

# Prostate-specific membrane antigen (PSMA) as diagnostic biomarker in prostate cancer: a cross-sectional study



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## ABSTRACT

**Introduction:** Prostate cancer is the second most common malignancy among men in the world. Prostate-specific membrane antigen (PSMA), a type II membrane protein, is produced by all prostate cells in any stage of prostate malignancy. This recently recognized attribute may prove useful in future diagnosis and therapy of prostate cancer. The aim of this study was to compare PSMA expression in both prostate cancer and benign prostate disease.

**Methods:** PSMA antigen expression was examined using polymerase chain reaction (PCR). Total of 20 samples from each prostate cancer and benign prostate group were examined at the Department of Pathology Anatomy, Dr. Sardjito Hospital. The data was analyzed using version 21 of SPSS.

**Results:** The mean PSMA gene expression in benign groups was 13.49 [95% CI: 11.27 – 15.72] and the mean PSMA gene expression in the malignant group was: 25.14 [95% CI: 20.95-29.33], the p-value was <0.01. Using an independent T-test analysis, we found that the increase in PSMA gene expression in the prostate cancer group was statistically significant.

**Conclusion:** The expression of the PSMA gene was correlated with prostate cancer. Increased PSMA gene expression in prostate tissue could be used as a biomarker to diagnose prostate cancer.

**Keywords:** gene expression, PCR, PSMA, prostate cancer

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## INTRODUCTION

Prostate cancer is the second most common malignancy among men in the world.<sup>1</sup> When detected at an early stage, prostate cancer has nearly 100 percent of the 5-year survival rate. Prostate-specific antigen (PSA) is currently the main marker used in screening settings. PSA has a high sensitivity and low specificity. Increased prostate-specific antigen does not only occur in prostate cancer, but can occur in several other conditions, resulting in a high false-positive rate.<sup>2</sup> The incidence of overdiagnosis and overtreatment will have a negative effect on the quality of life of patients diagnosed with prostate cancer. Thus, another diagnostic tool for prostate cancer is needed to prevent the increasing number of malignancies in the prostate and reduce the mortality rate due to prostate cancer, one of which is the prostate-specific membrane antigen.

Prostate-specific membrane antigen

(PSMA), a type II membrane protein which has glutamate-hydroxypeptidase hydrolysis activity, is produced by all prostate cells in any stage of prostate malignancy.<sup>3</sup> PSMA is expressed in normal tissue forms found in the prostate, brain, kidney tubules, and intestinal mucous membranes, including carcinoma. PSMA, characterized by the presence of murine monoclonal antibody (mAb) 7E11 - C5, has an internalization signal that allows the protein to be internalized on the cell surface to the endosomal compartment. Another study stated that PSMA is a biomarker that has high potential as a diagnostic test tool as well as therapy. A total of 100,000 proteins were found in prostate carcinoma, both primary and metastatic prostate carcinoma.<sup>10</sup> Using the enzyme-linked immunoadsorbent assay (ELISA) and western blot, PSMA was found in the serum of patients diagnosed with prostate cancer. The elevation in serum

PSMA levels seen in patients diagnosed with prostate cancer is consistent with low prostate-specific antigen levels. This recently recognized attribute may prove useful in future diagnosis and therapy of prostate cancer.<sup>4,5</sup> This study assessed PSMA gene expression in prostate tissue in two different groups: prostate cancer and benign prostate disease. The aim of this study was to compare PSMA expression in both prostate cancer and benign prostate disease.

## METHODS

This study is a non-experimental retrospective study to evaluate PSMA expression between prostate cancer tissue samples and benign prostate disease patients at Dr. Sardjito Hospital, Yogyakarta. This research included 40 tissue samples, of which 20 tissue samples were collected from patients with prostate cancer, and 20 other tissue samples

collected from patients with prostate cancer who had met the inclusion and exclusion criteria. Inclusion criteria were patients diagnosed with prostate cancer and benign prostate hyperplasia (BPH), and tissue samples has been carried out to see the PSMA image using PCR. Results were documented and analyzed for differences in prostate-specific membrane antigen in prostate cancer and benign prostate hyperplasia. Statistical measurement was performed using an independent T-test analysis with SPSS 21. Ethics committee approval was received from the Ethics Committee of Faculty of Medicine, Universitas Gadjah Mada/Dr. Sardjito Hospital with No. KE/FK/1105/EC/ 2020.

