ORIGINAL ARTICLE

Journal of International Surgery and Clinical Medicine (*JISCM*) 2022, Volume 2, Number 2: 40-43
E-ISSN: 2807-7008

Published By :
Surgical Residency Program
Universitas Syiah Kuala

Association of prostate-specific antigen and prostate volume in benign prostatic hyperplasia patients with urinary tract infection

Feren Altagracia Da Leo[1], Tejo Jayadi[2*], Jonathan Willy Siagian[2]

[1]Faculty of Medicine, Universitas Kristen Duta Wacana, Indonesia;
[2]Department of Anatomical Pathology, Faculty of Medicine, Universitas Kristen Duta Wacana, Indonesia;

*Corresponding to:
Tejo Jayadi;
Department of Anatomical Pathology, Faculty of Medicine, Universitas Kristen Duta Wacana, Indonesia;
tejo_jayadi@staff.ukdw.ac.id

Received: 2022-10-30
Accepted: 2022-12-09
Published: 2022-12-28

ABSTRACT

Introduction: One of the most common diseases in men is benign prostatic hyperplasia (BPH). In this condition, the prostate gland becomes larger, thus it can clamp the urinary tract area and cause obstruction. Obstruction in the lower urinary tract increases the high risk of urinary tract infections (UTI). When the prostate volume becomes larger, the levels of prostate-specific antigen increase. This research aims to determine the correlation between PSA levels and prostate volume in BPH patients with urinary tract infections (UTI).

Methods: This study used an analytic observational method with a cross-sectional design. Data were taken from the medical records of BPH patients suffering from UTIs at Bethesda Hospital Yogyakarta from January 2018 to December 2020. Data collection was carried out from January 17 2022 to March 17 2022. The data used in this study were selected using inclusion and exclusion criteria so that the obtained 33 medical record data were analyzed. The data used in this study were analyzed using SPSS software. The univariate analysis describes the distribution of data. Bivariate analysis used the chi-square test so that it could show the relationship between the independent variable (prostate volume) and the dependent variable (PSA level).

Result: The data show moderate prostate volume (30-80cc) in 17 (51.5%), high prostate volume (>80ml) in as many as 9 patients (27.3%) and normal prostate volume (<30 ml) in as many as 7 patients (21.2%). High PSA levels are 26 (78.8%) and normal PSA levels are 7 patients (21.2%) that noted. Bivariate analysis data with a chi-square test shows that the significant score is 0.019 ($p<0.05$).

Conclusion: The research shows an association of PSA levels and prostate volume in BPH patients with UTI.

Keywords: Prostatic Hyperplasia, Prostate-Specific Antigen, Urinary Tract Infections.
Cite This Article: Leo, F.A.D., Jayadi, T., Siagian, J.W. 2022. Association of prostate-specific antigen and prostate volume in benign prostatic hyperplasia patients with urinary tract infection. *Journal of International Surgery and Clinical Medicine* 2(2): 40-43. DOI : 10.51559/jiscm.v2i2.28

INTRODUCTION

The prostate gland is a single gland that lies below bladder. It has its own function that produces liquid that contains acid pH about 6.5 and other substances.[1] Prostate gland can have a benign or malignant growth. The prevalence rate of BPH varies in many countries. BPH is a specific histopathological picture that showing a benign proliferation from epithelial cells and stroma gland, active proliferation, varied size of gland and fibromuscular stroma, corpus amilaceum in lumen.[2] In general, BPH can be found in men at the age of 40 years old.[3] However, another percentage rates show that 20% until 62% can be found in men at the age of 50 years old.[4] In Indonesia, prevalence rate at Cipto Mangunkusumo hospital is 3.804 BPH patients with an average age of 66.61 years old.[5] In this condition, prostate gland becomes larger, thus it can clamp the urinary tract area and cause of obstruction. Obstruction in lower urinary tract increases a high risk for urinary tract infections (UTI). This incidence can create lower urinary tract symptoms (LUTS). LUTS is proven to have a correlation with increasing age as much as 50% in men over 50 years old.[6] On the other hand, LUTS can increase a risk of UTI.[7]

