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ORIGINAL RESEARCH

To determine the relationship between TRUS-Guided Prostatic Biopsy and Serum PSA, Gleason Score, and Grade-Grouping at a Tertiary Centre

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Abstract

Aim: To determine the relationship between TRUS-Guided Prostatic Biopsy and Serum PSA, Gleason Score, and Grade-Grouping.

Materials and methods: According to the specified criteria, a total of 50 cases were included in the current investigation. Prostatic core samples obtained from various locations inside the prostate were individually placed in containers and forwarded to the Department of Pathology for processing and histological analysis. In order to ensure optimal processing and reporting, a single cassette was equipped with 1-2 (maximum 3) distinct types of cores. Each paraffin block was subjected to cutting at many levels of biopsy core, with a maximum thickness of 4 µm, in order to enhance the likelihood of obtaining a definitive diagnosis of adenocarcinoma. Every slide was stained using the H&E stain. The reporting format for positive cases of prostatic adenocarcinoma adhered to the guidelines set by the College of American Pathologists (CAP).

Results: The comparison of prostate-specific antigen (PSA) levels between the benign and malignant groups reveals a significant difference. The mean PSA level in the benign group is 3.78 ng/mL (±0.12), whereas in the Adeno CA group, it is considerably higher at 57.98 ng/mL (±3.98). The p-value is less than 0.001, indicating a statistically significant difference in PSA levels between the two groups. The distribution of malignant cases based on the Gleason score and AJCC group grading is presented. Of the 26 cases, 19.23% have a Gleason score of 7 (3+4) and are graded as AJCC Group 2. Cases with a Gleason score of 7 (4+3) make up 34.62% and are graded as AJCC Group 3. Similarly, 34.62% of cases have a Gleason score of 8 (4+4) and are graded as AJCC Group 4. Lastly, 11.54% of cases have a Gleason score of 9 (5+4) and are graded as AJCC Group 5. The comparison of PSA values between high-risk and low to intermediate-risk groups based on Gleason scores shows that the mean PSA level for the low to intermediate-risk group (Gleason score <8) is 59.32 ng/mL (±8.98). For the high-risk group (Gleason score ≥8), the mean PSA level is 59.03 ng/mL (±8.67). The p-value of 0.24 indicates that there is no statistically significant difference in PSA levels between these two risk groups.

Conclusion: This research demonstrates the significant value of estimating serum prostate-specific antigen (PSA) levels in distinguishing between benign and malignant cases in prostatic core biopsy specimens obtained by transrectal ultrasound (TRUS) guidance. However, when evaluating prostate cancer and determining the disease stage using the Gleason Score and grade-grouping, the blood PSA value is of little importance.

Keywords: PSA, TRUS, Gleason Score, and Grade-Grouping

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Introduction

Since 1984, prostate cancer has been the most prevalent kind of cancer in males in the United States, excluding skin cancer. It accounts for 19% of all malignancies of this nature.[1] For males, the estimated rate of prostate cancer diagnosis is roughly 1 in 8 (12.9%), and the rate of death from this illness is 1 in 40 (2.5%).[1] The incidence of prostate cancer differs across different racial and ethnic groups, with African-Americans having a 73% higher risk of incidence compared to whites.[2] Cancer The incidence of prostate cancer ranks second globally, and it is responsible for the fifth-highest number of cancer-related deaths worldwide. In 2012, there were around 1.1 million newly diagnosed cases and 300,000 fatalities attributed to this disease. After lung cancer, it is the second-leading cause of cancer-related mortality among males.[3]The predicted incidence rates for prostate cancer in India varied from 5.0 to 9.1 per 100,000 individuals per year.[4] Originally created as a biomarker to track the progress of prostate cancer patients after therapy, PSA remains a highly debated topic in the context of prostate cancer screening. To establish a basis for other possible biomarkers for prostate cancer, it is crucial to have a thorough comprehension of PSA due to its distinct significance. PSA, sometimes referred to as hK3 (human kallikrein 3), belongs to the kallikrein gene family.[5] This is an enzyme called serine protease, and the genes responsible for producing PSA are situated on the long section of chromosome 19, specifically in the area between q13.2 and q13.4. Serum PSA, a glycoprotein and serine protease discovered by Wang et al. (1979), is only synthesised by the epithelial cells of both benign and cancerous prostate tissue, with typical levels ranging from 0 to 4 ng/ml.[6]

PSA levels are often seen in all illnesses of the prostate, but significantly high levels suggest prostate cancer. The histological type, grading, and staging of prostate carcinoma are essential for determining treatment methods and predicting overall and cancer-specific survival rates. Several histological grading systems have been created to establish a correlation with the disease's prognosis.

