Original Article

The prevalence and risk factors of upgrading of Gleason grade group between transrectal ultrasound prostate biopsy and prostatectomy specimens

Worapong Promsen, Satit Siriboonrid, Nattapong Binsri, Sarayut Kanjanatarayon, Weerayut Wiriyabanditkul, Vittaya Jiraanankul

Department of Surgery, Division of Urology, Phramongkutklao Hospital, Bangkok, Thailand

ABSTRACT

Background: The risk stratification of prostate cancer using Gleason grade group (GG), serum prostate-specific antigen (PSA), and T staging has an important role for appropriate treatment. In fact, the GG of biopsy was not the same as the prostatectomy specimen. The upgrading of GG has a significant risk of delay treatment. The study aims to evaluate the concordance of GG between biopsy and prostatectomy specimens and the factors of upgrading GG.

Materials and Methods: Retrospectively reviewed data from January 2010 to December 2019, 137 patients underwent prostate biopsy and followed by prostatectomy. Patients' data include pathological reports, imaging reports, serum PSA, PSA density (PSAD), and free PSA were analyzed by univariate and multivariate analysis.

Results: The concordance between the pathology was found in 54 specimens (39.4%) with the upgrading of GG in the prostatectomy was 57 specimens (41.6%). Furthermore, the downgrading was 26 specimens (18.9%). Serum PSA >10 ng/ml (*P* 0.003), PSAD >0.2 ng/ml/cm^3 (*P* 0.002), free/total PSA ratio (*P* 0.003), margin positive for malignancy (*P* 0.033), and extraprostatic involvement (*P* 0.039) were significantly related with upgrading at the univariate analysis. Only a PSAD >0.2 (*P* 0.014) was found to be an independent factor that is predictive of upstaging in multivariate analysis.

Conclusions: The prevalence of upgrading of GG from prostate biopsy to radical prostatectomy is as high as the other study. The factor that related to upstaging of GG was PSAD. Therefore, additional tools for biopsy were required to enhance the accurate diagnosis and staging of prostate cancer.

Keywords: Concordance, Gleason grade group, prostate biopsy, prostatectomy

Address for correspondence: Dr. Vittaya Jiraanankul, Department of Surgery, Division of Urology, Phramongkutklao Hospital, 315 Ratchawithi Road, Ratchathewi, Bangkok 10400, Thailand.
E-mail: jiraanankul_v@pmk.ac.th

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INTRODUCTION

Prostate cancer is the fourth-ranking of malignancy in Thai male.[1] The screening program of prostate cancer is mainly performed using digital rectal examination and serum prostate-specific antigen (PSA). Random prostatic biopsy through the rectum or perineum by ultrasound

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is considered the standard to retrieve the tissue for the diagnosis of cancer. Both routes of biopsy have a comparable detection rate of cancer.[2,3]

The risk stratification of prostate cancer using Gleason grade group (GG), serum PSA, and T staging has an important role in choosing an appropriate treatment.[4] GG of biopsy was not the same as the prostatectomy specimen due to multifocality of prostate cancer, pathology errors, borderline grades, and sampling errors.[5] Several studies have evaluated the concordance between preoperative biopsy and postprostatectomy specimen GG show a correlation ranging between 30% and 60%.[6] The upgrading of GG has a significant risk of delay appropriate treatment in prostate cancer patients, especially in the active surveillance group. In the present time, using targeted biopsy guided by magnetic resonance imaging (MRI) or MRI fusion with ultrasound may increase the diagnostic accuracy of cancer detection in postprostatectomy specimens.[7]

The aim of this study was to evaluate the concordance of GG between biopsy and prostatectomy specimens and the prognostic factors of upgrading GG in prostatectomy specimens.

MATERIALS AND METHODS

We retrospectively reviewed data of 137 prostate cancer patients who underwent transrectal prostate biopsy at our institution or other centers, at least 12 samples (extended-core biopsy) and followed by open radical retropubic or laparoscopic radical prostatectomy at Phramongkutklao Hospital from January 2010 to December 2019**.** The data of the population were collected for age, serum PSA level, a ratio of free and total PSA, PSA density (PSAD) (ratio of PSA and prostate size), prostate volume calculated by preoperative ultrasound or cross-sectional imaging, and clinical stage. The patients that received any chemotherapy or metastases to the bone of solid organs were excluded from this study.

