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ORIGINAL ARTICLE

Gleason scores in prostate needle biopsy and prostatectomy specimens in prostatic adenocarcinoma: A correlation study

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Abstract

Introduction: Gleason scoring (GS) categorised prostatic adenocarcinoma into five prognostic grade groups (PGGs); associated with different prognosis and treatment. This study aims to correlate between Gleason scores of needle biopsies with the corresponding total prostatectomy specimens, and to assess the relationship between the percentage of Gleason 4 tumour pattern (GP4) within Gleason score 7 (GS7) needle biopsy groups with the pathological staging. *Materials and Methods:* Seventy-eight specimens of needle prostate biopsy and its subsequent radical prostatectomy were retrospectively studied. The GSs of the needle biopsy were compared with the corresponding prostatectomy specimens. The percentage of GP4 in GS7 needle biopsy groups was calculated and correlated with the pathological staging. *Results:* More than half (60%) of GS 6 needle biopsy cases (PGG 1) were upgraded in the prostatectomy specimen, while the majority (80%) of the GS7 needle biopsy groups (PGG 2 and 3) remain unchanged. Cohen's Kappa shows fair agreement in the Gleason scoring between needle biopsies and prostatectomy specimens, K = 0.324 (95% CI, 6.94 to 7.29), p <0.0005 and in the percentage of GP4 in GS7 needle biopsy groups and their corresponding radical prostatectomy specimens, K = 0.399 (95% CI 34.2 – 49.2), p<0.0005. A significant relationship was seen between the percentage of GP4 in GS7 needle biopsy with the pT and pN stage of its radical prostatectomy (p = 0.008 and p=0.001 respectively). *Conclusion:* A higher percentage of GP4 in GS7 tumour is associated with worse tumour behaviour, therefore it is crucial for clinicians to realise this in deciding the optimal treatment.

Keywords: Prostate adenocarcinoma, Gleason grading, Gleason pattern 4, Needle biopsy, Radical prostatectomy, Prognostic grade group

INTRODUCTION

Prostate cancer is one of the most common cancers in men. In Peninsular Malaysia, this cancer accounted for 7.3% of the total cancers in males and was more commonly seen in Chinese followed by Indians and Malays.[1] According to the Global Cancer Statistics 2012, an estimated 1.1 million new prostate cancer cases were diagnosed in the year 2012 however, the mortality has been steadily declined.

The original Gleason grading system for prostate carcinoma was introduced in the 1960s as a histological architectural pattern grading system. Generally, a Gleason score (GS) is obtained by adding up the primary and secondary Gleason patterns. The GS in needle biopsy has been shown to be the most significant predictor of pathologic result at radical prostatectomy and predicts clinical outcome after the surgery.[2]

A few clinically important modifications were introduced in 2005 during the "International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma". The definition of pattern 3 was only limited to discrete and well-formed malignant glands. The scope of pattern 4 carcinoma was also widened to include all cribriform glands and ill-defined glands with

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poorly formed lumina. These changes result in homogenisation of GS 6 (3+3) and disease upgrading of GS 7 (either predominantly Gleason pattern 4 with secondary pattern 3 (4+3) or vice versa of Gleason pattern 3 + 4).[3]

A later update of Gleason grading in 2014 has introduced prognostic grade groupings (PGG). The PGG was suggested to provide a more definite grade stratification and uncomplicated classification to only five groups, each of which has different prognostic significance. For example, a GS 6 tumour belongs to PGG 1, which has a good prognosis and might not necessarily require radical prostatectomy. On the other hand, a GS 7 (3+4) tumour which falls under the PGG 2 shows a relatively less aggressive behaviour as opposed to GS 7 (4 + 3), PGG 3.[4]

This 2014 update also propose to report the percentage of Gleason pattern 4 tumours within GS7 adenocarcinoma.[5] The differentiating factor for PGG2 and PGG3 is the percentage of its Gleason pattern 4 tumour. Standardisation of labelling the malignant glands as either Gleason pattern 3 or 4 as well as giving the percentage of Gleason pattern 4 is vital as it will reflect the tumour behaviour. This information is important especially in needle biopsies to aid in the next step of patient care and treatment.