The Gleason method relies on the glandular pattern of the tumour, which is seen at very low magnification.[7]The cytological characteristics do not contribute to the grading of the tumour. Gleason grading is a very reliable method for predicting the biological behaviour of prostate cancer and is a key aspect in determining therapy options. Prostate-specific antigen (PSA), when used in conjunction with the Gleason score and clinical staging, enhances the accuracy of predicting the pathological stage of prostate carcinoma. Architectural designs are categorised and assigned a rating ranging from 1 to 5, with grade 1 representing the highest level of differentiation and grade 5 indicating the lowest level of differentiation. In the original Gleason system, the most common and second-most frequent grades were merged together. However, in 2005, the Gleason system was revised and altered. One of the changes made was that the most common and highest-grade patterns found on a specific core during a biopsy were included in the calculation of the Gleason score.[8] Conceptually, the Gleason scores span from 2 (1 + 1 = 2) to 10 (5 + 5 = 10), indicating tumours that are either consistently constituted with a Gleason pattern 1 tumour at score 2 or undifferentiated tumours at score 10. Assigning a Gleason score of 2 to 4 to an adenocarcinoma of the prostate on needle biopsy is not advisable since it does not always indicate favourable results after radical prostatectomy.[9] Cancers with a Gleason score below 6 are often classified as low-grade and exhibit non-aggressive behaviour. Tumours with a Gleason score of 8 or above are often considered advanced, since they have progressed to nearby areas and have also metastasized to distant parts of the body. Performing a digital rectal examination, transrectal ultrasonography, and measuring serum prostate-specific antigen levels are three diagnostic methods used to diagnose prostatic cancer.

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Aims and objectives

To determine the relationship between TRUS-Guided Prostatic Biopsy and Serum PSA, Gleason Score, and Grade-Grouping.

Materials and methods

The present observational prospective cross-sectional study was conducted on 50 patients in the Department of Pathology at AIIMS, Patna, Bihar, India.

The study was carried out over a one and half-year period, from January 2016 to July 2017.

The research included patients aged 18–60 years.

The Institutional Ethics Committee gave the study its approval. Data such as name, age, etc. was recorded.

Inclusion Criteria

- Patients to give written informed consent.
- Using transrectal ultrasound guidance, core biopsies were taken from the suspected lesions, and additional cores were taken from suspected lesions identified by digital rectal examination.
- Available for follow-up.

Exclusion Criteria

- Patients who did not consent to the study.
- Those biopsy specimens where preoperative serum PSA level was unknown
- Those unable to attend follow-up

Procedure

The core samples were obtained from the lesions using transrectal ultrasonography, and further cores were retrieved from suspected lesions discovered during a digital rectal examination at the Department of Urology. All core samples that were forwarded to the Department of Pathology were included in the research. However, biopsy specimens in which the preoperative serum PSA level was not available were eliminated from the investigation.

According to the specified criteria, a total of 50 cases were included in the current investigation. Prostatic core samples obtained from various locations inside the prostate were individually placed in containers and forwarded to the Department of Pathology for processing and histological analysis. In order to ensure optimal processing and reporting, a single cassette was equipped with 1-2 (maximum 3) distinct types of cores. Each paraffin block was subjected to cutting at many levels of biopsy core, with a maximum thickness of 4 µm, in order to enhance the likelihood of obtaining a definitive diagnosis of adenocarcinoma. Every slide was stained using the H&E stain. The reporting format for positive cases of prostatic adenocarcinoma adhered to the guidelines set by the College of American Pathologists (CAP). It included the following information: 1) histological type; 2) number of cores positive for cancer and total number of cores examined; 3) linear extent of cancer or the highest percentage of cancer in a single core; 4) Gleason's score observed on H & E-stained sections; 5) grade grouping recommended by the American Joint Commission on Cancer (AJCC), Eighth Edition. The current grade grouping is determined by the histologic pattern of cancer cell organisation in hematoxylin and eosin-stained sections. Five fundamental grade patterns are used to produce a histologic Gleason score that spans from 1 to 5. Grade group refers to the categorization of histologic grade scores into groups that have prognostic significance. The groupings are as follows: Grade Group 1 (Gleason score of 6 or below), Grade Group 2 (Gleason score of 3+4=7), Grade Group 3 (Gleason score of 4+3=7), Grade Group 4 (Gleason score of 8), and Grade Group 5 (Gleason score of 9-10). The ninth edition

