CORRELATION OF BODY MASS INDEX WITH PROSTATE VOLUME IN BENIGN PROSTATIC HYPERPLASIA PATIENTS

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Introduction: Benign prostatic hyperplasia (BPH) is the most common prostatic disease in men. Multiple factors influence the pathogenesis of BPH, and one of them is obesity. Various studies about the correlation between obesity and prostate volume show inconsistent results. Some studies reported that obesity correlates with prostate volume, whereas others didn't find the correlation between obesity and prostate volume. Therefore, this study aims to find the correlation between obesity and prostate volume.
Purpose: To find the relationship between body mass index (BMI) and BPH patients' prostate volume.
Methods: BMI was measured by BMI formula, and prostate volume was measured by transabdominal ultrasound (TAUS). This study was conducted in RSUD Ibnu Sina Kabupaten Gresik by looking at medical records in January 2016-September 2017. This study was an analytical observational study with a cross-sectional approach. This study uses Linear Regression Test to analyze the correlation of in-between variables. This study's population was patients with a diagnosis of BPH that undergo hospitalization in RSUD Ibnu Sina (273 medical records). The study sample that corresponding to inclusion and exclusion criteria are 27 medical records.
Result: The average prostate volume in underweight criteria was 44,5 cm3, in normal criteria is 42,4 cm3. Highest average of prostate volume found in overweight criteria, which was 64,3 cm3. In the obese criteria, the average prostate volume was 32,2 cm3. The average prostate volume was 46,0 cm3. From the linear regression test, we found the value of p=0,881 and R2=0,01.
Conclusion: There is no significant correlation between BMI and prostate volume in this study

Keywords: BPH, obesity, BMI, prostate volume

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INTRODUCTION

Progress in the health sector today has not been accompanied by health awareness in the community. According to population census data, Indonesia's life expectancy has increased from 1971, namely 45.7 years old, to 70.7 years old in 2010. The female's life expectancy is higher (72.6 years old) than the male's life expectancy (68,7 years old)[1]. Although the life expectancy has increased, the trend of obesity has also increased significantly. According to RISKESDAS 2013, the prevalence of obese adult male population in 2013 was 19.7 percent, higher than in 2007 (13.9%) and 2010 (7.8%). [2]

Obesity in adult society causes increased health problems, such as cardiovascular disease, type 2 diabetes mellitus, osteoarthritis, hypertension, and dyslipidemia[3]. Obese men also experience prostate disease (prostatitis, benign prostatic hyperplasia (BPH), and prostate cancer).

The prostate gland is an organ in men that most often undergoes neoplastic changes, both benign and malignant. Benign prostatic hyperplasia (BPH) is the most common benign tumor that grows in men, and the incidence is related to age. The prevalence of BPH on autopsy examinationhistologically increased by 20% at 41-50 years old, 50% at 51-60 years old, and more than 90% in patients over 80 years old. Although clinically less frequent, the symptoms caused by a prostate obstruction are also age-related. At 55 years old, 25% of men reported experiencing obstructive voiding symptoms, by the age of 75 years old, 50% of men complained of experiencing a decrease in the urine flow's strength.

BPH occurs in the transitional zone and causes obstruction of the bladder neck and urethra, known as bladder outlet obstruction (BOO). BOO caused specifically by BPH is known as benign prostate obstruction (BPO). This enlargement causes BPH patients to develop Lower Urinary Tract Symptoms (LUTS), which consists of symptoms and signs of obstruction and irritation. [6]

Symptoms and signs of urinary tract obstruction are that the patient has to wait for the first urinary discharge, interrupted micturition, dripping at the end of the micturition, weakened micturition, and feeling unsatisfied after micturition. Symptoms of irritation due to the detrusor muscle's hypersensitivity mean increased frequency of micturition, nocturia, difficulty tolerating micturition, and dysuria. The obstruction occurs because the detrusor fails to contract strongly enough or fails to acquire long

enough intermittent contractions. The symptoms of irritation occur due to incomplete emptying at the time of urination or enlargement of the prostate, stimulating the bladder. The bladder often contracts even though it is not yet full. These symptoms and signs are scored and expressed in the form of I-PASS (International Prostate Symptoms Score). [7]

