의학석사학위논문

근치적 전립선절제술 후 종양 국소 용적에 따른 위험도 분류의 비교

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2018년 2 월

서울대학교대학원

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이 논문을 의학석사학위논문으로 제출함

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김태진의 석사학위논문을 인준함

2017 년 12 월

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ABSTRACT

Comparison of Localized High Volume Tumor and Locally Advanced Low Volume Tumor after Radical Prostatectomy According to Risk Classification

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Purpose: To investigate the relevance of the pathologic tumor volume (PTV) among patients who underwent radical prostatectomy (RP).

Materials and Methods: We reviewed 3080 patients who underwent RP between September 2003 and March 2015 and with a postoperative follow up for more than 1 year. The patient population was stratified into 4 disease risk groups according to tumor stage and PTV (T2 low volume -T2LV, T2 high volume – T2HV, T3 low volume – T3LV and T3 high volume – T3HV).

Probability of biochemical recurrence (BCR)-free survival was determined using Kaplan-Meier curves. PTV was evaluated by Multivariate Cox proportional hazard analysis for predicting BCR. Subgroup analyses were performed according to preoperative risk.

Results: The median PSA was 7.87ng/ml, and PTV was 10%. Among a total of 2964 patients, T2LV had 1473(49%), T2HV was 598(20%), T3LV with 199(6%), and T3HV was 694(23%). When comparing T2HV and T3LV, Gleason score and positive surgical margin rate was higher in T3LV. During a 50 months follow-up, BCR free survival rate was higher in the T2HV group ($p < 0.001$). PTV was a significant factor to predict BCR in multivariate Cox analysis. In subgroup analyses, T2HV group had similar BCR free survival rates to T3LV group in the preoperative high risk group while PTV was significant in the high risk group.

Conclusion: PTV was a significant predictor of BCR among prostate cancer patients after RP, however T2HV had favorable BCR results. Among patients with a preoperative high PSA and Gleason score, T2HV had similar BCR results to T3LV.

Keywords: prostate; prostate cancer; recurrence; tumor volume

Student Number: 2016-2194

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Introduction

Prostate cancer (PCa) is the second most frequently diagnosed cancer and the fifth leading cause of cancer death in males worldwide. It was accountable for 15 % of the total new cancer cases and 7 % of total male cancer deaths in 2012.[1] Currently, radical prostatectomy (RP) is the only surgical option for patients with localized PCa.[2] While most localized PCa patients have an excellent 10-year biochemical recurrence (BCR)-free survival rates of 73 to 99 %, some cancers will eventually recur.[3, 4] Previous studies have identified variables such as prostate specific antigen (PSA), pathological sub-stage, Gleason score and/or positive surgical margins (PSM) as predictors of BCR. However, the aforementioned studies had limited accuracy and predictive power. Therefore, studies concerning increased accuracy and prediction of BCR are necessary.

Traditionally, in solid organ cancer, tumor size or tumor volumes are important factors to predict cancer related outcomes and prognosis.[5] The size of a tumor is an important reflection of its biology, determined by complex interacting factors such as cell proliferation, apoptosis and angiogenesis.[6, 7] Tumor volume (TV) at the time of treatment for clinically localized prostate cancer could reflect important properties that influence its clinical behavior. Despite the biological relevance of tumor size, the status of TV in prostate

cancer as an independent predictor of outcome after RP has not been well defined. Some studies demonstrated a positive relationship between TV and cancer progression;[8] others argued that TV is not an independent predictor of prostate cancer progression when incorporating the more readily determined tumor grade and stage in the analysis.[9-11]

Additionally, several studies have reported the predictive value of pathologic tumor volume (PTV) in prediction of BCR.[12-17] Even though tumor volume shows potential to be a significant factor, there were no studies done on the comparison of localized high volume PCa and low volume advanced PCa. Therefore we investigated the aforementioned issue among prostate cancer patients who underwent RP using PTV.

Material and Methods

Patients

After obtaining institutional review board approval, we reviewed the data of 3,080 patients who underwent RP for prostate cancer between September 2003 and March 2015 at our institution and were postoperatively followed up for more than 1 year. After excluding patients who underwent neoadjuvant, adjuvant hormone or radiation therapy and pathologic T4 and node positive disease and those with inadequate data, a total of 2,964 patients were included in the final analysis.

