Original Article

Positive association between preoperative lymphocyte-to-monocyte ratio and risk of the status of positive surgical margins by prostate cancer: results in 497 consecutive patients treated only by radical prostatectomy

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Background: Positive surgical margins (PSM) is one of the most important factors affecting the prognosis of prostate cancer (PCa) patients after radical prostatectomy (RP). Although some studies have found the preoperative systematic inflammation-based scores the neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR) can predict the incidence and prognosis of PCa, few studies have explored the predictive value of preoperative systematic inflammation-based scores on the PSMs for PCa patients after RP.

Methods: From June 2014 to September 2020 a total of 497 patients underwent RP at our institution. Blood samples from all patients were collected within one week before surgery. Preoperative clinical characteristics including age, body mass index (BMI), prostate-specific antigen (PSA), and biopsy Gleason sum (BGS) were assessed. Postoperatively pathological specimens were assessed for pathological Gleason sum (PGS), pathological stage, and margin status.

Results: In the multivariable analysis including preoperative variables, PSA and LMR were the independent predictive factors for PSM (OR: 2.817; 95% CI, 1.836–4.320, P<0.001; OR: 1.124; 95% CI, 1.018–1.240, P=0.021. Considering pre-, intra-, and postoperative variables, BGS, perineural invasion, seminal vesicle invasion (SVI), pathologic Gleason sum (PGS) combined, were associated with increased risk of PSM in the univariable analysis (P<0.001 for all variables). However, in the multivariable analysis, perineural invasion (OR: 2.672; 95% CI, 1.649–4.330; P<0.001), PGS (OR: 2.52; 95% CI, 1.556–4.082; P<0.001) were independent predictive factors for the incidence of PSM. Finally, LMR was shown to be an independent predictive factor (OR: 0.881; 95% CI, 0.779–0.996; P=0.043) for apical PSMs, with increasing LMR predicting the lower incidence of apex location. And we also found that LMR was an independent factor that predicts multifocal positive margins (OR: 1.179; 95% CI, 1.023–1.358; P=0.023).

Conclusions: Preoperative LMR could be used as an independent predictor to predict the incidence of PSMs after RP. And Considering pre-, intra-, and postoperative variables, we also found that preoperative LMR could predict the occurrence of apical and multifocal PSMs.

Keywords: Prostate cancer (PCa); positive surgical margins (PSM); lymphocyte-to-monocyte ratio (LMR)

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Introduction

Prostate cancer (PCa) is the most common male malignant tumor and the second leading cause of male cancer-related mortality (1). At present, radical prostatectomy (RP) is the gold standard treatment for localized PCa. With the development of surgical techniques and technology, it has gradually shifted from open radical prostatectomy (ORP) to laparoscopic radical prostatectomy (LRP). The development of technology has made the surgical treatment of localized PCa safer and more minimally invasive, and greatly improved the quality of life and prognosis of PCa patients (2).

Although patients with PCa can obtain a clinical cure or a good prognosis through RP, there are still some important factors that can lead to tumor recurrence and progression.

According to previous literature reports, the incidence rate of positive surgical margins (PSM) after RP is approximately 10–35%, and PSMs are considered to be one of the most significant indicators for cancer recurrence and poor prognosis in PCa patients (3-5). Compared with patients with negative surgical margins, PSMs may not only cause tumor recurrence after surgery but also cause mental stress to PCa patients (6). Recent studies have confirmed that tumor-related inflammation affects the malignancy of tumors, including tumor proliferation and survival, angiogenesis, metastasis, and treatment response (7). In some studies, some cancer-related inflammatory indexes including neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), and prognostic nutritional index play an important role in predicting the prognosis of different tumors, these are serum-based and not pathology review based (8-12). However, few articles reported the association between tumor-related inflammation scores and PSMs status after RP. Therefore, we performed this study to explore whether these inflammation scores can be used as important predictors to predict PSMs status. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/tau-20-1447).