Several studies have found that there are differences in the pathologic and prognostic outcome between the subgroups of 4+3 with primary Gleason pattern 4 and the subgroup of 3+4 with primary Gleason pattern 3. The prostatic carcinoma with GS7 (4+3) was found to have a worse prognosis than those with a GS7 (3+4), both in needle biopsies and radical prostatectomies.[4,6,7] These findings illustrate the diversity of tumour behaviour and prognosis in cases with GS7 and the importance of stratifying GS7 into (3+4) or (4+3).[8]

The staging system that is commonly used for prostate cancer is the TNM staging of Prostate Cancer, AJCC 2009 7th edition which indicates the spread of the disease as well as having a prognostic purpose. The PGG is comprised of five essential information including the extent of the primary tumour (T category), nearby lymph nodes involvement (N category), distant metastases (M category), PSA level at the time of diagnosis and GS on the prostate biopsy or the prostatectomy specimen.[9]

This study aims to assess the correlation between GS of needle biopsies and those of corresponding total prostatectomy specimens. The relationship between the percentage of Gleason pattern 4 (GP4) in GS7 needle biopsy groups and the pathological staging was also evaluated.

MATERIALS AND METHODS

This was a cross-sectional study using retrospective data by reviewing archival histological material and patients' medical record. Seventy-eight patients who were diagnosed with prostatic adenocarcinoma by transurethral ultrasound (TRUS) biopsy (needle biopsy) who subsequently underwent radical prostatectomy in Hospital Kuala Lumpur between year the 2010 and 2015 were selected. We have excluded cases who had underwent pre-operative chemotherapy, radiotherapy or hormonal therapy, and cases that were diagnosed by prostatic chips obtained from transurethral resection of the prostate (TURP). The patient's demographical data were obtained from the Lab Information System and their needle biopsy and radical prostatectomy slides were retrieved and reviewed.

The GS and percentage of Gleason pattern 4 in GS 7 groups from needle biopsies were recorded. The length of each core of needle biopsy tissue and as well as the length of the tumour area of pattern 4 and pattern 3 were measured in millimeter and the percentage of tumour area was calculated. The GS, percentage of Gleason pattern 4 in GS 7 groups, tumour volume, extra-prostatic extension, and lymph nodes involvement from the radical prostatectomy slides were also recorded. The cases were also categorised into different prognostic grade groups according to their total GS in the needle biopsy and the radical prostatectomy respectively (Table 1). The data were analysed by using SPSS version 17 software.

RESULTS

The patient's age at diagnosis ranges from 49 to 76 years old with a mean of 67. The patients were comprised of 37 Chinese (49%), 27 Malays (34%), 13 Indians (16%) and 1 of other ethnicity (1%). The Gleason score (GS) at needle biopsies were as follows; 29 patients (38%) had GS 6, (Prognostic grade group (PGG) 1); 25 patients (32%) with GS 7(3+4), (PGG 2); 15 patients (19%) with GS 7(4+3), (PGG 3); 6 patients (7%) with GS 8, (PGG 4); and 3 patients (3%) with GS 9, (PGG 5).

The subsequent radical prostatectomy specimens showed that 36 patients (46%) had GS 7(3+4), 23 patients (29%) GS 7(4+3), 10 patients

(12%) with GS 6, 8 patients (10%) with GS 9 and 1 patient (2%) with GS 8. Out of these, the tumours in 13 needle biopsies (48%) with GS 6 were upgraded in the subsequent prostatectomy to GS 7 (3+4), 3 cases (11%) were upgraded to GS 7 (4+3) and 1 case (3%) was upgraded to GS 8 (3+5). Within the GS 7 needle biopsy group, GS in 34 cases (80%) remained unchanged (Table 2). Cohen's Kappa shows fair agreement between the needle biopsy and prostatectomy Gleason scoring, K = 0.324 (95% CI, 6.94 to 7.29), p <0.0005.

The Cohen's Kappa also shows fair agreement between the percentage of Gleason pattern 4 in subgroup GS 7 of the needle biopsy and its radical prostatectomy specimen, K = 0.399 (95% CI 34.2 – 49.2), p<0.0005. Thirty-five cases (45%) of the radical prostatectomy specimens were pT2c, 23 cases (29%) were pT3a, 10 cases (13%) were pT3b, 7 cases (9%) were pT2a, 2 cases (2%) were pT2b and 1 case (3%) was pT4 (Table 2).

Forty-seven cases (60%) did not have regional nodes sampled. 31 cases that had the regional lymph nodes sampled, out of which 22 cases (28%) had no regional nodes involvement while metastases were seen in the remaining 9 cases (12%) (Table 3). In the subgroup of GS 7 in needle biopsy, there is a significant relationship between the percentage of Gleason pattern 4 and the pathological staging of its radical prostatectomy, pT and pN (p = 0.008 and p=0.001 respectively).

