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Prevalence of Histopathological Grades in Prostate Adenocarcinoma at Tobruk Medical Center

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الدرجة النسيجية المرضية السائدة للسرطان الغدة للبروستاتا في مركز طبرق الطبي

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Abstract: Prostate adenocarcinoma is one of the most common malignant tumors affecting males worldwide. Histopathological grading, particularly the Gleason scoring system and International Society of Urological Pathology (ISUP) Grade Group classification, plays an essential role in evaluating tumor aggressiveness, prognosis, and treatment planning. Prostatic adenocarcinoma is graded by the Gleason system, based on glandular architecture at low magnification. The system assigns patterns 1 to 5, with pattern 1 most differentiated and pattern 5 undifferentiated, and sums the primary and secondary patterns into a score from 2 to 10. The 2014 ISUP Grade Group classification maps this to five groups: Group 1 [3+3=6], Group 2 [3+4=7], Group 3 [4+3=7], Group 4 [4+4=8], Group 5 [9-10]. Grade is a key predictor of behavior and treatment decisions. Transrectal ultrasound-guided 16-core prostate biopsy series and contemporary literature evaluating distribution of Gleason scores and Grade Groups

Keywords: International Society of Urological Pathology, Adenocarcinoma, Histopathological

الملخص

يُعد السرطان الغدة للبروستاتا من أكثر الأورام الخبيثة شيوعًا بين الذكور حول العالم. ويُعتبر التقييم النسيجي المرضي، وخاصة نظام غليسون للتدرج وتصنيف المجموعة النسيجية للجمعية الدولية لعلم أمراض المسالك البولية (ISUP)، من أهم العوامل المستخدمة لتحديد شدة الورم، والتنبؤ بسلوكه، وتوجيه الخطة العلاجية. يُصنّف سرطان غدة البروستاتا وفقًا لنظام غليسون، بناءً على تركيبة الغدد تحت تكبير منخفض. يُخصّص النظام أنماطًا من 1 إلى 5، حيث يُمثّل النمط 1 التمايز الأكثر وضوحًا، بينما يُمثّل النمط 5 عدم التمايز. ويُجمع النمطان الأساسي والثانوي في درجة تتراوح من 2 إلى 10. يُصنّف تصنيف ISUP لعام 2014 مجموعات الدرجات إلى خمس مجموعات: المجموعة 1 [3+3=6]، المجموعة 2 [4+3=7]، المجموعة 3 [3+4=7]، المجموعة 4 [4+4=8]، المجموعة 5 [9-10]. تُعدّ الدرجة مؤشرًا رئيسيًا لسلوك الورم وقرارات العلاج. خزعات البروستاتا المتسلسلة تحت توجيه الموجات فوق الصوتية عبر المستقيم (16 عينة) والدراسات الحديثة التي تُقيّم توزيع درجات غليسون ومجموعات الدرجات.

الكلمات المفتاحية: الجمعية الدولية لأمراض المسالك البولية، سرطان الغدة الدرقية، علم الأمراض النسيجية

1. Introduction

Prostate cancer is one of the most common malignant neoplasms affecting men worldwide and represents a major global public health challenge. It is currently the second most frequently diagnosed cancer and one of the leading causes of cancer-related mortality among men. According to the Global Cancer Statistics (GLOBOCAN 2022), approximately 1.4 million new cases and nearly 400,000 deaths due to prostate cancer were estimated worldwide in 2022 (Bray et al., 2024). The global burden of prostate cancer is expected to increase substantially in the coming decades due to population growth, aging, and increased life expectancy, with projections indicating a marked rise in the number of cases and deaths by 2040 (Ferlay et al, 2020; Withrow et al., 2022). In the United States, prostate cancer remains the most commonly diagnosed non-cutaneous malignancy among men and represents a significant cause of cancer morbidity and mortality. Despite improvements in early detection, risk stratification, and treatment strategies, prostate cancer continues to contribute considerably to cancer-related health burden among males (Raychaudhuri et al., 2025). In Libya, prostate cancer has become an important health concern. Available national cancer statistics indicate that prostate cancer is among the most common malignancies affecting Libyan men, representing approximately 10–11% of newly diagnosed male cancers. However, published studies describing the histopathological characteristics, Gleason grading patterns, and clinicopathological features of prostate adenocarcinoma in the Libyan population remain limited. Therefore, local epidemiological and pathological investigations are necessary to improve understanding of disease patterns within the Libyan population. The incidence of prostate cancer increases significantly with advancing age, making elderly men the most affected group. Age represents the strongest established risk factor for prostate cancer development. Other recognized risk factors include family history, inherited genetic alterations, hormonal influences, environmental factors, and lifestyle-related factors. Individuals with affected first-degree relatives have an increased risk of developing prostate cancer, supporting the important contribution of hereditary susceptibility in disease pathogenesis (Rawla, 2019). The prostate gland is an essential component of the male reproductive system. It is located inferior to the urinary bladder and surrounds the proximal portion of the urethra. The gland contributes to reproductive function through secretion of prostatic fluid, which forms part of the seminal plasma. Due to its dependence on androgen signaling and age-associated cellular changes, the prostate is susceptible to malignant transformation. Although many prostate cancers demonstrate slow biological progression, a proportion of tumors exhibit aggressive behavior characterized by local invasion, lymph node involvement, and distant metastasis, particularly to bone (Mottet et al., 2021).

