

# HYPERTENSION EFFECTS ON THE DECREASED KIDNEY FUNCTION PROGRESIVITY IN BENIGN PROSTATIC HYPERPLASIA PATIENTS

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## ABSTRACT

**Objective:** A comprehensive knowledge about BPH and hypertension is needed to reduce morbidity and mortality in patients with decreased kidney function due to the two diseases. **Material & Methods:** This research used the observational analytics method with cross-sectional design. This research used secondary data from medical records of BPH patients in Bina Sehat Hospital and Paru Hospital from January 1<sup>st</sup> to December 1<sup>st</sup> 2019. **Results:** Comparative serum creatinine test results in hypertensive BPH patients with non-hypertensive BPH patients using the Mann Whitney test, obtained  $p = 0.000$ . Based on these results it can be concluded that there are significant differences in serum creatinine between hypertensive BPH patients and non-hypertensive BPH patients. Correlation test results using the Spearman test between serum creatinine with blood pressure systole and diastole all samples obtained each  $p = 0.000$   $r = 0.399$  for systolic blood pressure and  $p = 0.000$   $r = 0.337$  for diastole blood pressure. Based on these results it can be concluded that there is a significant correlation between serum creatinine with systolic and diastolic blood pressure of the patient. **Conclusion:** Hypertension will worsen the kidney function decline in BPH patients seen from an increase in serum creatinine.

**Keywords:** BPH, hypertension, kidney function, creatinine, blood pressure.

## ABSTRAK

**Tujuan:** Pengetahuan yang komprehensif tentang BPH dan hipertensi diperlukan untuk menurunkan angka kesakitan dan kematian pada pasien dengan penurunan fungsi ginjal akibat kedua penyakit tersebut. **Bahan & Cara:** Penelitian ini menggunakan metode analitik observasional dengan desain cross sectional. Penelitian ini menggunakan data sekunder dari rekam medis pasien BPH di RS Bina Sehat dan RS Paru dari tanggal 1 Januari sampai dengan 1 Desember 2019. **Hasil:** Hasil uji komparatif kreatinin serum pada penderita BPH hipertensi dengan penderita BPH non hipertensi menggunakan uji Mann Whitney didapatkan  $p = 0.000$ . Berdasarkan hasil tersebut dapat disimpulkan bahwa terdapat perbedaan kreatinin serum yang signifikan antara pasien BPH hipertensi dan pasien BPH non hipertensi. Hasil uji korelasi menggunakan uji Spearman antara kreatinin serum dengan tekanan darah sistol dan diastol semua sampel didapatkan masing-masing  $p = 0.000$ ,  $r = 0.399$  untuk tekanan darah sistolik dan  $p = 0.000$ ,  $r = 0.337$  untuk tekanan darah diastol. Berdasarkan hasil tersebut dapat disimpulkan bahwa terdapat hubungan yang signifikan antara kreatinin serum dengan tekanan darah sistolik dan diastolik pasien. **Simpulan:** Hipertensi akan memperburuk penurunan fungsi ginjal pada penderita BPH dilihat dari peningkatan kreatinin serum.

**Kata Kunci:** BPH, hipertensi, fungsi ginjal, kreatinin, tekanan darah.

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## INTRODUCTION

Benign Prostatic Hyperplasia (BPH) is defined as the abnormal growth of epithelial cells and prostate stromal cells in the transition zone and the periurethral area which manifests as an enlarged prostate gland.<sup>1</sup> In BPH, prostate enlargement that occurs will result in urinary tract obstruction that

manifests as lower urinary tract symptoms (LUTS). Histologically, prevalent BPH at autopsy increased from 20% at age 41-50 years, 50% at age 51-60 years, and > 90% at age over 80 years.<sup>2</sup> Hypertension is a frequent accompaniment to BPH. Both of these diseases increase in prevalence with age. It is estimated that 25% of men over 60 years experience BPH with hypertension.<sup>3</sup>

Hypertension and BPH are disorders that are closely related to aging. Although hypertension and BPH are two different groups of diseases, both have the same etiological form, namely age, and involvement of the sympathetic nervous system.<sup>4</sup> Based on the description above, it is said that hypertension is one of the most common comorbidities in BPH patients. Hypertension will accelerate the progression of the severity of lower urinary tract symptoms in BPH. In addition, hypertension also causes disorders in the kidney glomerulus which will increase the risk of kidney failure.

