

# Prognostic variables associated with biochemical recurrence after radical prostatectomy for pT3b prostate cancer

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## Abstract

**Objectives:** The objectives of the current study were to determine long-term biochemical recurrence rates stratified by adverse pathologic features and to identify predictive factors of biochemical recurrence rates following radical prostatectomy performed by either retropubic prostatectomy or robot-assisted laparoscopic prostatectomy from single tertiary center prostate cancer database.

**Material and Methods:** The Seoul National University Hospital prostate cancer database was queried for all patients treated with radical prostatectomy from 1999 to 2015. Among the 2680 patients who underwent radical prostatectomy, 331 patients with seminal vesicle invasion (pathologic T3bN0-1M0 stage) were identified. The primary endpoint was biochemical recurrence, defined as two consecutive postoperative prostate specific antigen values  $\geq 0.2$  ng/ml. Comparative analysis based on adverse pathologic characteristics and operation type was performed.

**Results:** Five and 10-year biochemical recurrence-free survival in the entire cohort was 59.0% and 42.9%. The Kaplan-Meier survival analysis demonstrated 5-year biochemical recurrence free survival rates differences in patients with different lymph node involvement (70.6% vs. 52.4%, log-rank,  $p=0.01$ ). Variables including age, extracapsular extension, lymph node invasion, surgical margin, perineural invasion, multicentricity and Capra-S score were similar between the groups of patients who underwent either retropubic or robot-assisted laparoscopic radical prostatectomy. The mean prostate specific antigen level, seminal vesicle invasion laterality, tumor volume, and pathologic Gleason score were lower in the cohort of patients who underwent robot-assisted laparoscopic prostatectomy. No statistically significant differences were found in 5-year biochemical recurrence-free survival rates stratified by operation type (58.1% vs. 65%, log-rank,  $p=0.8$ ), by Capra-S score (72.5% vs. 56.8%, log rank,  $p=0.1$ ), or by surgical margin status (69.4% vs. 59.3%, log-rank,  $p=0.8$ ). In univariate and multivariate Cox proportional regression analysis lymph node involvement ( $p=0.01$ ) was found to be a statistically significant predictor of biochemical recurrence.

**Conclusion:** Patients with positive lymph node involvement have a poor prognosis. Capra-S score was unable to predict biochemical recurrence in patients with pathologic T3b stage prostate cancer. Robot-assisted laparoscopic prostatectomy is comparable to retropubic radical prostatectomy in terms of the biochemical progression of prostate cancer with seminal vesicle invasion.

**Keywords:** prostate cancer, seminal vesicle invasion, pathologic T3b stage, outcomes, radical prostatectomy

## РТЗВ ҚУЫҚ АСТЫ ОБЫРЫНЫҢ РАДИКАЛЬДІ ПРОСТАТЭКТОМИЯДАН КЕЙІН БИОХИМИЯЛЫҚ РЕЦИДИВПЕН БАЙЛАНЫСТЫ БОЛЖАМДЫҚ АЙНЫМАЛЫЛАР

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### ТҰЖЫРЫМДАМА

**Мақсаттары:** Осы зерттеудің мақсаттары, жоғарғы деңгейлі орталықтың қуық асты безінің обыры мәліметтер базасында ең нашар патологиялық көрсеткіштермен стратификацияланған биохимиялық рецидивтардың жиілігі анықтау менен ашық және робот-ассистенцияланған лапароскопиялық простатэктомиядан кейін биохимиялық рецидивтің прогностикалық факторларын сәйкестендіру болған.

**Әдістері:** Сеул Ұлттық Университетінің ауруханасының қуық асты обырының мәліметтер базасында 1999-шы 2015-ші жылдар арасында радикалды простатэктомиямен емделген науқастардың деректері зерттелген. 2680 радикальді простатэктомия мен емделген науқастардың

арасында, 331 обьёрынын тұқымдық везикуларына басып кіруімен науқастар (патологиялық T3bN0-1M0 ауруының сатысымен) табылды. Біріншілік соңғы нүкте, отадан кейін ПСА деңгейі  $\geq 0.2$  нг/мл екі рет анықталғаннан кейін биохимиялық рецидив деп есептелетін. Ең нашар патологиялық көрсеткіштермен операция түріне негізделген салыстырмалы талдау жүргізілді.