2. Materials and Methods

Study Design

A retrospective descriptive study was conducted to determine the prevalent histopathological grade of prostate adenocarcinoma among patients diagnosed at Tobruk Medical Center. The study focused on evaluating the histopathological characteristics of confirmed prostate adenocarcinoma cases, including Gleason patterns, Gleason scores, and the International Society of Urological Pathology (ISUP) Grade Group classification.

Study Setting

The study was conducted at the Onco-Urology Department, Tobruk Medical Center, Tobruk, Libya. The center provides diagnostic and therapeutic services for patients with urological malignancies, including prostate cancer.

Study Duration

The study included patients diagnosed with prostate adenocarcinoma from January 2018 to March 2026. Patient data were collected retrospectively from medical records, and histopathology reports available at the study center.

Study Population

The study population consisted of all patients with histopathologically confirmed prostate adenocarcinoma who were diagnosed at Tobruk Medical Center during the study period.

Sample Size

A total sample of 60 histopathologically confirmed cases of prostate adenocarcinoma diagnosed at Tobruk Medical Center during the retrospective study period from January 2018 to March 2026 was included in the analysis.

Inclusion Criteria

Patients were included according to the following criteria:
Histopathologically confirmed diagnosis of prostate adenocarcinoma.
Availability of pathology reports containing tumor grading information.
Diagnosis established during the study period (2018–2026).

Exclusion Criteria

Patients were excluded if they met any of the following criteria:
Incomplete medical records.
Absence of histopathological reports.
Diagnosis of prostate malignancies other than adenocarcinoma.

Data Collection

Data were retrospectively collected from patients' medical records and histopathology reports. The collected variables included:

Age at diagnosis.
Histopathological subtype.
Gleason primary pattern.
Gleason secondary pattern.
Gleason score.
ISUP Grade Group classification.
Prostate-specific antigen (PSA) level before and after treatment (when available).
Tumor stage (when available).

Data Analysis

Collected data were entered and analyzed using IBM SPSS Statistics software. Descriptive statistics were used to summarize the study variables. Continuous variables were presented as mean $\pm$ standard deviation (SD) for normally distributed data and as median with interquartile range (IQR) for non-normally distributed data, whereas categorical variables were expressed as frequencies and percentages. The normality of continuous variables was assessed using the Shapiro–Wilk test. Age was compared between lower-grade (ISUP Grades 1–3) and high-grade (ISUP Grades 4–5) disease using the independent-samples t-test, as it demonstrated an approximately normal distribution. Because PSA values before and after treatment showed significant positive skewness, comparisons between paired PSA measurements were performed using the Wilcoxon signed-rank test. Associations between categorical variables, including age group, ISUP Grade Group, Gleason score, and tumor stage, were evaluated using the Chi-square test. A binary logistic regression analysis was performed to identify independent predictors of high-grade disease (ISUP Grades 4–5). Owing to the marked positive skewness of baseline PSA values, a base-10 logarithmic transformation [$\log_{10}(\text{PSA} + 1)$] was applied before inclusion in the regression model. Multicollinearity among predictor variables was assessed using the Variance Inflation Factor (VIF), and model calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test. All statistical tests were two-tailed, and a p-value <0.05 was considered statistically significant.

Ethical Considerations

Ethical approval was obtained from the appropriate authorities at Tobruk Medical Center prior to data collection. Patient confidentiality was strictly maintained throughout the study. All collected data were anonymized, and no personal identifying information was recorded. The data were used solely for scientific research purposes.

