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Comparison of Gleason score V/S Gleason grade group for prostatic carcinoma: A tertiary health care centre study

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Abstract

Introduction: Prostatic carcinoma accounts for 10% of cancer deaths in adults. And, benign prostatic hyperplasia (BPH) is benign enlargement of the prostate gland and is the most common disorder in elderly males. Gleason Score is the gold standard for the diagnosis of prostate carcinoma.

Material & Methods: This study was conducted over a period of 5 years on TURP chips, biopsies and prostatectomy specimens.

Results: According to International Society of Urological Pathology (ISUP) 2005, maximum cases 15/41 (36.5%) had 3+4 score and according to ISUP 2014, Grade Group 2 had the maximum frequency of 15/41 cases (36.5%).

Conclusion: The use of newly emerged Gleason Grade Grouping system (ISUP 2014) has led to reduced stress and confusion about the grades among the patients regarding prostate carcinoma.

Keywords: Prostate, gleason, benign prostatic hyperplasia (BPH), prostate specific antigen (PSA)

1. Introduction

The prostate is a retroperitoneal organ, about the size of a walnut, weighing approximately 20 grams encircling the neck of the bladder and the first part of the urethra in a normal male [1]. Carcinoma of the prostate is the most common internal malignancy among men, occurs in men older than 50 years. The incidence of BPH is the most common urological disorder in men above 40 years. Androgens play an important role in prostate cancer and BPH. Measurement of serum PSA level is used to diagnose and manage prostatic cancer. Prostate cancer is graded using the Gleason's system that stratifies the cancer into 5 grades on the basis of glandular patterns of differentiation and further Gleason score is given [2]. Lately, there has been development of a new grading system 2014 known as modified ISUP with the goal of less number of grades and each with its own distinct prognosis. Benefits of the new grading system include more accurate stratification, the lowest grade in new system is 1 as opposed to 6 in the Gleason system [3].

2. Material & Methods

This study was a retrospective and prospective study from June 2013- July 2018 conducted in the Department of Pathology, Subharti Medical College and the associated Chhatrapati Shivaji Hospital, Meerut. There were 41 malignant and 72 benign cases. All TURP chips, prostate needle biopsy and prostatectomy specimens diagnosed as non-neoplastic and neoplastic lesions were included. Specimens were received in 10% formalin. Gross findings were noted. Representative sections were taken from prostatectomy specimens and biopsies were processed in to. Biopsies which were inadequate for reporting were excluded from the study. Paraffin embedded sections were be taken and stained by routine Haemotoxylin and Eosin (H & E stain). Slides were studied and categorised into non-neoplastic and neoplastic lesions. Neoplastic lesions were further classified according to WHO classification. Prostatic adenocarcinoma was graded according to both modified Gleason scoring system (2005) and new contemporary grading system (2015) The grading done by both methods was compared. Pre-operative PSA was also correlated with various parameters.

3. Results

The patient's age ranged from 44-90 years. Mean age of all patients was 68.5 ± 9.0 years.

Age of patients were divided into 5 groups. Maximum number of cases were present in the 6th -7th decade of life 42/113(37.1%) cases. Different types of specimens received were – TURP chips, prostate biopsy and prostatectomies. TURP chips was the most common type of specimen- 91/113 cases (80.6%) followed by prostate biopsy 11/113 (9.7%) and prostatectomy specimen 11/113 (9.7%). The weight of the specimens ranged from 2-36 g. Mean weight of all specimens was 16.9 g. Weight of specimens were divided into groups : 0-10,11-20,21-30 and >30 g. Maximum number of cases were in the 11-20 category 49/113 (43.3%), followed by 31/113(27.4%) in the 0-10g category. 25/113 cases (22.1%) were in the 21-30g category and only 9/113 (7.9%) cases had weight >30g. Out of 72 benign cases, maximum cases 33/72(45.8%) had weight 11-20g. 0-10g and 21-30 g category both had 17/72 cases (23.6%). 5/72 cases (6.9%) had weight >30g. Out of 41 malignant cases, maximum cases 15/41(36.5%) had weight 11-20g. 14/41 cases (34.1%) were in the 0-10g category. 8/41 cases (19.5%) were in the 21-3-g category. Only 4/41 cases (9.7%) were in the >30g category.

Out of 113 cases, pre-operative PSA was available in 96 cases. PSA was divided into 4 groups : <2, 2-4, 4-10 and > 10ng/dl. Maximum number of cases were seen in the 4-10ng/dl category 44/96 (45.8%), followed by 4-10ng/dl 34/96 (35.4%), <2 ng/dl had 11/96 cases (11.5%) and PSA >10 ng/dl was present in 7/96 cases (7.3%). The age range of the 3 group's i.e < 2, 2-4 and 4-10 ng/dl was 5th-8th decade. PSA > 10 ng/dl was seen in the age range of 4th-8th decade. Out of 64 benign cases with available pre-operative PSA, 28/64 cases (43.7%) had a PSA range of 4-10 ng/dl, 26/64 cases (40.6 %) were in the PSA range of 2-4 ng/dl. 8/64 cases (12.5%) had PSA value < 2ng/dl and only 2/64 cases(3.1%) had PSA >10 ng/dl.