Pathologic Evaluation

Specimens from RPs were weighed, fixed intact in 20% neural buffered formalin, and sectioned at 3 to 4 mm intervals with the apical and bladder neck portion sectioned radially to allow evaluation of margin status parallel to urethra. For each pathologic slide, the percent of tumor involvement per slide was estimated, and PTV was determined by averaging the estimates from all slides using methods previously reported by others. [13, 18]

Statistical Analysis

Data assessment included patient age, preoperative PSA level, prostate specimen weight, PTV, pathologic Gleason score, pathologic stage, surgical margin status, lymph node involvement, and postoperative follow-up PSA data, and was compared according to groups via tumor stage and PTV by the Mann-Whitney U or Kruskal-Wallis test. The patient population was stratified into 4 disease risk groups according to tumor stage and PTV (median PTV value of 10%) – T2 low volume group (T2LV), T2 high volume group (T2HV), T3 low volume group (T3LV) and T3 high volume group (T3HV). Biochemical recurrence (BCR) was defined as two consecutive rises in PSA of 0.2 ng/ml or higher at a minimum of 2 months following RP.[19] Probability of biochemical recurrence-free survival was determined using Kaplan-Meier curves with log rank test used to assess statistical significance. Effects of various variables on biochemical recurrence-free survival were assessed using the Cox proportional hazards model. An additional subgroup analysis was performed via clinical risk classification. The SPSS software package version 15.0 (Statistical Package for Social Sciences™, Chicago, IL, USA) was used for statistical analysis. A 2-tailed $P < 0.05$ was considered significant for all analyses.

Results

Baseline Characteristics

Patient characteristics are shown in Table 1. When stratified into groups (T2LV, T2HV, T3LV and T3HV), 1,473 (49.7%) patients had pathologic T2 and PTV less than 10% (T2LV), 598 (20.2%) patients had pathologic T2 and PTV ≥ 10% (T2HV), 199 (6.7%) patients were T3LV and 694 (23.4%) patients were T3HV. Among total patients, the median PSA was 7.87 ng/ml, and median PTV was 10% (mean value; 16.9%). In pT2 patients (n=2,071), the T2HV group had a higher pathologic Gleason score, positive surgical margin (PSM) rate and BCR rate than T2LV ($p < 0.001$). In pT3 patients (n=893), the T3HV group also had a higher pathologic Gleason score, PSM rate, seminal vesicle invasion (SVI) and BCR rate than T2LV ($p < 0.001$). When comparing T2HV and T3LV groups, pathologic Gleason score ($p < 0.001$), PSM ($p = 0.002$) and BCR ($p < 0.001$) were higher in the T3LV group.

Biochemical Recurrence Free Survival Analysis

Univariate analysis showed that PTV was associated with BCR-free survival among total patients (log rank $p < 0.001$). A multivariate Cox proportional hazards regression model demonstrated that PTV was an independent predictor of biochemical recurrence-free survival ($p < 0.001$) in the study population after adjusting for age, PSA, prostate volume, pathologic Gleason score, extracapsular extension (ECE), SVI and PSM (Table 2). Among the 4 groups, BCR free survival rates were significantly different as shown in Figure 1 (log rank test, all $p<0.001$). The 10 year BCR free survival was calculated as 86.1% in T2LV, 76.0% in T2HV, 59.7% in T3LV and 26.2% in T3HV.

Subgroup Analysis According To Risk Group

In a subgroup analysis according to stratification of risk classification, PTV was a significant predictor to BCR only in the high risk group and not in the low-intermediate risk group (Table 3). As shown in Figure 2a-c, T2LV PCa had a significantly higher BCR free survival rate compared to other groups (vs. T2HV, $p = 0.003$; vs. T3LV, $p < 0.001$; T3HV, $p < 0.001$). However, in the low risk classification groups, there were no significant differences. In the intermediate risk group, T2LV and T2HV had similar BCR free survival rate and T3LV and T3HV had also similar results for BCR rate. Cox proportional multivariate analysis also showed that PTV was not a significant predictor to BCR in the low and intermediate risk group (Table 3). However in the high risk group, the T2HV group had similar BCR free survival rates when compared to the T3LV group (Figure 2c) ($p = 0.543$). As shown in Table 3, PTV was a significant predictor to BCR only in the high risk group (HR : 1.914, 95%CI 1.325-2.765, $p < 0.001$) after adjusting for other factors.

Discussion

In our study, PTV was observed to be an independent predictor of BCR-free survival following RP among the total subjects. In high PTV organ confined PCa, BCR free survival rates are favorable compared to locally advanced PCa regardless of PTV. However in high risk groups who have a higher PSA and Gleason score, PTV could be a significant factor to predict BCR, and our study shows that T2HV disease had similar BCR related results compared to T3LV after RP.

Our finding that tumor volume is an independent prognosticator of biochemical recurrence agrees with several independent studies.[8,20–22] Humphrey *et al.* reported that intraglandular tumor extent measured as percent of carcinoma correlated with disease progression following RP among patients with clinically localized prostate cancer.[23,24] Moreover, Carvalhal *et al.* and Ramos *et al.* observed that PTV was an independent predictor of biochemical recurrence among patients who underwent RP for pathologically organ confined disease.[13,25] Furthermore, a study done by Rampersaud *et al.* showed that PTV was a significant factor in disease progression following RP even after adjusting for multiple clinical and pathological characteristics for margin positive or extraprostatic extension of tumor as well as those with pathologically organ-confined disease.[18] On the other hand, Epstein *et al.*

reported from their series of clinically localized prostate cancer patients treated with RP that PTV did not provide independent information beyond that offered by other factors.[9]