3. Results

The dataset included 60 patients diagnosed with prostatic adenocarcinoma. The mean age was 70.37 years (SD = 9.01). The most prevalent recorded Gleason histopathological pattern was 4+3=7, accounting for 19 cases (31.7%). The most common ISUP grade was Grade 3, observed in 19 patients (31.7%), while Stage 4 was the dominant tumor stage, observed in 39 patients (65.0%). High-grade disease, defined as ISUP Grades 4-5, was present in 13 patients (21.7%). A p-value <0.05 was considered statistically significant.

This analysis first examined the normality of age, PSA before treatment, PSA after treatment, and the paired PSA difference. Age was approximately normally distributed overall and within the lower-grade and high-grade groups. By contrast, PSA before treatment, PSA after treatment, and the paired PSA difference were significantly non-normal. Therefore, the Wilcoxon signed-rank test was used as the primary paired PSA comparison test. For logistic regression, the non-normality of PSA does not violate logistic regression assumptions directly; however, because raw PSA was highly right-skewed and contained extreme values, $\log_{10}(\text{PSA before} + 1)$ was used in the final logistic regression model to reduce skewness and improve model stability.

Descriptive Statistics for Continuous Variables

Table 1 shows that the mean age was 70.37 years and the median age was 71.00 years. The closeness of the mean and median, together with the Shapiro-Wilk result reported later, indicates that age was approximately normally distributed in this cohort.

Table 1. Descriptive statistics for age

Variable	N	Mean	SD	Median	Minimum	Maximum
Age	60	70.37	9.1	71.00	49.00	89.00

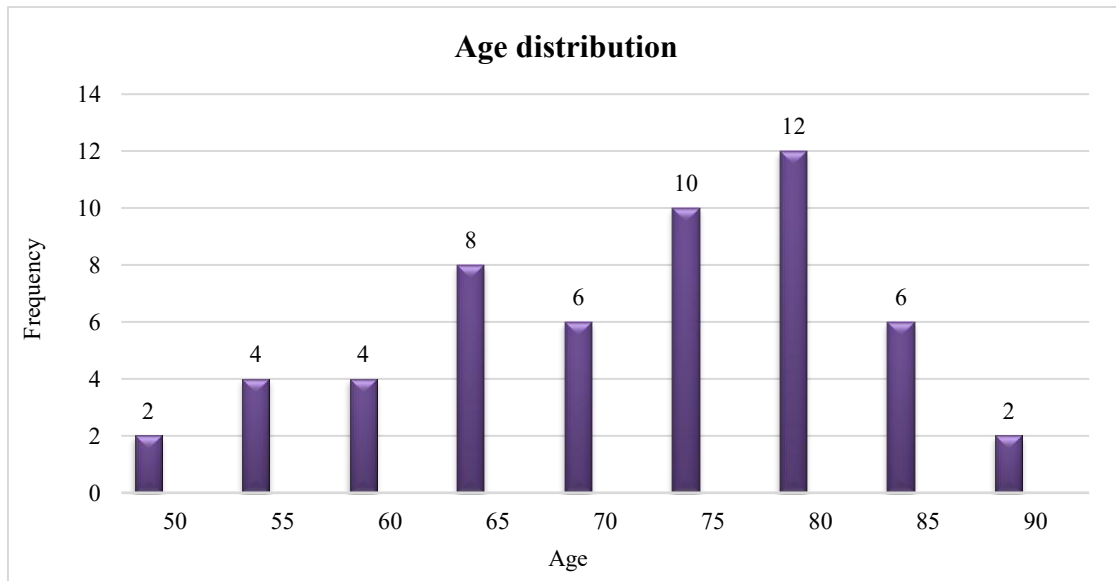


Figure 1. Age histogram showing an approximately balanced age distribution (N=60).

Table 2 presents descriptive statistics for PSA levels before and after treatment. Before treatment, the mean PSA was 72.21 ng/mL (SD = 87.01), and the median was 41.80 ng/mL. After treatment, the mean PSA decreased to 19.65 ng/mL (SD = 32.16), while the median decreased to 2.85 ng/mL. The large standard deviations and the marked difference between mean and median values indicate strong positive skewness. Therefore, median, quartiles, and non-parametric testing are more appropriate for PSA interpretation than mean-based inference alone.

Table 2. Descriptive statistics for PSA before and PSA after

Variable	N	Mean	SD	Median	Q1	Q3	IQR	Minimum	Maximum
PSA before	60	72.21	7.01	41.80	17.80	100.00	82.20	0.22	470.00
PSA after	60	19.65	32.16	2.85	0.39	22.8	22.41	0.01	100.00

3. Normality Test Analysis for Age and PSA Variables

Normality was evaluated using the Shapiro-Wilk test. We assessed age overall and within the two grade categories because we later compared age between lower-grade and high-grade patients using an independent samples t-test. PSA before treatment, PSA after treatment, and the paired PSA difference were also tested because the assumption behind a paired-samples t-test concerns the distribution of within-patient differences.

