CANCER DIAGNOSIS & PROGNOSIS *5*: 313-318 (2025)
doi: 10.21873/cdp.10443

Preoperative Predictive Factors for Seminal Vesicle Invasion (pT3b) in Robotic-assisted Radical Prostatectomy

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Abstract

Background/Aim: Robot-assisted radical prostatectomy (RARP) outcomes improve with surgical experience, but preoperative prediction of disease stage is crucial to avoid unexpected T stage upgrades, such as pT3b. This study aimed to identify preoperative predictive factors for pT3b (seminal vesicle invasion) following RARP.

Patients and Methods: Out of 299 RARP performed between 2013 and 2020, 246 cases without preoperative hormone therapy were included. Of these, 19 cases (7.7%) were pT3b. T classification was performed using magnetic resonance imaging (MRI), and 12-site prostate biopsies were conducted. Cox proportional hazards, logistic regression analysis, and Kaplan-Meier analyses were used.

Results: The 3-year prostate specific antigen (PSA) recurrence-free survival rate was 87% but significantly lower at 70% for pT3b cases. Multivariate logistic regression analysis identified the International Society of Urological Pathology (ISUP) grade group at biopsy as the only significant preoperative predictor of pT3b.

Conclusion: pT3b is associated with increased postoperative biochemical recurrence risk, and ISUP grade group at biopsy serves as a significant preoperative predictive factor for pT3b.

Keywords: Prostate cancer, robot-assisted radical prostatectomy, seminal vesicle invasion, biochemical recurrence, grade group.

Introduction

In recent years, robotic-assisted radical prostatectomy (RARP) has become the standard procedure for radical prostatectomy (RP) in cases of localized prostate cancer. A systematic review by Novara *et al.* reported that there was no significant difference in positive surgical margins or postoperative biochemical recurrence between RARP, laparoscopic radical prostatectomy (LRP), and retropubic radical prostatectomy (RRP) (1). Subsequently, a randomized controlled trial (RCT) comparing RARP and RRP found that although RARP resulted in shorter hospital

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Received February 25, 2025 | Revised March 18, 2025 | Accepted March 19, 2025

stays and less blood loss, it did not demonstrate superior cancer control outcomes (2). Similarly, a multicenter RCT comparing LRP and RARP showed no significant differences in cancer control (3). In contrast, several studies suggest that surgical experience plays a crucial role in improving oncological outcomes. It has been reported that the rate of positive surgical margins in pT2 cases decreases after approximately 100 RARP cases, while the rate in pT3/4 cases improves after 200-300 cases, indicating that extensive surgical experience may enhance cancer control (4, 5). Despite improved surgical techniques, cases involving seminal vesicle invasion (SVI; pT3b) continue to demonstrate poor prognosis. Among 6,740 radical prostatectomy cases, 566 cases (8.4%) had SVI, with 5-year and 10-year biochemical recurrence-free survival (RFS) rates of 38.0% and 25.6%, respectively (6). Additionally, SVI is associated with a significant incidence of lymph node metastasis, with rates of 12-38% reported during surgery and 26% detected by MRI (7-15). Locally advanced prostate cancer with SVI poses a high risk of recurrence, limiting the efficacy of radical therapy. Therefore, accurate preoperative prediction of SVI is critical to guide treatment strategies and provide information on potential salvage therapy. Given the limited research on predictive factors for SVI in RARP, this study aimed to examine both prognosis and preoperative predictive factors for pT3b cases treated with RARP at our institution.

Patients and Methods

Study participants. This study retrospectively analyzed 246 cases from a total of 299 RARP procedures performed at Showa University Hospital between 2013 and December 2020. This study was approved by Showa University Institutional Review Board (No.22-049-B). Informed consent was obtained by an opt-out approach.

Cases with preoperative hormone therapy were excluded. Among the cases included, 19 (7.7%) were diagnosed with seminal vesicle invasion (SVI, pT3b). Prognostic outcomes and preoperative predictive factors were examined.

Imaging and biopsy procedures. In order to more accurately assess the presence or absence of seminal vesicle invasion preoperatively, T classification was determined using magnetic resonance imaging (MRI). MRI was performed according to the institution's standard protocol. Prostate biopsies were systematically performed at 12 sites transrectally using an 18G needle under local anesthesia.

Statistical analysis. Prostate specific antigen (PSA) recurrence was defined as a persistent increase in PSA levels exceeding 0.2 ng/ml. PSA recurrence-free rates were estimated using the Kaplan-Meier method and compared using the log-rank test. Cox regression analysis was employed to evaluate the impact of SVI on PSA recurrence-free survival rates, while multivariate logistic regression analysis was used to identify preoperative predictive factors for SVI. Statistical analyses were conducted using JMP Pro15 software (SAS Institute, Cary, NC, USA). A p-value of less than 0.05 was considered statistically significant.