The aforementioned studies are a reflection of the ongoing controversy surrounding the actual value of PTV as a potential prognostic indicator in patients who underwent RP. There are several possible explanations for the disagreement of the role of volume in risk of recurrence. One explanation of these differences is in the methods used to measure tumor volume. In several series, objective measures of tumor volume, such as by computerized planimetry or measurement of the greatest tumor dimension, have demonstrated prediction of biochemical recurrence after radical prostatectomy independent of other clinical and pathological variables.[26,27] Subjective measures, such as visual estimates of tumor size or percentage of gland involvement, have failed to provide prognostic information, although the literature is conflicting.[25] A second explanation could be due to a small study cohort or small tumor volume in series in which volume has failed to correlate with outcome. Finally, some studies include large numbers of patients with relatively low grade cancers. Merrill *et al.* found that in patients with a pathologic Gleason score of 6 or less, tumor volume failed to predict for biochemical recurrence.[15] Therefore, the inclusion of patients with Gleason grade 3+3 disease in prognostic models will corrupt the predictive power of tumor volume.

Results from our study show that PTV was an independent predictor of BCR-free survival following RP. However, the predictive value of PTV was only significant in the high risk D'Amico classified group, which shows that PTV could be a significant factor to predict BCR in highly aggressive tumors and in the low or intermediate risk groups, tumor staging is a much more important factor compared to tumor volume.

The Gleason grade represents tumor differentiation while PTV reflects the tumor burden; these are principal outcome determinants in any solid organ cancer. Pathologic stage represents the disease extent resulting directly from the combination of both factors; all other clinicopathologic factors may have potential to influence outcome. Therefore, in pT2 prostate cancer, prognosis may be primarily determined by PTV and the Gleason grade; T2HV disease with high a PSA and Gleason score disease should treated and managed in similar fashion to locally advanced PCa.

Tumor volume or size is considered as an important prognostic indicator in many cancer types and is often included in pathological staging.[20–22] However, the importance of tumor volume in the prognosis of prostate cancer has been debated. The main reason for this ongoing debate has been a lack of consensus on the best way to assess cancer volume or extent.[28] Some proposed the direct measurements of tumor volume, while others have used percent cancer as a ratio of tumor volume to total prostate volume as an estimate of the percentage of the gland involved with cancer.[21, 22] To date, tumor volume and

percent cancer have not been compared directly.

Potential limitations of our study include the retrospective nature of study design. Moreover, we could not control for intra- or inter observer variability in assessing PTV. Although PTV in all specimens were calculated by an experienced single uro-pathologist, PTV measurement done by computerized morphometric methods would be regarded as a more accurate estimate of the actual tumor burden. The present study was a retrospective analysis with a short median follow up duration was 48 months in our study. Due to the lack of long term follow up, time to BCR rather than cancer-specific survival was designated as the primary endpoint in our study. A final limitation of the present study is that the different number of subjects according to each group could affect the interpretation of our results. Therefore, the results of this study should be validated in a large scaled cohort study

Conclusion

The present study demonstrated that PTV was a significant predictor of BCR among patients who underwent RP. Patients with a high PTV, organ confined disease had a favorable BCR free survival rate compared to locally advanced PCa regardless of PTV. However in the high risk group, T2HV disease had similar BCR related results when compared to T3LV after RP, therefore, patients with T2HV with a high PSA and Gleason score disease should be approached and managed similarly to locally advanced PCa.

Acknowledgements

This work was supported by grant no SNUBH-02-2016-015 from the SNUBH (Seoul National University Bundang Hospital) Research Fund and supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2014R1A1A2059658).

References

1. Torre LA1, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A Global cancer statistics, 2012. CA Cancer J Clin. 2015 Mar;65(2):87-108. doi: 10.3322/caac.21262. Epub 2015 Feb 4

2. Heidenreich A1, Bastian PJ, Bellmunt J, Bolla M, Joniau S, van der Kwast T, Mason M, Matveev V, Wiegel T, Zattoni F, Mottet N; European Association of Urology. EAU guidelines on prostate cancer. part 1: screening, diagnosis, and local treatment with curative intent-update 2013. Eur Urol. 2014 Jan;65(1):124-37. doi: 10.1016/j.eururo.2013.09.046. Epub 2013 Oct 6.

3. Han M1, Partin AW, Zahurak M, Piantadosi S, Epstein JI, Walsh PC. Biochemical (prostate specific antigen) recurrence probability following radical prostatectomy for clinically localized prostate cancer. J Urol. 2003 Feb;169(2):517-23.

4. Caso JR1, Tsivian M, Mouraviev V, Polascik TJ, Moul JW. Pathological T2 sub-divisions as a prognostic factor in the biochemical recurrence of prostate cancer. BJU Int. 2010 Dec;106(11):1623-7. doi: 10.1111/j.1464-410X.2010.09439.

