Frontiers in Health Informatics
ISSN-Online: 2676-7104
www.healthinformaticsjournal.com
2024; Vol 13: Issue 8
Open Access

COMPARISON OF CONVENTIONAL AND MODIFIED GLEASON GRADING SYSTEMS

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Cite this paper as: Farhana Ali, Madiha Arshad, Sana Afroze, Khadija Saleem, (2024) Comparison Of Conventional And Modified Gleason Grading Systems. Frontiers in Health Informa .4904-4311

ABSTRACT

OBJECTIVE: To determine the frequency of patients who show change in conventional Gleason score of prostate adenocarcinoma by the application of modified Gleason grading system

STUDY DESIGN Cross sectional survey.

PLACE AND DURATION OF STUDY: Department of pathology, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore. Six months after approval of synopsis time duration

MATERIAL AND METHODS:100 cases of prostatic adenocarcinoma were given a Gleason score by applying conventional Gleason grading system and Modified (ISUP 2005) Gleason grading. Information was collected on a Performa. Patient's name, age, histology numbers, the change in Gleason score, presence of tertiary tumor grade pattern and any other morphological variation were recorded.

RESULTS: 41 cases showed change in gleason score after the application of modified gleason grading system. the gleason score was upgraded in these cases. none of the case showed downgraded .gleason score .

CONCLUSION: The application of modified gleason grading system changes gleason score in significant number of cases with upward migration.

KEY WORDS:
gleason garding, prostatic adenocarcinoma, tertiary pattern

INTRODUCTION

Prostate cancer arises from prostate gland present in pelvis of males. It is the most common internal cancer of men and accounts 10% of the cancers in the men. In 2009, the new prostate

cancers case reported in United States were 1,479,350[1] and was found to be the second leading cause of cancer related deaths.[2] According to collective cancer registry report 2008 of Shaukat Khanum Memorial Cancer hospital and Research Centre Lahore, prostate cancer is sixth most common cancers among males above 18years.[3] The prostate cancer is a common solid malignant neoplasm seen in routine practices.[4]

Ninety five percent of the prostate cancers are adenocarcinomas.[5] The diagnosis of prostate cancer is based on light microscopic examination of prostate tissue. Treatment and prognosis of patients having prostate adenocarcinoma depends on the behavior of tumor which is predicted by Gleason grading. In this system different patterns of neoplasm are given grade patterns from 1 to 5 and the sum of two most common patterns (primary and secondary) are added to get a total score of 2-10.[6]

In 2005, International society of urological pathology (ISUP) held a consensus conference on Gleason grading system of prostate carcinoma to review conventional Gleason grading.[7] This revision was needed because of several recent developments like screening of prostate cancers and diagnosis of prostate cancer at early stages,[8] new methods of tissue sampling like needle biopsy, advanced surgical methods like radical prostatectomy, use of immunohistochemistry and recognition of unusual morphological patterns.[9]

The ISUP consensus conference on Gleason grading is an attempt to develop consensus in the problematic areas of conventional Gleason grading. This consensus has developed as a result of the discussions held by the experts in urological pathology. There is a need to apply this scoring system in biopsies of prostate carcinoma and to evaluate its impact on Gleason scoring in pathology practices. In one of the study the difference in Gleason score (GS) distribution was analyzed and after the application of current modifications the Gleason score (GS) was changed in overall 43.14%. It was upgraded in 30.9% cases and downgraded in 12.3% cases.[10]

The accurate assessment of Gleason score has great impact on the risk stratification of patients, their treatment and follow up options. The studies[10,11] in this context emphasize the fact that the modified Gleason grading system has marked change on Gleason score and when this change has been incorporated in making clinical decisions these provided with better stratification of patients in different risk groups and is being helpful in the avoidance of under or over treatment of patients. It is also suggested that the patients in which Gleason score is upgraded, it indicates the early chances of biochemical recurrence and other bad prognostic effects and such patients can be put under effective and timely follow up. However in our set up no such comparative data is available. We intend to compare the both Gleason grading systems and to see the effect of modified Gleason grading system on our pathology practices. Any significant change in Gleason score, if occurs after the application of modified Gleason grading system, will encourage in adoption of modified Gleason grading system. The more accurate Gleason score in return shall be helpful for clinicians to decide treatment and follow up options.