**Нәтижелері:** Бес және 10 жылдық биохимиялық қайталанбайтын өмір сүру барлық когортада 59,0% және 42,9% құрады. Каплан-Мейердің өмір сүру талдауы лимфа түйіндеріне ауру тарауы жоқ және бар науқастарда 5-жылдық биохимиялық қайталанудан босату жылдамдығының айырмашылығын көрсетті (70,6% vs. 52,4%, log-rank,  $p=0.01$ ). Жас, экстракапсулярлы тарау, лимфа түйіндеріне шабуылы, хирургиялық маржа, перинеоваральды шабуыл, мультицентризм және Capra-S рейтингісі ретропубикалық немесе роботпен қамтамасыз етілген лапароскопиялық радикалды простатэктомиямен ауыратын топтар арасында ұқсас болды. Роботпен қамтамасыз етілген лапароскопиялық простатэктомиямен емделген науқастарда простата спецификалық антиген деңгейі, тұқымдық везикулаға инвазияның латералдығы, ісік көлемі және патологиялық Глисон баллдары ашық әдіс простатэктомиямен емделген науқастардан төмен рек болған. Capra-S-тің бағалауы бойынша (72.5% vs. 56.8%, log rank,  $p=0.1$ ) немесе хирургиялық шеті бойынша (69.4% vs. 59.3%, log-rank,  $p=0.8$ ) және операцияның түрі бойынша (58.1% vs. 65%, log-rank,  $p=0.8$ ) 5-жылдық биохимиялық рецидивсыз өмір сүру деңгейлерінде статистикалық маңызды айырмашылықтар табылмады. Унивариативті және мультивариативті Сох пропорционалды регрессиялық талдау кезінде лимфа түйіндеріне қатерлі ісік тарауы бар болуы ( $p = 0.01$ ) биохимиялық қайталанудың статистикалық маңызды предикторы болып табылды.

**Қорытынды:** Лимфа түйіндеріне қатерлі ісік тарауы бар науқастарда нашар болжам бар. Capra-S бойынша T3b простата қатерлі ісігі бар науқастарда биохимиялық рецидив туралы болжау жасауға мүмкіндік бермейді. Роботпен қамтамасыз етілген лапароскопиялық простатэктомия мен ретропубикалық радикалды простатэктомиямен емделген простатикалық қатерлі ісіктерді тұқымдық везикулярлық шабуылмен биохимиялық прогрессияға байланысты тең болып табылды.

**Негізгі сөздер:** құық асты безінің обьёры, қатерлі ісіктін тұқымдық везикулаға шабуылы, патологиялық T3b сатысы, ем нәтижелері, радикалды простатэктомия

## ПРОГНОСТИЧЕСКИЕ ФАКТОРЫ АССОЦИИРОВАННЫЕ С БИОХИМИЧЕСКИМ РЕЦИДИВОМ ПОСЛЕ РАДИКАЛЬНОЙ ПРОСТАТЭКТОМИИ У ПАЦИЕНТОВ С КАРЦИНОМОЙ ПРЕДСТАТЕЛЬНОЙ ЖЕЛЕЗЫ РТ3b

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### РЕЗЮМЕ

**Цели:** Задачами данного исследования были определение частот биохимического рецидива стратифицированных по наличию наихудших патологических признаков и идентификация прогностических факторов биохимического рецидива после простатэктомии выполненной открытым или робот-ассистированным лапароскопическим способом по данным базы данных рака предстательной железы одного третичного центра.

**Материалы и методы:** В базе данных рака предстательной железы госпиталя Сеульского Национального Университета исследованы данные пациентов перенесших радикальную простатэктомию с 1999 по 2015 годы. Среди 2860 пациентов перенесших радикальную простатэктомию, у 331 была идентифицирована инвазия опухолевого процесса в семенные пузырьки (патологическая T3bN0-1M0 стадия заболевания). Первичной конечной точкой был биохимический рецидив, определенный как два последовательных повышения значений простата специфического антигена  $\geq 0.2$  ng/ml. Был выполнен сравнительный анализ основанный на наихудших патологических признаках и типе выполненной операции.