5. Lee KC1, Kim HJ, Sung K, Choi YE, Lee SH, Lim S, Lee KB, Shin JW, Park CY, Kim YS, Sym SJ, Shim YS, Choi SJ. The Predictive Value of Tumor Size, Volume, and Markers During Radiation Therapy in Patients With Cervical Cancer. Int J Gynecol Cancer. 2016 Oct 18.

6. Nicholson B1, Theodorescu D. Angiogenesis and prostate cancer tumor growth. J Cell Biochem. 2004 Jan 1;91(1):125-50.

7. Abdulkadir SA1, Carvalhal GF, Kaleem Z, Kisiel W, Humphrey PA, Catalona WJ, Milbrandt J. Tissue factor expression and angiogenesis in human prostate carcinoma. Hum Pathol. 2000 Apr;31(4):443-7

8. Stamey TA1, McNeal JE, Yemoto CM, Sigal BM, Johnstone IM. Biological determinants of cancer progression in men with prostate cancer. JAMA. 1999 Apr 21;281(15):1395-400

9. Epstein JI1, Carmichael M, Partin AW, Walsh PC. Is tumor volume an independent predictor of progression following radical prostatectomy? A multivariate analysis of 185 clinical stage B adenocarcinomas of the prostate with 5 years of followup. J Urol. 1993 Jun;149(6):1478-81.

10. Graefen M1, Karakiewicz PI, Cagiannos I, Klein E, Kupelian PA, Quinn DI, Henshall SM, Grygiel JJ, Sutherland RL, Stricker PD, de Kernion J, Cangiano T, Schröder FH, Wildhagen MF, Scardino PT, Kattan MW. Validation study of the accuracy of a postoperative nomogram for recurrence after radical prostatectomy for localized prostate cancer. J Clin Oncol. 2002 Feb 15;20(4):951-6.

11. Salomon L1, Levrel O, Anastasiadis AG, Irani J, De La Taille A, Saint F, Vordos D, Cicco A, Hoznek A, Chopin D, Abbou CC. Prognostic significance of tumor volume after radical prostatectomy: a multivariate analysis of pathological prognostic factors. Eur Urol. 2003 Jan;43(1):39-44.

12. Ahyai SA, Zacharias M, Isbarn H, Steuber T, Eichelberg C, Kollermann J, Fisch M, Karakiewicz PI, Huland H, Graefen M, Chun FK (2010) Prognostic significance of a positive surgical margin in pathologically organ-confined prostate cancer. BJU Int 106(4):478–483. doi:10.1111/j.1464-410X.2009.09162.x

13. Ramos CG, Roehl KA, Antenor JA, Humphrey PA, Catalona WJ (2004) Percent carcinoma in prostatectomy specimen is associated with risk of recurrence after radical prostatectomy in patients with pathologically organ confined prostate cancer. J Urol 172(1):137–140. doi:10.1097/01.ju.0000132139.40964.75

14. Palisaar RJ, Graefen M, Karakiewicz PI, Hammerer PG, Huland E, Haese A, Fernandez S, Erbersdobler A, Henke RP, Huland H (2002) Assessment of clinical and pathologic characteristics predisposing to disease recurrence following radical prostatectomy in men with pathologically organ-confined prostate cancer. Eur Urol 41(2):155–161

15. Merrill MM, Lane BR, Reuther AM, Zhou M, Magi-Galluzzi C, Klein EA (2007) Tumor volume does not predict for biochemical recurrence after radical prostatectomy in patients with surgical Gleason score 6 or less prostate cancer. Urology 70(2):294–298.

16. Song C, Kang T, Yoo S, Jeong IG, Ro JY, Hong JH, Kim CS, Ahn H (2011) Tumor volume, surgical margin, and the risk of biochemical recurrence in men with organ-confined prostate cancer. Urol Oncol. doi:10.1016/j.urolonc.2010.11.005

17. Chun FK, Briganti A, Jeldres C, Gallina A, Erbersdobler A, Schlomm T, Walz J, Eichelberg C, Salomon G, Haese A, Currlin E, Ahyai SA, Benard F, Huland H, Graefen M, Karakiewicz PI (2007) Tumour volume and high grade tumour volume are the best predictors of pathologic stage and biochemical recurrence after radical prostatectomy. Eur J Cancer 43(3):536–543. doi:10.1016/j.ejca. 2006.10.18

18. Rampersaud EN1, Sun L, Moul JW, Madden J, Freedland SJ. Percent tumor involvement and risk of biochemical progression after radical prostatectomy. J Urol. 2008 Aug;180(2):571-6; discussion 576. doi: 10.1016/j.juro.2008.04.017. Epub 2008 Jun 12.

