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# Analysis of risk factors for positive margins in robot-assisted laparoscopic radical prostatectomy with Retzius-sparing (RS-RARP)

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## Abstract

**Objective** This study aims to analyze the risk factors for positive surgical margins following robot-assisted laparoscopic radical prostatectomy with Retzius-sparing (RS-RARP) to provide a basis for clinical preoperative evaluation and intraoperative decision-making.

**Methods** A retrospective analysis was conducted on the clinical data of 103 patients who underwent RS-RARP at the First Hospital of Shanxi Medical University from May 2022 to May 2024. Patients were divided into positive margin and negative margin groups, as well as apical positive margin and apical negative margin groups based on surgical margin status. Patient demographics, preoperative data, and postoperative data were collected. Univariate and multivariate logistic regression analyses were used to evaluate the relationship between various factors and surgical margin status.

**Results** A total of 103 patients were included, with 31 cases (30.1%) in the positive margin group and 72 cases (69.9%) in the negative margin group. The results of the Logistic Regression With Variable Reduction indicated that prostate volume (OR = 10.90, 95% CI: 3.49–34.04,  $p < 0.001$ ) and  $\geq pT3$  stage tumors (OR = 8.78, 95% CI: 2.54–30.42,  $p < 0.001$ ) were independent risk factors for positive surgical margins. Additionally, they were also significantly associated with an increased risk of positive surgical margins at the prostate apex.

**Conclusion** The study indicates that prostate volume and pT stage are notable predictors of positive surgical margins in RS-RARP.

**Keywords** Prostate cancer, Retzius-sparing, Robotic surgery, Positive surgical margins

## Introduction

According to Globocan statistics in 2020, there were nearly 1.4 million new cases of prostate cancer (PCa) and approximately 375,000 deaths worldwide. PCa has become the second most common malignant tumor in men in 2020 [1, 2]. Robot-Assisted Radical Prostatectomy

(RARP) is currently one of the main surgical methods for treating localized prostate cancer [3]. In 2010, Professor Galfano proposed the Retzius-Sparing Robot-Assisted Radical Prostatectomy (RS-RARP) to improve patient prognosis, such as reducing urinary incontinence and accelerating the recovery of sexual function [4].

However, a key challenge in prostate cancer surgery is to ensure negative resection margins, as positive surgical margins (PSM) are associated with an increased risk of biochemical recurrence and cancer progression [5]. Although RS-RARP may have potential advantages, there is insufficient evidence to support its superiority in

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short-term and long-term prognosis of resection margins compared with standard RARP, RS-RARP changes the anatomical approach to prostatectomy and may have an impact on oncological outcomes, including PSM rates [6].

The aim of this study was to systematically evaluate independent clinical factors that significantly influence surgical margins in a target population, using logistic regression methods to provide a deeper understanding of potential relationships.

