Original Article

Relationship between Prostate Volume and Risk of Chronic Kidney Disease (CKD) in Benign Prostate Hyperplasia (BPH) Patients After Transurethral Resection of the Prostate (TURP): An Observational Study

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Abstract

Introduction: *Benign Prostate Hyperplasia (BPH) is an enlarged prostate gland that causes problems in micturition and results in disruption of urine flow. Factors that cause prostate enlargement from a combination of chronic and progressive urine retention, high bladder pressure and ureterohydronephrosis can cause progressive kidney injury. The obstructive process changes the cells and physiological conditions in the bladder muscle and collagen contributes to increasing bladder pressure and the inability to empty the bladder and ends up causing kidney failure. This study was to determine the prevalence of chronic kidney disease (CKD) in BPH patients undergoing transurethral resection of the prostate (TURP) surgery.*
Method: *Using non-probability sampling method with consecutive sampling technique. Data were analyzed by univariate analysis using data frequency tables and bivariate analysis using the chi-square test.*
Result: *Of the total 178 BPH patients, 15 of them suffered from CKD (8.4%). BPH prevalence was highest in the age category 61-70 (39.3%), the majority had prostate volume > 50 ml (59%), the most common symptoms were severe lower urinary tract symptoms (LUTS) (83.1%) and urine retention (74.7%), some of them were accompanied by comorbidities such as hypertension (33.7%). The most common indication for surgery in patients who underwent TURP was recurrent retention (79.2%). The chi-square test showed an association between BPH and the incidence of CKD.*
Conclusion: *The prevalence of CKD at all stages in BPH patients who underwent TURP surgery was 8.4%. The most influential factors for the occurrence of CKD in BPH patients are prostate volume 30-40 ml, prostate volume 41-50 ml, and men aged 71-80 years.*

Keywords: *Chronic kidney disease, Benign prostate hyperplasia, Prevalence.*

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Hubungan Antara Volume Prostat dan Risiko Chronic Kidney Disease (CKD) pada Pasien Benign Prostate Hyperplasia (BPH) Pasca Transurethral Resection of the Prostate (TURP): Sebuah Studi Observasional

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Abstrak

Pendahuluan: *Benign Prostate Hyperplasia (BPH) merupakan pembesaran kelenjar prostat yang menimbulkan gangguan miksi dan mengakibatkan terganggunya aliran urin. Faktor-faktor penyebab pembesaran prostat yang berasal dari kombinasi faktor retensi urine kronis dan progresif, tingginya tekanan kandung kemih dan ureterohydronephrosis dapat menyebabkan cedera ginjal yang progresif. Proses obstruktif merubah sel dan kondisi fisiologis pada otot kandung kemih dan kolagen berkontribusi meningkatkan tekanan kandung kemih dan terjadi ketidakmampuan untuk mengosongkan kandung kemih dan berakhir menyebabkan gagal ginjal. Penelitian ini bertujuan untuk mengetahui prevalensi chronic kidney disease (CKD) pada pasien BPH yang menjalani tindakan operasi transurethral resection of the prostate (TURP).*
Metode: *Menggunakan metode pengambilan non-probability sampling dengan teknik consecutive sampling. Data dianalisis dengan analisis univariat menggunakan tabel frekuensi data dan analisis bivariat menggunakan uji chi-square.*
Hasil: *Dari total 178 pasien BPH, 15 diantaranya menderita CKD (8,4%). Prevalensi BPH tertinggi pada kategori usia 61-70 (39,3%), mayoritas memiliki volume prostat >50 ml (59%), gejala terbanyak dimiliki adalah lower urinary tract symptoms (LUTS) berat (83,1%) dan retensi urine (74,7%), beberapa diantaranya disertai komorbid seperti hipertensi (33,7%). Indikasi operasi tersering pada pasien yang dilakukan TURP yaitu retensi berulang (79,2%). Dari hasil uji chi-square menunjukkan adanya hubungan antara BPH dengan kejadian CKD.*
Kesimpulan: *Prevalensi CKD pada semua stadium terhadap pasien BPH yang menjalani operasi TURP sebesar 8,4%. Faktor yang paling berpengaruh terhadap terjadinya CKD pada pasien BPH adalah volume prostat 30-40 ml, volume prostat 41-50 ml, dan pria usia 71-80 tahun.*

