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The consistency of Gleason scores may effect the operation outcomes for laparoscopic radical prostatectomy: a single surgeon and a single pathologist data

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Abstract. – INTRODUCTION: To evaluate the effects of consistency in preoperative and postoperative Gleason scores to the operation outcomes in patients who underwent laparoscopic radical prostatectomy.

MATERIALS AND METHODS: 204 of 347 patients were included the study. 143 patients whose preoperative prostate biopsies were evaluated in the other Institute were not included into the study. The preoperative data of patients and operation outcomes were investigated from institute's files of patients. Patients were divided to three groups by using consistence of pre and postoperative Gleason scores. The tumor, node and metastasis classification were used for staging prostate cancer.

RESULTS: Mean age was 63 and the mean PSA level was 11 ng/dl overall. In statistical analysis PSA levels, Gleason score and rate of positive score were significantly low in Group I ($p < 0,05$). As in operative data, nerve sparing surgical technique was performed statistical significance higher in Group 1 than other Groups. External bleeding rate of Group II was significantly lower than the other Groups. In univariate and multivariate analysis, postoperative pathologic stage was statistical significant for consistency of pre and postoperative Gleason scores.

CONCLUSIONS: The modified Gleason scoring system is safe and usable for evaluating prostate biopsies and operative specimens. The consistency in pre and postoperative Gleason score effect the operation technique and also operation outcomes. Working with an experienced uro-pathologist provides to inform patients more accurate and better.

Key Words:
Laparoscopy, Neoplasm grading, Pathology, Prostate cancer, Prostatectomy.

Introduction

Prostate cancer (PCa) is the most commonly diagnosed cancer among men in the world[1]. Nearly two thirds of PCa cases are confined to the prostate and can be treated by radical prostate removal or radiotherapy[2]. After prostate specific antigen (PSA) was described and then introduced in clinics, diagnosis of PCa increased rapidly. Additionally, PSA provides early diagnosis of PCa and early diagnosis of PCa may ensure early treatment[3]. Recently, rectal examination, serum PSA levels and prostate biopsies are used together for diagnosis of PCa. The Gleason scoring system is used for histopathological evaluation of prostate cancer, in addition, this scoring system may provide us to determinate its aggressiveness[3,4]. After diagnosis there are different treatment options for PCa that include watchful waiting, radical prostatectomy, radiotherapy, brachytherapy, androgen deprivation therapy[4]. In the first step after diagnosis, patients have to be provided by clinicians with accurate information about PCa. This information must include risks of PCa, operation outcomes and postoperative follow-up period. Before treatment, we have to analyze the risk of PCa in patients who have prostate confined PCa. The risks depend on PSA, Gleason score and clinical stage. In addition, clinicians must know the success rate of treatments, rate of tumor positive surgical margins, operation outcomes, and complications of operation[5]. According to the data, we evaluated the effects of consistency in preoperative prostate biopsies' Gleason scores and postoperative

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prostate materials' Gleason scores to the operation outcomes in patients who underwent laparoscopic radical prostatectomy (LRP). We aimed to predict operation outcomes by using preoperative Gleason score which was prepared by experienced uropathologist before operation. This is the first study which evaluates the consistency of preoperative and postoperative Gleason score for predicting operation data for laparoscopic radical prostatectomy in the literature.

Patients and Methods

This is a retrospective study. Patients who underwent LRP between December 2004 and February 2010 were included into the study. 204 of 347 patients were included in the study. 143 patients whose preoperative prostate biopsies were evaluated in the other Institute were not included into the study. All of the patients signed the Helsinki Declaration form and our Institute's form for LRP. The preoperative data of patients which included age, body mass index (BMI), PSA levels, preoperative Gleason scores, rate of positive cores in preoperative prostate biopsy, prostate volume, preoperative and operation outcomes which included complications in operation, hemoglobin levels, operation time, bleeding volume in operation, pathologic stage, positive surgical margin rate were investigated from Institute's files of patients. All of the preoperative prostate biopsies and LRP were performed by a single surgeon, also pre and postoperative prostate materials were evaluated by a single pathologist by using Modified Gleason scoring system. The modified Gleason scoring system was described in literature[6]. The tumor, node and metastasis (TNM) were used for staging prostate cancer[7].

