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New Gleason grade groups; epidemiologic data from Isfahan, Iran based on the new classification

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Key point

The purpose of the Gleason grade grouping system is to provide a simplified and user-friendly classification of disease and to assist patient counseling, however does it enhance the prediction of prognosis and the patient's clinical condition? In a study on 305 prostate cancer cases, we found the new Gleason grading system provides a more accurate estimation of disease progression and recurrence, confirmed by other studies. Among patients diagnosed with prostate cancer, 28.6% had a Gleason score of less than 6 (GGG 1) which indicates that about one fourth of patients do not need aggressive treatment.

Abstract

Introduction: A new five-tier Gleason grade grouping (GGG) has recently been proposed and approved by the World Health Organization. In this new classification, GGG 1 (Gleason score≤6), GGG 2 (Gleason score 3+4=7), GGG 3 (Gleason score 4+3=7), GGG 4 (Gleason score 8) and GGG 5(Gleason score 9-10) are the new grade groups based on the Gleason score.

Objectives: We examined the epidemiologic data of prostate cancer based on the new Gleason system in Isfahan, Iran. International Society of Urological Pathology (ISUP) proposed the new Gleason grade groups in order to make accurate prognostic classification for prostate cancer.

Patients and Methods: Around 305 prostate cancer cases which diagnosed by biopsy admitted to Khorshid university hospital and Ordibehesht surgical center were included (from 2014 to 2016).

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Pathological examination of the samples was conducted by pathologists with genitourinary expertise.

Results: Among 305 biopsy specimens, 28.6% of cases had a Gleason score less than 6, 23.7% Gleason score 3+4=7, 10.9% Gleason score 4+3=7, only 0.7% Gleason score 4+4=8 and 36.1% Gleason score 9 and 10.

Conclusion: The new Gleason grade groups provide a simplified, user-friendly and clear classification system for predicting prognosis and disease progression before and after treatment.

Key words: Prostate cancer, Gleason score, International society of urological pathology, Gleason grade group

Introduction

Prostate cancer is one of the leading causes of death from cancer among Asian men (1). The Gleason grading system was first developed in the 1960s and it remains one of the main predictors of outcome among men diagnosed with prostate cancer (2). In addition, the Gleason score plays an important role in choosing the treatment strategy(3). In this scoring system, structural characteristics of the cancer cells are identified and the results are closely related to the clinical behavior of the tumor(4). Higher score in this system indicates further spread of disease in the affected person(5). Based on the characteristics of cell proliferation and the degree of differentiation of cells in the prostate biopsy sample, each cellular pattern has a score of 1 to 5, as the score 1 represents the highest cellular differentiation, and the score 5 represents the lowest cellular differentiation(6). The Gleason score is obtained from the sum of the two common patterns in the sample(7). Higher score in this system indicates more likelihood of disease progression in the affected person(5). The Gleason grading system has been under review and updated several times since its first introduction, the latest one in November 2014(8). Finally, several changes were made to the morphology and grouping of the system therefore the new system would better represent the biological behavior of the tumor and helps identify the treatment strategy(7). The new classification system does not replace the Gleason classification system however, based on the Gleason score, scheduled the patients in five groups and provides a more accurate estimation of relapse. This system uses a scale of 1 to 5, unlike the previous system, in which scores are reported from 2 to 10(9). This new classification system has been approved by the World Health Organization and has been adopted in the 2016 World Health Organization (WHO) classification of genitourinary tumors (10). 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 8), and grade group 5 (Gleason score 9-10) are the new grading groups based on Gleason scores(10). However, due to the recent introduction of the system, the statistical evaluation of various indicators is still needed. This has become important as the treatment and follow-up of patients with prostate cancer are increasingly conducted on the basis of this new system in diagnostic and therapeutic centers.

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Objectives

As far as we know, there is insufficient epidemiologic data using the new grouping system in Iran. Therefore, our goal in this study was to determine the distribution of prostate cancer frequency and serum prostate-specific antigen (PSA) level of the affected patients, at the time of biopsy, based on the new Gleason grading system. In addition, we aimed to investigate the frequency of perineural invasion in each group.

Patients and Methods

Study design

In this descriptive comparative study, 305 prostate cancer cases diagnosed by biopsy in the population of patients from Khorshid university hospital and Ordibehesht surgical center from 2014 to 2016 were included. All clinical parameters contained in these collected samples were categorized for classification purposes. All macroscopic and microscopic characteristics of each biopsy specimen were determined, and finally, the Gleason score of each sample was identified. In addition, at the same time serum PSA levels were checked in all patients. Previously reported samples were re-examined by the same laboratory and the results were reported. In the next step, the Gleason scores were converted to the new Gleason groups in accordance with the method described by the International Society of Urological Pathology (ISUP). After the grade groups were identified, the distribution of samples in each group was determined. In addition, the prevalence of perineural invasion and median level of serum PSA in each group were calculated.

Statistical analysis

All quantitative The data are expressed as medians and ranges.

Results

About 305 biopsies from prostate cancer patients from 2014 to 2016 were studied. Of them, 28.6% of cases had a Gleason score less than six, 23.7% had a Gleason score 3+4=7, 10.9% had a Gleason score 4+3=7, only 0.7% had a Gleason score 4+4=8 and 36.1% of cases had a Gleason score 9-10. Patient characteristics are shown in Table 1. The highest prevalence of perineural invasion was 84.9% in the first group. The information about perineural invasion in other groups is shown in Table 2.