## Method

1. The study retrospectively analyzed the clinical data of 103 patients who underwent RS-RARP in the First Hospital of Shanxi Medical University from May 2022 to May 2024. According to the resection margin, they were divided into two groups, namely, the resection margin positive group and the resection margin negative group. Inclusion criteria: a. Preoperative prostate puncture and postoperative pathology confirmed prostate cancer; b. Complete clinical medical records. Exclusion criteria: a. Pathology was non-adenocarcinoma samples; b. Preoperative prostate surgery history; c. Case data missing. In the data collection stage of this study, to ensure data transparency, if there is a missing value of some data, we will exclude the sample.
2. The basic data of the patients were collected, including age, BMI (1=BMI< 28, 2=BMI≥ 28), history of hypertension (0=no, 1=yes), history of diabetes (0=no, 1=yes), and history of coronary heart disease (0=no, 1=yes); preoperative data, including total prostate-specific antigen (TPSA) (0=TPSA< 20, 1=TPSA≥ 20), prostate volume ml (0=< 50, 1=≥ 50), prostate MRI PI-RADS score (3–5), Extraprostatic extension(lymph node metastasis/seminal vesicle invasion/bone metastasis) (0=no, 1=yes), interval from puncture to surgery (0=< 4 weeks, 1=≥ 4 weeks), puncture ISUP grade (1–5), puncture positive needle number ratio (0=< 25%, 1= 25%≤< 49%, 2=≥ 50%), D'Amico risk score (1 = medium risk/low risk, 2 = high risk), preoperative endocrine therapy(take Bicalutamide) (0 = no, 1 = yes); intraoperative data, including operation time and intraoperative blood loss; postoperative data, including postoperative pathological stage (≤pT2, ≥ pT3), postoperative ISUP grade (1–5), nerve invasion (0 = no, 1 = yes), vascular tumor thrombus (0 = no, 1 = yes), margin status (0 = negative margin, 1 = positive margin), location of positive margin (0 = non-apical, 1 = apical). After the postoperative specimen was stained with ink, the tumor visible at the edge of the ink stain was defined as PSM under microscopic observation after fixation, embedding and sectioning.
3. Pneumoperitoneum was established, the robot arms were connected, and the robot laparoscope was inserted to see that the abdominal cavity could be expanded. After freeing the pelvic tissue, the peritoneum was cut along the bladder-rectal pouch through the retroprostatic approach, and the bilateral seminal vesicles and vas deferens were freed and exposed. The vas deferens were fully freed, and the vas deferens were cut off. Carefully freed along the recto-vesical gap and the Diers fascia, and the bladder neck was exposed along the boundary between the bladder neck and the prostate. The bladder neck was cut. Continue to free forward to the prostate apex close to the prostate capsule, expose the urethra at the prostate apex, and cut the urethra. Reconstruct the bladder neck, use 3 -0 V-loc sutures to continuously anastomose the bladder neck and urethra under the guidance of the urethra, replace the urethra, and insert the F18 three-lumen catheter from the external urethral opening to the bladder. A drainage tube was left in the surgical area, and the gauze and instruments were counted to be correct. The Trocars were removed, the specimens were taken out, and the puncture holes were sutured layer by layer. The operation was completed.
4. The patient data were divided into positive margin group and negative margin group. Univariate analysis: Univariate logistic regression analysis was performed to evaluate the relationship between each individual factor (age, hypertension, diabetes, coronary heart disease, body mass index (BMI), total prostate specific antigen (TPSA), prostate volume, prostate imaging reporting and data system (PIRADS), lymph node metastasis, seminal vesicle invasion, bone metastasis, preoperative International Prostate Cancer Pathological Grading System (ISUP), time between puncture and surgery, proportion of positive needles, preoperative endocrine therapy, pT stage, postoperative ISUP, D'Amico classification, nerve invasion and vascular cancer thrombus) and the outcome variable surgical margin. This step helps to identify factors that have a potential relationship with the outcome variable. Through inspection, it was discovered that there is multicollinearity and overfitting among the independent variables. Lasso regression was used for variable selection, removing variables with regression coefficients of zero, and the selected variables were then re-substituted into the original ordinary regression analysis.

**Table 1** Univariate analysis of prostate PSM

Characteristic	OR <sup>1</sup>	95% CI <sup>1</sup>	p-value <sup>2</sup>
Age	0.98	0.93, 1.05	0.617
Hypertension			
0	—	—	
1	0.90	0.39, 2.12	0.814
Diabetes			
0	—	—	
1	1.32	0.47, 3.72	0.595
Coronary heart disease			
0	—	—	
1	1.17	0.20, 6.76	0.859
BMI			
1	—	—	
2	1.68	0.54, 5.21	0.369
TPSA			
0	—	—	
1	2.28	0.97, 5.38	0.059
Prostate volume			
0	—	—	
1	10.83	3.87, 30.33	< 0.001***
PIRADS			
3	—	—	
4	3.49	1.01, 12.03	0.048*
5	6.34	1.79, 22.54	0.004**
Extraprostatic extension			
0	—	—	
1	2.71	0.86, 8.53	0.089
The time between puncture and surgery			
0	—	—	
1	0.74	0.29, 1.91	0.534
Preoperative ISUP			
1	—	—	
2	1.71	0.48, 6.07	0.404
3	2.00	0.52, 7.76	0.316
4	2.18	0.60, 7.96	0.237
5	3.11	0.86, 11.29	0.084
The ratio of positive needle count			
0	—	—	
1	4.12	0.46, 36.67	0.204
2	6.24	0.75, 51.76	0.090
Preoperative endocrine therapy			
0	—	—	
1	1.92	0.60, 6.09	0.268
Operation time	1.00	0.99, 1.01	0.995
Amount of bleeding	0.99	0.99, 1.00	0.249
pT			
2	—	—	
3	8.71	3.04, 24.90	< 0.001***
Postoperative ISUP			
1	—	—	

**Table 1** (continued)

Characteristic	OR <sup>1</sup>	95% CI <sup>1</sup>	p-value <sup>2</sup>
2	2.31	0.44, 12.20	0.325
3	3.60	0.59, 21.93	0.165
4	1.64	0.23, 11.70	0.624
5	4.62	0.84, 25.49	0.079
D'Amico			
2	—	—	
1	0.82	0.35, 1.92	0.645
Nerve invasion			
0	—	—	
1	2.60	0.89, 7.62	0.082
Vascular cancer thrombus			
0	—	—	
1	1.17	0.20, 6.76	0.859

<sup>1</sup> OR Odds Ratio, CI Confidence Interval<sup>2</sup> \**p* < 0.05; \*\**p* < 0.01; \*\*\**p* < 0.001

The status of the prostate apex resection margin was selected as the outcome variable, and the above statistical analysis was performed again. In our study, all statistical analyses were performed using R software (version 4.2.2) and MSTATA software.