Patients were divided into three groups by using consistence of pre and postoperative Gleason scores. In the first group (Group I) the Gleason scores were the same in pre and postoperative. In the second group (Group II) the Gleason scores of postoperative materials were higher than the Gleason scores of preoperative prostate biopsies. In the third group (Group III) the Gleason scores of postoperative materials were lower than the Gleason scores of preoperative prostate biopsies. We compared preoperative data and operation outcomes in these three groups.

The prostate biopsies were performed in Urology Outpatient Clinic and 10-12 core biopsies were taken by using trans-rectal ultrasound[8]. Additionally, the prostate volume was diagnosed by rectal ultrasonography, preoperative. The prilocaine was used for peri-prostatic nerve block (10cc prilocaine was injected) and also gel with lidocaine was used intrarectal.[9] The patients who underwent prostate biopsy, stopped to use anticoagulants and they began to use quinolone before trans-rectal prostate biopsy[10-12]. The patients who undervent prostate biopsies continued to use quinolone for 4 days after biopsy.

LRP were performed transperitoneal or extraperitoneal (148 extraperitoneal LRP, and 58 transperitoneal LRP) when prostate cancer diagnosed and patients wanted to be operated for prostate cancer. LRP procedures were performed as described in literature[13-15].

Statistical Analysis

Descriptive statistics were reported for all parametres. All statistical analyses were performed by SAS 9.2. Polytomous logistic regressions were used to define predicting factors for consistency of pre and postoperative Gleason scores. Continuous variables were compared using the ANOVA (Analyses of variance) and Fisher LSD test used for post hoc comparison between groups. Categorical variables were compared by Chisquare or Fisher's exact test. Significant level was accepted $p < 0.05$ for all statistical tests.

Results

In group I there is 106 (52%) patients, 77 (38%) patients in group II and 21 (10%) patients in group III. Mean age was 63.01 and the mean PSA level was 10.78 ng/dl overall. In statistical analysis, PSA levels were significantly low in Group I ($p < 0.05$, $p = 0.0024$) but not significant difference between group II and group III ($p > 0.05$) was observed. Pre and postoperative Gleason scores were significantly high in group III ($p < 0.05$) but no difference between Group I and Group II ($p > 0.05$) was observed. Rate of positive cores in biopsy were significantly low in Group I but not significant difference between group II and group III ($p > 0.05$) was observed. Tumor volume in group I is lower than group II and III but not significant difference group II and III was observed. Age, BMI, prostate volume were not statistically significant in three groups ($p > 0.05$). Table I shows the preoperative data of patients.

The Gleason scores were accepted as total for statistical analysis as well in Table I. Because,

Table I. Descriptive statistics for preoperative data of patients.

Parameter	Group I, n = 106	Group II, n = 77	Group III, n = 21	All, n = 204	F; *p*
Mean age (year)	63.05 (± 6.50)	63.01 (± 6.49)	62.81 (± 6.07)	63.01 (± 6.42)	0.01; 0.9882
Mean BMI# (kg/m^2)	26.32 (± 3.39)	26.44 (± 3.55)	26.01 (± 2.24)	26.60 (± 3.37)	1.70; 0.1867
Mean PSA*	8.42 (± 6.05)	13.37 (± 13.71)	13.37 (± 11.17)	10.78 (± 10.36)	6.08; 0.0027
Mean Gleason score*	6.22 (± 0.53)	6.05 (± 0.87)	7.10 (± 1.04)	6.25 (± 0.79)	16.63; 0.0000
Mean rate of positive core* (%)	0.30 (± 0.22)	0.38 (± 0.25)	0.46 (± 0.30)	0.35 (± 0.24)	4.94; 0.0081
Mean prostate volüme (cc)	50.37 (± 18.73)	47.82 (± 18.07)	53.09 (± 23.20)	49.69 (± 18.96)	0.78; 0.4678
Mean tumor volume* (cc)	3.77 (± 6.23)	7.61 (± 8.06)	6.30 ± (9.49)	5.49 (± 7.52)	6.14; 0.0026

#Body mass index; *Statistical significant.

there is contradiction with the prognosis of Gleason score 3+4 and 4+3, they are all accepted as "7" in statistical analysis[5,16]. As well preoperative data were not significant statistical in analysis, postoperative mean operative time, complication rate in operation were not significant statistical. Table II shows logistic regression summary statistics.