Kata kunci: *Gagal ginjal kronis, Hiperplasia kelenjar prostat, Prevalensi*

Introduction

Theoretically, *Benign Prostate Hyperplasia* (BPH) is a diagnosis of an enlarged prostate gland where there is proliferation of benign tumors and epithelium causes micturition disorders and results in disruption of urine flow. BPH is a disease that commonly occurs in men and its occurrence is closely related to the aging process.[1] An enlarged prostate in BPH causes the lumen of the prostatic urethra to narrow and inhibits urine flow, increasing intravesical pressure. The bladder requires more contractions to expel urine. Continuous contractions cause hypertrophy of the detrusor muscle, trabeculation, formation of saccules, cells, and bladder diverticula. These stricture changes are generally complained of in the lower urinary tract or are known as *lower urinary tract symptoms* (LUTS). LUTS consists of obstruction that causes a decrease in the quality of life of BPH patients.[2]

In addition, it was found that comorbidities such as diabetes mellitus and hypertension

were independent risks of BPH. Insulin resistance in diabetes patients allows the IGF receptor to stimulate prostate growth by causing excessive activity in prostate cells. In patients with hypertension, systolic and diastolic pressure are significantly associated with the rate of prostate enlargement.[3] Increased sympathetic activity and/or 1-adrenoceptor responsiveness in hypertension patients may be a common pathophysiological factor for essential hypertension and BPH.

Chronic Kidney Disease (CKD) is an abnormality of kidney function and found in progressive decline in the Glomerular filtration rate (GFR). The relationship between CKD and BPH begins with an enlarged prostate in BPH causes kidney insufficiency. The occurrence of CKD in BPH originates from a combination of chronic and progressive urinary retention, high bladder pressure and ureterohydronephrosis causes progressive kidney injury. The obstructive process of cell and physiological changes in the bladder muscle and collagen contributes to persistent increases in bladder pressure and an inability to empty the bladder and ultimately leads to kidney failure. Other renal risk factors such as diabetes mellitus, cardiovascular disease, hypertension, obesity, and dyslipidemia also need to be considered in patients with BPH.[1]

The highest prevalence of BPH in the world is in the age group ≥ 70 years has a median prevalence of 25.2% (19-37.9%).[4] Meanwhile, CKD in the world affects > 10% of the general population worldwide, amounting to >800 million people.[5] CKD and BPH also have a high disease prevalence in Indonesian society. The results of Riskesdas in 2018, state that the prevalence of BPH is in second place with 50% of men aged 50 years suffering from BPH. It also stated that the prevalence of CKD was 3.8% with the lowest prevalence being 1.8% and the highest being 6.4%.[2] However, there has been no research regarding the incidence or prevalence of CKD in BPH patients so researchers are interested in conducting this research.

Methods

The type of research used is descriptive analytical research with observational studies and a cross sectional approach. The variables used in this study consisted of the independent variable, namely BPH status consist of age, main complaint (LUTS, urinary retention), prostate volume, and comorbidities (hypertension and diabetes mellitus) and the dependent variable was CKD. This research was declared free from ethical clearance by the Health Research Ethics Commission, Faculty of Medicine Universitas Brawijaya. This research was carried out at Dr. Saiful Anwar General Hospital Malang by taking secondary data in the form of medical records. The population in this study were BPH patients who underwent TURP surgery in 2018-2022. Samples are using a non-probability sampling technique, namely consecutive sampling in accordance with the inclusion criteria (BPH patients who underwent TURP surgery in 2018-2022 at RSSA Malang) and exclusion criteria (patients with incomplete medical record data). The total number of samples was 178. Data were analyzed using univariate tests carried out by analyzing each variable with frequency and bivariate tests using chi-square analysis tables.

Result

The results of the univariate analysis test are the distribution of the numbers for each variable. The distribution of research data can be seen in Table 1.

