E-ISSN 2667-4610

# bulletin of UROONCOLOGY

galenos yayinevi

UROONCOLOGY ASSOCIATION - 1999

December
2025
Volume
24(4)

The Official Journal of Urooncology Association of Turkey

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**Publisher Certificate Number:** 14521

**Online Publication Date:** December 2025
E-ISSN: 2667-4610
International scientific journal published quarterly.

# Contents

## Original Articles



## Case Report



## Index

bulletin of
UROONCOLOGY

BEST REVIEWER of ISSUE
Cemil AYDIN

*Original Article*

DOI: 10.4274/uob.galenos.2025.2024.11.4

*Bull Urooncol 2025;24(4):92-96*

# *The Additive Value of MRI Targeted Biopsy on Prostate Cancer Detection in Patients with Serum Prostate-specific Antigen 20-100 ng/mL and Normal Digital Rectal Examination*

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## Abstract

**Objectives:** The study investigates whether multiparametric magnetic resonance imaging (mpMRI) targeted biopsy (MRI-TB) is necessary in the setting of prostate-specific antigen (PSA) 20-100 ng/mL and normal digital rectal examination (DRE).
**Materials and Methods:** Patients undergoing MRI-TB and concomitant systematic biopsies (SB) with a PSA 20-100 ng/mL and normal DRE were retrospectively reviewed in Prostate Cancer Database of Turkish Urooncology Association. Pathological data of MRI-TB was compared to the SB data. All patients underwent mpMRI followed by transrectal/transperineal MRI-TB of any Prostate Imaging Reporting and Data System lesion and 12-core SB. The prostate cancer (PCa) and clinically significant PCa (csPCa) (grade group ≥2) detection on MRI-TB, SB and MRI-TB+SB were determined for all patients. A subgroup analysis of combined (MRI-TB+SB) group was also performed to identify performances of MRI-TB alone, SB alone and combination of MRI-TB+SB for the prediction of final pathology at radical prostatectomy (RP). Statistical significance was set at $p<0.05$.
**Results:** In the study 65 patients were evaluated. Among them, 35 have PCa and 32 of them were csPCa. The detection rate of PCa for MRI-TB+SB, MRI-TB and SB were 53%, 46% and 36%, respectively, and csPCa detection rates were 49%, 41% and 33%, respectively. TB added 31.4% of any grade PCa and 31.25% csPCa detection over SB. csPCa detection rate improved with increased PSA density for TB. Among 15 patients who underwent RP, 6 patients were found to have csPCa on final pathology which went undetected or undergraded with SB biopsy initially.
**Conclusion:** MRI-TB based on mpMRI presents a valuable addition to SB in patients with PSA 20-100 ng/mL and normal DRE.
**Keywords:** Prostate cancer, targeted biopsy, MRI/US fusion, prostate biopsy, concordance

**Cite this article as:** Aslan G, Çelik S, Çetin S, et al. The additive value of MRI targeted biopsy on prostate cancer detection in patients with serum prostate-specific antigen 20-100 ng/mL and normal digital rectal examination. Bull Urooncol. 2025;24(4):92-96.

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**Received:** 29.11.2024 **Accepted:** 07.02.2025 **Publication Date:** 24.12.2025

## Introduction

Prostate cancer (PCa) is the second most common malignancy among men worldwide (1). Previous researches have shown that multiparametric magnetic resonance imaging (mpMRI) targeted biopsy (MRI-TB) identifies clinically significant PCa (csPCa) more accurately than conventional systematic biopsy (SB) in men with PCa (2-5). MRI-TB has resulted in greater detection of csPCa with less detection of clinically insignificant PCa than SB alone (6,7). Nevertheless, 12-core SB is often performed in addition to MRI-TB in a combination schema is increased detection of csPCa (3,8). Additionally, such a practice allows for the non-lesional sampling beyond suspicious lesions, as 10-24% of csPCa are not visualized on mpMRI (9).

Patients with prostate specific antigen (PSA) >20 represent csPCa (≥ Gleason grade group 2) between 72-90% of all cases (10-14). Given the high prevalence of such csPCa in these patient population, the utility of MRI-TB is uncertain. Few studies suggested omitting mpMRI and MRI-TB in patients with PSA >10 ng/mL and abnormal digital rectal examination (DRE) (14). Low evidence suggests that patients with PSA >10 and an abnormal DRE do not benefit from pre-biopsy mpMRI and MRI-TB (14). On the contrary, in the analyzing of 91 patients, it was shown that a significantly higher detection rate of csPCa with MRI-TB compared with SB in patients with both normal and abnormal DRE (15). The authors stated that the contribution of mpMRI and MRI-TB was more pronounced in patients with normal DRE compared with those with abnormal DRE.

Little or no data exist in the current literature about the value added from performing MRI-TB in patients with PSA 20-100 ng/mL with normal DRE. In this context, we aimed to investigate the utility of MRI-TB in addition to SB in patients with PSA 20-100 ng/mL to determine whether some patients can be spared from additional or unnecessary mpMRI and MRI-TB.

## Materials and Methods

We retrospectively reviewed data from completely anonymized patients enrolled by nation-wide tertiary centers in Prostate Cancer Database of Turkish Urooncology Association. MRI-TB in conjunction with 12-core SB for PSA 20-100 ng/mL and normal DRE at our database were included in the study. All patients gave consent for the study.

All mpMRI for TB were reviewed by specified institutional radiologists. In patients with a Prostate Imaging Reporting and Data System (PI-RADS)-lesion 1-5 (according to PI-RADS-v2 classification) (10), MRI targeted ultrasound fusion biopsy using different software-based platforms according to participant center's property [MIMS Symphony Dx® (MIM Software), bk3000® (BKMedical), UroNav® (Invivo Corp, Philips)] were conducted. MRI image fusion biopsies (MRI-TB) were taken, obtaining ≥3-core samples, from each lesion. In addition to MRI-TB, SB were also performed using a 12-core biopsy schema.

All patients underwent both MRI-TB and SB. PCa detection rate was obtained from combination of both methods and then from each method separately. MRI-TB cancer detection determined when only target lesions yielded as cancer, and SB cancer detection rate was determined when target lesions were negative but SB were positive for cancer. A missed cancer rate is determined by subtracting individual performance of each biopsy methods from combined method cancer ratio.

Prostate biopsies were performed by transrectal or transperineal route in 55 and 10 patients, respectively. Sedation anesthesia was administered during the biopsy procedures. An indwelling foley urethral catheter was used to visualize the urethra on ultrasound images. A transrectal ultrasound (TRUS) probe was used for needle placement and guidance. MRI-TB cores are taken via the appropriate grid holes to ensure sampling of the designated area. If patients had more than one PI-RADS lesion, lesions were analyzed together (such that per patient rather than per lesion). Analysis was performed by reporting percentages of PCa and csPCa for MRI-TB, SB and MRI-TB+SB.

