THE CORRELATION BETWEEN SERUM PSA LEVEL AND PROSTATE HISTOLOGIC AGGRESSIVENESS WITH PROSTATIC VOLUME IN BPH PATIENTS

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ABSTRACT

Objective: Prostate inflammation is one of pathophysiology of prostate hyperplasia in benign prostatic hyperplasia (BPH). There are several factor that involved in prostatic inflammation, such as prostate specific antigen (PSA) that play a role as an autoantigen. The objective of this study was to assess the correlation between free PSA level with prostate histologic aggressiveness, and also the correlation between prostate histologic aggressiveness with prostatic volume in BPH patients. Material & Methods: The design of this study was cross-sectional analytic observational study to determine correlation between serum PSA level with prostatic aggressiveness, and prostatic volume with prostatic aggressiveness. This study was performed from June to November 2016 in Sanglah Public Hospital, Surya Husadha, Balimed, Bhakti Rahayu, and Ganesa Hospital. Eighty three patients with BPH undergoing transurethral resection of the prostate (TURP) were recruited. Results: The result of gamma correlation analysis using Chi-square of PSA level with aggressiveness (p=0.000) and aggressiveness with prostatic volume (p=0.012). Conclusion: Serum PSA level were correlated with prostatic aggressiveness. Prostatic aggressiveness also correlated with prostatic volume.

Keywords: Prostate specific antigen, prostatic volume, aggressiveness.

ABSTRAK

Tujuan: Inflamasi prostat merupakan salah satu patofisiologi terjadinya hiperplasia prostat. Terdapat banyak faktor yang terlibat pada inflamasi prostat, seperti prostate specific antigen (PSA) yang berperan sebagai auto antigen. Tujuan penelitian ini adalah untuk menilai hubungan antara serum PSA dengan agresifitas prostat, dan hubungan antara agresifitas prostat dengan volume prostat pada pasien benign prostatic hyperplasia (BPH). Bahan & Cara: Desain dari studi ini adalah observasional analitik potong lintang untuk menentukan hubungan antara serum PSA dengan agresifitas prostat serta volume prostat dengan agresifitas prostat. Penelitian ini dikerjakan pada bulan Juni sampai November 2016 di RSUP Sanglah, RS Surya Husadha, RS Balimed, RS Bhakti Rahayu, dan RS Ganesa. Total sampel yang dilakukan operasi transurethral resection of the prostate (TURP) sebanyak 83 pasien BPH. Hasil: Hasil analisa korelasi gamma dengan menggunakan Chi-square, didapatkan korelasi bermakna antara serum PSA dengan agresifitas prostat (p=0.000) dan agresifitas prostat dengan volume prostat (p=0.012). Simpulan: Serum PSA berhubungan dengan agresifitas prostat dan agresifitas prostat berhubungan dengan volume prostat.

Kata kunci:Prostate specific antigen, prostatic volume, aggressiveness.

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INTRODUCTION

Benign prostatic hyperplasia (BPH) is the most frequent benign tumor in elderly male. Based on epidemiology study in USA in year of 2000, BPH is main causes of 4.4 million case of clinical referral, 117.000 emergency department cases, and 105.000 hospitalized cases.[1,2] In 2013 at Sanglah Hospital Denpasar, there were 101 BPH patients undergoing operation between 1161 urological operation.[3]

Prostatic inflammation is an important pathophysiology that involved in prostatic growth and progressiveness of Lower Urinary Tract Symptoms (LUTS). Many growth factor and cytokine give an implication to inflammatory process. Potential causes of inflammation including hormonal change, infection, diet or environmental factors, autoimmune responses, or urine reflux in prostate collecting duct. Pattern of inflammation in prostatic tissue in BPH patients was also examined widely. Irani et al, proposed a four point scale classification of prostatic tissue inflammation based on hypothesis of histological grading about extension of inflammatory cells. Furthermore, they described about aggressiveness grading system based on effect of inflammatory cells existence in prostatic tissues.[4,5]