Methods

Patients

This study reviewed all patients from June 2014 to September 2020, 497 patients of PCa who underwent RP in the second hospital of Tianjin Medical University were included. The retrospective data were collected following criteria: no neoadjuvant or adjuvant treatment, distant metastasis confirmed by surgery or imaging. Excluded criteria: Patients with genetic immunodeficiency, acquired immunodeficiency syndrome, immunosuppressive drugs, and other immune deficiency diseases; patients with hematological diseases; long-term immunotherapy; patients with other malignant tumors; incomplete record. The surgical techniques for RP with or without lymph node dissection differed among patients: open RP or laparoscopic RP. Both interventions were conducted by two experienced surgical teams. The protocol for processing RP specimens was similar across sites, the remaining specimen was sectioned transversely at intervals of 3–5 mm formalin-fixed and embedding all sections for analysis. PSMs was defined as the appearance of tumor cells on the surface of the surgical specimen and were categorized into five groups based on their locations: apex, proximal (bladder neck), peripheral, focal, and multifocal. Determine the occurrence and location of positive margins based on previous studies (13). A pathologist performed all histopathological diagnoses and prepared prostate specimens using the same method during the research. Focal positive margins are considered to be only a single positive location in the surgical specimen, and multifocal positive margins are defined as more than 1 positive location in the surgical specimen. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Regional Ethical Review Board in Tianjin medical university second hospital and individual consent for this retrospective analysis was waived.

Definitions and of LMR, NLR, PLR, prognostic nutritional index

The definitions of prognostic nutritional index, NLR, and PLR were shown as follows: prognostic nutritional index = albumin (g/L) + 5 × total lymphocyte counts (10^9/L); SII = platelet × neutrophil/lymphocyte counts; NLR = neutrophil/lymphocyte counts; and PLR = platelet/lymphocyte counts. Blood samples of all patients were collected within one weeks before surgery.

Statistical analysis

The entire statistical process was performed with SPSS 22.0 software. Measurement values for continuous variables are expressed as the median (range). Qualitative data were

expressed as a percentage (%) and analyzed by the χ^2 test. The receiver operating characteristic (ROC) curve was plotted by referring to the sensitivity *vs.* 1-specificity of the LMR level. The areas under the curve (AUCs) and cut-off values were also calculated. Sensitivity, specificity was used to estimate the value of LMR based on the cut-off value. Univariate and multivariate logistic regression analysis was used to screen out the independent risk factors for the incidence, location of PSMs. All analyses are bilateral analysis, P<0.05 has statistical significance.

Results

Patient Features are shown in *Table 1*. A total of 497 patients were enrolled in our study, from June 2014 to September 2020. The overall PSMs rate was 53.7% (267 of 497). The distribution of these PSMs by location was 69.3% (185 of 267) in the apex, 23.3% (116 of 267) peripheral, 34.5% (92 of 267) proximal. Focal PSM was 59.2% (158 of 267) and multifocal PSM was 40.8% (104 of 267).

Model 1: preoperative and postoperative factors in PSMs

In preoperative factors, no association was observed in the univariable analysis (*Table 2*) between PSM and age (P=0.904), BMI (P=0.441), NLR (P=0.44), PLR (P=0.116), LMR (P=0.074), prognostic nutritional index (P=0.46). In the multivariable analysis including preoperative variables, LMR was a significant predictive factor, with higher PSM rates (OR: 1.124; P<0.021) and also in PSA (OR: 2.817; P<0.001) (*Table 2*). As for postoperative pathological factors, perineural invasion, SVI and pathologic Gleason sum (PGS) were associated with increased risk of PSM in the univariable analysis (P<0.001 for all variables; *Table 2*). In the multivariable analysis, perineural invasion (P<0.001) and PGS (P<0.001) were the only independent predictive factors for PSMs.

