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Can the Free/Total PSA Ratio Predict the Gleason Score Before Prostate Biopsy?

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Key Words

PSA • Percent free PSA prostate cancer • Gleason score • Prostate biopsy

Abstract

Objectives: To determine whether there is a correlation between high Gleason score and free/total (f/t) prostate specific antigen (PSA) in patients newly diagnosed with prostate carcinoma. ***Materials and Methods:*** The study included 272 prostate biopsy patients whose total PSA value ranged from 4 - 10 ng/ml. The patients were divided into 2 groups according to the f/t PSA ratio: Group 1 ≤ 15% and Group 2 > 15%. Furthermore, the groups were also compared to each other in terms of mild (≤ 6), moderate (= 7), and high (≥ 8) Gleason score. ***Results:*** Group 1 consisted of 135 (49.6%) patients and Group 2 consisted of 137 (50.4%) patients. While 27 (20%) patients had a high Gleason score in Group 1, only 10 (7.3%) patients had a high Gleason score in Group 2 ($p = 0.008$). Using Spearman's correlation test, we found that the f/t PSA ratios were observed to decrease significantly in all patients with increased Gleason scores ($p = 0.002$, $r = -0.185$). ***Conclusion:*** According to our study, there is a relationship between higher Gleason score and decreased f/t PSA ratio. Therefore, f/t PSA can be an indicator for predicting the Gleason score.

Introduction

Prostate carcinoma (PCa) is the most common occurring cancer type for men in the USA, and for elderly men in Europe [1, 2]. It is the second most common cause of cancer-related death in men [1]. It is a serious health problem, especially in developed countries where the elderly population is proportionally higher [3]. Histopathological diagnosis of PCa can be established by transrectal ultrasound-guided (TRUS) biopsy after an abnormal finding in digital rectal examination or finding an augmentation in prostate specific antigen (PSA) level [3]. An increased PSA level is not specific for PCa; it can also elevate due to benign prostate hyperplasia, prostatitis, and other nonmalignant events [3]. Catalona et al. [4] suggests using a total PSA cut-off value of 4 ng/ml in order to recommend a prostate biopsy for diagnosing PCa. In numerous studies, the importance of free/total (f/t) PSA ratio was shown and this ratio is usually lower in patients with PCa than in those with benign prostate hyperplasia [5]. Catalona et al. [6, 7] suggest using a cut-off f/t PSA ratio between 0.20–0.25 be used for recommending evaluation to diagnose PCa. High Gleason scores also indicate a greater likelihood of PCa and correlate with increased total PSA levels [8, 9]. Today, a 25% cut-off

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Table 1. Clinical and demographic characteristics of the patients

	First group (n = 135)	Second group (n = 137)	p
Age (year)	65.27 ± 8.01	66.04 ± 7.55	0.4
Total PSA (ng/ml)	7.02 ± 1.94	6.38 ± 2.04	0.008
Free PSA (ng/ml)	0.72 ± 0.31	1.37 ± 0.61	< 0.001
Free/Total PSA	0.1 ± 0.03	0.21± 0.06	< 0.001
Prostate volume (ml)	38.13 ± 15.5	45.37 ± 20.01	0.003
Gleason score	6.60 ± 0.94	6.35 ± 0.8	0.037

First Group: free/total PSA ≤ 15%; Second Group: free/total PSA > 15%; PSA = prostate specific antigen

Table 2. Mild, moderate and high-risk cancer distributions according to patients' Gleason score in Group 1 and Group 2

	Mild (Score ≤ 6)	Modarate (Score = 7)	High (Score ≥ 8)	Total	p
Group 1	88 (65.2%)	20 (14.8%)	27 (20%)	135	
Group 2	100 (73%)	27 (19.7%)	10 (7.3%)	137	
Total	188 (69.1%)	47 (17.3)	37 (13.6%)	272	0.008

f/t PSA ratio for patients with total PSA levels between 4–10 ng/ml (gray zone) is recommended for diagnosing PCa. When this ratio is used, it has a 95% probability of correctly diagnosing PCa [10]. Also the f/t PSA ratio is useful for diagnosing more aggressive cancer and eliminating the need for redundant histopathological diagnoses [11, 12]. In our study, we evaluated whether there is a correlation between the f/t PSA ratio and Gleason score in newly diagnosed PCa patients, and we evaluated the importance of using a 15% f/t PSA ratio cut-off value.