19. Cookson MS1, Aus G, Burnett AL, Canby-Hagino ED, D'Amico AV, Dmochowski RR, Eton DT, Forman JD, Goldenberg SL, Hernandez J, Higano CS, Kraus SR, Moul JW, Tangen C, Thrasher JB, Thompson I. Variation in the definition of biochemical recurrence in patients treated for localized prostate cancer: the American Urological Association Prostate Guidelines for Localized Prostate Cancer Update Panel report and recommendations for a standard in the reporting of surgical outcomes. J Urol. 2007 Feb;177(2):540-5.

20. D'Amico AV, Whittington R, Malkowicz SB, et al. Calculated prostate cancer volume greater than 4.0 cm3 identifies patients with localized prostate cancer who have a poor prognosis following radical prostatectomy or external beam radiation therapy. JCO 1998;16:3094–100.

21. Ates M, Teber D, Gozen AS, et al. Do tumor volume, tumor volume ratio, type of nerve sparing, and surgical experience affect prostate specific antigen recurrence after laparoscopic radical prostatectomy? A matched pair analysis. J Urol 2007;177:1771– 6.

22. Guzzo TJ, Vira MA, Neway W, et al. Minimal tumor volume may provide additional prognostic information in good performance patients after radical prostatectomy. Urology 2007;69:1147–51.

23. Humphrey PA and Vollmer RT. Intraglandular tumor extent and prognosis in prostatic carcinoma: application of a grid method to prostatectomy specimens. *Hum Pathol* 1990; 21: 799-804.

24. Humphrey PA, Walther PJ, Currin SM, Vollmer RT. Histologic grade, DNA ploidy, and intraglandular tumor extent as indicators of tumor progression of clinical stage B prostatic carcinoma. A direct comparison. *Am J Surg Pathol* 1991; 15: 1165-70.

25. Carvalhal GF, Humphrey PA, Thorson P, Yan Y, Ramos CG, *et al.* Visual estimate of the percentage of carcinoma is an independent predictor of prostate carcinoma recurrence after radical prostatectomy. Cancer 2000; 89: 1308-14.

26. Noguchi M, Stamey TA, McNeal JE, et al. Assessment of morphometric measurements of prostate carcinoma volume. Cancer 2000;89: 1056–64.

27. Renshaw AA, Richie JP, Loughlin KR, et al. The greatest dimension of prostate carcinoma is a simple, inexpensive predictor of prostate specific antigen failure in radical prostatectomy specimens. Cancer 1998;83:748 –52.

28. Grignon DJ, Sakr WA. Pathologic staging of prostate carcinoma what are the issues? Cancer 1996;78:337– 40.

Table 1. Baseline characteristics of entire patients according to tumor volume and pathologic stage

	T2 LV	T2 HV	T3 LV	T3 HV	p-value
Number	1473	598	199	694	
Age (mean ± SD), yr	65.45 ± 6.99	65.58 ± 6.91	67.36 ± 6.08	66.66 ± 6.51	<0.001
Body mass index (mean ± SD),	24.43 ± 6.85	24.32 ± 2.91	25.75 ± 16.59	24.45 ± 2.84	0.059
Prostate specific antigen (median ± SD), ng/ml	6.21 ± 8.84	8.57 ± 11.21	7.45 ± 6.40	14.61 ± 22.20	<0.001
Pathological Gleason score, (%)					<0.001
6	291 (19.8)	28 (4.7)	4 (2.0)	6 (0.9)	
7	1123 (76.2)	524 (87.6)	162 (81.4)	474 (68.3)	
≥8	59 (3.0)	46 (7.7)	33 (14.6)	214 (30.8)	
Prostate volume (mean ± SD), cc	42.46 ± 16.11	36.19 ± 11.46	40.13 ± 12.58	38.96 ± 13.30	<0.001
Tumor volume ratio (mean ± SD), %	4.88 ± 2.85	22.99 ± 61.73	7.24 ± 2.30	38.66 ± 89.87	<0.001
Seminal vesicle invasion	0	0	29 (14.6)	221 (31.8)	<0.001
Positive surgical margin (%)	141 (9.6)	151 (25.3)	73 (36.7)	409 (58.9)	<0.001
Biochemical recurrence (%)	87 (5.9)	77 (12.9)	49 (24.6)	310 (44.7)	<0.001
Mean follow up duration (months)	46.25	46.94	50.11	45.59	0.480

Table 2. Multivariate Cox proportional hazard analysis to predict biochemical recurrence after radical prostatectomy among total patients

variables	HR	95%CI	p-value
Age	0.995	0.981-1.008	0.439
PSA	1.010	1.006-1.013	<0.001
Prostate volume	1.002	0.995-1.008	0.602
Pathologic Gleason score	3.409	1.935-6.007	<0.001
ECE	2.553	2.039-3.196	<0.001
SVI	2.727	2.195-3.389	<0.001
PSM	1.951	1.597-2.384	<0.001
PTV (10%)	1.569	1.248-1.973	<0.001

ECE = extracapsular extension; SVI = seminal vesicle invasion; PSM = positive surgical margin; PTV = pathologic tumor volume

