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Reproducibility of Modified Gleason Scoring System and Grade Group in Prostate Carcinoma on Microphotographs

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Abstract

Background: Pathologists can quickly transmit the microscopic images photographed in a certain location to remote centers for analyzing the images. Gleason scoring system forms an important prognostic parameter for therapeutic decision and in the overall management of prostate cancer patients. *Aims*: 1. To study various histopathological patterns of prostatic carcinoma. 2. To evaluate the reproducibility of modified Gleason scoring system and Grade group in prostate carcinoma on microphotographs. *Material and Methods:* A retrospective study of invasive prostate cancer cases was conducted from January 2014 to October 2016. It was an analytical type of study at a rural tertiary care institute. Histopathology slides of prostate adenocarcinoma slides were retrieved, reviewed, scored and graded according to World Health Organization [WHO] 2016. The representative images captured by 13 megapixel mobile camera were sent to two pathologists by E-mail and were evaluated separately. The primary Gleason pattern, secondary Gleason pattern, total Gleason score and Grade groups were documented. Concordance and kappa statistics was applied. *Results*: Twelve cases were analyzed. Concordance was better in secondary Gleason pattern when compared with primary Gleason pattern, total Gleason score and Grade group. The present study showed substantial agreement in primary Gleason pattern; and substantial to almost perfect agreement in secondary Gleason pattern, Gleason total score and grade group. The overall performance of both the pathologists was satisfactory. *Conclusions*: Modified Gleason scoring system and grade group has good reproducibility in prostate carcinoma on microphotographs. The analysis of representative images is a feasible and time saving exercise.

Keywords: Adenocarcinoma; Gleason Score; Histopathology.

Introduction

Pathologists can quickly transmit the microscopic images photographed in a certain location to remote centers for analyzing the images. The method of storing and analyzing images at a later time allows us to transmit the images captured by a digital camera of suitable resolution, as an electronic mail file and to analyze them at opportune time [1]. Invasive prostate cancer is the second most frequently diagnosed cancer and the sixth leading cause of cancer death in males. In 2005, the ISUP [International Society of Urological Pathology] introduced modifications of Gleason scoring system. Gleason scoring system forms an important prognostic parameter for therapeutic decision and in the overall management of prostate cancer patients [2]. The inconsistency in histological grading may invalidate its use in treatment decision [3]. The current study was undertaken to evaluate the reproducibility of modified Gleason scoring system and grade groups in prostate carcinoma on microphotographs.

Materials and Methods

The study was conducted at histopathology section in the department of Pathology at a tertiary care institute. It was a retrospective study of invasive prostate cancer cases from January 2014 to October 2016. It was an analytical type of study. Twelve cases were analysed.

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Inclusion Criteria

All cases of invasive prostate carcinoma confirmed by histopathological examination were included in the study.

Exclusion Criteria

Those cases in which biopsies performed are unsatisfactory for interpretation were excluded from the study.

Histopathology slides of prostate adenocarcinoma slides were retrieved. The histological characterization of prostate carcinoma was reviewed and findings were documented according to the new grading system accepted by World Health Organization [WHO] 2016. Representative image of tumor pattern corresponding to primary grade and secondary grade was captured by 13 megapixels primary mobile camera. The images were sent to two pathologists by E-mail and were evaluated separately. The primary Gleason pattern, secondary Gleason pattern, total Gleason score and Grade groups were documented. The findings were documented and analyzed.

Statistical Analysis

The socio-demographic variables were represented using frequencies and percentages. The extent of reproducibility of interpreting the Gleason score on microphotograph was analyzed by concordance and kappa statistics.

Results

Twelve cases were analyzed. Prostatic adenocarcinoma ranged from 25 yr to 91 yr. Lesions were most common in eighth decade [mean = 69.33 yr]. Transurethral resection of prostate [TURP] specimens were the most common type of specimens received constituting seven cases [58.33%] followed by five cases [41.67%] of needle biopsies.

The distribution of various patterns of malignant lesions in primary Gleason pattern and secondary Gleason pattern was analyzed [Table 1]. Fused glands pattern and sheets were the most common primary Gleason pattern, constituting four cases [33.33%] each. Cribriform pattern was the least common primary Gleason pattern constituting only one case [8.33%]. Sheets were the most common secondary Gleason pattern, constituting four cases [33.33%]. Fused glands pattern and solid nests were the least common pattern, constituting only one case each [8.33%].

The distribution of scores in primary Gleason pattern, secondary Gleason pattern and total Gleason score; and distribution of grade groups were analyzed. [Table 2]. Score 4 was most common in primary Gleason pattern, constituting five cases [41.67%] and score 3 was the least common score in primary Gleason pattern, constituting three cases [25%]. Score 5 was most common in secondary Gleason pattern, constituting eight cases [66.67%], followed by score 4 constituting four cases [33.33%]. Score 9 and Score 10 were the most common total Gleason score, constituting four cases each [33.33%]. Score 8 was the least common total Gleason score constituting only one case [8.33%]. Grade group 5 was the most common grade group, constituting 8 cases [66.67%] and Grade group 4 was the least common grade group, constituting only one case [8.33%].