In operation outcomes, in Group I the nerve sparing technique was used more than the other groups. This was statistically significant when the groups were compared to each other (33.9%, $p < 0.05$). In addition, there was significant difference for external bleeding volume between only group I and group II ($p < 0.05$). Table III shows operation outcomes of patients.

After polytomous logistic regression analysis, only the postoperative pathologic stage was the effective factor on consistency of pre and postoperative Gleason scores ($p < 0.05$). Odd's ratios and confidence limits were presented (Table IV).

In logistic regression analysis, group I accepted as reference group. Although the complication rate in Group II (6,4%) is lower than the other groups this is not significant statistically in logistic regression analysis. In addition positive surgical margin rates are not significant statistically ($p > 0.05$).

Table II. Logistic regression summary statistics.

Parameter	Wald Chi-Square Statistic	*p*
Rate of cancer in biopsy	3.4671	0.1767
Intra operative complications	1.0616	0.5881
Nerve sparing rate	0.1218	0.9409
Anastomosis time	0.7822	0.6763
Delta hemoglobin	0.8250	0.6620
External bleeding	4.3453	0.1139
Operation time	2.3921	0.3024
Tumor volume	1.3180	0.5174
Specimen volume	2.4944	0.2873
PSA#	4.5160	0.1046
BMI*	2.6135	0.2707
Age	0.8283	0.6609

#PSA: Prostate specific antigen.
*BMI: Body mass index.

Discussion

The Gleason scoring system which was described in 1966 is used for defining treatment options, predicting prognosis and staging risk of prostate cancer. However, recently modified Gleason scoring system is used for diagnosis and

Table III. Operative data of patients.

Parameter	Group I, n = 106	Group II, n = 7	Group III, n = 21	*p* value
Nerve sparing technique rate*	33.9 %	22%	28%	< 0.05 = 0.00172
Mean operation time (minute)	212.2 ± 59.55	208.1 ± 55.65	233.1 ± 53.64	> 0.05
External bleeding (cc)*	556.1 ± 357.4	435.2 ± 252	586.2 ± 247.1	< 0.05, = 0.0197
Complication rate (%)	9.2	6.4	9.5	> 0.05
pT3 and pT4 patients	28.7 %	55.8 %	47.6 %	> 0.05
Positive surgical margin rate	5 (4.71%)	3 (3.89%)	1 (4.76%)	> 0.05

*Statistical significant.

Table IV. Distribution of categorical parameters according to groups in multivariate analysis.

Parameter	Clinical Stage	Group I		Group II		Group III		Total	
		n	%	n	%	n	%	n	%
Pathologic Stage*	T1 + T2	75	36.76	34	16.67	10	4.90	119	58.33
$p = 0.0009$	T3 + T4	31	15.20	43	21.08	11	5.39	85	41.67

*Statistical significant.

also risk analysis for PCa instead of the Gleason scoring system[17-18]. In this study all of the preoperative and postoperative prostate materials were evaluated by using modified Gleason grading system by a single experienced uro-pathologist. The clinical prostate cancer staging were diagnosed by using TNM classification[7].

PSA has some limitations for diagnosis of PCa but PSA levels may help to predict the spread of PCa, prognosis of PCa and recurrence of PCa. Additionally, in previous series PSA was related to tumor volume and Gleason scores[19]. In this study, PSA levels were significant statistical in group I but not significant in multivariate analysis. In our opinion this is related with tumor's features. As well this is related with Gleason score indirectly.

In this study, the rate of positive cores in biopsy chips and tumor volume which was detected postoperatively had been statistically significant lower in Group I than the other groups. This may help us to define the prostate confined disease before operation by using the Gleason scores[20-22].