All the patients were proceeded to radical prostatectomy within 6 months after the diagnosis of prostate cancer. Pelvic lymphadenectomy was performed following the European Association of Urology Guidelines.[8] The specimens were evaluated by pathologists according to the TNM staging. Upgrading or downgrading was defined as the difference of GG between prostatectomy and biopic specimens. The grading of specimens was defined to the Gleason score range from 6 to 10. We converted the Gleason score to GG 1–5 according to the risk stratification of prostate cancer.

For the statistical analysis, the continuous variables were analyzed using mean and standard deviation. The association between upgrading or upstaging and age, serum PSA, PSAD, ratio of free to total PSA, and prostate volume were evaluated using the Student's *t*-test or the Mann–Whitney *U* test for continuous data and Chi-square test for categorical data. Statistical analyses were performed using the SPSS software, version 16.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Clinicopathological characteristics

The clinical and pathological characteristics of the study population are shown in Table 1. The mean age of the population was 66.95 years. The mean PSA level was 14.45 ng/ml, with a free/total mean ratio of 6.68%. The majority of the population (68.0%) presented with a negative physical examination. The mean prostate volume was 37.46 cm^3. Furthermore, the mean PSAD was 0.49 $ng/ml/cm^3$.

Upgrading and downgrading

The most frequently represented bioptic pathology was GG1 (42.3%) followed by GG2 (34.3%), whereas the most frequent prostatectomy pathology was GG2 (30.6%), followed by GG1 (21.0%). The concordance between bioptic and prostatectomy GG is shown in Table 2. The correspondence between the pathology was found

Table 1: Baseline clinical and pathological characteristics of the participants

Characteristics	Total participants=137 (mean±SD)
Age (years)	66.95±5.75
PSA (ng/ml)	14.45±29.77
Free to total PSA ratio	6.68±7.92
Prostate volume (cm^3)	37.46±18.56
PSAD ($ng/ml/cm^3$)	0.49±1.54
Clinical stage, *n* (%)	
T1c	103 (68)
T2a	26 (16.5)
T2b	9 (6.5)
T2c	11 (8)
Positive cores, *n* (%)	22.79±21.89
Bioptic Gleason grade group, *n* (%)	
1	58 (42.3)
2	47 (34.7)
3	18 (13)
4	8 (5.5)
5	6 (4.5)
Prostatectomy Gleason grade group, *n* (%)	
Negative	9 (6.5)
1	29 (21.5)
2	42 (30.6)
3	20 (14.4)
4	16 (11.6)
5	21 (15.4)

PSA: Prostate-specific antigen, SD: Standard deviation

in 54 specimens (39.4%) with the upgrading of GG in the prostatectomy was 57 specimens (41.6%). While the downgrading was 26 specimens (18.9%). The correspondence was decreasing according to GG1-4, excepting GG5 that has the most correlation between histopathologic studies as shown in Table 2. The lowest correspondence was found in GG4, only one specimen (12.5%) that was accurate between pathologic studies. We found that 28 specimens (48.2%) in bioptic GG1 were upgraded to GG2-5. In addition, the upgrading was found in 21 (44.68%), 5 (27.8%), and 3 (37.5%) in bioptic GG 2, 3, and 4, respectively.

Univariate and multivariate analysis

We evaluated the relationship between age group, preoperative serum PSA, prostate volume, PSAD, ratio of free and total PSA, digital rectal examination, extraprostatic involvement, and margin positive. We found that serum PSA >10 ng/ml (*P* 0.003), PSAD >0.2 ng/ml/cm^3 (*P* 0.002), the ratio of free and total PSA (*P* 0.003), margin positive for malignancy (*P* 0.033), and extraprostatic involvement (*P* 0.039) were significantly related with upgrading at the univariate analysis. Only a PSAD >0.2 (*P* 0.014) was found to be an independent factor that predictive of upgrading in multivariate analysis [Table 3].

DISCUSSION

The determination of the GG was important in the evaluation of prostate cancer patients in the management of this disease, which may range from active surveillance to surgery, radiation, or chemotherapy. Several previous studies have analyzed the concordance of tissue Gleason grading between preoperative biopsy and the prostate obtained from surgery.