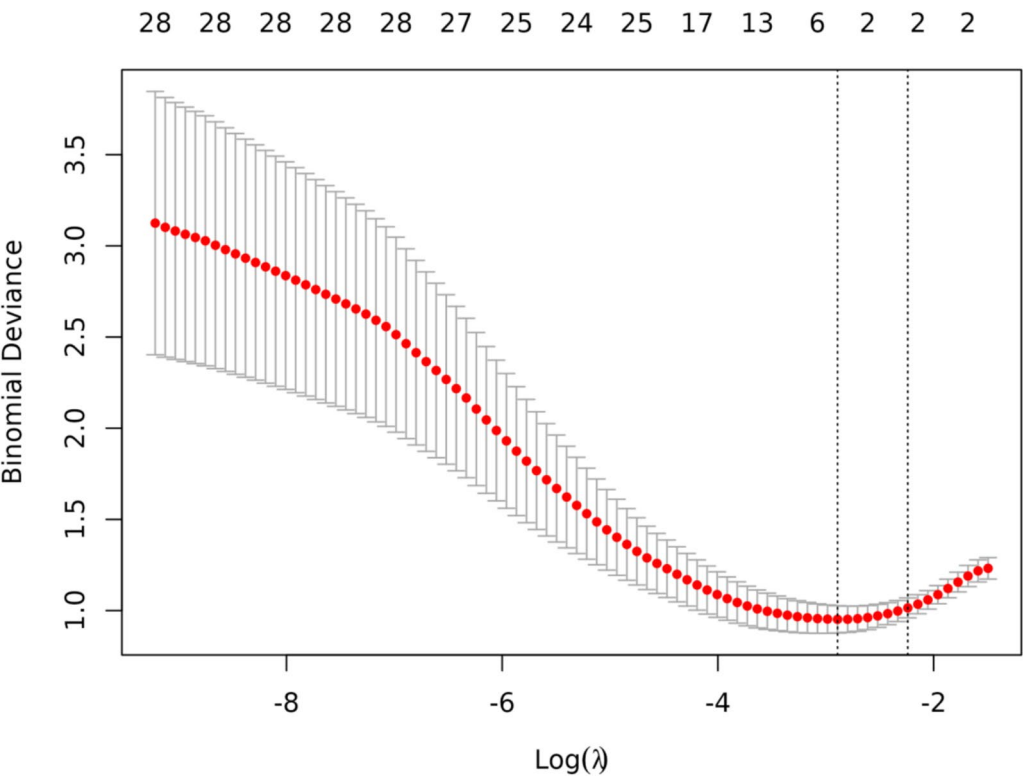
## Results

A univariate logistic regression analysis was conducted to identify potential factors associated with positive surgical margins (PSM). The results are summarized in Table 1: Patients with a prostate volume of  $\geq 50$  ml had a significantly higher risk of PSM (OR = 10.83, 95% CI: 3.87–30.33, *p* < 0.001). Higher PI-RADS scores (4 and 5) were associated with an increased risk of PSM (OR = 3.49, 95% CI: 1.01–12.03, *p* = 0.048 for PI-RADS 4; OR = 6.34, 95% CI: 1.79–22.54, *p* = 0.004 for PI-RADS 5). Patients with  $\geq$ pT3 stage tumors had a significantly higher risk of PSM compared to those with  $\leq$ pT2 stage tumors (OR = 8.71, 95% CI: 3.04–24.90, *p* < 0.001). Other factors such as age, BMI, hypertension, diabetes, coronary heart disease,

