Validation of the WHO 2016 new Gleason score of prostatic carcinoma

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INTRODUCTION

The Gleason grading system is the most powerful prognostic indicator of prostatic carcinoma and has undergone significant changes since its adoption for grading of prostate cancer. The Gleason grading system originated from a well-controlled, prospective, randomized study from 1959 to 1964 by Veteran’s Affairs Cooperative Research Group. This is based on clinicopathological correlation of over 2900 patients. The architectural patterns were given Gleason score (GS) 1–5, and the net result was obtained by adding the most common and the second most common patterns.[1] In 2005, the International Society of Urological Pathology (ISUP) conducted a consensus
The present study is aimed at applying the revised Gleason grading and assigning PGGs according to 2016 WHO classification for carcinoma prostate.

**SUBJECTS AND METHODS**

All the patients who underwent core biopsies, transurethral resection of prostate (TURP), and radical prostatectomy (RP) with a clinical suspicion of carcinoma prostate from January 2014 to June 2016 were included in the study. The patients diagnosed on core biopsy and subsequently underwent RP were included in radical specimen only. The patients who underwent core biopsy or TURP were numbered separately. The demographic and clinical data were noted from the medical records. The hematoxylin- and eosin-stained slides were reviewed, and biopsies with no evidence of carcinoma were excluded from the study. All the slides were seen separately by two pathologists trained in oncopathology and uropathology. GS was done on all samples diagnosed as carcinoma, and

**Figure 1:** Evolution of Gleason grading system
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prognostic group was assigned as per the recommendations of the consensus meeting of ISUP in 2014 which was later adopted by 2016 WHO classification of tumors of the urinary system and male genital organs. Accordingly, cribriform, fused, and glomeruloid glands were assigned pattern 4, forming two groups of GS 7 (3 + 4 and 4 + 3). The patients were grouped into prognostic groups based on GS into Group 1 (3 + 3); Group 2 (GS 3 + 4); Group 3 (GS 4 + 3); Group 4 (GS 3 + 5; 4 + 4; 5 + 3); and Group 5 (GS 5 + 4; 4 + 5; 5 + 5). The number of patients with change in GS and PGG was calculated. The prognostic group was correlated with the follow-up data wherever available and correlated with the prostate-specific antigen (PSA) at the time of diagnosis, at 12th and 24th month.

RESULTS

There were 215 patients who underwent prostate biopsies in the study period. The samples included 153 core biopsies, 51 TURP, and 11 RP specimens. There were 143 (67%) malignant and 72 (33%) benign lesions. The patients with malignancy (143) were included for further analysis. The age ranged from 40 to 90 (median-65) years. The initial and revised GS along with initial and revised PGG were given in Tables 1 and 2. There was change in GS and prognostic group from 1 to 2 in 1 case; Group 2–3 in 8 cases; and Group 3–4 in 2 cases. There was no change in prognostic group in the other patients. There was an upgradation of prognostic groups in 11 (7.69%) patients. All the upgraded patients had high persistent PSA levels, one was asymptomatic, seven were symptomatic, and three developed skeletal metastasis.

Follow-up

Follow-up at 2 years was available for 22 patients. About 11 were clinically asymptomatic, however, were not biochemically free of disease. Two were clinically symptomatic with persistent elevated PSA levels. Nine patients died of disease, and 8 (88.9%) patients had high-grade prostatic carcinoma (GS 8–10). The GS, PGG, and PSA levels of the 22 patients are given in Table 3.

The GS and PSA levels did not correlate well with the patients who were alive and clinically asymptomatic. However, the patients who were symptomatic and expired had persistent high levels of PSA with higher grade carcinoma. Kaplan–Meier graphs with survival data were not attempted as the data are limited.

DISCUSSION

Prostate cancer is globally the second frequently diagnosed cancer and the sixth leading cause of cancer death in males. In India, its prevalence was considered to be lower, however, with changing lifestyle, better awareness, and access to medical facilities, more patients are diagnosed, and the incidence is estimated to be 8/100,000 persons.

Previous Gleason grading systems

Studies before the 2005 ISUP classification reported 41%–46% patients with GS 5–7. With the modified Gleason system in 2005, there was a shift toward higher GS being reported. An Indian study showed that 60% of carcinoma cases presented with GS 5–7. In a series of thin core biopsies, regrading by the 2005 ISUP criteria resulted in increase of Score 7 tumors from 25.5% to 67.9%. In a review of 97,168 patients newly diagnosed of prostate cancers on needle biopsy in Sweden from 1998 to 2011, it was found that, after the standardization for stage and PSA, there was an increase of GS 7–10 diagnoses from 59% to 72%. Among low-risk cases (clinical stage T1 and serum PSA 4–10 ng/mL), the increase was from 16% to 40% whereas among high-risk cases (stage T3 and PSA 20–50 ng/mL), the increase was from 65% to 94%. At the same time, diagnoses of GS 2–5 decreased from 27% to 1% whereas GS 2–4 was almost discontinued. Relocation of original Gleason pattern 3 cribriform growths into