TABLE 1: Comparison between prognostic grade group in the needle biopsy and its corresponding radical prostatectomy specimens

		Prognostic Grade Group (PGG) in Radical Prostatectomy[a]					
		PGG 1	**PGG 2**	**PGG 3**	**PGG 4**	**PGG 5**	**Total**
		GS [b] 6 (3+3)	**GS 7** (3+4)	**GS 7** (4+3)	**GS 8** (4+4, 3+5, 5+3)	**GS 9** (4+5, 5+4) **GS 10** (5+5)	
Prognostic Grade Group (PGG) in Prostate Needle Biopsy	**PGG 1 GS 6** (3+3)	10 (37%)	13 (48%)	3 (11%)	1(3%)	0	27
	PGG 2 GS 7 (3+4)	0	22 (81%)	3 (11%)	0	2 (7%)	27
	PGG 3 GS 7 (4+3)	0	1 (7%)	12 (80%)	0	2 (13%)	15
	PGG 4 GS 8 (4+4, 3+5, 5+3)	0	0	2 (33%)	0	4 (67%)	6
	PGG 5 GS 9 (4+5, 5+4) **GS 10** (5+5)	0	0	1 (33%)	0	2 (67%)	3
	Total	10	36	21	1	10	78

[a]PGG: Prognostic Grade Group, [b]GS: Gleason Score

TABLE 2: Number of cases according to its primary tumour pathologic staging

Primary tumour pathologic staging, pT	Number of cases (%)
pT1, clinically inapparent tumour	0 (0%)
pT2, organ confined	0 (0%)
pT2a, unilateral, one-half of one side or less	7 (9%)
pT2b, Unilateral, involving more than one-half of side but not both sides	2 (2%)
pT2c, bilateral disease	35 (45%)
pT3, extra-prostatic extension	0 (0%)
pT3a, extra-prostatic extension or microscopic invasion of bladder neck	23 (29%)
pT3b, seminal vesicle invasion	10 (13%)
pT4, invasion of rectum, levator muscle, and/or pelvic wall	1 (3%)

DISCUSSION

Gleason grading of prostate needle biopsy is essential in deciding the appropriate treatment and the extent of the neurovascular bundle and pelvic lymph node dissection at radical prostatectomy.[2] The new suggested prognostic grade groups (PGG) which is based on Gleason grade is expected to give more simplified but definite grade stratification.

There were a few studies looking at the reliability of Gleason grades in the needle biopsy by comparing the grade of the needle biopsies with those of radical prostatectomy specimens. In the current study, 48% of PGG 1 needle biopsies were upgraded to PGG 2 in the subsequent radical prostatectomy (RP) and 14% were upgraded to PGG 3 or PGG 4. One large population-based study which involved a total of 1116 cases showed about similar findings in which more than 40% of cancers graded with GS of ≤6 in the biopsy were upgraded to a ≥7 in the RP specimen.[10] There are many factors that may contribute to the upgrading of the tumour. One of the reasons is due to tumour sampling whereby prostate needle biopsy represents just a small percentage of the whole gland (<0.05 cc) and with the nature of multifocality of prostate cancer making chance of not sampling higher grade areas remain high.[11]

The differentiating factor for PGG 2 and 3 is the predominance of its Gleason pattern 4 tumours. Recognition and labelling of malignant glands as Gleason pattern 3 or Pattern 4 will differentiate the cases of prostatic adenocarcinoma into either PGG1 or PGG 2 and 3 with different prognostic implication.

Our study showed fair agreement between the percentage of Gleason pattern 4 in subgroup GS 7 of the needle biopsy and its radical prostatectomy specimen. In 27 cases that are classified as PGG 2 by needle biopsy specimens, 81% (22 cases) had matching score with the radical prostatectomy specimen while 11% (3 cases) were upgraded to PGG3 and 7% (2 cases) were upgraded to PGG 5. Similarly, in 15 cases of PGG 3 group needle biopsy, 80% (12 cases) had a similar score in radical prostatectomy specimen while 7 % (1 case) was downgraded to PGG 2 and 13% (2 cases) were upgraded to PGG 5.

