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Original Research Article

FACTORS AFFECTING BIOCHEMICAL RECURRENCE IN POST RADICAL PROSTATECTOMY PATIENTS WITH CARCINOMA PROSTATE - A PROSPECTIVE STUDY

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Abstract

Background: Radical prostatectomy remains the standard treatment for clinically localized prostate cancer. However, biochemical recurrence (BCR) continues to occur in a considerable proportion of patients. Identification of pathological predictors of recurrence is essential for postoperative risk stratification and patient management. **Objective:** To evaluate the association of clinicopathological factors with pathological stage and biochemical recurrence following radical prostatectomy in patients with localized prostate cancer. **Materials and Methods:** This retrospective observational study included 116 patients who underwent radical prostatectomy for clinically localized prostate cancer at Department of Urology, The Oxford Medical College Hospital & Research Centre, Bangalore between January 2020 and January 2024. Histopathological parameters including Gleason score, tumor volume, extraprostatic extension (EPE), seminal vesicle invasion (SVI), perineural invasion (PNI), lymphovascular invasion (LVI), positive surgical margins (PSM), high-grade prostatic intraepithelial neoplasia (HGPIN), necrosis, and tertiary Gleason pattern were evaluated. **Results:** The mean age was 67 years, with 65.5% of patients having pT2 disease and 34.5% having pT3 disease. Higher preoperative PSA, larger tumor volume, and higher Gleason score were significantly associated with advanced pathological stage (all $p<0.001$). During follow-up, biochemical recurrence occurred in 38 (32.8%) patients. Multivariable analysis identified preoperative PSA ($p=0.001$), tumor volume ($p<0.001$), Gleason score ($p<0.001$), extraprostatic extension ($p=0.002$), seminal vesicle invasion ($p<0.001$), positive surgical margins ($p=0.012$), lymphovascular invasion ($p=0.032$), and tumor necrosis ($p=0.017$) as independent predictors of biochemical recurrence. **Conclusion:** Preoperative PSA, tumor volume, Gleason score, extraprostatic extension, seminal vesicle invasion, positive surgical margins, lymphovascular invasion, and necrosis are significant predictors of biochemical recurrence after radical prostatectomy.

INTRODUCTION

Prostate cancer is one of the most common malignancies affecting men worldwide and remains a major cause of cancer-related morbidity and mortality. It is the most frequently diagnosed non-cutaneous cancer in men in many developed countries and constitutes a significant public health challenge due to its increasing incidence with advancing age.[1] Although prostate cancer is uncommon before the age of 50 years, the majority of cases occur in men older than 65 years, with the average age at diagnosis declining following the widespread adoption of prostate-specific antigen (PSA) screening. Improvements in early detection have resulted in a greater proportion of patients being diagnosed with localized, organ-confined disease, contributing to a reduction in prostate cancer-specific mortality.[2]

The development of prostate cancer is influenced by several established risk factors, including advancing age, ethnicity, and a positive family history. Men with first-degree relatives affected by prostate cancer have a significantly higher lifetime risk of developing the disease. Geographic and ethnic variations in incidence further suggest contributions from genetic predisposition, environmental influences, and differences in healthcare access and

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screening practices.[3] Lifestyle factors such as obesity, dietary fat intake, and smoking have also been investigated, although evidence regarding their role in disease initiation remains inconsistent. Smoking, however, has been associated with poorer survival and increased prostate cancer-specific mortality among affected patients.[4]

Prostate cancer develops through uncontrolled proliferation of epithelial cells within the prostate gland, with the potential for local invasion and distant metastasis. Early detection is essential because treatment outcomes are strongly related to disease stage at diagnosis. The two most commonly employed screening methods are digital rectal examination (DRE) and measurement of serum prostate-specific antigen (PSA). PSA is an organ-specific glycoprotein produced by prostatic epithelial cells and serves as an important biomarker for prostate disorders.[5] However, PSA lacks tumor specificity, as elevated levels may also occur in benign prostatic hyperplasia, prostatitis, and other non-malignant conditions. Conversely, clinically significant prostate cancer may be present despite normal PSA values, limiting its diagnostic accuracy. While PSA screening has facilitated earlier diagnosis and reduced advanced-stage disease, concerns regarding overdiagnosis and overtreatment persist. Many screen-detected tumors are indolent and may never become clinically significant during a patient's lifetime.[6] Consequently, unnecessary diagnostic procedures and treatments may expose patients to urinary, sexual, and bowel dysfunction, adversely affecting quality of life. Large randomized screening trials have produced conflicting evidence regarding the mortality benefits of PSA-based screening, emphasizing the need for improved diagnostic strategies capable of distinguishing clinically significant from insignificant disease.