Table 3. Shapiro-Wilk normality tests for age, PSA variables, and transformed PSA

Variable	N	Shapiro-Wilk W	P value	Skewness	kurtosis	Decision
Age	60	0.987	0.763	-0.17	-0.27	Approximately normal
Age among lower grade	47	0.985	0.792	-0.25	-0.00	Approximately normal
Age among high grade	13	0.966	0.848	0.06	-0.67	Approximately normal
PSA before	60	0.710	<0.001	2.71	9.28	Non-normal
PSA after	60	0.644	<0.001	1.68	1.43	Non-normal
Paires PSA different	60	0.636	<0.001	3.26	13.30	Non-normal
Log1(PSA before +1	60	0.949	0.014	-0.70	0.36	Non-normal

Note. A significant Shapiro-Wilk test indicates departure from normality. Age was approximately normally distributed overall and within grade groups. PSA before, PSA after, and the paired PSA difference were non-normal. Log10(PSA before + 1) reduced skewness but remained slightly non-normal; nevertheless, predictor normality is not an assumption of logistic regression.

The Shapiro-Wilk test showed that age was normally distributed overall ($W = 0.987$, $p = 0.763$), among lower-grade patients ($W = 0.985$, $p = 0.792$), and among high-grade patients ($W = 0.966$, $p = 0.848$). Therefore, the age variable was suitable for parametric description and for the independent-samples t-test comparing age between grade categories. Conversely, PSA before treatment ($W = 0.710$, $p < 0.001$), PSA after treatment ($W = 0.644$, $p < 0.001$), and the paired PSA difference ($W = 0.636$, $p < 0.001$) were clearly non-normal. This finding supports replacing the paired-samples t-test with the Wilcoxon signed-rank test for the before-after PSA comparison.

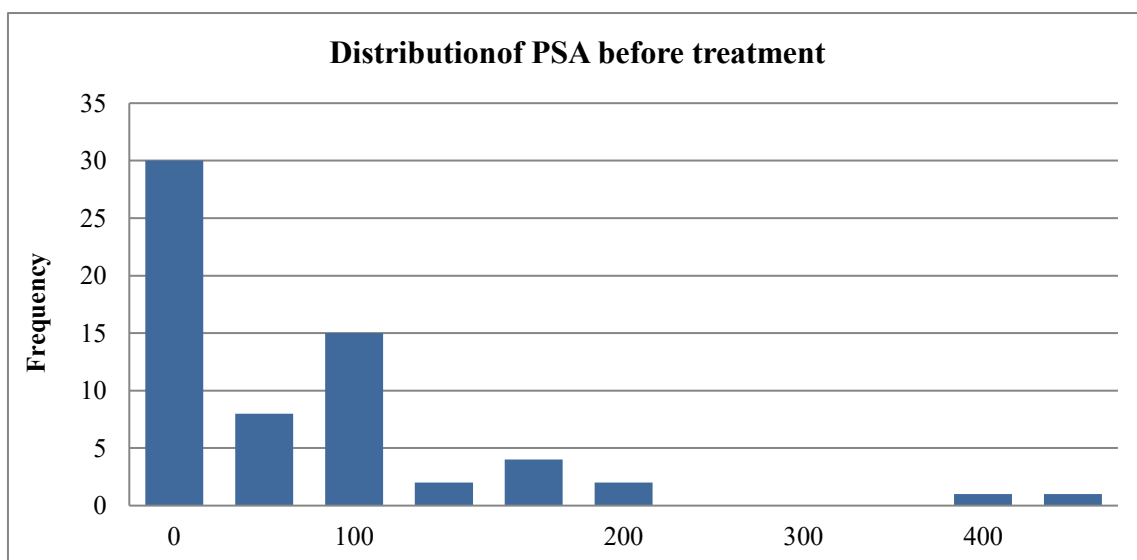


Figure 2. Histogram showing the positively skewed distribution of PSA before treatment (N=60).