Apart from using I-PASS, other tests that can be used in determining the diagnosis of BPH are digital rectal, measuring the remaining urine after urination with catheterization or ultrasound of the bladder, uroflowmetry to measure the strength of the urine emission at the time of urination, or with an ultrasound imaging modality to determine the size of the prostate.[7]

Theoretically, in obese patients, adipose tissue causes an increase in estrogen due to the aromatization of testosterone. This change in hormonal balance plays a role in the pathogenesis of BPH.[8] Another conceptual approach is that obesity causes systemic inflammation and occurs in the prostate tissue resulting in the enlargement of prostate size. several studies show that obesity plays a role in prostate gland enlargement[3,4,10,11], but several other studies do not show the role of obesity in the prostate gland's enlargement[3,12,13,14]. Obesity can be measured by calculating the body mass index. Because of the discrepancy in the previous studies results, the researchers wanted to prove that the increase in BMI would be followed by an enlargement of the prostate volume in BPH patients with transabdominal ultrasonography (TAUS) examination at Ibnu Sina Regional Hospital, Gresik Regency.

METHODS

this research is an observational study. data was analyzed using the cross-sectional method. This study took medical record data of BPH patients at the Ibnu Sina Regional Hospital, Gresik Regency, from January 2016 to September 2017. This study's population were all BPH patients hospitalized at the Ibnu Sina Regional Hospital, Gresik Regency during the period January 2016 to September 2017. The research sample was BPH patients at the Ibnu Sina Hospital, Gresik Regency, from January 2016 to September 2017 who met the inclusion criteria and were not included in the exclusion criteria. This study's inclusion criteria were patients with a radiological diagnosis of BPH, and data on height, weight, and prostate volume were obtained by TAUS examination. This study's exclusion criteria were patients with prostate cancer, prostatitis patients, incomplete medical records, and patients

over 65 years of age. The sampling technique was non-probability sampling through purposive sampling. Purposive sampling is data collection based on the researcher's assessment criteria, considering that the sample meets the inclusion requirements and follows the research objectives. The minimum sample size for this study was 22 samples. In this study, out of 105 medical records, there were 84 medical records with weight and height data, from 84 medical records, there were 27 medical records that had complete prostate volume data (height, width, and length), four medical records only had data for length and height, one medical record only has width data, and 52 medical records have no data. Therefore, the number of samples analyzed was 27 medical records that matched the inclusion and exclusion criteria.

Based on the data collection that has been carried out, the data obtained are described in the table of age, weight, height, body mass index, and prostate volume. we used a linear regression test with the equation y = a + bx to examine how much the BMI variable will affect the prostate volume variable..

RESULT

The number of BPH patients at Ibnu Sina Hospital in 2016 was 158 people, and from January 2017 to September 2017 was 115 people. The total number of BPH patients in Ibnu Sina from 2016 to September 2017 was 273 people. However, the number of BPH patients who had complete prostate volume data was 27.

Table 1 Number of BPH Patients in 2016 and 2017 at Ibnu Sina Regional Hospital

Year	Patients Number
2016	158
2017*	115
Total	273

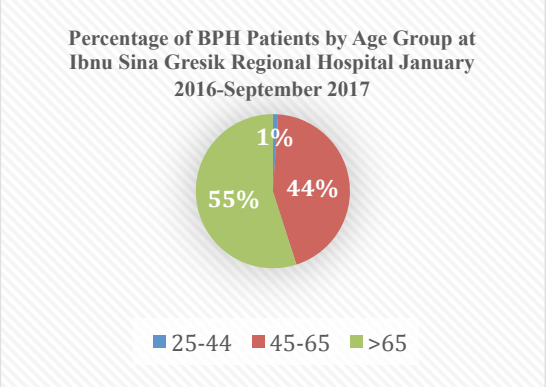

Diagram 1 Percentage of BPH Patients by Age Group at Ibnu Sina Gresik Regional Hospital January 2016-September 2017