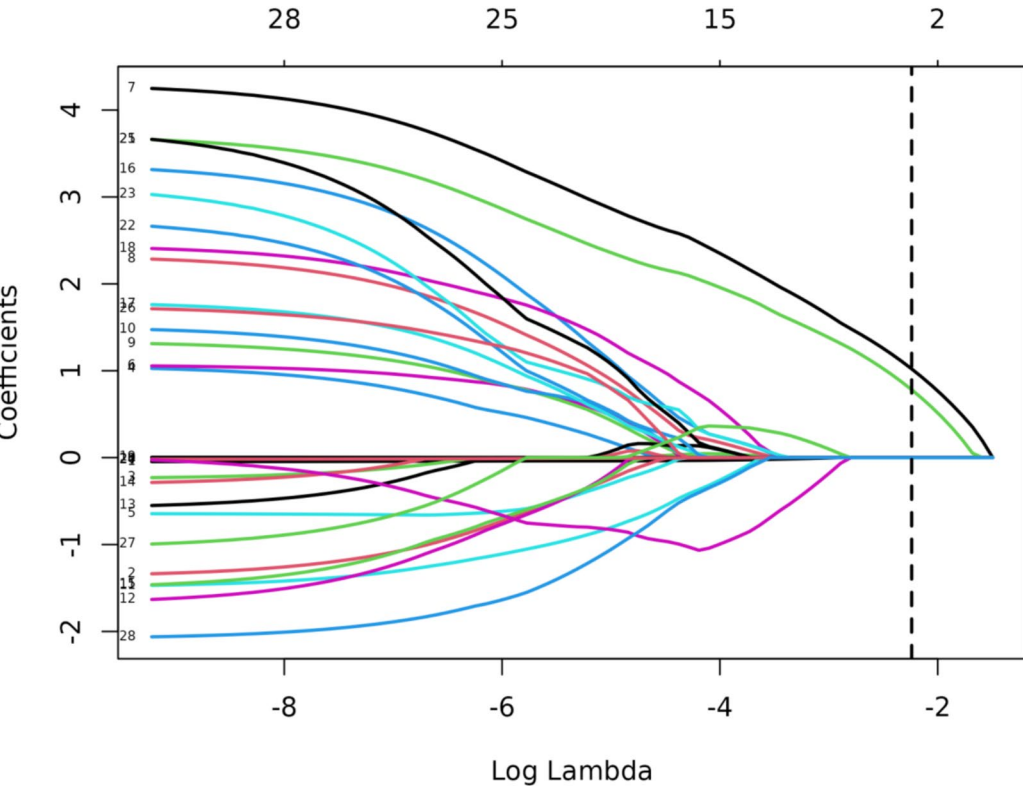
**Table 2** Logistic regression with variable reduction (variables selected by regularized regression)

Characteristic	N	Event N	OR <sup>a</sup>	95% CI <sup>a</sup>	p-value
Prostate volume					
0	58	6	—	—	
1	45	25	10.90	3.49, 34.04	< 0.001
pT					
2	81	16	—	—	
3	22	15	8.78	2.54, 30.42	< 0.001

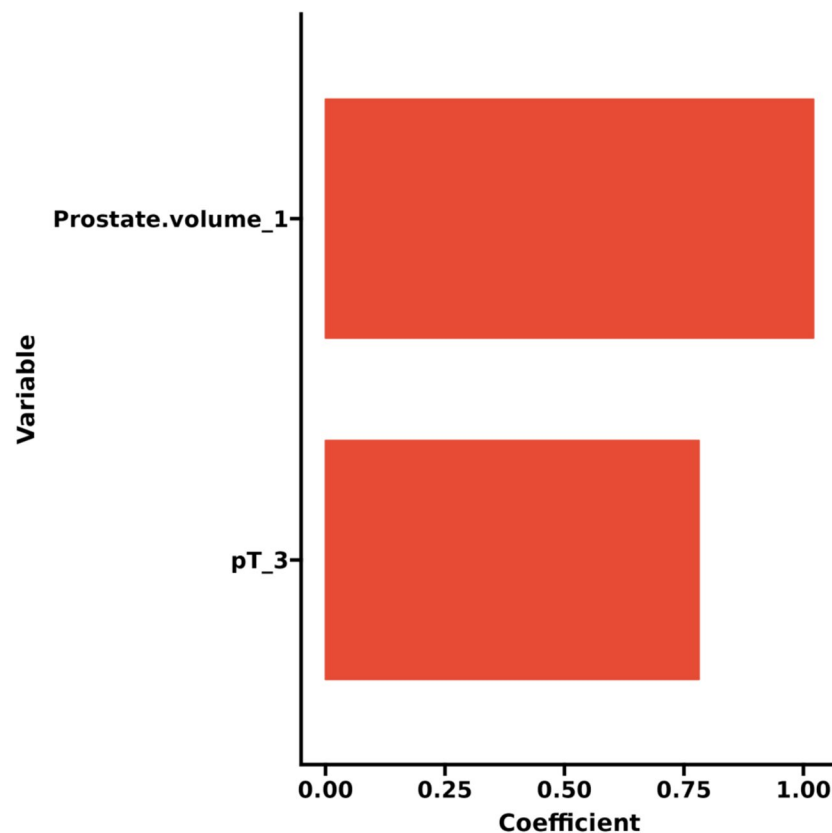
<sup>a</sup> OR Odds Ratio, CI Confidence Interval



**Fig. 1** Cross-validation curve for screening risk factors of PSM after RS-RARP in prostate cancer patients based on Lasso regression



**Fig. 2** Path diagram for screening risk factors of PSM after RS-RARP in prostate cancer patients based on Lasso regression



**Fig. 3** Visualization of variable screening results based on prostate PSM

TPSA, extraprostatic extension, preoperative ISUP grade, interval from biopsy to surgery, ratio of positive biopsy cores, preoperative endocrine therapy, operation time, and intraoperative blood loss did not show a statistically significant association with PSM ( $p > 0.05$ ).