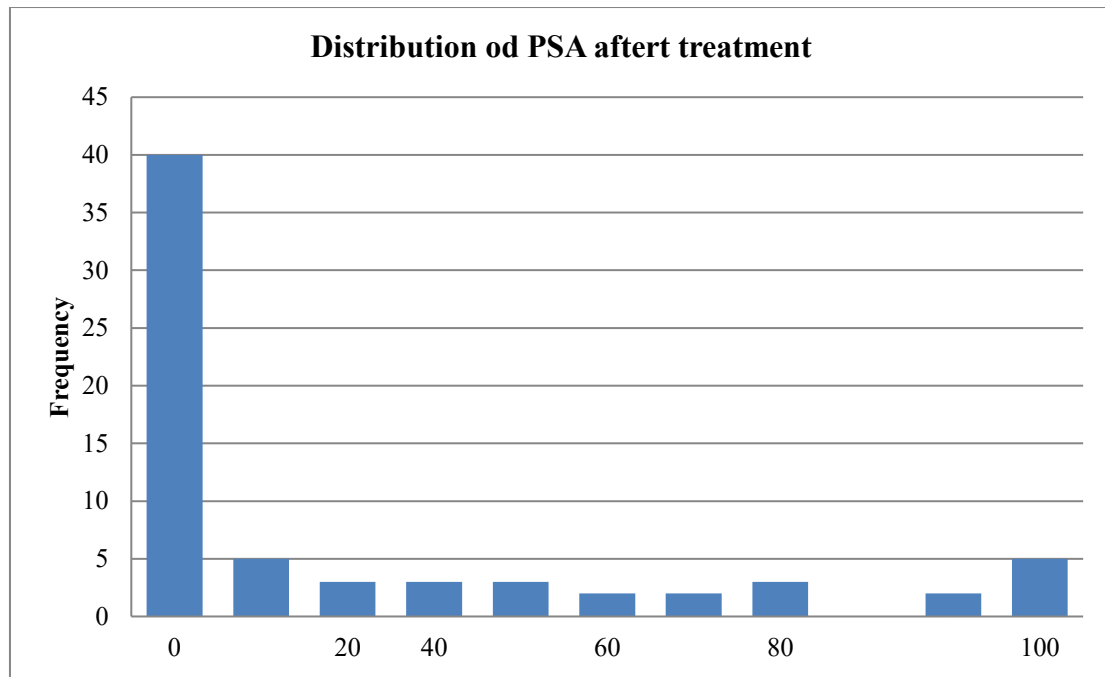


Figure 3. Histogram showing the positively skewed distribution of PSA after treatment (N=60).

In Figure 4, the orange horizontal line inside each box represents the median PSA. Before treatment, the median PSA is clearly higher, around 41.8 ng/mL. After treatment, the median falls sharply to around 2.85 ng/mL, indicating a strong overall biochemical reduction after treatment.

The green triangle represents the mean PSA. The mean is much higher than the median in both groups, especially before treatment. This means the PSA distribution is positively skewed, because a few patients had very high PSA values.

The box represents the middle 50% of patients. Before treatment, the box is much taller, showing large variability in PSA levels. After treatment, the box is compressed near the lower values, showing that most patients had much lower PSA after treatment.

The circles above the whiskers are outliers. Before treatment, there are extreme PSA outliers around 400–470 ng/mL. After treatment, some outliers remain, around 60–100 ng/mL, suggesting that a small number of patients continued to have relatively high PSA levels despite treatment.

4. Age Group Distribution

Table 4 shows that most patients were aged 70-79 years, representing 43.3% of the total sample. The second most common age group was 60-69 years at 30.0%, followed by patients aged ≥ 80 years at 16.7%. Only 10.0% of patients were younger than 60 years.

Table 4. Age group distribution (N=60)

Category	Frequency	Percentage
<60	6	10.0%
60-69	18	30.0%
70-79	26	43.3%
≥ 80	10	16.7%

