Risk factors for the development of vesicourethral anastomotic stenosis following laparoscopic radical prostatectomy

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Abstract. The present study aimed to investigate the preoperative and perioperative clinical variables associated with the development of vesicourethral anastomotic stenosis (VUAS) following laparoscopic radical prostatectomy (LRP). A total of 281 patients who underwent LRP for localized prostate cancer between January 2020 and January 2025 at the Department of Urology, Bursa City Hospital, University of Health Sciences (Bursa, Türkiye), were retrospectively included. Preoperative laboratory parameters, biopsy and radical prostatectomy pathological findings, perioperative variables and postoperative follow-up data were collected. Patients were stratified according to the development of VUAS. Univariate analyses, exploratory multivariable logistic regression and receiver operating characteristic (ROC) curve analyses were performed. Results of the present study demonstrated that VUAS developed in 11 patients (3.9%). The median follow-up time was 12 months (range, 3-16 months). Larger prostate volume (PV), longer operative time, adjuvant radiotherapy (RT), intraoperative blood transfusion, prolonged hospital stay, delayed drain removal and delayed catheter removal were significantly associated with VUAS in the univariate analyses. Although lymph node metastasis was more frequent in the VUAS group, it did not reach statistical significance and was not independently associated with VUAS. In the exploratory multivariable logistic regression model, adjuvant RT [odds ratio, (OR), 5.380; 95% confidence interval (CI), 1.326-21.836; P=0.019], PV (OR, 1.027; 95% CI, 1.011-1.043; P=0.001) and operative time (OR, 1.017; 95% CI, 1.004-1.030; P=0.012) were independently associated with VUAS. ROC curve analysis identified an optimal PV cutoff of 62.5 cc [area under the curve (AUC), 0.715] and an operative time cutoff of 262.5 min (AUC, 0.758). In conclusion, adjuvant RT, larger PV and longer operative time were independently associated with postoperative VUAS in this exploratory multivariable analysis.

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Abbreviations: VUAS, vesicourethral anastomotic stenosis; LRP, laparoscopic radical prostatectomy; PV, prostate volume; RT, radiotherapy; LN, lymph node; ISUP, International Society of Urological Pathologists; LVI, lymphovascular invasion; PSA, prostate-specific antigen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; MCH, mean corpuscular hemoglobin; RDW, red cell distribution width; ROC, receiver operating characteristic; AUC, area under the curve; OR, odds ratio; CI, confidence interval

Key words: LRP, prostate cancer, VUAS, risk factors, logistic regression

Introduction

Prostate cancer is one of the most commonly diagnosed malignancies among men worldwide; it is the second most common cancer in men after non-melanoma skin cancer and remains a leading cause of cancer-related mortality (1). The GLOBOCAN 2022 report estimated ~1.5 million new cases and 397,000 deaths worldwide, making prostate cancer the second most frequently diagnosed cancer and the fifth leading cause of cancer-related death among men in 2022 (2). Despite advances in early detection and treatment, the management of treatment-associated complications continues to present a clinical challenge (3,4).

Vesicourethral anastomotic stenosis (VUAS) is a clinically important urological complication following laparoscopic radical prostatectomy (LRP) that substantially impairs quality of life and often requires additional invasive interventions (5). The reported incidence of VUAS ranges from 1.4 to 4.8% (6). Fibrotic narrowing of the vesicourethral anastomosis may result in lower urinary tract symptoms, including reduced urinary flow, urinary urgency and recurrent urinary tract infections. Differences in surgical techniques, patient populations and follow-up duration may contribute to variation in reported incidence rates (7).

The etiology of VUAS is multifactorial. Established risk factors include advanced age, obesity, chronic kidney disease, coronary artery disease and active smoking (8,9). Adjuvant radiotherapy (RT), which may induce obliterative endarteritis and tissue fibrosis, has also been associated with an increased risk of VUAS, and may complicate subsequent management. In addition to patient-associated factors, surgical technique, the method of vesicourethral anastomosis, pelvic hematoma

formation and urinary extravasation have all been implicated in the development of VUAS (10).

The present study aimed to investigate the preoperative, perioperative and pathological factors associated with the development of VUAS following LRP in a single-center cohort.

Materials and methods

Study design. The present retrospective study was approved by the Ethics Committee of the University of Health Sciences, Bursa City Hospital (Bursa, Türkiye; approval no. 2024-15/5) and was conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective study design.