### Statistical Analysis

Study data were collected and managed using Research Electronic Data Capture (REDCap) electronic data capture tools hosted at Turkish Urooncology Association (16,17). REDCap is a secure and web-based software platform designed to support data capture for research studies, providing an intuitive interface for validated data capture, automated export procedures for seamless data downloads to common statistical packages, audit trails for tracking data manipulation and export procedures and procedures for data integration and interoperability with external sources (16,17).

In the statistical analysis, Statistical Package for the Social Sciences (SPSS) version 22.0 was used. The Mann-Whitney U test, t-test and chi-square test were used to analyze the relationship of categorical and continuous variables between two biopsy methods and three biopsy schemes of combined biopsy method. In the multivariate analysis, regression model was used to identify independent risk factors for csPCa detection. P-values less than 0.05 were considered statistically significant.

## Results

Data from 65 patients who underwent MRI-TB+SB, with PSA levels of 20-100 ng/mL and normal DRE were evaluated. Demographic data of the study cohort stratiŞed by biopsy approach are given in Table 1. Median number of MRI-TB cores sampled per region of interest was 5.8. Mean age and PSA were 65.3 years, 33.2 ng/mL respectively.

PI-RADS 5 lesions were detected in 44% of the patients. PCa was detected in 35 patients with combined MRI-TB+SB (53.8%) patients. PCa detected in 30 and 24 patients by targeted and systematic only biopsy, respectively. SB alone missed 11 patients and MRI-TB missed only 5 patients of any grade cancer. There was significant difference in missed PCa ratio between MRI-TB and SB (14.2% vs 31.4%) of any grade PCa, but csPCa detection by SB alone was significantly lower than MRI-TB alone. Most of the patients with cancer identified as csPCa (91.4%). SB alone missed 10 patients and MRI-TB missed only 5 patients with csPCa. TB added 10/32 (31.25%) of csPCa detection.

We analyzed that clinical factors impact csPCa detection risk by MRI-TB-SB. In the multivariate analysis, the regression model proved that the following clinical parameters were significantly

increasing the probability of PCa detection: prostate volume, PSA density (PSAD) >0.75 ng/mL$^2$ and higher PI-RADS scores (Table 2).

Fifteen patients who underwent radical prostatectomy (RP) were evaluated for concordance analysis. MRI-TB showed significantly higher concordance over SB at RP (Table 3). Six patients were found to have significant PCa on RP whom went undetected or undergraded with SB biopsy. Gleason score downgrading at final pathology was lowest in both methods.

**Table 1. Descriptive characteristics and pathologic results of patients**

| | | PSA 20-100 DRE normal (n=65) |
|---|---|---|
| Age | | 65.3±8 |
| BMI | | 27±6.7 |
| PSA | | 33.2±16.4 (20-100) |
| PV | | 82.3±57.7 |
| PSAD | | 0.50±0.51 |
| mpMR-PI-RADS | PI-RADS <3 | 1 (1.5%) |
| | PI-RADS 3 | 12 (18.5%) |
| | PI-RADS 4 | 23 (35.4%) |
| | PI-RADS 5 | 29 (44.6%) |
| PCa<br>• MRI-TB+SB<br>• MR-TB<br>• SB | | <br>35 (53.8%)<br>30 (46.2%)<br>24 (36.9%) |
| csPCa<br>• MRI-TB+SB<br>• MR-TB<br>• SB | | <br>32 (49.2%)<br>27 (41.5%)<br>22 (33.8%) |
| RP (n=57)<br>• Upgrade<br>• Concordance<br>• Downgrade | | (n=15)<br>4 (26.7%)<br>9 (60%)<br>2 (13.3%) |

BMI: Body mass index, PSA: Prostate specific antigen, PSAD: PSA density, PV: Prostate volume, DRE: Digital rectal examination, RP: Radical prostatectomy, SB: Systematic biopsies, PI-RADS: Prostate Imaging Reporting and Data System, MRI: Magnetic resonance imaging, TB: Targeted biopsy

**Table 2. Multivariable logistic regression analyses predicting factors effecting biopsy results**

| | | PSA 20-100 ng/mL MRI-TB | | |
|---|---|---|---|---|
| | | Benign (n=35) | PCa (n=30) | p-value |
| Age | | 63.2±6.2 | 67.8±9.1 | 0.068 |
| PV | | 111.1±58 | 47.3±33.3 | <0.001 |
| PSAD | | 0.28±0.23 | 0.75±0.63 | 0.002 |
| mpMRI-PI-RADS | PI-RADS <3 | 1 (2.9%) | 0 (0%) | <0.001 |
| | PI-RADS 3 | 9 (25.7%) | 3 (10%) | |
| | PI-RADS 4 | 19 (54.3%) | 4 (13.3%) | |
| | PI-RADS 5 | 6 (17.1%) | 23 (76.7%) | |
| Number of cores per lesion | | 7.2±4.4 | 5.8±4.4 | 0.146 |

PSAD: Prostate specific antigen density, PV: Prostate volume, PI-RADS: Prostate Imaging Reporting and Data System, MRI: Magnetic resonance imaging, PCa: Prostate cancer, TB: Targeted biopsy

**Table 3. Concordance at radical prostatectomy**

| | | RP insPCa (n=2) | RP csPCa (n=13) |
|---|---|---|---|
| PSA | | 24.6±5:2 | 29±10 |
| mpMRI-PI-RADS | PI-RADS <3 | 0 (0%) | 0 (0%) |
| | PI-RADS 3 | 0 (0%) | 3 (23.1%) |
| | PI-RADS 4 | 0 (0%) | 4 (30.8%) |
| | PI-RADS 5 | 2 (100%) | 6 (46.2%) |
| MRI-TB+SB<br>• insPCa<br>• csPCa | | <br>2 (100%)<br>0 (0%) | <br>1 (7.7%)<br>12 (92.3%) |
| MRI-TB<br>• benign<br>• insPCa<br>• csPCa | | <br>1 (50%)<br>1 (50%)<br>0 (0%) | <br>2 (15.4%)<br>2 (15.4%)<br>9 (69.2%) |
| SB<br>• benign<br>• insPCa<br>• csPCa | | <br>0 (0%)<br>2 (100%)<br>0 (0%) | <br>6 (46.2%)<br>0 (0%)<br>7 (53.8%) |

insPCA: Insignificant prostate cancer, RP: Radical prostatectomy, SB: Systematic biopsies, PI-RADS: Prostate imaging-reporting and data system, MRI: Magnetic resonance imaging, TB: Targeted biopsy, PCa: Prostate cancer

## Discussion

The main goal of our study was to investigate whether omitting MRI-TB in PSA 20-100 ng/mL and normal DRE could impact the csPCa detection rate. Our results confirmed that in these patients MRI-TB has a significantly higher csPCa detection rate compared to SB, 41% vs 33%, respectively. We also confirmed that omitting MRI-TB may contribute to a significant reduction in the csPCa detection rate by 31.25%.

