

Original Research Article

New perspectives in modified Gleason's grading for prostatic cancer and its comparison with original Gleason's

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ABSTRACT

Background: The Gleason score is the most widely accepted histopathological grading system for prostate cancer since decade despite having many deficiency that can potentially impact patient health care. So ISUP agreed on developing a system of prognostic grade groups from I-V. Aim and objective was to study the new perspectives of modified Gleason's grading and to compare it with original Gleason's System with focus on the prognostic significance of the modifications.

Methods: A retrospective study of 60 patients, who underwent TURP and Sextant biopsy and diagnosed as prostatic carcinoma in our institute were included in this study. Laboratory requisition forms with clinical history, PSA levels and histopathology reports of these patients were reviewed and graded accordingly to the newer gleasons. New Gleason grade includes five distinct Grade Groups based on the modified Gleason score groups. Grade Group 1 = Gleason score ≤ 6 , Grade Group 2 = Gleason score $3 + 4 = 7$, Grade Group 3 = Gleason score $4 + 3 = 7$, Grade Group 4 = Gleason score 8, Grade Group 5 = Gleason scores 9 and 10 were assigned. The change in the grading system is tabulated and compared separately.

Results: Patients age ranged from 55-80 years. The number of cases were 3,12,15,19 and 11 categorized under grade group I, grade group II, grade group III, grade group IV, grade group V cancer respectively according to modified gleason grading.

Conclusions: Modified Gleason is a simplified grading system which may reduce over treatment of indolent prostate cancer. New gleasons grading clarifies the clinicians about the dilemma of gleason scores, offering an excellent prognostic stratification of this carcinoma.

Keywords: Gleason grading, Gleason score, Modified, New perspectives, Prognosis, Prostatic cancer

INTRODUCTION

Prostate cancer is the second most commonly occurring cancer in men and the fourth most commonly occurring cancer overall. There were 1.3 million new cases in 2018.¹ There are several diagnostic tools such as serum PSA, DRE and imaging modalities like transrectal ultrasonography which are helpful in picking of this cancer before prostatectomy, but it is the biopsy specimens that is considered to be the gold standard.^{2,3} The Gleason histologic grade of prostate adenocarcinoma

is one of the most powerful predictors of biologic behaviour and often has an important role in determining patient treatment. The most widely used method for prostatic carcinoma grading was developed by Donald Gleason and is known as the Gleason scoring system.⁴ The sum of two most common (primary or predominant + Secondary or second most common) grade patterns and is reported as Gleason score. 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. 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 tumors.⁵

In this system with changing pathological and clinical practice, several controversial areas were found which can potentially impact the patients health care.⁶⁻⁹ An International Society of Urological Pathology (ISUP) arranged consensus conferences in 2014 in Chicago (USA), participants were urologists, pathologists, radiation therapists and oncologists. 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.¹⁰⁻¹³

This new grading system includes five distinct Grade Groups based on the modified Gleason score groups.

Grade Group 1 = Gleason score ≤ 6 , Grade Group 2 = Gleason score 3 + 4 = 7, Grade Group 3 = Gleason score 4 + 3 = 7, Grade Group 4 = Gleason score 4 + 4 = 8, Grade Group 5 = Gleason scores 9 and 10. It has been accepted by the World Health Organization (WHO) for the 2016 edition of Pathology and Genetics: Tumours of the Urinary System and Male Genital Organs.¹⁴

METHODS

A retrospective study from May 2017 to October 2018 of 60 patients, who underwent TURP and Sextant biopsy, diagnosed as prostatic carcinoma at L.N. Medical College and Research Centre, Department of Pathology, were included in this study. Laboratory requisition forms with clinical history, PSA levels and histopathology reports of these patients were reviewed and graded accordingly to the Modified Gleasons scoring system for prostatic cancer (Table 1).

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
	Gleason score 3+4=7	Grade group- II
	Gleason score 4+3=7	Grade group- III
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. Comedonecrosis)	Gleason score 4+5=9	Grade group V
	Gleason score 5+4=9	
	Gleason score 5+5=10	

Slides were examined for assigning modified Gleason grade groups to the already diagnosed prostatic cancers with old Gleason scores. If there was no consensus between the pathologists or there was some ambiguity regarding the pattern of cancer, then deeper sections or serial sections were taken of their respective blocks, processed and stained as per the standard protocol followed in our histopathology department.