Following Institutional Review Board approval, the medical records of patients who underwent LRP for localized or locally advanced prostate cancer at University of Health Sciences, Bursa City Hospital between January 2020 and January 2025 were retrospectively reviewed. Medical records were retrieved from the hospital database between May and June 2025, and statistical analyses were performed between July and August 2025. Patients who underwent radical prostatectomy as part of multimodal treatment for intermediate- or high-risk disease were also eligible for inclusion.

Patients with a history of bladder neck contracture, urethral stenosis, previous pelvic radiotherapy, active urinary tract infection or inflammatory disease at the time of surgery, or incomplete preoperative laboratory data were excluded. Of the 332 patients initially identified, 51 were excluded due to incomplete clinical data, inadequate follow-up or treatment via open radical prostatectomy. The final study cohort comprised 281 patients.

The following variables were collected: Age (range, 45-78 years; median, 66 years); comorbidities, including diabetes mellitus, hypertension, coronary artery disease and chronic obstructive pulmonary disease; and preoperative laboratory parameters, including complete blood count with differential [white blood cell count, neutrophils, lymphocytes, monocytes, eosinophils, basophils, red blood cell count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin (MCH), MCH concentration, red cell distribution width (RDW)-standard deviation and RDW-coefficient of variation], platelet count, plateletcrit, mean platelet volume and platelet distribution width], total and free prostate-specific antigen (PSA), PSA density, free-to-total PSA ratio, aspartate aminotransferase (AST), alanine aminotransferase (ALT), the De Ritis ratio (AST/ALT), neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, lymphocyte-to-monocyte ratio and prostate volume (PV).

Biopsy variables included Gleason score (11), International Society of Urological Pathology (ISUP) grade (11), perineural invasion and lymphovascular invasion (LVI), as determined from transrectal ultrasound-guided biopsy specimens. Radical prostatectomy pathology variables included Gleason score, ISUP grade, pathological upgrading, surgical margin status, LVI, extraprostatic extension, seminal vesicle invasion, lymph node (LN) involvement and pathological T stage (12). Distant metastases were assessed via imaging. Perioperative variables included operative time, intraoperative blood transfusion, postoperative hemoglobin concentration, Clavien-Dindo complications (13), length of hospital stay, timing of drain removal, timing of catheter removal and administration of adjuvant RT.

Table I. Characteristics of the overall cohort (n=281).

Characteristic	Value
Mean age ± SD, years	65.5±6.0
Mean total PSA ± SD, ng/ml	14.7±12.9
Pathological stage	
T1, n (%)	1 (0.4)
T2, n (%)	128 (45.6)
T3, n (%)	147 (52.3)
T4, n (%)	5 (1.8)
Biopsy ISUP grade ≥3, n (%)	102 (36.3)
RP ISUP grade ≥3, n (%)	133 (47.3)
Lymphovascular invasion, n (%)	87 (31.0)
Extraprostatic extension, n (%)	142 (50.5)
Seminal vesicle invasion, n (%)	77 (27.4)
Positive surgical margin, n (%)	81 (28.8)
Lymph node dissection performed, n (%)	67 (23.8)
Lymph node metastasis, n (%)	39 (13.9)
Distant metastasis, n (%)	4 (1.4)
Adjuvant radiotherapy, n (%)	51 (18.1)
Any intraoperative blood transfusion, n (%)	35 (12.5)
VUAS, n (%)	11 (3.9)
Median follow-up time (range), months	12 (3-16)

Percentages are calculated using the total cohort (n=281). Categorical totals were reconstructed from the subgroup counts reported in Table II. Values for stage T1 are retained from the proof pending verification against source records. SD, standard deviation; PSA, prostate-specific antigen; ISUP, International Society of Urological Pathology; RP, radical prostatectomy; VUAS, vesicourethral anastomotic stenosis.

All patients underwent transperitoneal LRP. A vesicourethral anastomosis was performed using a continuous running technique with 3-0 or 2-0 monofilament absorbable barbed suture. Interrupted or non-barbed sutures were not used during the study period. Anastomotic integrity was routinely assessed intraoperatively by filling the bladder with saline through a Foley catheter. As the anastomotic technique was standardized and suture size was not consistently documented in the retrospective database, the effect of suture size on VUAS could not be evaluated.

Patients presenting with symptoms suggestive of VUAS, including a weak urinary stream, incomplete bladder emptying, urinary retention or persistent urinary incontinence, underwent evaluation with uroflowmetry and flexible cystoscopy. VUAS was confirmed when a 16-Fr flexible cystoscope could not be advanced through the vesicourethral anastomosis into the bladder. Ultrasonography, post-void residual urine measurement or urodynamic studies were performed when clinically indicated.