The complication rate was significantly lower in Group II than other groups. This is related to that the Gleason score shows the ability of tumor's aggressivity and invasivity. During the past 20 years, urologic laparoscopic surgery has become popular worldwide, especially in Europe[23-27]. Early series with more than 5 years follow-up report no difference in oncologic outcomes between open and laparoscopic series[28,29]. Laparoscopic complications have been reported only for some series of specific procedures, and few multi-institutional series with a large number of procedures published[14,27,30-37]. In our investigation the complication rate was 8.3% and this rate is lower than literature. Our unique situation of having one well-organized fellowship-trained surgeon (more than 9 months) dominantly performing laparoscopic surgeries[38,39]. In Group I, there was extended bleeding in 6 patients, bladder perforation in 2 patients, bladder neck perforation in 1 patient and open conversation in 1 patient. The rate of complication is 9.2% in group I. In Group II, there was extended bleeding in 2 patients, subcutaneous emphysema in 2 patients and rectal injury in 1 patient. The rate of total complication In Group II is 6.4 %. In Group III, there was extended bleeding in 1 patient and bladder perforation in 1 patient. The overall complication rate is 9.5% in Group III. All of the complications except subcutaneous emphysema and open conversation were fixed during operation.

The nerve sparing technique was used in Group I much more than other groups[40]. This is much more than group II and III but this rate is not significant in logistic regression analysis ($p = 0.940$). In one year follow-up period, Group I patients had lower erectile dysfunction rate than the other groups.

The rate of erection was 19.4% in Group I, 12.9% in Group II and 9.5% in Group III. The rate of erectile dysfunction in Group I is statistically significant lower than other groups ($p < 0.05$). But more comprehensive studies which have long follow-up period are needed for better evaluation in erectile dysfunction.

We detected that the external bleeding rate was statistically lower in Group II than in the other groups ($p < 0.05$, $p = 0.01973$). The external bleeding rate of Group II is lower than other groups, especially lower than Group I. In our opinion this operative data is related with rate of nerve-sparing technique, in addition our series' bleeding rate is consistent with literature[27].

This is the first study which evaluates the consistency of pre and postoperative Gleason scores for predicting LRP's operation data in the literature. The Group I represented the consistency of pre and postoperative Gleason score and it is also used as reference group for statistical analysis. However, the postoperative Gleason scores are higher than preoperative usually in the literature. In this study, the most of pre and postoperative Gleason scores are the same, and this can be seen

in Table I[41-43]. The number of patients in Group I is higher than in other groups, nearly 52% of all patients. In the literature this is related to PSA, experience of pathologist, clinical stage, numbers of biopsies, prostate volume, the rate of cancer in biopsies and tumor volume[44]. In our report we determined that only the postoperative pathologic stage was significant statistically for consistency of preoperative and postoperative Gleason scores. As well the biopsy technique and the experience of surgeon who perform prostate biopsy is very important, this phenomenon also may be related to experience of pathologist, especially. Additionally, the Gleason scores are related to clinical stage. Clinical stage helps us to define the anatomical spread of disease, benefits of treatment, complication of treatment. If the tumor is confined into the prostate, the disease has chance to be treated surgically. In addition, there are lower rates of capsular invasion and lymphatic metastasis for this tumor. As well it is important to inform the patients in the light of this data, the experience of uro-pathologist has an important role for this confirmation. It is recommended that the prostate biopsy materials and operation materials have to be evaluated by the same experienced uro-pathologist[45]. In pathologic evaluation, the preoperative prostate biopsies' features which include the Gleason scores were not considered when evaluating postoperative specimens. Working with experienced uro-pathologist may give us a chance to predict operation outcomes, so we can provide patients with accurate information. This may also increase the confidence of patient's in urologists[46].

There is no doubt that, the consistency in pre and postoperative Gleason grades should not influence therapeutic decisions, directly. The rate of consistency in preoperative and postoperative Gleason scores may be helpful in defining quality standards of pre-therapeutic diagnosis and risk assessment, indirectly. Additionally, we did not aim to prepare or discuss a new nomogram for prostate cancer in this study.

Conclusions

The modified Gleason scoring system is safe and usable for evaluating prostate biopsies and operative materials. The consistency in pre and postoperative Gleason scores effect the operation technique and also operation outcomes. By using nerve sparing technique, we may reduce the rate of erectile dysfunction in 1 year follow-up period. Additionally, it is important to give more accurate information to patients with prostate cancer who will be performed LRP. Working with an experienced uro-pathologist enables us to inform patients in a more accurate and better way. More comprehensive studies which have long follow-up periods on this issue by holding the light of findings in this study may provide better treatment modalities and new forms of Gleason grading system for diagnosis.

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