REVIEW ARTICLE

A COMPREHENSIVE REVIEW OF 2016 GLEASON'S CRITERIA FOR SCORING OF PROSTATE ADENOCARCINOMA.

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ABSTRACT

Gleason's scoring system was introduced by Dr. Donald Gleason in 1960 and till date it is widely accepted to score the prostate adenocarcinoma. This remained the best predictor for treatment and prognosis of the patients. This system depends upon the histological features of the prostate adenocarcinoma and morphological patterns. The most common and second most common patterns identified on biopsy are used to be added up to score the prostate adenocarcinomas. However, certain limitations, in particular to scores; 7, 8 and 9 along with Gleason's relation to tumor variants, is having a large impact on prognosis and course of treatment. To overcome these limitations, John Hopkins university proposed a new scoring system for the prostate adenocarcinoma in 2013, consisting of 5 grade 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. The updated grade groups provide proper scoring for the prostate adenocarcinoma to address the present limitations.

KEY WORDS: Prostate cancer, Grading, Prognosis, Gleason grade.

BACKGROUND

Gleason's scoring system for the prostate cancer based on histological pattern was introduced in 1960s by Dr. Donald Gleason, a pathologist at the Minneapolis Veterans Affairs Hospital. Adenocarcinoma of prostate usually graded by Gleason's scoring system[1]. The Gleason system is based exclusively on the glandular architecture of the prostate adenocarcinoma. It evaluates the ability of cancer cells to organize and structure themselves into glands resembling those of the normal prostate[2]. A well differentiated tumor exhibits uniform glandular architecture and represents a least aggressive biological behavior, whereas reverse is the case for poor differentiation [3].

Gleason's score remained the most common and useful prognostic pattern for prostate adenocarcinoma. Gleason's scoring is universally applied on various prostate biopsy specimens; including TURP, needle biopsy and radical prostectomy [4]. Briefly, two predominant morphological patterns were assigned after careful evaluation. Primary and secondary morphological features are characterized from least to most aggressive on the scale of 1 to 5. The two grades are added together produce the cumulative Gleason score. A higher cumulative score represents an aggressive behavior [5].

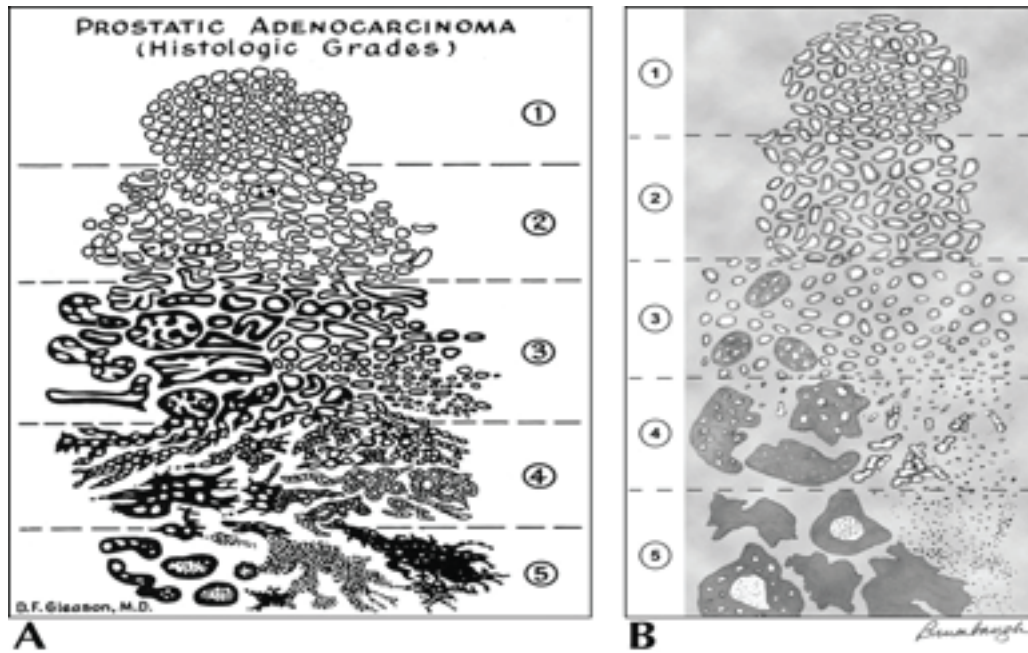*Corresponding Author: Santosh Kumar Sidhwani**

Figure 1: Comparison of Gleason grades 2005 (A) and 2015 (B) for prostate adenocarcinoma.