**Результаты:** Уровни 5 и 10-летней свободы от биохимического рецидива во всей когорте составили 59.0% и 42.9% соответственно. Анализ выживаемости по Каплану-Мейеру продемонстрировал разницу в уровнях 5-летней выживаемости без биохимического рецидива у пациентов без наличия вовлечения лимфатических узлов и с наличием (70.6% vs. 52.4%, log-rank,  $p=0.01$ ). Такие переменные как возраст, экстракапсулярное распространение, поражение лимфатических узлов, хирургический край, перинеоваральная инвазия, мультицентричность и число Capra-S не различались между группами пациентов перенесших позадилоновую или робот-ассистированную лапароскопическую радикальную простатэктомию. Средние уровни ПСА, латеральность инвазии семенных пузырьков, объем опухоли, и число Глиссона при патологическом исследовании было ниже в когорте пациентов перенесших робот-ассистированную лапароскопическую простатэктомию. Не было выявлено статистически значимой разницы в уровнях 5-летней выживаемости у пациентов в зависимости от перенесенного типа операции (58.1% vs. 65%, log-rank,  $p=0.8$ ), от числа Capra-S (72.5% vs. 56.8%, log rank,  $p=0.1$ ), или от статуса хирургического края (69.4% vs. 59.3%, log-rank,  $p=0.8$ ). В унивариативном и мультивариативном пропорциональном регрессионном анализе Кокса вовлечение лимфоузлов ( $p=0.01$ ) было обнаружено как статистически достоверный предиктор биохимического рецидива.

**Закключение:** У пациентов с поражением лимфатических узлов отмечен более худший прогноз. Число Capra-S не обладало прогностической значимостью при оценке риска биохимического рецидива у пациентов с патологической T3b стадией рака предстательной железы. Робот-ассистированная лапароскопическая простатэктомия и позадилоновая простатэктомия у пациентов с наличием инвазии в семенные пузырьки сопоставимы с друг другом в плане риска биохимического рецидива.

**Ключевые слова:** рак предстательной железы, инвазия в семенные пузырьки, патологическая T3b стадия, результаты, радикальная простатэктомия

## Background

дениям о влиянии тиреоидных гормонов на синтез биорSeminal vesicle invasion (SVI) is found in almost 18% of patients who undergo radical prostatectomy, which is considered an established adverse pathologic feature and is strongly correlated with poor prognosis [1-4]. In contemporary literature, 5-year biochemical recurrence (BCR) rates in patients with SVI vary from 8% to 68% [5-7]. The objectives of our current study were to determine 5- and 10-year BCR rates stratified by adverse pathologic features and to identify predictive factors of BCR. As only a few centers have performed robot assisted laparoscopic prostatectomy (RALP) for more than 10 years at this time, there are only a few studies that have reported comparable oncologic outcomes after RALP and retropubic radical prostatectomy (RRP) in pT3b patients. The majority of these reports were single-center studies with small cohorts and short-term follow-

up periods [8-11]. In our study we compare 5-year biochemical recurrence-free survival (BCRFS) in patients with pT3b after RRP or RALP from the Seoul National University Hospital (SNUH) prostate cancer database. The SNUH commenced in robot assisted laparoscopic radical prostatectomy since May 2008.

## Material and Methods

The Institutional Review Boards (IRBs) of the Seoul National University Hospital approved this study (Approval number: H-1608-118-791). As the present study was carried out retrospectively, written informed consent from patients was waived by the IRBs. Personal identifiers were completely removed, and the data were analyzed anonymously. Our study was conducted according to the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

The SNUH database was queried for all patients with prostate cancer who were treated with radical prostatectomy from 1999 to 2015. Among the 2680 patients who underwent radical prostatectomy, 331 patients with seminal vesicle invasion (SVI) (pT3b disease) were identified. The SVI diagnosis was confirmed using standard protocols with SVI defined as a tumor invading the muscular wall of the seminal vesicle (SV). After excluding patients with bone metastasis and those who underwent laparoscopic prostatectomy, 331 patients with pT3bN0-1M0 prostate cancer remained. All patients underwent radical prostatectomy by either RRP or RALP. The number of patients who underwent immediate radiation treatment was 17 (5%), the number of patients who underwent salvage radiation treatment was 26 (7.8%). Retropubic radical prostatectomy (RRP) or robot-assisted laparoscopic prostatectomy (RALP) was conducted by several surgeons during the involving period. A pelvic lymph node dissection (PLND) was performed in 241 of the 331 men based on individual surgeon preference.

