Does the New Proposal for Prostate Cancer Grading Correlate With CAPRA Score?

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Purpose: To determine if there is a correlation between the newly proposed Gleason grading system by the International Society of Urological Pathology and the Cancer of the Prostate Risk Assessment (CAPRA) score.

Material and Methods: The records of all patients that underwent radical prostatectomy at our hospital between 2007 and 2013 were retrospectively reviewed. The study parameters included patient demographics, the percentage of pre-operative prostate biopsies positive for PCa, biopsy Gleason Score (GS), and pre- and post-operative PSA values.

Result: The study included 146 patients with complete medical records and follow-up data. Mean age of the patients was 66.6 ± 6.08 years. According to the newly proposed Gleason grading system, 97 (66.4%) patients were grade 1, 20 (13.7%) were grade 2, 8 (5.5%) were grade 3, 11 (7.5%) were grade 4, and 10 (6.8%) were grade 5. The distribution of CAPRA scores was as follows: 1: n = 43 (29.5%); 2: n = 53 (36.3%); 3: n = 22 (15.1%); 4: n = 14 (9.6%); 5: n = 8 (5.5%); 6: n = 4 (2.7%); 7: n = 1 (0.7%); 8: n = 1 (0.7%). Correlation analysis showed that the CAPRA score was significantly correlated with GS based on the newly proposed Gleason grading system (Correlation Coefficient=0.361, $P < 0.001$).

Conclusion: As a strong correlation was noted between these 2 independent grading systems, we think clinicians that seek to predict the prognosis in PCa patients should take into consideration both the newly proposed ISUP grading system and the CAPRA score.

Keywords: biochemical recurrence; CAPRA; Gleason pattern; pathologic examination; prostatectomy

INTRODUCTION

Prostate cancer (PCa) is the most common solid neoplasm in Europe, with an incidence of 214 cases per 1000 men[(1)]. Nowadays, patient counseling and patient-oriented treatment form the core of PCa treatment, because each treatment modality can have serious effects on patient quality of life;[(2)] as such, stratification and grading of PCa continue to increase in importance. The treatment of PCa is based on clinical stage and risk status, and treatment options for localized PCa include active surveillance, radical prostatectomy (RP), radiation therapy, brachytherapy, cryosurgical ablation, and high-intensity focused ultrasound (HIFU)[(1)].

The Gleason grading system is the most common system used to grade prostate cancer aggressiveness. The system uses a scale of 1 to 5 to calculate the Gleason score (GS) (range: 2-10), which is the sum of the most common and second most common grade patterns. The most commonly reported GSs in clinical practice is ≥ 6. Many patients and clinicians consider a GS of 6 indicative of an intermediate prognosis and seek immediate treatment;[(3,4)] however, there is a lack of consensus concerning the cancerous pattern of PCa with a GS of 6[(5)]. Due to deficiencies, the International Society of Urological Pathology (ISUP) has updated the Gleason grading system from time to time; the latest update was in 2014. The newly proposed system stratifies patients into 5 distinct prognostic groups, which enables more accurate and simplified classification of tumors. Moreover, the lowest grade in the newly proposed system is 1 not 6, as in the Gleason system, which might result in reducing the incidence of overtreatment of indolent cancer[(3)].

There are several pre- and post-treatment assessment tools used to predict prognosis after definitive treatment of PCa, including the Kattan nomogram, D'Amico classification, and the Cancer of the Prostate Risk Assessment (CAPRA) score[(6-8)]. The CAPRA score is a pre-treatment score based on patient age, preoperative prostate-specific antigen (PSA), prostate biopsy GS, clinical stage, and the percentage of positive cores in a prostate biopsy specimen. Although the CAPRA score is an externally validated and easy to use tool; biopsy GS, clinical stage, and the percentage of positive biopsy cores are approximations by nature and, therefore, might over- or underestimate the actual grade or extension of disease[(8)]. As such, the present study aimed to determine the correlation between the newly proposed Gleason grading system and the CAPRA score. A possible correlation might help clinician in patient risk stratification and treatment planning.

