

Grading Intraductal Carcinoma of the Prostate; ISUP versus GUPS Recommendations

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ABSTRACT

Objective: To evaluate the frequency of intraductal component (IDC-P) in prostatic adenocarcinoma and its effect on the final grade using the ISUP and GUPS grading system.

Study Design: Descriptive study.

Place and Duration of the Study: Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, between June 2021 and June 2022.

Methodology: The study included 250 cases of prostatic adenocarcinoma. The presence of the intraductal carcinoma prostate (IDC-P) was confirmed by patchy or complete staining of the basal cell layer by p63 immunohistochemical stain. Cases with IDC-P were then graded using two different methods, first using the grading criteria based on the ISUP recommendations and then by the grading criteria based on the GUPS recommendations.

Results: Two hundred and fifty cases showed invasive prostatic carcinoma ranging from Gleason grade group 2-5. IDC-P was identified in 5 of the 250 biopsies (2%). The final Gleason grade remained unchanged in these cases, when they were graded using the ISUP and GUPS recommendations.

Conclusion: Although the present results are based on a relatively small sample size, IDC-P was not frequently present in biopsies of patients with adenocarcinoma in the studied population. Grading IDC-P in invasive prostate cancer led to only a minor change in grade group assignment of prostate cancer biopsies.

Key Words: Prostatic adenocarcinoma, Intraductal carcinoma, IDC-P, ISUP, GUPS, Gleason Grade group.

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INTRODUCTION

Grading of prostate cancer plays a vital role in patient management and risk stratification.¹ Gleason grading and grouping is a widely used system for this purpose.² Since its original description by Gleason, various changes have been incorporated into this grading system.³ One of the latest recommendations by the two international bodies, namely the International Society of Urological Pathology (ISUP) and the Genitourinary Pathology Society (GUPS) has created a controversy,⁴ regarding the grading of intraductal component (IDC) if present along with the invasive carcinoma. ISUP recommends that the intraductal component should be included in the final grade, whereas GUPS does not recommend grading the intraductal component.^{5,6} WHO has not endorsed either of the two and states that whether the architectural pattern of IDC-P should additionally be incorporated into prostate cancer grading remains controversial at this time owing to insufficient data.⁷

Therefore, this study was undertaken to evaluate the frequency of the intraductal component of invasive prostate carcinoma and whether grading / not grading it makes any real difference in a significant number of cases.

METHODOLOGY

Two hundred and fifty cases of prostatic biopsies (needle core and TURP) with invasive prostatic adenocarcinoma diagnosed between June 2021 and June 2022 at the Histopathology Department of Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan, were identified. Intraductal carcinoma (IDC-P) was defined using criteria laid down by 2014 ISUP guidelines. Inclusion criteria were all diagnosed cases of invasive prostatic carcinoma by histology at Shaukat Khanum Memorial hospital received either as TURP or needle core biopsy. Exclusion criteria were all cases of prostatic adenocarcinoma with a previous history of treatment with endocrine therapy, radiation, or chemotherapy, variants such as ductal adenocarcinoma, sarcomatoid, small cell carcinoma, tumour at metastatic sites, recurrent carcinoma and isolated IDC-P cases without the invasive disease.

Institutional ethical approval was taken for the use of tissue samples for scientific purposes. All Haematoxylin and Eosin (H&E) stained sections were evaluated in each case. P63 immunohistochemical (IHC) stain (for basal cells) was then

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applied in cases showing dense cribriform glands and/or solid nests and/or marked pleomorphism or necrosis to distinguish IDC-P from invasive carcinoma.

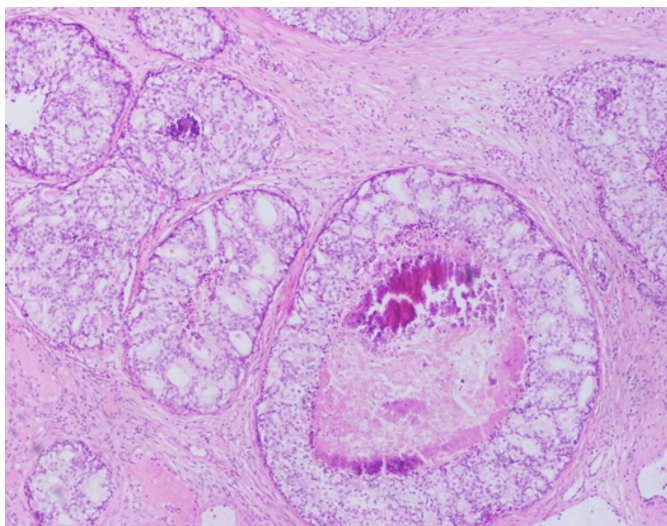


Figure 1: Comedonecrosis associated with IDC-P.

