The Discrepancy between Needle Biopsy and Radical Prostatectomy Gleason Score in Patients with Prostate Cancer

Amir Reza Abedi[1], Abbas Basiri[2], Nasser Shakhssalim[2], Ghazal Sadri[3], Mahsa Ahadi[4], Seyyed Ali Hojjati[1],*
Samad Sheykhzadeh[5], Sajjad Askarpour[2], Saleh Ghiasy[1]

Purpose: Gleason score (GS), as well as other prognostic and diagnostic modalities, can predict the possibility of tumor growth and metastasis during the life of patients with prostate cancer. Based on the prostate biopsy GS, clinicians choose the most appropriate therapy for managing patients. The objective of this cross-sectional study was to determine the discrepancy between needle biopsy and radical prostatectomy GS and to identify its predictive factors in the Iranian population.

Materials and Methods: A total of 1147 patients who underwent radical prostatectomy from 2009 to 2019 were initially enrolled in this study. After consideration of the inclusion and exclusion criteria, 439 patients were finally included. The demographic variables and clinical data including age, PSA level, prostate volume, PSA density, GS derived from ultrasonography-guided core needle biopsy specimen, and GS derived from radical prostatectomy specimen were collected from the medical records of patients with prostate adenocarcinoma and were reviewed by a urology resident.

Results: The average age of patients was 64.5 years (range 48-84 years), and the average preoperative PSA level was 14.8 ng/mL. On histopathological examination, no changes in GS were observed in 237 (53.9%) patients, whereas GS was upgraded in 144 (32.8%) patients and downgraded in 58 (13.2%) patients at radical prostatectomy. The number of patients who had extracapsular extension, seminal vesicle invasion, and positive lymph nodes was significantly higher in the upgraded group compared with the non-upgraded group.

Conclusion: In this study, there was a steady decrease in GS upgrading with the prostate size extending up to 49.7 g. There was also an association between downgrading and extending prostate size. Due to the greater risk of high-grade disease in men with small prostates, smaller prostate bulks are most probably upgraded after radical prostatectomy. A higher maximum percentage of involvement per core was an independent predictive factor of upgrading from biopsy grade 1 to grade $\geq$ 2. Our study showed that patients' age was not predictive of upgrading, which is consistent with other studies. Also, we demonstrated a non-significant relationship between PSA level and upgraded GS. Findings in this study did not demonstrate a significant relationship between PSA level and upgrading.

Keywords: Gleason score; needle biopsy; prostate cancer; PSA; radical prostatectomy

INTRODUCTION

Gleason score (GS), as well as other prognostic and diagnostic modalities including serum prostate specific antigen (PSA) and prostate volume, can predict the possibility of tumor growth and metastasis during the life of patients with prostate cancer[1,2]. Since PSA and prostate volume are not as accurate as GS, most physicians rely on biopsy results, especially Gleason score, in order to counsel their patients[3]. Based on the prostate biopsy GS, clinicians choose the most appropriate treatment for the management of patients; these therapeutic approaches range from non-invasive therapies such as active surveillance to invasive therapies such as ablative therapies (radiation therapy or cryotherapy) and even more invasive therapies such as radical prostatectomy (RP)[4-6]. Therefore, GS, as one the main diagnostic and prognostic factors, must be reliable enough so that physicians could make the best clinical decision.

More recently, literature has emerged that offers contradictory findings about the discrepancy between

[1]Department Of Urology, Shohadae-tajrish Hospital, Shahid Beheshti University Of Medical Sciences, Tehran, Iran.
[2]Department Of Urology, Shahid Labbafinejad Medical Center, Urology and Nephrology Research Center, Shahid Beheshti University Of Medical Sciences, Tehran, Iran.
[3]Department Of Radiology, Iran University of Medical Sciences, Tehran, Iran.
[4]Department Of Pathology, Shohadae-tajrish Hospital, Shahid Beheshti University Of Medical Sciences, Tehran, Iran.
[5]Department Of Urology, Shahid Modares Hospital, Shahid Beheshti University Of Medical Sciences, Tehran, Iran.
*Correspondence: Department Of Urology, Shohadae-tajrish Hospital, Shahid Beheshti University Of Medical Sciences, Tehran, Iran. Phone: +989112166808. Email: sah_hojjati@yahoo.com
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Table 1. A comparative analysis between the upgraded and the non-upgraded groups.

