

Prognostic Stratification of Prostatic Cancer According to Modified Gleason Grading System

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Abstract

Background : To assess the prognostic stratification of prostatic cancer according to modified Gleason Grading System

Methods: In this observational study 65 patients having prostatic carcinoma, who underwent prostatectomy by different surgical procedures were included. Lab request forms and histopathology reports of these patients were reviewed for prognostic grade groups. Gleason grade ≤ 6 ; 3 + 4; 4 + 3; 8 and 9-10 were assigned by two histopathologists separately to each prostatic cancer in addition to already assigned Gleason grades.

Results: Sixty five patients were found to be diagnosed with prostatic carcinoma. Age ranged from 64-85 years. Eight patients were found incidentally to have prostatic cancer in T1 stage with six having grade group I cancer, one with grade group II and the one with a grade group III cancer. The remaining 57 cases were already diagnosed before surgery by different diagnostic tests. Out of these 57 cases 15 had Gleason grade 7 cancer (7 with grade group II and 8 with grade group III), 18 had Gleason grade 8 (All with grade group IV) and 24 cases had combined Gleason grade 9 and 10 cancer (All with grade group V). Cancer of all of these 57 cases was beyond T1 stage. Thirty cases were in stage T2, 20 in stage T3 and only 7 in stage T4.

Conclusion: While retaining the essence of the conventional Gleason system, the 2014 modified system of grade groups categorize patients of prostatic carcinoma, prognostically with more accuracy acceptable to both clinicians and patients.

Key Words: Prognostic Stratification, Prostatic Cancer, Modified Gleason Grading System

Introduction

Prostate cancer (PCa) is the second most commonly diagnosed cancer and 6th leading cause of death due to cancer in males through out the world.¹ There are several diagnostic tools including serum PSA, DRE and imaging modalities like transrectal ultrasonography which are helpful in picking of this

cancer before prostatectomy, but it is the histopathology of biopsy specimens that is considered to be the gold standard.^{2,3}

To evaluate prostate cancer in prostatectomy specimens a grading system based on its histological architecture was developed by Donald Gleason in 1966 and is considered a strong predictor of prognosis since the time of its inception.^{4,5,6} In this system grade is the sum of two most common (primary or predominant + Secondary or second most common) grade patterns and is reported as Gleason score.⁵ To avoid ambiguity Gleason score is reported in the form of a mathematical equation i.e. Gleason score 3+4=7.⁷ Synonyms for Gleason score are Gleason sum or combined Gleason grade.⁵ Both the primary and the secondary architectural patterns are identified and assigned a number from 1 to 5. Pattern-1 is considered as the most differentiated while pattern 5 the least differentiated one. When a carcinoma has one histologic pattern instead of two then same number is assigned to both primary and secondary patterns and is added. Range wise Gleason scores range from 2 (1+1=2) to 10 (5+5=10). Grade 2 tumors are composed uniformly of Gleason pattern-1 and are most differentiated while Gleason score 10 are uniformly composed of Gleason pattern-5 and are the most undifferentiated tumors⁵. With changing pathological and clinical practice, several controversial areas were found in this system.⁸ More than 30 % cases of prostate cancer comprised of pattern 1 and 2 in the original publications by Gleason which are presently not reported on biopsy specimens. Reporting of multiple prostatic cores and radical prostatectomy specimens having tertiary pattern were also not described by the initial scoring system. Similarly a minor component of high grade cancer, if present was not reported in this initial system.^{6,8}

To address these and many unmentioned issues an International Society of Urological Pathology (ISUP) arranged consensus conferences in 2005 in San Antonio, Texas (USA) and subsequently in 2014 in Chicago (USA). In 2005 conference only pathologists participated while in 2014 conference urologists,

pathologists, radiation therapists and oncologists participated. They agreed on developing a system of prognostic grade groups from I-V to be used in conjunction with original Gleason grades. They incorporated Gleason scores into this new system of grade groups (Table 1).^{6,7,9,10,11-13}

Table 1: Modified Gleason Scoring for prostatic cancer

Gleason pattern	Gleason score	Grade Group
Gleason Patterns 1-3 (Distinct and discrete individual glands)	Gleason score ≤ 6	Grade group- I Grade group- II Grade group- III
	Gleason score 3+4=7	
	Gleason score 4+3=7	
Gleason Patterns 4 (cribriform, fused or poorly formed glands)	Gleason score 4+4=8	Grade group IV
	Gleason score 3+5=8	
	Gleason score 5+3=8	
Gleason Patterns 5 (cords, solid nest, sheets, single cells, comedo necrosis)	Gleason score 4+5=9	Grade group V
	Gleason score 5+4=9	
	Gleason score 5+5=10	