Model 2: positive surgical margin location

Tables 3-5 summarize clinical and pathologic features according to the location of PSMs including apex, peripheral, proximal. LMR, analyzed as a continuous variable, was shown to be an independent predictive factor for apical PSMs, with increasing BMI predicting the lower incidence of apex location (OR: 0.881; P=0.043). ROC curve indicated that a LMR of 7.01 had maximum Youden index value (*Figure 1*) (sensitivity =89.7%, Specificity =22%). The higher the preoperative LMR value, the lower the risk of the positive apex. Regarding peripheral PSM location, PSA (OR: 2.209; P=0.006) and perineural invasion (OR: 1.934; P=0.014) were determined to be significantly predictive factors, which predicts the incidence risk of peripheral location.

Model 3: focal and multifocal positive margins

In univariate analysis (*Table 6*), PSA (OR 2.721; P<0.001), perineural invasion (OR 2.452; P<0.001), SVI (OR 2.714; P=0.001), PGS (OR 2.4; P<0.001) associated with the risk of focal surgical margins. In multivariate analysis (*Table 6*), PSA (OR 2.374; P<0.001), perineural invasion (OR 2.349; P=0.002), PGS (OR 1.78; P=0.039) were independent factors that associated with the risk of focal PSMs. And in the multivariate analysis presented in *Table 7*, LMR (OR 1.179; P=0.023), PSA (OR 3.5; P<0.001), perineural invasion (OR 3.446; P<0.001), PGS (OR 3.931; P<0.001) were significant with the risk of multifocal PSMs.

Discussion

PSMs after RP is considered to be one of the important factors leading to postoperative tumor recurrence and local progression, and it is also a key factor in determining whether PCa patients should proceed with the second treatment (14). With the development of surgical techniques and instruments, the probability of PSMs after RP is decreasing. However, in high-risk PCa patients, the incidence rate of PSMs after RP remains relatively stable (15). There are two main causes for the incidence risk of PSMs, including tumor progression and the experience of the surgeon. With the development of the current surgical technique, the surgical technique of the surgeon is constantly improving. In addition to the surgical experience, the more important reason is the biological behavior of the tumor cell, which is an independent risk factor that affects the PSMs (14,16). Patel *et al.* performed a muti-institutional study and demonstrated that the apex of the prostate is the most common site for PSMs after robotic-assisted RP, and pathological staging and preoperative PSA are the most important independent risk factors for predicting positive margins (17). Yossepowitch *et al.* reported that the incidence of PSMs is strongly influenced by the surgeon's experience irrespective of the surgical approach through evidence synthesis and they also thought PSMs are associated with a twofold increased hazard of biochemical relapse, but

Table 1 Association between individual categorical and continuous variables with positive surgical margins