Table 1: Prostate adenocarcinoma–Gleason grade: Group wise number of patients before and after following the new grading system (n=143)

| GS | Number of patients with initial GS (%) | Number of patients with revised GS (%) | PGG - initial | PGG - revised |
|----|---------------------------------------|---------------------------------------|---------------|---------------|
| 3+3| 14 (9.7) | 13 (9) | PGG-1=14 | PGG-1=13 |
| 3+4| 20 (13.9) | 13 (9) | PGG-2=20 | PGG-2=13 |
| 4+3| 28 (19.6) | 34 (23.8) | PGG-3=28 | PGG-3=34 |
| 4+4| 31 | 33 | PGG-4=32 | PGG-4=34 |
| 3+5 | 00 | 00 | 00 | 00 |
| 5+3 | 01 | 01 | 01 | 01 |
| 4+5 | 23 | 23 | PGG-5=49 | PGG-5=49 |
| 5+4 | 20 | 20 | 06 | 06 |
| 5+5 | 06 | 06 | 143 | 143 |
| Total | 143 | 143 | 143 | 143 |

GS: Gleason score, PGG: Prognostic grade group

Figure 2: Change in prognostic grade group

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Table 2: Change in prognostic grade group with following data of prostate-specific antigen levels at the time of diagnosis, 12th, and 24th month, respectively, with clinical course

| Procedure    | Age (years) | Initial GS | Modified GS | PSA levels (at the time of diagnosis) | PSA levels follow-up at 12th month | PSA levels follow-up at 24th month | Clinical course |
|--------------|-------------|------------|-------------|--------------------------------------|-----------------------------------|-----------------------------------|-----------------|
| Core biopsy  | 68          | 3+3        | 3+4         | 11.5                                 | 5.6                               | 6.2                               | Asymptomatic    |
| Core biopsy  | 59          | 3+4        | 4+3         | 26.2                                 | 14.4                              | 4.0                               | Symptomatic     |
| Core biopsy  | 74          | 3+4        | 4+3         | 6.2                                  | 12.6                              | 5.5                               | Symptomatic     |
| Core biopsy  | 78          | 3+4        | 4+3         | 2.2                                  | 14.8                              | 5.0                               | Symptomatic     |
| Core biopsy  | 52          | 3+4        | 4+3         | 35.5                                 | 52.3                              | 12.5                              | Skeletal metastasis |
| Core biopsy  | 63          | 3+4        | 4+3         | 10.3                                 | 6.5                               | 5.0                               | Symptomatic     |
| Core biopsy  | 65          | 3+4        | 4+3         | 147                                  | 38                                | 36                                | Skeletal metastasis |
| Core biopsy  | 65          | 3+4        | 4+3         | 15.5                                 | NA                                | 8.0                               | Symptomatic     |
| Core biopsy  | 58          | 3+4        | 4+3         | 78                                   | 22.2                              | 18.3                              | Symptomatic     |
| Core biopsy  | 73          | 4+3        | 4+4         | 434                                  | 151                               | 82.2                              | Skeletal metastasis |
| Core biopsy  | 69          | 4+3        | 4+4         | 1.5                                  | NA                                | 9.2                               | Symptomatic     |

PSA level units-ng/ml, NA: Not available, PSA: Prostate-specific antigen, GS: Gleason score

Table 3: Prostate adenocarcinoma: Follow-up at 2 years (n=22), patients’ condition- I. Alive and asymptomatic, II. Alive and symptomatic, III. Patient expired