## OBJECTIVE

Comprehensive knowledge of BPH and hypertension is needed to reduce morbidity and mortality in patients with decreased kidney function due to the two diseases.

## MATERIAL & METHODS

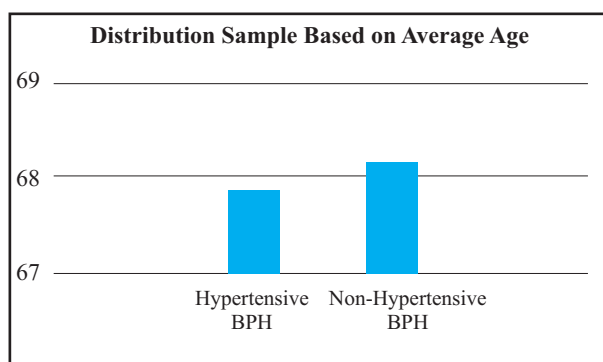
This research used the observational analytics method with cross-sectional design. This research used secondary data from medical records of BPH patients in Bina Sehat Hospital and Paru Hospital from January 1<sup>st</sup> to December 1<sup>st</sup> 2019. The serum creatinine, blood pressure data were collected from the patients medical record. This study was exempted the ethical clearance from Faculty of Medicine, University of Jember ethical commission.

## RESULTS

The total number of research samples was 128. The number of samples that met the criteria in Bina Sehat Hospital Jember was 102 samples and in the Paru Hospital in Jember as many as 26 samples. Then from 128 samples were divided into 2 groups,

71 samples of non-hypertensive BPH and 57 samples of hypertensive BPH. The distribution sample based on age and serum creatinine can be seen in Table 1.

From the sample used by researchers, BPH was mostly found in the age range of 61-70 years. The average age of BPH patients with hypertension is lower than non-hypertensive BPH patients. The lowest and highest age for BPH subjects with hypertension were 49 years and 89 years respectively, while the lowest and highest ages for non-hypertensive BPH subjects were 48 years and 90 years, respectively. The distribution of subjects based on average age can be seen in Figure 1.

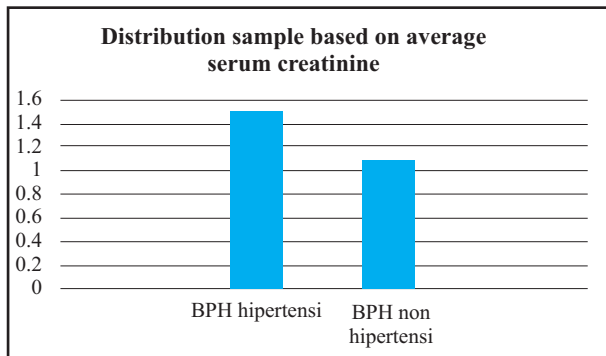


**Figure 1.** Distribution sample based on average age.

BPH patients with hypertension have average serum creatinine levels higher than non-hypertensive BPH patients. The lowest and highest serum creatinine in BPH subjects with hypertension were 1.12 mg/dl and 6.96 mg/dl, respectively, while the lowest and highest serum creatinine in non-hypertensive BPH subjects were 0.4 mg/dl and 2, respectively, 57 mg/dl. The distribution of subjects based on serum creatinine can be seen in Figure 2.

