in developed

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and developing countries, including Indonesia. Hypertension is when the systolic blood pressure is more than 140 mmHg and diastolic blood pressure is more than or equal to 90 mmHg. Hypertension is categorized into two types, primary/essential and secondary hypertension. The etiology of primary hypertension is still unknown, while the etiologies for secondary hypertension include kidney disease/disorders, endocrine, and heart diseases. Hypertension often causes no symptoms, while persistently high blood pressure for a long time could cause complications. Therefore, hypertension should be identified early by regularly checking blood pressure.⁹

Based on a study conducted by Hwang et al.,⁹ men with hypertension have a high risk of having severe LUTS and explained that men with hypertension have a high IPSS score. The pathophysiology is an increase in sympathetic activity and alpha-1 adrenoreceptor activity. Hypertension causes vascular damage, resulting in resistance, then continued by prostate gland growth. This study aimed to investigate the association between LUTS and hypertension in BPE patients.

Methods

The population of this study was 324 patients from Urology Department in Dr. Hasan Sadikin General Hospital from January 2017 to December 2020. Patients were grouped into two categories based on their blood pressure: the hypertensive and non-hypertensive groups.

This was a retrospective cohort observational analytic study. The subjects were BPE patients in the urology clinic at Dr. Hasan Sadikin General Hospital Bandung who met the inclusion criteria and was not included in the exclusion criteria. The inclusion criteria were BPE patients at the urology clinic of Dr. Hasan Sadikin General Hospital Bandung who never consumed BPE (alpha-blocker, 5-alpha-reductase inhibitor) and hypertension medication; and approved to be included in this study. The exclusion criteria included; diagnosed BPE patients who get routine control; urology patients diagnosed with secondary hypertension, alcohol dependence, hyperthyroidism, and liver disease; BPE-diagnosed urology patients, either new or control patients, who have already taken BPE drugs; patients with other conditions or diseases related to LUTS symptoms (urethral strictures, bladder stones, urinary tract infections, urinary

tract cancer); and patients with severe cognitive impairment.

The study was written following STROBE. The research sample was taken by consecutive sampling. Data were taken from 2017 to 2020 and were analyzed using SPSS ver 26.0. Dr. Hasan Sadikin General Hospital Bandung Health Research Ethics Committee approved informed consent and ethical clearance with register number: LB.02.01/X.6.5/305/2020.

The normality test was carried out on numerical data with the Shapiro-Wilk test to assess whether the data were normally distributed or not. Based on the p-value, data including age, blood pressure, and body mass index were not normally distributed with a p-value <0.05. In this study, we obtained 32 (10%) patients with mild LUTS degrees (IPSS score 1–7), 170 (52.4%) patients with moderate LUTS degrees (8–19), and 122 (37.6%) patients with severe LUTS degrees. The correlation coefficients are interpreted between -1 to 0 and 0 to 1.

The International Prostate Symptom Score (IPSS) questionnaire comprises eight questions. Seven questions are about symptoms over the last month, and one question evaluates the quality of life. The seven questions of symptoms include frequency, urgency, intermittency, weak stream, incomplete emptying, nocturia, and straining. Each symptom is counted as 0 to 5, with a maximum of 35 points. To classify the severity, the total scores of each question were added. The severity includes mild - 0-7, moderate - 8-19, and severe - 20-35. The quality of life is evaluated from the eighth question, with a score of 0 to 6. Hypertension categories are explained in Table 1.

Results

This study obtained three hundred and twenty-four patients of the urology clinic. The median age was 67, with a median prostate volume of $48 \pm (35-65)$ mL, as shown in Table 2.