Variables	Population (n=497)	Surgical margin		P value
		Negative (n=230; 46.3%)	Positive (n=267; 53.7%)	
Age, years, median (IQR)	68 [63–73]	68 [63–72]	67 [63–73]	0.904
BMI, kg/m^2, median (IQR)	25.14 (23.5–27)	24.97 (23.53–26.83)	25.2 (23.38–27.16)	0.442
Diabetes, (%)				0.238
Absent	420 (84.5)	191 (83.0)	229 (85.8)	
Present	77 (15.5)	39 (17.0)	38 (14.2)	
Hypertension, (%)				0.503
Absent	254 (51.1)	118 (51.3)	136 (50.9)	
Present	243 (48.9)	112 (48.7)	131 (49.1)	
Coronary heart disease, no. (%)				0.458
Absent	402 (80.9)	187 (81.3)	215 (80.5)	
Present	95 (19.1)	43 (18.7)	52 (19.5)	
PSA, (%)				<0.001*
<20 ng/mL	314 (63.2)	179 (77.8)	135 (50.6)	
≥20 ng/mL	183 (36.8)	51 (22.2)	132 (49.4)	
Serum albumin, g/L, median (IQR)	44.7 (41.7–47.2)	44.56 (42–47.05)	44.8 (41.4–47.5)	0.795
Serum neutrophil, 10^9/L, median (IQR)	3.6 (2.98–4.42)	3.58 (2.98–4.4)	3.6 (2.99–4.46)	0.896
Serum lymphocyte,10^9/L, median (IQR)	1.79 (1.44–2.27)	1.78 (1.37–2.26)	1.79 (1.47–2.27)	0.132
Serum monocyte, 10^9/L, median (IQR)	0.37 (0.31–0.45)	0.38 (0.3–0.45)	0.37 (0.31–0.46)	0.828
Serum platelet, 10^9/L, median (IQR)	202 [171–240]	203.5 (170.5–243.5)	201 [172–239]	0.768
NLR, median (IQR)	2 (1.53–2.7)	2.05 (1.54–2.83)	1.94 (1.51–2.6)	0.437
PLR, median (IQR)	113 (89.81–147.01)	118.4 (90.87–157.25)	109.5 (89.45–138.82)	0.111
LMR, median (IQR)	4.8 (3.86–5.97)	4.54 (3.78–5.58)	5 (4.02–6.08)	0.072
Prognostic nutritional index, median (IQR)	53.85 (50.45–57.13)	53.4 (50.34–56.95)	53.59 (50.5–57.35)	0.461
Biopsy Gleason sum, n (%)				<0.001*
<8	292 (58.8)	155 (67.4)	137 (51.3)	
≥8	205 (41.2)	75 (32.6)	130 (48.7)	
Perineural invasion, n (%)				<0.001*
Absent	375 (75.5)	197 (85.7)	178 (66.7)	
Present	122 (24.5)	33 (14.3)	89 (33.3)	
SVI, n (%)				<0.001*
Absent	414 (83.3)	211 (91.7)	203 (76.4)	
Surgical approach, n (%)				
ORP	28 (5.6)	14 (50.0)	14 (50.0)	0.415
LRP	469 (94.4)	216 (46.1)	253 (53.9)	
Present	83 (16.7)	19 (8.3)	64 (23.6)	

Table 1 (*continued*)

Table 1 (*continued*)

Variables	Population (n=497)	Surgical margin		P value
		Negative (n=230; 46.3%)	Positive (n=267; 53.7%)	
Pathologic stage				
Organ confined: pT1/pT2, no. (%)	211 (42.4)	211 (91.7)	0	
Non-organ confined: pT3a, no. (%)	200 (40.2)	0	200 (74.9)	
Non-organ confined: pT3b, no. (%)	78 (15.7)	19 (8.3)	59 (22.1)	
Non-organ confined: pT4, no. (%)	8 (1.7)	0	8 (4)	
Pathologic Gleason sum, no. (%)				<0.001*
<8	308 (62.0)	176 (76.5)	132 (49.4)	
≥8	189 (38.0)	54 (23.5)	135 (50.6)	
Location of PSM, no. (%)				
Any	267 (53.7)		267 (100.0)	
Apical	185 (37.2)		185 (69.3)	
Peripheral	116 (23.3)		116 (23.3)	
Proximal	92 (18.5)		92 (34.5)	
Number of PSM, no. (%)				
Focal positive (single)	158 (31.8)		158 (59.2)	
Multifocal positive (more than 1)	109 (21.9)		109 (40.8)	

*, statistically significant. BMI, body mass index; PSA, prostate specific antigen; NLR, neutrophil to lymphocyte ratio; PLR, platelets to lymphocyte ratio; LMR, lymphocyteto monocyte ratio; SVI, seminal vesicle invasion; ORP, open radical prostatectomy.