Among the five age groups, there were a significant number of 70 research subjects in the 61 - 70 age (39.3%). The prevalence of BPH begins to increase after the 4th decade of life with a percentage of 1.1%, 39.3% in the 6th decade, until finally decreasing in the 8th decade of life. These are associated with an increase in prostate volume with increasing age in elderly men.

The largest prostate volume of the four categories has a volume of more than 50 ml with a prevalence of 59%. Normal prostate volume is in the range of 20-30 ml. Prostate volume increase serves as an independent predictor in determining treatment. Prostate volume has a correlation with PSA levels which also influences the choice of treatment if indicated.

The main complaints of BPH patients in this study were LUTS and urinary retention, with the results that all research subjects experienced LUTS, with varying degrees of LUTS. The severe LUTS category was the most common with a prevalence of 83.1%. Meanwhile, 74.7% of the research subjects were confirmed to have urinary retention. LUTS is closely related to BPH where it identified as a clinical diagnosis of BPH. BPH patients who did not get any treatment can cause urinary retention. In addition, urinary retention is often associated as an extreme form of LUTS so that the prevalence of urinary retention in BPH patients has a high percentage.

Table 1. Characteristics of BPH Patients

Characteristic	N	%
Age (Years)		
<50	2	1.1
50-60	37	20.8
61-70	70	39.3
71-80	55	30.9
>80	14	7.9
Prostate Volume (ml)		
<30	23	12.9
30-40	26	14.6
41-50	24	13.5
>50	105	59
Chief Complain		
LUTS: Mild	7	3.9
Moderate	23	12.9
Severe	148	83.1
Urinary Retention	133	74.7
Comorbid		
Hypertension	60	33.7
Diabetes Melitus	10	5.6
Smoking	20	11.2
Disfunction Erection	11	6.2
Stroke	3	1.7
Indication of Surgery		
Medical Therapy Failure	16	9.0
Complications:		
Recurrent Urinary Retention	141	79.2
Urinary stones	39	21.9
CKD:	15	13.4
Normal	163	91.6
Stage 1	0	0
Stage 2	2	1.1
Stage 3a	0	0
Stage 3b	2	1.1
Stage 4	7	3.9
Stage 5	4	2.2
Clot retention	11	6.2
Inguinal hernia/ Hemorrhoids	23	12.9
Total	178	100

There are various comorbid factors that can influence BPH, including hypertension, diabetes mellitus, smoking, erectile dysfunction, and stroke. Hypertension is the highest prevalence of comorbid BPH with 33.7% percentage, followed by smoking, erectile dysfunction, diabetes mellitus and stroke. Hypertension in BPH is related to age because diastolic blood pressure decreases, and systolic blood pressure increases in elderly. Diabetes mellitus is related to hypertension by causing kidney damage, then causing retention, which results in increased blood pressure. The percentage of diabetes mellitus in research subjects was 5.6% One of the treatment options for BPH is surgery. Indications for BPH surgery to continue surgical intervention include recurrent retention, failed therapy, stones, CKD, hernia/hemorrhoids, and clots. In addition, BPH patients may undergo surgery with other additional indications such as the desire to stop medical treatment, and financial constraints related to medical therapy. The highest prevalence of indications for BPH surgery was recurrent retention with a 79.2% percentage, followed by stones, hernias, failed treatment, CKD, and clots. Urinary retention is the most common indication for BPH surgery due to the discomfort and discomfort it causes. Repeated urinary retention that is not treated immediately in BPH patients not only worsens the condition of BPH but can cause complications in the urinary tract, bladder and kidney damage. One of the kidney damage due to urinary retention is CKD which is also an indication for surgery with a percentage of 8.4% with the highest stage is CKD Stage 4 at 3.9%.