Out of 32 malignant cases with pre-operative PSA, maximum cases 16/32 (50%) had a PSA range of 4-10ng/dl, followed by 8/32 cases (25%) with PSA range 2-4ng/dl. 5/32 cases (15.6 %) had PSA > 10 ng/dl. 3/32 cases (9.4 %) had PSA < 2ng/dl. We also studied the correlation of Grade Group with mean PSA.

Mean PSA of Grade Group1 was 5.8ng/dl, Grade Group 2 was 7.9ng/dl, Grade Group 3 was 4.9ng/dl, Grade Group 4 was 5.1ng/dl, Grade Group 5 was 7.7 ng/dl.

Inflammation was present in 111/113 cases: 98.2% and absent in 2/113 cases: 1.8%. Associated hyperplasia was present in 95/113 cases: 84.1% and absent in 18/113 cases: 15.9%. Perineural invasion was seen in only 10/113 cases (8.8%), out of which all 10 cases were malignant: 100%. Cases with no perineural invasion were 103/113 (91.2%) and 31/113 (27.5%) cases were malignant. Out of 113 cases, adenocarcinoma cases were 35/113 (31.9%). BPH cases were 72 /113 (63.7%) and 5/113 cases (4.4 %) were cases of BPH with neoplastic foci and 1 case of PIN with adenocarcinoma.

According to ISUP 2005, maximum cases 15/41 (36.5%) had 3+4 score, followed by 10/41 cases: 24.3 % with <6 score. 9-10 score was observed in 6/41 cases (14.6 %). 4+3 scoring was seen in 5/41 cases (12.1 %). 4+4 and 5+3 scores were reported in 2/41 cases (4.8%).

3/41 cases (7.3 %) were cases with no grading as shown in Table 1.

Table 1: Patterns according to ISUP 2005

Gleason score 2005	No. of cases	%
< 6	10	24.3
3+4=7	15	36.5
4+3=7	5	12.1
4+4, 5+3	2	4.8
9-10	6	14.6
No Grading*	3	7.3
Total	41	100

*These were retrospective cases and not graded at that time. Slides of these cases were retrieved from the archives of Histopathology (SMC, Meerut) and now were graded according to ISUP2014 (GGG).

According to ISUP 2014, Grade Group 2 had the maximum frequency of 15/41 cases (36.5%). 10/41 cases (24.3 %) had Grade Group 1. 7/41 cases (17 %) were cases of Grade Group 3. Grade Group 4 cases were 6/41 (14.6 %). 3/41 cases (7.3 %) were Grade Group 5 as shown in Table 2.

Table 2: Grade Groups according to ISUP 2014

Gleason grade group	No. of cases	%
Grade Group 1	10	24.3
Grade Group 2	15	36.5
Grade Group 3	7	17
Grade Group 4	6	14.6
Grade Group 5	3	7.3

On correlating the 2005 ISUP, Gleason score (GS) with 2014 ISUP Grade Grouping (GG) system, it was observed that 10 cases of GS < 6 are now GGG 1 (24.3%), 14 cases of GS 3+4=7 are now GGG2 (36.5%), 6 cases of 4+3=7 are now GGG 3(12.1%), 4+4 and 5+3 GS are now GGG 4 (4.8%) and 6 cases of 9-10 GS are now GGG 5 (14.6%). 3 cases were not graded by earlier GS, now they were categorised into 2 cases of GGG 1 and 1 case of GGG3 as shown in Table 3.

Table 3: Correlation between 2005 & 2014 grading

Gleason score (2005)	No. of cases	Gleason grade group (2014)
< 6	10	GGG 1
3+4=7	14	GGG 2
4+3=7	6	GGG 3
4+4, 5+3	2	GGG 4
9-10	6	GGG 5
No Grading*	3	GG1: 2 GG3: 1

*These were retrospective cases and not graded at that time. Slides of these cases were retrieved from the archives of Histopathology and now were graded according to ISUP2014 (GGG).

4. Discussion

The Gleason grading system developed in the 1960's remains a strong predictor of outcome of men diagnosed with prostate carcinoma. With most recently proposed modifications (ISUP2014), improved correlation with risk stratification and biochemical free – recurrence have been observed. [4] In the present study it was observed that with increasing age, the prevalence of histologically identifiable BPH and carcinoma increases progressively with highest frequency at 7th decade of life (37.1%).The patients age ranged from 44-90 years with the mean age of 68.5 years. Similar age group distribution was observed by Oesterling

and Bal *et al.* [22,38] In our study, prostate chips (80.6%) was the most common type of tissue received, followed by prostate biopsy (9.7%) and prostatectomy (9.7%) specimens. Similarly, Cheng *et al.* [20] examined all 102 specimens of TURP chips. Also, Egevad *et al.* studied 121 patients who had underwent TRUS guided core biopsies. [21] The mean weight of all specimens was 16.9 g. Maximum cases belonged to 11-20g category with 29.2% of BPH cases. Mean weight of BPH specimens was 19 grams according to Arshad *et al.* [33]. 24.6 ±18 g was the mean weight of TURP specimens reported by Cheng *et al.* [20].

