



Can Invasion of the Vas Deferens be Considered a Prognostic Marker in pT3b Prostate Cancer?

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¹University of Health Sciences Türkiye, Ankara Etlik City Hospital, Department of Urology, Ankara, Türkiye

²Ankara University Faculty of Medicine, Department of Urology, Ankara, Türkiye

³Ankara University Faculty of Medicine, Department of Pathology, Ankara, Türkiye

Abstract

Objective: To assess the impact of vas deferens invasion (VDI) on prognosis, as well as clinical and pathological outcomes in patients with pT3b prostate cancer.

Materials and Methods: Patients reported as pT3b between 2010 and 2020 were included in the study. Patients were divided into two groups: Group 1 (VDI-) and Group 2 (VDI+). Biochemical recurrence-free survival (BCRFS) was compared using the Kaplan-Meier method with the log-rank test. Univariate and multivariate regression models were used to investigate the relationship between VDI and the risk of BCR.

Results: The study included 199 patients with seminal vesicle invasion (SVI) on radical prostatectomy (RP) pathology. VDI was detected in 95 patients (47.7%). No differences were found between the two groups with respect to clinical and perioperative factors, including age, preoperative prostate-specific antigen (PSA), prostate volume, PSA density, biopsy International Society of Urological Pathology (ISUP) grade, clinical N stage, preoperative European Association of Urology risk group, surgery type (open or robotic), nerve-sparing approach, surgical margin status, number of resected lymph nodes (LN), and pathological LN positivity rates. The VDI+ group exhibited higher rates of extraprostatic extension and bilateral SVI, and a more advanced ISUP grade in RP pathology ($p<0.05$). The number of patients who received adjuvant hormone therapy was higher in the VDI+ group. Sixth-week PSA values were higher in the VDI+ group ($p<0.05$). No significant difference in BCRFS was observed (log-rank test; $p=0.127$). In multivariate logistic regression analysis, pN+ and RP ISUP grade were found to be significant predictors of BCR ($p<0.05$).

Conclusion: Although the current study found that patients with VDI had lower BCRFS, the difference was not statistically significant. This condition may result from disparities in adjuvant treatments and other clinicopathological variables. Since the effect of VDI on prognosis in pT3b patients is not known, the results should be interpreted with caution. Patients with T3b prostate cancer may exhibit heterogeneous survival rates. Therefore, the indication of VDI in the pathology report appears to be an important consideration that can guide patient management.

Keywords: Biochemical recurrence, prostate cancer, seminal vesicle, survival, vas deferens

Introduction

Pathologic T stage, pathologic N stage, surgical margin positivity, and Gleason grade in radical prostatectomy (RP) specimens are significant predictors of biochemical recurrence (BCR) following RP (1,2). The presence of seminal vesicle invasion [(SVI); pT3b] is also a significant prognostic factor, and the prognosis differs significantly from that of extraprostatic invasion (pT3a). Even though it is an organ adjacent to the prostate, SVI can also be considered an independent organ invasion. The likelihood of

recurrence and lymph node (LN) invasion is higher in cases with SVI (3). The prognostic significance of seminal vesicle invasion is well established; however, the prognostic implications of vas deferens invasion (VDI), an adjacent structure to the prostate and seminal vesicles, remain unclear. The scarcity of research in this field is likely due to the fact that vas deferens sampling is not routinely recommended (4) and VDI by prostate cancer is a relatively uncommon event (5). Nevertheless, VDI is extremely rare in pT2 and pT3a stages, with most cases occurring in patients with pT3b or pT4 disease (6). The primary pathway

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Address for Correspondence: Ahmet Furkan Özsoy, MD, Ankara University Faculty of Medicine, Department of Urology, Ankara, Türkiye

E-mail: furkanozsoy22@gmail.com **ORCID:** orcid.org/0000-0001-8134-7484

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of SVI is extraprostatic extension (EPE) of prostate carcinoma into the soft tissue adjacent to the ipsilateral seminal vesicle (7). This indicates that invasion of the vas deferens, which is located adjacent to the seminal vesicle, may occur via EPE. However, the histological structures of the seminal vesicle and the vas deferens are quite different; the vas deferens is firmer and more durable, suggesting that invasion of the vas deferens may be more difficult. Therefore, we suspect that tumors infiltrating the vas deferens may exhibit more aggressive features. In this study, we investigated whether VDI affects biochemical recurrence-free survival (BCRFS) in pT3b patients.