Parameters	Total	Group 1 (upgraded)	Group 2 (Non-upgraded)	*P*-value
Number (%)	439 (100)	144 (32.8)	295 (67.2)	-
Age, mean ± SD (years)	64.5 ± 7.2	64.3 ± 8.2	64.6 ± 6.7	0.7
PSA (ng/mL/gr)	14.8 (2.5-107)	18.7 (6.1-107)	14.7 (2.5-54)	0.2
Abnormal finding in DRE, n (%)	77 (17.6%)	37 (25.7%)	40 (13.5%)	0.01
Prostate volume, mL	44.4 ± 16.4	32 ± 5.7	49.7 ± 14.6	0.0001
Positive cores, mean ± SD	4.3 ± 1.4	5.1 ± 1.4	3.8 ± 1.2	0.0001
Maximum % cancer per core	50.7	52	47.2	0.2
Gleason Score upgrading, n (%)				
Grade 1	179 (41)	94 (52)	85 (48)	0.0001
Grade 2	54 (12)	11 (17)	43 (83)	0.1
Grade 3	41 (9)	15 (35)	26 (65)	0.7
Grade 4	76 (17)	24 (31)	52 (69)	0.8
Grade 5	89 (20)	0 (0)	89 (100)	0.0001
Pathologic T stage, n (%)				
pT2a	18 (4)	0 (0)	18 (6.1)	0.02
pT2b	15 (3)	10 (6.9)	5 (1.6)	0.2
pT2c	165 (37)	57 (27.7)	108 (36.6)	0.8
pT3a	144 (32)	51 (35)	93 (31.5)	0.4
pT3b	128 (29)	40 (30)	88 (29.8)	0.4
Perineural invasion, n (%)	235 (53.5)	97 (67.3)	138 (46.7)	0.5
Extracapsular extension, n (%)	216 (49.2)	89 (61.9)	127 (43)	0.002
Positive surgical margins, n (%)	135 (30.7)	50 (34.7)	85 (29)	0.3
Seminal vesicle invasion, n (%)	44 (10)	28 (19)	16 (5.4)	0.001
Positive lymph nodes, n (%)	21 (4.7)	14 (9.6)	7 (2.3)	0.008

Abbreviations: PSA, prostate specific antigen; DRE, digital rectal examination; SD, standard deviation

preoperative GS and RP GS. Upgrading of GS on RP specimens compared with transrectal ultrasound-guided biopsy (TRUS-GB) GS is observed in 31.8% to 52% of the cases, according to different studies[7,8]. In a study conducted by Dolatkhah et al. that included 100 patients, the rate of discrepancy for group and individual scoring of GS was 41% and 56%, respectively. The findings of their study indicated that although the agreement between core needle biopsy (CNB) GS and RP GS is fair to moderate, the feature of discrepancy, i.e. under-grading in low and intermediate grades and over-grading in high grades of CNB GS, could help in making more appropriate clinical decisions [9]. In addition, although many studies have assessed the discrepancy between CNB GS and RP GS, there is a paucity of evidence regarding its predictive factors. Identification of these factors can help clinicians to perform additional diagnostic tests and take more effective treatment measures for patients who have a higher risk of tumor progression when compared with their initial biopsy. Consequently, the mismanagement of patients who have been incorrectly classified as low-risk could be significantly reduced.

Few articles have analyzed the discrepancy of GS between transrectal biopsy and radical prostatectomy in Iran. In addition, we found no studies that have assessed the predictive factors of discrepancy in GS among the Iranian population. Therefore, in this cross-sectional study, we aimed to determine the discrepancy between CNB GS and RP GS and to identify its predictive factors among the Iranian population.

MATERIALS AND METHODS

Study design and setting

This retrospective cross-sectional study was conducted between December 2017 and September 2019 in Tehran, Iran. This study was performed in the urology department of three affiliated hospitals of Shahid Beheshti University of Medical Sciences (SMBU), Labbafinezhad Hospital, Shohadaye Tajrish Hospital, and Shahid Modarres Hospital that are located in the east, north, and west of Tehran, respectively.