Patient data were collected by physicians at diagnostic, preoperative, and postoperative evaluations. The data included preoperative clinical characteristics (PSA level, clinical stage, and biopsy Gleason scores) and pathologic characteristics (disease stage, histology, and surgical margin (SM) status) of the specimens carefully registered by a specialized staff pathologist with genitourinary expertise.

Prostate specimens were staged using the 2002 tumor, node, metastasis (TNM) classification. The percent tumor volume was determined by dividing the sum of all visually estimated tumor foci by the prostate volume on each section. The positive surgical margin was defined as the tumor extending to the inked surface of the specimen and in areas without a definite, identifiable capsule [12]. All histologic slides were reviewed by hospital staff pathologist, and past report was changed, which recorded using grade classification according to 1973 World Health Organization (WHO) classification (G1/G2/G3) to report using grade classification according to 2004 WHO classification (Low grade/High grade). Gleason scores were determined according to the International Society of Urological Pathology modified Gleason grading system [13]. Supersensitive PSA levels were measured every 3 months after surgery during the first year, then every 6 months up to 3-years, and annually thereafter. The median follow-up period was 49 months (mean 55.0±35.9 months). Median follow-up period for RRP was 58 months, while the median follow-up for RALP was 41 months. The primary endpoint was BCR, defined as two consecutive postoperative PSA values ≥0.2 ng/ml. In case of determining PSA level more than 0.2, PSA levels checked in short term 1 to 3 months considering rising velocity.

Appropriate comparative tests (t-test and chi-square tests) were used to determine differences in patient clinicopathological characteristics. The Kaplan-Meier method was used to determine 5-year BCRFS rates and compare with log-rank tests. Univariate and multivariate Cox proportional hazard models were used to determine predictive factors for BCR. The variables identified as significant in the univariate analysis were then entered into a multivariate Cox regression model to evaluate definitive predictors. All analysis was done using SPSS version 21 (Armonk, NY: IBM Corp.) and statistical significance was defined as  $p < 0.05$ .

## Results

In the entire cohort, 231 (69.7%) patients were treated by RRP and 100 (30.2%) were treated with RALP. The clinical and pathological characteristics are summarized in Table 1.

**Table 1** Clinicopathological parameters of pT3b patients

	Total	RRP	RALP
Number of patient, n (%)	331 (100)	231(69.7)	100(30.3)
Age, [Mean ± SD]	66.3±6.9	66.7±6.7	65.4±7.4
Preoperative PSA, ng/ml, [Mean ± SD]	25.4±37.4	29.3±43.1	16.4±15.4**
PSA group, n (%)			
<10 ng/ml	109 (32.9)	66 (28.5)	43 (43)
>10-20 ng/ml	96 (29)	61 (26.4)	35 (35)
>20 ng/ml	126 (38)	104 (45)-	22 (22) **
SVI laterality, n (%)			
Unilateral	54 (16.3)	35 (15.1)	19 (19)
Bilateral	45 (13.5)	23 (9.9)	22 (22)
Missing data	232 (70.0)	173 (74.8)	59 (59)*
Tumor volume [Mean ± SD]	19.9±16.9	20.2±15.1	14.1±11.9*
ECE, n (%)			
No	57 (17.2)	36 (15.5)	21 (21)
Yes	274(82.7)	195 (84.4)	79 (79)
pGs, n (%)			
≤7	194(58.6)	124 (53.6)	70 (70)
≥8	111 (33.5)	84(36.3)	27 (27)
Missing data	26(7.9)	23(9.9)	3(3)*
LNI, n (%)			
Negative	189 (57.1)	114(49.3)	75 (75)
Positive	57 (17.2)	32 (13.8)	25 (25)
SM, n (%)			
Negative	98 (29.6)	67 (29)	31 (31)
Positive	233 (70.3)	164 (70.9)	69 (69)
PNI, n (%)			
Negative	35 (10.5)	18 (7.7)	17 (17)
Positive	211(63.7)	128 (55.4)	83 (83)
Missing data	85(25.6)	85 (36.7)	-
Patients with BCR, n (%)	94 (28.3)	71 (30.7)	23 (23)
Multicentricity, n (%)			
Yes	124 (37.4)	73 (31.6)	51(51)
No	121 (36.5)	73 (31.6)	48(48)
Missing	86(25.9)	85(36.7)	1(1)
Capra-S score, [Mean ± SD]	8.2±2.1	8.3±2.1	7.8±2