Table 3. Multivariate Cox proportional hazard analysis to predict biochemical recurrence after radical prostatectomy according to risk group

	Low risk group			Intermediate risk group			High risk group		
variables	HR	95%CI	p-value	HR	95%CI	p-value	HR	95%CI	p-value
Age	0.964	0.924-1.006	0.091	0.984	0.959-1.010	0.236	1.000	0.983-1.018	0.992
PSA	1.111	0.961-1.284	0.206	1.045	1.006-1.086	0.024	1.004	0.996-1.008	0.087
Prostate volume	0.982	0.955-1.010	0.206	0.988	0.974-1.003	0.111	1.004	0.996-1.012	0.302
Pathologic Gleason score	1.226	0.585-2.567	0.590	3.586	1.983-6.484	<0.001	2.110	1.672-2.663	<0.001
ECE	2.567	1.329-4.959	0.005	2.324	1.601-3.375	<0.001	2.016	1.470-2.766	<0.001
SVI	14.917	3.355-66.330	<0.001	1.761	1.058-2.932	0.029	2.011	1.566-2.582	<0.001
PSM	3.795	1.965-7.332	<0.001	2.073	1.460-2.944	<0.001	1.547	1.191-2.010	0.001
PTV (10%)	1.063	0.550-2.054	0.856	0.828	0.569-1.203	0.321	1.914	1.325-2.765	0.001

ECE = extracapsular extension; SVI = seminal vesicle invasion; PSM = positive surgical margin; PTV = pathologic tumor volume

Figure 1. Biochemical recurrence free survival rate according to tumor stage and pathologic tumor volume (blue line – T2 low volume group, green line – T2 high volume group, yellow line – T3 low volume group and purple line – T3 high volume group)

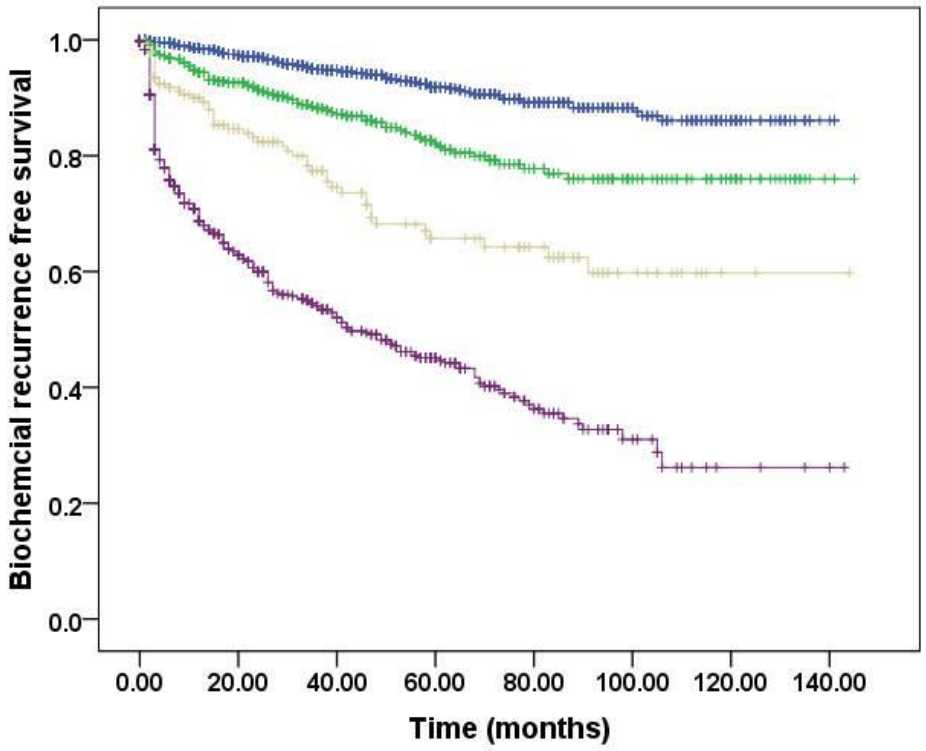


Figure 2a. Biochemical recurrence free survival rate according to tumor stage and pathologic tumor volume (blue line – T2 low volume group, green line – T2 high volume group, yellow line – T3 low volume group and purple line – T3 high volume group) (A) among D'amico low risk group, (B) intermediate risk group, (C) high risk group.