Study participants

A total of 1147 patients who underwent radical prostatectomy from 2009 to 2019 in the three previously mentioned hospitals were initially enrolled in the study. After consideration of the inclusion and exclusion criteria, 439 patients were finally included. Among the 708 excluded patients, 423 patients had incomplete medical records, and 285 patients had received neo-adjuvant hormone therapy, chemotherapy, or radiotherapy. All the patients had undergone standard 12 core biopsy. Patients who had undergone fusion biopsy or saturation biopsy were not included in this study.

Variables and data collection

The demographic variables and clinical data including age, PSA level, prostate volume, PSA density, GS derived from ultrasonography-guided core needle biopsy CNB specimens, GS derived from RP specimens were collected from the medical records of patients with prostate adenocarcinoma and were reviewed by a urology resident. Incomplete medical records were also completed after direct phone calls to the patients.

Radical prostatectomies were performed with the retropubic method by expert urologists. Prostate volume was measured using prostate ellipse dimension theory. The specimens that were extracted from CNB and RP were reviewed by a single pathologist in order to reduce possible diagnostic biases. Upgrading of GS was defined as an increase in GS of the pathological specimen derived from RP compared with GS of the pathological specimen derived from CNB, whereas downgrading of GS was defined as a decrease in RP GS compared with CNB GS.

Statistical analysis

Statistical analysis was done by using the Social Sciences Software version 21. Qualitative data were analyzed

Table 2. Comparing Peak flow rate (Q max) and International prostate symptom score (IPSS) variables in OP and TURP group without Re-operation.

Variable	TURP (N=61)	OP (N=80)	*P*- value
Peak flow rate (Q max), Mean ± SD (Range)			
Before	9.1 ± 1.3 (8-11)	9.2 ± 1.3 (8-11)	0.61
After 1 month	14.2 ± 1.5 (10-16)	14.3 ± 1.5 (13-16)	0.99
After 3 month	16 ± 1.6 (13-17)	16.4 ± 2.3 (15-18)	0.25
After 6 month	16.7 ± 2.2 (13-18)	17.2 ± 2.4 (16-19)	0.48
After 9 month	16.7 ± 1.9 (14-18)	17.1 ± 2.2 (16-19)	0.23
After 12 month	17 ± 2.4 (14-19)	17.3 ± 1.6 (16-19)	0.14
International prostate symptom score (IPSS)			
Before	28.4 ± 3.2 (23-30)	29.2 ± 3.1 (27-32)	0.11
After 3 month	19.3 ± 2.8 (17-22)	18.4 ± 2.6 (16-20)	0.53
After 6 month	17.6 ± 3.1 (15-19)	17.5 ± 2.4 (16-20)	0.93
After 12 month	17.5 ± 2.5 (15-19)	17.3 ± 2.4 (16-20)	0.82

Abbreviations: OP, open prostatectomy; TURP, transurethral resection of the prostate; SD, standard deviation; IPSS, International prostate symptom score

using the chi-square test, and quantitative data were analyzed using the independent T-test and Mann-Whitney U test. A p-value of 0.05 or less was considered statistically significant in this study.

RESULTS

A total of 439 patients were finally included in our study. The average age of patients was 64.5 years (range 48-84 years), and the average preoperative PSA was 14.8 ng/mL. After histopathological examination, no changes in GS were observed in 237 (53.9%) patients, whereas GS was upgraded in 144 (32.8%) patients and downgraded in 58 (13.2%) patients at RP (**Table 1**). Prostate volume in the upgraded group was significantly lower than the non-upgraded group ($P < .001$). The number of positive core biopsies and patients with an abnormal finding in DRE were significantly higher in the upgraded group compared with the non-upgraded group ($P < .001$, $P = .01$, respectively).

The highest increase in GS was seen in the grade 1 group ($P < .001$). The non-upgraded group had a lower pathology stage as opposed to the upgraded group ($P = .02$). The number of patients who had extracapsular extension, seminal vesicle invasion and positive lymph nodes was significantly higher in the upgraded group compared with the non-upgraded group ($P = .002$, $P = .001$, $P = .008$, respectively) (**Table 1**).