MATERIALS AND METHODS

After approval of the study by the college of physicians and surgeons of Pakistan, the tissue specimen of 100 patients fulfilling the inclusion criteria were taken. Each case was given a case number and medical record number. The demographic data like age and name was recorded. The prostate specimen was be fixed over night in 10% formalin. After gross examination, sections were stained with eosin and hematoxiline stains. Microscopic findings of these slides were noted by the single consultant pathologist (five year post fellowship experience). Each case was given a Gleason score by applying conventional Gleason grading system and Modified (ISUP 2005) Gleason grading .The change in Gleason score which had occurred after the application of modified system were be noted. The presence of tertiary tumor grade pattern and any other morphological variation were also noted. All the data was recorded in especially designed Proforma .The collected information entered and analysed through SPSS version

10.Quatitative variables like age shown as mean and standard deviation.Qalitative variables shown as frequency and percentages.

RESULTS

During the study period, 100 cases diagnosed as prostatic adenocarcinoma, were studied and gleason scores were noted by applying both conventional and modified gleason grading systems. The age of the patients, participating in the study ranged from 50years to 120 years (mean 69.47±9.471Std) (table 1).Of all the cases gleason score was changed in 41 cases (41%) after applying modified gleason grading system. however, 59 cases(59%)(table2) showed no change in gleason score. none of the case showed downgradation of gleason grading.Among the hundred cases, morphological variants of prostatic adenocarcinoma were observed in four cases only ,three of which showed glomerulation and one case showed large duct differentiation.

The minimum gleason score encountered in conventional gleason grading systems was score 5 and the maximum score was 10 . The minimum gleason score encountered in modified gleason grading systems was score 6 and the maximum score was 10 . the most common gleason score with conventional gleason grading system was score 7(31%) and with modified gleason grading system was score 9(39%).the percentages of cases with different gleason score by applying conventional gleason grading system were score1=zero%, score2=zero%, score3=zero%, score4=zero%, score5=7%, score6=22%, score7=31%, score8=19%, score9=22%, score10=9%. The percentages of cases with different gleason score by applying modified gleason grading system were score1=zero%, score2=zero%, score3=zero%, score4=zero%, score5=zero%, score6=20%, score7=21%, score8=13% , score9=39%, score10=7%.

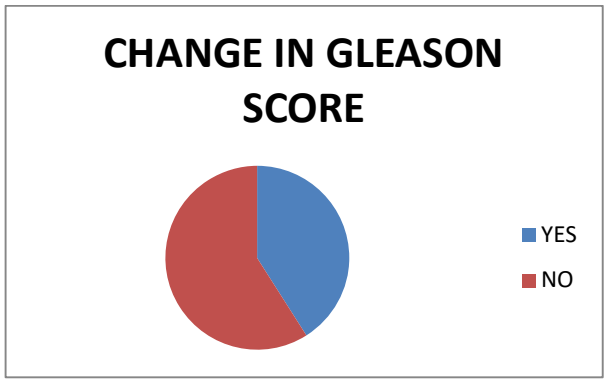
The tertiary pattern was observed in 21% cases.the most common tertiary pattern was grade 3 pattern(95.23%).the other tertiary pattern seen was grade 4 pattern(4.76%).none of the case had grade 5 tertiary pattern..The commonest primary grade pattern in convention gleason grading system was grade 3 pattern(43%) and in modified gleason grading system was grade 4 pattern(40%) . The commonest secondary grade pattern in conventional gleason grading system was grade 4 pattern(37%) and in modified gleason grading system was grade 4 pattern(35%)cases. The grade 2 pattern was only observed as secondary grade pattern in 7% cases by applying conventional gleason grading system