Bivariate analysis of the relationship between CKD and non-CKD with BPH patients showed the results sequentially from highest to lowest, namely: Prostate volume category 31-40 ml (p value: 0.002); Prostate volume category > 50 ml (p value: 0.002); Age category 71-80 years (p value: 0.049); severe LUTS (p value: 0.289); Hypertension (p value: 0.267); Diabetes Mellitus (p value: 0.854); Urine retention (p value: 0.897). Based on the results of the bivariate analysis, there were only three variables that had significant values, namely prostate volume in the 31-40 ml category, prostate volume in the >50 ml category, and age in the 71-80 age category so that a multivariate test could not be carried out. The research failed to conduct multivariate analysis, which limited its ability to observe complex relationships between multiple variables. As a result, the study lacked a thorough understanding of how various variables interacted with each other and influenced the outcomes. Additionally, it became challenging to identify the most relevant and significant variables. The results bivariate

Table 2. Relationship Between Patients' Characteristics and CKD Stages

Variable	Normal		*P value*	CKD Stage 1		*P value*	CKD Stage 2		*P value*
	N	%		N	%		N	%	
Age (years)									
<50	2	1.2	0.666	0	0	-	0	0	0.879
50-60	36	22.1	0.159	0	0	-	0	0	0.466
61-70	64	39.3	0.955	0	0	-	2	100	0.077
71-80	47	28.8	0.049	0	0	-	0	0	0.342
>80	14	8.6	0.237	0	0	-	0	0	0.678
Prostate Volume (ml)									
<30	21	12.8	0.960	0	0	-	0	0	0.584
30-40	18	11.4	0.002	0	0	-	1	50	0.128
41-50	21	12.9	0.141	0	0	-	1	50	0.141
>50	101	62	0.002	0	0	-	2	100	0.092
LUTS									
Mild	6	3.7	0.569	0	0	-	0	0	0.774
Moderate	20	12.3	0.393	0	0	-	0	0	0.584
Severe	137	84	0.289	0	0	-	2	100	0.522
Urinary Retention	122	74.8	0.897	0	0	-	2	100	0.408
Comorbid									
Hypertension	53	32.5	0.267	0	0	-	1	50	0.624
Diabetes Melitus	9	5.5	0.854	0	0	-	2	100	0.729

analysis of the relationship between CKD at each stage and BPH patients in tables 5.3 and 5.4 have varying results. There are stages of CKD that cannot be tested, namely stages 1 and stadium 3a because there were no research subjects suffering from CKD at that stage. The normal variable (Non-CKD) there are three significant variables, namely prostate volume category 31-40 ml (*p* value: 0.002), prostate volume category >50 ml (*p* value: 0.002), and age category 71-80 years (*p* value: 0.049). CKD stage 2 does not have significant variables, but there are variables that have a closer relationship, namely age 61-70 years (*p* value: 0.077) and prostate volume >50 ml (*p* value: 0.092). Just like CKD stage 2, CKD stage 3b also does not have significant variables but has variables that are related, including prostate volume 31-40 ml (*p* value: 0.128) and prostate volume 41-50 ml (*p* value: 0.141). CKD stage 4 has more significant variables compared to other stages, these variables are age 71-80 years (p value: 0.018), moderate LUTS (*p* value: 0.016), severe LUTS (*p* value: 0.004), and urinary retention (*p* value: 0.048). CKD stage 5 only has one significant variable, prostate volume of 31-40 ml has a p value of 0.000 as strong evidence to reject the null hypothesis.

Discussion

The results of the study showed a positive relationship with the prevalence of CKD in BPH patients who underwent TURP surgery. This is proven by data findings with a percentage of 8.4% who experienced CKD overall and CKD stage 4 was the most common stage (3.9%). In addition, the results of the study showed that the highest prevalence of BPH was suffered by patients aged 61-70 (39.3%), prostate volume >50 ml (59%) being the largest volume, the majority of BPH patients had LUTS symptoms with the highest degree of complaint, namely Severe LUTS (83.1%), some of which were accompanied by comorbidities such as hypertension (33.7%), and in the advanced stages of BPH patients underwent surgical procedures with the most common indication for surgery being repeated retention (79.2%).