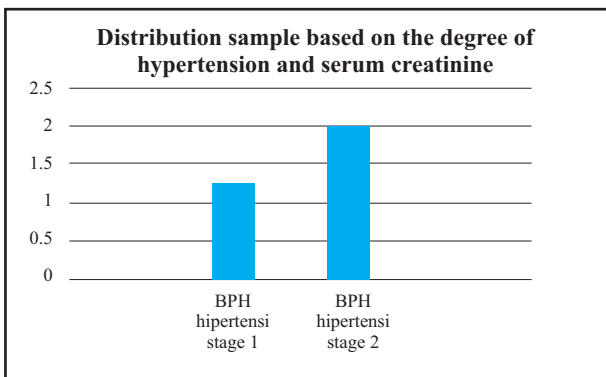
**Table 1.** Distribution sample based on age and serum creatinine.

Variable	Total n= 128	Hypertensive BPH n= 57	Non-hypertensive BPH n= 71
<b>Age (years)</b>	68.04 ± 9.03	67.89 ± 8.69	68.16 ± 9.35
Average 41-50	4 (3.12%)	2 (3.5%)	2 (2.81%)
51-60	19 (14.84%)	9 (15.78%)	10 (14.08%)
61-70	57 (44.53%)	24 (42.1%)	33 (46.47%)
71-80	37 (28.9%)	18 (31.57%)	19 (26.76%)
81-90	11 (8.59%)	4 (7.01%)	7 (9.85%)
<b>Serum creatinine (mg/dl) (avg)</b>	1.27 ± 0.67	1.52 ± 0.87	1.07 ± 0.36



**Figure 2.** Distribution sample based on average serum creatinine.

BPH patients with stage 2 hypertension have average serum creatinine levels higher than BPH patients with stage 1 hypertension. The average serum creatinine in BPH samples with stage 1 hypertension is 1.27 mg/dl while the average serum creatinine level is BPH samples with stage 2 hypertension were 2.02 mg/dl. The lowest and highest serum creatinine in BPH subjects with stage 2 hypertension was 0.78 mg/dl and 6.96 mg/dl respectively, while the lowest and highest serum creatinine in BPH subjects with stage 1 hypertension was 0.77 mg/dl respectively dl and 2.53 mg/dl. The distribution of subjects based on the degree of hypertension and serum creatinine can be seen in Figure 3.



**Figure 3.** Distribution sample based on the degree of hypertension and serum creatinine.

**Table 2.** Comparative test results for serum creatinine samples.

Variable	Total n= 128	Hypertensive n= 57	Non-hypertensive BPH n= 71	P
Serum Creatinine(mg/dl) (avg)	1.27 ± 0.67	1.52 ± 0.87	1.07 ± 0.36	0.000

The comparative test in this study aims to compare the dependent variables in BPH patients with hypertension and non-hypertensive BPH patients. The dependent variable compared was the patient's serum creatinine level. In the comparative test results with the Mann Whitney test p values obtained are smaller than 0.05. These results indicate that there are significant differences in serum creatinine levels between BPH patients with hypertension and non-hypertensive BPH patients. Comparative test results for serum creatinine samples can be seen in Table 2.

The correlation test in this study aims to find the relationship between variables in BPH patients with hypertension and non-hypertensive BPH. The variables to be tested for correlation were serum creatinine levels in patients with systolic and diastolic blood pressure. In the correlation test results using the Spearman test p values obtained are smaller than 0.05. These results indicate that there is a significant relationship between serum creatinine levels with systolic and diastolic blood pressure in patients. These results also showed that serum creatinine levels were positively correlated with elevated systolic and diastolic blood pressure. Correlation test results can be seen in Table 3.

**Table 3.** Correlation test results.

Variable	P
Serum creatinine–Systolic blood pressure	0.000
Serum creatinine–Diastolic blood pressure	0.000

## DISCUSSION

In this study, it was found that the average age of the sample that experienced BPH was 68 years. With the youngest sample aged 48 years and the oldest sample aged 90 years. This is consistent with Lim's 2017 study which said that the prevalence of BPH increased after the age of 40 years, with a prevalence rate of 8% -60% at the age of 90 years.<sup>5</sup> This result is also supported by data from Krimpen and Baltimore Longitudinal Study, a study conducted by Bosch, et al. in 2007 which said that

prostate volume increased by 2-2.5% every year in older men.<sup>6</sup>

Based on Table 1 it is found that BPH patients with hypertension have higher mean serum creatinine levels than BPH patients without hypertension. Figure 4 also shows that BPH patients with stage 2 hypertension have higher serum creatinine levels than BPH patients with stage 1 hypertension.