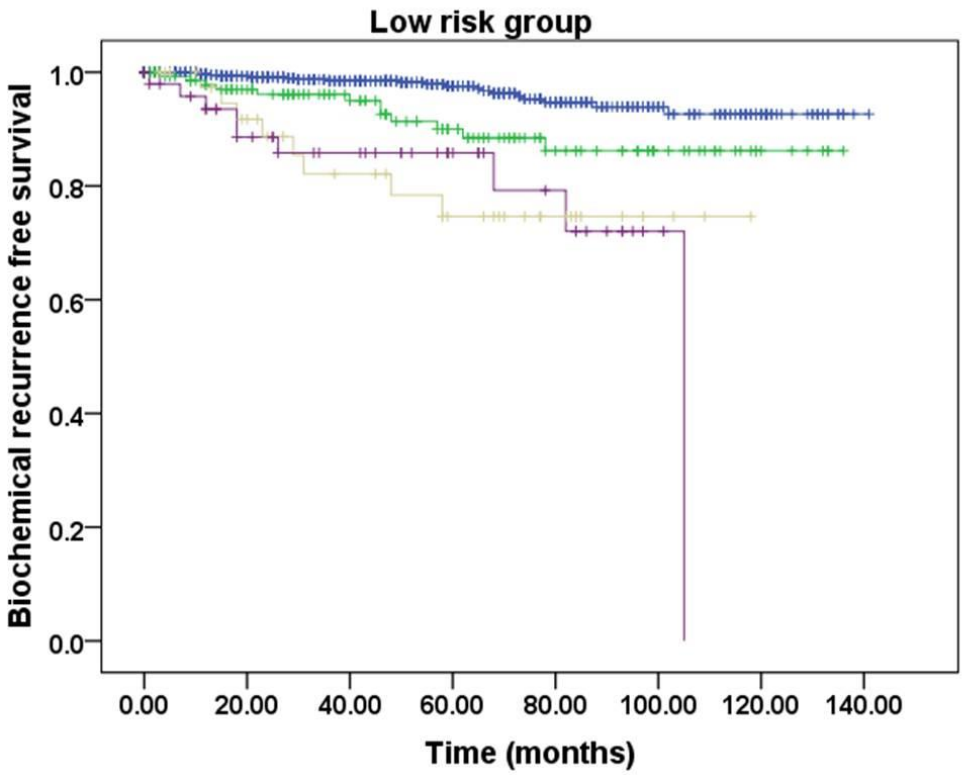


Figure 2b. Biochemical recurrence free survival rate according to tumor stage and pathologic tumor volume (blue line – T2 low volume group, green line – T2 high volume group, yellow line – T3 low volume group and purple line – T3 high volume group) (A) among D'amico low risk group, (B) intermediate risk group, (C) high risk group.

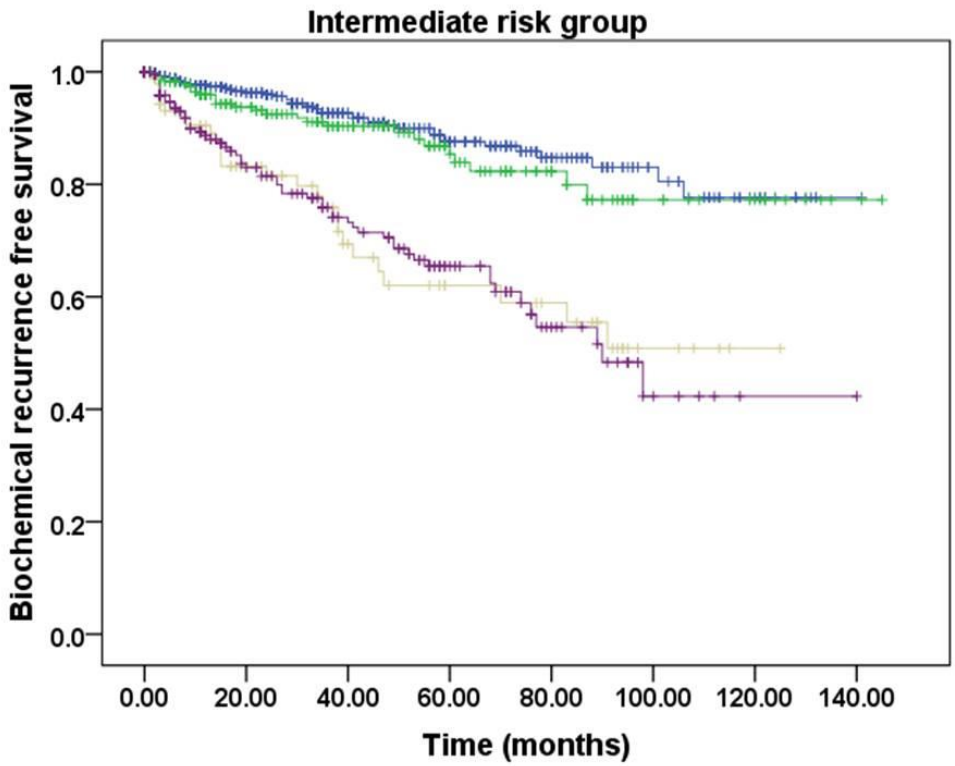
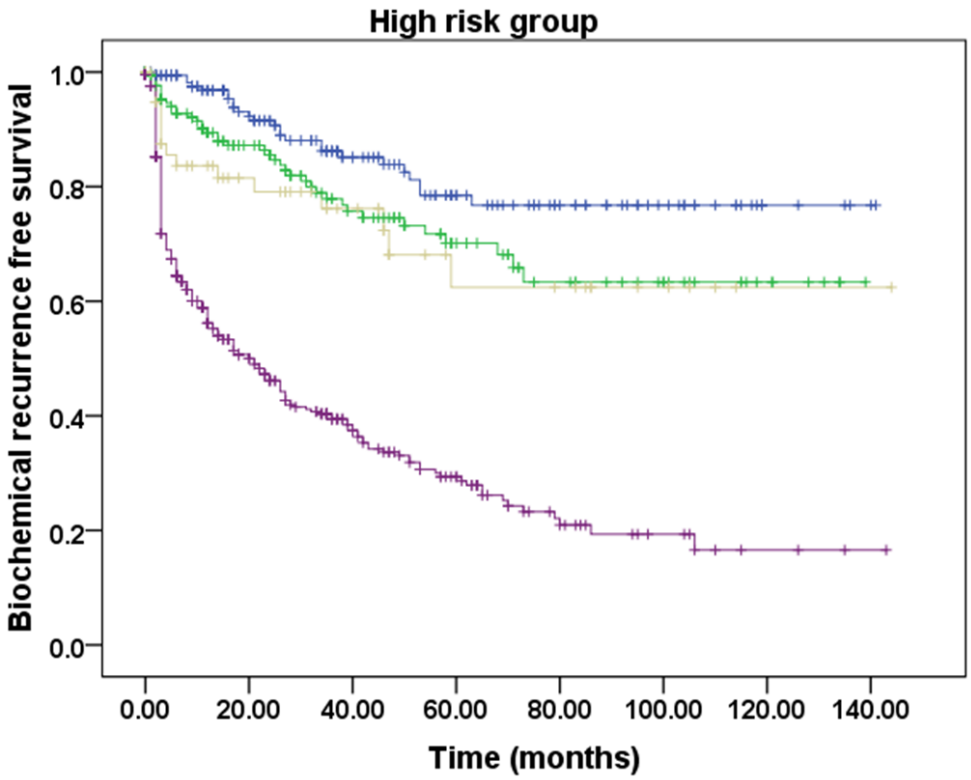