Materials and Methods

Patient Population

This study was approved by the Ankara University Human Research Ethics Committee (decision no: İ03-264-24, date: 22.04.2024). After institutional review board approval, the medical records of the patients who had undergone RP at a tertiary referral academic center between 2010 and 2020 and who were reported as pT3b were retrospectively reviewed. Of 1376 patients who had RP, 307 classified as pT3b were assessed for inclusion in the study. Patients with at least twelve core biopsies were included in the study. Patients who received neoadjuvant treatments or had inadequate follow-up data were excluded. Additionally, patients whose VDI status was unreported or inconsistently assessed were excluded from the study. A total of 199 patients with pT3b prostate cancer were included in the study. Patients were categorized into two groups based on the presence or absence of invasion of the VDI. Preoperative staging was performed according to the 8th edition of the tumor-node-metastasis classification. The grade category was assigned according to the 2014 International Society of Urological Pathology (ISUP) grading system. Patients in both groups were classified according to European Association of Urology (EAU) risk groups (low, intermediate, high, and locally advanced) based on their clinical characteristics.

Postoperative prostate-specific antigen (PSA) monitoring begins 6-8 weeks after RP and is performed every three months for the ensuing two years, then every six months. BCR is defined as two consecutive increases in PSA, with the last PSA being ≥ 0.2 ng/mL following RP.

Pathological Analysis

Two expert uropathologists (S.K. and D.E.) at our institute performed the pathological analysis of RP specimens. The RP grossing protocol in our pathology laboratory is as follows: specimens are fixed in 10% neutral buffered formalin overnight and labeled with two colors of ink for anatomical orientation. After fixation, the specimen is weighed and the dimensions of the prostate, seminal vesicles, and bilateral vas deferens are recorded. The apex and base are coned, following the ISUP consensus recommendations. Serial 4 mm sagittal sections, from apex to base, are oriented according to their anatomical positions (right, left, anterior, and posterior) and embedded as whole mounts. As with the prostate, the bilateral seminal vesicles and vas deferens are excised and submitted in their entirety. The surgical margins of the bilateral vas deferens are also submitted separately.

Microscopic evaluation includes sketching the entire specimen and tumor to fully document tumor localization and extent. The reporting of RP specimens is performed in accordance with the College of American Pathologists protocols (version: 4.2.0.0, June 2021). The histological type of the carcinoma, modified Gleason score, ISUP prognostic grade group, tumor volume, EPE, lymphovascular invasion, perineural invasion, seminal vesicle involvement, vas deferens involvement, margin status, and pathological stage are included in the final pathology report.

Statistical Analysis

The Mann-Whitney U test was applied to compare clinicopathological characteristics between groups for continuous variables, and the chi-square test was applied to compare categorical variables between groups. The Kaplan-Meier method and the log-rank test were used to estimate and compare BCRFS between groups. Additionally, univariate and multivariate Cox proportional hazards models were used to evaluate associations between variables and the risk of BCR. The multivariate model was constructed by incorporating significant variables from the univariate analysis. Statistical significance was assigned to comparisons with p-values of less than 0.05.

Results

A total of 199 patients reported as pT3b were included in the study. VDI was detected in 95 patients (47.7%) (Table 1). Preoperative patient characteristics are presented in Table 1. We were unable to demonstrate a statistically significant difference between groups in clinicopathological features such as age, American Society of Anesthesiology scores, preoperative PSA, prostate volumes, biopsy ISUP grades, and preoperative EAU risk groups ($p > 0.05$; Table 1). The time from biopsy to RP was longer in the VDI- group than in the VDI+ group (Table 1, 60 vs. 50 days, $p = 0.043$).