In the literature, studies regarding PSA thresholds and the biopsy technique were mainly focused on the patient groups who had PSA levels less than 20 ng/mL (10,14). Most of the clinicians and patients' perception is that once they had a PSA level of >20 ng/mL, there would be a high probability of having PCa. In the literature and guidelines however, there is a paucity of data for the exact cancer detection rates which would help significantly in counseling those patient groups.

In our study most patients had PI-RADS 5 lesions. A low csPCa detection rate in patients with PI-RADS 3 and 4 but high in those with PI-RADS 5 lesions was consistent with the findings of others indicating that mpMRI is beneficial to men with PSA 20-100 ng/mL and normal DRE. Overall, these results emphasize the advantages of the proposed combined strategy. Therefore, allocating time and resources for pre-interventional mpMRI is warranted in most patients with suspected PCa, since inaccurate initial risk stratification could lead to avoidable morbidities that significantly exceed the expenses of establishing a precise diagnosis.

There are several arguments that advise MRI-TB omission mostly in patients with PSA>20 and normal DRE.

For patients presenting with PSA levels >20 ng/mL and abnormal DRE, some reports suggest that performing only SB may be a reasonable option, as it reduces the need for cost-effective diagnostic procedures prior to prostate biopsy (18). In line

with this, skipping pre-interventional mpMRI to avoid delays in diagnosis and the associated psychological burden could be considered, particularly in settings with limited resources and inadequate infrastructure (18). Nevertheless, such an approach should be carefully weighed against available facilities and potential limitations. On the other hand, in an analysis of 91 patients, demonstrated a significantly higher detection rate of csPCa with MRI-TB compared to SB, both in cases with normal and suspicious DRE findings (15). In that study, Omri et al. (15) emphasized that the added value of mpMRI and TB was more evident in patients with a negative DRE, although they still recommended the combined use of TBx and SBx for those with suspicious DRE. Similarly, Morote et al. (13) assessed the impact of mpMRI and MRI-TB in 34 men with PSA >20 ng/mL and normal DRE, showing that MRI-TB could enhance SB in identifying the highest proportion of csPCa in this context. In the subgroup analysis of patients with PSA >20 ng/mL revealed a mean PSA of 58 ng/mL, with levels reaching up to 912 ng/mL, indicating a heightened likelihood of csPCa presence, including metastatic disease. Importantly, 95% of these patients were diagnosed with csPCa, and SB alone yielded accurate diagnoses in 87% of cases (13). Still, even in this subset, the combination of biopsy methods of MRI-TB+SB provided superior diagnostic performance. Overall, evidence suggests that mpMRI offers greater benefit in patients with a normal DRE; however, both MRI-TB and SB remain advisable regardless of DRE status (13,15,18,19).

Beyond PSA levels, several additional factors are being investigated as potential predictors of csPCa detection through MRI-TB, including PSAD, DRE findings, lesion location, prostate volume and biopsy procedure. To date, however, no clear risk-adapted model or nomogram has been proposed to omit TB. In our analysis, a PSAD threshold of 0.75 ng/mL$^2$ emerged as an important data for identifying csPCa. These findings align with existing literature, which consistently highlights PSAD and PI-RADS score as strong predictors of csPCa detection. Abnormal DRE remains one of the classic indications for biopsy and also provides clinical insight into disease extent. Yang et al. (12) reported PCa detection rates of 66.3% in patients with PSA 20-100 ng/mL and positive DRE, compared with 64.9% in those with negative DRE. In our cohort, overall PCa detection was 53.8%. Higher PSA values were shown to correlate with abnormal DRE findings, and among patients with PSA levels between 20-99.99 ng/mL, positive DRE findings were significantly linked with PCa diagnosis (10,12). Interestingly, while PSA level did not correlate with PCa in men presenting with palpable nodules on DRE, a higher PSA was associated with PCa diagnosis in patients without nodules on DRE (10,12).

In our cohort, 15 patients who underwent RP were evaluated for concordance. MRI-TB was superior in prediction of the final histopathological results than SB. MRI-TB showed significantly higher concordance over SB at RP. Six patients were found to have csPCa on RP whom went undetected or undergraded with SB only. If MRI-TB omitted, our results showed that 6 patients (40%) with csPCa at RP would be missed initially. This supports previous researches that has highlighted the superior concordance of combined biopsy of MRI-TB+SB with final pathological tumor grading, emphasizing the signifcance of performing both SB and MRI-TB to reduce the risk of misdiagnosis (15,19).

### Study Limitations

The major limitations of our study are its retrospective nature and analysis. Our study is multi-centric and retrospective. Given the specific patient population definition as normal DRE with PSA 20-100 ng/mL, our study sample size is not low and provides important insights for clinical practice. The study population was heterogeneous, as it included both transperineal and transrectal biopsies. The analysis did not include epidemiological factors such as body mass index or comorbidities. Part of the mpMRI images were obtained from external radiological centers, and they were read by radiologists with different experiences; therefore, wider inter-observer variability is certainly possible in the assessment of the PI-RADS scores. Another limitation is that MRI-TB data was obtained from 5 different centers performed by 7 different urologists using different MRI and MRI-US fusion devices. Failure of mpMRI fusion biopsy due to incorrect mpMRI image registration or mismatch of image planes, inaccurate sampling and intralesion Gleason score heterogeneity may have impacted our results. Another important limitation is that there was no centralized pathological examination, multicentric pathological examinations by uropathologists at respective centers. The comparisons of biopsy methods were performed per patient rather than per lesion. Nevertheless, our data reflect the real-life nationwide picture and therefore important.

## Conclusion

The results of our study indicate that in patients with normal DRE and PSA 20-100 ng/mL, the probability of detecting csPCa in SB is significantly lower than in MRI-TB. Omitting MRI-TB is associated with the risk of missing csPCa in one-third of cases. In patients with PSA 20-100 ng/mL and normal DRE, MRI-TB adds non-negligible clinical value. Therefore, sparing these patients from MRI-TB should not be considered to reduce patient morbidity and cost in order to avoid reduced cancer detection, local staging error and misleading therapeutic decisions.

### Ethics

**Ethics Committee Approval:** Ethics committee approval is not required.

**Informed Consent:** All patients gave consent for the data collection.

### Acknowledgements

We acknowledge for their contribution of data collection to Members of Turkish Urooncology Association; Sertaç Yazıcı, İlker Akarken, Cenk Yücel Bilen, Evren Süer, Ahmet Güdeloğlu, Saadettin Eskiçorapçı.