Gleason's 2005 in practice/application

Grade 1 is rarely used in practice, as it differs slightly from grade 2; based on glandular arrangement. Grade 1 and 2 are less important compared to others both rarely exist [6]. Histologically, grade 1 can only be distinguish from grade 2 by more compact and non-invasive neoplastic glandular architecture. Both grades represent slow growth pattern and better prognosis[7].

Gleason's grade 3 is most common pattern seen in practice [8]. Grade 3 exhibits variation in shape and size of neoplastic glands with prominent invasion and occasional cribriforming. However, these features are not consistent with poor prognosis. [9].

Gleason Grade 4 adversely affects patient's survival, which make it an important prognostic determinant [10]. Disruption and loss of the normal gland unit is the hallmark feature of grade 4[11]. In grade 4 the glands lost their ability to form an individual gland unit with separate lumen that makes it to be distinct. Differentiating grade 4 tumors from grade 3 pattern is a difficult task and requires expert skills [12].

Gleason's grade 5 is the most aggressive of all and has a worst prognosis. It is rarely considered as diagnosis in early stage of tumor development and is less common than grade 4 [13]. Grade 5 exhibits variety of patterns, all of which demonstrate no evidence of any attempt to form gland units; constituting an undifferentiated form of tumor [14].

Figure 1 compares photomicrograph of different Gleason's patterns presently used in practice.

Limitations of 2005 Gleason's system

Although Gleason's scoring system is widely used as a prognostic marker for prostate adenocarcinoma however, it has some limitations. Firstly, the Gleason's 7 can be derived by 4+3 or 3+4[15]. The two largely differs in terms of prognosis as predominant histological pattern in latter case represents a more aggressive behavior and requires a more intense approach to treatment[16]. Secondly, Gleason's score up to 5 is no longer used for grading of prostate adenocarcinoma[17]. Thirdly, Gleason's 6 is usually over diagnosed as Gleason 7 by most pathologist. Lastly Gleason's 8-10 is often considered as a single group presenting high grade disease; thus requiring as aggressive treatment[18].

Revised Gleason's system

To address these controversial limitations Johns Hopkins university and hospitals proposed a new scoring system in 2015, composed of 5 grading 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 v[19]. Fig. 1 compares histological differentiation of old and new Gleason's criteria. The proposed system is based on a study done on more than 20,000 patients treated with radical prostectomy and 5,000 patients treated with the radiotherapy [20]. Table 1 presents the proposed grading system approved by ISUP, 2015.

The modified Gleason's system is largely beneficial in patients presented with low grade tumor[21]. Table 2 displays the 5 years risk free survival of updated

grade groups. As Gleason's group 1 can be assigned easily, follow up and active surveillance of patients with less aggressive tumor is now possible, which was neglected in the old Gleason's system [22]. The new grading system is easier and simpler to grade prostate adenocarcinomas and this system also gives proper histology of the tumor[23]. This system has been accepted worldwide by World Health Organization (WHO) to grade the tumors of urinary and male genital origin[24].

Application of revised scoring on histological variants
Intraductal carcinoma of Prostate (IDC) is considered as an aggressive tumor with extension into neighboring prostate ducts and a decrease disease free survival with high incidence of recurrence[25]. Therefore, the tumor was usually awarded a high score, thus requires an aggressive course of treatment. However, occasionally IDC may occur as a precursor lesion of noninvasive nature, identified on radical prostatectomy. In such instances, the tumor usually behaves less aggressively with a lower recurrence rate, and biopsy with a usual high Gleason's score would be misleading [26]. Therefore, in ISUP 2015 it was not decided by consensus; not to score IDC but rather add a comment in report that the tumor may be associated with an aggressive prostate cancer of invasive nature [16].

Mucinous adenocarcinoma of prostate is consid-

ered as a diagnosis when at least 25% of tumor volume consists of pool of extracellular mucin[27]. Previously, it was believed that tumor morphology is best represented by Gleason grade 4. However, few studies have reported that the biological behavior of mucinous cancer may be similar to other types of prostate cancer [28]. Thus, a consensus was built in 2015 ISUP to grade the tumor with respect to its growth pattern [16].