New Gleason grade includes five distinct Grade Groups based on the modified Gleason score groups. Grade Group 1 = Gleason score ≤ 6 , Grade Group 2 = Gleason score 3 + 4 = 7, Grade Group 3 = Gleason score 4 + 3 = 7, Grade Group 4 = Gleason score 8, Grade Group 5 = Gleason scores 9 and 10 were assigned. The change in the grading system is tabulated and compared separately.

Inclusion criteria includes all cases diagnosed with adenocarcinoma. Exclusion criteria includes all cases

other than of adenocarcinoma and inadequate biopsy samples

RESULTS

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 showing the distribution of prostatic cancer cases (Table 2).

Patient's age ranged from 55-80 years. Number of cases were maximum 32, in age group from 65-75 years and 19 cases among 55-65, Only 9 cases were seen in more than 75 years (Table 3). As per original Gleason, only three cases were of gleason grade 6. Majority of cases 27 and 19 were categorized under gleason score 7 and 8 respectively. Whereas only 9 and 2 cases in grade 9 and grade 10 respectively.

Table 2: Distribution of prostatic cancer cases (n=60).

Gleason Grade	Grade groups	No. of cases according to new Gleason Grading	No. of cases according to old Gleason Grading
3+3 = 6	I	3	3
3+4 = 7	II	12	27
4+3 = 7	III	15	
4+4 = 8	IV	10	19
3+5 = 8		6	
5+3 = 8		3	
4+5 = 9	V	5	9
5+4 = 9		4	
5+5 = 10		2	

Table 3: Age wise distribution of patients.

(n=60) Age Group (years)	No. of cases
55-64	19
65-74	32
>75	9

As per recent ISUP 2014 system of grade groups the three cases having prostatic carcinoma of grade 3+3=6 were kept in grade group I. The twelve cases having gleason grade 3+4=7 was kept in grade group II while the other fifteen cases having 4+3=7 was kept in grade group III. As per recommendations of new grading system all 19 cases of Gleason grade 8 cancer were accommodated in grade group IV cancer while 11 cases of combined Gleason grade 9 and 10 cancers were kept in grade group V.

DISCUSSION

The original study by Gleason did not benefit from the use of immunohistochemistry and it is likely that Gleason’s original 1 + 1 = 2 adenocarcinomas were in fact adenosis. In addition, with the current changes in Gleason grading, nearly all the previously considered Gleason pattern 2 adenocarcinomas are now classified as Gleason grade 3. Over the last decade there has been a dramatic decrease in the current incidence of pathologists diagnosing Gleason score 2-4 compared to 22.3% of the biopsies in 1994.^{15,16}

Gleason pattern 3 consists of well-formed, individual glands of various sizes including branching glands (Figure 1). The glands should form discrete units, well-formed and not fused. Gleason pattern 4 includes poorly-formed, fused, and cribriform glands (Figure 2).

Gleason pattern 5 consists of sheets of tumor, individual cells, and cords of cells (Figure 3). A more uncommon pattern 5 morphology is comedonecrosis (Figure 4) within solid nests or cribriform glands. It is important to

distinguish intraluminal eosinophilic secretions from true necrosis. Gleason pattern 5 is frequently undergraded by pathologists.¹⁷

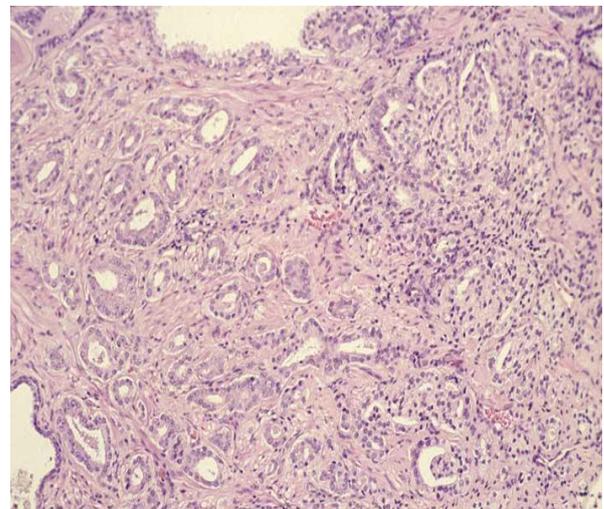


Figure 1: Gleason pattern 3.