MINIMUM	50
MAXIMUM	120
MEAN	69.47
STANDARD DEVIATION	9.471

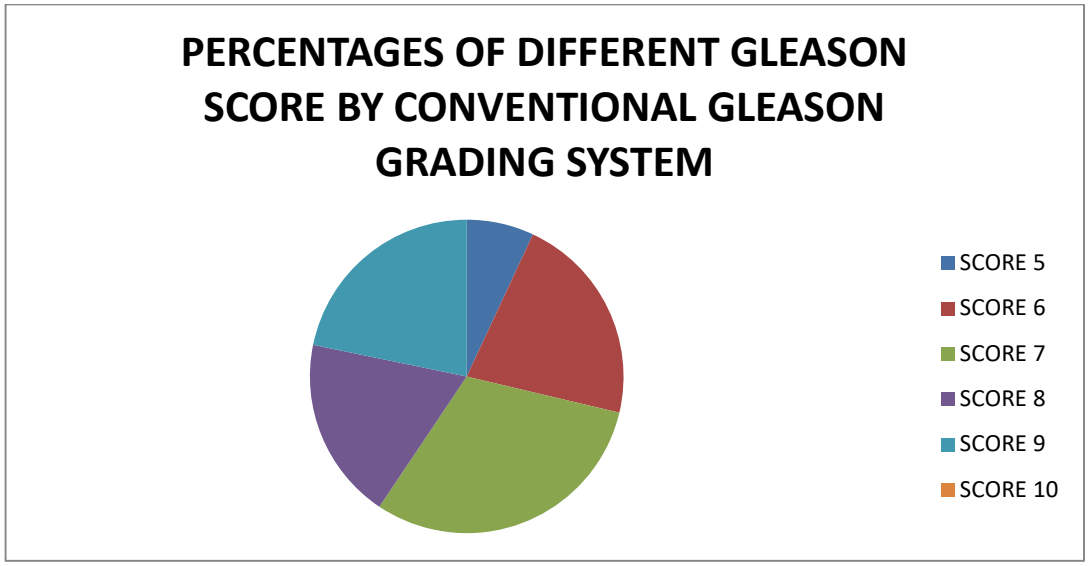
TABLE 1: DESCRIPTIVE STATISTICS FOR AGE

CHANGE IN GLEASON SCORE	FREQUENCY	% OF CASES
no	59	59.0
Yes	41	41.0
Total	100	100.0

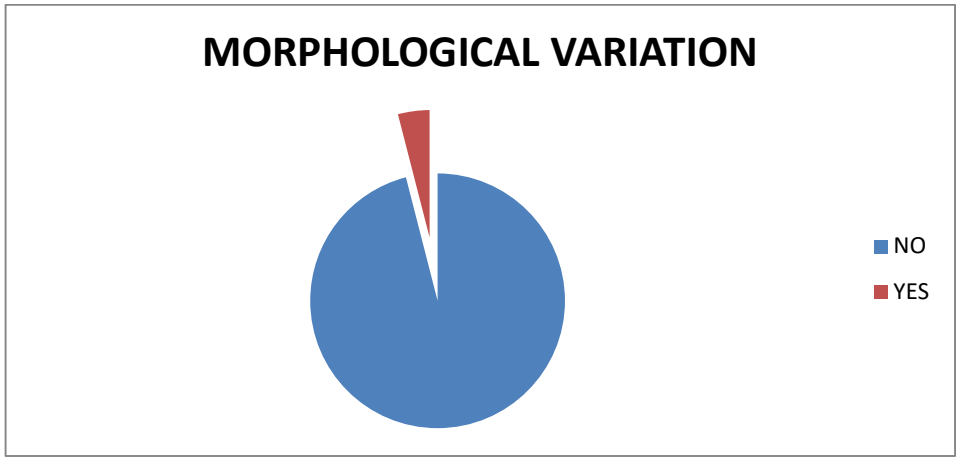
TABLE 2:FREQUENCY OF CASES WITH CHANGE IN GLEASON SCORE



PERCENTAGE OF CASES WITH CHANGE IN GLEASON SCORES



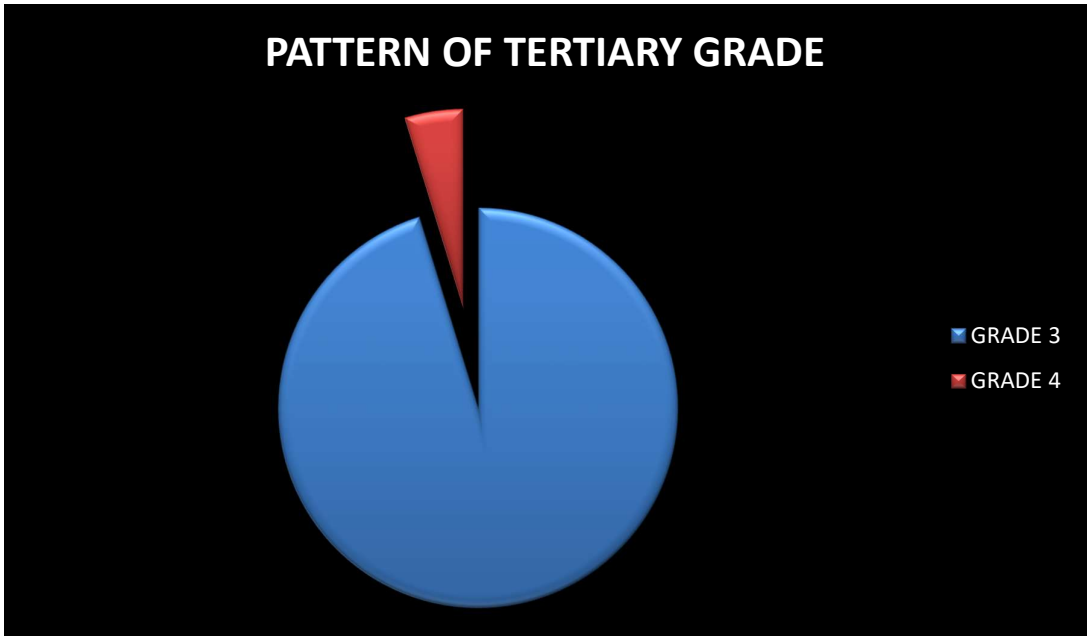
PERCENTAGE OF DIFFERENT GLEASON SCORES BY CONVENTION GLEASON GRADING SYSTEM



TERTIARY PATTERN	PERCENTAGE CASES

YES	21%
NO	79%

PERCENTAGE OF CASES WITH MORPHOLOGICAL VARIANTS



PERCENTAGE OF CASES WITH TERTIARY PATTERN

DISCUSSION

In last three decades over forty grading systems have been presented for prostatic adenocarcinoma .However, the most commonly used and accepted grading system is gleason grading. Currently the most widely used grading system in the United States and worldwide is the Gleason system.[12] .

The Gleason grading system is recommended for use by the 2004 World Health Organization 'blue book' and the 2002 American Joint Committee on Cancer/Union International Centre le Cancer (AJCC/UICC) cancer staging manual. uptill now this system has been modified several times, the most major modification occurring after isup consense conference of urologists in 2005. The Multiple studies have confirmed that Gleason score is a very powerful prognostic factor. It predicts pathological stage, margin status, biochemical failure, local recurrences, disease progression, lymph node or distant metastasis after prostatectomy.[13]The clinical

management of patients is largely determined by gleason score besides TNM staging.

