

Correlation of Preoperative and Radical Prostatectomy Gleason Score: Examining the Predictors of Upgrade and Downgrade Results

Gholamreza Pourmand, Shahram Gooran, Seyed Reza Hossieni, Fateme Guitynavard, Majid Safavi, Amirsina Sharifi, and Ehsan Mokhtari

Department of Urology, Sina Hospital, Urology Research Center, Tehran University of Medical Sciences, Tehran, Iran

Received: 22 Apr. 2016; Accepted: 05 Jan. 2017

Abstract- Preoperative Gleason score (GS) obtained from Trans Rectal Ultra Sonography (TRUS) is the most common grading system to evaluate the appropriate treatment for patients with clinically localized prostate cancer. But this method showed upgraded and downgraded results in comparison to Gleason score obtained from radical prostatectomy. The current study aimed to determine clinical or pathological variables to reduce the differences between biopsy and radical prostatectomy Gleason scores. Through retrospective review of 52 patients with radical prostatectomy, this study examined the correlations of preoperative Gleason score with age, prostate volume, PSA level, PSA density, digital rectal exam findings and percentage of positive core needle biopsies across two groups, including patients with preoperative $GS \leq 6$ (i.e. group one) and patients with preoperative $GS \geq 7$ (group two). The discordance between biopsy GS and radical prostatectomy GS was observed to be 52% in the current study. Among patients with preoperative $GS \leq 6$, prostate volume ($P=0.026$), PSA density ($P=0.032$) and percentage of positive core needle biopsies ($P=0.042$) were found to be significant predictors for upgrade. There was no significant predictor for downgrade in patients with preoperative $GS \geq 7$. Findings of this study revealed that in patients with preoperative $GS \leq 6$, smaller prostate volume, higher prostate density and higher positive results of core needle biopsies were associated with the upgrade of GS. Therefore, it should be considered when selecting treatment modalities among these patients.

© 2017 Tehran University of Medical Sciences. All rights reserved.

Acta Med Iran 2017;55(4):249-253.

Keywords: Grade change; Prostate adenocarcinoma; Radical prostatectomy; Gleason score

Introduction

Prostate cancer is the most prevalent cancer among men and the second major cause of cancer death among males (1). Gleason score is used to evaluate prostate adenocarcinoma and associated with tumor aggressiveness, prognosis and treatment modalities (2). Biopsy Gleason score is obtained from histological examinations of the specimen from TRUS-guided core needle biopsies (3). Gleason score is considered for decision making about the modality of treatment to be either surgical or non-surgical (active surveillance, watchful waiting, and hormone therapy) (4,5). Despite the importance of biopsy Gleason score for evaluating prostate adenocarcinoma, it has shown very low correlations with Gleason scores obtained from radical prostatectomy (lymph node and/or nerve sparing) (6,7). Therefore, it is essential to improve its accuracy.

This study aimed to identify the preoperative clinical or pathological factors to enhance the accuracy of biopsy Gleason score in prediction of tumor grades before radical prostatectomy.

Materials and Methods

We retrospectively reviewed 103 patients, who had proven prostate adenocarcinoma from March 2012 to March 2013 in Sina hospital. Among these patients, 52 had retro pubic radical prostatectomy. To avoid any influence on Prostate Specific Antigen (PSA) level and Gleason scores, we excluded patients with preoperative therapies such as hormone and radiation therapy. Additionally, patients who had any invasive interventions on prostate which could affect its volume and PSA level were excluded from the study.

The objectives of this study were two-fold. First, to

Corresponding Author: S. Gooran

Department of Urology, Sina Hospital, Urology Research Center, Tehran University of Medical Sciences, Tehran, Iran
Tel: +98 21 6312484, Fax: +98 21 66348560, E-mail address: shahram_gooran@yahoo.com

Preoperative gleason score

influence of age, prostate volume, PSA level, PSA density, digital rectal exam findings and transrectal ultrasonography-guided core needle biopsy as predictors of adenocarcinoma. Second, to determine correlations of age, prostate volume, PSA levels, PSA density, digital rectal exam findings and percentage of positive core needle biopsies for adenocarcinoma with an upgrade in patients with preoperative $GS \leq 6$ (group A) or with downgrade in patients with preoperative $GS \geq 7$ (group B).

Upgrading was defined as an increase in Gleason score in pathological specimen derived from radical prostatectomy. Downgrading was defined as a decrease in Gleason score in conditions similar to upgrading.