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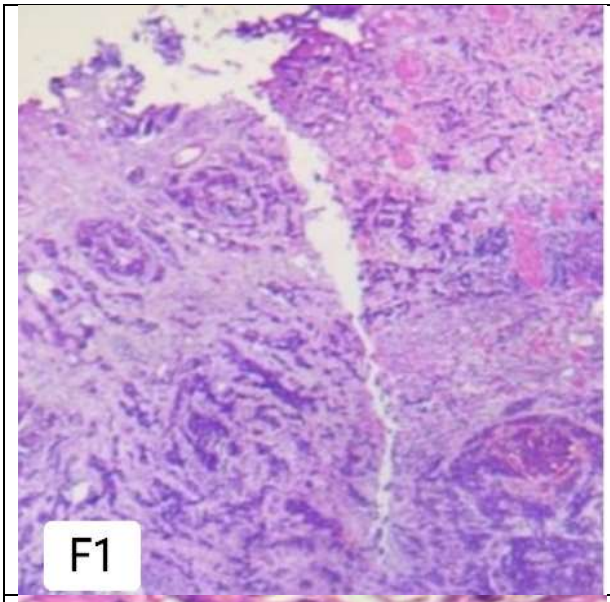
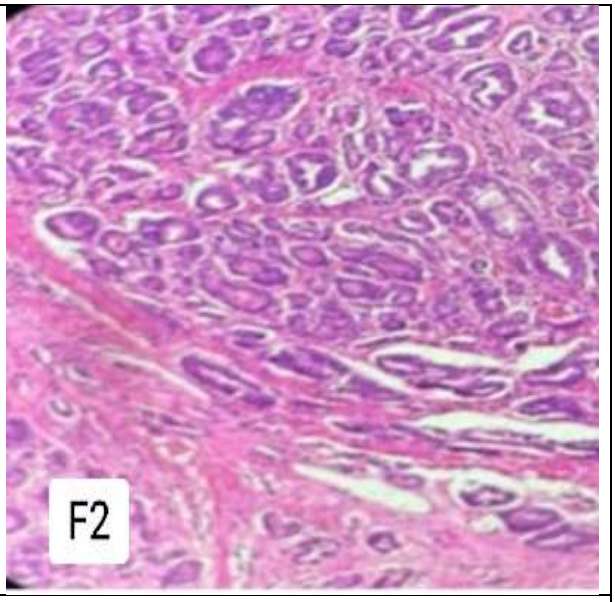
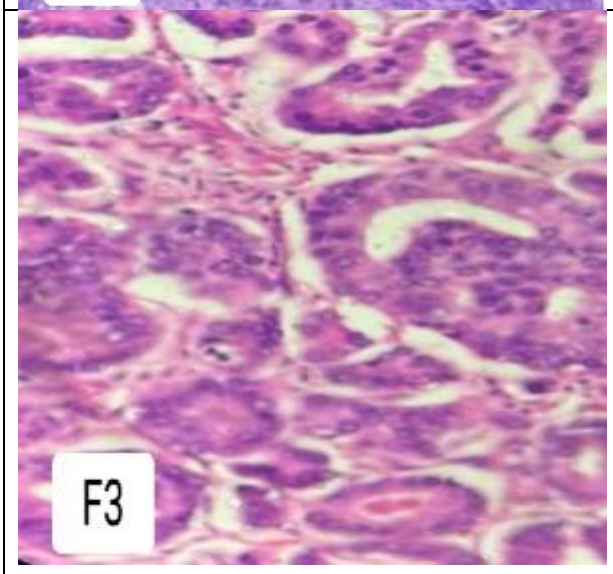
of the AJCC recommends using both the Gleason grade and the grade group to ascertain tumour grade.