Perioperative and postoperative patient characteristics are outlined in Table 2. The median follow-up time of the patients in the VDI- and VDI+ groups was 65 months [interquartile range (IQR), 45-107 months] and 61 months (IQR, 39-86 months), respectively (Table 2, $p = 0.076$). The VDI+ group exhibited a greater degree of EPE and bilateral seminal vesicle invasion. In the RP specimens, EPE was identified in all but one patient in the VDI+ group, compared with 94 patients (90.4%) in the VDI- group. (Table 2, $p = 0.008$). While 43% of patients in the VDI- group had bilateral seminal vesicle invasion, 82% of patients in the VDI+ group did (Table 2, $p < 0.001$). The VDI+ group had a higher number of ISUP grade 5 patients, resulting in a significant difference in RP ISUP grades between the two groups (Table 2, $p = 0.001$). Although surgical margin positivity and pathologic LN positivity were higher in the VDI+ group, these differences did not reach statistical significance. The median PSA values at postoperative week 6 were significantly higher in the VDI+ group (Table 2; 0.04 vs. 0.14; $p < 0.001$). Although 61% of patients in the VDI- group received adjuvant RT, only 47% of patients in the VDI+ group did (Table 2, $p = 0.051$). Conversely, more patients in the VDI- group received than in the VDI+ group (Table 2, 44% vs. 77%, $p < 0.001$). BCR was detected

Parameters	Vas deferens invasion (-) n=104 (52.3%)	Vas deferens invasion (+) n=95 (47.7%)	p-value
Age, year, mean ± SD	71.51±7.55	69.71±6.8	0.08
Preoperative PSA, median (IQR)	10.7 (7.6-26.6)	15 (7.1-23.7)	0.368
Prostate MRI volume, median (IQR)	43 (32-58)	45 (37-60)	0.329
PSA density	0.28 (0.15-0.54)	0.31 (0.16-0.67)	0.622
ASA score ASA 1 ASA 2 ASA 3	43 (41.1%) 59 (56.7%) 3 (2.2%)	49 (51.1%) 44 (46.6%) 2 (2.3%)	0.397
Biopsy ISUP grade group 1 2 3 4 5	16 (15.4%) 29 (27.9%) 23 (22.1%) 21 (20.2%) 15 (14.4%)	15 (15.8%) 16 (16.8%) 29 (30.5%) 13 (13.7%) 22 (23.2%)	0.121
Preoperative EAU risk group Low Intermediate High Locally advanced	9 (8.5%) 37 (35.3%) 44 (41.9%) 15 (14.3%)	8 (8.4%) 25 (26.3%) 48 (50.5%) 14 (14.7%)	0.612
Time from biopsy to RP day, median (IQR)	60 (42-90)	50 (39-65)	0.043

Student's t-test, Mann-Whitney U test, chi-square
SD: Standard deviation, PSA: Prostate-specific antigen, IQR: Interquartile range, ISUP: International Society of Urological Pathology, RP: Radical prostatectomy, EAU: European Association of Urology, ASA: American Society of Anesthesiologists, MRI: Magnetic resonance imaging

in 34 patients (32.7%) in the VDI- group and in 38 patients (40%) in the VDI+ group (Table 2, p=0.284).

The 5-year BCRFS rates were 67% [confidence interval (CI): 58-76] and 60% (CI: 50-70) for the VDI- and VDI+ groups, respectively. Kaplan-Meier curves demonstrated no statistically significant difference in BCRFS between the 2 groups (log-rank p=0.127; Figure 1).

Cox regression models were applied to analyze the association between VDI and the risk of BCR. VDI was not associated with BCR on uni- and multivariate analysis (Table 3, p=0.3 and 0.8, respectively). Bilateral seminal vesicle invasion (p=0.006) in RP pathology, ISUP grade group 3 in biopsy (p=0.033), ISUP grade group 2 (p=0.004) and ISUP group 3 (p=0.002) in RP specimen, and pathologic LN positivity (p=0.001) were all significantly associated with BCR on univariate analysis (Table 3). On multivariate regression analysis, pathological ISUP grade groups 2 [hazard ratio (HR): 13, 95% CI: 2.3-71.4; p=0.04] and 3 (HR: 7.2, 95% CI: 1.5-33.3; p=0.012) on RP pathology, and pathological LN positivity (HR: 2.5, 95% CI: 1.3-4.5; p=0.004) were found to be significant predictors of BCR (Table 3).