Materials and Methods

After receiving local ethics committee approval at our hospital, the data of 272 patients who received TRUS biopsies due to high PSA levels or suspicious findings during digital rectal examination and were diagnosed with PCa according to the outcome of biopsies, were evaluated retrospectively between the dates of January 2012 and December 2014. Twelve core TRUS biopsies were received from all patients whose total PSA levels were between 4 - 10 ng/ml. Each biopsy was performed with the patient in the lateral decubitis position, and in all cases, an anesthetic block of the periprostatic plexus was applied by administering 0.2% prilocaine. A 25 cm 18 gauge Tru-cut® needle was used in each case. The patients were divided into 2 groups according to f/t PSA ratio: Group 1 (≤ 15%) and Group 2 (> 15%). Ages, f/t PSA, prostate volumes, and Gleason scores of the groups were compared. Furthermore, the groups were compared with each other in terms of mild (≤ 6), moderate (= 7), and high (≥ 8) Gleason score.

The data analysis was performed by using SPSS for Windows, version 16 (SPSS Inc., Chicago, IL, United States). Descriptive statistics for variables with a normal distribution and categorical variables are shown as mean ± standard deviation and the number of cases and percentage (%), respectively. Student's t-test was used for the intergroup analysis of continuous variables, and $p < 0.05$ was accepted as statistically significant.

Results

Group 1 consisted of 135 (49.6%) patients and Group 2 consisted of 137 (50.4%) patients. The mean age in Group 1 was 65.2 ± 8.01 years and in Group 2 was 66.04 ± 7.55 years (p = 0.4). The prostate volumes of the patients in Group 1 and Group 2 were found as 38.13 ± 15.5 and 45.37 ± 20.01 ml, respectively. The other comparative data for both groups are shown in table 1.

Patients from each f/t PSA group were further divided into 3 groups, low (score ≤ 6), moderate (score = 7), and high (score ≥ 8), according to their Gleason scores. A statistically significant difference was observed regarding PCa incidence between each f/t PSA group with high Gleason scores while there was statistically no significant difference between each f/t PSA group with low and moderate-risk Gleason scores (p = 0.601). While 27 patients (20%) had high Gleason score in Group 1, the patient number in Group 2 was only 10 (7.3%) (p = 0.008, table 2).

Using Spearman's correlation test, we found that the f/t PSA ratios were observed to decrease significantly in relation to increased Gleason scores for all PCa patients (p = 0.002, r = -0.185).

Discussion

Partin nomogram, for indicating whether disease is organ-limited before radical surgery, was used as a guide in our studies [13]. Using the nomograms as a guide, we determined whether f/t PSA ratio has a correlation with Gleason score, or at least in patients with a high Gleason score. Previous studies have shown the clinical importance of a series of markers as well as tPSA for diagnosing PCa, while also showing the clinical importance of f/t PSA ratio for diagnosing PCa [14, 15]. Pannek et al. [16] emphasized in their study that the f/t PSA ratio can be of crucial predictive value for Gleason score. In similar

studies, Noldus et al. [17] were unable to show the predictive significance of the f/t PSA ratio in organ-limited disease. However, Sakai et al. [18] reported that the f/t PSA ratio had a predictive significance for determining the PCa stage for patients in the gray zone between 4 –10 ng/ml total PSA. Likewise, in our study, a significant negative correlation was detected between f/t PSA ratio and Gleason score. In another study from Turkey, Erdem et al. [19] were unable to show that the predictive significance of the f/t PSA ratio was more valuable than tPSA in patients who underwent radical prostatectomy. Southwick et al. [20] obtained results supporting our study. They emphasized that using a 15% cut-off value for f/t PSA in patients with < 7 Gleason scores improved prediction of T1c PCa. Morote et al. [21] determined a predictive cut-off value for f/t PSA ratio in T1c PCa patients as 11%, but then evaluated radical prostatectomy patients' data in their subsequent study and found that a 15% cut-off value for f/t PSA ratio had greater predictive accuracy. Aus et al. [22] reported that in low-risk patients who underwent radical prostatectomy, those with f/t PSA ratios that were < 10.7% had more aggressive PCa. When the patients were divided into 2 groups according to f/t PSA ratio, our study showed that patients below 15% (Group 1) had a higher Gleason score.

In conclusion, according to our study, PCa patients with higher Gleason score correlate with increased tPSA and decreased fPSA. Therefore, the f/t PSA ratio can be used for predicting the Gleason score. We believe that our work will be helpful for future research and may provide an impact for clinical considerations.

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