DISCUSSION

In terms of prostate cancer management, GS determined by CNB has an important role in treatment selection [10,11]. Precision of GS is of significant importance in patients undergoing active surveillance or radiotherapy. Underestimated GS contributes to an inappropriate treatment strategy and thus, patients may not receive the best treatment.

Although TRUS-GB is the most cost-benefit modality for prostate cancer diagnosis, pathology errors, borderline pathology grades, and sampling errors contribute to a mismatch between CNB GS and the corresponding RP GS [12]. The most common sampling error happens when biopsies are taken from different places of the higher grade components at RP, which leads to the undergrading of prostate cancer. Sampling a tertiary higher grade component on CNB, which is not routinely mentioned in RP reporting, results in an apparent upgrading on ultrasound-guided biopsy. An underestimated GS is the most common problem associated with TRUS-GB [13]. Our study showed that GS was upgraded at RP in 32.8% of the cases; consistent with other studies.

According to many studies, an enlarged prostate size is associated with lower rates of upgrading [14,15]. In our study, there was a steady decrease in upgrading with the prostate size extending up to 49.7 g. There was also an association between downgrading and extending prostate size. In multivariate logistic regression analysis, we discovered that smaller prostate volumes (< 32 mL) were independent predictors of upgraded GS at RP. Likewise, Freedland et al.[16] showed that smaller bulks of the prostate are associated with advanced GS. Due to the greater risk of high-grade disease in men with small prostates, smaller prostate volumes are most probably upgraded after RP. The other reason is that prostate size has an effect on the PSA level; hence, the prostate size is a confounding factor in the interpretation of PSA levels.

Several studies have shown a correlation between the number of positive cores on biopsy and upgrading[17-19]. The number of involved cores and the maximum percentage of involvement per core were predictive factors of upgrading in our study. In addition, a higher maximum percentage of involvement per core was an independent predictive factor of upgrading from biopsy grade 1 to grade ≥ 2.

Our results showed that patients' age was not predictive of upgrading, which is in parallel with other studies [17,20]. Also consistent with other studies, we demonstrated that the clinical stage of disease was not a predictive factor[21,22].

Most of the previous studies have stated that serum PSA levels weakly predict upgrading[15,18,21]. Higher PSA levels are correlated with larger tumor bulks, and on the other hand, a relationship exists between tumor size and tumor grade after RP. Therefore, it is highly likely that patients with GS 6 on transrectal biopsy and higher PSA levels will be upgraded at RP. Our study demonstrated a relationship, although non-significant, between serum PSA level and upgraded GS.

One study revealed a correlation between the percentage of free PSA and upgrading[23]. PSA velocity and free PSA percentage were not evaluated in our study. Because both higher serum PSA levels and lower pros-

tate weights are correlated with upgrading, PSA density is speculated to be more specifically associated with upgrading rather than PSA level alone[24]. However, the findings of this study did not demonstrate a significant relationship between PSA level and upgrading.

Many studies have reported that widespread biopsies are correlated with decreased rates of upgrading [20,25,26]. However, in our study, widespread transrectal biopsies were not performed and were regarded as the yardstick of care; hence, this factor was not considered in our study.

A few studies have mentioned GS downgrading after RP, with percentages ranging from 29% to 56% [15,17] (16, 21). In the current study, the reported GS on needle biopsy was lower than RP GS in 13.2% of the cases. Moussa et al. mentioned a 7.3% occurrence of downgrading from GS 3 + 4 = 7 to GS $\leq$ 6 [14,15].

Furthermore, some researchers have reported that MRI-ultrasound fusion guided biopsy is less likely associated with GS upgrading; however, this issue was not investigated in our study.

CONCLUSIONS

According to previous studies, an enlarged prostate size is associated with lower rates of upgrading. In our study, there was a steady decrease in upgrading with the prostate size extending up to 49.7 g. There was also an association between downgrading and extending prostate size. Due to the greater risk of high-grade disease in men with small prostates, smaller prostate volumes are most probably upgraded at RP. A higher maximum percentage of involvement per core was an independent predictive factor of upgrading from biopsy grade 1 to grade $\geq$ 2. Our results showed that patients' age was not predictive of upgrading, which is consistent with other studies. Also, our study demonstrated a non-significant relationship between PSA level and upgraded GS.

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CONFLICT ON INTEREST

The authors declare that they have no conflict of interest.

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