The modified gleason grading has systematically addressed contemporary thinking on gleason grading. The key issues are grade assigning, redefining patterns, emphasis on quantification of a particular pattern(pattern 4) as it is prognostically important. Other issues include reporting high pattern in small biopsies,tertiary pattern , its significance and morphological variants.
In present study ,100 cases of prostate cancer were studied. Of all cases modified gleason grading system changed score in 41% cases. The score was upgraded in all of the 41 cases . The most common reason for change of score was the redefined pattern 4 in modified system. These cases had pattern 3(cribriform) in conventional system which was now assigned as pattern 4 except few controversial area of cribriform Gleason pattern 3. The consensus panel required extremely stringent criteria for the diagnosis of cribriform pattern 3, with remaining cribriform
patterns typically falling into Gleason pattern 4 (e.g: pattern 3+3=score 6/10 in conventional gleason grading is now 3+4=7/10 in modified gleason grading). The criteria used to diagnose cribriform pattern 3 were rounded, well-circumscribed glands of the same size of normal glands. When various images were shown to the consensus panel of potential candidates for cribriform Gleason pattern 3,almost none of them met the criteria based on subtle features, such as slight irregularities of the outer border of the cribriform glands. Therefore all such cases were rendered grade 4 pattern. This finding is similar as observed in a cohort study of 904 and 423 patients by Zareba P,Zhang J et al [14.]Another contributing reason is that low grade cancers commonly confined to central portion of prostate and are not sampled by the biopsy techniques used in routine like needle biopsies and transurethral resections.
None of our case showed downgradation in gleason score owing to the fact that none of our study case was a radical prostatectomy.as per modified gleason grading system.the report of radical prostatectomy comprises of two most predominant patterns and a tertiary pattern. the down gradation of gleason score is noted in radical prostatectomy cases as compared to the gleason score in prior needle biopsies of same patients.[15.]None of the cases was assigned gleason score less than six after using modified gleason system as observed by Cedars-Sinai et al in his study.[16]The modifeied system defines a very strict criteria for assigning low gleason score(2-5).many studies prove that such low score diagnosis on small biopsies was proved wrong in final radical prostatectomy specimens.[17].
The change in gleason score eventually changes the clinical management. The patients with gleason score 2-4 are kept in no aggressive cancer group,score 5-6 in intermediate aggressive cancer group,score 7 in moderate aggressive and score 8-10 in highly aggressive cancer groups.the patients with score 2-6 are given I/V prognostic grade group, score 7(3+4) II/V group ,score 7(4+3) III/Vgroup, score 8 as IV/V group and score 9,10 are assigned prognostic grade group V/V.Four of the cases showed morphological variation i.e glomerulation in three and large duct differtiation in one of the case.These variants have a peculiar gleason grade. Glomerulation is assigned grade 4 and large duct differentiation is assingned grade 5 as per modifeied gleason grading system. **[18]**
In our 59 cases with unchanged gleason score after applying modified gleason grading system ,14 cases showed change in primary and secondary patterns but overall score remained same. four cases changed patterns from 3+4 to 4+3 and five cases changed patterns from 4+5 to 5+4. After carefull quatification. the overall score remained 7 and 9 in these cases respectively. However it is important to correctly quatify the patterns for assigning them as primary and secondary as 4+3 pattern verses 3+4 is considered prognostincally important in modified gleason grading system. According to a study patients with gleason score 4+3 are 3.1 times more likely to develop any lethal event in disease course as compared to patients with score 3+4. .**[19]**

The most frequent tertiary pattern we encountered was grade 3.we did not encountered any higher grade tertiary pattern probably because none of our the case was radical protatectomy. The reporting pattern in radical prostatectomy is two most predominat patterns and a tertiary pattern as compared to reporting the most predominant pattern and a highest grade pattern in needle biopsies and transurethral resection specimens. High grade Tertiary pattern (5) is associated with adverse pathological features.[20]

CONCLUSION

We have observed that there is an upward trend of assigning gleason score with modified gleason grading system. The change in score changes the treatment options,therefore clinical trial and follow up studies should be carried out to see the ultimate outcome of this score upgradation..it should also be clearly mentioned which grading system has been used in a particular case for better interpretation by the clinician.

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