Concordance and discordance were analyzed with respect to the reviewed histopathological evaluation of the slides. The values were calculated for both the pathologist who evaluated the microscopic images sent by E-mail. Concordance was better in secondary Gleason pattern when compared with primary Gleason pattern, total Gleason score and Grade group.

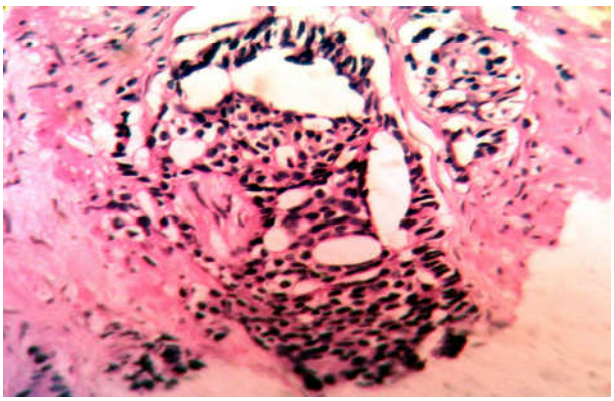

Fig. 1: Microphograph of invasive prostatic carcinoma showing tumor cells arranged in cribriform pattern. [X 400, H&E].

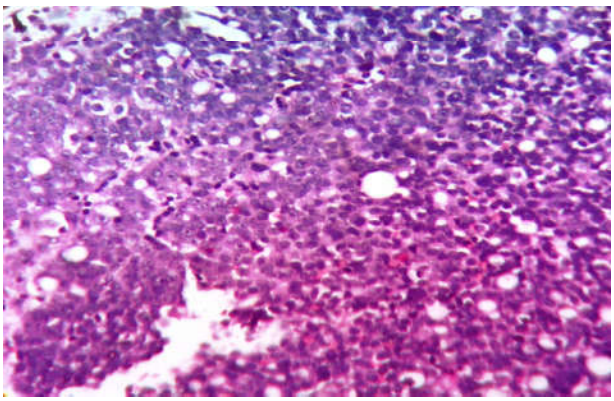

Fig. 2: Microphograph of invasive prostatic carcinoma showing tumor cells arranged in sheets. [X 400, H&E].

Table 1: The distribution of various patterns of prostatic adenocarcinoma in primary Gleason pattern and secondary Gleason pattern

Sl. No	Patterns	Cases	Percent
	Primary pattern		
1	Fused smaller glands	4	33.33
2	Sheets	4	33.33
3	Discrete infiltrating glandular units	3	25
4	Cribriform	1	8.33
	Total	12	100
	Secondary pattern		
1	Sheets	4	33.33
2	Cribriform	3	25
3	Infiltrating cords	3	25
4	Fused smaller glands	1	8.33
5	Solidnest	1	8.33
	Total	12	100

Table 2: The distribution of scores in primary Gleason pattern, secondary Gleason pattern and total Gleason score and grade groups

Sl. No	Scores	Cases	Percent
	Primary gleason pattern scores		
1	Score 3	3	25
2	Score 4	5	41.67
3	Score 5	4	33.33
	Total	12	100
	Secondary gleason pattern scores		
1	Score 4	4	33.33
2	Score 5	8	66.67
	Total	12	100
	Total gleason score		
1	Score 7	3	25
2	Score 8	1	8.33
3	Score 9	4	33.33
4	Score 10	4	33.33
	Total	12	100
	Grade group		
1	Grade group 2	3	25
2	Grade group 4	1	8.33
3	Grade group 5	8	66.67
	Total	12	100

Table 3: Distribution of concordance values, Kappa values and discordance values

Concordance Parameters	**Pathologist 1**	**Pathologist 2**
Primary gleason pattern score	10 cases [83.33%]	9 cases [75%]
Secondary gleason pattern score	11 cases [91.67%]	10 cases [83.33%]
Total gleason score	9 cases [75%]	8 cases [66.67%]
Grade group	10 cases [83.33%]	9 cases [75%]
Kappa statistics Parameters	**Pathologist 1**	**Pathologist 2**
Primary gleason pattern score	0.80 [substantial]	0.68 [substantial]
Secondary gleason pattern score	0.82 [Almost Perfect]	0.66 [substantial]
Total gleason score	0.81 [Almost Perfect]	0.68 [substantial]
Grade group	0.81 [Almost Perfect]	0.73 [substantial]
Discordance Parameters	**Pathologist 1**	**Pathologist 2**
Primary gleason pattern score	2 cases [16.67%]	3 cases [25%]
Secondary gleason pattern score	1 case [8.33%]	2 cases [16.67%]
Total gleason score	3 cases [25%]	4 cases [33.33%]
Grade group	2 cases [16.67%]	3 cases [25%]