Table II. Comparison of clinically relevant variables between groups.

Variable	Non-VUAS group (n=270)	VUAS group (n=11)	P-value
Age, years[a]	66 (45-78)	66 (59-70)	0.695
Biopsy ISUP grade ≥3, n (%)	98 (36.3)	4 (36.4)	1.000
RP ISUP grade ≥3, n (%)	128 (47.4)	5 (45.5)	1.000
Pathological stage T3-T4, n (%)	147 (54.4)	5 (45.5)	0.759
Lymphovascular invasion, n (%)	81 (30.0)	6 (54.5)	0.101
Extraprostatic extension, n (%)	137 (50.7)	5 (45.5)	0.768
Seminal vesicle invasion, n (%)	75 (27.8)	2 (18.2)	0.733
Positive surgical margin, n (%)	78 (28.9)	3 (27.3)	1.000
Lymph node dissection performed, n (%)	62 (23.0)	5 (45.5)	0.140
Lymph node metastasis, n (%)	35 (13.0)	4 (36.4)	0.051
Distant metastasis, n (%)	3 (1.1)	1 (9.1)	0.148
Adjuvant radiotherapy, n (%)	45 (16.7)	6 (54.5)	0.006
Prostate volume, cc[a]	50 (10-216)	72 (23-180)	0.016
Total PSA, ng/ml[a]	11.1 (0.6-133.0)	10.2 (6.2-24.8)	0.898
PSA density[a]	0.2 (0.0-3.3)	0.2 (0.0-0.8)	0.076
Operative time, min[a]	245 (110-435)	270 (225-380)	0.004
Any intraoperative blood transfusion, n (%)	31 (11.5)	4 (36.4)	0.035
Postoperative hemoglobin, g/dl[a]	12.6 (4.1-16.7)	10.7 (8.1-14.3)	0.009
Hospital stay, days[a]	4 (2-29)	5 (3-63)	0.024
Drain removal day[a]	4 (2-8)	4 (3-18)	0.039
Catheter removal day[a]	12 (9-35)	15 (10-60)	0.004

[a]Data are presented as median (min-max). Categorical variables were compared using Fisher's exact test or χ^2 test, as appropriate; continuous variables were compared using the Mann-Whitney U test. VUAS, vesicourethral anastomotic stenosis; ISUP, International Society of Urological Pathologists; RP, radical prostatectomy; PSA, prostate-specific antigen.

Patients were stratified according to the development of VUAS. Preoperative, pathological and perioperative variables were subsequently compared between patients who developed VUAS and those who did not.

Statistical analysis. Statistical analyses were performed using SPSS (version, 21.0; IBM Corp.). The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Overall cohort age and total PSA level are additionally summarized as the mean ± standard deviation (SD). Non-normally distributed variables are presented as the median (interquartile range) and were compared using the Mann-Whitney U test. Categorical variables are presented as frequencies and percentages and were compared using the χ^2 test or Fisher's exact test, as appropriate.

Variables with P<0.05 in the univariate analyses were considered candidates for logistic regression analysis. From these, four clinically relevant variables, namely, adjuvant RT, LN metastasis, PV and operative time, were selected for inclusion in the exploratory multivariable logistic regression model based on biological plausibility and to minimize overfitting given the limited number of outcome events. Variables considered likely to represent perioperative or postoperative consequences rather than independent etiological factors, including intraoperative blood transfusion, postoperative hemoglobin concentration, length of hospital stay, timing of drain removal and timing of catheter removal, were not included in the multivariable model. Complete-case analysis was used for all multivariable analyses.

A post hoc assessment of the events-per-variable ratio was also performed. With 11 VUAS events and four candidate predictors, the events-per-variable ratio was 2.75. Based on the conventional recommendation of ~10 events per predictor variable in logistic regression, at least 40 events would have been required for a four-variable model. At the observed VUAS incidence of 3.9%, this would correspond to a study population of ~1,022 patients (14,15). Accordingly, the multivariable regression results and receiver operating characteristic (ROC)-derived cutoff values should be considered exploratory rather than constituting a validated prediction model. P<0.05 was considered to indicate a statistically significant difference.