## Footnotes

### Authorship Contributions

Surgical and Medical Practices: G.A., S.S., L.T., S.Y., C.Y.B., İ.A., E.S., Concept: G.A., S.Ç., Design: G.A., S.Ç., Data Collection or Processing: S.Çet., S.S., S.Y., İ.A., S.E., B.Ş., C.Y.B., Analysis or Interpretation: B.Ş., S.Ç., G.A., Literature Search: S.Çet., B.Ş., Writing: G.A.

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*Original Article*

DOI: 10.4274/uob.galenos.2025.2024.11.3

*Bull Urooncol 2025;24(4):97-102*

# *Can the Preoperative Systemic Immune-inflammation Index be Used to Predict Biochemical Recurrence in Patients with Localized Prostate Cancer After Radical Prostatectomy: A Retrospective Cohort Study*

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## Abstract

**Objective:** The purpose of study was to identify the clinical utility of preoperative systemic immune-inflammation index (SII) in predicting biochemical recurrence (BCR) after robot-assisted radical prostatectomy (RARP).

**Materials and Methods:** A retrospective analysis was performed using data from our robotic surgery database, which included 531 patients with localized prostate cancer (PCa) who received RARP from March 2015 through June 2021. Patients' characteristics and outcomes were recorded. The preoperative SII of each patient was calculated. Patients with and without BCR were confronted. The predictive ability of the SII was determined by receiver operating characteristic (ROC) curve analysis.

**Results:** After applying the exclusion criteria, the study included 400 patients. Among them, 90 patients (22.5%) experienced BCR. Analysis of the relationship between BCR and preoperative variables demonstrated that prostate-specific antigen, biopsy International Society of Urological Pathology (ISUP) grade, clinical stage, and D'Amico classification statistically significant. Although the SII was higher in patients with BCR, the difference was not statistically significant (p=0.198). Previously reported pathological factors, such as ISUP grade at prostatectomy, pathological stage, lymphovascular invasion, perineural invasion, extraprostatic extension, seminal vesicle invasion, and positive surgical margin, were associated with BCR. The ROC curve for the SII demonstrated poor predictive ability for BCR (95% confidence interval: 0.412-0.545; p=0.532).

**Conclusion:** SII did not appear to be a prognostic indicator for BCR after RARP in localized PCa patients.

**Keywords:** Systemic immune-inflammation index, prostate cancer, biochemical recurrence, pathology

## Introduction

Prostate cancer (PCa) represents the leading cancer diagnosis in the male population (1). Currently, radical prostatectomy (RP) remains the primary surgical treatment approach for managing localized PCa. The main purpose of RP is to provide tumor removal, achieve final staging, and eradicate sources of prostate-specific antigen (PSA), while preserving continence and erectile function. Biochemical recurrence (BCR) was observed in 35% of the patients after RP (2). Patients with BCR may require additional treatment and are reported to have worse oncological outcomes. The pathological results have a significant impact on prognosis in patients with localized PCa who undergo RP. The identification of biomarkers that can accurately predict pathological and oncological outcomes is needed to inform the decision-making process.

Inflammation plays a key role in the advancement and progression of multiple cancers (3). Furthermore, the host inflammatory response to malignancy has been shown to be associated with tumorigenesis and progression (4). Recently, the relationship between inflammation and cancer has received increasing attention, and the prognostic value of inflammatory

**Cite this article as:** Karamık K, Ölçücü MT, Demir Y, et al. Can the preoperative systemic immune-inflammation index be used to predict biochemical recurrence in patients with localized prostate cancer after radical prostatectomy: a retrospective cohort study. Bull Urooncol. 2025;24(4):97-102.

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**Received:** 29.11.2024 **Accepted:** 24.08.2025 **Publication Date:** 24.12.2025

markers has been studied extensively. Multiple inflammatory markers were evaluated to estimate prognosis in patients with various cancers. Neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR) were the most examined biomarkers (5-7). Recently, the systemic immune-inflammation index (SII) has been suggested as a biomarker that integrates neutrophils, platelets, and lymphocytes. It was proposed that the SII was superior to known biomarkers because the SII showed better the equality between host inflammatory and immune response (8-10).

So far, the prognostic ability of SII has been evaluated in metastatic PCa patients (11-14). However, the role of SII in patients with localized PCa has rarely been reported (15-17). Therefore, we aimed to explore the prognostic ability of SII in patients with localized PCa who undergone robot-assisted RP (RARP), which may contribute to the literature.

## Materials and Methods

### Study Cohort

After Institutional Ethics Committee for University of Health Sciences Türkiye, Antalya Training and Research Hospital (decision no: 15/14, date: 30/09/2021) was obtained for this retrospective study, we retrospectively determined the robotic surgery data of 531 patients who undergone RARP between March 2015 and July 2021. Patients with the subsequent circumstances were excluded from the study: (1) initially received neoadjuvant androgen deprivation therapy (n=4); (2) evidence of chronic and/or acute infection (n=13); (3) history of the autoimmune or inflammatory disease (n=11); (4) a follow-up time shorter than one year (n=94); (5) lack of detailed clinical information (n=3); and (6) persistent PSA after surgery (n=6). Thus, the final study population included 400 patients. Patient selection flowchart is demonstrated in Figure 1.

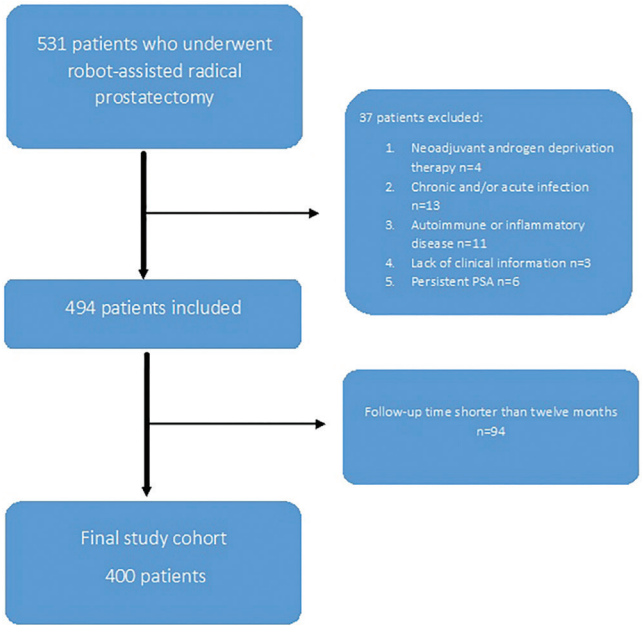


**Figure 1.** Patient selection flowchart

### Study Parameters

Preoperative demographic data (age, body mass index), clinical information [PSA, biopsy International Society of Urological Pathology (ISUP) grade, clinical stage, D'Amico risk group, SII level], pathological outcomes [prostatectomy ISUP grade, pathological stage, surgical margin status, presence, of perineural invasion (PNI), lymphovascular invasion (LVI), extraprostatic extension (EPE), seminal vesicle invasion (SVI), positive lymph node metastasis], and follow-up data were recorded.