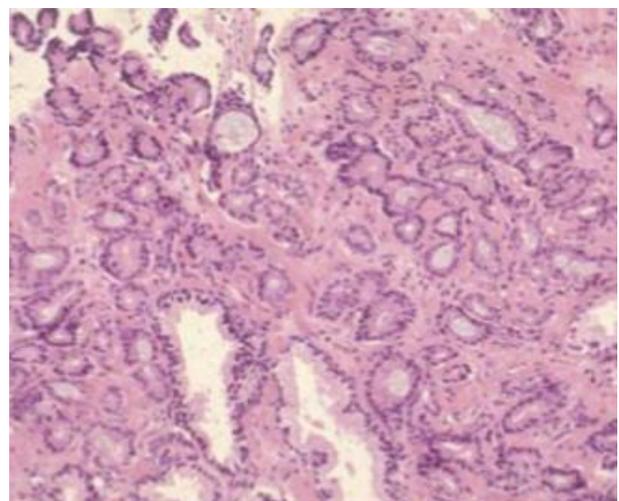


Figure 2: Gleason pattern 4.

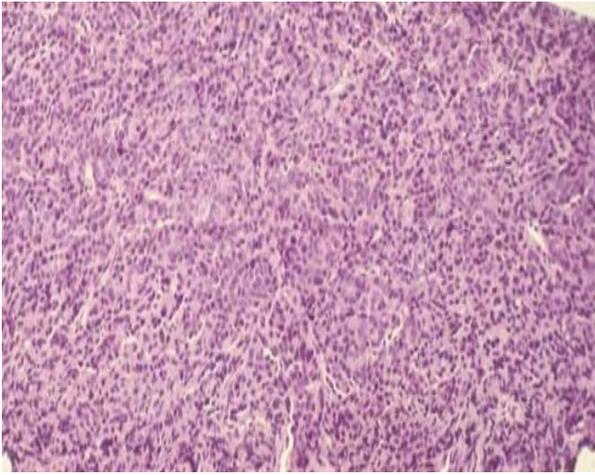


Figure 3: Gleason pattern 5.

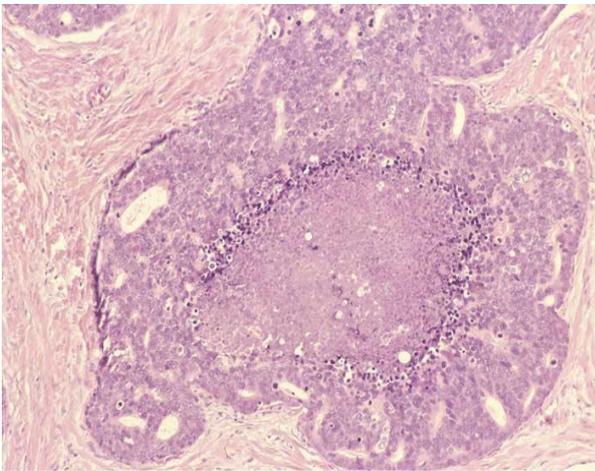


Figure 4: Comedonecrosis.

A common critique on the Gleason score is that the majority of patients is categorised into one group (Gleason score 6-7) with highly variable outcomes, suggesting the Gleason scoring system to be insufficient as prognostic tool.¹⁸ Several studies have tried to address this problem by subdividing Gleason score 7 into Gleason score 3 + 4 = 7 and Gleason score 4 + 3 = 7.¹⁹

A major weakness of the Gleason system is the large amount of patients with intermediate Gleason score 7, whose prognosis is still highly unpredictable, contrasting with Gleason score 6 or 10, having a good and bad prognosis respectively. In practice the lowest score is now assigned a 6, although it is on a scale of 2-10. This leads to a logical yet incorrect assumption on the part of patients that their cancer is in the middle of the scale, compounding the fear of their cancer diagnosis with the belief that the cancer is serious, thus leading to an expectation that treatment is necessary.