Results

A total of 281 patients were included in the present study. The mean age was 65.5±6.0 years, and the mean total PSA level was 14.7±12.9 ng/ml. Pathological staging was T1 in 1 patient (0.4%), T2 in 128 patients (45.6%), T3 in 147 patients (52.3%) and T4 in 5 patients (1.8%). Adjuvant RT was administered to 51 patients (18.1%), and LN dissection was performed in 67 patients (23.8%). The median follow-up time was 12 months (range, 3-16 months). Overall cohort characteristics are summarized in Table I.

Table III. Exploratory univariate and multivariable logistic regression analysis for vesicourethral anastomotic stenosis development.

	Univariate analysis		Multivariate analysis	
Variable	OR (95% CI)	P-value	OR (95% CI)	P-value
LN metastasis	3.837 (1.068-13.782)	0.039	2.633 (0.601-11.546)	0.199
Adjuvant radiotherapy	6.000 (1.755-20.511)	0.004	5.380 (1.326-21.836)	0.019
Prostate volume	1.021 (1.007-1.035)	0.003	1.027 (1.011-1.043)	0.001
Operative time	1.014 (1.004-1.025)	0.007	1.017 (1.004-1.030)	0.012

ORs are from logistic regression. The multivariable model was restricted to four clinically selected variables as only 11 VUAS events occurred. Complete-case n=280 due to one missing operative time value. OR, odds ratio; CI, confidence interval; LN, lymph node.

Table IV. Exploratory multivariable logistic regression analysis for vesicourethral anastomotic stenosis development.

Variables	β	SE	OR	95% CI for OR	P-value
Adjuvant radiotherapy	1.883	0.693	6.575	1.692-25.550	0.007
Prostate volume, cc	0.025	0.008	1.026	1.010-1.042	0.001
Operative time, min	0.017	0.007	1.017	1.004-1.031	0.009

The model included 280 patients as operative time was missing for 1 patient. VUAS developed in 11 patients. OR, odds ratio; CI, confidence interval; SE, standard error.

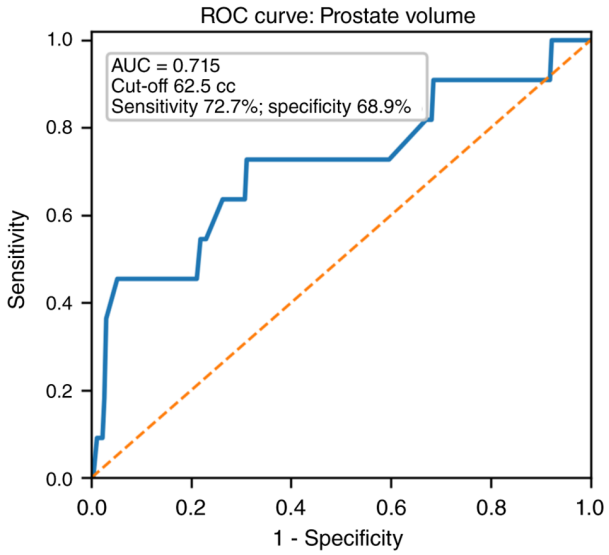


Figure 1. ROC curve for prostate volume as an exploratory marker of vesicourethral anastomotic stenosis risk. The curve shows the sensitivity/specificity trade-off for prostate volume; cut-off value, 62.5 cc; sensitivity, 72.7%; specificity, 68.9%; AUC, 0.715 (95% confidence interval, 0.532-0.898); P=0.016. ROC, receiver operating characteristic; AUC, area under the curve.

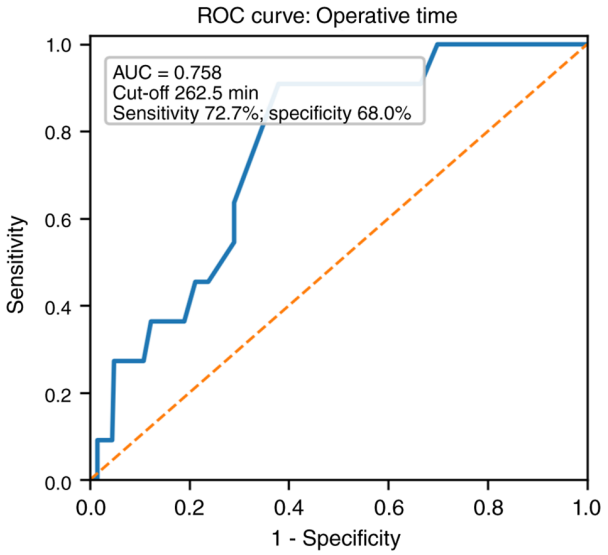


Figure 2. ROC curve for operative time as an exploratory marker of vesicourethral anastomotic stenosis risk. The curve shows the sensitivity/specificity trade-off for operative time; cut-off value, 262.5 min; sensitivity, 72.7%; specificity, 68.0%; AUC, 0.758 (95% confidence interval, 0.644-0.872); P=0.004. ROC, receiver operating characteristic; AUC, area under the curve.