Therefore, the present study aims to evaluate the role of multiparametric MRI in the diagnosis of prostate cancer and to correlate imaging findings with histopathological results in the Indian population.

MATERIALS AND METHODS

This retrospective observational study was conducted in the Department of Urology, The Oxford Medical College Hospital & Research Centre, Bangalore. The study included patients who underwent radical prostatectomy (RP) for clinically localized prostate cancer between January 2020 and January 2024. Institutional ethical approval was obtained prior to data collection, and patient confidentiality was maintained throughout the study. A total of 116 men with histopathologically confirmed localized prostate adenocarcinoma who underwent radical prostatectomy during the study period were included. Clinical records, operative notes, histopathology reports, and follow-up data were reviewed to evaluate pathological characteristics and postoperative outcomes.

Patients with clinically localized, histopathologically confirmed prostate cancer who underwent radical prostatectomy and had a Gleason score >5 were eligible for inclusion. Only patients who achieved an undetectable postoperative prostate-specific antigen (PSA) level following surgery were included. Patients with metastatic disease, Gleason score ≤5, those who had received neoadjuvant chemotherapy, hormonal therapy, or radiotherapy, those receiving adjuvant postoperative chemotherapy, radiotherapy, or hormonal therapy, and patients who failed to achieve an undetectable postoperative PSA level were excluded.

Patients were initially evaluated with serum PSA measurement three months after radical prostatectomy. Only patients with undetectable PSA levels at this assessment were enrolled for long-term follow-up. Thereafter, serum PSA estimation and digital rectal examination were performed every three months during the first postoperative year, every six months during the second year, and annually thereafter. Biochemical recurrence was defined as two consecutive serum PSA measurements ≥0.2 ng/mL. Patients with biochemical recurrence underwent radionuclide bone scintigraphy and other appropriate imaging studies when clinically indicated to detect distant metastasis. Radiological or histopathological evidence of metastatic disease was considered confirmation of distant recurrence.

Statistical Analysis

Data were analyzed using appropriate statistical software. Continuous variables were expressed as median with minimum, maximum, and interquartile range (IQR), while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using the Mann-Whitney U test for non-parametric continuous variables and the Chi-square or Fisher's exact test for categorical variables. Cox proportional hazards regression analysis was used to identify independent predictors of biochemical recurrence following radical prostatectomy. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Baseline demographic and pathological characteristics (n = 116)

Variable	N	%
Age group		
<60 years	32	27.6
≥60 years	84	72.4
Pathological stage		
pT2	76	65.5
pT3	40	34.5

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A total of 116 patients who underwent radical prostatectomy for clinically localized prostate cancer were included in the study. The mean age was 67 years (range: 48–76 years). Most patients (72.4%) were older than 60 years. On final histopathological examination, 76 patients (65.5%) had organ-confined disease (pT2), while 40 patients (34.5%) had locally advanced disease (pT3).

Table 2: Distribution of Gleason score

Gleason score	n	%
6	24	20.7
7	56	48.3
• 3+4	22	39.3*
• 4+3	34	60.7*
8	24	20.7
9	12	10.3

Percentage calculated among Gleason 7 patients.

The majority of patients had a Gleason score of 7 (48.3%). Among these, Gleason 4+3 was more frequent than Gleason 3+4.

Table 3: Comparison of continuous tumor characteristics according to pathological stage

Variable	pT2 Median (IQR)	pT3 Median (IQR)	P value
PSA (ng/mL)	7.15 (5.27)	16.30 (21.80)	<0.001
Tumor volume (%)	10 (15)	40 (55)	<0.001
Gleason score	6 (1)	7 (2)	<0.001

Patients with pT3 disease had significantly higher preoperative PSA levels, larger tumor volumes, and higher Gleason scores than those with pT2 disease. Advanced pathological stage was significantly associated with elevated PSA, increased tumor volume, and higher Gleason score.