Table 2 Univariate and Multivariate analysis for positive surgical margins

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age	0.998	0.973–1.025	0.904			
BMI	1.025	0.963–1.091	0.441			
PSA	3.432	2.317–5.083	<0.001*	2.817	1.836–4.32	<0.001*
NLR	0.952	0.841–1.078	0.44			
PLR	0.997	0.994–1.001	0.116			
LMR	1.086	0.992–1.189	0.074	1.124	1.018–1.24	0.021*
Prognostic nutritional index	1.013	0.979–1.047	0.46			
Biopsy Gleason sum (≥8 *vs.* <8)	1.961	1.361–2.826	<0.001*	0.902	0.566–1.439	0.665
Perineural invasion	2.985	1.907–4.672	<0.001*	2.672	1.649–4.33	<0.001*
SVI	3.501	2.026–6.051	<0.001*	1.778	0.96–3.29	0.067
Pathologic Gleason sum (≥8 *vs.* <8)	3.333	2.261–4.913	<0.001*	2.52	1.556–4.082	<0.001*

*, statistically significant. BMI, body mass index; PSA, prostate specific antigen; NLR, neutrophil to lymphocyte ratio; PLR, platelets to lymphocyte ratio; LMR, lymphocyteto monocyte ratio; SVI, seminal vesicle invasion.

Table 3 Univariate and multivariate analysis for apical PSMs

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age	1.039	1.001–1.078	0.043*	1.036	0.998–1.076	0.062
BMI	1.001	0.913–1.099	0.977			
PSA	0.73	0.433–1.230	0.237			
NLR	1.085	0.888–1.325	0.424			
PLR	1.004	0.998–1.009	0.219			
LMR	0.875	0.775–0.988	0.031*	0.881	0.779–0.996	0.043*
Prognostic nutritional index	1.001	0.954–1.050	0.963			
Biopsy Gleason sum (≥8 *vs.* <8)	0.805	0.478–1.355	0.415			
Perineural invasion	1.052	0.606–1.827	0.857			
SVI	0.91	0.505–1.638	0.753			
Pathologic Gleason sum (≥8 *vs.* <8)	0.963	0.572–1.620	0.886			

*, statistically significant. BMI, body mass index; PSA, prostate specific antigen; NLR, neutrophil to lymphocyte ratio; PLR, platelets to lymphocyte ratio; LMR, lymphocyteto monocyte ratio; SVI, seminal vesicle invasion.

Table 4 Univariate and Multivariate analysis for peripheral PSMs

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age	0.975	0.941–1.009	0.144			
BMI	0.946	0.867–1.032	0.213			
PSA	1.926	1.179–3.145	0.009*	2.029	1.226–3.357	0.006*
NLR	1.039	0.891–1.212	0.625			
PLR	0.996	0.991–1.001	0.13			
LMR	1.123	0.997–1.265	0.057	1.128	0.999–1.275	0.053
Prognostic nutritional index	0.993	0.950–1.039	0.768			
Biopsy Gleason sum (≥8 *vs.* <8)	1.401	0.862–2.278	0.173			
Perineural invasion	1.962	1.173–3.281	0.01*	1.934	1.143–3.274	0.014*
SVI	1.456	0.840–2.526	0.181			
Pathologic Gleason sum (≥8 *vs.* <8)	1.387	0.853–2.254	0.187			

*, statistically significant. BMI, body mass index; PSA, prostate specific antigen; NLR, neutrophil to lymphocyte ratio; PLR, platelets to lymphocyte ratio; LMR, lymphocyteto monocyte ratio; SVI, seminal vesicle invasion.

their association with more robust clinical endpoints is controversial (18). In our research results, we found that preoperative PSA, perineural invasion, and postoperative GS are related to the occurrence of PSMs (all P<0.001). Although there is currently no conclusion on the role of preoperative inflammatory factors in the occurrence of PSMs after RP, inflammatory indicators did have a greater impact on the prognosis of PCa. Peng *et al.* performed a meta-analysis in 2019 and reported that pretreatment LMR, NLR, PLR might be an effective biomarker for poor