Diagram 1 shows the percentage of BPH patients by age group at the Ibnu Sina Gresik Regional Hospital from January 2016 to September 2017. The age group with the least percentage of BPH patients is the age group 25-44 years, with 1% (3 people). The age group with the second-highest percentage of BPH patients was 45-65 years old with 44% (120 people), and the age group with the highest

percentage was over 65 years old with 55% (150 people).

Table 2 BMI Distribution Table of BPH Patients Who Have Complete Prostate Volume Data

IMT	Category	Patients Number
< 18,5	Skinny	4
18,5-24,9	Normal	16
25,0-27,0	Overweight	5
>27	*Obese*	2
Total		27

Table 3 Distribution of BMI Data Distribution of BPH Patients Who Have Complete Prostate Volume Data

	IMT (kg/m^2)
Mean	22,46
Median	22,03
Modus	16,11
Minimum	16,11
Maximum	31,22
Standard Deviation	3,61
n	27

Table 2 shows the number of BPH patients with body mass index data with complete prostate volume; there were 27 patients. The highest number of BPH patients was in the normal category, as many as 16 people, and the least number of BPH patients were in the obese category, where there were two people. In the skinny category, there are four people, and the overweight category is over five people.

Table 3 shows the distribution of the BMI data distribution of BPH patients who have complete prostate volume data. The average was 22.46 kg/m2, median 22.03 kg/m2, mode 16.11 kg/m2, patients with the smallest BMI was 16.11 kg/m2, the patient with the largest BMI was 31.22 kg/m2, the standard deviation value was 3.61, and the number of patients was 27.

To calculate the volume of the prostate, use the ellipsoid formula, which is by knowing the largest anteroposterior height (H), transverse width (W), cephalocaudal length (L), then entering into the formula: $Volume = H \times w \times L \times \frac{\pi}{6}$. The greatest anteroposterior height (H), transverse width (W), cephalocaudal length (L) are known from ultrasound examination. The ultrasound machine used was the Toshiba Aplio 400.

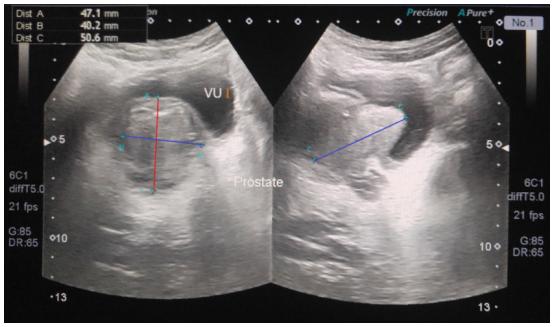

Figure 1 Prostate ultrasound image

From the prostate ultrasound image above, we can determine a BPH patient's prostate volume, where line A is the largest anteroposterior (H) height, measuring 47.1 mm. Line B is cephalocaudal (L) length, measuring 40.2 mm. Line C is the transverse width (W), measuring 50.6 mm. Then these numbers are entered into the formula ellipsoid:

$$Volume = H \times w \times L \times \frac{\pi}{6}$$

$$Volume = 47{,}1mm \times 40{,}2mm \times 50{,}6mm \times \frac{\pi}{6}$$

$$Volume = 50.164\ mm^3 = 50{,}164\ cm^3;$$

then the prostate volume above is 50.164 cm3.