Over the past years, a few modifications on the original Gleason pattern in which some of the previously Gleason pattern 3 glands are now being reclassified as Gleason pattern 4[5]. Under calling borderline grades (especially between small glands of pattern 3 and small cribriform glands of pattern 3 with poorly formed or

TABLE 3: Cases according its pathologic regional lymph nodes involvement

Pathologic regional lymph nodes, pN	Number of cases (%)
pNX, regional nodes not sampled	47 (60%)
pN0, no positive regional lymph nodes	22 (28%)
pN1, metastases in regional node(s)	9 (12%)

cribriform glands of Gleason pattern 4) and under calling small foci of Gleason pattern 5 may contribute in the discrepancy of needle biopsy with radical prostatectomy Gleason score.[11]

Our study also showed that there was a significant relationship between the percentage of Gleason pattern 4 and the pathological staging of its radical prostatectomy, pT and pN. One large multi-institutional study using the latest contemporary Gleason grading demonstrated that tumour that is categorised as PGG 1 at radical prostatectomy which comprises of Gleason grade 6(3+3) has a 96% cure rate at 5-years.[12] Another separate study showed that pure GS 6(3+3) tumour diagnosed in radical prostatectomy specimen has no potential for metastatic behaviour.[13] It was also illustrated that PGG 2 had a very good prognosis with rare metastases while PGG 3 has a significantly worse prognosis than PGG 2.[12] These studies illustrate the importance of categorising prostatic carcinoma in the needle prostate biopsy specimen as either PGG 1, PGG 2 or PGG 3 because it may influence successive management.

CONCLUSION

The tumour grade of prostatic adenocarcinoma assessed via needle biopsy specimen may be upgraded in the successive radical prostatectomy specimen as more tumour areas are available for evaluation. The percentage of Gleason pattern 4 in needle biopsy is significantly related to the final pathological staging. Reporting the percentage of pattern 4 especially on needle biopsies may have clinical importance, as it may reflect the tumour behaviour and aid the next step in patient care and management. It is thereby important for treating clinicians to realise this trend when taking the Gleason score of needle biopsy into consideration in deciding the subsequent treatment of choice for prostatic adenocarcinoma.

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REFERENCES

1. Lim GCC, Rampal S, Yahaya H. Cancer Incidence in Peninsular Malaysia, 2003-2005: The Third Report of the National Cancer Registry, Malaysia. National Cancer Registry; 2008.
2. Fine SW, Amin MB, Berney DM, *et al.* A contemporary update on pathology reporting for prostate cancer: biopsy and radical prostatectomy specimens. Eur Urol. 2012; 62(1): 20-39.
3. Zareba P, Zhang J, Yilmaz A, Trpkov K. The impact of the 2005 International Society of Urological Pathology (ISUP) consensus on Gleason grading in contemporary practice. Histopathology. 2009; 55(4): 384-91.
4. Brimo F, Montironi R, Egevad L, *et al.* Contemporary grading for prostate cancer: implications for patient care. Eur Urol. 2013; 63(5): 892-901.
5. Chen N, Zhou Q. The evolving Gleason grading system. Chin J Cancer Res. 2016; 28(1): 58-64.
6. Pierorazio PM, Walsh PC, Partin AW, Epstein JI. Prognostic Gleason grade grouping: data based on the modified Gleason scoring system. BJU international. 2013; 111(5): 753-60.
7. Stark JR, Perner S, Stampfer MJ, *et al.* Gleason score and lethal prostate cancer: does 3+ 4= 4+ 3? J Clin Oncol. 2009; 27(21): 3459-64.
8. Berg KD, Røder MA, Brasso K, Vainer B, Iversen P. Primary Gleason pattern in biopsy Gleason score 7 is predictive of adverse histopathological features and biochemical failure following radical prostatectomy. Scand J Urol Suppl. 2013;47.
9. Moch H, Humphrey PA, Ulbright TM. Who classification of tumours of the urinaryt system and male genital organs. Who classification of tumours of the urinary system and male genital organs 2016.
10. Kvåle R, Møller B, Wahlqvist R, *et al.* Concordance between Gleason scores of needle biopsies and radical prostatectomy specimens: a population-based study. BJU international. 2009; 103(12): 1647-54.
11. Trpkov K. Contemporary Gleason grading system. Genitourinary Pathology: Springer; 2015: 13-32.
12. Epstein JI, Zelefsky MJ, Sjoberg DD, *et al*. A contemporary prostate cancer grading system: a validated alternative to the Gleason score. Eur Urol. 2016; 69(3): 428-35.
13. Ross HM, Kryvenko ON, Cowan JE, Simko JP, Wheeler TM, Epstein JI. Do adenocarcinomas of the prostate with Gleason score (GS)≤ 6 have the potential to metastasize to lymph nodes? Am J Surg Pathol. 2012; 36(9): 1346-52.