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Table 1. Upstaging between prostate biopsy and final pathology results

Gleason Score	Prostate Biopsy GS	RP Specimen GS
Gleason 6 (3+3)	115 (78.8 %)	97 (66.4 %)
Gleason 7 (3+4)	14 (9.6 %)	20 (13.6%)
Gleason 7 (4+3)	4 (2.7 %)	8 (5.4%)
Gleason 8 (3+5)	12 (8.2 %)	8 (5.4%)
Gleason 8 (4+4)	1 (0.7 %)	2 (1.3%)
Gleason 8 (5+3)	-	1 (0.6%)
Gleason 9 (4+5)	-	6 (4.1%)
Gleason 9 (5+4)	-	4 (2.7%)

MATERIALS AND METHODS

After the approval of the study protocol by Turkiye Yuksek Ihtisas Training and Research Hospital review board, the records of all patients that underwent radical prostatectomy at our hospital between 2007 and 2013 were retrospectively reviewed. Patients who had a biopsy confirmed localized PCa were treated with radical prostatectomy. Patients that received neoadjuvant treatment for PCa were excluded from the study. The study parameters included patient demographics, the percentage of pre-operative prostate biopsies positive for PCa, biopsy GS, and pre- and post-operative PSA values. The CAPRA score was calculated using The University of California, San Francisco (UCSF), web-based calculator[9] by S.T.. Needle biopsies and radical prostatectomy materials were examined by the same pathologist (G.A.). Samples that could not be diagnosed via hematoxylin & eosin staining were studied using p63, HMWK, and AMACR immunohistochemistry.
Mean ± SD was used to describe quantitative variables. Quantitative measurements were compared using non-parametric Spearman's correlation analysis. Data were analyzed using IBM SPSS Statistics for Windows v.21.0 (IBM Corp., Armonk, NY). The level of statistical significance was set at $P < .05$.

RESULTS

The study included 146 patients with complete medical records and follow-up data. Mean age of the patients was 66.6 ± 6.08 years. The mean pre-operative PSA value was 9.3 ± 9.6 mg dL−1 and the mean number of PCa-positive prostate biopsy cores was 3.1 ± 1.3 (range: 1-6). The distribution of prostate biopsy GSs was as follows: GS 6: n = 115 (78.7%); GS 7: n = 18 (12.3%); GS 8: n = 13 (8.9%). An upstaging of GS was observed via final pathologic examination of some RP specimens, as shown in **Table 1**. According to the newly proposed Gleason grading system, 97 (66.4%) patients were grade 1, 20 (13.7%) were grade 2, 8 (5.5%) were grade 3, 11 (7.5%) were grade 4, and 10 (6.8%) were grade 5.
The distribution of CAPRA scores was as follows: 1: n = 43 (29.5%); 2: n = 53 (36.3%); 3: n = 22 (15.1%); 4: n = 14 (9.6%); 5: n = 8 (5.5%); 6: n = 4 (2.7%); 7: n = 1 (0.7%); 8: n = 1 (0.7%). According to CAPRA risk categorization 96 patients (65.7%) had low risk, 44 patients (30.1%) had intermediate risk and 6 patients (4.4%) had high-risk disease.
Among the 146 patients, 25 (17.1%) patients developed biochemical recurrence; 18 within 2 years and 7 within 5 years of treatment. Correlation analysis showed that the CAPRA score was significantly correlated with GS based on the newly proposed Gleason grading system (Correlation Coefficient=0.361, $P < .001$).
On univariate regression analysis both CAPRA score and newly proposed Gleason grading system were found significantly predict biochemical recurrence after radical prostatectomy ($P < .01$ for both correlations) (**Table 3**).