Blood tests were routinely obtained 3-10 days before the surgery. The SII was calculated as (platelet × neutrophil)/lymphocyte.

### Surgical Technique and Follow-up

Surgeries were performed via transperitoneal and retzius-sparing approach with the da Vinci XI robotic system. Previously, we described our surgical technique of RARP (18). Extended lymph node dissection was performed in patients whose Briganti nomogram-calculated risk of lymph node metastasis was greater than 5%. PSA value of the patients was measured every 3 months during postoperative follow-up. BCR was determined when two successive PSA measurements reached or exceeded 0.2 ng/mL.

### Statistical Analysis

Continuous variables were reported as mean ± standard deviation or median (interquartile range), and categorical variables as counts (percentages). The assumption of normality was tested using the Shapiro-Wilk test. Categorical variables were analyzed with the chi-square test or Fisher's exact test. Based on data distribution characteristics, we utilized either Student's t-test or Mann-Whitney U test for continuous variable comparisons. ROC curve analysis was employed to evaluate the predictive capacity of SII for BCR. Stepwise multivariate logistic regression was utilized to determine which variables independently predicted BCR following RP. The initial model included the following clinicopathological variables: prostatectomy ISUP grade, LVI, PNI, EPE, surgical margin status, lymph node involvement, D'Amico risk classification, clinical stage, SII, and preoperative PSA level. All statistical analyses were performed with IBM SPSS Statistics version 27.0, with statistical significance set at $p<0.05$.

## Results

The relationship between BCR and preoperative clinical characteristics and SII was summarized in Table 1. BCR was determined in 90 patients (22.5%). PSA, biopsy ISUP grade, clinical stage, and D'Amico risk were statistically significant ($p=0.006$, $p=0.006$, $p=0.010$, and $p=0.005$, respectively). Although the SII was higher in patients with BCR, there was no statistically significant difference observed ($p=0.198$).

Table 2 shows the association between BCR and postoperative outcomes. ISUP grade at prostatectomy and pathological stage were correlated with BCR. Furthermore, the presence of LVI, PNI, EPE, SVI, and surgical margin positivity were correlated with BCR ($p<0.05$, for all).

As shown in Figure 2, the ROC curve of the SII for BCR estimation was was 0.478 [95% confidence interval (CI): 0.412-0.545; $p=0.532$].

Following the stepwise selection process, three variables remained statistically significant in the final model (Table 3). EPE presence correlated with an approximately two-fold elevation in BCR risk [odds ratio (OR)=1.923; 95% CI: 1.107-3.342; p=0.020]. Similarly, SVI independently predicted recurrence, with an odds ratio of 2.551 (95% CI: 1.331-4.889; p=0.005). Moreover, the preoperative PSA level was a continuous predictor of BCR, with each 1 ng/mL increase in PSA corresponding to a 2.4% increase in recurrence risk (OR=1.024; 95% CI: 1.0031.045; p=0.027). These results highlight EPE, SVI, and preoperative PSA as the most robust independent predictors of BCR following RP in this cohort.

**Table 1. Preoperative characteristics compared between patients experiencing and not experiencing biochemical recurrence**

| Variables | BCR | | p-value |
|---|---|---|---|
| | Yes (n=90) | No (n=310) | |
| Age, years (mean ± SD) | 65.73±6.13 | 64.50±6.08 | 0.093 |
| BMI, kg/m$^2$ (mean ± SD) | 27.09±2.72 | 27.53±3.63 | 0.463 |
| PSA, ng/mL (median, IQR) | 9.87 (10.48) | 8.00 (6.34) | **0.006** |
| Biopsy ISUP, n (%) | | | **0.006** |
| 1 | 41 (45.5%) | 196 (63.2%) | |
| 2 | 28 (31.1%) | 67 (21.6%) | |
| 3 | 7 (7.8%) | 23 (7.4%) | |
| 4 | 11 (12.2%) | 23 (7.4%) | |
| 5 | 3 (3.3%) | 1 (0.03%) | |
| Clinical stage, n (%) | | | **0.010** |
| T1 | 53 (58.9%) | 216 (69.7%) | |
| T2 | 35 (38.9%) | 92 (29.7%) | |
| T3 | 2 (2.2%) | 2 (0.6%) | |
| D'Amico risk classification, n (%) | | | **0.005** |
| Low | 25 (27.8%) | 142 (45.8%) | |
| Intermediate | 40 (44.4%) | 116 (37.4%) | |
| High | 25 (27.8%) | 52 (16.8%) | |
| SII (mean ± SD) | 608.87±780.07 | 537.79±311.62 | 0.198 |

BMI: Body mass index, SD: Standard deviation, BCR: Biochemical recurrence, PSA: Prostate-spesific antigen, ISUP: International Society of Urological Pathology, SII: Systemic immune-inflammation index, IQR: Interquartile range

**Table 2. Postoperative characteristics compared between patients experiencing and not experiencing biochemical recurrence**

| Variables | BCR | | p-value |
|---|---|---|---|
| | Yes (n=90) | No (n=310) | |
| Prostatectomy ISUP, n (%) | | | **0.001** |
| 1 | 25 (27.8%) | 134 (43.2%) | |
| 2 | 27 (30.0%) | 103 (33.2%) | |
| 3 | 22 (24.4%) | 39 (12.6%) | |
| 4 | 4 (4.4%) | 20 (6.5%) | |
| 5 | 12 (13.3%) | 14 (4.5%) | |
| Pathological stage, n (%) | | | **<0.001** |
| T2 | 39 (43.3%) | 222 (71.6%) | |
| T3 | 51 (56.7%) | 88 (28.4%) | |
| Lymphovascular invason, n (%) | | | **<0.001** |
| Absent | 59 (65.6%) | 261 (84.2%) | |
| Present | 31 (34.4%) | 49 (15.8%) | |
| Perineural invasion, n (%) | | | **0.024** |
| Absent | 13 (14.4%) | 77 (24.8%) | |
| Present | 77 (85.6%) | 233 (75.2%) | |

| Table 2. Continued | | | |
|---|---|---|---|
| **Variables** | **BCR** | | **p-value** |
| | **Yes (n=90)** | **No (n=310)** | |
| Extraprostatic extension, n (%) | | | **<0.001** |
| Absent | 44 (48.9%) | 230 (74.2%) | |
| Present | 46 (51.1%) | 80 (25.8%) | |
| Seminal vesicle invasion, n (%) | | | **<0.001** |
| Absent | 63 (70.0%) | 280 (90.3%) | |
| Present | 27 (30.0%) | 30 (9.7%) | |
| Surgical margin, n (%) | | | **0.015** |
| Positive | 31 (34.4%) | 69 (22.3%) | |
| Negative | 59 (65.6%) | 241 (77.7%) | |
| Lymph node involment, n (%) | | | 0.279 |
| Positive | 5 (5.5%) | 11 (3.5%) | |
| Negative | 85 (94.5%) | 299 (96.5%) | |
| Mortality, n (%) | | | 0.333 |
| Yes | 8 (8.9%) | 35 (11.3%) | |
| No | 82 (91.1%) | 275 (88.7%) | |
| ISUP: International Society of Urological Pathology, BCR: Biochemical recurrence | | | |