To address issues of multicollinearity and overfitting, Lasso regression was used for variable selection. The final multivariate logistic regression model identified prostate volume and pT stage as independent predictors of PSM (Table 2, Figs. 1, 2 and 3): A prostate volume of  $\geq 50$  ml remained a significant predictor of PSM (OR = 10.90, 95% CI: 3.49–34.04,  $p < 0.001$ ).  $\geq$ pT3 stage tumors were significantly associated with PSM (OR = 8.78, 95% CI: 2.54–30.42,  $p < 0.001$ ).

A univariate analysis was also performed specifically for apex PSM, identifying the following significant factors (Table 3): A prostate volume of  $\geq 50$  ml was associated with an increased risk of apical PSM (OR = 11.13, 95% CI: 3.01–41.21,  $p < 0.001$ ). A PI-RADS score of 5 was associated with apical PSM (OR = 6.64, 95% CI: 1.30–33.88,  $p = 0.023$ ). The presence of extraprostatic extension was associated with apex PSM (OR = 4.02, 95% CI: 1.21–13.37,  $p = 0.023$ ).  $\geq$ pT3 stage tumors were associated with apex PSM (OR = 5.92, 95% CI: 2.03–17.23,  $p = 0.001$ ).

After variable selection using Lasso regression, the final multivariate logistic regression model for apex PSM included prostate volume and pT stage as independent predictors (Table 4, Figs. 4, 5 and 6): A prostate volume of  $\geq 50$  ml remained a significant predictor of apical PSM (OR = 9.62, 95% CI: 2.51–36.88,  $p < 0.001$ ).  $\geq$ pT3 stage tumors were significantly associated with apex PSM (OR = 4.71, 95% CI: 1.45–15.32,  $p = 0.010$ ).

## Discussion

This study aimed to explore the clinical risk factors for postoperative positive surgical margins (PSM) in patients with RS-RARP. By analyzing the clinical data of 103 patients undergoing RS-RARP, we found that prostate volume and prostate MRI PI-RADS score were independent predictors of postoperative PSM. Prostate volume was closely related to postoperative PSM at the prostate apex. This result has important clinical significance for RS-RARP surgical planning.

First, the correlation between prostate volume and PSM was fully verified in this study. In radical prostatectomy, it is crucial to ensure complete removal of tumor tissue while avoiding excessive removal of normal tissue. Previous studies have different views. One study showed

**Table 3** Univariate analysis of prostate apex PSM

Characteristic	OR <sup>a</sup>	95% CI <sup>1</sup>	p-value <sup>2</sup>
Age	1.02	0.95, 1.09	0.641
Hypertension			
0	Reference	Reference	
1	1.07	0.40, 2.85	0.895
Diabetes			
0	Reference	Reference	
1	2.11	0.69, 6.45	0.189
Coronary heart disease			
0	Reference	Reference	
1	2.19	0.37, 12.92	0.385
BMI			
1	Reference	Reference	
2	1.04	0.26, 4.11	0.951
TPSA			
0	Reference	Reference	
1	2.05	0.76, 5.50	0.154
Prostate volume			
0	Reference	Reference	
1	11.13	3.01, 41.21	< 0.001***
PIRADS			
3	Reference	Reference	
4	4.50	0.90, 22.54	0.067
5	6.64	1.30, 33.88	0.023*
Extraprostatic extension			
0	Reference	Reference	
1	4.02	1.21, 13.37	0.023*
The time between puncture and surgery			
0	Reference	Reference	
1	0.73	0.24, 2.22	0.581
Preoperative ISUP			
1	Reference	Reference	
2	1.94	0.43, 8.78	0.391
3	2.82	0.60, 13.24	0.189
4	2.38	0.52, 11.01	0.266
5	2.58	0.56, 12.02	0.226
The ratio of positive needle count			
0	Reference	Reference	
1	2.44	0.26, 22.72	0.432
2	3.18	0.37, 26.94	0.289
Preoperative endocrine therapy			
0	Reference	Reference	
1	1.16	0.29, 4.60	0.838
Operation time	1.01	1.00, 1.02	0.254
Amount of bleeding	0.99	0.98, 1.01	0.363
pT			
2	Reference	Reference	
3	5.92	2.03, 17.23	0.001**
Postoperative ISUP			
1	Reference	Reference	