In addition, many former Gleason score 6 tumors are now reclassified as Gleason score 7 in the modified system. Modern Gleason score 6 tumors have a much better

prognosis than reported in the older literature. Studies have shown that virtually no pure Gleason score 6 tumors are associated with disease recurrence after radical prostatectomy and lacks the potential for lymph node metastases.^{20,21} These Grade Groups were shown to be more accurate in predicting progression than the Gleason risk stratification groups (≤ 6 , 7, 8-10).

Many clinicians consider Gleason score 7 on biopsy to be intermediate risk, multiple studies have shown that Gleason score 4 + 3 = 7 demonstrates worse pathological stage and biochemical recurrence rates than 3 + 4 = 7.²²⁻²⁴ Recommendations have been made to split up and refine the Gleason score 7 group, on the molecular level. Several studies reported molecular signatures and pathways based on mRNA expression to distinguish tumors according to Gleason grade.²⁵⁻²⁷ 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. 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.

Several studies have been conducted about merits and demerits of this modified system of grade groups.^{6,10} All of them have concluded that this system is simpler and accurate when used in conjunction with already prevalent Gleason grading system. This study also recommend the same. Until now no reliable alternative for the Gleason system exists, and it is not likely that in the next years an alternative non-histological system will appear that will have the same reproducibility and prognostic strength.²⁸

CONCLUSION

Gleason score continues to be the single most powerful predictor of prostate cancer prognosis and plays a significant role in clinical management. Modified Gleason is a simplified grading system which may reduce over treatment of indolent prostate cancer, offering an excellent 5-tiered prognostic stratification of this carcinoma. If the Gleason system is regularly monitored and updated it is expected to stay a key element in the prostate cancer diagnostic algorithm, even in the molecular era.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality

- worldwide for 36 cancers in 185 countries. *CA: a Cancer J Clinicians.* 2018 Nov;68(6):394-424.
2. Varghese J, Kuruvilla PM, Mehta N, Singh R. Incidentally detected adenocarcinoma prostate in transurethral resection of prostate specimens: a hospital based study from India. *Asian Pac J Cancer Prev.* 2016;17(4):2255-58.
 3. Sakamoto H, Matsumoto K, Hayakawa N, Maeda T, Sato A. Preoperative parameters to predict incidental (T1a and T1b) prostate cancer. *Can Urol Assoc J.* 2014;8(11-12):815-20.
 4. Gleason DF, Mellinger GT. Prediction of prognosis for prostatic adenocarcinoma by combined histological grading and clinical staging. *J Urol.* 1974;111(1):58-64.
 5. Baydar DE, Epstein JI. Gleason Grading System: Modifications and additions to the original scheme. *Turkish J Pathol.* 2009;25(3):59-7.
 6. Kryvenko ON and Epstein JI. Prostate cancer grading a decade after the 2005 modified Gleason grading system. *Arch Pathol Lab Med.* 2016;140:1140-52.
 7. Gordetsky J, Epstein J. Grading of prostatic adenocarcinoma: current state and prognostic implications. *Diagnostic Pathol.* 2016;11(25):1-8.
 8. Egevad L, Mazzucchelli R, Montiron R. Implications of the international society of urological pathology modified Gleason grading system. *Arch Pathol Lab Med.* 2012;136:426-34.
 9. Loeb S, Montorsi F, Catto JW. Future-proofing Gleason Grading: What to Call Gleason 6 Prostate Cancer? *Euro Urol.* 2015;68:1-5.
 10. Chen N and Zhou Q. The evolving Gleason grading system. *Chin J Cancer Res.* 2016;28(1):58-64.
 11. Pierorazio PM, Walsh PC, Partin AW. Prognostic Gleason grade grouping: data based on the modified Gleason scoring system. *BJU Int.* 2013;111:753-60.
 12. Epstein JI, Egevad L, Amin MB, Delahunt B. The 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma: definition of grading patterns and proposal for a new grading system. *Am J Surg Pathol.* 2016;40(2):244-52.
 13. Kryvenko ON, Epstein JI. Changes in prostate cancer grading: Including a new patient centric grading system. *Prostate.* 2016;76:427-33.
 14. Epstein JI, Egevad L, Amin MB, Delahunt B, Srigley JR, Humphrey PA. The 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma: definition of grading patterns and proposal for a new grading system. *Am J Surg Pathol.* 2016;40(2):244-52.
 15. Steinberg DM, Sauvageot J, Piantadosi S, Epstein JI. Correlation of prostate needle biopsy and radical prostatectomy Gleason grade in academic and community settings. *Am J Surg Pathol.* 1997;21(5):566-76.
 16. Fine SW, Epstein JI. A contemporary study correlating prostate needle biopsy and radical prostatectomy Gleason score. *J Urol.* 2008;179(4):1335-8.
 17. Fajardo DA, Miyamoto H, Miller JS, Lee TK, Epstein JI. Identification of Gleason pattern 5 on prostatic needle core biopsy: frequency of under diagnosis and relation to morphology. *Am J Surg Pathol.* 2011;35(11):1706-11.
 18. Andren O, Fall K, Franzen L, Andersson SO, Johansson JE, Rubin MA. How well does the Gleason score predict prostate cancer death? A 20-year followup of a population-based cohort in Sweden. *J Urol.* 2006;175(4):1337-40.
 19. Bostwick DG, Grignon DJ, Hammond ME, Amin MB, Cohen M, Crawford D, et al. Prognostic factors in prostate cancer. College of American Pathologists Consensus Statement 1999. *Arch Pathol Lab Med.* 2000;124(7):995-1000.
 20. Pierorazio PM, Walsh PC, Partin AW, Epstein JI. Prognostic Gleason grade grouping: data based on the modified Gleason scoring system. *BJU Int.* 2013;111:753-60.
 21. Miyamoto H, Hernandez DJ, Epstein JI. A pathological reassessment of organ-confined, Gleason score 6 prostatic adenocarcinomas that progress after radical prostatectomy. *Hum Pathol.* 2009;40:1693-8.
 22. Burdick MJ, Reddy CA, Ulchaker J, Angermeier K, Altman A, Chehade N, et al. Comparison of biochemical relapse-free survival between primary Gleason score 3 and primary Gleason score 4 for biopsy Gleason score 7 prostate cancer. *Int J Radiat Oncol Biol Phys.* 2009 Apr 1;73(5):1439-45.
 23. Chan TY, Partin AW, Walsh PC, Epstein JI. Prognostic significance of Gleason score 3 + 4 versus Gleason score 4 + 3 tumor at radical prostatectomy. *Urol.* 2000;56:823-7.
 24. Kang DE, Fitzsimons NJ, Presti Jr JC, Kane CJ, Terris MK, Aronson WJ, et al. Risk stratification of men with Gleason score 7 to 10 tumors by primary and secondary Gleason score: results from the SEARCH database. *Urol.* 2007 Aug 1;70(2):277-82.
 25. True L, Coleman I, Hawley S, Huang CY, Gifford D, Coleman R, et al. A molecular correlate to the Gleason grading system for prostate adenocarcinoma. *Proc Natl Acad Sci.* 2006;103(29):10991-6.
 26. Kim H, Lapointe J, Kaygusuz G, Ong DE, Li C, van de Rijn M, et al. The retinoic acid synthesis gene *ALDH1a2* is a candidate tumour suppressor in prostate cancer. *Cancer Res.* 2005;65(18):8118-24.
 27. Tomlins SA, Rhodes DR, Perner S, Dhanasekaran SM, Mehra R, Sun XW, et al. Recurrent fusion of *TMPRSS2* and *ETS* transcription factor genes in prostate cancer. *Sci.* 2005;310(5748):644-8.
 28. Gevaert T, Van Poppel H, Joniau S, De Ridder D, Lerut E. Current perspectives on the use of the Gleason grading system for prostate cancer. *Belgian J Med Oncol.* 2012 Apr 1;6(2):45-51.

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