| Patient condition | Serial number | Type of biopsy | Age (years) | Gleason score | PSA levels (at the time of diagnosis) | PSA levels at follow-up (12th month) | PSA levels at follow-up (24th month) |
|-------------------|---------------|----------------|-------------|---------------|--------------------------------------|--------------------------------------|---------------------------------------|
| I                 | 1             | Core biopsy    | 68          | 3+4          | 24.9                                 | 11.94                               | 5.05                                 |
|                   | 2             | Radical specimen | 65         | 3+4          | 34.1                                 | 17.6                               | 10.5                                 |
|                   | 3             | Core biopsy    | 70          | 4+3          | 147.2                                | NA                                 | 0.22                                 |
|                   | 4             | Core biopsy    | 59          | 4+3          | 38.5                                 | 5.2                                | 1.0                                  |
|                   | 5             | Core biopsy    | 73          | 4+4          | 12.8                                 | 4.9                                | 0.19                                 |
|                   | 6             | TURP biopsy    | 64          | 4+5          | 515                                  | 27.5                               | 11.7                                 |
|                   | 7             | Core biopsy    | 60          | 4+5          | 72.7                                 | 4.68                               | 1.26                                 |
|                   | 8             | Core biopsy    | 49          | 4+5          | 90.1                                 | 3.2                                | 3.73                                 |
|                   | 9             | Core biopsy    | 65          | 5+4          | 973                                  | NA                                 | 2.5                                  |
|                   | 10            | TURP biopsy    | 64          | 5+4          | 17.8                                 | 3.5                                | 2.02                                 |
|                   | 11            | Core biopsy    | 62          | 5+5          | 38.2                                 | 5.5                                | 10.56                                |
| II                | 12            | Core biopsy    | 72          | 3+4          | 11.3                                 | 22.4                               | 15.2                                 |
|                   | 13            | Core biopsy    | 68          | 4+4          | 400                                  | 153                                | 110                                  |
| III               | 14            | Core biopsy    | 62          | 3+4          | 13.5                                 | 22.8                               | *                                    |
|                   | 15            | Core biopsy    | 68          | 4+4          | 16.8                                 | 12.5                               | 15.4                                 |
|                   | 16            | Core biopsy    | 75          | 4+4          | 34.2                                 | 153.2                              | *                                    |
|                   | 17            | Core biopsy    | 69          | 4+5          | 12.6                                 | 17.8                               | *                                    |
|                   | 18            | TURP biopsy    | 60          | 4+5          | 10.2                                 | 44.3                               | 29.3                                 |
|                   | 19            | Core biopsy    | 63          | 4+5          | 90.1                                 | *                                  | *                                    |
|                   | 20            | Core biopsy    | 72          | 5+4          | 19.8                                 | NA                                 | 68.9                                 |
|                   | 21            | Core biopsy    | 55          | 5+4          | 77.9                                 | *                                  | *                                    |
|                   | 22            | Core biopsy    | 65          | 5+4          | 48.5                                 | *                                  | *                                    |

*Patient expired. NA: Not available, TURP: Transurethral resection of prostate

Gleason pattern 4 has shown to be valuable in predicting biochemical recurrence after RP.[4,5] New Gleason grading system

The major revision in the WHO 2016 classification was to include cribriform, fused, and poorly formed glands into Gleason pattern 4 and also differentiate the GS 7 into two PGGs (3 + 4 = 7 and 4 + 3).[4,5] The identification of major pattern in the GS was correlated with the prognosis. In the present study, there was a decrease in GS 3 + 4 from 13.9% to 9% and an increase of GS 4 + 3 from 19.6% to 23.8% in the GS 7. There was mild increase in the other group; GS 8 increased from 22.4% to 23.8%. The 5-grade prognostic groups were shown to be more accurate in predicting progression than the 3 GS groups (<6, 7, 8–10).[4] The 5-year biochemical risk-free survival for the 5-grade groups based on RP grade was 96%, 88%, 63%, 48%, and 26%.[18] The overall grading of needle biopsy and RP specimens increased (e.g., from 58% to 72%) after the adoption of the modified system, particularly for biopsies with GS of 3 + 4 = 7 (88%).[19] Thus, increase of high-risk category tumors from 31.3% to 41.1% was noted.[20] Few studies appreciated no significant change in level of agreement between scores of needle biopsies and subsequent RP specimens, particularly with predominant pattern of GS7.[21,22] There was no change in both GS as well as prognostic group between core biopsies and RP specimens in the present study.

There was a strong correlation between the 5-grade groups and prostate cancer death. The new grade groups were simpler to apply and helpful for better stratification that correlated with the prognosis.[23,24] The biochemical
risk-free survival and hazard ratio were reported to be in correlation with the new (2016) grading system. With the 2016 criteria, the change in the prognostic group was into higher grade, and it was seen in 11 (7.69%) patients in the present study. Follow-up showed poor prognosis in the patients who were upgraded to the higher prognostic group. The patients who were symptomatic and expired had persistent high levels of PSA with higher grade carcinoma, highlighting the importance of prognostic grade grouping.

CONCLUSIONS

The application of the WHO 2016 modified Gleason scoring system and prognostic grade grouping criteria retrospectively to 143 carcinoma prostate biopsies resulted in the upgradation of prognostic groups in 11 (7.69%) patients. The identification of major pattern in the GS 7 correlated with the prognosis. There was no change in GS in core biopsies and RP specimens. The number of patients with the upgraded group is small but significant. Hence, awareness about the architectural pattern as per the revised Gleason Scoring system and assigning PGGs is essential for prognostication.

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Conflicts of interest
There are no conflicts of interest.

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