**Table 3** (continued)

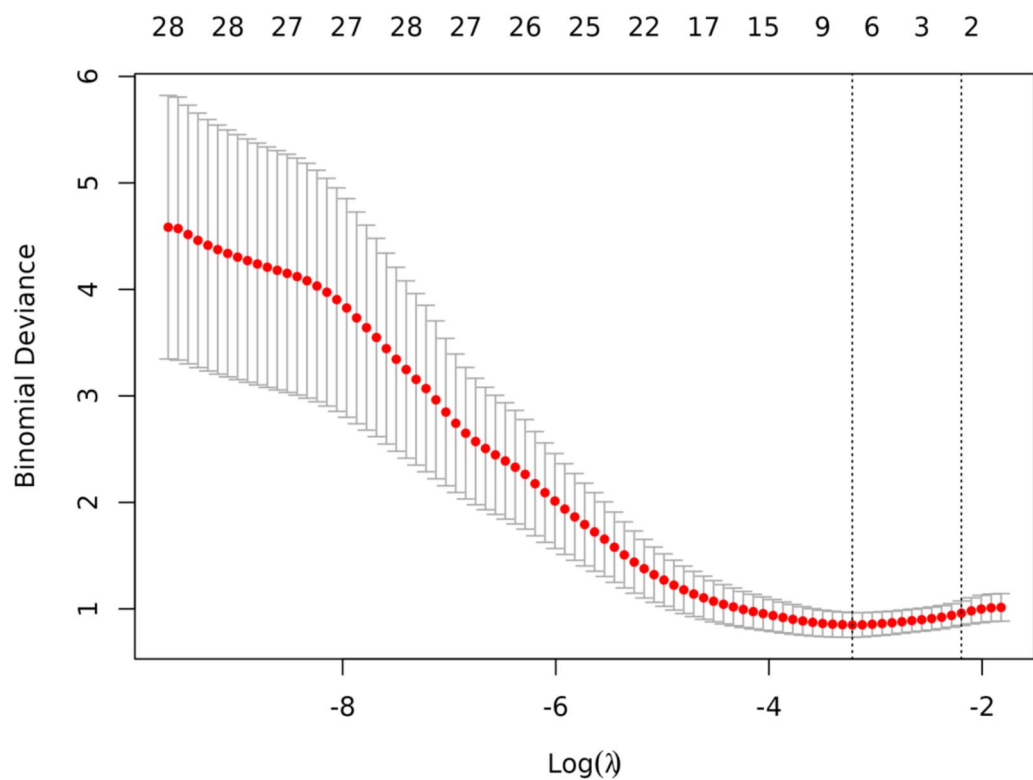
Characteristic	OR <sup>a</sup>	95% CI <sup>1</sup>	p-value <sup>2</sup>
2	0.55	0.08, 3.67	0.533
3	3.60	0.59, 21.93	0.165
4	1.64	0.23, 11.70	0.624
5	2.12	0.36, 12.34	0.404
D'Amico			
1	Reference	Reference	
2	1.52	0.57, 4.04	0.406
Nerve invasion			
0	Reference	Reference	
1	1.72	0.52, 5.68	0.370
Vascular cancer thrombus			
0	Reference	Reference	
1	2.19	0.37, 12.92	0.385

<sup>1</sup> OR Odds Ratio, CI Confidence Interval<sup>2</sup> \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$ **Table 4** Logistic regression of apex PSM with variable reduction (variables selected by regularized regression)