VUAS developed in 11 patients (3.9%), with a median time to diagnosis of 12 months (range, 3-16 months). No significant differences were observed between the VUAS and non-VUAS groups with respect to age and the majority of the pathological variables, including, total PSA level and PSA density. Baseline patient characteristics are summarized in Table II.

PV was significantly greater in the VUAS group than in the non-VUAS group (median, 72 compared with 50 cc; P=0.016). Adjuvant RT was significantly more common among patients who developed VUAS (54.5% compared with 16.7%; P=0.006) and operative time was significantly longer (median, 270 min compared with 245 min; P=0.004). LN metastasis was more

frequent in the VUAS group (36.4% compared with 13.0%); however, the difference did not reach statistical significance (P=0.051 calculated using Fisher's exact test; P=0.079 calculated using continuity-corrected χ^2 test). Intraoperative blood transfusion was also more common in the VUAS group (36.4% compared with 11.5%; P=0.035). Postoperative hemoglobin concentration, length of hospital stay, timing of drain removal and timing of catheter removal also differed between groups; however, these variables were considered perioperative or postoperative markers rather than independent etiological predictors.

In the univariate logistic regression analyses, LN metastasis (OR, 3.837; 95% CI, 1.068-13.782; P=0.039), adjuvant RT (OR, 6.000; 95% CI, 1.755-20.511; P=0.004), PV (OR, 1.021; 95% CI, 1.007-1.035; P=0.003) and operative time (OR, 1.014; 95% CI, 1.004-1.025; P=0.007) were associated with VUAS (Table III). The univariate logistic regression result for LN metastasis differs from the Fisher's exact test result (P=0.051; Table II) because these are different statistical tests. In the four-variable multivariable model, adjuvant RT (OR, 5.380; 95% CI, 1.326-21.836; P=0.019), PV (OR, 1.027; 95% CI, 1.011-1.043; P=0.001) and operative time (OR, 1.017; 95% CI, 1.004-1.030; P=0.012) remained independently associated with VUAS, whereas LN metastasis did not (OR, 2.633; 95% CI, 0.601-11.546; P=0.199) (Table III). The reduced three-variable model, which omitted LN metastasis, yielded ORs of 6.575 for adjuvant RT (95% CI, 1.692-25.550; P=0.007), 1.026 for PV (95% CI, 1.010-1.042; P=0.001) and 1.017 for operative time (95% CI, 1.004-1.031; P=0.009) (Table IV). As only 11 VUAS events occurred, these findings should be interpreted as exploratory.

ROC analysis identified a PV cutoff value of 62.5 cc for predicting VUAS, with a sensitivity of 72.7% and a specificity of 68.9% [area under the curve (AUC), 0.715; 95% CI, 0.532-0.898; P=0.016; Fig. 1]. The optimal cutoff for operative time was 262.5 min, with a sensitivity of 72.7% and a specificity of 68.0% (AUC, 0.758; 95% CI, 0.644-0.872; P=0.004; Fig. 2). These cutoff values should be considered exploratory and require validation in independent cohorts.

Discussion

VUAS is a recognized complication following LRP that can substantially impair quality of life and often necessitates additional intervention (16). In the present study, VUAS developed in 11 out of 281 patients (3.9%), with a median time to diagnosis of 12 months, which is consistent with the previously reported incidence of 1.4-4.8% (6). In the exploratory three-variable multivariable logistic regression model, adjuvant RT, larger PV and longer operative time remained independently associated with VUAS. These findings should be interpreted cautiously due to the limited number of VUAS events; however, the identified variables are clinically plausible and consistent with mechanisms that may impair anastomotic healing.

The association between larger PV and VUAS is clinically relevant, with ROC analysis identifying an optimal cutoff value of 62.5 cc. Larger prostates may increase the technical difficulty of vesicourethral anastomosis, resulting in greater anastomotic tension, reduced tissue apposition and compromised vascularity, all of which may impair wound healing and promote stricture formation. Gillitzer *et al* (17) similarly identified PV as an independent predictor of VUAS in a cohort of >2,000 patients undergoing RP, supporting the present findings (17). Likewise, Borboroglu *et al* (18) reported larger prostate size as a risk factor for anastomotic stricture following RP (18).