Table 5 Univariate and Multivariate analysis for proximal PSMs

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age	0.99	0.955–1.026	0.568			
BMI	0.979	0.894–1.072	0.644			
PSA	1.651	0.992–2.749	0.054	1.436	0.847–2.433	0.179
NLR	1.018	0.870–1.191	0.826			
PLR	0.999	0.994–1.003	0.556			
LMR	1.084	0.965–1.218	0.173			
Prognostic nutritional index	0.995	0.950–1.043	0.846			
Biopsy Gleason sum (≥8 *vs.* <8)	1.414	0.852–2.346	0.181			
Perineural invasion	0.86	0.502–1.474	0.584			
SVI	2.413	1.373–4.240	0.002*	2.052	1.124–3.746	0.019*
Pathologic Gleason sum (≥8 *vs.* <8)	1.765	1.058–2.945	0.03*	1.329	0.762–2.317	0.316

*, statistically significant. BMI, body mass index; PSA, prostate specific antigen; NLR, neutrophil to lymphocyte ratio; PLR, platelets to lymphocyte ratio; LMR, lymphocyteto monocyte ratio; SVI, seminal vesicle invasion.

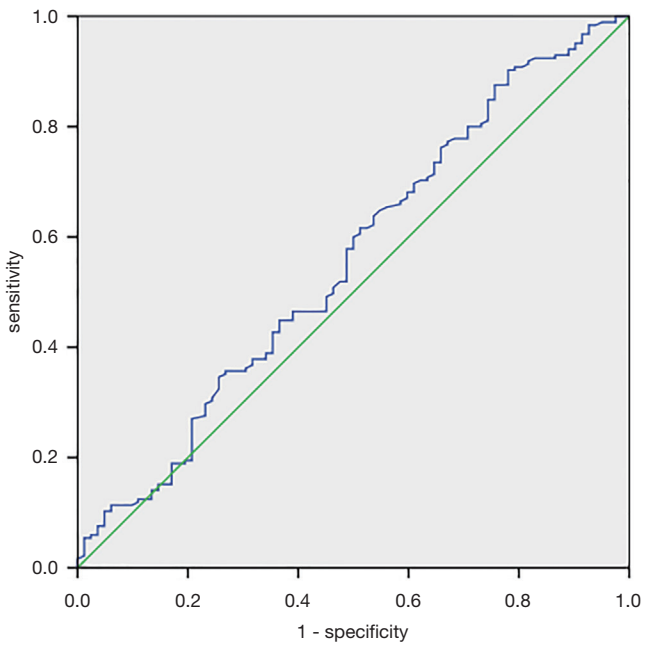

Figure 1 ROC curves in predicting apex PSMs by LMR (continuous, AUC =0.557). ROC receiver operating characteristic, AUC area under the curve.

prognosis in patients with PCa (19). And Zhou *et al.* also suggested that LMR played a significant role in initial PCa diagnosis (20). These articles showed that LMR played an important role in the occurrence and development of PCa. In our research, we found that preoperative PSA, LMR, and postoperative perineural invasion, PGS can be used as independent factors to predict the incidence risk of PSMs after RP. And also, in terms of predicting the location of PSMs, LMR may have an inverse relationship with the apical PSMs (P=0.043). The lower the LMR before surgery, the higher the probability of apical PSMs. Shigeta *et al.* also showed that high monocyte count predicts poor clinical outcomes in PCa patients. This conclusion indicated that lower LMR may have a worse prognosis in PCa patients (21). At the same time, Lian *et al.* found that patients with apical PSMs had a higher risk of biochemical recurrence than patients with other PSMs in 2020 (22). These findings lead us to speculate that the impact of LMR on the prognosis of PCa patients may be caused by the incidence of apical PSMs after RP. However, we found that higher LMR may have a greater risk of PSMs. This is contrary to our hypothesis. The reason for this contradiction is still unclear. It may be related to the small number of the population included in this study. Besides, we also found that LMR may be used as an independent predictor of multifocal PSMs. Coelho *et al.* reported that the clinical stage was the only independent variable that was associated with PSM after RARP (23). They did not find a positive correlation between preoperative PSA and PSMs. Porcaro *et al.* collected 476 PCa patients after RP, and they also demonstrated that