Table 4: Association between pathological stage and adverse histopathological features

Variable	pT2 n (%)	pT3 n (%)	P value
Perineural invasion	50 (65.8)	40 (100)	0.002
Seminal vesicle invasion	0 (0)	18 (45.0)	<0.001
Extraprostatic extension	16 (21.1)	36 (90.0)	<0.001
Positive surgical margin	26 (34.2)	36 (90.0)	<0.001
Lymphovascular invasion	0 (0)	10 (25.0)	0.003
HGPIN	60 (78.9)	30 (75.0)	0.645
Necrosis	0 (0)	4 (10.0)	0.115
High-grade tertiary pattern	8 (10.5)	2 (5.0)	0.005

Perineural invasion, seminal vesicle invasion, extraprostatic extension, lymphovascular invasion, and positive surgical margins were significantly associated with pT3 disease, whereas HGPIN and necrosis were not.

Table 5: Distribution of pathological features during follow-up (n = 94)

Variable	n	%
Perineural invasion	78	83.0
HGPIN	67	71.3
Extraprostatic extension	22	23.4
Positive surgical margin	48	51.1
Lymphovascular invasion	6	6.4
Necrosis	3	3.2
Seminal vesicle invasion	12	12.8

Among the 116 patients, 94 (81.0%) were available for follow-up with a median follow-up duration of 14 months. Sixteen patients were lost to follow-up, and six patients died during the study period, including three deaths unrelated to prostate cancer. Perineural invasion and HGPIN were the most frequently observed pathological findings during follow-up.

Table 6: Biochemical recurrence according to Gleason score

Gleason score	BCR (n)	%	Time to BCR (months)	PSADT (months)
6	8	21.1	48–108	24–48
7	8	21.1	48–72	12–48
8	10	26.3	12–60	6–12
9	12	31.6	3–36	3–9

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Biochemical recurrence (BCR) occurred in 38 patients (32.8%), with a median recurrence time of 19 months. Higher Gleason scores were associated with earlier recurrence and shorter PSA doubling time (PSADT).

Table 7: Biochemical recurrence by pathological stage

Stage	No BCR n (%)	BCR n (%)
pT2 (n=66)	43 (69.7)	23 (30.3)
pT3 (n=28)	13 (46.4)	15 (53.6)

Biochemical recurrence was more frequent among patients with pT3 disease than those with pT2 disease.

Table 8: PSA doubling time in patients with biochemical recurrence (n = 38)

Stage	Patients	PSADT (months)
pT2	23	24–108
pT3	15	3–18

Patients with pT3 disease demonstrated substantially shorter PSA doubling times, indicating more aggressive tumor biology.

Table 9: Cox proportional hazards regression analysis for biochemical recurrence

Variable	HR (95% CI)	P value
PSA level	1.04 (1.01–1.05)	0.001
Tumor volume	1.03 (1.02–1.07)	<0.001
Gleason score	2.27 (1.51–3.40)	<0.001
Extraprostatic extension	7.42 (2.07–26.47)	0.002
Positive surgical margin	13.35 (1.76–101.39)	0.012
Seminal vesicle invasion	14.13 (4.71–42.41)	<0.001
Lymphovascular invasion	3.36 (1.11–10.03)	0.032
Necrosis	4.12 (1.29–13.12)	0.017
Age	NS	0.889
Perineural invasion	NS	0.116
HGPIN	NS	0.388
Tertiary pattern	NS	0.685

Elevated preoperative PSA, larger tumor volume, higher Gleason score, extraprostatic extension, seminal vesicle invasion, lymphovascular invasion, positive surgical margins, and tumor necrosis were independent predictors of biochemical recurrence. Age, HGPIN, perineural invasion, and tertiary Gleason pattern were not significantly associated with recurrence.

DISCUSSION

The present study evaluated the clinicopathological factors associated with pathological stage and biochemical recurrence (BCR) following radical prostatectomy in 116 patients with clinically localized prostate cancer. Among the variables studied, preoperative PSA, tumor volume, Gleason score, extraprostatic extension (EPE), seminal vesicle invasion (SVI), positive surgical margins (PSM), lymphovascular invasion (LVI), and tumor necrosis demonstrated significant associations with adverse pathological features and recurrence, whereas age, high-grade prostatic intraepithelial neoplasia (HGPIN), perineural invasion (PNI), and tertiary Gleason pattern were not independent predictors of BCR.