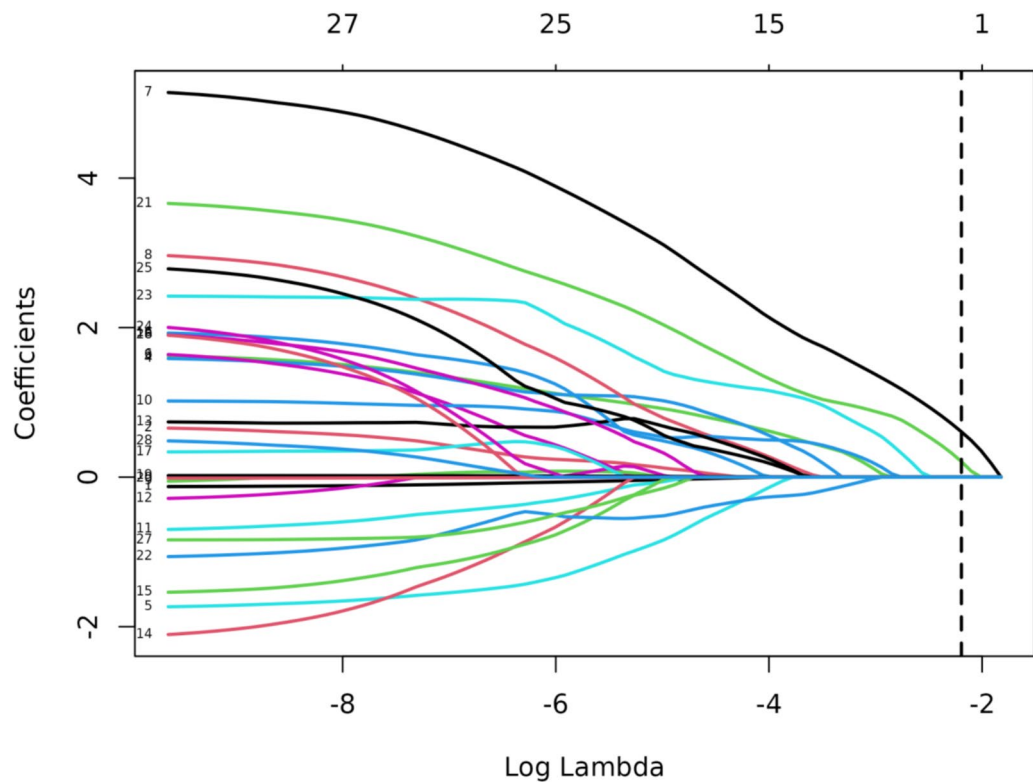
Characteristic	N	Event N	OR <sup>a</sup>	95% CI <sup>a</sup>	p-value
Prostate volume					
0	58	3	—	—	
1	45	17	9.62	2.51, 36.88	< 0.001
pT					
2	81	10	—	—	
3	22	10	4.71	1.45, 15.32	0.010

<sup>a</sup> OR Odds Ratio, CI Confidence Interval

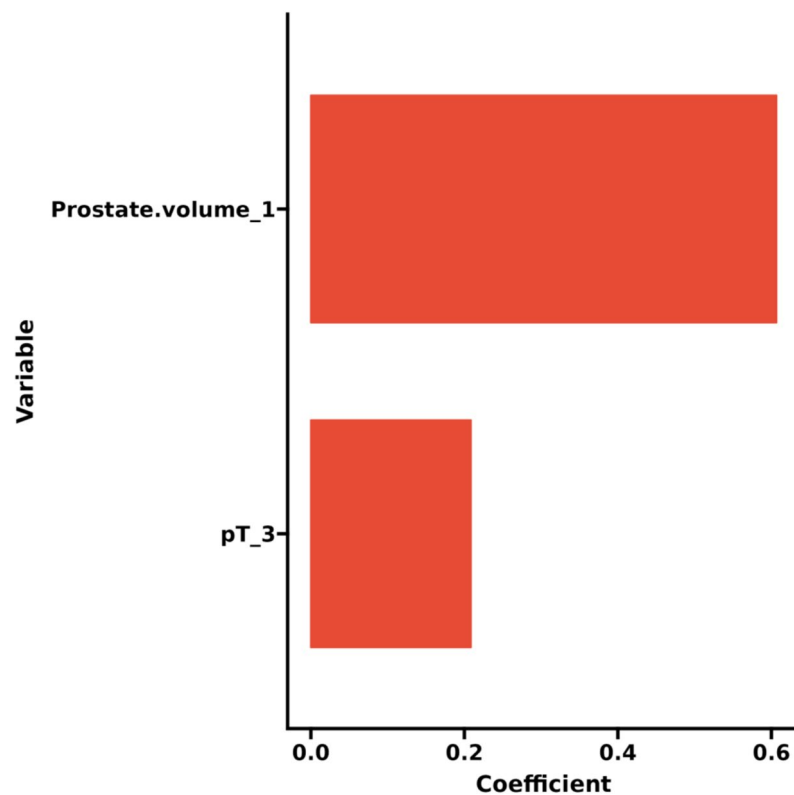
that patients with smaller prostate volume were more likely to have positive margins during robot-assisted radical prostatectomy, and smaller prostate volume was more likely to be associated with higher incidence and invasiveness [7–9]. Related studies have suggested that the pressure exerted by prostate enlargement/mechanical deformation may inhibit PCa growth, which may explain why smaller prostates are associated with higher PSM [10]. The prostate transition zone (TZ) is the main area of benign prostatic hyperplasia, and prostate tumors usually originate from the peripheral zone (PZ). One theory is that when the transition zone increases, it will have a compression effect on the peripheral zone, causing the volume of the peripheral zone to decrease relatively. This compression may cause the peripheral zone to become thinner and shrink, thus affecting its tissue structure and function. When the transition zone is too large, it may compress the peripheral zone, resulting in reduced local blood flow and tissue hypoxia, thereby changing the cellular environment of the peripheral zone [11]. Hypoxic