Table 4 Prostate Volume Distribution Table for BPH Patients Who Have Complete Prostate Volume Data

Volume Prostate (cm^3)	Grade	Patients Number
<30	Grade I	6
30-50	Grade II	9
50-85	Grade III	11
>85	Grade IV	1
Total		27

Table 5 Prostate Volume Grading Distribution Table based on BMI

IMT	Volume Prostat								Total	
	Grade I		Grade II		Grade III		Grade IV			
	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)
Kurus	0	0%	3	11,1%	1	3,7%	0	0%	4	14,8%
Normal	4	14,8%	4	14,8%	8	29,6%	0	0%	15	59,3%
BB lebih	1	3,7%	1	3,7%	2	7,4%	1	3,7%	5	18,5%
Obese	1	3,7%	1	3,7%	0	0%	0	0%	2	7,4%
Total	6	22,2%	9	33,3%	11	40,7%	1	3,7%	27	100%

Table 6 Table of Average Prostate Size Volume by BMI Category

Category	Mean
Skinny	44,5 cm^3
Normal	42,4 cm^3
Overweight	64,3 cm^3
Obese	32,2 cm^3
Mean Total	46,0 cm^3

Table 4 shows that the highest number of BPH patients according to prostate volume grading was at Grade III with 11 people, and the least number was at Grade IV with one person. The number of BPH patients with Grade I was six and Grade II was 9.

From Table 5, the highest prostate volume grade in the thin BMI group was grade II with a rate of 3 people (11.1%). The highest prostate volume grade in the group with normal BMI was Grade III with eight people (29.6%). Only one person (3.7%) had Grade IV.

Table 6 explains that in the thin category group, the mean prostate volume was 44.5 cm3; in the normal category, it was 42.4 cm3. The largest mean prostate volume was found in the overweight category group, namely 64.3 cm3. In the obese group, the mean prostate volume was 32.2 cm3. The overall mean of BPH patients at the Ibnu Sina Regional Hospital was 46.0 cm3.

To examine how much the BMI variable will affect the prostate volume variable, the researcher will use a linear regression test with equations $y = a + bx$.

In this study it was found that the data have normal distribution values. The BMI variable has a Skewness value = 0.92; Kurtosis = 0.32; and Shapiro-Wilk = 0.758. The prostate volume variable has a Skewness value = 0.95; Kurtosis = -0.07; and Shapiro-Wilk = 0.787.

To find out whether the data on the variables in this study had a homogeneous variant, the Levene test was used. In the Levene test, the variable prostate volume has a value of p = 0.232, and the BMI variable is p = 0.302. Because both variables have p> 0.05, the two variables have a homogeneous variant.

From the results of the regression calculation according to the IBM SPSS Statistic 24 program, it was found that p-value = 0.881, which can be concluded that there is no significant relationship between BMI and prostate volume. Because there was no significant relationship between BMI and prostate volume, a regression equation between BMI and prostate volume could not be made. The scatter diagram found that the data distribution between prostate volume (y-axis) and BMI (x-axis) were randomly distributed and did not describe a linear relationship.

DISCUSSION

Based on the data obtained from the index of BPH inpatients at the Ibnu Sina Hospital, Gresik Regency, we can find out the number of patients and the patients' age in the period January 2016 to September 2017. Out of 273 people, the number of BPH patients is in the 25-44 years old group. There were three people (1.1%), in the 45-65 years age group, there were 120 people (44%), and in the age group over 65 years old, there were 150 people (55%). This result shows similarities with other studies that there is an increase in BPH incidence with age.

In this study, from 105 medical record files submitted to researchers, seven medical records were sampled in the study because they had complete data on height, weight, prostate volume and were under the inclusion and exclusion criteria. Four people had a BMI under 18.5 and were categorized as skinny, 16 people had a BMI between 18.5 and 24.9 and were categorized as normal, and five people had a BMI between 25 and 27 and were categorized as overweight. Two people were included in the obese category because they had a BMI above 27. The number of obese patients in this study was two, which is one of the study's weaknesses because the number is small and does not represent the obese BMI group. This study's limitation was that not all medical records had complete prostate volume data, and only two obese patients had complete prostate volume data. This incomplete medical record data also causes researchers to be unable to use probability sampling techniques (stratified random sampling).