Adjuvant RT was also independently associated with VUAS (OR, 5.380) in the present study. Radiation-induced endarteritis and progressive perivascular fibrosis may impair anastomotic healing and increase the risk of stenosis formation. Patients requiring adjuvant RT may also represent a subgroup with more advanced pathological disease requiring multimodal treatment, which could further contribute to postoperative complications. By contrast, Munoz *et al* (19) reported no difference in VUAS incidence between patients who did and did not receive postoperative RT in a cohort of 258 patients undergoing RP (19). Differences in radiation technique, dose, timing and patient selection may account for the discrepancy in these findings.

Longer operative time was independently associated with VUAS in the present study, with an optimal cutoff value of 262.5 min (AUC, 0.758). Operative time should not be interpreted as a direct causal factor but rather as a surrogate marker of surgical complexity, challenging pelvic anatomy, larger PV, greater tissue manipulation or intraoperative technical difficulties. These factors may have contributed to local inflammation, tissue ischemia or impaired anastomotic healing, thereby increasing the risk of VUAS. Erickson *et al* (20) identified excessive blood loss and pelvic hematoma formation as operative factors associated with bladder neck contracture, although operative time itself was not identified as an independent predictor (20).

Although LN metastasis was more frequent among patients who developed VUAS in the present study, it was not included in the exploratory multivariable model due to concerns regarding overfitting resulting from the limited number of VUAS events. The observed association may therefore reflect more advanced disease, more extensive pelvic surgery or a greater likelihood of receiving adjuvant therapy rather than an independent effect of LN metastasis itself.

Several additional variables, including postoperative hemoglobin concentration, length of hospital stay, timing of drain removal and timing of catheter removal, also differed between the two groups. However, these variables may be more likely to reflect perioperative recovery, urinary extravasation or postoperative management than independent preoperative or intraoperative etiological factors. Wang *et al* (21) identified urinary leakage as an independent predictor of VUAS, which is consistent with the prolonged drain duration observed in the VUAS group in the present study. Similarly, Altinova *et al* (22) reported an association between prolonged catheterization and VUAS, whereas Spek *et al* (23) found no association, which may be due to differences in tumor stage and surgical experience (22,23).

Intraoperative blood transfusion was also more common in the VUAS group in the univariate analysis of the present study. However, this finding likely reflected greater surgical complexity, increased blood loss or more extensive tissue manipulation rather than a direct causal effect of transfusion itself. Consequently, this variable was not included in the exploratory multivariable model.

With respect to surgical technique, Wang *et al* (21) and Modig *et al* (24) both reported a lower incidence of VUAS following robotic RP compared with that following open RP (21,24). The present study included only patients undergoing LRP using a standardized continuous barbed suture technique, resulting in a relatively homogeneous surgical cohort for risk factor analysis. However, this also precluded evaluation of the influence of different anastomotic techniques or suture materials.

The key limitation of the present study was the small number of VUAS events. Although the multivariable model was intentionally restricted to three clinically relevant variables, the events-per-variable ratio remained below the conventional recommendation for logistic regression. Accordingly, the multivariable analysis and ROC-derived cutoff values should be regarded as exploratory and hypothesis-generating rather than constituting a validated prediction model. Additional prospective multicenter studies with larger sample sizes and sufficient event numbers are required to confirm these findings and establish robust predictors of VUAS following LRP.

In conclusion, adjuvant RT, larger PV and longer operative time were independently associated with VUAS following LRP in an exploratory multivariable analysis. These findings suggested that patients with larger prostates, those requiring adjuvant RT and those undergoing more complex surgical procedures may be at increased risk of postoperative VUAS. Given the limited number of VUAS events, these findings should be interpreted cautiously and require validation in larger, prospective multicenter studies.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

EO and OE conceived and designed the study. UA, OY, AE and GA acquired and collected the clinical data. ES and SA performed the statistical analysis. EO, UA, OY, AE, OE, SO and VC analyzed and interpreted the data. EO, AE and VC conducted the literature review and drafted the manuscript. OE, SO, GA, UA, OY, ES and SA critically revised the manuscript for important intellectual content. SO supervised the study and contributed to the interpretation of the clinical findings. EO and UA confirm the authenticity of all the raw data. All authors have read and approved the final manuscript, and agree to be accountable for all aspects of the work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of University of Health Sciences, Bursa City Hospital (IRB no. 2024-15/5) and performed in accordance with the principles of the Declaration of Helsinki. Informed consent was waived given the retrospective nature of the data.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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