Serum prostate specific antigen (PSA) can be used to know BPH progression. PSA was synthesized by epithelial cells of prostatic tissue and it's organ specific but not cancer specific. Prostatic volume progression can be predict by serum PSA level. Serum PSA level can increased in inflammation, prostatic manipulation (biopsy of TURP), acute urine retention, instrumentation, prostatic malignancy and, aging process. PSA is a risk factor of moderate and severe inflammation in BPH.[4,6,7]

OBJECTIVE

The utility of serum PSA was widely described as free PSA, PSA density, PSA velocity. The objective of this study was to assess the correlation between free PSA level with prostate histologic aggressiveness, and also the correlation between prostate histologic aggressiveness with prostatic volume in BPH patients.

MATERIAL & METHODS

We examined medical record of 83 BPH patients undergone TURP in 5 hospital in Denpasar and one hospital in Gianyar regency from June to November 2016. The mean age of the patients was 64.4 (range 50-84) years. BPH was defined according to BPH clinical study guidelines and histopathology examination result. Patient with chronic systemic inflammation, diabetes mellitus, or obesity was excluded. PSA level was categorized by PSA cutoff 4ng/ml (defined as low PSA <4ng/ml, and high PSA ≥ 4 ng/ml), and prostatic volume was categorized by median of prostatic volume (40 ml) as a cut off, then categorized as as low volume <40 ml, and high volume ≥ 40 ml. Prostatic volume measurement was done by Radiologist using trans abdominal ultrasonography.

Pathological examination of prostatic aggressiveness was examined by single Pathologist based on four point classification by Irani et al (grade 0, 1, 2, 3), then categorized as low grade (grade 0 and 1), and high grade (grade 2 and 3) based on previous study by Kwon et al.[5,8]

Shapiro-Wilk's and Levene's tests were used to test the normality and variance homogeneity of data. Values of numerical data is described as mean, median and range. Categorical data were compared by Chi-square distribution. Gamma correlation was used for correlation analysis.

RESULTS

The baseline characteristic of research subject is summarize at table 1. The mean age of the patients was 64.4 (range 50-84) years old.

There was a significant correlation between PSA level with aggressiveness (p=0.000). Correlation coefficient R=0.672 showed a positive strong correlation between PSA level with prostatic aggressiveness. Prevalence ratio (PR 2.873 with CI 95% 2.00-3.05) means that high level of PSA serum (PSA ≥ 4ng/ml) have a tendency to have a high prostatic aggressiveness 2.873 times higher than low level of PSA serum (PSA <4ng/ml).

There was a significant correlation between histologic aggressiveness with prostatic volume (p=0.012). Correlation coefficient R=0.575 showed a positive moderate correlation between histologic aggressiveness with prostatic volume. Prevalence

**Table 1.** Baseline characteristics of research subject.

	Mean	SD	Median (Max -Min)
Age (years)	64.4	8.188	
PSA (ng/dl)			4.85 (0.22-43.20)
Prostatic volume (ml)			40 (20.68-81.94)

Table 2. Data distribution determined by frequency and percentage.

Variable	Category	Frequency (n)	Percentage (%)
PSA	Low (<4ng/ml)	37	44.6
	High (≥4ng/ml)	46	55.4
Prostatic volume	Low (<40ml)	42	50.6
	High (≥40ml)	41	49.4
Aggressiveness	Low grade	51	61.4
	High grade	32	38.6

Table 3. Bivariate analysis (gamma correlation).