The comparisons between the biopsy compared to the surgical specimen showed a accuracy equal to 50%.[9-12] The difference in histopathology was described by several reasons, such as error evaluation by the pathologist, sampling errors, and the multifocality of cancer.[5]

Table 2: Number of concordance of the Gleason grade group between bioptic and prostatectomy specimen

Number of bioptic GG (%)	Number of RP GG *n* (%)						Total
	Negative	1	2	3	4	5	
1	6 (10.3)	24 (41.4)	13 (22.4)	6 (10.3)	5 (8.6)	4 (6.9)	58
2	2 (4.3)	4 (8.5)	20 (42.6)	7 (14.9)	7 (14.9)	7 (14.9)	47
3	1 (5.6)	1 (5.6)	6 (33.3)	5 (27.8)	2 (11.1)	3 (16.7)	18
4	0	0	3 (37.5)	1 (12.5)	1 (12.5)	3 (37.5)	8
5	0	0	0	1 (16.7)	1 (16.7)	4 (66.7)	6
Total	9	29	42	20	16	21	137

RP: Radical prostatectomy, GG: Gleason grade group

Table 3: Univariate and multivariate analysis of factors between upgrading and nonupgrading of the Gleason grade group

	Number of nonupgraded GG (%)	Number of upgrade GG (%)	*P*	Adjusted odd ratios (95% CI)	*P*
Age (mean±SD)	66.61±6.05	67±5.63	0.702		
PSA ratio (mean±SD)	8.4±7.9	4.37±6.91	0.003	0.97 (0.88–1.09)	0.653
DRE					
Negative	57 (60)	38 (40)	0.567		
Positive	23 (54.8)	19 (45.2)			
Margin					
Negative	59 (64.8)	32 (35.2)	0.033	2.19 (0.98–4.89)	0.056
Positive	21 (45.7)	25 (54.3)			
SVI					
Negative	71 (60.2)	47 (39.8)	0.297		
Positive	9 (47.4)	10 (52.6)			
EPE					
Negative	78 (60.9)	50 (39.1)	0.039	2.89 (0.54–15.37)	0.214
Positive	2 (22.2)	7 (77.8)			
PSA (ng/ml)					
≤10	49 (71)	20 (29)	0.003	1.27 (0.27–5.98)	0.759
>10	31 (45.6)	37 (54.4)			
PSAD (ng/ml/cm^3)					
≤0.2	28 (82.4)	6 (17.6)	0.002	3.75 (1.31–10.73)	0.014
>0.2	52 (50.5)	51 (49.5)			
Prostate size (g)					
<30	31 (60.8)	20 (39.2)	0.662		
≥30	49 (57)	37 (43)			

GG: Gleason grade group, CI: Confidence interval, DRE: Digital rectal examination, SVI: Seminal vesicle involvement, EPE: Extraprostatic involvement, PSA: Prostatic-specific antigen, PSAD: Prostatic-specific antigen density, SD: Standard deviation

In 2012, Epstein *et al*.[5] evaluated the largest series in the literature, with 7,643 patients, analyzing the accuracy between bioptic and prostate Gleason scores. The study shown that patients with Gleason score 3 + 3 (GG1), 36.3% underwent an upgrading, and approximately 20% of the patients exhibited a low grade of cancer. Moreover, in 2014, D'Elia *et al*.[6] reviewed 300 patients who correlated with bioptic and definitive Gleason score 35.3% and upgrading 39.7%. Xu *et al*., 2018,[13] reported factors that helped to predict the outcome accurately for prostate cancer biopsy, including PSAD, prostate volume <30 cm^3, and biopsy modality.

In our series, we found the correlation between bioptic and prostatectomy GG about 39.4%, upgrading about 41.6%, and downgrading about 18.9% close to others studies, variables predictive of upgrading of GG was PSAD >0.2.

In total, there are nine cases of negative tumor at prostatectomy; we can review the histology only two cases. The first case was reported bioptic GG1, and we confirmed the negative tumor in the final pathology report. The second case was reported bioptic GG1; however, for the final pathology review, we found a high-grade prostatic intraepithelial neoplasia from immunohistochemistry after that patient had PSA progression, and we found the local recurrence at prostatic bed with the histopathology shown Gleason 3 + 5 (GG4).

