

# AGE, TOTAL PSA, PSA DENSITY AND GLEASON SCORE, TAUS AS PREDICTIVE FACTORS IN PATIENTS WITH PROSTATE CANCER

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## ABSTRACT

**Objective:** To find the factors related as predictive factors for Gleason score in prostate cancer patients. **Material & methods:** This study obtained a total sample of 144 patients with prostate cancer in Sardjito General Hospital Yogyakarta in 2009-2013. Of the total 144 patients, only 64 patients had complete medical records. All patient samples were patients who had biopsy of the prostate. This study is a retrospective case-control study to predict the Gleason Score in patients with prostate cancer in terms of age, total prostate specific antigen (PSA), PSA density (PSAD) and transabdominal ultrasonography (TAUS). Normality test assessed the distribution of the data. Pearson test assessed normal distribution and Spearman test for normal distribution. All data were analyzed using SPSS version 18. **Results:** Analysis of data from 64 patients with prostate cancer with a normal distribution of the variables obtained on age and TAUS with  $p > 0.05$  whereas abnormal distribution obtained on total PSA, PSAD with  $p < 0.05$ . Of the data on the data with a normal distribution, age and TAUS with values obtained  $p 0.039$  and  $p 0.738$ . From these data it can be said there is a relationship between age and Gleason score where the higher the age the higher the Gleason score. TAUS of the data can be said there is no relationship between TAUS and Gleason score. Then the abnormal distribution of the data obtained with a total PSA  $p < 0.001$  and PSA density  $p < 0.001$ . The data is obtained from the relationship between total PSA and PSAD with Gleason score. **Conclusion:** It was found that age, total PSA, PSAD affect the increase in Gleason score where the higher the age, total PSA and PSAD the higher the Gleason score in patients.

**Keywords:** Prostate cancer, total prostate specific antigen, prostate specific antigen density, transabdominal ultrasonography, Gleason score.

## ABSTRAK

**Tujuan:** Mencari faktor-faktor yang berhubungan sebagai faktor prediksi Gleason score pada pasien kanker prostat. **Bahan & cara:** Pada penelitian ini didapatkan total sampel 144 pasien dengan kanker prostat di RSU Sardjito Yogyakarta pada tahun 2009-2013. Dari total 144 pasien, hanya 64 pasien yang mempunyai data rekam medis lengkap. Semua sampel pasien adalah pasien yang dilakukan biopsi prostat. Penelitian ini merupakan penelitian case control retrospektif untuk memprediksi Gleason score pada pasien dengan kanker prostat ditinjau dari usia, total prostate specific antigen (PSA), prostate specific antigen density (PSAD) dan transabdominal ultrasonography (TAUS). Uji normalitas untuk menilai sebaran data. Kemudian dilakukan tes Pearson untuk menilai distribusi normal dan tes Spearman untuk distribusi tidak normal. Seluruh data dianalisa dengan menggunakan SPSS versi 18. **Hasil:** Analisa data dari 64 pasien dengan kanker prostat didapatkan variabel dengan distribusi normal pada usia dan TAUS dengan  $p > 0.05$  sedangkan didapatkan distribusi tidak normal pada PSA total, PSAD dengan  $p < 0.05$ . Dari data tersebut pada data dengan distribusi normal, yaitu usia dan TAUS didapatkan nilai usia  $p 0.039$  dan  $p 0.738$ . Dari data tersebut dapat dikatakan terdapat hubungan antara usia dengan Gleason score dimana semakin tinggi usia maka semakin tinggi Gleason score. Dari data TAUS dapat dikatakan tidak terdapat hubungan antara TAUS dengan Gleason score. Kemudian dari data distribusi tidak normal didapatkan PSA total dengan  $p < 0.001$  dan PSA density  $p < 0.001$ . Dari data tersebut didapatkan hubungan antara PSA total dan PSAD dengan Gleason score. **Simpulan:** Dari penelitian ini didapatkan bahwa usia, PSA total, PSAD mempengaruhi peningkatan Gleason score dimana semakin tinggi usia, PSA total dan PSAD maka akan semakin tinggi Gleason score pada pasien.

**Kata Kunci:** Karsinoma prostat, total prostate specific antigen, prostate specific antigen density, transabdominal ultrasonography, Gleason score.