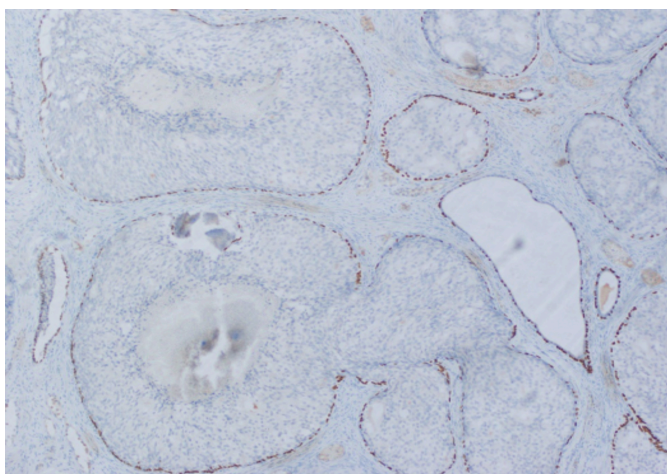


Figure 2: P63 immunohistochemical stain highlighting the intact basal cell layer around the same glands.

All the cases with IDC-P were reviewed by two genitourinary pathologists. The presence of IDC-P was confirmed by patchy or complete staining of the basal cell layer by p63 immunohistochemical stain (Figures 1 and 2). These cases were then graded using two different methods. Both invasive carcinoma and IDC-P components were graded (invasive and IDC). Grading was done based on the International Society of Urological Pathology (ISUP) 2014 guidelines. Only invasive carcinoma was graded, without incorporating the IDC-P component (invasive only). Grading was done based on Genitourinary Pathology Society (GUPS) guidelines. The parameters recorded in each case were the presence/absence of intraductal carcinoma associated with invasive carcinoma; and the Gleason score/grade using the two different grading methods and the subsequent change in grade.

RESULTS

In total 250 prostatic biopsies in men aged between 50-76 years were evaluated. The types of biopsies selected were TURP and

needle core biopsies. All the cases chosen for this research were the patients with invasive carcinoma graded from Gleason grade group 2-5.

Intraductal carcinoma (IDC-P) was identified in 5 out of 250 biopsies (2%), using p63 immunohistochemical stain. Overall, the respective Gleason score and grade in the cases with IDC-P was 4+5=9/5 in 2 cases, 5+4=9/5 in another 2 cases, and 4+3=7/3 in 1 case. The pattern of intraductal carcinoma was dense cribriform and was associated with comedonecrosis.

Using the ISUP system, where the intraductal component was included in the final grade, the grades and scores of these 5 cases were changed. The first biopsy was scored 5+4=9/10 and assigned Gleason group 5. The second was scored 4+5=9/10 and assigned as Gleason group 5. The third was scored 4+5=9/10 and assigned Gleason group 5. The fourth was scored 5+4=9/10 Gleason group 5, and the fifth was scored 4+3=7/10 Gleason group 3.

In these 5 cases, the overall Gleason group/score using the GUPS system when the intraductal component was excluded from the final grade was compared. The first biopsy was scored 5+4=9/10 in Gleason group 5. The second was scored 4+5=9/10 Gleason in group 5. The third was scored 4+5=9/10 in Gleason group 5. The fourth was scored 5+4=9/10 in Gleason group 5 and the fifth was scored 4+3=7/10 in Gleason group 3.

The final group remained unchanged in the 5 cases, and none of the patients was reclassified. This was because 4 out of the 5 cases were associated with comedonecrosis and were already in Gleason Group 5 and therefore, the impact of excluding IDC from the final grade did not affect the overall grade group. And the fifth case (Gleason 4+3=7/10 group 3) had IDC-P in the dense cribriform pattern along with invasive carcinoma in pattern 4 therefore, excluding IDC-P from the score did not affect the overall group (Table I).

DISCUSSION

The Gleason grading system for prostatic adenocarcinoma was established by Dr. Donald Gleason. It has evolved from its original scheme laid out in the 1960s, to a substantially modified system after two major consensus meetings were held by the International Society of Urologic Pathology (ISUP) in 2005 and 2014.⁸

The ISUP meeting held in 2014 released a revised prostate cancer grading system called the Grade Groups. This was basically a new grading system, although based on Gleason patterns.¹ One of the main reasons behind the development of this new system was to guide the clinical management and this system does so by stratifying patients into various risk groups.^{9,10} As the treatment varies considerably in these groups the distinction is essential. For example, group 1 patients are usually just put on active surveillance whereas group 2 patients need additional investigations, radio and hormonal therapy and sometimes even pelvic lymph node dissection.¹⁻³ Another reason was to better communicate the prognosis to the patients. In addition, it also had a major impact on the practising pathologists.