Gleason score 6 cancer, managed presently by active surveillance is perceived by patients as more ominous than grade group 1 cancer and in the same way over-treated sometimes by the oncologists. Patients feel uneasy with this grade 6 cancer and suffer usually from psychological problems like depression and inclination towards suicide.⁹ On the contrary, grade group 1 cancer out of 5 in the recent modified system sounds more indolent as compared to Gleason grade 6 cancer out of 10 in the previous system.⁴ Previously Gleason grade 3+4=7 and 4+3= 7 tumours were considered to have the same gravity of aggressiveness regarding stage and biochemical recurrence. In the recent grade group system, grade groups-II and III are assigned to Gleason grade 3+4=7 and 4+3= 7 tumors respectively as grade 4+3=7 cancer is more aggressive compared to grade 3+4=7 and vice versa. Similarly all cribriform patterns, fused glands, poorly formed glands and glomeruloid morphology were considered Gleason pattern 4 instead of 3 in the modified system for the purpose of simplicity and interobserver reproducibility.^{4,7} This new grade group system is incorporated into the recent 2016 edition of WHO classification of prostatic tumors due to its simplicity, provision of accurate prognostic stratification and

reflection of prostate cancer biology more accurately as compared to original system of Gleason score.^{6, 7,10 12}

Patients and Methods

In this observational study all the patients were having prostatic carcinoma and operated at LRH or elsewhere by any surgical method. Patient having inadequate or autolysed specimens in spite of having presurgically diagnosed prostatic cancer by serum prostate specific antigen (PSA), digital rectal examination (DRE) or transrectal ultra-sonography were excluded from the study. Slides patients (n=65) were examined by two histopathologists for assigning recently adopted grade groups to the already diagnosed prostatic cancers with allocated old Gleason scores. If there was no consensus between the pathologists or there was some ambiguity regarding the pattern of cancer, then deep sections or serial sections were taken of their respective blocks, processed and stained as per standard protocol followed in the department. New grade groups were assigned to all the cases and arranged in parallel to the previously assigned Gleason scores. Data obtained from evaluation by both old and new systems was arranged in a tabulated form to compare the simplicity and applicability of both the systems. Gleason score = 7 cancers were also divided into two different prognostic grade groups. Data thus collected was analyzed by Microsoft excel software.

Results

Sixty five patients having age of 64–85 years (mean = 74 years) were found from the record of the laboratory to have prostatic carcinoma. They were operated by different surgical procedures. Eight cases were found incidentally to have prostatic cancer while evaluating their prostatic chips removed by transurethral resection of prostate (TURP) for the treatment of benign prostatic hyperplasia (BPH) without any presurgical knowledge of cancer in them. The remaining 57 cases were diagnosed presurgically by various diagnostic methods like DRE, serum PSA level estimation, transrectal ultrasound etc. All of these 57 cases were subjected to radical prostatectomy being a planned treatment option for their health problem..All the patients either diagnosed incidentally in the TURP specimens or diagnosed presurgically for prostatic cancer were having age above 60 years (Table 2)

Table 2:Age wise distribution of patients (n=65)

Age Group (years)	No of cases
60-70	16
71-80	28
81-90	65

Pattern 3 (Fig. I), 4 (Fig. II) and 5 (Fig. III) were the patterns commonly observed in our study. Pattern 2 (Fig. IV) was also observed but in less percentage not qualifying for primary or secondary pattern in any case to be recorded in grading of the tumor. No case of pattern 1 was observed in this study. As per old system of Gleason scoring six out of the eight incidentally found cancers were assigned Gleason score 6 with all having 3+3=6 grade while two had score of 7 with one having 3+4=7 grade and the other having 4+3=7 grade. According to recent ISUP 2014 system of grade groups the six cases having prostatic carcinoma of grade 3+3=6 were kept in grade group I. The one having Gleason grade 3+4=7 cancer was kept in grade group II while the other having grade 4+3=7 cancer was kept in grade group III. Out of these eight specimens, six had a tumor volume of less than 5% of the total resected chips (T1a cancer) while two had a tumor volume of more than 5% of the total resected specimens (T1b cancer). Out of the remaining 57 cases of prostatic cancer 15 cases had Gleason grade 7 cancer according to old Gleason score, 18 had grade 8 cancer while 11 and 13 cases had Gleason grade 9 and 10 cancer respectively. No Gleason grade 6 cancer was found in these 57 prostatectomy specimens. During microscopic evaluation, according to ISUP 2014 system seven cases were kept in grade group II and eight cases were given grade group III out of 15 cases already diagnosed with Gleason grade 7 cancer. As per recommendations of new grading system all 18 cases of Gleason grade 8 cancer were accommodated in grade group IV cancer while 24 cases of combined Gleason grade 9 and 10 cancers were kept in grade group V (Table-3). All of these cancers were beyond T1 stage. Thirty cases were in stage T2, 20 in stage T3 and seven in stage T4. Nodal (N) status of all these cases except the last 7 cases was N0. Seven cases of stage T4 had N1 status. There was no distant metastasis (M0) in all the 65 cases of prostate cancer.