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## INTRODUCTION

Pathology prediction in patients diagnosed with prostate cancer is still far from our expectations and requires a combination of other variables examination, such as digital rectal examination, prostate specific antigen (PSA) serum and biopsy results data, such as Gleason score and percentage of positive biopsy results. Achievement from multi parameter is essential when viewed from the PSA is not very accurate due to the influence of age and often there are several conditions that influence such as benign prostate hyperplasia (BPH) and prostatitis.<sup>1-3</sup>

Gleason score is the most frequently used system for classifying characteristics of prostate cancer where the assessment glandular structures in the tumors. The predominant pattern and two dominant patterns are given a score of 1-5 each. Gleason score then summed. Scoring systems assessed by two of the most numerous and heterogeneous patterns in prostate cancer. In addition, this method is more superior in predicting the prognosis of the disease than single scoring system.<sup>4-6</sup>

## OBJECTIVE

This study aims to find the factors associated as a factor predictive of Gleason scores in prostate cancer patients. Factors used include age, total PSA, PSA density and transabdominal ultrasonography (TAUS). By knowing some of these factors are expected to treat prostate cancer patients with a treatment option that is more appropriate and not excessive.

## MATERIAL & METHOD

This is a case control study that conducted at Sardjito General Hospital Yogyakarta from April to May 2013, retrospectively. Data were collected from medical records of Sardjito Hospital, Yogyakarta. Researchers are beginning the procedure to apply for a permit implementation of research at research supervisor in the Department of Urology Faculty of Medicine, University of Gadjah Mada, then the obtained permission submitted to the Research Department of Sardjito General Hospital Yogyakarta. Then perform retrieval of data through medical records of patients.

Prostate cancer patients with histopathologic biopsy results (Gleason score), age, total

PSA and TAUS were included in this study. Patients with no histopathologic results with prostate carcinoma were excluded. After undergoing the selection of samples obtained total samples that meet the inclusion and exclusion criteria were 64 patients. Descriptive and correlative data were assessed among variables. Pearson tests were conducted to assess the normal distribution and Spearman test for abnormal distribution. All data were analyzed using SPSS version 18.

## RESULT

In this study, it was found that 144 patients histopathologically diagnosed with prostate cancer in January 2009-May 2013 by means of prostate biopsy, prostatectomy, or transurethral resection (TURP). Of the total 144 patients, who met the inclusion and exclusion criteria were 64 patients. From the processed data, mean age was 70.5 years with the youngest 50 and the oldest 85 years. Then the total PSA value of the data obtained a mean value of total PSA 62.4 ng/dl with the lowest total PSA value 1.89 ng/dl and the highest > 150 ng/dl. PSA density value of the data obtained average value 1.77ng/dl with the lowest values of 0.6 ng/dl and the highest 8.88 ng/dl. As for TAUS, the mean prostate volume 43.87 grams with the smallest volume of 9.56 grams and the largest volume of 107.84 grams (table 1).

**Table 1.** Variable characteristic.

Variable	
Age, X $\pm$ SD (median)	70.5 $\pm$ 8.1 (70.5)
PSAt	62.4 $\pm$ 54.6 (41.2)
TAUS	43.9 $\pm$ 19.1 (45.9)
PSAd	1.8 $\pm$ 1.9 (1.1)
Score Gleason, medium (min - max)	6 (2-10)

## DISCUSSION

The mean value obtained Gleason score of 6.45 with the lowest 2 and the highest 10. For Gleason score can only be the accumulated then categorized including low risk, medium risk or high risk. Gleason scores are supposed to be read in conjunction the first and second pattern shown in histopathological tissue. Because Gleason score 4 + 3 with Gleason score of 3 + 4 has a different

prognosis where Gleason score 4 + 3 has a worse prognosis than 3 + 4 although the result in number is equal.<sup>7</sup>

It is necessary to note that in patients with Gleason score above 7 has a success rate of biopsy more highest.<sup>2</sup> Also stated that the extension biopsy had superior results in terms of diagnostic and also results in a more highest Gleason score.<sup>8</sup> Total PSA, PSA density and PSA density transition zone has an advanced ability to detect prostate cancer, as well as the invasion of seminal vesicles and lymph nodes or metastasis but difficult if it is used to detect early-stage prostate cancer.<sup>6</sup> Patients with early-stage prostate cancer, PSA levels inspection, the number of biopsies performed may be used as a predictive risk factor for the increase Gleason score.<sup>9</sup> Biopsy extension prostate cancer patients at least 10 core can increase the positive detection rate of prostate cancer in accordance with the findings at prostatectomy.<sup>10</sup>

On this study, 14 patients with a total PSA >150 ng/dl accompanied by Gleason score of 10. From these data show that the higher the value the higher the PSA will follow Gleason score and from previous studies say, the progressive increase of the increase in the incidence of metastasis bone in patients with high PSA scores with high Gleason proven results. In the PSA levels over 100 have predictive value to 100% for malignancy.<sup>11</sup> By knowing PSA, it can be used to predict bone metastasis in prostate cancer patients will provide savings in terms of economy.<sup>11</sup>