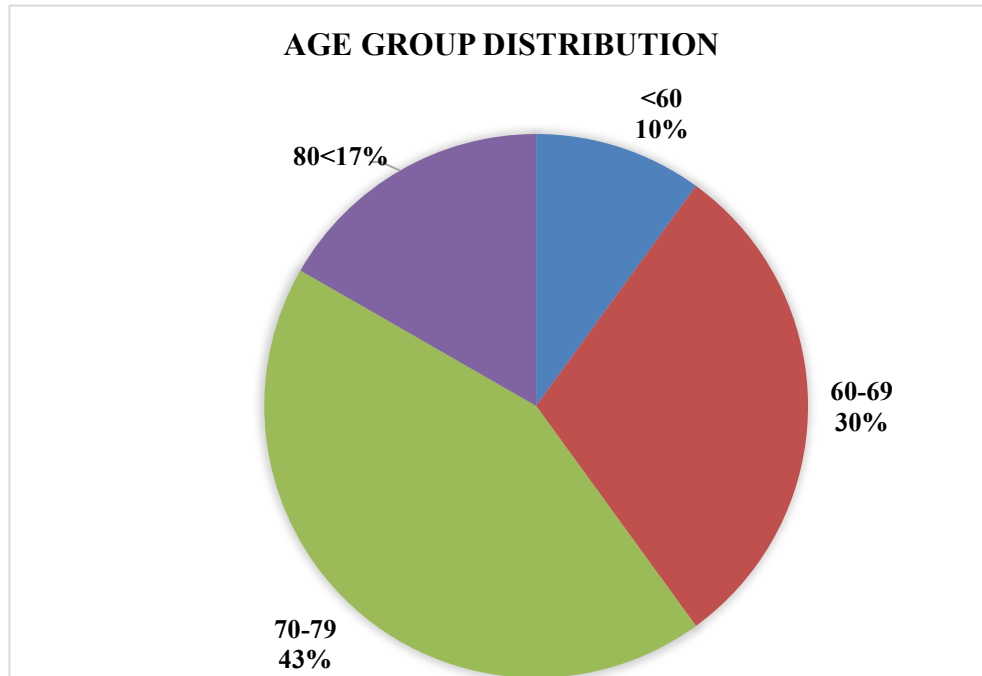


Figure 4. Pie chart of age group distribution (N=60)

5. Gleason Histopathological Pattern Distribution

Table 5 presents the distribution of Gleason histopathological patterns. The most prevalent pattern was Gleason score 4+3=7, accounting for 31.7% of all cases. This was followed by Gleason score 3+4=7, which represented 11.7% of cases. Gleason scores 5+4=9 and 3+3=6 each accounted for 8.3% of cases, while the remaining patterns were less common.

Table 5. Gleason histopathological pattern distribution (N=60)

Category	Frequency	percentage
4+3=7	19	31.7%
3+4=7	7	11.7%
5+4=9	5	8.3%
3+3=6	5	8.3%
2+2=4	4	6.7%
2+5=7	3	5.0%
4+4=8	3	5.0%
1+3=4	2	3.3%
2+3=5	2	3.3%
5+2=7	2	3.3%
5+3=8	2	3.3%
5+5=10	1	1.7%
3+5=8	1	1.7%
1+1=2	1	1.7%
4+5=9	1	1.7%
2+1=3	1	1.7%
2+4=6	1	1.7%

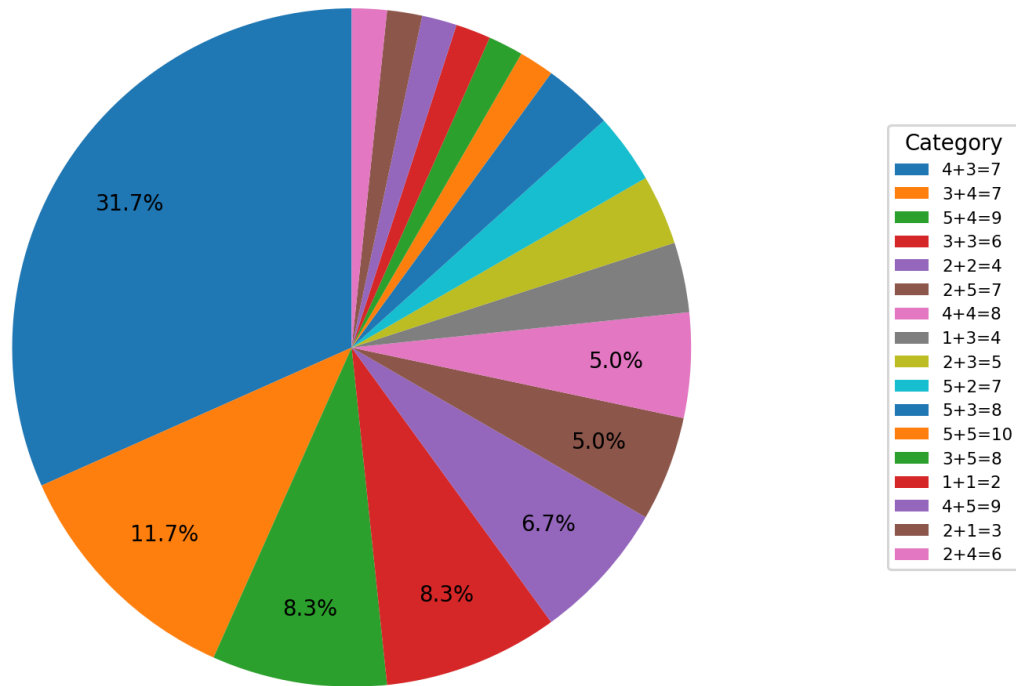


Figure 5. Pie chart of Gleason histopathological pattern distribution (N=60).