BPH can happen because of many factors there are androgen, dihydrotestosterone, and testosterone hormones which promoting proliferation in stroma and prostate gland. Testosterone and dihydrotestosterone will bind to androgen receptors which promoting proliferation especially in prostate gland.[2] The second factor is a genetic factor. This factor shows in a cohort study that people in blood relation are way riskier of having a severe BPH, and monozygotic twins have high rates of having LUTS. Ethnicity also shows a correlation with prostate volume.[6] The third factor is metabolic syndrome which consist of hypertension, insulin resistance, and dyslipidemia. Other presumption of obesity that can affect development of BPH, because of systemic inflammation mechanisms and rising estrogen hormones.[6]

Prostate-specific antigen is a serin protease that is a product from epithelial cells of prostate gland also part of seminal fluid.[8] Normal PSA levels are less than 4 ng/ml. Variation results of PSA levels in patients are caused by several factors like BPH, prostate cancer, UTI, prostatitis, age,

α1-blocker, 5α-reductase inhibitor, and antimuscarinic medication.[5] Therefore, this research aims to determine the association between PSA levels and prostate volume in BPH patients with UTI.

METHODS

This research uses an analytic observational method with a cross-sectional design. Analytic observational method means not giving intervention to subjects and analyze the correlation between PSA levels and prostate volume in BPH patients with UTI. Data were collected from medical records of BPH patients who suffer from UTI at Bethesda Hospital in Yogyakarta from January 2018 until December 2020. The researcher collects the data from 17th January 2022 until 17th March 2022. The researcher is not taking any samples from patients.

The data collected must meet the inclusion and exclusion criteria. The inclusion criteria in this study were BPH patients suffering from UTI. UTI can be diagnosed using clinical findings, laboratory tests, and radiological examinations. Then, BPH patients underwent PSA examination and BPH patients underwent radiological examination to determine prostate volume. Exclusion criteria in this study were incomplete patient medical records.

The independent variable in this study was prostate volume which was categorized into three categories such as normal prostate volume was <30 ml, moderate prostate volume was 30-80 ml and high prostate volume was >80 ml. Meanwhile, the dependent variable in this study was PSA levels which were divided into two categories, namely normal PSA <4 ng/ml and high PSA, namely > 4 ng/ml.[5]

Prostate volume categorized as ordinal scale of data and PSA levels categorized as nominal scale of data. The total sample size of this research based on the sample that fulfills the inclusion and exclusion criteria. There are 33 data collected. This data can contribute to this research in which some other research uses the 30 data.[9,10] Data analysis used in this research are univariate analysis and bivariate analysis using SPSS. Univariate analysis describe the distribution of data. Bivariate analysis show the association between independent variable (prostate volume) and dependent variable (PSA levels). Prostate volume and PSA levels were statistically using Ci-square test with p-value less than 0.05 were taken as significant. Odds ratio (OR) with Confident Interval (CI) 95% were analyzed. For the analysis, the prostate volume would be categorized into two groups normal prostate volume < 30 ml and high prostate volume ≥ 30 ml based on the followed research.[11]

RESULTS

The total data collected from January 2018 until December 2020 is 318 data. Nonetheless, from 318 data, patients who undergo PSA examination were 56 data and patients who undergo urine examination is 20 data. Therefore, researcher uses a clinical result, laboratory examination, and radiology examination to confirm UTI's patients. Final data is collected from as many as 33 data. Data analysis uses a Statistical Product and Service Solutions (SPSS) version 25. The result of univariate analysis between prostate volume and PSA levels shows in Table 1.

The most prostate volume in BPH patients with UTI were 17 (51.5%) patients with moderate prostate volume (30-80ml), then following by high prostate volume (>80ml) as many as 9 patients (27.3%) and normal prostate volume (<30 ml) as many as 7 patients (21.2%). From 33 data patients, most of them have high PSA levels (> 4ng/ml) as 26 patients (78.8%). For normal PSA levels are 7 patients (21.2%) that noted.