Table 2. The Newly Proposed Grading System Groups for Prostate Cancer by ISUP

Prognostic Grade Group	Definition
Grade group 1	Gleason score ≤ 6
Grade group 2	Gleason score 3+4=7
Grade group 3	Gleason score 4+3=7
Grade group 4	Gleason score 8 (4+4, 3+5, 5+3)
Grade group 5	Gleason score 9–10 (4+5,5+4,5+5)

DISCUSSION

PCa is the most common solid malignancy diagnosed in men in Europe and the United States,[1,10] and is the second leading cause of death in the United States[10]. Most patients with PCa die due to other causes; however, PCa does cause mortality in some cases. Due to the ambiguous behavior of the disease and the potential side effects of its treatment, risk stratification of PCa patients has become an important facet of its management[11].
The Gleason grading system was developed in the 1960's to categorize adenocarcinoma of the prostate according to 5 patterns, ranging from well differentiated (1) to poorly differentiated (5)[12]. The GS is the sum of the most common (primary) and the second most common (secondary) grade patterns, ranging from 2 to 10;

Table 3. Association Between Different Grading Systems And Frequency Of Biochemical Recurrence (BR).

	Biochemical recurrence, n (%)	*P* value
International Society of Urological Pathology (ISUP) Grade Group		< 0,01
1	9/97 (9,3)	
2	6/20 (30)	
3	2/8 (25)	
4	1/11 (9,1)	
5	7/10 (70)	
Cancer of the Prostate Risk Assessment (CAPRA) score		< 0,01
1	2/43 (4,7)	
2	6/53 (11,3)	
3	7/22 (31,8)	
4	4/14 (28,6)	
5	3/8 (37,5)	
6	1/4 (25)	
7	1/1 (100)	
8	1/1 (100)	

however, nowadays the most commonly reported GS in clinical practice is ≥ 6. Despite being the most popular grading system, the Gleason grading system is not perfect[4]. A rational patient could consider a GS of 6 (on a scale of 10) to indicate an intermediate prognosis or to indicate that immediate treatment is required, whereas, in fact, GS 3 + 3 = 6 is a good score indicating that treatment with active surveillance is sufficient. In addition, although both are GS 7, GS 3 + 4 = 7 has a better prognosis than GS 4 + 3 = 7[4]. Due to Gleason grading system deficiencies, the need for a better grading system emerged and in 2014 ISUP proposed a new grading system, as shown in **Table 2**[3].

During the past 20 years several research groups have proposed various nomograms and statistical models for predicting recurrence-free survival following definitive treatment and for determining pre-treatment pathologic stage of PCa; the most well-known being the Kattan nomogram and D'Amico classification,[6,13] and the CAPRA score[14]. Cooperberg et al.[14] developed the CAPRA score for preoperative prediction of biochemical recurrence-free survival after RP in patients with clinically localized PCa, as appropriate preoperative risk assessment is an integral component of counseling such patients[15]. The CAPRA score is the sum of the weighted risk factors, including age and PSA value at diagnosis, biopsy GS, clinical tumor stage, and the percentage of biopsy cores positive for PCa[16]. The external validation of the CAPRA score was studied by multiple researchers,[17, 18] and was reported to accurately predict recurrence-free survival and stratify patients according to their risk.

In the past, PCa patients were stratified according to GS as low risk (GS < 7), intermediate risk (GS = 7), and high risk (GS = 8-10); however, now it is well known that all GS 7 and GS 8-10 PCa cannot be grouped in the same categories and treated in that manner. In the present study the CAPRA score was significantly correlated with the newly proposed ISUP grading system. Based on this finding, we think that both the newly proposed ISUP grading system and the CAPRA score can be considered reliable instruments for predicting the prognosis in PCa patients. None of the patients in the present study had a GS of 9 or 10, which might have been due the widespread use of PSA screening in Turkey, which facilitates early detection of PCa. Also patients with high GS in prostate biopsy might have chosen or been directed to alternative treatment modalities.

Our study is also not without limitations. First of all, this is a retrospective study with a relatively small number of patients. And as mentioned above there are not many patients with high grade/high risk PCa.

CONCLUSIONS

The literature includes multiple studies on the validity of the CAPRA score for predicting PCa recurrence; however, to the best of our knowledge the present study is the first to determine the correlation between the newly proposed Gleason grading system and the CAPRA score. As a strong correlation was noted between these 2 independent grading systems, we think clinicians that seek to predict the prognosis in PCa patients should take into consideration both the newly proposed ISUP grading system and the CAPRA score.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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