**Fig. 4** Cross-validation curve for screening risk factors of PSM after RS-RARP in prostate apex of prostate cancer patients based on Lasso regression



**Fig. 5** Path diagram for screening risk factors of PSM after RS-RARP in prostate apex of prostate cancer patients based on Lasso regression



**Fig. 6** Visualization of variable screening results based on prostate apex PSM

environment may promote the expression of certain tumor-related genes, thereby affecting the development and progression of cancer. However, the larger prostate volume usually limits the surgical operating space, increasing the complexity and challenge of surgery [12]. Larger prostates may lead to insufficient intraoperative exposure and increase the risk of PSM. Furthermore, large volume prostates are often accompanied by a higher proportion of tumor volume, a higher proportion of high-grade or locally advanced tumors, and a more aggressive nature of the tumor, increasing the risk of residual tumor during surgery. These findings suggest that prostate volume can be used as an important factor in preoperative evaluation and has important reference value in surgical planning.

Secondly, the role of PI-RADS score as an imaging assessment tool in predicting the risk of PSM was also significantly verified in this study. PI-RADS score is an important tool for grading prostate cancer based on multi-parameter MRI (mpMRI). The higher the score, the more aggressive the tumor is and the greater the tumor burden, all of which increase the risk of PSM. Related studies suggest that the PSM of the PI-RADS group is lower than that of the non-PI-RADS group in the preoperative MRI assessment scheme (31.3% vs. 40.9%) [13].

PI-RADS score is closely related to the pathological characteristics and prognosis of prostate cancer. Patients with higher PI-RADS scores (such as scores of 4 or 5) may need to undergo more extensive resection of surrounding tissue during surgery to ensure a negative resection margin [14, 15]. In addition, there is a certain correlation between the imaging features of the PI-RADS score and the molecular characteristics of the tumor, suggesting that imaging and molecular markers can be combined in the future to further improve the accuracy of PSM risk prediction.

Our research results indicate that pathological staging is significantly associated with positive surgical margins in prostate cancer, with higher pathological stages potentially leading to a higher rate of positive surgical margins, which is consistent with many previous studies [16–18]. The core reason why a higher pathological stage of prostate cancer (such as  $\geq T3$  stage) leads to an increased rate of positive surgical margins is the combined effect of increased tumor invasiveness and anatomical complexity. High-stage tumors often break through the prostatic capsule and invade adjacent structures such as the seminal vesicles, and the proportion of multifocal distribution significantly increases. During surgery, to protect urinary control function (such as the urethral sphincter) or the

neurovascular bundle (NVB), the tumor must be resected close to the capsule, leading to an increased risk of tumor residue. To avoid postoperative incontinence or sexual dysfunction, surgeons may reduce the extent of resection, resulting in a significantly higher rate of positive surgical margins in high-risk areas such as the apex and base.

The main shortcomings of this article are insufficient sample size, lack of multicenter data, and potential confounding factors. First, the small sample size may lead to insufficient statistical power of the model and increase the possibility of error. Second, the study is based only on data from a single center, which limits the applicability of the model in different patient populations. Multicenter data can cover more diverse patient characteristics and treatments, which helps to improve the generalization ability of the model and the reliability of external validation. In addition, potential confounding factors have not been adequately controlled, such as patients' comorbidities, lifestyles, and specific pathological characteristics of tumors, which may affect the positive results of resection margins and thus affect the evaluation of results. It is worth noting that this study was conducted by the same surgeon, and the surgeon's surgical proficiency may also have unpredictable potential impacts on the results. Future studies should expand the sample size, introduce multicenter data, and more comprehensively incorporate and control relevant confounding factors to improve the accuracy of the results.

## Conclusion

The study indicates that prostate volume and pT stage are notable predictors of positive surgical margins in RS-RARP. Emphasizing these factors in preoperative planning and surgical decisions is crucial for minimizing PSM risk and enhancing oncological outcomes.

## Acknowledgements

None.

## Clinical trial number

Not applicable.

## Authors' contributions

Yangjie Gao and Pengliang Shen conducted the literature search. Xiaoming Cao designed the study and provided guidance. Kaiyuan Jia and Junyuan Bing performed data collection and organization. Hua Yang, Bo Wu, and Xuchang Liu wrote the manuscript and conducted the statistical analysis. All authors reviewed the manuscript.

## Funding

This work is supported by The Key Research and Development Program Projects of Shanxi Province (Grant No. 201803D31110).

## Data availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

This study was approved by the Ethics Committee of First Hospital of Shanxi Medical University (NO.KYLL-2024-100). Patients were consented by an informed consent process that was reviewed by the Ethics Committee of First Hospital of Shanxi Medical University and certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

Received: 16 February 2025 Accepted: 14 April 2025

Published online: 30 April 2025

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