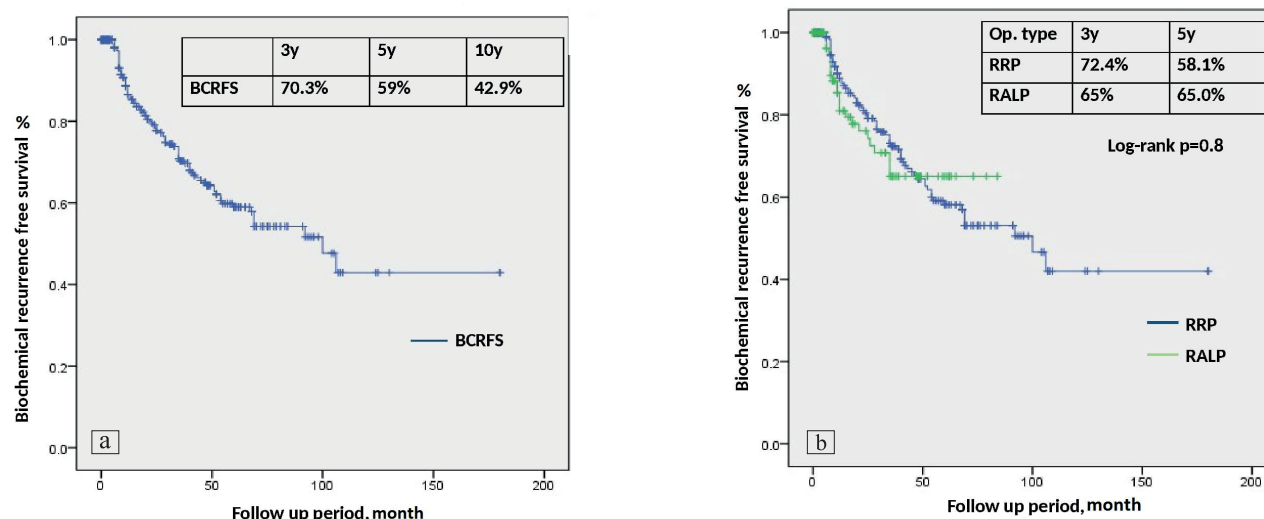
The mean patient age was 66.3±6.9 years, the mean PSA was 25.4±37.4, and the mean CAPRA-S score was 8.2±2.1. A total of 54 (16.3%) patients had unilateral SVI, 274(82.7%) had extracapsular extension (ECE), 111(33.5%) patients had pathologic Gleason score (pGs) 8 or more, 58 (17.5%) patients had lymph node involvement (LNI), 233(70.3%) patients had a positive surgical margin (PSM). Perineural invasion (PNI) rate was positive in 211 (63.7%) patients. The average yield of LN's removed was 58% and the average yield of positive lymph nodes were 17.5%.

At a median follow-up of 49 months, 94 (28.3%) patients experienced BCR. Kaplan-Meier survival analysis for the overall cohort showed estimated 5- and 10-year BCR free rates of 59% and 42.9%, respectively (Figure 1a). Table 2 summarizes the data of the univariable and multivariable analyses for predictors of BCR. Among the clinicopathologic features, positive lymph node involvement (HR=2.21,  $p=0.02$ ) was the strongest predictor of BCR.

BCRFS rates stratified by positive lymph node involvement ( $n=57$ , 17.2%) versus negative involvement ( $n=189$ , 57.1%) are presented in Figure 2a. Log-rank tests revealed that rates of freedom from BCR are significantly lower in patients with positive lymph node involvement ( $\chi^2(1)=6.62$ ,  $p=0.01$ ).