Discussion

This study examines the prognostic significance of invasion of the vas deferens in patients with pT3b prostate cancer. BCR-free survival was lower in patients with VDI; however, the difference was not statistically significant. Cox regression analysis of BCR-related factors revealed that VDI was not associated with BCR. Pathological ISUP grade group in the RP specimen and pathological LN positivity were significant predictors of BCR.

Sampling of the vas deferens is not a mandatory step in the routine pathologic examination of RP specimens. Additionally, at the ISUP consensus conference reviewing the pathologic evaluation of RP specimens, it was noted that although almost half of the pathologists examined for and reported VDI, the consensus was that routine sampling of the vas deferens was not mandatory (4). An important reason for sampling the vas deferens is to evaluate the surgical margin. The rationale is that pathologists performing vas deferens sampling consider this area to be also the surgical margin of the specimen. However, the current study was planned not only because the vas deferens is the surgical margin but also because it is a distinct organ whose invasion may have prognostic significance. We support routine VD sampling in all cases because it serves both as a surgical margin and, it is believed, has prognostic significance. Because existing literature on this topic is inadequate, it is not possible to make a definitive recommendation about whether to perform VD sampling based solely on the results of this study.

Although a positive surgical margin is significant for prognosis, it is possibly not the most critical factor. Accordingly, pathologic T stage, pathologic N stage, and Gleason grade seem to be more significant prognostic factors. Würnschimmel et al. (1) presented their 20-year study of oncological outcomes in patients with localized prostate cancer at Martini-Klinik. As expected, the lowest BCRFS, metastasis-free survival, and cancer-specific survival were observed in the very high-risk group according to the National Comprehensive Cancer Network risk classification. Additionally, a survival analysis was conducted by integrating pathologic T stage and surgical margin status. The lowest BCRFS was observed in patients exhibiting seminal

Parameters	Vas deferens invasion (-) n=104 (52.3%)	Vas deferens invasion (+) n=95 (47.7%)	p-value
Follow up time, month, median (IQR)	65 (45-107)	61 (39-86)	0.076
Surgical procedure			
Open	59 (56.7%)	55 (57.9%)	0.629
Robotic	45 (43.3%)	40 (42.1%)	
Nerve sparing surgery			
No	82 (78.6%)	63 (66.3%)	0.074
Yes	22 (21.4%)	32 (33.7%)	
Extraprostatic extension			
No	10 (9.6%)	1 (1.1%)	0.008
Yes	94 (90.4%)	94 (98.9%)	
Seminal vesicle invasion			
Unilateral	59 (57.3%)	17 (17.9%)	<0.001
Bilateral	45 (43.2%)	78 (82.1%)	
ISUP grade at final pathology			
1	7 (6.7%)	-	0.001
2	18 (17.3%)	14 (14.7%)	
3	26 (25%)	28 (29.5%)	
4	17 (16.4%)	4 (4.2%)	
5	36 (34.6%)	49 (51.6%)	
Positive surgical margin, n (%)			
Yes	43 (41.3%)	45 (47.4%)	0.393
No	61 (58.7%)	50 (52.6%)	
Pathological lymph node status			
pNO	67 (64.4%)	50 (52.6%)	0.156
pN+	37 (35.6%)	45 (47.4%)	
Number of removed LNs, median (IQR)	13 (9-20)	14 (12-20)	0.086
Number of positive LNs, median (IQR)	1 (0-2)	2 (0-4)	0.202
Postoperative 6th week PSA, median (IQR)	0.04 (0.01-0.17)	0.14 (0.02-0.87)	<0.001
Adjuvant radiotherapy			
Yes	64 (61.5%)	45 (47.4%)	0.051
No	49 (38.5%)	50 (52.6%)	
Adjuvant hormonotherapy			
Yes	46 (44.2%)	73 (76.8%)	<0.001
No	58 (55.8%)	22 (23.2%)	
BCR			
Yes	34 (32.7%)	38 (40%)	0.284
No	70 (67.3%)	57 (60%)	