Prostate volume category's were changed into normal value of < 30ml and high value of ≥30ml just to find out odds ratio value. Most of normal prostate volume have high value in normal PSA levels as 4 data (12.1%) and high PSA levels was 3 (9.1%). The result of high prostate volume was followed by high PSA levels as much as 23 data (69.7%) and just 3 data (9.1%) for normal PSA levels. Total frequency of normal prostate volume were 7 (21.2%) and 26 (78.8%) of high prostate volume. Total of PSA levels were 7 (21.2%) of normal PSA levels and 26 (78.8%) of high PSA levels. Value of 95% coefficient interval for the minimum score 1.498 and 69.761 for the maximum score. Odds ratio value from prostate volume and PSA levels correlation were 10.222. A correlation of prostate volume and PSA levels was determined with *p-value* of 0.019 based on three categories of prostate volume; normal, moderate, and high.

Table 1. Distribution of prostate volume and PSA level frequencies (n=33).

Variable	Frequency	Percentage (%)
Prostate Volume		
Normal (<30ml)	7	21.2
Moderate (30-80ml)	17	51.5
High (>80ml)	9	27.3
PSA Levels		
Normal (<4 ng/ml)	7	21.2
High (>4 ng/ml)	26	78.8

Table 2. Bivariate analyze between prostate volume and PSA levels (n=33).

Variable		PSA Levels		Total Frequency	CI 95%	OR	*P value*
		Normal (<4 ng/ml)	High (>4 ng/ml)				
Prostate volume	Normal (< 30ml)	4 (12.1%)	3 (9.1%)	7 (21.2%)	1.498-69.761	10.222	0.019*
	High (≥ 30 ml)	3 (9.1%)	23 (69.7%)	26 (78.8%)			

Note: *significant at p<0.05 by chi-square test

DISCUSSION

In this study, according to the result of prostate volume in BPH patients with UTI at Bethesda Hospital Yogyakarta, there were 17 (51.5%) patients with moderate prostate volume (30-80ml), following by high prostate volume (>80ml) as many as 9 patients (27.3%) and normal prostate volume (<30 ml) as many as 7 patients (21.2%). Comparing this result, it was different from the research by Putra et al., that distinguishes prostate volume into five categories in details ≤ 30 ml, 31-40 ml, 41-50ml, 51-100ml, and > 100ml; and the highest score for prostate volume was 31-40 ml as much 442 patients (27%) from 1.638 data. There are 436 patients (26.6%) for ≤ 30 ml, 296 patients (18.1%) for 41-50 ml, 430 patients (26.3%) for 51-100ml, and 34 patients (2.1%) for prostate volume > 100 ml.[12] Another research by Levissa et al. also distinguishes prostate volume into five categories in details <20cc, 20.00-39.99cc, 40.00-59.99cc, 60.00-79.99cc, and >80cc - with total sample is 52 data. The 16 (30.7%) data, out of 52 data, have prostate volume 20-39.99 ml. There are 0 data (0%) for prostate volume < 20ml, 14 patients (26.9%) for 40-59.99ml, 20 patients (19.2%) for 60-79.99ml, and 12 patients (23.2%) for prostate volume > 80ml.[13] Research by Deori et al. made four categories of prostate volume based on age group.[14] Another research by Fadila et al. state that high prostate volume (>25 ml) is 90.9% data in BPH patients and normal prostate volume (≤ 25 ml) is 9.1%.[9]

The statement and all the research results show that prostate volume size in BPH patients does not only vary but also has a larger size. Especially, in this research, the population of sampling is BPH patients with UTI. Distinction of prostate volume size is caused by many factors like age or the aging process and hormones. This factor is proved by Deori et al and Levissa et al research, showing the correlation between aging and prostate volume.[13,14] Moreover, research by Levissa et al also explains that people who are likely to have a size 20-39.99 ml and > 80 ml are people from the age of 61 until 70 years old.[13] On the other hand, Krisna et al. research's result does not interpret statistically between age and prostate volume.[15] Another factor that can affect prostate volume is race or ethnicity. It is shown in Mubenga et al research's that there is a different prostate size in race or ethnic group in Sud-Kivu Republic of Congo. Its research shows other result such as prostate volume has a correlation with age, living place, fasting blood glucose, and prostate volume do not have a relationship with anthropometry parameter and body fat composition.[16] Research by Heidler et al. conforms that higher prostate volume is found in all patients who have positive (+) bacteria in culture urine.[17]