Blood pressure is divided into systolic and diastolic pressures. A correlation test of blood pressure to prostate volume and IPSS was performed. The result showed a positive correlation ($r=0.761, p=0.000$) between systolic blood pressure and prostate volume, which was statistically significant. The IPSS also showed a weak positive correlation ($r=0.152, p=0.006$) with systolic blood pressure. This study found a weak positive correlation between diastolic

Table 1 Blood Pressure Classification

Blood pressure Classification	Systolic Blood Pressure mmHg	Diastolic Blood Pressure mmHg
Normal	<120	and <80
Prehypertension	120-139	or 80-89
Stage 1 hypertension	140-159	or 90-99
Stage 2 hypertension	≥160	or ≥100

Table 2 Mean Age, Prostate Volume, and International Prostate Symptom Score (IPSS)

Variable	n	p-value
Age (Median ± IQR)	67 ± (61-74)	p=0.027
Prostate volume	48 ± (35-65)	p=0.000
IPSS (n (%))		
Mild	32 (10%)	
Moderate	170 (52.4%)	
Severe	122 (37.6%)	

blood pressure with prostate volume ($r=0.066$, $p=0.245$) and IPSS ($r=0.015$, $p=0.784$), but both were not statistically significant. (Table 3). Patients were then grouped into 2 categories based on blood pressure: the hypertensive and non-hypertensive groups. Based on this grouping, it was found that the hypertension group was dominated by patients with moderate LUTS complaints, as much as 53%. In the group with mild LUTS complaints, only 10.2% of patients were classified as hypertension, while in the group with severe LUTS complaints, the number of hypertensive patients was 36.7%. As many as 27.3% of patients with severe LUTS

were non-hypertensive patients (Table 4). Based on these findings, hypertension appears to play a role in the level of LUTS complaints ($p=0.001$).

The figure shows the distribution of systolic (blue) and diastolic (red) blood pressure data based on the total IPSS value (Figure 1). It appears that there is a positive relationship or correlation between the IPSS value with systolic and diastolic blood pressure, meaning that the increase in the total IPSS value causes an increase in the systolic and diastolic blood pressure values. The correlation of the total IPSS value obtained was weak with systolic blood pressure ($r=0.152$, $p=0.006$) and diastole ($r=0.015$, $p=0.784$) but

Table 3 Correlation of Blood Pressure with Prostate Volume And IPSS

Variable	Systolic blood pressure		Diastolic blood pressure	
	Spearman Correlation	P-value	Spearman Correlation	P-value
Prostate volume	0.761	0.000	0.065	0.245
Total IPSS	0.152	0.006	0.015	0.784

Table 4 Distribution of LUTS severity between Hypertensive and Non-Hypertensive Patients

	Hypertensive (n/%)	Non-hypertensive (n/%)
Mild LUTS	32 (10.2)	5 (45.5)
Moderate LUTS	166 (53)	3 (27.3)
Severe LUTS	115 (36.7)	3 (27.3)

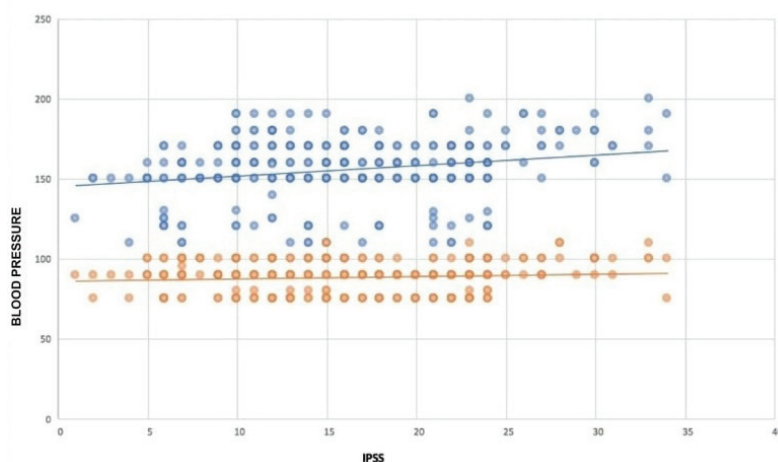


Figure Scatter Plot of Blood Pressure Correlation and IPSS

not statistically significant.

Discussion

Hwang et al.⁹ determined that hypertension, diabetes, and dyslipidemia were categorized as risk factors for cardiovascular disease. From those factors, it is known that hypertension has a significant difference in IPSS, especially in obstructive symptoms, compared to the group without symptoms. Similar to this result, there is a positive relationship or correlation between the IPSS value and systolic and diastolic blood pressure, meaning that the increase in the total IPSS value causes an increase in the systolic and diastolic blood pressure values in this study. Many studies have investigated factors causing filling and urination symptoms, such as age, physical status, psychiatric factors, lifestyle, socioeconomic status, and metabolic factors. This result was also supported by the study conducted by Güven et al.,¹⁰ which evaluated the relationship between hypertension and LUTS.