Student's t-test, Mann-Whitney U tests, chi-square tests
 PSA: Prostate-specific antigen, IQR: Interquartile range, BCR: Biochemical recurrence, LN: Lymph node, ISUP: International Society of Urological Pathology, RP: Radical prostatectomy, EAU: European Association of Urology, ASA: American Society of Anesthesiologists

vesicle invasion (pT3b) and positive surgical margins (R1), and higher grade group correlated with poorer survival rates (1). It has also been shown that having 3 or more LNs decreases survival. In the multivariable Cox regression analysis examining the associations of these factors with BCR, Gleason grade group 4-5 (HR: 1.6), pT3a (HR: 2.5), pT3b (HR: 4.5), R1 (HR: 1.3), and pN1 (HR: 1.7) tumors were identified as significant risk factors for increased BCR (1). We can infer that seminal vesicle invasion is the most hazardous scenario identified in this study. While Würnschimmel et al.'s (1) study included a more pathologically diverse patient population, our study focused exclusively on patients with pathologic SVI, which was the patient group with the largest HR in that study. Despite the differences in samples, the findings of our study generally align with existing literature. We found that bilateral SVI was associated with BCR in univariate analysis; however, it was not statistically significant

in multivariate analysis. We can conclude that bilateral SVI does not pose an additional disadvantage with respect to BCR. In contrast to our study, the current literature indicates that bilateral SVI is associated with BCR (8,9). The study by Suh et al. (8) showed that bilateral SVI correlated with BCR, yielding a p-value of 0.049. However, the relatively low (HR: 1.197) in this study suggests that the associated risk remains minimal (8). Likewise, the study by Lee et al. (9) which involved 93 patients, identified a significant association between bilateral SVI and BCR in multivariate analysis, with a p-value of 0.047. Nonetheless, this study's small patient sample and limited p-value hinder drawing definitive conclusions about the effects of bilateral SVI on prognosis.

Another critical aspect of our study is that the pathological ISUP grade was significantly associated with BCR in multivariate