Radical prostatectomy was performed through the open retro-pubic method by expert surgeons. The prostate volume was measured using prostate ellipse dimension theory. PSA density was calculated by dividing PSA level to prostate volume. The positive answer for core needle biopsy was set as any pathological finding that matched prostate adenocarcinoma cellular features.

SPSS software (version 21) was used for data analysis through chi-square test for comparing categorical variables in each group and stepwise multivariable logistic regression analysis for determining the significant predictors of

adenocarcinoma. Patients with no changes in Gleason score before and after operation were chosen as control group. P of smaller than 0.05 were regarded as statistically significant for all tests.

Results

Following the screening criteria, 51 patients were excluded from the study. This resulted in the inclusion of only 52 patients in the study, with mean age of 69.2 years ranging from 54 to 91 years. The mean preoperative PSA level for these patients was 9.9 (ng/mL), mean PSA density was 0.16 (ng/mL²) and mean prostate volume was 61.3 (mL).

No changes were observed in Gleason score of 25 patients (48%), whereas 27 patients showed the difference in GS score (52%), with 19 patients marked as upgraded (36%) and 8 patients marked as downgraded (16%), as summarized in Table 1. Moreover, Tables 2 and 3 show the evaluation of age, prostate volume, PSA level, PSA density, digital rectal exam findings and percentage of positive core needle biopsies for each group.

Evaluation of independence for the aforementioned predictors of prostate adenocarcinoma is shown in Table 4.

Table 1. Relation between predict values and biopsy and radical prostatectomy GS

Characteristics	Difference between preoperative and postoperative GS			P
	Equal	Upgrade	Downgrade	
No. patients, n (%)	25(48)	19(36)	8(16)	--
Age(years)	71.7±7.8	65.5±5.9	70.4±1.8	0.555
Prostate volume(mL)	62.8±15.3	59.2±13.9	62.0±24.1	0.928
PSA level(ng/mL)	11.0±3.07	10.6±2.4	8.2±2.1	0.326
PSA density(ng/ml ²)	0.17±0.05	0.16±.04	0.15±0.08	0.442
DRE findings	Normal (%)	51	50	53
	Nodule (%)	28	27	26
	Abnormal (%)	21	23	21
Positive core needle biopsy (%)	65.6	62.3	64.5	0.516

Table 2. Patients characteristics with preoperative $GS \leq 6$

Characteristics	No upgrade	Upgrade	P
NO. Patients, n (%)	12	19	--
Age(years)	68.7±8.0	70.2±7.65	0.738
Prostate volume (mL)	59.0±15.63	60.4±12.83	0.032*
PSA level (ng/mL)	10.5±2.5	12.3±2.6	0.629
PSA density(ng/mL ²)	0.14±0.01	0.15±0.03	0.0122*
DRE findings	Normal (%)	52	57
	Nodule (%)	26	27
	Abnormal (%)	22	16
Positive core needle biopsy (%)	67.8	65.9	0.028*

Table 3. Patients characteristics with preoperative GS \geq 7

Characteristics	No upgrade	Downgrade	P
NO. Patients, n (%)	13	8	--
Age(years)	70.4 \pm 1.04	71.4 \pm 2.1	0.952
Prostate volume (mL)	60.5 \pm 12.6	59.6 \pm 11.9	0.441
PSA level (ng/mL)	9.4 \pm 2.9	11.7 \pm 3.4	0.852
PSA density(ng/mL ²)	0.15 \pm 0.03	0.17 \pm 0.02	0.328
DRE findings	Normal (%)	56	58
	Nodule (%)	22	25
	Abnormal (%)	22	17
Positive core needle biopsy (%)	68.3	66.9	0.237

Table 4. Multivariate analysis of predictive values in different groups

Predictor value	P	
Characteristics	Group A	Group B
Age(years)	0.482	0.623
Prostate volume (mL)	0.026*	0.248
PSA level(ng/mL)	0.591	0.613
PSA density(ng/mL ²)	0.032*	0.521
DRE findings	Normal (%)	
	Nodule (%)	0.726
	Abnormal (%)	0.429
Positive core needle biopsy (%)	0.042*	0.754

Prostate volume ($P=0.026$), PSA density ($P=0.032$), and positive core needle biopsy ($P=0.042$) were found to be significant predictors of upgrade in Gleason score among patients with preoperative GS \leq 6. However, these factors do not play a prediction role for patients with preoperative GS \geq 7. A cut-off value for each factor is as follows: prostate volume $<$ 57.5 (mL), PSA density $>$ 0.165 (ng/mL²), positive core needle biopsy $>$ 60(%).