Age has been inconsistently associated with prostate cancer aggressiveness in previous studies. While some investigators have reported poorer outcomes with increasing age, others have found no independent association between age and disease progression. In the present study, age was not significantly associated with biochemical recurrence (p=0.889), indicating that chronological age alone may not predict recurrence following radical prostatectomy. This finding supports the concept that tumor biology rather than patient age is the principal determinant of prognosis.[7,8]

Tumor volume remains an important indicator of disease burden. Consistent with previous reports, larger tumor volume was significantly associated with advanced pathological stage and biochemical recurrence. Patients with pT3 disease had substantially greater tumor volumes than those with pT2 disease, and tumor volume emerged as an independent predictor of recurrence on Cox regression analysis (p<0.001). These findings emphasize the importance of tumor extent in predicting postoperative outcomes.[9]

Gleason score continues to be one of the strongest prognostic indicators in prostate cancer. Nearly half of the patients in the present study had Gleason score 7 disease, with Gleason 4+3 being more frequent than Gleason 3+4. Increasing Gleason score was associated with higher pathological stage, earlier biochemical recurrence, and shorter PSA doubling time (PSADT). Multivariate analysis further confirmed Gleason score as an independent predictor of recurrence (HR=2.27, p<0.001). Patients with Gleason scores 8 and 9 demonstrated

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the earliest recurrence and most rapid PSADT, highlighting the aggressive biological behavior of poorly differentiated tumors.

Extraprostatic extension represents local tumor spread beyond the prostatic capsule and is an established adverse prognostic factor. In this study, EPE was significantly more common in pT3 tumors (90%) and independently predicted biochemical recurrence (HR=7.42, p=0.002). These findings are consistent with previous studies demonstrating that capsular extension reflects aggressive disease and increased likelihood of postoperative recurrence.[8,9,10]

Positive surgical margins were identified in over half of the follow-up cohort and were significantly associated with both pathological stage and recurrence. Multivariate analysis demonstrated that PSM independently increased the risk of biochemical recurrence (HR=13.35, p=0.012). Although the extent and location of margin positivity were not analyzed separately, the findings reinforce the prognostic importance of achieving complete surgical excision during radical prostatectomy.

Perineural invasion was frequently observed, particularly in pT3 disease, where all patients demonstrated PNI. Although significantly associated with advanced pathological stage, PNI did not independently predict biochemical recurrence (p=0.116). Similar observations have been reported in several contemporary studies, suggesting that PNI reflects aggressive pathological characteristics but loses independent prognostic significance after adjustment for established clinicopathological variables.[11,12]

Tumor necrosis was observed in only a small proportion of patients, predominantly among those with advanced disease. Although necrosis was not significantly associated with pathological stage, it independently predicted biochemical recurrence (HR=4.12, p=0.017). Because of the small number of affected cases, this observation should be interpreted cautiously but suggests that necrosis may reflect highly aggressive tumor biology.

A high-grade tertiary Gleason pattern was identified in only ten patients and showed a significant association with pathological stage but not with recurrence. The absence of recurrence among the limited number of patients available for follow-up likely reflects inadequate statistical power rather than a lack of biological significance. Larger studies with longer follow-up are required to clarify its prognostic value.

The present study has several limitations. First, the median follow-up duration was relatively short, which may have underestimated late biochemical recurrence. Second, the single-center design and modest sample size limit the generalizability of the findings. Third, positive surgical margins were not categorized according to focal or extensive involvement, and extraprostatic extension was not quantified by extent. Finally, uncommon pathological variables such as tumor necrosis and tertiary Gleason pattern were present in relatively few cases, reducing the statistical power to determine their true prognostic significance. Future multicenter studies with larger cohorts and longer follow-up are warranted to validate these observations.

CONCLUSION

This study demonstrates that preoperative PSA level, tumor volume, Gleason score, extraprostatic extension, seminal vesicle invasion, positive surgical margins, lymphovascular invasion, and tumor necrosis are significant predictors of biochemical recurrence following radical prostatectomy. Among these, Gleason score, pathological stage, and tumor volume remain the most important prognostic indicators for postoperative risk stratification and treatment planning. Although perineural invasion was strongly associated with advanced pathological stage, it did not independently predict recurrence, while high-grade prostatic intraepithelial neoplasia showed no significant prognostic value. Lymphovascular invasion and tumor necrosis, though less frequently encountered, were independently associated with recurrence and may serve as additional markers of aggressive disease. Patients with advanced pathological stage also exhibited shorter PSA doubling times, reflecting a /higher risk of disease progression. Overall, comprehensive pathological evaluation combined with PSA monitoring provides valuable prognostic information for identifying patients at increased risk of recurrence and guiding postoperative surveillance and individualized management after radical prostatectomy.

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