6. Gleason Score Distribution

Table 6 shows that the most common Gleason score was 7, observed in 31 patients (51.7%). This indicates that more than half of the study population had intermediate-grade prostate adenocarcinoma. Gleason scores 4, 6, 8, and 9 were each reported in 10.0% of patients, while very low scores and the highest score of 10 were uncommon.

Table 6. Gleason score distribution (N=60)

Category	Frequency	Percentage
2	1	1.7%
3	1	1.7%
4	6	10.0%
5	2	3.3%
6	6	10.0%
7	31	51.7%
8	6	10.0%
9	6	10.0%
10	1	1.7%

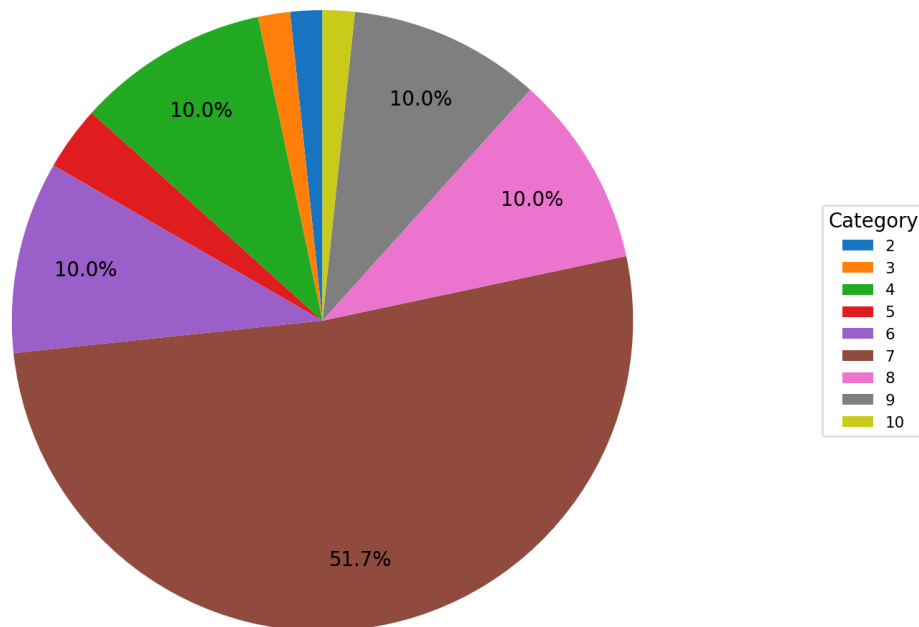


Figure 6. Pie chart of Gleason score distribution (N=60).

4. Results

Summary of the Study Population

The present retrospective study included 60 patients diagnosed with histopathologically confirmed prostate adenocarcinoma at Tobruk Medical Center, Department of Oncourology, during the period from January 2018 to March 2026. The mean age of the patients was 70.37 ± 9.01 years, with an age range of 49–89 years.

The age distribution showed that the majority of patients were in the 70–79 years age group, representing 26 cases (43.3%), followed by the 60–69 years group with 18 cases (30.0%). Patients aged ≥ 80 years accounted for 10 cases (16.7%), while patients younger than 60 years represented the smallest group with 6 cases (10.0%).

Gleason Histopathological Pattern Distribution

The analysis of Gleason histopathological patterns demonstrated considerable variation among the studied cases.

The most prevalent Gleason pattern was Gleason score $4+3=7$, identified in 19 patients (31.7%). The second most frequent pattern was $3+4=7$, observed in 7 patients (11.7%).

Other detected patterns included $5+4=9$ and $3+3=6$, each occurring in 5 patients (8.3%). Less frequent patterns included $2+2=4$, $2+5=7$, $4+4=8$, and other combinations with lower frequencies.

Gleason Score Distribution

Regarding the overall Gleason score distribution, Gleason score 7 was the most common score, detected in 31 cases (51.7%) of the studied population.

Gleason scores 4, 6, 8, and 9 were each observed in 6 patients (10.0%). The lowest scores (2 and 3) and the highest score (10) were uncommon, each representing 1.7% of cases.

These findings indicate that the majority of patients had intermediate-grade prostate adenocarcinoma.