Discussion

Gleason score is the most common predictor for evaluating the prognosis of prostate cancer (8,9). Patients with high-grade prostate cancer are more likely to have progression (10). According to recent studies, such patients show more recurrence intervals in PSA levels and lower survival rates. Therefore, treatments should be more aggressive in these patients. However, there is a price to pay as more aggressive treatments often result in more side effects, as well as lower quality of life and survival rates. As such, the most beneficial and appropriate treatments should be considered for these patients (11-13).

Today, PSA screening helps to diagnose prostate cancer in early stages. Therefore, the rates of well-differentiated adenocarcinomas have increased even

though the mortality rate has decreased (14). As discussed earlier, overtreatment should be avoided in patients who could benefit from conservative therapies such as watchful waiting and active surveillance. Recent guidelines suggest these treatments for patients with the following features: PSA level $<$ 10 ng/mL, biopsy GS \leq 6 and clinical stage \leq T2a. More aggressive treatments are required for patients with biopsy GS \geq 7 (15-17). Thus, accurate staging of a patient is necessary for proper selection of treatment.

Several recent studies have reported a mismatch in the biopsy and radical prostatectomy Gleason score (18,19). The current study showed 52% of discordance, which is very important for patients who are not indicated for aggressive treatments. Therefore, finding clinical or pathological criteria that might predict Gleason score upgrade is crucial. Besides, identifying these criteria could overtreatment of patients in many cases.

The relation between PSA level and post radical prostatectomy GS upgrade is controversial, with prior studies both supporting and rejecting it (20,21). This study did not find any statistically significant evidence to support this relation. Our findings demonstrated that smaller prostate volume is a predictor of upgrading in patients with preoperative GS \leq 6 ($P=0.026$), which has been supported in some recent studies (22,23). However,

Preoperative gleason score

no significant correlation was observed between upgrading and age and DRE findings. PSA density was first described as a predictor of the upgrade by Stavros Sfoungaristos, MD and Petros Perimenis, MD (24). Data analysis revealed that increase in this ratio increases GS upgrade ($P=0.032$). In line with the current guidelines on treatment selection for patients with $GS \leq 6$, it is crucial to correctly measure the Gleason score before attempting to run conservative therapies for these patients (25). While the percentage of positive core needle biopsies has not been reported as a predictor of GS upgrade, the current study found that higher percentage of positive core needle biopsies is associated with upgrade in patients with preoperative $GS \leq 6$ ($P=0.042$).

This research did not show any statistically significant correlation between age, prostate volume, PSA level, PSA density, DRE findings and percentage of positive core needle biopsies for patients with preoperative $GS \geq 7$.

Although Gleason score is used for evaluation of tumor aggressiveness, prognosis and treatment modalities, it accompanies some upgrade and downgrade results. Factors such as prostate volume < 57.5 (mL), PSA density > 0.165 (ng/mL²) and positive core needle biopsies > 60 (%) can predict upgrade results in patients with preoperative $GS \leq 6$.