Pre-operative PSA was available in 96 cases out of 113 in our study. Highest distribution of cases were seen in the 5th-7th decade. Out of malignant cases, mean PSA of Grade Group 1 was 5.8ng/dl, Grade Group 2 was 7.9ng/dl, Grade Group 3 was 4.9ng/dl, Grade Group 4 was 5.1ng/dl, and Grade Group 5 was 7.7 ng/dl. We could not find any study in literature to the best of our knowledge to compare, PSA level with Grade Group system (ISUP2014). However, Bal *et al.* studied that the average PSA level in Gleason score (Original scoring 1974), 2-4 was 32.13 ng/ml, 5-7 was 31.06 ng/ml, and 8-10 was 44 ng/ml. Thus, concluding that higher Gleason score correlated with higher PSA values. [38] In our study, the maximum number of cases were seen in the 4-10ng/dl category: 45.8%, followed by 2-4ng/dl: 35.4%, <2ng/dl: 11.5% and >10 ng/dl: 7.3%. [60] In a study by Goldner, pre-operative PSA was <10 ng/ml in 58%, >10–20 ng/ml in 31% and >20 ng/ml in 11% of patients [61].

Inflammation was seen in 98.2% of cases in our study. Silverio *et al.* [31] studied that inflammation was mild in 78%, moderate in 21% cases and severe in 1% only out of 1700 cases. Associated hyperplasia was seen in 84.1% of total cases and absent in 15.9% of total cases. We observed perineural invasion in 10/32 malignant cases. Grade Group 1 and 2 showing the maximum number of cases associated with perineural invasion. A significant correlation between perineural invasion and Gleason score >3 (p<0.001) was reported by Lee *et al.* [40] Since perineural invasion is considered as a tool for disease aggressiveness, we could not correlate it due to lack of patient follow-up. Our study comprised of 36 cases of adenocarcinoma, 5 cases of BPH with neoplastic foci, 1 case of PIN and 72 cases of BPH.

On the basis of grading by ISUP 2005, we studied that Gleason score 3+4=7 was the most common (36.5%), followed by <6 score (24.3%), 4+3 score was (12.1%), 9-10 scoring was (14.6%), 4+4 and 5+3 score was only (4.8%). 7.3% cases were of no grading. Primary pattern 3 by ISUP 2005 and 7.4 % cases of Gleason score 8-10 was also observed by Kryvenko *et al.* [48]. Rasiah *et al.* observed similar findings: 75% had primary Gleason Pattern 3 tumors, 25% had primary Gleason pattern 4 tumors [47]. Stark *et al.* in 2009 concluded that 3+4 does not equal 4+3 because they found that patients with Gleason score 4+3 had 3 times risk of prostate cancer than in patients with GS 3+4 [46].

According to ISUP 2014 grading, in the present study, Grade Group 2 (36.5%) was identified as the most common. Second, was Grade Group 1 (24.3%), followed by Grade Group 3 (17%), Grade Group 4 (14.6%) and Grade Group 5 (7.3%). [6] Evans *et al.* found 74.7% Grade Group 2, followed by Grade Group 3 (18.6%) and Grade Group 1 (3.4%) on needle biopsy specimens. [54] On correlating the 2005 ISUP, Gleason score (GS) with 2014 ISUP Gleason Grade Grouping (GG) system, it was observed that 10 cases of GS < 6 are now GGG 1 (24.3%), 14 cases of GS 3+4=7 are now

GGG2 (34.2%), 6 cases of 4+3=7 are now GGG 3(12.1%), 4+4 and 5+3 GS are now GGG 4 (4.8%) and 6 cases of 9-10 GS are now GGG 5 (14.6%). 3 cases were not graded by earlier GS, now they were categorised into 2 cases of GGG 1 and 1 case of GGG3. Almost similar findings were analysed by Loeb *et al.* 67% men had GGG 1 (former G.S 6), 20% had GGG 2 (former G.S 3 + 4), 7% had GGG 3 (former G.S 4 + 3), 4% had GGG 4 (former G.S 8), and 1% had GGG 5 (Gleason score 9–10) on biopsy. [6] So finally, Gleason Grade Group 2 was found to be the most common grade according to IUSP 2014.

5. Conclusion

By undertaking the present study, the use of newly emerged Gleason Grade Grouping system has led to reduced stress and confusion about the grades among the patients. In addition, post-operative findings are equally important to predict prognosis of the patient.

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Conflict of Interest: None

Ethical approval: The study was approved by the institutional ethics committee

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