The role of hypertension in the pathogenesis of BPH is significant, mainly from the dynamic and static components. One study has shown that hypertension is associated with a high prevalence of lower urinary tract symptoms (LUTS).⁹ In our study, there were 32 (10%) patients with mild LUTS (IPSS score 1-7), 170 (52.5%) patients with moderate LUTS degrees (8-19), and 122 (37.7%) patients with severe LUTS degrees. There are anthropometric risk factors for hypertension; higher odds of hypertension were

found in patients who are overweight, obese, and with abdominal/central obesity. Risk factors, including gender, age, occupation, marital status, tobacco use, abdominal/central obesity, and BMI, were significantly associated with hypertension. Similar to the results of this study, Zeng et al.¹¹ conducted a study to determine the risk factors for BPH. The study found that African-American men with a history of hypertension were 1.76 times more likely to develop moderate to severe LUTS symptoms (OR=1.76 95% CI=1.26-2.45) and moderate to severe obstructive symptoms of LUTS (OR=1.76, 95% CI=1.20-2.58). Also, the subjects had twice the higher risk of having moderate to severe irritative symptoms of LUTS (OR=2.10.95 % CI=1.54-2.86). According to the National Health and Nutrition Examination Survey (NHANES III), it was stated that men with a history of hypertension had an increased risk factor for LUTS-related BPH than men without a history of hypertension (OR=1.76, 95% CI=1.20-2.59).¹⁰

Results of this study found that the hypertension group was dominated by patients with moderate LUTS complaints, as much as 53%. In the group with mild LUTS complaints, only 10.2% of patients were classified as hypertension, while in the group with severe LUTS complaints, the number of hypertensive patients was 36.7%. As many as 27.3% of patients with severe LUTS were non-hypertensive patients. Based on these findings, it appears that hypertension plays a role in the level of LUTS complaints ($p=0.001$). This result is similar to a study conducted by Fujimura, et al¹³,

which reported that men with hypertension did not have more severe LUTS compared to those without hypertension, but this study excluded patients with chronic and acute prostate and bladder diseases.¹³ On the contrary, Hwang et al.⁹ found that men with hypertension will get more severe symptoms of LUTS than those without hypertension. The study investigated the effect of hypertension on LUTS in BPH patients receiving α 1-adrenoceptor antagonist therapy and calculated the relationship between blood pressure and the severity of LUTS. The effect of age on the relationship between LUTS and hypertension was also found. From this study, it was stated that hypertension and LUTS play a role in pathophysiological pathways and increase sympathetic activity and α 1 adrenoceptor activity.¹⁰

This study showed a positive correlation ($r=0.761$, $p=0.000$) between systolic blood pressure and prostate volume, which was statistically significant. This result was supported by Guven et al.,¹⁰ which explained a positive correlation between systolic pressure and storage problems in LUTS, with the problem of urgency as the most significant complaint. Diastolic blood pressure showed a weak, non-statistically significant positive correlation with prostate volume ($r=0.065$, $p=0.245$) and IPSS ($r=0.015$, $p=0.784$).

A study by Zeng et al.¹³ showed a positive but insignificant association between hypertension and BPH. The study also revealed an insignificant association between hypertensive patients with BPH-related LUTS in the Chinese population. The differences and wide variations in LUTS definition, study population, survey methods, and data collection may cause this contradiction. Other cofactors, such as cardiovascular risk, also influenced the study results. This study found that men with hypertension experienced severe LUTS more often than men without hypertension. The limitation of this study is the small number of samples. Nevertheless, this study can be used as a preliminary study for a multicenter study or other comparative studies. Further studies are needed with a larger number of samples.

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D Stefanus & S Siregar: Association of Lower Urinary Tract Symptoms and Benign Prostatic Enlargement in Patients with Hypertension

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