Table I: Changes in overall grade group between the two grading methods.

Prostatic carcinoma with associated IDC-P	ISUP recommendation (invasive +IDCP)	GUPS recommendation (invasive only)	Overall change in Gleason score
Case 1	5+4=9, Group 5	5+4=9, Group 5	Not seen
Case 2	4+5=9, Group 5	4+5=9, Group 5	Not seen
Case 3	4+5=9, Group 5	4+5=9, Group 5	Not seen
Case 4	5+4=9, Group 5	5+4=9, Group 5	Not seen
Case 5	4+3=7, Group 3	4+3=7, Group 3	Not seen

Intraductal carcinoma (IDC-P) is defined as a proliferation of malignant epithelial cells confined within the glands. In the majority of the cases, it is accompanied by invasive carcinoma. It is an independent adverse prognostic factor.^{4,11-15} In biopsy specimens, IDC-P is typically seen with high-grade, high-volume prostate cancer and is associated with adverse clinical outcomes.

In 2019, both ISUP and GUPS published proceeding papers on the grading of prostate cancer.¹⁶ ISUP recommended to incorporate IDC-P into the Gleason score in IDC-P associated with invasive carcinoma with a comment stating its presence and significance.¹⁷ GUPS had opposing views regarding the inclusion of IDC-P associated with invasive carcinoma in the final grade group. According to GUPS recommendations, IDC-P would not be included in the final Gleason score and instead be reported separately.

The rationale behind ISUP recommendation is that previous data suggests that only a small proportion of total cases might see grade changes if IDC-P is excluded from the final grade.¹⁸ Secondly, IDC-P is typically seen with high-grade cancer and adverse clinical outcomes therefore, including IDC-P to the final grade in cases already associated with high-grade carcinoma would not affect the patient prognosis.¹⁹ Then, there is the practical aspect to it. It would be cumbersome and costly to perform immunohistochemical stain on every case to confirm the presence of IDC-P.

Whereas, the rationale behind GUPS recommendations stands true for grade group 1 cases with admixed IDC-P where including IDC-P in the final grade would upgrade the cases by 1 or 2 groups. Emerging data suggest that in a small number of cases with IDC-P (20%) there might be a change in grade.²⁰

In this study, IDC-P was not a very frequently reported finding in invasive prostate carcinoma. Five out of 250 prostatic biopsies (2%) had an associated intraductal carcinoma. The overall group was unchanged in these 5 cases when scored following the ISUP recommendations and then the GUPS recommendations.

These results (2%) are comparable to the results of another study (2.8%) conducted by Katherine Watts *et al.* to see the frequency of intraductal carcinoma in prostatic biopsies.²¹

As almost all the cases of IDC-P identified in this research were already associated with high-grade tumours (group 4 or 5) there was 0% shift in global grade groups after the exclusion of IDC-P from the invasive tumour in the cases. This is

also in concurrence with many studies done previously,^{22,23} where approximately 90% cases of IDC-P were associated with high-grade tumours (Gleason >7). A study conducted by Van Leenders *et al.* showed a shift in 1.6% of the prostate biopsies.¹⁶ Similarly, in a study conducted by Chen-Maxwell *et al.* there was a shift in 1% of the prostate biopsies and they also similarly reported that IDC-P has minimal impact on grade group in most of the cases.¹⁹ All these studies have results comparable with the present results. The findings of there being a 0% shift in global grade groups indicates that inclusion or otherwise does not make any real difference in the management of patients.

To the author's knowledge, this is the first study in Pakistan. Further such studies are important to compare the results of the current study at the national and international levels to set grading guidelines for IDC-P. The current study was limited by its retrospective nature and the limited number of cases.

CONCLUSION

Even though, this study is limited by a relatively small sample size, IDC-P was not frequently present in prostatic biopsies of patients with prostatic adenocarcinoma and grading IDC-P associated with invasive prostate cancer leads to a minor change in Grade Group assignment of prostate cancer biopsies. Therefore, more such studies with larger sample size need to be carried out and this controversy needs to be resolved to facilitate general histopathologists in their daily practice.

ETHICAL APPROVAL:

The institutional review board (IRB) of Shaukat Khanum Memorial hospital had granted exemption prior to initiation of research work.

PATIENTS' CONSENT:

Not applicable as the data were obtained retrospectively.

COMPETING INTEREST:

There was no competing interest related to this research.

AUTHORS' CONTRIBUTION:

AS: Acquisition of data and drafting the work.

SM: Conception of work and reviewing it critically.

HM: Design of work and reviewing the slides.

UH: Critical analysis of the final draft.

MH: Acquisition of data.

MS: Interpretation of data.

All the authors have approved the final version of the manuscript to be published.

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