The BMI table data distribution shows that the mode values do not approach the mean and median values because the BMI distribution has a multimodal distribution and does not have twin values.

Prostate volume was obtained using the ellipsoid formula after knowing the largest anteroposterior height (H), transverse width (W), cephalocaudal length (L) from ultrasound examination. The ultrasound machine used in this examination is the Toshiba Aplio 100 with the TAUS examination method.

If divided into 4 grades, the classification of prostate volume grading is as follows:

Table 7 Classification of Prostate Volume

Grade	Volume Prostat (cm^3)
Grade I	<30
Grade II	30-50
Grade III	50-85
Grade IV	>85

In this study, of 27 people, there were six people with grade I BPH, nine people with grade II BPH, 11 people with grade III BPH, and one with grade IV BPH. The patient with the smallest prostate volume was 12.01 cm3, while the patient with the largest prostate volume was 94.1 cm3. The mean prostate volume of BPH patients in this study was 46.0 cm3. The prostate volume table's data distribution shows that the mode values do not approach the mean and median values because the prostate volume distribution has a multimodal distribution and does not have twin values.

The mean prostate volume in patients with an obese BMI category (32.2 cm3) was smaller than that of the other BMI category groups and does not follow the existing theory. This could be due to decreased quality of ultrasound imaging results in obese patients so that the prostate volume is found to be less accurate. In obese patients, sound waves attenuate due to thick adipose tissue. Increased attenuation of sound waves goes straight along with an increase in the thickness of the adipose tissue. The higher the frequency used, the higher the attenuation of sound waves. The difference in the thickness of the fat layer also causes the speed of sound that passes through the adipose tissue to be different, and when received by a transducer, it will reduce the quality of the ultrasound imaging results.

In this study, we wanted to determine how much the BMI variable would affect the prostate volume variable to use a linear regression test with the equation $y = a + bx$. For the linear regression test to be carried out, the parametric test research requirements must be met, namely having a normal distribution and a

homogeneous data variant. Based on the values of Skewness, Kurtosis, and Shapiro-Wilk, it was found that the data for the two variables had a normal distribution. Based on the Levene test shows that the two variables have a homogeneous variant. Furthermore, the linear regression test was carried out, from the results of the linear regression test, the value of p = 0.881 or p> 0.05. The p value> 0.05 indicates that prostate volume and body mass index do not have a significant relationship, with a value of R2 = 0.01, which means that the effect of BMI on prostate volume is 1%. This result is under the research conducted by Ambeng Y., et al., which was conducted in Dr. Soetomo Surabaya, which showed that there was no significant relationship between BMI and prostate volume (r = 0.018 and p = 0.936) 18, but research conducted by Yelsel K., et al. showed different results, where the study they conducted showed that BMI has a positive correlation with prostate volume (r = 0.630 and P <0.001) .10

The study's difference could be due to differences in the characteristics of the study sample, the number of the study sample, and the methods of measuring prostate volume and BMI used in the study. In a study conducted by Yelsel K. et al., Patients who were sampled had an age range of 56-90 years; wherein this study, the sample used was patients under 65 years of age to minimize the age factor on prostate volume. Research conducted by Yelsel K. et al., Excluded patients who took 5-α-reductase inhibitors or antiandrogens because they could affect prostate volume, whereas, in this study, the consumption of 5-α-reductase inhibitors or antiandrogens were not excluded.

Because it uses a broader age range, in the study of Yelsel K., et al., the sample used was larger, namely 211 people, while in this study due to the lack of complete data in the medical record archives, the number of research samples was only 27 people. The difference in the number of samples in the study also affects the results of the investigation.