Results

Patient characteristics. In the pT3b cases, the median age was 70 years (range=57-78 years), and the median PSA level was 9.47 ng/ml (range=3.50-32.5 ng/ml). According to the National Comprehensive Cancer Network (NCCN) risk classification, one case was classified as very low to low risk, eight cases as intermediate risk, and 10 cases as high to very high risk. Clinical T classifications were distributed as: T1c in three cases, T2 in 15 cases, and T3a in one case. Positive surgical margins were identified in 11 cases (57.9%), and six cases (31.6%) experienced biochemical recurrence. Patients characteristics are presented in Table I.

Recurrence-free survival. The overall 3-year PSA recurrence-free survival rate was 87%, and the 5-year RFS rate was 84%. However, for pT3b cases, the 3-year PSA recurrence-free survival rate was significantly lower at 70%. PSA recurrence-free survival rates, stratified by the presence or absence of SVI, were analyzed using the Kaplan-Meier

Table I. *Patient characteristics.*

		All (n=246)	SVI (n=19)	Non-SVI (n=227)
Age at diagnosis, years, median		69 (53-80)	70 (57-78)	69 (53-80)
PSA at diagnosis (ng/ml), median		7.20 (0.85-57.6)	9.47 (3.50-32.5)	7.51 (0.85-57.6)
ISUP Grade group at biopsy, n (%)	1	72 (29.3)	3 (15.8)	69 (30.4)
	2	75 (30.5)	4 (21.1)	71 (31.3)
	3	37 (15.0)	6 (31.6)	31 (13.7)
	4	51 (20.7)	3 (15.8)	48 (21.1)
	5	11 (44.7)	3 (15.8)	8 (3.5)
Clinical T stage, n (%)	T1-T2a	119 (48.4)	6 (31.6)	113 (49.8)
	T2b	51 (20.7)	6 (31.6)	45 (19.8)
	T2c	67 (27.2)	6 (31.6)	61 (26.9)
	T3a	9 (3.7)	1 (5.3)	8 (3.5)
NCCN risk classification, n(%)	Very low-Low	43 (17.5)	1 (5.3)	42 (18.5)
	Intermediate	137 (55.7)	8 (42.1)	129 (56.8)
	High-Very high	66 (26.8)	10 (52.6)	56 (24.7)
Biopsy positive core rate (%), median		30 (8.3-100)	33 (17-83)	25 (8.3-100)
Observation period, months, median		30 (0-87)	10 (0-64)	32 (0-87)
PSA recurrence, n(%)		40 (16.3)	6 (31.6)	34 (15.0)
Resection margin positive, n(%)		95 (38.6)	11 (57.9)	84 (37.0)
Extraprostatic extension, n(%)		54 (22.0)	16 (84.2)	38 (16.7)

SVI: Seminal vesicle invasion; PSA: prostate specific antigen; ISUP: International Society of Urological Pathology; NCCN: National Comprehensive Cancer Network.

method and compared with the log-rank test (Figure 1). Patients with SVI had a significantly shorter RFS period, with a hazard ration (HR) of 4.07 (p=0.01).

Predictive factors. Multivariate logistic regression analysis revealed that the ISUP grade group at biopsy was the only significant preoperative predictor of SVI. The odds ratio (OR) for ISUP grade group was 1.556 (p=0.027) (Table II).

Discussion

pT3b prostate cancer is defined as cancer that has invaded one or both seminal vesicles (16). Among patients with clinical stage T1-T2 disease, pT3b is detected in 6-26% of cases following radical prostatectomy (9, 17-19). Although the D'Amico risk classification system (20) bases T stage assessment on digital rectal examination, MRI is now recognized as the most effective staging modality. With the increasing use of multiparametric MRI, the number of cases clinically staged as T3b prostate cancer may rise. However, if diagnostic accuracy improves and surgical intervention can be optimized, the number of unexpected pT3b cases may decrease. The spread of robotic-assisted RARP is expected to enhance surgical outcomes for locally advanced prostate cancer. Nevertheless, as previously noted, no evidence has demonstrated that RARP is superior to other surgical techniques in terms of cancer control. Although reports indicate that the incidence of pT3b is decreasing, the survival rates for pT3b cases have not significantly improved. In this study, pT3b status was significantly associated with increased PSA recurrence risk. Ohori *et al.* developed a nomogram that highlights clinical stage, PSA levels, Gleason score at biopsy, and the presence of cancer at the base of the prostate as critical predictors of SVI (21). MRI remains the most accurate preoperative tool for predicting SVI, with a reported sensitivity of approximately 60% and specificity of around 95%. Accuracy may be further enhanced when MRI is combined with nomograms or seminal vesicle biopsy (22, 23). However, in this study, no cases of pT3b were detected through preoperative MRI, indicating limitations in using MRI alone for SVI evaluation. In 2014, the International Society of Urological Pathology (ISUP) introduced a new grading system for prostate cancer, which stratifies tumors into five grade groups (24). Grade group 1 corresponds to a Gleason