Comparison of BCRFS rates stratified by Capra-S score





**Figure 1** - Kaplan-Meier BCRFS curves for the entire cohort (a) and stratified by operation type (b).

**Table 2**

Cox regression analysis predicting biochemical recurrence (BCR) rate

Univariable analysis BCR		
	HR	CI
Prostate volume	1.000	(0.98, 1.01)
In PSA		
0-10	ref	-
10-20	1.079	(0.66, 1.74)
>20	1.035	(0.62, 1.72)
pGs sum	1.001	(0.99, 1.00)
pGs ≤7	ref	
pGs 8	0.834	(0.51, 1.35)
pGs >8	1.445	(0.69, 2.99)
ECE (positive vs negative)	1.016	(0.78, 1.31)
Bilateral ECE	30.65	(0.00, 34.97)
Perineural inv (posit vs negative)	0.432	(0.15, 1.20)
LNI (posit vs negative)*	2.12	(1.17, 3.83)
SVI laterality (bilateral vs unilateral)	0.723	(0.27, 1.87)
Operation type RRP vs RALP	0.959	(0.59, 1.54)
PSM	1.043	(0.67, 1.60)
Multicentricity	1.034	(0.58, 1.82)
Capra Score		
3-5	ref	-
6-7	0.579	(0.27, 1.21)
8-12	1.112	(0.70, 1.75)
Number of positive lymph nodes	1.048	(0.87, 1.26)
Total lymph nodes removed	1.004	(0.97, 1.03)
Tumor volume >36%	0.690	(0.24, 1.95)
Multivariable analysis BCR		
LNI (posit vs negative)*	2.21	(1.08, 4.53)

showed that 5-year BCRFS rates were higher in patients with Capra-S scores between 3-5 than in patients with Capra-S scores  $\geq 6$  (72.5% vs. 56.8%), but differences were not statistically significant in log-rank tests ( $\chi^2(1)=2.570$ ,  $p=0.10$ ) (Figure 2b). In univariable Cox proportion analysis, the Capra-S score did not predict BCR.

Main clinicopathologic characteristics of patients who underwent either RRP or RALP are presented in Table 1.

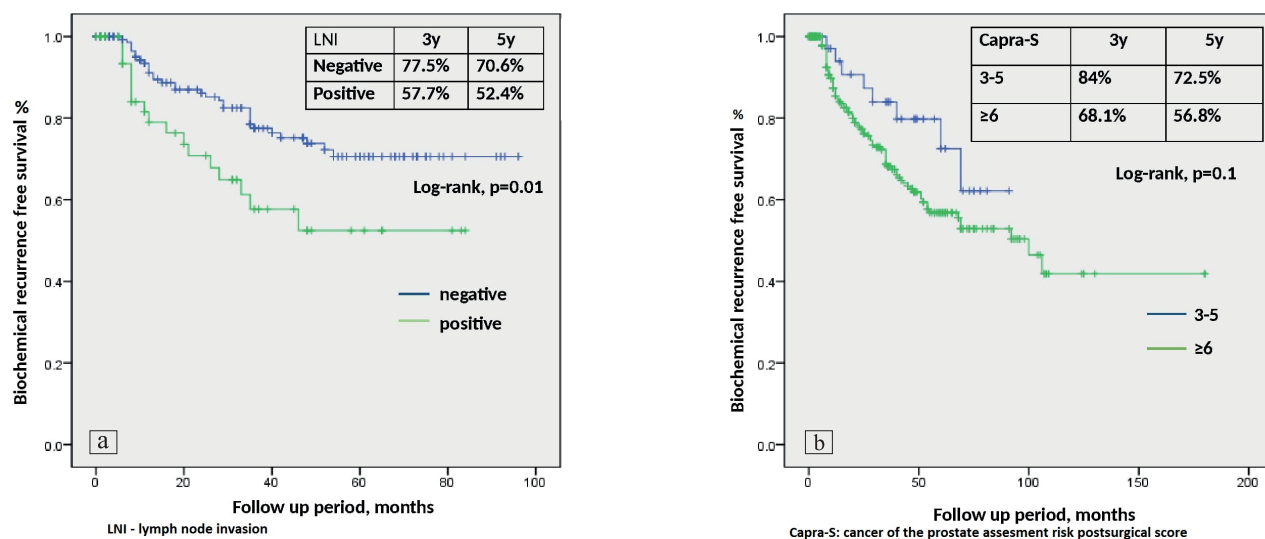
Variables including age, ECE, LNI, surgical margin (SM), PNI, multicentricity and Capra-S score were similar between the RRP and RALP groups. The mean PSA level, SVI laterality, tumor volume, and pGs were lower in the RALP cohort. There were no statistically significant differences in 5-year BCRFS rates among RRP and RALP patients (58.1% vs. 65.0%,  $p=0.3$ ) (Figure 1b).