The Ibnu Sina Hospital's ultrasound machine used in this study was the Toshiba Aplio 400. In contrast, Yelsel K. et al. did not include the ultrasound machine. The method of measuring prostate volume used in this study was Transabdominal Ultrasound (TAUS), while the study conducted by Yelsel K., et al., used the Trans Rectal Ultrasound (TRUS) examination. Although TRUS may be better at

estimating prostate size, Sutapa et al. did not show a significant difference between the measurement of prostate volume using the TRUS method and the TAUS method. Examination using ultrasound is very dependent on operator expertise (operator-dependent) so that the results of the examination can be different from one person to another. We used the Kappa coefficient test to find the degree of consistency of the results of ultrasound examinations carried out by more than one examiner.

The weight and height used in this study were only by recording what was stated in the medical records so that researchers could not measure the errors that occurred when measuring height and weight. Errors that occur during this measurement can cause errors in calculating the patient's BMI. In a study conducted by Yelsel K. et al., measurement of body weight and height was carried out for the sake of research to measure errors that can occur during measurement. The timing of BMI data collection was also a factor that led to the absence of a significant relationship between BMI and prostate volume. We cannot see whether the BMI the patient has was temporary or has been since the incident or before BPH appeared[14].

The following are differences in several factors that can affect the differences in the results of the two studies:

Table 8. Research Differences between Tritanto R. dan Yelsel K., et al

Items	Tritanto R.	Yelsel K., et al.
Age mean	59,61	68.0 ± 6.3
Age range	48-65	56-90
Sample count	27	211
Prostate Volume Measurement method	TAUS	TRUS
USG Machine	Toshiba Aplio 400	None
Height and weight measurement	Recording medical records	Direct evaluation
Consumption of 5-α-reductase inhibitors or antiandrogens	Not excluded	Excluded
Bladder stones	Not excluded	Excluded
Neurogenic bladder dysfunction	Not excluded	Excluded
Reapeated ISK	Not excluded	Excluded

Apart from the method and method of data collection, other confounding variables may affect the finding of insignificant relationship between BMI and prostate volume. Metabolic syndrome such as insulin resistance can affect prostate growth. In insulin resistance conditions, there is a decrease in cell response to insulin so that pancreatic beta cells will produce more insulin and hyperinsulinemia occurs.[21] Insulin is known as a mitogen and becomes a growth factor for prostate epithelial cells. Increased insulin will lead to increased transcription of genes involved in sex

hormone metabolism. Hyperinsulinemia is also associated with decreased sex hormone-binding globulin, resulting in an increase in the number of androgens and estrogens in the prostate and an increased BPH risk.

Insulin-like growth factor 1 (IGF-1) also promotes prostate epithelial growth. Homologous insulin receptors with IGF-1 receptors, so that insulin can bind to the IGF-1 receptor and activate the IGF signaling pathway that promotes prostate growth.[22] Nandeesha et al. found that insulin was an independent risk factor for increased prostate volume. Patients with fasting plasma insulin levels less than 7mU / mL had prostate growth of 0.84 mL per year, whereas patients with preeclamptic plasma levels were also higher.

CONCLUSION

Research on the correlation between BMI and prostate volume in BPH patients at the Gresik District Hospital can be concluded as follows:

1. The number of BPH patients in the 25-44-year-old age group is three people (1.1%), in the 45-65-year-old age group, there are 120 people (44%), and in the age group over 65 years old, there are 150 people (55 %). There is an increase in the incidence of BPH with increasing age.
2. The average prostate size in BPH patients at the Ibnu Sina Regional Hospital, Gresik Regency, is 46 cm3.
3. There is no correlation between BMI and prostate volume in BPH patients.

Based on the research that has been done, there are several suggestions for further study.

1. Improve the sample distribution of each BMI group so that the study results are representative of each BMI group and the results obtained have better statistical power. Hospitals and clinicians' role is to complete data and carry out more complete examinations so that all medical records can be used and provide better research results.
2. Measuring body weight and height directly to minimize the measurement error factor.
3. In this study, researchers found it difficult to get complete prostate volume data from ultrasound machine. For further research, it is recommended that the researcher communicates with the clinician (surgeon and/or radiologist) who treats and examines the patient so that they know the picture or approximate sample that will be met during the study.

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