This study shows that there are significant differences in elevated serum creatinine levels in hypertensive BPH patients and non-hypertensive BPH patients in Bina Sehat Hospital and Jember Pulmonary Hospital. These results are in accordance with the research of Lee et al. (2009) which said that BPH patients who experienced an increase in serum creatinine all had comorbidities such as hypertension and diabetes.<sup>7</sup> In the study of Kaplan et al. (2011) also said there was a significant relationship between hypertension and diabetes on the incidence of chronic kidney disease (CKD) in BPH patients.<sup>8</sup>

This study also showed a significant relationship between systolic blood pressure and diastole with elevated serum creatinine levels in hypertensive BPH patients. These results are in accordance with Coresh et al. in 2001 which said that the higher the systolic and diastolic pressure, the higher the patient's serum creatinine would be.<sup>9</sup>

Urinary retention is the main mechanism for kidney failure in BPH patients. Increased intravesical pressure will cause urine reflux to return to the upper urinary tract. Upper urinary dilatation or an increase in serum creatinine is found in half of the patients with urinary retention due to BPH. Recurrent urinary tract infections in chronic urinary retention also play a role in the occurrence of kidney failure in BPH.<sup>10</sup>

Hypertension causes kidney failure because of its effect which increases blood pressure in the kidneys. Uncontrolled hypertension will cause an increase in intraglomerular pressure and disrupt the glomerular filtration process.<sup>11</sup> Hypertension also contributes to the decline in kidney function through its role in the course of BPH. In BPH, hypertension will cause microvascular dysfunction and decrease blood flow to the prostate tissue. This causes the prostate tissue and nerves that invade it to experience hypoxia. This tissue hypoxia will reduce the amount of nitrite oxide, increase the activity of phosphodiesterase, and increase the production of reactive oxygen species. Nitrate-related nerves are most affected by this oxidative stress and play an important role in the occurrence of lower urinary tract symptoms (LUTS).<sup>12</sup>

Under physiological conditions, nitric oxide (NO) acts as an endothelial related vasodilator because this substrate is produced mainly by endothelial blood vessels. Increased NO production will trigger vasodilation mediated by cyclic guanosine monophosphate (cGMP). NO will increase intracellular cGMP production which triggers phosphorylation of intracellular proteins and activates GMP-dependent kinase enzymes which will reduce intracellular calcium levels. In hypertensive conditions where blood vessel endothelium is dysfunctional, NO production will decrease. This decrease in NO production will ultimately reduce intracellular cGMP levels and increase intracellular calcium levels which will trigger vasoconstriction. This vasoconstriction, if it occurs chronically in the blood vessels of the kidneys, will cause kidney dysfunction and if it occurs in vascularisation of the lower urinary tract, especially in the prostate in BPH, it will exacerbate the degree of lower urinary tract obstruction.<sup>13</sup>

Besides being influenced by NO, intracellular cGMP regulation is also influenced by the enzyme phosphodiesterase. This enzyme will degrade cGMP and convert it to GMP. In hypertensive conditions, the activity of this enzyme will increase so that the intracellular cGMP level decreases resulting in conditions as described above. This enzyme is also an important target for therapy in BPH patients. Phosphodiesterase inhibition in BPH patients has been shown to improve clinical symptoms and reduce morbidity through the mechanism of vasodilation and relaxation of smooth muscles around the prostate.<sup>14</sup>

In BPH accompanied by hypertension, therapy using alpha-blockers has been shown to reduce blood pressure and improve clinical symptoms of BPH, but this medication has a lower protective effect for stroke and heart failure than other hypertension drugs. This proves that BPH and hypertension are related to pathophysiological aspects but not from therapeutic aspects.<sup>15</sup>

## CONCLUSION

Hypertension will worsen the kidney function decline in BPH patients seen from an increase in serum creatinine.

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