Figure 2c. Biochemical recurrence free survival rate according to tumor stage and pathologic tumor volume (blue line – T2 low volume group, green line – T2 high volume group, yellow line – T3 low volume group and purple line – T3 high volume group) (A) among D'amico low risk group, (B) intermediate risk group, (C) high risk group.



요약 (국문초록)

근치적 전립선절제술 후 종양 국소 용적에 따른 위험도 분류의 비교

김태진

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서론: 근치적 전립선절제술 (RP)을 받은 환자에서 병리학 적 종양 부피 (PTV)의 관련성을 조사하고자 하였다.

대상 및 방법: 본 연구에서는 2003년 9월부터 2015년 3월까지 근치적 전립선 절제술 (RP)을 시행 받은 환자 중 1년 이상 추적 관찰한 3080명을 후향적으로 분석하였다. 해당 환자군은 병기 등급 및 병리학적 종양 크기(PTV)에 따라 4가지 위험군 (T2 + 저용량 : T2LV, T2 + 고용량 : T2HV, T3 + 저용량 : T3LV, T3 + 높은 용적 : T3HV)으로 분류되었다. 생화학적 재발 확률 (BCR)은 Kaplan-Meier 곡선을 사용하여 분석하였으며, 콕스 다변량 분석을 통해 PTV의 BCR 예측 정도를 평가하였다.

결과: 환자들의 PSA의 중앙값은 7.87ng/ml이었으며 PTV는 10 %으로 확인되었다. 총 2964명의 환자 중 T2LV 군은 1473명 (49 %), T2HV 군은 598명 (20%), T3LV 군은 199명 (6%), T3HV 군은 694 (23 %)명 확인되었다. T2HV 군과 T3LV 군을 비교할 때, 글리슨 점수 및 절제부에 종양이 있을 가능성은 T3LV에서 더 높았다. 추적 관찰 기간 (50개월) 동안 BCR 미발생 생존율은 T2HV 군에서 더 높았다 ($p < 0.001$). 콕스 다변량 분석 결과 PTV는 BCR의 유의미한 예측 인자로 확인되었다. 하위 그룹 분석에서 수술 전 고위험군 환자들을 대상으로 할 경우 T2HV 군은 T3LV 군에 비해 BCR 미발생 생존율 면에서는 유의미한 차이가 없었으나, PTV는 유의미한 차이를 보였다.

결론: PTV는 RP을 시행 받은 전립선 암 환자에서 BCR의 중요한 예측 인자로 확인되었나 T2HV의 BCR 결과는 긍정적이었다. 수술 전 PSA와 글리슨 점수가 높을 경우, T2HV 군은 T3LV 군과 BCR 결과가 비슷하였다.

주요어: 전립선암, 근치적 전립선적출술, 재발

학 번: 2016-21945