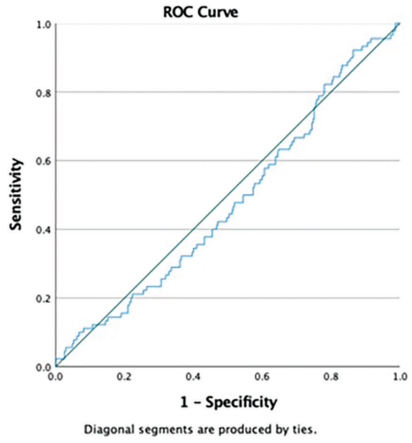


**Figure 2.** The ROC curve of the SII

ROC: Receiver operating characteristic, SII: Systemic immune-inflammation index

## Discussion

In recent years, markers based on blood tests have shown great potential for predicting oncological outcomes in patients with malignancies. The NLR is one of the most extensively studied biomarkers, and it has been shown to have prognostic value in many malignancies. Subsequently, it was suggested that the SII better reflects immune status and its prognostic significance in cancers has frequently been studied. In the present study, we assessed the ability of preoperative SII to predict BCR in localized PCa patients treated with RP. We observed that the SII was not identified as a predictor of BCR.

Many studies have reported the association between inflammation and cancer, suggesting that immune cells play an essential role in promoting tumor development and progression by secreting various cytokines and chemokines (3,4). Neutrophils facilitate tumor development, progression, and metastasis by inducing angiogenesis (19). Lymphocytes exert an antitumor effect by inhibiting tumor cell proliferation (20). Therefore, lymphopenia indicates an insufficient host immune response. Furthermore, platelets have been shown to protect cancer cells from immune cells and promote metastasis (21). In light of this information, inflammatory biomarkers such as NLR, PLR, and LMR have been proposed as indicators of cancer prognosis. Inflammatory markers have been extensively studied as predictors of prognosis in various cancers (5-8). Inflammation markers can be readily calculated from routine blood tests without additional cost or examination. Recently, SII has been proposed based on the proportions of neutrophils, platelets, and lymphocytes. SII has been suggested as a better predictive biomarker. Because it projects better the equation between host inflammatory and immune response status when compared to NLR, PLR, and LMR (22,23). As a simple, convenient, easily obtained, inexpensive, and non-invasive marker, the capacity of the SII to estimate oncological outcomes in cancer patients is promising. SII could provide an information regarding prognosis and treatment response in cancer patients.

The prognostic importance of SII in PCa patients has mostly been studied in metastatic disease (11-14). Few studies have investigated SII to predict prognosis in localized PCa (15-17). In a multicenter study, Rajwa et al. (15) showed that high preoperative SII (≥620) was associated with BCR in the preoperative multivariable model but not in the postoperative multivariable model. In another study, high preoperative SII (>528) was associated with an increased risk of BCR in localized PCa after RP (17). Unlike these studies, there was not a significant predictive role of SII for BCR in our study. A recent meta-analysis demonstrated that SII was not correlated with biochemical recurrence free survival in patients with localized PCa, which supports our findings (24). Conflicting results may have been

| Table 3. Stepwise logistic regression model for predicting BCR after radical prostatectomy | | | | | | |
|---|---|---|---|---|---|---|
| **Variables** | **Beta** | **SE** | **p-value** | **OR** | **95% CI** | |
| Extraprostatic extension | | | | | | |
| Absent (reference) | | | | | | |
| Present | 0.654 | 0.282 | **0.020** | 1.923 | 1.107 | 3.342 |
| SV invasion | | | | | | |
| Absent (reference) | | | | | | |
| Present | 0.937 | 0.332 | **0.005** | 2.551 | 1.331 | 4.889 |
| Preoperative PSA, ng/mL | 0.023 | 0.011 | **0.027** | 1.024 | 1.003 | 1.045 |
| BCR: Biochemical recurrence, SE: Standard error, OR: Odds ratio, CI: Confidence interval, SV: Seminal vesicle, PSA: Prostate-spesific antigen | | | | | | |

obtained in previous studies due to differences in sample sizes, SII cut-off values, and follow-up periods. The optimal cut-off values of SII reported in prior literature were not uniform, ranging from 300 to 1600. Therefore, optimal cut-off values should be clarified in larger prospective studies. Small sample size and short follow-up duration may also affect the efficacy of SII in predicting BCR after RP.

We also evaluated the potential role of conventional parameters in BCR following RP. PSA, biopsy ISUP grade, clinical stage, D'Amico risk classification, prostatectomy ISUP grade, pathological stage, LVI, PNI, EPE, SVI, and positive surgical margin were associated with BCR. Furthermore, EPE, SVI, and PSA were independent predictors of BCR, which is consistent with a recent meta-analysis. This meta-analysis involving 21,682 patients reported that clinicopathological features, including SVI, EPE, LVI, PNI, lymph node positivity, and surgical margin positivity were related with biochemical recurrence free survival (25).

### Study Limitations

This study has certain limitations that warrant consideration. The primary limitation involves the retrospective design, limited patient cohort size, and relatively brief follow-up duration. The time range for preoperative blood collection may introduce variability in SII. Furthermore, the SII can be a variable biomarker that can be affected by various situations such as smoking, medications, inflammatory diseases, and cardiovascular diseases. Larger sample-sized prospective studies can help to negate these issues.

### Conclusion

We evaluated the association between SII and BCR after RP. SII did not appear to be a prognostic biomarker for BCR after RP in localized PCa patients. SII, an easily calculated and cost-effective marker, has potential utility in cancer prognosis. However, the optimal cut-off value of SII should be determined by prospective studies.

### Ethics

**Ethics Committee Approval:** Approval was received from the Institutional Ethics Committee of University of Health Sciences Türkiye, Antalya Training and Research Hospital (decision no: 15/14, date: 30/09/2021).