Variables		p value	Coefficient correlation	Prevalence ratio
PSA	Aggressiveness	0.000	0.672	2.873 (2.00 -3.05)
Aggressiveness	Prostatic volume	0.012	0.575	2.254 (2.00 -3.04)
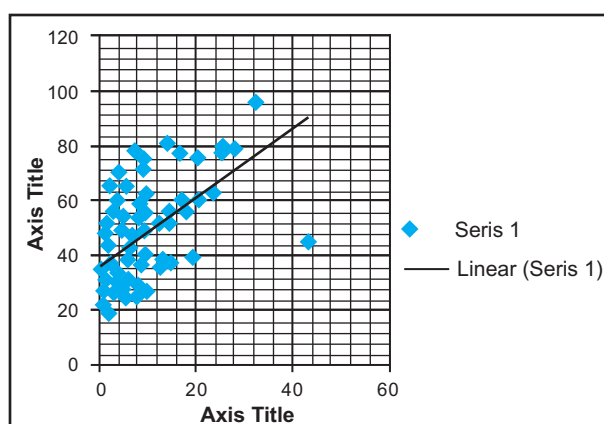
Figure 1. The correlation between free PSA and prostatic volume (p=0.00; R 0.572).

ratio (PR 2.254 with CI 95% 2.00-3.04) means that high prostatic histologic aggressiveness have a tendency to have a high prostatic volume 2.254 times higher than low prostatic aggressiveness.

There was a significant correlation between PSA level with prostatic volume (p=0.000). Correlation coefficient R=0.572 showed a positive moderate correlation between PSA level with prostatic volume. It means that higher level of PSA serum have a tendency the higher prostatic volume.

DISCUSSION

Recently, role of prostatic inflammation has been proposed in pathogenesis and progression of BPH. It was hypothesized that inflammation infiltrate caused tissue damage and lead to chronic wound healing and caused prostatic hyperplasia.

Tezval et al., proposed that inflammatory infiltrate is proportional with enlargement or volume of prostatic tissue.[9-11] Serum prostate specific antigen (PSA) can be used to know BPH progression. PSA was synthesized by epithelial cells of prostatic tissue and it's organ specific but not cancer specific. Prostatic volume progression can be predicted by serum PSA level. Serum PSA level can increased in inflammation, prostatic manipulation (biopsy of TURP), acute urine retention, instrumentation, prostatic malignancy, and aging process. PSA is a risk factor of moderate and severe inflammation in BPH.[4,6,7]

Pattern of inflammation in prostatic tissue in BPH patients was also examined widely. Irani et al., proposed a four point scale classification of prostatic tissue inflammation based on hypothesis of histological grading about extension of inflammatory

cells. Furthermore, they described about aggressiveness grading system based on effect of inflammatory cells existence in prostatic tissues.[4,5]

In our study most of research subject (61.4%) were have low grade prostatic aggressiveness. Aggressiveness in prostatic tissue showed extension of inflammatory infiltrate until reach contact with prostatic epithelial.[5] This is supported by inflammation phenomena, which is proposed that chronic low grade basal inflammatory condition accompanied by local hypoxia, then followed by release of reactive oxygen species and nitric oxide then lead to prostatic enlargement.[12]

Overall proportion of research subject in this study (55.4%) have a high level of PSA (>4ng/ml). Maybe this finding is consistent with condition of overall subject that were in complication of urine retention which was done urine catheter insertion before hospital admitted. Few study suggested that many factors that play a role in increasing PSA level, such as duration of urine retention, urinary catheter insertion, digital rectal examination, TURP procedure, and post sexual intercourse.[4,6,7]

In this research we found that there was a significant correlation between PSA level with aggressiveness (p=0.000, R=0.672, PR 2.873 with CI 95% 0.000-0.035). Significant correlation was also found between prostatic volume with aggressiveness (p=0.012, R=0.575, PR 2.254 with CI 95% 0.000-0.036). PSA level and prostatic volume was statistically correlated with prostatic aggressiveness. PSA has auto antigenicity characteristic that can stimulate chronic inflammation, and inflammatory infiltrate can caused chronic wound healing process. Prostatic aggressiveness itself is an effect that caused by the existence of inflammatory cells in the prostatic tissue. Overall of pathogenic process lead to prostatic enlargement.[5,9,10,13,14]

CONCLUSION

Serum PSA level is correlated with prostate histologic aggressiveness in BPH patients. Prostatic aggressiveness is correlated with prostatic volume in BPH patients.

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