Table 4: Comparison of kappa statistical inference

Sl. No.	Authors	Total cases	Number of pathologists Participated	Scale used	Primary gleason pattern score	Secondary gleason pattern score	Total gleason score
1	Singh RV et al [2011]	20	21	Cohen	Fair to moderate agreement [60%]	Slight to fair agreement [78%]	Slight to fair agreement [80%]
2	Abdollahi A et al [2012]	101	5	-	-	-	Fair agreement
3	Francisco RDAS et al [2014]	50	3	Landis and Koch			Moderate agreement
4	Salmo EN et al [2015]	96	3	-	-	-	Substantial agreement [72%]
5	Allsbrook WC et al [2017]	46	10				Substantial agreement
6	Present study [2017]	12	2	Cohen	Substantial	Substantial to Almost perfect	Substantial to Almost perfect

Kappa was calculated to know the strength of agreement for both the pathologists with respect to primary Gleason pattern, secondary Gleason pattern, total Gleason score and Grade groups. Concordance, Kappa values and discordance are depicted in Table 3. With respect to the original findings in each of the parameters, the performance of first pathologist was better than second pathologist. However, the overall performance of both the pathologists was satisfactory.

Discussion

Telepathology is a branch of telemedicine, and is defined as the practice of pathology at a distance through visualization of microscopic images sent for consultation on a computer screen rather than direct analysis of the slides under microscope [1]. Good quality digital images can be safely interpreted and used for patient care [4]. Prostate cancer is morphologically heterogeneous neoplasm displaying several patterns of differentiation [5]. The histopathological examination is considered as gold standard in the diagnosis of prostate cancer [6]. The Gleason histological grade of prostate adenocarcinoma is thought to be the most powerful predictors of biological behavior [7]. Gleason histopathological classification shows high level of subjectivity [5]. Gleason grading system has led to a new "Grade Group" system proposed by 2014 ISUP consensus, and has been adopted by 2016 WHO classification of tumors of prostate [8]. The present study deals with evaluation of the reproducibility of modified Gleason scoring system and grading system in prostate carcinoma on microphotographs.

In the present study, most of the cases were from TURP specimen. In contrast, Singh RV et al [3], Abdollahi A et al [6] and Allsbrook WC et al [9] documented needle biopsies as most common type of specimen analyzed in their study. Abdollahi A et al [6] analyzed most number of cases (101 cases). In the present study, only 12 cases were analyzed and constituted least number of cases. The number of pathologists participated was also less [Two] in comparison with other studies. [Table 4] But the reproducibility was analyzed on microscopic images sent to pathologists. Thus the present study can be considered as a unique one.

The present study was compared with the other studies. Singh RV et al [3] and the present study used Cohen scale for categorizing the strength of agreement. In contrast, Abdollahi A et al [6] used Landis and Koch scale. However, other studies had not specified the scale used. Except for Singh RV et al [3], Most of the studies focused on agreement in total Gleason score. Singh RV et al [3] focused on agreement with respect to primary Gleason pattern, secondary pattern and total Gleason score. In the present study, even the Gleason grade group was assessed.

Singh RV et al [3] documented fair to moderate agreement in primary Gleason pattern and slight to fair agreement in secondary Gleason pattern. In contrast, the present study showed substantial agreement in primary Gleason pattern and substantial to almost perfect agreement in secondary Gleason pattern. With respect to total Gleason score,

Singh RV et al [3] documented slight to fair agreement, Abdollahi A et al [6] documented fair agreement and Francisco RDAS et al [10] documented moderate agreement. In contrast, Salmo EN et al [2] and Allsbrook WC et al [9] observed substantial agreement in their study.

In the present study, substantial to almost perfect agreement was documented. However, among discordant cases, it was found that all the cases were under-scored. In contrast, Singh RV et al [3] under-scoring was seen in 23% and over-scoring was seen in 33.7%.

But, it has been observed that general pathologists more frequently under-score than over-score. The difference in the strength of agreement in the present study could be because, the representative images were sent to the pathologist to analyze. This may not only minimise the interpretation errors, but also saves time.

However the accuracy of the diagnosis depends on factors like quality of the image sent, the pathologist who captures and sends the image; and experience and enthusiasm of the pathologist who receives the images and reports the findings.

Limitations

In comparison with other studies, the sample size the present study was very less. But the method of assessment was a unique one. The reproducibility was assessed on microscopic images sent to pathologists by E-mail.

In addition to primary Gleason pattern, secondary Gleason pattern, total Gleason score and grade group, reproducibility could also be assessed with respect to recognition of specific pattern in primary and secondary Gleason pattern. This may increase the strength of agreement. Such evaluation may be suggested for any similar studies that may be undertaken in future.

Most of the studies assessed the agreement between the participating pathologists. In the present study, the agreement was assessed for both pathologists separately with respect to the diagnosis and findings reviewed with respect to recent reporting pattern guidelines.

This is because the reviewed findings would serve as a control for assessment. In some instances the observations of participating pathologists may significantly differ from the original findings. Agreement between the participating pathologists may not reflect the true deviation from the control.

Conclusion

Modified Gleason scoring system and grade group has good reproducibility in prostate carcinoma on microphotographs. The analysis of representative images is a feasible and time saving exercise. Recognition of specific pattern in primary and secondary Gleason pattern may be considered for evaluation in future studies of such kind. The accuracy of the diagnosis depends on factors like quality of the image sent, the pathologist who captures and sends the image; and experience and enthusiasm of the pathologist who receives the images and reports the findings.

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