Discussion

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The Gleason scoring system has proven to be a robust and durable method for evaluating prostate cancer and is employed as an important factor in determining prognosis(8). Through several evaluations and reviews, the predictive ability of the system has improved, and as a result, its function has become more complicated. The complexity of the latest version of the Gleason grading system can lead to confusion among pathologists, urologists and patients alike. For example, the Glasson score six is the lowest score that is typically given to biopsy specimens, while the score in this system is from 2 to 10. This raises concern for patients because they reasonably think that since grade 6 is in the middle of the 2 to 10, scale their disease is also in the high-risk group and therefore seek unnecessary treatment and expensive care. However in the modified Gleason scoring system, grade 6 is placed in the first category while, the patient's concerns about the severity of the illness and its prognosis are moderated and costly diagnostic techniques and overtreatment will be avoided. Although the score in the Gleason system is between 2 and 10, there are practically 25 potential scores (e.g. 1+2, 1+3, 1+4, 2+1). Another change in the new Gleason system is applied to the definition of Gleason pattern 4 on histological examination. In the previous Gleason system, only the irregular cribriform architecture and fused glands were placed in Gleason pattern 4, while in the new system, almost all cribriform patterns are considered Gleason pattern 4(11). Even in a set of selected images that seemed to be mostly consistent to pattern 3, most of the pathologists with genitourinary expertise, interpret cribriform pattern as pattern 4. Additionally, 73% of the samples that were identified as category 3 were more compatible with pattern 4 elsewhere on the biopsy specimen (12).

The changes in the reclassification of many previous Gleason scores 6 and 7 had various prognostic consequences, including improvement in prognosis of newly diagnosed Gleason score 6. At present, tumors with a score of 6 are generally more homogenous and all have a better prognosis than a score of 7(13). The study by Pierorazio et al, showed patients with a recently diagnosed Gleason score 6 based on the new system did not experience progression after radical prostatectomy, while in the previous Gleason system, some of these patients suffered from relapse and disease progression(8). Of course, as mentioned in this study, it is not possible to predict disease severity based on the Gleason score alone and other factors such as extra-prostatic extension, margin involvement in the radical prostatectomy specimen, serum PSA levels, and clinical stage are involved. However, in general, the prognosis of patients with a score of 6 is excellent (14).

The difference between the score 3+4 and 4+3 is well documented in various studies. These studies are based on both biopsy and radical prostatectomy specimens. Although these studies have different and sometimes conflicting results, most have proven that clinical behavior and recurrence are worse in patients with prostate cancer with Gleason score 4+3(15-17), while Gleason score 3+4=7 has a good prognosis with an estimated 2-year biochemical-free survival of 90.6% for biopsy specimens(8).

The Glasson score 8 has a significantly worse prognosis, but still has a better prognosis than

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Gleason scores 9-10. Although some urologists consider Gleason score 8 similar to Gleason scores 9-10 regarding prognosis and response to treatment, Gleason scores 9-10 tumors have almost twice the risk of recurrence and disease progression(18).

Generally, prostate cancer risk stratification is evolving rapidly, for example, the use of magnetic resonance imaging (MRI) and different methods of genetic testing are under investigation (19, 20). Histopathologic examination and tumor grade evaluation are key elements in decision-making and patient management, and the new GGG system has proved useful in this regard and will be an important part of decision-making in the future. The main purpose of using the GGG system is to provide a simplified and user-friendly classification and to assist patient counseling, although, it has improved the prediction of prognosis and the patient's clinical condition.

Table 1. Characteristics and demographics by Gleason grade group for men diagnosed with prostate cancer in 2014 to 2016

Biopsy GGG GGG5(%)	GGG1 (%)	GGG2 (%)	GGG3 (%)	GGG4 (%)
No. of men 115 (36.1)	86 (28.6)	71 (23.7)	32 (10.9)	1 (0.7)
Age (years)				
Median (Range) 68 (42-91)	67 (42-84	67 (49-89)	70.5 (49-85)	61
Serum PSA (ng/ml)				
Median (Range) 10 (3.7-132)	9 (0.8-29)	14.5 (0.6-132)	11.3 (5.8-11)	10.4

Table 2. Perineural invasion in GGGs

New Gleason grade group GGG5	GGG1	GGG2	GGG3	GGG4
Perineural invasion (%) 89 (77.4)	73 (84.9)	53 (74.6)	25(78.1)	1 (100)

Conclusion

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The new Gleason grading system provides a more accurate estimation of disease progression and recurrence, confirmed by other studies. Among patients diagnosed with prostate cancer, 28.6% had a Gleason score of less than 6 (GGG 1) which indicates that about one fourth of patients do not need aggressive treatment.

Limitations of the study

This study has some limitations. Most importantly, only biopsy specimens were included while no radical prostatectomy specimen was studied. Second, due to the nature of cross-sectional studies, patients were not followed up which is required for further validation of the findings. Finally, biopsy schemes and techniques vary among surgeons and hospital disciplines which alter the accuracy of data.

Authors' contribution

MY and ASN were the principal investigators of the study. MY, ASN were included in preparing the concept and design. ASN and AY collected the samples and coordinated the execution of the study. All authors revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. Informed consents were obtained from all patients. The study was approved by the ethical committee of Isfahan University of Medical Sciences (ethical code; IR.AJUMS.REC. 295143). This study was extracted from the M.D thesis of Amir Salar Nourbakhsh (#295143) in Isfahan University of Medical Sciences. Besides, ethical issues (including plagiarism, data fabrication and double publication) have been completely observed by the authors.

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Competing interests

The authors declare that they have no competing interests.

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