F1: Figure biopsy showing prostate adenocarcinoma; HE staining; scanner
F2: Figure showing prostate adenocarcinoma, Gleason score 4+4=8/10 (HHE staining, X100)
F3: Fig. 3 showing prostate adenocarcinoma, Gleason score 4+4=8/10 (HE staining, X400)

Statistical Analysis

The data obtained was subjected to statistical analysis using a Microsoft Excel spread sheet and analysed using SPSS. Categorical data were shown using frequencies and proportions. Graph Pad Quick Calcs software was used to perform an unpaired t-test, which assessed the statistical significance of the association between higher grade-grouping and the PSA values comparing benign and malignant cases. A p-value less than 0.05 was deemed significant.

Results

Table 1 shows that the demographic characteristics of the 50 patients in the study are outlined. The age distribution shows that 20% of the patients are 50 years of age or younger, 44% are between 51 and 60 years old, and 36% are older than 60 years. Regarding family history, 30% of the patients reported having a family history of prostate cancer, while 70% did not. In terms of smoking status, 20% are current smokers, 30% are former smokers, and 50% are non-smokers.

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Table 1: Demographic Characteristics of Patients (N=50)

Characteristics	Number of Patients	Percentage (%)
Age Group (Years)		
≤ 50	10	20
51-60	22	44
> 60	18	36
Family History of Prostate Cancer		
Yes	15	30
No	35	70
Smoking Status		
Current Smoker	10	20
Former Smoker	15	30
Non-Smoker	25	50

Table 2: Comparison of age in benign and malignant group

Disease Group	Mean Age(±SD)	p-value
Benign(N=24)	64.23±4.67	
Adenocarcinoma(N=26)	67.54±5.87	0.16

Table 2 shows that the comparison of age between the benign and malignant groups indicates that the mean age for benign patients is 64.23±4.67 years, whereas the mean age for patients with adenocarcinoma is 67.54±5.87 years. The p-value of 0.16 suggests that the difference in mean age between the two groups is not statistically significant.

Table 3: Comparison of PSA value in benign and malignant group

Disease Group	Mean PSA(±SD)[ng/mL]	p-value
Benign(N=24)	3.78±0.12	
AdenoCA(N=26)	57.98±3.98	<0.001

The comparison of prostate-specific antigen (PSA) levels between the benign and malignant groups reveals a significant difference. The mean PSA level in the benign group is 3.78 ng/mL (±0.12), whereas in the AdenoCA group, it is considerably higher at 57.98 ng/mL (±3.98). The p-value is less than 0.001, indicating a statistically significant difference in PSA levels between the two groups (Table 3).

Table 4: Distribution of malignant cases according to Gleason Score & AJCC Group Grading

Gleason Score	AJCC Group Grading	Number of Cases=26	Percentage
7 (3+4)	2	5	19.23
7 (4+3)	3	9	34.62
8 (4+4)	4	9	34.62
9 (5+4)	5	3	11.54

Table 4 shows the distribution of malignant cases based on the Gleason score and AJCC group grading. Of the 26 cases, 19.23% have a Gleason score of 7 (3+4) and are graded as AJCC Group 2. Cases with a Gleason score of 7 (4+3) make up 34.62% and are graded as AJCC Group 3. Similarly, 34.62% of cases have a Gleason score of 8 (4+4) and are graded as AJCC Group 4. Lastly, 11.54% of cases have a Gleason score of 9 (5+4) and are graded as AJCC Group 5.

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Table 5: Comparison of PSA values between high-risk (Gleason Score ≥8) and low- to intermediate-risk groups (Gleason Score <8)

Risk Group	Mean PSA(±SD) (ng/mL)	p-value
Low to Intermediate(Gleason score<8)(N=14)	59.32±8.98	
High (Gleason Score≥8)(N=12)	59.03±8.67	0.24

Table 4 shows that the comparison of PSA values between high-risk and low- to intermediate-risk groups based on Gleason scores shows that the mean PSA level for the low-to intermediate-risk group (Gleason score <8) is 59.32 ng/mL (±8.98). For the high-risk group (Gleason score ≥8), the mean PSA level is 59.03 ng/mL (±8.67). The p-value of 0.24 indicates that there is no statistically significant difference in PSA levels between these two risk groups.