**Informed Consent:** Retrospective study.

### Acknowledgements

**Publication:** The results of the study were not published in full or in part in form of abstracts.

**Contribution:** There is not any contributors who may not be listed as authors.

### Footnotes

### Authorship Contributions

Surgical and Medical Practices: M.A., Concept: K.K., M.T.Ö., M.R.İ., M.A., Design: K.K., M.T.Ö., H.A., K.Y., M.A., Data Collection or Processing: Y.D., M.R.İ., H.A., Analysis or Interpretation: Y.D., M.R.İ., H.A., Literature Search: K.K., M.T.Ö., H.A., K.Y., Writing: K.K., M.T.Ö.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

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*Original Article*

DOI: 10.4274/uob.galenos.2025.2025.8.1

*Bull Urooncol 2025;24(4):103-108*

# *The Role of Neoadjuvant Chemotherapy in the Pathological T-staging of Patients Undergoing Radical Cystectomy*

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## Abstract

**Objective:** For eligible patients with muscle-invasive bladder cancer, the current standard of care is neoadjuvant chemotherapy (NAC) using cisplatin-based regimens followed by radical cystectomy (RC) with pelvic lymph node dissection. We evaluated the role of NAC in the pathological T-staging of tumors in patients who underwent RC and the effect of pathological T-stage regression on disease-free survival (DFS) and overall survival (OS).
**Materials and Methods:** We evaluated 29 patients who underwent RC following NAC between 2015 and 2023 at our hospital. Eligible participants had histologically confirmed urothelial carcinoma of the bladder with stage cT2-T4a N0-N2 M0 disease and had received cisplatin-based NAC. The primary endpoint was the effect of NAC on pathological T-stage regression, DFS, and OS. The secondary endpoint was to determine the factors affecting DFS following RC.
**Results:** Cystectomy pN0 rate, in patients with T regression, was significantly higher than that in the other group (86.7% vs. 42.9%, p=0.021). The rate of lymphovascular invasion following cystectomy was significantly lower in the T regression group (57.1%) compared to the non-T regression group (93.3%; p=0.023). T2 pathology to RC time (hazard ratio=1.620, 95% confidence interval: 1.004-2.613, p<0.048) was the only independent predictor for DFS following RC in the multivariate analysis.
**Conclusion:** Detection of pathological tumor regression in cystectomy pathology after NAC is associated with better DFS and OS. T2 pathology to RC time was an independent predictor of DFS.
**Keywords:** Neoadjuvant chemotherapy, radical cystectomy, muscle-invasive bladder cancer

## Introduction

For eligible patients with muscle-invasive bladder cancer (MIBC), the current standard of care is neoadjuvant chemotherapy (NAC) using cisplatin-based regimens followed by radical cystectomy (RC) with pelvic lymph node dissection (1). This treatment schedule, which includes cisplatin-based NAC, has demonstrated improved oncological outcomes, with an 8% increase in 5-year overall survival (OS) after RC. Further research is needed to identify the most effective regimen of NAC (2,3).

The most frequently employed regimens for NAC treatment are methotrexate, vinblastine, doxorubicin, cisplatin, and gemcitabine-cisplatin (GC). While both regimens demonstrate comparable levels of tumor reduction, the GC regimen has been associated with lower OS rates following RC (4). Some studies have examined how NAC affects the T-stage of MIBC in RC patients. These studies, including both phase 2 and phase 3 trials, have demonstrated that certain NAC regimens can significantly contribute to the pathological downstaging of the tumor (5)

Our study evaluated the influence of NAC on the pathological T-staging of patients with MIBC who underwent RC. Furthermore, the study investigated the correlation between NAC-induced pathological T-stage regression and subsequent disease-free survival (DFS) and OS.

## Materials and Methods

Ethics committee approval, numbered 2025/0081, was secured on 31.07.2025 from İstanbul Provincial Health Directorate, Göztepe Prof. Dr. Süleyman Yalçın City Hospital. For this retrospective case-control study. We analyzed data from patients who were treated with NAC before undergoing

**Cite this article as:** Zada İH, Arıkan Ö, Kazan Ö, Çakıcı MÇ, Yıldırım A. The role of neoadjuvant chemotherapy in the pathological t-staging of patients undergoing radical cystectomy. Bull Urooncol. 2025;24(4):103-108.

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**Received:** 01.08.2025 **Accepted:** 22.09.2025 **Publication Date:** 24.12.2025

RC at our hospital between 2015 and 2023. Eligible participants had histologically confirmed urothelial carcinoma of the bladder with stage cT2-T4a N0-N2 M0 disease and had received cisplatin-based NAC. We collected data on patient demographics, comorbidities, smoking status, length of hospitalization, antiaggregant/anticoagulant therapy use, the time interval between bladder cancer diagnosis and RC, the interval between muscle-invasive pathology diagnosis and cystectomy, pathological T-stage and grade determined by primary transurethral resection of the bladder tumor (TUR-BT), presence of carcinoma *in situ*, lymphovascular invasion and post-TUR-BT intravesical therapy. Additionally, cystectomy pathological T-stage and grade, as well as the presence of carcinoma in situ and lymphovascular invasion, were evaluated.

Patients were ineligible for inclusion in the study if they had evidence of metastatic disease, non-urothelial tumors, a history of pelvic radiation, or incomplete medical records.

The primary endpoint was the effect of NAC on pathological T-stage regression and its effect on DFS and OS. The secondary endpoint was determining the factors affecting DFS following RC.

### Statistical Analysis

Statistical analyses were conducted using SPSS software, version 22. (IBM Corp, Armonk, NY). Continuous normally distributed variables were summarized as mean ± standard deviation. The t-test was used for group comparisons. The chi-square test was used for categorical variables, with a significance level of $\alpha$ =0.05 for all tests. Multivariate logistic regression analyses were conducted to determine independent prognostic factors influencing treatment decisions, using variables that had shown statistical significance in univariate analyses. Univariate and multivariate logistic regression analyses were performed to determine the odds ratios and 95% confidence intervals (CI) of risk factors predicting T-stage regression. A p-value threshold of less than 0.005 was considered statistically significant.

## Results

Twenty-nine patients met the inclusion criteria, comprising 20.6% women (n=6) and 79.4% men (n=23). There were 15 people in the T regression group and 14 people in the non-T regression group. No statistically significant differences were observed between groups regarding age, gender, smoking status, comorbidities, and family history. The pN0 rate following cystectomy was significantly higher in the T regression group compared to the other group (86.7% vs. 42.9%, p=0.021). Additionally, lymphovascular invasion in cystectomy specimens was significantly lower in the T regression group (57.1% vs. 93.3%, p=0.023). Operation time was longer in patients with non-T regression (218.5±44.7 vs. 202.67±28.6 min., p=0.035). In contrast, blood loss (217.8±72.3 vs. 306.6±174.1 mL, p=0.014) was significantly lower in this group. The demographic characteristics and pathological results of the patients are summarized in Table 1. Median follow-up was 41.6 months [interquartile range (IQR: 6-76)] in the T regression group; 29.7 months (IQR: 3-97) in the other group.