The limitations of our study were single-center and retrospective data. Unable to completely review all of the histological studies that do not correspond between biopsy and prostatectomy specimen. For many cases of biopsies were not performed in our institute. In this study, we do not include the oncological outcomes of the patients, so we cannot correlate the discordance of results with the malignancy outcomes.

CONCLUSIONS

The discordance of GG from prostate biopsy to prostatectomy is an important topic and maybe of important value at the clinical level for treatment planning, as well as for the prediction of cancer outcomes. The factor that related to upstaging of GG from our study was PSAD. Therefore, additional tools for biopsy were required to enhance the accuracy of histopathologic study, to increase the accuracy for staging of prostate cancer.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. National Cancer Institute Department of Medical Services Ministry of Public Health Thailand. Hospital-Based Cancer Registry 2019. Bangkok: New Thammada Press (Thailand) Co., Ltd.; 2020.
2. Hara R, Jo Y, Fujii T, Kondo N, Yokoyoma T, Miyaji Y, *et al*. Optimal approach for prostate cancer detection as initial biopsy: Prospective randomized study comparing transperineal versus transrectal systematic 12-core biopsy. Urology 2008;71:191-5.
3. Takenaka A, Hara R, Ishimura T, Fujii T, Jo Y, Nagai A, *et al*. A prospective randomized comparison of diagnostic efficacy between transperineal and transrectal 12-core prostate biopsy. Prostate Cancer Prostatic Dis 2008;11:134-8.
4. Epstein JI, Zelefsky MJ, Sjoberg DD, Nelson JB, Egevad L, Magi-Galluzzi C, *et al*. A contemporary prostate cancer grading system: A validated alternative to the Gleason score. Eur Urol 2016;69:428-35.
5. Epstein JI, Feng Z, Trock BJ, Pierorazio PM. Upgrading and downgrading of prostate cancer from biopsy to radical prostatectomy: Incidence and predictive factors using the modified Gleason grading system and factoring in tertiary grades. Eur Urol 2012;61:1019-24.
6. D'Elia C, Cerruto MA, Cioffi A, Novella G, Cavalleri S, Artibani W. Upgrading and upstaging in prostate cancer: From prostate biopsy to radical prostatectomy. Mol Clin Oncol 2014;2:1145-9.
7. Wegelin O, van Melick HH, Hooft L, Bosch JL, Reitsma HB, Barentsz JO, *et al*. Comparing three different techniques for magnetic resonance imaging-targeted prostate biopsies: A systematic review of in-bore versus magnetic resonance imaging-transrectal ultrasound fusion versus cognitive registration. Is there a preferred technique? Eur Urol 2017;71:517-31.
8. Heidenreich A, Bellmunt J, Bolla M, Joniau S, Mason M, Matveev V, *et al*. EAU guidelines on prostate cancer. Part 1: Screening, diagnosis, and treatment of clinically localised disease. Eur Urol 2011;59:61-71.
9. 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.
10. Sengupta S, Slezak JM, Blute ML, Leibovich BC, Sebo TJ, Myers RP, *et al*. Trends in distribution and prognostic significance of Gleason grades on radical retropubic prostatectomy specimens between 1989 and 2001. Cancer 2006;106:2630-5.
11. Melia J, Moseley R, Ball RY, Griffiths DF, Grigor K, Harnden P, *et al*. A UK-based investigation of inter- and intra-observer reproducibility of Gleason grading of prostatic biopsies. Histopathology 2006;48:644-54.
12. Kvåle R, Møller B, Wahlqvist R, Fosså SD, Berner A, Busch C, *et al*. Concordance between Gleason scores of needle biopsies and radical prostatectomy specimens: A population-based study. BJU Int 2009;103:1647-54.
13. Xu N, Wu YP, Li XD, Lin MY, Zheng QS, Chen SH, *et al*. Risk of upgrading from prostate biopsy to radical prostatectomy pathology: Is magnetic resonance imaging-guided biopsy more accurate? J Cancer 2018;9:3634-9.