Analysis of data from 64 patients with prostate cancer obtained variables with normal distribution on age and TAUS with  $p > 0.05$  whereas abnormal distribution obtained on total PSA, PSA density at  $p < 0.05$ . From these data at the data with a normal distribution, the age and the age of the value obtained TAUS  $p = 0.039$  and  $p = 0.738$ . From these data it can be said there is a relationship between age and Gleason scores where the higher the age, the higher the Gleason score. TAUS data can be said there is no relationship between TAUS with Gleason score. Then from the data distribution is not normal total PSA obtained with  $p < 0.001$  and PSA density  $p < 0.001$ . From the data obtained relationship between total PSA and PSA density with Gleason score. From other studies say, total PSA has a false negative numbers were lower when compared with the figures because the PSA density PSA in patients with non-malignancy of the gland is not eliminated by the formula or method used to calculate PSA.<sup>6</sup> In the cohort studies with a total sample of 1662

patients had significant thing about the worsening results of histopathological results in patients with high PSA density. Previous research said that PSA density may be obtained from the weight of the prostate or TRUS as a strong predictor for cases of high risk for recurrence. There are other studies that say, both total PSA and PSA density has the same parameters and significant in predicting tumor borders and extracapsular expansion of tumor but there is a difference in the total PSA in predicting an increase in blood PSA levels and prostate volume. From this it can be said, PSA density showed a strong predictor for extracapsular T1c disease accompanied by clinical preoperative PSA Gleason score while more inferior.<sup>6</sup>

## CONCLUSION

From this study, it was found that age, total PSA, PSA density affects the increase in Gleason score where the higher the age, total PSA and PSA density, the higher the Gleason score in patients. With higher Gleason score, then the risk for the occurrence of metastases is also high.

## REFERENCES

1. Stacy L, Herbert B. Early detection, diagnosis, and staging of prostate cancer, in Campbell-Walsh Urology. 10<sup>th</sup> ed. Saunders: Philadelphia USA; 2012. p. 2764.
2. Bittner N, Gregory S, Andreini H, Taunbenslag W, Allen ZA, Butler WM, et al. Prebiopsy PSA velocity not reliable predictor of prostate cancer diagnosis, Gleason score, tumor location, or cancer volume after TTMB. J Urol; 2009.
3. Giannarini G, Scott C, Moro U, Pertoldi B, Beltrami CA, Selli C. Are PSA density and PSA density of the transition zone more accurate than PSA in predicting the pathological stage of clinically localized prostate cancer. Urology Oncology : Seminars and Investigation; 2008. p. 353-60.
4. Stav K, Judith S, Merald H, Leibovici H, Lindner A, Zisman A. Does prostate biopsy Gleason score accurately express the biologic features of prostate cancer. Urology Oncology; 2007. p. 382-86.
5. Andre N, Roemeling S, Krane Ries, Scholder FH, Van Der Kwast TH. Should we replace the Gleason score with the amount of high-grade prostate cancer. European Association of Urology; 2007. p. 931-39.
6. Divrik RT, Eroglu A, Sahin A, Zorlu F, Ozen H. Increasing the number of biopsies increases the concordance of Gleason scores of needle biopsies and prostatectomy specimens. Urology Oncology: Seminars and Investigation; 2007. p. 376-82.

7. Hong SK, Han BK, Lee ST, Kim SS, Min KE, Jeong SJ, et al. Prediction of Gleason score upgrading in low-risk prostate cancers diagnosed via multi (,12)-core prostate biopsy. *J Urol*; 2009. p. 271-76.
8. Munterner M, Epstein J, Hernandez DJ, Gonzalgo ML, Mangold L, Humphreys E, et al. Prognostic Significance of Gleason Score Discrepancies between Needle Biopsy and Radical Prostatectomy. *European Association of Urology*; 2008. p. 767-76.
9. Alenda O, Ploussard G, Mouracade P, Xylinas E, Taille AD, Allory Yves, et al. Impact of the primary Gleason pattern on biochemical recurrence-free survival after radical prostatectomy: a single-center cohort of 1,248 patients with Gleason 7 tumors. *J Urol*; 2011. p. 671-76.
10. Rapiti E, Schaffar R, Iselin C, Mirabell R, Pelte MF, Weber D, et al. Importance and determinants of Gleason score undergrading on biopsy sample of prostate cancer in a population-based study. *BMC Urology*; 2011. p. 13-19.
11. Krane LS, Menon M, Kaul SA, Siddiqui SA, Wambi C, Peabody JO, et al. Role of PSA velocity in predicting pathologic upgrade for Gleason 6 prostate cancer. *Urology Oncology: Seminars and Investigation*; 2011. p. 372-77.