References

1. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics 2010. *CA Cancer J Clin* 2010;60:277-300.
2. Epstein JI, Partin AW, Sauvageot J, Walsh PC. Prediction of progression following radical prostatectomy. A multivariate analysis of 721 men with long-term follow-up. *Am J Surg Pathol* 1996;20:286-92.
3. Hull GW, Rabbani F, Abbas F, Wheeler TM, Kattan MW, Scardino PT. Cancer control with radical prostatectomy alone in 1,000 consecutive patients. *J Urol* 2002;167:528-34.
4. Rubin MA, Bismar TA, Curtis S, Montie JE. Prostate needle biopsy reporting: how are the surgical members of the Society of Urologic Oncology using pathology reports to guide treatment of prostate cancer patients? *Am J Surg Pathol* 2004; 28:946-52.
5. Makarov DV, Trock BJ, Humphreys EB, Mangold LA, Walsh PC, Epstein JI, et al. Updated nomogram to predict pathologic stage of prostate cancer given prostate-specific antigen level, clinical stage, and biopsy Gleason score (Partin tables) based on cases from 2000 to 2005. *Urology* 2007; 69:1095-101.
6. Epstein JI, Partin AW, Sauvageot J, Walsh PC. Prediction of progression following radical prostatectomy. A multivariate analysis of 721 men with long-term follow-up. *Am J Surg Pathol* 1996;20:286-92.
7. Moussa AS, Li J, Soriano M, Klein EA, Dong F, Jones JS. Prostate biopsy clinical and pathological variables that predict significant grading changes in patients with intermediate and high grade prostate cancer. *BJU Int* 2009;103:43-8.
8. Herman CM, Kattan MW, Ohori M, Scardino PT, Wheeler TM. Primary Gleason pattern as a predictor of disease progression in Gleason score 7 prostate cancer: a multivariate analysis of 823 men treated with radical prostatectomy. *Am J Surg Pathol* 2001;25:657-60.
9. King CR, McNeal JE, Gill H, Presti JC Jr. Extended prostate biopsy scheme improves reliability of Gleason grading: implications for radiotherapy patients. *Int J Radiat Oncol Biol Phys* 2004;59:386-91.
10. Altay B, Kefi A, Nazli O, Killi R, Semerci B, Akar I. Comparison of Gleason scores from sextant prostate biopsies and radical prostatectomy specimens. *Urol Int* 2001;67:14-8.
11. Mosse CA, Magi-Galluzzi C, Tsuzuki T, Epstein JI. The prognostic significance of tertiary Gleason pattern 5 in radical prostatectomy specimens. *Am J Surg Pathol* 2004;28:394-8.
12. Kojima M, Troncoso P, Babaian RJ. Use of prostate-specific antigen and tumor volume in predicting needle biopsy grading error. *Urology* 1995;45:807-12.
13. Cookson MS, Fleshner NE, Soloway SM, Fair WR. Correlation between Gleason score of needle biopsy and radical prostatectomy specimen: accuracy and clinical implications. *J Urol* 1997;157:559-62.
14. Schmid H, Oberpenning F, Pummer K. Diagnosis and staging of prostatic carcinoma: what is really necessary? *Urol Int* 1999;63:57-61.
15. Partin AW, Kattan MW, Subong EN, Walsh PC, Wojno KJ, Oesterling JE, et al. Combination of prostate-specific antigen, clinical stage, and Gleason score to predict pathological stage of localized prostate cancer. A multi-institutional update. *JAMA* 1997;277:1445-51.
16. Arellano L, Castillo O, Metrebian E. Concordance of Gleason histological scoring for prostatic cancer in needle biopsies and the surgical piece obtained during radical prostatectomy. *Rev Med Chil* 2004;132:971-8.
17. Rubin MA, Bismar TA, Curtis S, Montie JE. Prostate needle biopsy reporting: how are the surgical members of the Society of Urologic Oncology using pathology reports to guide treatment of prostate cancer patients? *Am J Surg Pathol* 2004;28:946-52.
18. Nayyar R, Singh P, Gupta NP, Hemal AK, Dogra PN,

- Seth A, et al. Upgrading of Gleason score on radical prostatectomy specimen compared to the pre-operative needle core biopsy: An Indian experience. *Indian J Urol* 2010;26:56-9.
19. Carlson GD, Calvanese CB, Kahane H, Epstein JI. Accuracy of biopsy Gleason scores from a large uropathology laboratory: use of a diagnostic protocol to minimize observer variability. *Urology* 1998;51:525-9.
 20. Wolff JM, Boeckmann W, Mattelaer P, Handt S, Adam G, Jakse G. Determination of prostate gland volume by transrectal ultrasound: correlation with radical prostatectomy specimens. *Eur Urol* 1995;28:10-2.
 21. 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 mult (> or =12)-core prostate biopsy. *World J Urol* 2009;27:271-6.
 22. Sved PD, Gomez P, Manoharan M, Kim SS, Soloway MS. Limitations of biopsy Gleason grade: implications for counseling patients with biopsy Gleason score 6 prostate cancer. *J Urol* 2004;172:98-102.
 23. Fukagai T, Namiki T, Namiki H, Carlile RG, Shimada M, Yoshida H. Discrepancies between Gleason scores of needle biopsy and radical prostatectomy specimens. *Pathol Int* 2001;51:364-70
 24. Sfoungaristos S, Perimenis P. Clinical and pathological variables that predict changes in tumor grade after radical prostatectomy in patients with prostate cancer. *Can Urol Assoc J* 2013;7:E93-7.
 25. Mian BM, Lehr DJ, Moore CK, Fisher HA, Kaufman RP Jr, Ross JS, et al. Role of prostate biopsy schemes in accurate prediction of Gleason scores. *Urology* 2006;67:379-83.