BPH usually begins to develop after the age of 40 and is progressive and chronic. The age spike in BPH patients can vary, in this study the age spike occurred in the age range 61-70 years. As men age, the ratio of estrogen to androgen increases, making BPH a very common disease suffered by elderly men. Observational studies from Europe, the US, and Asia also show older age to be a risk factor for the onset and clinical progression of BPH.[6] A study in the United States showed that the prevalence of BPH reached 70% in those aged between 60 and 69 years and more than 80% in those aged over 70 years.[7] Another study from Indonesia showed that TURP for BPH patients was mostly performed on patients aged 61-70 years

(39.5%).[8] Different demographic profiles and population increases throughout the world will of course show different prevalence. However, the largest age range for BPH shows consistent results between one study and another, with this study occurring most frequently at the age of 61-70 years.

reduction in quality of life but not experience BPE. A BPH patient survey by Park et al of 6,184 patients reported 33% with mild LUTS, 52% with moderate LUTS, and 15% with severe LUTS. It is estimated that 90% of men aged between 45 and 80 years suffer from LUTS.10 There are differences in the percent-

Table 3. Correlation of CKD in CKD Stage 3a, CKD Stage 3b, CKD Stage 4, and CKD Stage 5 at Each Stage with BPH Patients

Variable	CKD Stage 3a		*P value*	CKD Stage 3b		*P value*	CKD Stage 4		*P value*	CKD Stage 5		*P value*
	N	%		N	%		N	%		N	%	
Age (years)												
<50	0	0	-	0	0	0.879	0	0	0.774	0	0	0.829
50-60	0	0	-	0	0	0.466	1	14.3	0.665	0	0	0.300
61-70	0	0	-	1	50	0.756	1	14.3	0.166	2	50	0.658
71-80	0	0	-	1	50	0.557	5	71.4	0.018	2	50	0.403
>80	0	0	-	0	0	0.678	0	0	0.430	0	0	0.555
Prostate Volume (ml)												
<30	0	0	-	0	0	0.584	2	28.6	0.208	0	0	0.438
30-40	0	0	-	1	50	0.128	1	14.3	0.949	3	75	0.000
41-50	0	0	-	1	50	0.141	2	28.6	0.259	0	0	0.414
>50	0	0	-	0	0	0.092	2	28.6	0.102	1	25	0.170
LUTS												
Mild	0	0	-	0	0	0.774	1	14.3	0.150	0	0	0.682
Moderate	0	0	-	0	0	0.584	3	42.9	0.016	0	0	0.436
Severe	0	0	-	2	100	0.522	3	42.9	0.004	4	100	0.362
Urinary Retention	0	0	-	2	100	0.408	3	42.9	0.048	4	100	0.239
Comorbid												
Hypertension	0	0	-	0	0	0.311	4	57.1	0.181	2	50	0.486
Diabetes Melitus	0	0	-	0	0	0.729	0	0	0.510	1	25	0.089

Prostate volume >50 ml has the greatest prevalence of 59% compared to other prostate volumes. Based on data from Creampen and the Baltimore Longitudinal Study of Aging which shows a prostate growth rate of 2.0%–2.5% per year.[6] A study in Ghana explained that the prevalence of prostate volume ≥30ml was 36%. On the other hand, the USA reports a prostate volume prevalence of 36% across all races.[9] The difference in results on This research and other studies do not have significant differences. This is due to differences in the volume range groupings used.

The two main complaints of this study showed a significant number of LUTS in all BPH patients (99.9%) and urinary retention (74.7%). BPE is experienced by approximately 50% of men with histological BPH. Some patients may experience BPE but not experience significant LUTS, whereas other patients may experience LUTS and experience a significant

age of LUTS between each LUTS classification between that study and this study. This can be caused by a patient's level of awareness of diseases in developed and developing countries so that disease treatment can be addressed immediately. The percentage of LUTS in this study was mild LUTS 3.9%, moderate LUTS 12.9%, and severe LUTS 83.1%. Urinary retention in this study was suffered by 74.7% of subjects. One predictor of the development and worsening of BPH is urinary retention. It is estimated that 10% of men in their 70s and one third of men in their 80s will experience urinary retention.[11] 74.7% of BPH patients in this study had symptoms of urinary retention. This high percentage of urinary retention shows that the majority of BPH patients at Dr. Saiful Anwar General Hospital Malang experience worsening.