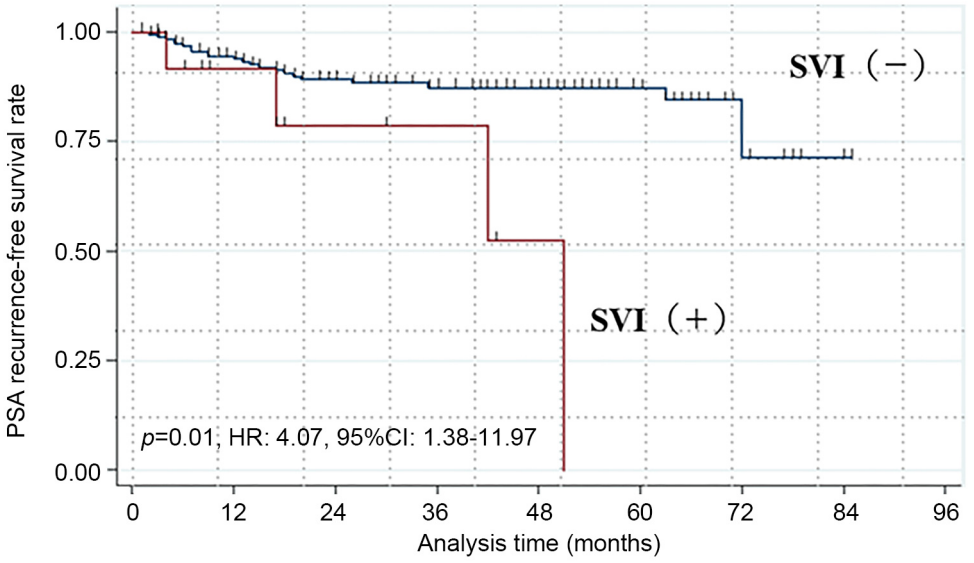

Figure 1. *PSA recurrence-free survival rate by the presence or absence of seminal vesicle invasion. SVI: Seminal vesicle invasion; HR: hazard ratio.*

score of 6 or less, grade group 2 to a Gleason score of 3+4=7, grade group 3 to a Gleason score of 4+3=7, grade group 4 to a Gleason score of 8, and grade group 5 to a Gleason score of 9 or 10. In this study, the ISUP grade group at biopsy was the only significant preoperative predictor of SVI. However, cases with higher grade groups may exhibit local progression that is not detectable through imaging, even when biopsy positivity rates were low. It has also been reported that long-term exposure to testosterone in rats is associated with the development of cancer in the dorsolateral part of the prostate and the seminal vesicles. In our case, age was not a predictor of seminal vesicle invasion (25). Mitsunari *et al.* reported that pathological T stage, Gleason score, and positive surgical margins are predictors of biochemical recurrence after RARP (26). The importance of surgical accuracy is also suggested in robot-assisted surgery, and pathological information such as Grade group and Gleason score play an important role in predicting prognosis.

Study limitations. First, it was retrospective in design and conducted at a single institution. In addition, the study population consisted of patients treated during the early phase of robotic surgery implementation, with multiple surgeons performing the procedures. Variability in surgical expertise may have influenced both prognosis and recurrence outcomes. In the future, multicenter studies and prospective designs will be required.

Table II. *Preoperative predictors of seminal vesicle invasion (pT3b) by logistic regression analysis.*

	OR	95%CI	*p*-Value
Age at diagnosis, years, median	1.036	0.9449-1.1364	0.4424
PSA at diagnosis (ng/ml), median	1.021	0.9648-1.0810	0.4497
Clinical T stage	1.023	0.6680-1.5687	0.9156
ISUP grade group	1.556	1.0482-2.3102	0.0266*
Biopsy positive core rate	4.334	0.5379-34.919	0.1754

OR: Odds ratio; CI: confidence interval; PSA: prostate specific antigen; ISUP: International Society of Urological Pathology. *Statistically significant.

Conclusion

Pathological stage pT3b after robot-assisted radical prostatectomy is a significant predictive factor for postoperative biochemical recurrence. Additionally, the ISUP grade group at biopsy is a key preoperative predictive factor for pT3b. Although various parameters influence pT3b

status, it is critical to recognize that cases with higher grade groups may experience local progression undetectable by imaging, irrespective of the biopsy positive rate. These findings highlight the need for enhanced preoperative risk assessment protocols that integrate biopsy-based grading with imaging and predictive models. Clinically, early identification of high-risk patients could improve treatment planning by informing decisions regarding salvage therapies or closer postoperative monitoring. Future research should explore the development of more accurate diagnostic strategies and conduct prospective, multicenter studies to validate these predictive factors across diverse patient populations.

Conflicts of Interest

The Authors have no conflicts of interest to declare in relation to this study.

Authors' Contributions

Kazuhiko Oshinomi: Methodology; Software; Data curation; Writing – original draft; Writing – review & editing; Visualization. Shota Kikuchi: Data curation. Hirotaka Kishi: Data curation; Anju Hayashi: Data curation. Sho Okada: Data curation. Masahiro Kurokawa: Data curation. Toshiki Mugita: Data curation. Tatsuki Inoue: Data curation. Motoki Yamagishi: Data curation. Yoshihiro Nakagami: Data curation; Supervision; Investigation. Masakazu Nagata: Supervision. Takashi Fukagai: Supervision; Project administration.

Acknowledgements

The Authors would like to thank Editage (www.editage.com) for English language editing.

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