## RESULTS

The analysis was performed on 40 tissue samples taken from two unpaired groups, namely the prostate cancer group and the benign prostate hyperplasia group. From the two groups, a statistical test was carried out in each group which can be seen in Table 1.

Based on the data table, it can be seen that as many as 20 samples were included in the prostate cancer group, and as many as 20 were included in the benign prostate hyperplasia group. The mean PSMA value for both prostate cancer and benign prostate hyperplasia is listed in Table 2. The mean PSMA value in prostate cancer is 25.14 with a 95% CI value: 20.95-29.30, which statistically has a higher mean value than the control group, namely PSMA in benign prostatic hyperplasia (13.49, 95% CI: 11.27-15.72).

An independent T-test was obtained with a 2-way significance value of 0.00 in both groups with a p-value of 0.01. There was a significant difference in PSA level between prostate cancer and benign prostate hyperplasia groups (Table 2). In the prostate cancer group, PSMA had a higher value than in the benign prostatic hyperplasia group and was statistically significant.

## DISCUSSION

Some study suggest that PSMA can be used as a serum-based marker option for prostate cancer using RT-PCR in

**Table 1. The characteristics of sample**

		N	Mean
Prostate-Specific Membrane Antigen (PSMA)	Prostate Cancer	20	25.14
	Benign prostate hyperplasia	20	13.49

**Table 2. The unpaired T-test results of the PSMA on tissue samples of patients diagnosed with prostate cancer and benign prostate hyperplasia**

		Sig. (2-tailed)	95% Confidence Interval	
			Lower	Upper
Prostate-specific membrane antigen	Prostate cancer	.000	20.95	29.3
	Benign prostate hyperplasia	.000	11.27	15.72

addition to histopathologic examination, but this has not been thoroughly verified.<sup>5</sup> The monoclonal antibody (mAb) 7E11 is an anti-PSMA antibody used to assess the PMSA expression in serum.<sup>3</sup> Increased PSMA expression was found in prostate adenocarcinoma and prostate intraepithelial neoplasia compared to benign prostatic hyperplasia. Therefore, PSMA expression can be used as a diagnostic tool and also as a criterion for a patient undergoing prostate cancer therapy.<sup>6</sup> In comparison to that study, a previous study looked at the expression of prostate-specific membrane antigen with anti-PSMA antibodies. In this study, immunoreactivity was shown to have a higher percentage of cancer cells than benign epithelial cells.<sup>7</sup>

Wright et al. compare the expression of PSMA in normal prostate tissue, benign prostatic hyperplasia (BPH), prostate intraepithelial neoplasia (PIN) tissue, and prostate cancer tissue. In that study, out of 27 tissue samples of BPH, 22 (81%) of the samples had positive PSMA result, with 29% mean positive cells, while in PIN, 100% of the tissue samples had positive PSMA result with 59% mean positive cells. The expression of PSMA had varying stain patterns, ranging from low-level diffuse cytoplasmic staining in the epithelium of normal prostate to very intense cytoplasmic and focal membrane staining in high-grade carcinomas and metastatic tissue.<sup>4</sup> Another study found PSMA expression in prostate cancer tissue, with 157 out of 165 (95%) samples had positive PSMA result, with 53% mean

positive cells.<sup>8</sup> The unique expression of PSMA makes it an important marker for prostate cancer.<sup>9-11</sup>

Several studies have suggested that although PSMA expression can be found in BPH tissue, the values were not as high as PSMA in prostate cancer tissue.<sup>12-15</sup> A number of cells with a positive result against PSMA-antigen have also been shown to be higher in prostate cancer tissue compared to BPH tissue samples.

## CONCLUSION

The expression of the PSMA gene was correlated with prostate cancer. Increased PSMA gene expression in prostate tissue could be used as a biomarker to diagnose prostate cancer at early stage, and also as a criterion for a patient undergoing prostate cancer therapy to avoid over-treatment due to false-positive results from another diagnostic test.

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## CONFLICT OF INTEREST

We declare that there were no conflicts of interest in this study.

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## AUTHOR CONTRIBUTION

All of authors are equally contributed to the study.

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