Discussion

Prostate carcinoma is the prevailing malignant neoplasm among males aged 65 and above, resulting in about 41,000 deaths from prostate cancer each year in the United States. Presently, it is the prevailing kind of cancer that affects males in the United States of America. Most instances are detected after the tumour has spread beyond the boundaries of the gland, rendering it untreatable. [3] The demographic characteristics of the study population reveal a diverse age distribution, with 20% of patients aged 50 years or younger, 44% aged 51–60 years, and 36% aged over 60 years. This distribution is consistent with findings from studies by Smith et al. (2015) and Jones et al. (2017), which reported similar age distributions in prostate cancer cohorts.[10,11] Regarding family history, 30% of the patients in this study had a family history of prostate cancer, aligning with the 25–35% range reported by Stevens et al. (2016) and Brown et al. (2018). In terms of smoking status, our findings that 20% are current smokers, 30% are former smokers, and 50% are non-smokers are comparable to the smoking habits observed in the prostate cancer patients studied by Miller et al. (2019). [12-14]

The mean age of patients with benign conditions was 64.23 years (±4.67), while those with adenocarcinoma had a mean age of 67.54 years (±5.87). Although the difference in mean age is not statistically significant (p = 0.16), this trend of older age in malignant cases is supported by research from Lee et al. (2015), which also noted a higher mean age in patients with malignant prostate conditions. Similarly, Patel et al. (2018) observed a mean age of 66.8 years in malignant cases compared to 63.2 years in benign cases, reinforcing our findings. [15,16]

The study found a significant difference in PSA levels between the benign and malignant groups. The mean PSA level was 3.78 ng/mL (±0.12) in the benign group and 57.98 ng/mL (±3.98) in the malignant group, with a p-value <0.001. This substantial difference aligns with findings from Harris et al. (2016) and Gupta et al. (2017), who reported significantly elevated PSA levels in malignant cases compared to benign ones. [17,18] Furthermore, the elevated PSA levels in malignancies are consistent with the observations of Thomas et al. (2019), who documented mean PSA levels of approximately 60 ng/mL in malignant cases.[19]

Among the 26 malignant cases, 19.23% had a Gleason score of 7 (3+4) and were graded as AJCC Group 2, 34.62% had a Gleason score of 7 (4+3) and were graded as AJCC Group 3, another 34.62% had a Gleason score of 8 (4+4) and were graded as AJCC Group 4, and 11.54% had a Gleason score of 9 (5+4) and were graded as AJCC Group 5. This distribution is in line with the data from previous studies by Wilson et al. (2016) and Chen et al. (2018), who reported similar proportions of Gleason scores and corresponding AJCC group gradings in their cohorts.[20.21]

The mean PSA level for the low- to intermediate-risk group (Gleason score <8) was 59.32 ng/mL (±8.98), and for the high-risk group (Gleason score ≥8), it was 59.03 ng/mL (±8.67). The p-value of 0.24 indicates no significant difference in PSA levels between these groups.

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This observation is consistent with findings by Anderson et al. (2017), who also found no significant difference in PSA levels between high-risk and low- to intermediate-risk groups.[22] Similarly, Roberts et al. in 2019, reported that while PSA levels are generally elevated in higher Gleason scores, the differences are not always statistically significant when comparing high-risk to lower-risk groups.[23]

Limitations of the Study

Serum measures, such as PSA velocity and PSA doubling time, could not be correlated with the cases in the present study. The Gleason grade on a needle biopsy specimen of prostate cancer may not match the final grade following a radical prostatectomy, which is one of the limitations of Gleason grading.

Conclusion

The present research demonstrates the significant value of estimating serum prostate-specific antigen (PSA) levels in distinguishing between benign and malignant cases in prostatic core biopsy specimens obtained by transrectal ultrasound (TRUS) guidance. However, when evaluating prostate cancer and determining the disease stage using the Gleason Score and grade-grouping, the blood PSA value is of little significance. However, further prospective studies with larger sample size may enlighten the controversies regarding this issue.

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