Table 3: Distribution of prostatic cancer according to modified grade group system. (n=57)

Gleason Grade	Grade groups	Number of prostatic cancer
3+4=7	II	7
4+3=8	III	8
4+4=8	IV	5
3+5=8	IV	7
3+5=8	IV	6
4+5=9	V	9
5+4=9	V	11
5+5=10	V	4
Total		57

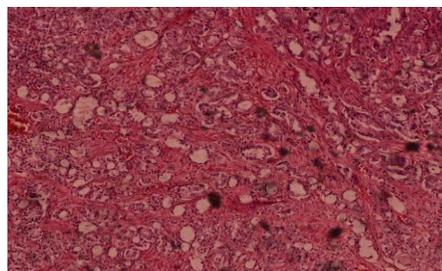


Figure 1. Prostatic Cancer - Pattern 3

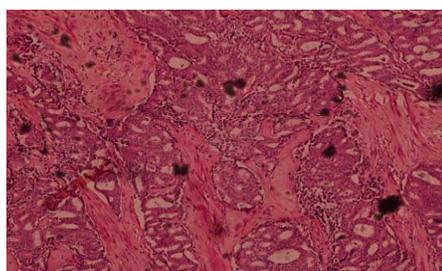


Figure 2. Prostatic Cancer - Pattern 4

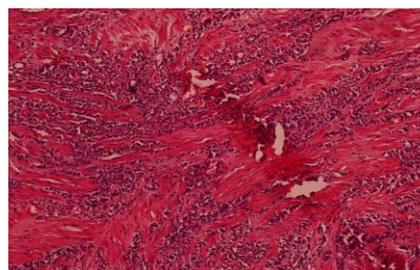


Figure 3. Prostatic cancer - Pattern 5

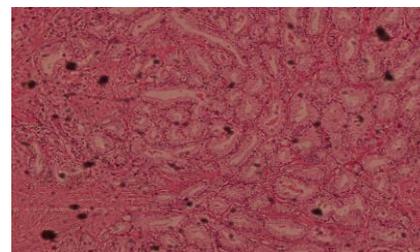


Figure 4. Prostatic cancer - Pattern 2

Discussion

This was an easy practice to assign grade groups to prostate cancer as per modified ISUP system while

evaluating it microscopically, in place of giving Gleason patterns and grades to them. As Gleason grading system is in practice for last 50 years and has gained vast acceptability, therefore the present system should be used in conjunction with it and grade group of each prostate cancer should be written in bracket along with the Gleason grade as accepted by the WHO for 2016 classification of prostatic tumors.⁷ We have also adopted this 2016 WHO criteria in the present study. In the previous system, Gleason grade 6 prostatic cancer, although considered an indolent cancer by the pathologists and oncologists, is taken worrisome by the patients. The figure of 6 being amid of 2 and 10 is perceived by a patient to be of an intermediate severity instead of low one and thus puts a lot of psychological burden on his mind.⁹ In the modified system of grade groups if the same patient is told that he has grade group-1 prostate cancer than it is easy to convince him about the indolent behavior of his tumor and easy to alleviate his anxiety.⁴ These Grade Groups predict progression of prostatic carcinoma more accurately as compared to conventional Gleason risk stratification groups (≤ 6 or low risk, 7 or intermediate risk and 8-10 or high risk).⁶ Several studies have been conducted about merits and demerits of this modified system of grade groups for prognostic stratification of prostatic carcinoma. ^{6,7,10,14,15} All of them have concluded that this system is simple and applicable being based on the already prevalent Gleason grading system. The present study has also shown simplicity and applicability of the modified system without facing any difficulty .

Conclusion

1. The modified grade group system of prostate cancer is simple and offers an excellent 5-tiered prognostic stratification of this carcinoma.
2. Modified grade group system in conjunction with conventional Gleason scoring system can improve the applicability in prognostic scoring of CA prostate.

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