Table 1: New ISUP Grading System for Prostate Cancer

2005 Modified Gleason Grading	2015 ISUP Grade
3+3, 3+2, 2+3, 2+2	1
3+4	2
4+3	3
4+4, 3+5, 5+3	4
4+5, 5+4, 5+5	5

Table 2: Five years risk free survival

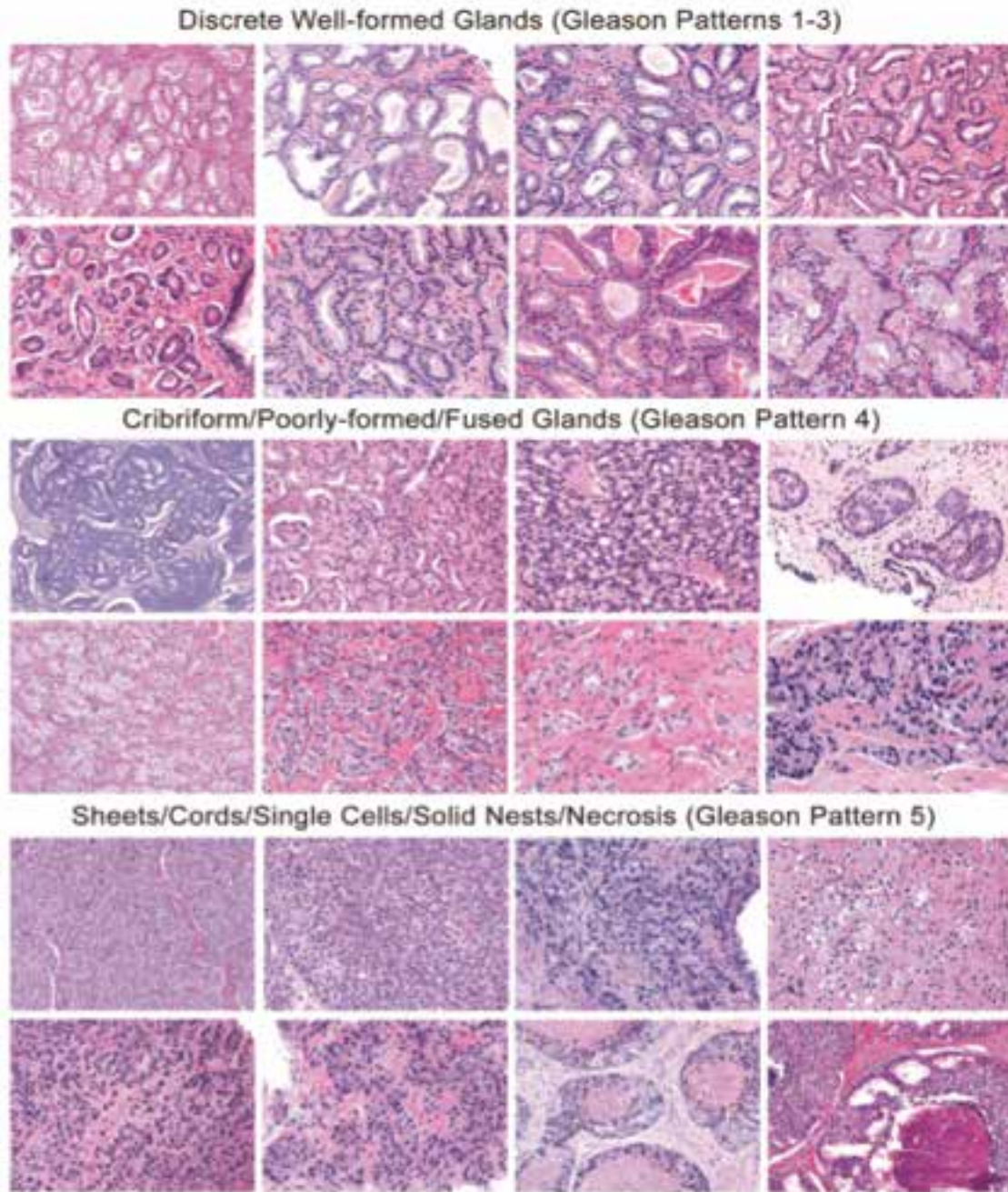| Grade group	Gleason's score	Risk free survival
1	3+3=6	96%
2	3+4=7	88%
3	4+3=7	63%
4	4+4=8	48%
5	9 and 10	26%

Figure 2: Morphological features comparing different Gleason's patterns

CONCLUSION

Gleason's scoring system remains the most important and powerful prognostic and therapeutic predictor of prostate adenocarcinoma. Proper diagnosis and grading of the prostate adenocarcinoma is important for its therapeutic management. So it is very essential to grade prostate adenocarcinoma so that proper treatment option can be provided by clinicians and to predict its prognosis. Therefore 2014 ISUP worked to improve the Gleason's scoring system for better therapeutic approach to relieve the sufferings of patients and thus improving the prognosis of prostate adenocarcinoma.

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