## Discussion

Invasion of prostate cancer into the seminal vesicle is related to poor prognosis and is considered a strong predictor of BCR [13, 14]. In current literature, only a few huge multicenter studies with large descriptive cohorts have been published reporting comparative analysis of outcomes after RRP and RALP treatment in patients with seminal vesicle invasion. Only limited data are available regarding long-term follow-up of oncologic outcomes among RRP and RALP cohorts. In our present study we compared 5-year BCRFS rates after RRP or RALP in patients with pT3b stage (Table 3).

Five-year BCRFS rates were 59% in the pT3b patients in our study: this corresponds with previously reported data from large multi-institutional series [4, 13, 15-17] (Table 3). Patients with isolated SVI on prostate specimen after RP had a 5-year BCRFS rate between 5 and 60%, with a median value of 36% [7]. Because of such wide spectrum of BCRFS rates, additional stratification of risk would be helpful in choosing further treatment [18]. The direction of our research was seeking predictors of BCR in pT3b patients, which helps to make a decision about adjuvant treatment.

Positive lymph node involvement was found in 17.2% of patients and differences in BCRFS rates stratified by lymph node involvement positivity was statistically significant as in previous reports [13, 15]. Lymph node metastasis has been associated with worse cancer-specific survival and a higher rate



**Figure 2** - Kaplan-Meier BCRFS curves for the entire cohort (a) and stratified by operation type (b).

**Table 3** Comparison with previous studies

	Pierorazio et al. [4]	Pagano et al. [15]	Kang et al. [16]	Secin et al [13]	Forgues et al [6]	Our study
Patients number	989	180	876	387	104	331
Age, mean	59 (40-73)	63.7 (58-67)	65.8±6,6	62 (56-66)	63.5(58-67)	66.3±6.9
Preoperative PSA ng/ml, mean	7.2 (0.8-67)	9.1(6.3-17.1)	22.3±26.0	10.8(6.9-20.3)	10.3(7-15)	25.4±37.4
Preoperative PSA group, n (%)						
<10 ng/ml	-	101(56.1)	-	168(46)	-	109 (32.9)
>10-						
20ng/ml		42(23.3)		103(28)		96 (29)
>20 ng/ml		37(20.6)		92(25)		126 (38)
pGs, n (%)						
≤6	92(9.3)			94(12.4)	15(14.4)	
7	542(54.8)	126(70)	398(49.7)	321(42.6)	71(68.3)	194 (58.6)
≥8	352(35.5)	54(30)	403(50.3)	336(44.6)	18(17.3)	111 (33.5)
Lymph node involvement, n (%)	242(24.2)	22(12.2)	130(16.2)	91(24)	-	57 (17.2)
PSM, n (%)	409(41.3)	74(41.1)	524(65.4)	146(38)	34(32.7)	233(70.3)
5 year BCRFS, %	36-40	39.5	30.1	38	55.8	59

of distant metastasis [19]. Positive lymph node involvement status was also found to be a statistically significant predictor of BCR in multivariate analysis in our cohort. These patients may benefit from early adjunctive therapy after surgery to improve outcomes.

The pGs was not a predictor of BCR as in our study, unlike in previous studies [5, 11]. Among the different prognosis factors, the presence of PSM appears to be the most important [7]. PSM rate in the entire cohort of patients with pT3b was 70.3%: this rate is higher than that in the findings from previous series in which rates of 41.3% [4], 38% [13], and 41.1% [15] were reported. PSM rates among two treatment method groups not revealed differences in PSM status in patients who underwent RRP and RALP (70.9% vs. 69%). Kaplan-Meier plots showed that BCRFS was higher in patients with PSM but differences in the log-rank test were not statistically significant ( $\chi^2(1)=0.037$ ,  $p=0.8$ ). The 5-year BCRFS rate was 59.3% in patients with PSM status, whereas in patients with negative surgical margin status the rate was 58.2%. Spahn et al [20] conducted a multivariate analysis of pT3b patients that demonstrated that SM status was an independent predictive factor of prostate cancer BCR. In previously reported studies [21, 22] PSM was independent