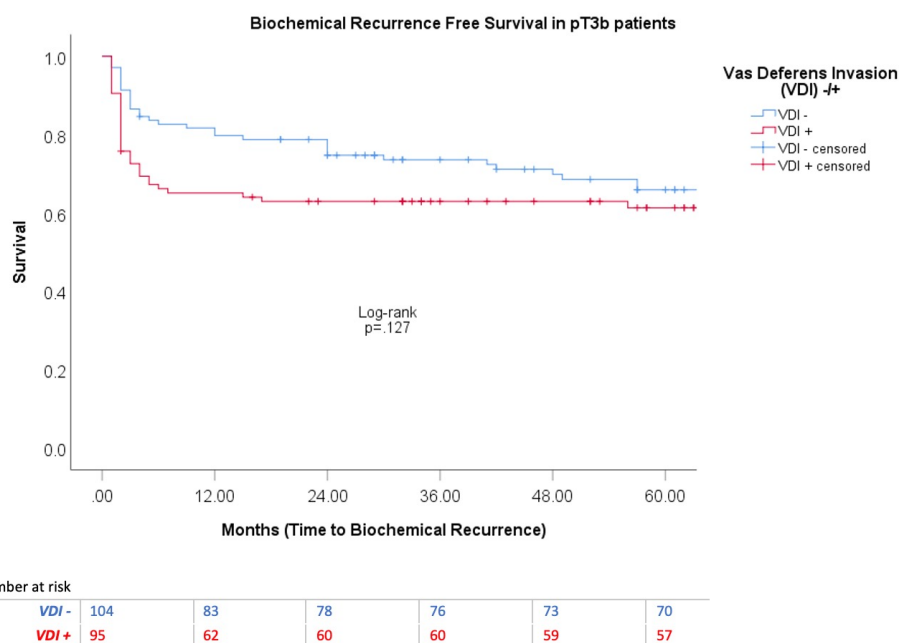


Figure 1: Biochemical recurrence free-survival Kaplan-Meier curve

	Biochemical recurrence (BCR)			
	Univariate analysis	Multivariate analysis		
	p-value*	HR	95% CI	p-value**
Age	0.2	0.982	0.947-1.018	0.4
Preoperative PSA	0.7	0.983	0.965-1.001	0.06
Biopsy ISUP grade groups				
ISUP grade 1	Reference	Reference		
ISUP grade 2	0.1	2.481	0.920-6.666	0.07
ISUP grade 3	0.033*	1.063	0.411-2.405	0.9
ISUP grade 4	0.6	1.754	0.642-4.784	0.3
ISUP grade 5	0.8	2.512	0.909-6.944	0.08
Bilateral seminal vesicle invasion	0.006*	1.757	0.962-3.245	0.063
Vas deferens invasion	0.3	1.093	0.621-1.924	0.8
ISUP grade at final pathology				
ISUP grade 1	Reference	Reference		
ISUP grade 2	0.1	12.987	2.320-71.428	0.04**
ISUP grade 3	0.004*	7.194	1.555-33.333	0.012**
ISUP grade 4	0.002*	3.875	0.645-15.151	0.2
ISUP grade 5	0.8	3.875	0.865-17.241	0.08
Positive surgical margin	0.1	1.146	0.665-1.975	0.6
Pathological lymph node positivity	0.001*	2.471	1.343-4.546	0.004**
Surgical procedure (open/robotic)	0.7	1.131	0.654-1.955	0.6

*: Univariate logistic regression analysis, **: Multivariate logistic regression analysis, HR: Hazard ratio, CI: Confidence interval, ISUP: International Society of Urological Pathology, PSA: Prostate-specific antigen

analysis, corroborating existing literature. Numerous studies have shown that higher ISUP grade groups are significantly associated with an increased risk of BCR (1,10). The absence of an association between pathologic ISUP grades 4 and 5 and BCR in our study may be attributable to other coexisting risk

factors in patients with these grades, including pathologic LN involvement, bilateral seminal vesicle invasion, and positive surgical margins. Given that the risk of BCR is already significantly elevated in patients with these characteristics, ISUP grades 4 and 5 may not further augment the risk of BCR. Multivariate analysis

of our study also demonstrated that pathologic LN positivity is one of the main risk factors for BCR. Pathologic LN positivity is a well-established risk factor for BCR in the literature (1,11). Although the effects of these factors on oncologic outcomes are well known, the impact of VDI by prostate cancer on oncologic outcomes remains unclear. Current knowledge reveals a scarcity of studies examining the impact of VDI on survival outcomes. Jang et al. (12) investigated the impact of VDI on oncological outcomes in patients with pT3b prostate cancer. The authors found that almost a quarter of the 350 pT3b prostate cancer patients had VDI; this group had worse 5-year BCRFS than the group without VDI (12). Additionally, VDI emerged as a significant predictor of BCR in the multivariate Cox analysis, with a HR of 1.39 ($p=0.039$) (12). In contrast, we observed that VDI did not affect BCRFS in our study, which was methodologically similar to this study. This difference between the two studies may be attributed to two reasons. The relatively low number of patients, a limitation of our study, may have contributed to this difference. To us, another significant factor is the exclusion of patients who received adjuvant treatment in the study by Jang et al. (12) In the current study, patients who underwent adjuvant treatment were included and examined. As is well known, adjuvant therapies are recommended by guidelines for locally advanced disease (2). The higher incidence of adjuvant HT among patients in the VDI+ group may account for the observed lower BCR within that cohort.

In a study, Saar et al. (6) examined the prevalence and extent of surgical-margin involvement of the vas deferens in 2701 consecutive RP specimens from two institutions. Of the 41 patients with positive VD surgical margins, the majority were classified as pT3b, one was pT3a, and six were pT4. The authors stated that although VD surgical margin positivity is rare, this region may sometimes be the only site of positive surgical margins. Consequently, they highlighted the significance of VD sampling. The distal segment of the vas deferens and the surgical margin are frequently investigated by pathological examination. Gözen et al. (5) investigated preperitoneal and distal VD samples in high-risk prostate cancer patients. A total of 332 individuals were sampled from the VD region between the internal inguinal ring and the obturator fossa. Among 130 pT3b patients, 18 patients (14%) exhibited distal VDI, and 1 patient presented with preperitoneal VDI. Conversely, among 104 pT3a patients, patient 1 demonstrated distal VDI and 1 patient showed preperitoneal VDI. In pT3b patients, distal VDI did not correlate with an increased risk of positive surgical margins or nodal disease. However, 2 patients with preperitoneal VDI exhibited bilateral distal VDI and features of highly aggressive disease. Of the 2 patients with preperitoneal VDI, 1 had seminal vesicle invasion, while the other did not. This also serves as a clear example that VDI can occur independently of SVI. Another study by Nguyen et al. (13) reported that local recurrences following RP were observed at the vas deferens resection site in 22% of cases. Although the study is limited by lack of specification of VDI in RP material, histological evidence at the recurrence site indicates that the majority of local recurrences arise at the anastomotic site. Therefore, the 22% rate of vas deferens involvement is noteworthy. Notably, one-third of patients with recurrence at the site of VD resection were