Table 6 Univariate and Multivariate analysis for focal PSMs

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age	1.001	0.971–1.032	0.961			
BMI	1.052	0.979–1.132	0.168			
PSA	2.721	1.748–4.235	<0.001*	2.374	1.482–3.803	<0.001*
NLR	0.857	0.712–1.031	0.102			
PLR	0.998	0.995–1.002	0.359			
LMR	1.065	0.964–1.178	0.217			
Prognostic nutritional index	1.024	0.982–1.067	0.272			
Biopsy Gleason sum (≥8 *vs.* <8)	1.73	1.140–2.626	0.01*	0.966	0.571–1.635	0.897
Perineural invasion	2.452	1.482–4.057	<0.001*	2.349	1.381–3.995	0.002*
SVI	2.714	1.487–4.955	0.001*	1.566	0.796–3.079	0.194
Pathologic Gleason sum (≥8 *vs.* <8)	2.4	1.547–3.721	<0.001*	1.780	1.032–3.076	0.039

*, statistically significant. BMI, body mass index; PSA, prostate specific antigen; NLR, neutrophil to lymphocyte ratio; PLR, platelets to lymphocyte ratio; LMR, lymphocyteto monocyte ratio; SVI, seminal vesicle invasion.

Table 7 Univariate and Multivariate analysis for multifocal PSMs

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age	0.99	0.962–1.029	0.772			
BMI	0.979	0.913–1.069	0.764			
PSA	1.651	2.947–7.856	<0.001*	3.5	1.993–6.147	<0.001*
NLR	1.018	0.884–1.173	0.799			
PLR	0.999	0.991–1.000	0.06			
LMR	1.084	0.996–1.256	0.059	1.179	1.023–1.358	0.023*
Prognostic nutritional index	0.995	0.961–1.044	0.936			
Biopsy Gleason sum (≥8 *vs.* <8)	1.414	1.474–3.747	<0.001*	6.867	0.461–1.630	0.658
Perineural invasion	4.04	2.375–6.875	<0.001*	3.446	1.863–6.372	<0.001*
SVI	4.822	2.588–8.985	<0.001*	2.064	0.991–4.298	0.053
Pathologic Gleason sum (≥8 *vs.* <8)	5.406	3.301–8.851	<0.001*	3.931	2.078–7.436	<0.001*

*, statistically significant. BMI, body mass index; PSA, prostate specific antigen; NLR, neutrophil to lymphocyte ratio; PLR, platelets to lymphocyte ratio; LMR, lymphocyteto monocyte ratio; SVI, seminal vesicle invasion.

preoperative PSA could not be an independent factor to predict the incidence of PSMs (24). Pooli *et al.* published an article in 2019 and reported that age and PSA were significantly associated with PSMs rate (25). In summary, the relationship between PSA and PSM is still controversial. Jayachandran *et al.* discovered that obesity was associated with an increased risk of overall PSMs. They also suggested that most obese men had a higher risk of apical PSMs (26). Although Coelho *et al.* did not found that there was a relationship between BMI and the risk of any PSMs, they

also believe that there was a statistical relationship between BMI and apical PSMs (23). Zilberman *et al.* thought although BMI was associated with advanced PCa, BMI did not show a correlation in the incidence rate and location of PSMs (27). In our research, we did not find an important association between BMI and incidence rate and the location of PSMs. Currently, the impact of BMI on PSMs after RP remains controversial.

Limitation

There were a few limitations to our study. First, our research was a retrospective study, so some information or data may be biased. Besides, other inflammatory factors may also affect the results of the study, but we did not include these factors. Furthermore, from our research, the incidence of PSMs in our population was more than 50%, which may also be caused by the experience of the surgeon and technical limitations.

Conclusions

In general, LMR could be used as a significant factor to predict the incidence of PSMs. Regarding PSMs location, LMR could be used as an independent variable to negatively correlate with the apical PSMs. Besides, LMR was the only preoperative variable independently associated with multifocal PSMs

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Regional Ethical Review Board in Tianjin medical university second hospital and individual consent for this retrospective analysis was waived.

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