Among BPH comorbidities, hypertension has a more dominant influence with

a percentage of 33.7%. Around 25% –30% of all men over 60 years old have BPH and hypertension that occur simultaneously.[12] Based on the results of research and other studies, it can be concluded that hypertension is the most common comorbidity in BPH patients. Hypertension that is not treated further can also cause damage to the kidney glomerulus which increases the risk of CKD. Diabetes mellitus is one of the comorbidities that has an influence, as many as 5.6% of BPH patients are accompanied by diabetes mellitus. Diabetes mellitus increases the risk of BPH and LUTS significantly based on epidemiological evidence, with pathophysiological mechanisms. Previous research suggests that BPH may be directly related to hyperglycemia and urinary retention. On the other hand, there are studies that do not show a relationship between the two, while other studies show an inverse relationship between diabetes and clinical BPH. However, most studies have shown a relationship between hyperglycemia and insulin resistance and the incidence of LUTS.[13]

Initial therapy for BPH includes observation with lifestyle modification and pharmacotherapy. Surgical intervention may be considered if less invasive treatment fails. The most common indication for BPH surgery in this study was recurrent retention (79.2%). Apart from that, there is CKD (8.4%) as indication for BPH surgery. In another study, men over 80 years old experienced decreased renal reserve function, poor compensatory ability, and sensitive response to external stimuli, including BPH and hypertension.[14]

Bivariate analysis between BPH and CKD in most cases had a prostate volume of 30-40 ml, a prostate volume of 41-50 ml, and age 71-80 being the variable with the most significant relationship with CKD. Prostate volume is an independent risk factor for changes in eGFR before and after treatment. Therefore, multiple linear regression analysis showed that baseline prostate volume was a factor influencing the improvement of renal function after BPH treatment. However, several clinical trials have not confirmed the correlation of prostate volume with the growth and progression of CKD.[14] The risk of developing CKD increases with age, resulting in damage to kidney function and getting worse every year. Men over 70 years, the average estimated glomerular filtration rate (eGFR) is 75 mg/mmol causes increasing prevalence of CKD in men aged over 70 years may occur.[15] Apart from the variables above, there are variables that also have a relationship with the incidence of CKD in BPH patients, namely LUTS, especially severe LUTS, urinary retention, hypertension and diabetes mellitus. Men with severe LUTS have a higher risk of developing CKD than other degrees of LUTS. This condition is related to complications caused by severe LUTS ultimately causes CKD.[14] There is a condition in urinary retention causes urine to flow back to the kidneys called reflux. This reflux causes damage to the kidneys. Apart from that, repeated urinary retention can also cause obstruction so that the kidneys cannot excrete urine and a buildup occurred can lead to CKD.[15]

Men with LUTS should undergo routine serum creatinine screening, according to the 1994 AUA clinical practice guidelines on BPH. However, after the 2003 update, routine screening is no longer advised. On the other hand, if an abnormal renal function is suspected based on the patient's medical history and clinical examination, the European Association of Urology guidelines on non-neurogenic LUTS recommend renal function evaluation prior to surgery, suggesting a potential correlation between renal function and LUTS.[14]

Over time, uncontrolled high blood pressure can cause the arteries around the kidneys to narrow, weaken, or harden. These damaged arteries are unable to deliver enough blood to the kidney tissue. Damaged kidney arteries cannot filter blood properly, so hypertension has a relationship in causing kidney damage and CKD. Diabetes mellitus has high glucose levels in the blood and by the time it can damage blood vessels, including blood vessels in the kidneys.[16]

Conclusion

In conclusion, the prevalence of CKD in BPH patients undergoing TURP surgery is 8.4%. The factors that most influence the occurrence of CKD in BPH patients are prostate volume 30-40 ml, prostate volume 41-50 ml, and men aged 71-80 years.

Conflicts of Interest

The authors declare no conflict of interest.

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