classified as pT2, nearly half as pT3, and almost half had the primary tumor located at the apex. The presence of recurrences in this region strongly suggests that VDI in RP specimens may have prognostic significance.

The pathology community defines invasion of the seminal vesicle as involvement of muscular tissue within the seminal vesicle wall (4,14). Ohori et al. (14) identified three distinct mechanisms for seminal vesicle invasion. type-1 involves direct internal spread along the ejaculatory duct complex into the seminal vesicles. Tumor migration does not occur within the lumen of the ejaculatory duct; instead, it invades the surrounding tissue. type-2 involvement extends beyond the prostate, penetrating the capsule and infiltrating the muscular layer of the seminal vesicle. Involvement may occur directly across the tissue plane between the base of the prostate and the seminal vesicles. The presence of isolated foci of cancer in the seminal vesicle, without direct continuity to the primary tumor, characterizes type-3 involvement. In 2007, Billis et al. (7) showed that the primary pathway of SVI is the EPE of prostate carcinoma into the soft tissue adjacent to the ipsilateral seminal vesicle, leading to infiltration of the seminal vesicle wall. The prevalence of invasion via EPE suggests that the vas deferens, located adjacent to the seminal vesicle, is also susceptible to this route. However, the histological structures of the seminal vesicle and the vas deferens are distinct. The consistency of the VD is considerably different and markedly harder than that of the adjacent structures and periprostatic tissues (15). Based on these findings, we can interpret that the muscular layer of the VD serves as a more resistant barrier to tumor invasion, similar to arterial walls. The biochemical behavior and clinical presentation of a tumor invading the VD are expected to be more aggressive. In this context, higher postoperative PSA levels, EPE rates, bilateral SVI rates, and ISUP grades at the final pathology in the VDI+ group in the current study indicate a potentially more aggressive disease course for this group of patients. However, the classification of tumors with VD invasion remains unclear due to a lack of comprehensive literature on the subject. Should these tumors be interpreted as EPE only, or as involvement of adjacent organs other than the seminal vesicle? Given the disparity in prognosis between the two groups, it is essential to clarify this issue.

The present study has some limitations, including its retrospective design and small sample size, because it was conducted at a single center and focused on a specific patient population. Although VD was fully sampled in all cases, the omission of the VD length measurement could be considered an additional limitation.

Conclusion

Patients with pT3b prostate cancer may have different survival rates depending on VD invasion status. This study revealed a difference in BCRFS between the groups with and without VDI, although it was not statistically significant. However, the results should be interpreted with caution, keeping in mind that this may be due to differences in adjuvant treatments and other clinical and pathologic parameters between the two groups. Since VDI may have prognostic significance, we recommend routine sampling of VD during RP. In order to draw more

definitive conclusions on this issue, prospective, multicenter studies with larger patient populations are needed.

Ethics

Ethics Committee Approval: This study was approved by the Ankara University Human Research Ethics Committee (decision no: 103-264-24, date: 22.04.2024).

Informed Consent: Retrospective study.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: Ç.G., K.T., S.B., E.S., Concept: Ç.A., E.S., Design: M.A.İ., Data Collection or Processing: M.C.K., A.F.Ö., E.D.S., S.K., D.E., Analysis or Interpretation: E.E., Literature Search: M.C.K., A.F.Ö., Writing: M.C.K.

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