predictive factor of BCR in pT2 and pT3a patients, but not in pT3b patients. In our pT3b cohort also, PSM was not found as a prognostic factor in univariate and multivariate analysis. As in the study of Yang et al. [23] where Kaplan-Meier analysis stratified by CAPRA-S scores of 3-5 vs.  $\geq 6$  resulted in differences among groups, in our cohort BCRFS rates also decreased with increasing Capra-S score. The 5-year BCRFS was higher in pT3b patients with Capra-S scores 3-5 vs.  $\geq 6$ , but log-rank test ( $\chi^2(1)=2.57$ ,  $p=0.109$ ) did not reveal statistically significant differences among the groups. This is likely due to small sample size because there were not any such problematic values in large CaPSURE [24, 25] and SEARCH data-sets [26]. Cox proportional regression did not demonstrate a prognostic probability of the Capra-S score in univariate analysis.

In Punnen et al.s' study [27] 4-year BCRFS rates after RRP and RALP were determined to be 66% vs. 68% respectively and differences among BCRFS rates were not significant. After that Pierorazio et al [28] and Menon et al [11] established 3-year and 5-year BCRFS rates, respectively, and they did not find statistically significant differences between the RRP and RALP cohorts. In our study BCRFS rates were lower in RRP group (58.1%) than in RALP group (65%), but differences were not

statistically significant. Therefore our study demonstrated comparable BCRFS rates stratified by operation type in pT3b patients similar to previous reports.

Our present study has several limitations resulting from its retrospective design, such as a small sample size and a small number of death events which limited the power to detect differences among variables. Further, the mean follow-up remains short and longer observation time and additional studies are required, especially with regard to overall survival and cancer specific survival.

## Conclusion

Patients with positive lymph node involvement, have a poor prognosis. The Capra-S score was unable to predict BCR in pT3b patients. RALP is comparable to RRP for prostate cancer with seminal vesicle invasion with respect to BCR.

### Clinical Practice Points

Five-year BCRFS rates in the pT3b patients in our study corresponds with previously reported data from large multi-institutional series.

There were no statistically significant differences in 5-year BCRFS rates among RRP and RALP patients.

Univariate and multivariate analyses have identified positive lymph node invasion as a poor prognostic factor.

Capra-S score was unable to predict BCR in pT3b stage prostate cancer patients

## Abbreviations

BCR: biochemical recurrence, RRP: retropubic radical prostatectomy, RALP: robot-assisted laparoscopic prostatectomy, BCRFS: biochemical recurrence-free survival, SVI: seminal vesicle invasion, SNUH: Seoul National University Hospital, IRB: Institutional Review Boards, SD = standard deviation, pGs = pathologic Gleason score, pN = pathologic n stage, SV: seminal vesicle, PSA: Prostate-specific antigen, TNM: Tumor Node Metastasis, ECE: extracapsular extension, LNI: lymph node involvement, PSM: positive surgical margin, PNI: Perineural invasion, CSS: cancer specific survival, OS overall survival.

## Declarations

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## Availability of data and materials

The dataset analyzed during the current study available from the corresponding author on reasonable request.

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## Competing interests

The authors declare no conflict of interest.

## Consent for publication

Not applicable (the manuscript does not include details, images, or videos to individual participants).

## Ethical approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was performed under approval of the appropriate ethics committee (Institutional Review Boards (IRBs) of the Seoul National University Hospital approved this study (Approval number: H-1608-118-791).

## Authors' contributions

UB had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis. UBB, JKK, CWJ, JHK, and CK designed the study. UB, JKK, BT, and MK performed data acquisition. UB and JKK analyzed and interpreted the data. UB and CWJ drafted the manuscript. CWJ performed critical revisions. UB, JKK, and BT performed the statistical analysis. CWJ, HHK, JHK, and CK supervised the study.

**Disclosures:** There is no conflict of interest for all authors.

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