PSA levels from 33 data have high PSA levels (> 4ng/ml) as 26 patients (78.8%). For normal PSA levels was 7 patients (21.2%) that noted. This result shows that most of all data was dominated by high PSA levels. In Levissa et al.'s research, the distribution of PSA levels was divided into four categories in which the most data are 24 (46.2%) of 2.6 until 9.9 ng/ml PSA levels.[13] Another study from Fadila et al. also shows high PSA levels are 84.8% from 33 data.[9]

PSA examination is one of the biomarker which indicates an organ-specific not disease-specific.[18] High PSA levels with UTI condition is proved by the result of 22 patients (28.9%) have positive (+) bacteria urine culture and 0% for patients with negative (-) bacteria urine culture.[19] Result of PSA levels are caused by some conditions like BPH, prostate cancer, UTI, prostatitis, age, urethral catheterization, α1-blocker, 5α-reductase inhibitor, and antimuscarinic medication. These medicine give a benefit to decrease PSA levels.[5] Urethral catheterization is common treatment to treat urinary retention. There are[1] studies show that urethral catheterization has not changed PSA levels. Besides, if the procedure was not sterile and make injury to patient, it can increase PSA levels.[18]

Another parameter that can be used by clinician is measure free PSA levels or total PSA levels. This examination is important to differentiate BPH and prostate cancer, even to do a biopsy procedure. The result of free/total PSA after catheterization is not increasing.[18] Free PSA is a strong predictor to measure prostate volume rather than age and total PSA.[20] Free PSA is also common in prostatitis condition or BPH condition.[2]

The significant value or *p* value from Chi-square test is 0.019 which this *p* value based on three categories of prostate volume and two categories PSA levels. Therefore, if the *p* value < 0.05, it means prostate volume and PSA levels in BPH patients who undergo with UTI has a correlation. This study conforms with study by Krisna et al. with a different correlation test – Pearson and multiple liner regression analysis – which has a correlation score 0.384.[15] Another study by Deori et al. shows a Pearson correlation of 0.933 between prostate volume and PSA levels.[14] The study from Fadila et al. found *p* value is 0.019 with the Spearman test.[9] In a study by Heidler et al. told there is a strong correlation between bacteria colonization with high prostate volume, also which in this study shows UTI condition such as pyuria and hematuria influences the high PSA levels because it can affect the prostate volume to produce more PSA as a reflect defense mechanisms by prostate gland.[17] The odds ratio from Table 2. shows that prostate volume and PSA levels is 10.222 means that high prostate volume tends ten times as much to have high PSA levels and normal prostate volume tends to have a normal PSA levels. The minimum score of 95% confident interval is 1.498 and 69.761 as the maximum score.

The limitation of our study was the small sample size than other researches. Another thing that can be improved is to analyze the confounding factors between PSA levels and prostate volume in BPH patients who undergo with UTI.

CONCLUSION

There were 33 data was analysised. The most prostate volume in BPH patients with UTI were moderate prostate volume (30-80ml), then following by high prostate volume and normal prostate volume. From 33 data patients, most of them have high PSA levels (> 4ng/ml). From the analytic data reported there were an association of PSA levels and prostate volume in BPH patients with UTI.

DISCLOSURES

Ethical Clearance

This study has received an ethical approval from Bethesda Hospital in Yogyakarta with number 72/KEPK-RSB/XII/21.

Funding
No funding resources.

Conflict of Interest
No conflict of interest.

Author Contribution
All authors contributed in this work.

ACKNOWLEDGEMENT

We acknowledge all the healthcare professional to aware about the correlation of PSA levels and prostate volume in BPH patients who undergo with urinary tract infections (UTI).

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