ISUP Grade Group Distribution

According to the International Society of Urological Pathology (ISUP) Grade Group classification, ISUP Grade Group 3 was the predominant grade, detected in 19 patients (31.7%).

ISUP Grade Group 1 was observed in 16 patients (26.7%), while Grade Group 2 occurred in 12 patients (20.0%).

High-grade categories included:

- ISUP Grade Group 4: 6 patients (10.0%)
- ISUP Grade Group 5: 7 patients (11.7%)

Overall, high-grade disease (ISUP Grades 4–5) was found in 13 patients (21.7%), whereas lower-grade disease (ISUP Grades 1–3) represented 47 patients (78.3%).

Tumor Stage Distribution

Tumor stage analysis revealed that Stage 4 disease was the most frequent stage, observed in 39 patients (65.0%).

Stage 2 disease was found in 17 patients (28.3%), whereas Stage 3 disease was observed in only 4 patients (6.7%).

5. Discussion

Prostate adenocarcinoma is one of the most common malignancies affecting elderly men worldwide. Histopathological grading, particularly the Gleason scoring system and International Society of Urological Pathology (ISUP) Grade Group classification, plays a crucial role in predicting tumor aggressiveness and guiding treatment decisions. The present retrospective study evaluated 60 patients with histopathologically confirmed prostate adenocarcinoma at Tobruk Medical Center during the period from 2018 to 2026.

In the current study, the mean age of patients was 70.37 ± 9.01 years, with the majority of cases occurring among patients aged 70–79 years (43.3%). This finding is consistent with the general epidemiology of prostate cancer, which predominantly affects elderly men. Similar results were reported in a local study conducted at Benghazi Medical Center involving 81 prostate cancer patients, where the mean age was 71.6 years, demonstrating comparable age distribution among eastern Libyan populations. This similarity may reflect the demographic characteristics and increased risk of prostate cancer with advancing age.

Regarding histopathological findings, Gleason score 7 was the most common score in our study, accounting for 51.7% of cases. The predominant Gleason pattern was 4+3=7, observed in 31.7% of patients. These findings indicate that intermediate-grade prostate adenocarcinoma represents the majority of cases in our population. Similar observations have been reported internationally, where Gleason score 7 is frequently identified as the most common category among diagnosed prostate cancers.

According to the ISUP Grade Group classification, ISUP Grade Group 3 was the most prevalent category in our study (31.7%), followed by Grade Group 1 (26.7%) and Grade Group 2 (20.0%). High-grade disease (ISUP Grades 4–5) represented 21.7% of cases. The predominance of intermediate and high-grade disease in our cohort may indicate delayed diagnosis or referral, as prostate cancer screening and early detection programs remain limited in many regions.

The present findings differ from a recent study performed at Benghazi Medical Center, where Grade I was reported as the most frequent histopathological grade. The difference between the two studies may be attributed to variations in patient selection, referral patterns, study populations, and differences in the stage of disease at presentation. Patients referred to tertiary medical centers may represent more advanced cases with higher-grade tumors.

Tumor stage distribution in our study demonstrated that Stage 4 disease was the most common stage, accounting for 65.0% of cases, while Stage 2 and Stage 3 represented 28.3% and 6.7%, respectively. The high proportion of advanced-stage disease may reflect late presentation, limited screening awareness, and delayed diagnosis. Early detection of prostate cancer through appropriate clinical evaluation and PSA testing could contribute to identifying tumors at earlier stages and improving outcomes.

The relationship between histopathological grade and clinical variables was evaluated in this study. No statistically significant association was found between age group, Gleason score, ISUP grade, and tumor stage. Similar findings have been reported in some studies, suggesting that age alone may not reliably predict tumor aggressiveness, and pathological assessment remains essential for accurate disease classification.

6. Conclusion

This study demonstrated that prostate adenocarcinoma in patients treated at Tobruk Medical Center predominantly affects elderly men, with a mean age of approximately 70 years. Gleason score 7, particularly Gleason pattern 4+3=7, was the most common histopathological finding, and ISUP Grade Group 3 represented the predominant grade category.

A considerable proportion of patients presented with advanced tumor stage, with Stage 4 disease being the most frequent presentation. These findings suggest that delayed diagnosis remains an important challenge in prostate cancer management in our population.

The significant reduction in PSA levels after treatment indicates a favorable biochemical response; however, the presence of advanced-stage and high-grade disease highlights the need for improved early detection programs.

Enhancing awareness, promoting screening, and improving access to specialized care are essential strategies to achieve earlier diagnosis, better treatment outcomes, and improved survival among prostate cancer patients in Libya.

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