**Table 1. Patient characteristics and pathological outcomes**

| | pT regression (no) (n=14) | pT regression (yes) (n=15) | p-value |
|---|---|---|---|
| **Gender, n (%)** | | | 0.411[c] |
| Female | 2 (14.3) | 4 (26.7) | |
| Male | 12 (85.7) | 11 (73.3) | |
| Age (years), mean ± SD | 64.2±6.7 | 61.4±8.9 | 0.954[T] |
| Operation time (minute), mean ± SD | 218.5±44.7 | 202.67±28.6 | **0.035**[T] |
| Blood loss (mL), mean ± SD | 217.8±72.3 | 306.6±174.1 | **0.014**[T] |
| Removed lymph node number, mean ± SD | 9.64±4.9 | 13.6±8.1 | 0.154[T] |
| Number of positive lymph nodes, mean ± SD | 0.8±0.8 | 0.4±1.1 | 0.860[T] |
| Smoking interval, median (min-max) | 37.5 (20-45) | 40 (20-200) | 0.399[M] |
| Diagnosis of bladder cancer to radical cystectomy time, mo, median (min-max) | 6.5 (3-78) | 5 (3-72) | 0.115[M] |
| T2 pathology - radical cystectomy time, mo, median (min-max) | 6 (3-13) | 5 (3-7) | 0.319[M] |
| Length of hospitalization, day, median (min-max) | 11.5 (7-31) | 10 (8-11) | 0.128[M] |
| **Family history, n (%)** | | | 0.227[c] |
| No | 13 (92.9) | 13 (86.7) | |
| Yes | 1 (7.1) | 2 (13.3) | |
| **Hypertension, n (%)** | | | 0.077[c] |
| No | 11 (78.6) | 7 (46.7) | |
| Yes | 3 (21.4) | 8 (53.3) | |
| **Coronary artery disease, n (%)** | | | 0.311[c] |
| No | 10 (71.4) | 13 (86.7) | |
| Yes | 4 (28.6) | 2 (13.3) | |
| **Diabetes mellitus, n (%)** | | | 0.909[c] |
| No | 10 (71.4) | 11(73.3) | |
| Yes | 4 (28.6) | 4 (26.7) | |
| **Pulmonary comorbidities, n (%)** | | | 0.924[c] |
| No | 11 (78.6) | 12 (80.0) | |
| Yes | 3 (21.4) | 3 (20.0) | |
| **Reason of hospitilization, n (%)** | | | 0.997[c] |
| Asymptomatic | 1 (7.1) | 1 (6.7) | |
| Hematuria | 12 (5.7) | 13 (86.7) | |
| LUTS | 1 (7.1) | 1 (6.7) | |

**Table 1. Continued**

| | pT regression (no) (n=14) | pT regression (yes) (n=15) | p-value |
|---|---|---|---|
| **Primary T-staging, n (%)** | | | 0.567[c] |
| Ta | 1 (7.1) | 0 (0.0) | |
| T1 | 2 (14.3) | 2 (13.3) | |
| T2 | 11 (78.6) | 13 (89.7) | |
| **Primary grade, n (%)** | | | 0.292[c] |
| Low grade | 1 (7.1) | 0 (0.0) | |
| High grade | 13 (92.7) | 15 (100.0) | |
| **Primary carcinoma *in situ*, n (%)** | | | 0.941[c] |
| No | 12 (85.7) | 13 (86.7) | |
| Yes | 2 (14.3) | 2 (13.3) | |
| **Primary lenfovascular invasion, n (%)** | | | 0.960[c] |
| No | 13 (92.9) | 14 (93.3) | |
| Yes | 1 (7.1) | 1 (6.7) | |
| **Tumor size, n (%)** | | | 0.060[c] |
| <3 cm | 2 (14.3) | 7 (46.7) | |
| >3 cm | 12 (85.7) | 8 (53.3) | |
| **Intravesical Bacillus Calmette-Guérin (BCG) therapy, n (%)** | | | 0.858[c] |
| No | 7 (50.0) | 8 (53.3) | |
| Yes | 7 (50.0) | 7 (46.7) | |
| **Intravesical mitomycin-c (MMC) therapy, n (%)** | | | 0.837[c] |
| No | 8 (57.1) | 8 (53.3) | |
| Yes | 6 (42.9) | 7 (46.7) | |
| **Pre-cystectomy T-staging, n (%)** | | | 0.367[c] |
| Ta | 1 (7.1) | 0 (0.0) | |
| T1 | 0 (0.0) | 1 (6.7) | |
| T2 | 13 (92.9) | 14 (93.3) | |
| **Pre-cystectomy carcinoma *in situ*, n (%)** | | | 0.249[c] |
| No | 11 (78.6) | 14 (93.3) | |
| Yes | 3 (21.4) | 1 (6.7) | |
| **Pre-cystectomy lymphovascular invasion, n (%)** | | | 0.960[c] |
| No | 13 (92.9) | 14 (93.3) | |
| Yes | 1 (7.1) | 1 (6.7) | |
| **Pre-cystectomy clinical T-staging, n (%)** | | | 0.287[c] |
| 0 | 9 (64.3) | 13 (86.7) | |
| 1 | 1 (7.1) | 1 (6.7) | |
| 2 | 4 (28.6) | 1 (6.7) | |

**Table 1. Continued**

| | pT regression (no) (n=14) | pT regression (yes) (n=15) | p-value |
|---|---|---|---|
| **Pre-cystectomy clinical N staging, n (%)** | | | 0.374[c] |
| N0 | 12 (85.7) | 12 (80.0) | |
| N1 | 1 (7.1) | 3 (20.0) | |
| N2 | 1 (7.1) | 0 (0.0) | |
| **Urinary diversion type, n (%)** | | | 0.367[c] |
| Ureterocutaneostomy | 1 (7.1) | 0 (0.0) | |
| Ileal Loop | 13 (92.9) | 14 (93.3) | |
| Ileal Neobladder | 0 (0.0) | 1 (6.7) | |
| **Cystectomy T-staging, n (%)** | | | **0.002** |
| pT0 | 2 (14.3)[a] | 13 (86.7)[b] | |
| pT1 | 1 (7.1)[a] | 2 (13.3)[a] | |
| pT2 | 1(7.1)[a] | 0 | |
| pT3 | 7 (50.0)[a] | 0 | |
| pT4 | 3 (21.4)[a] | 0 | |
| **Cystectomy pN stage, n (%)** | | | **0.021** |
| pN0 | 6 (42.9)[a] | 13 (86.7)[b] | |
| pN1 | 5 (35.7)[a] | 0 (0.0)[b] | |
| pN2 | 3 (21.4)[a] | 2 (13.3)[a] | |
| **Cystectomy lymphovascular invasion, n (%)** | | | **0.023** |
| No | 8 (57.1) | 14 (93.3) | |
| Yes | 6 (42.9) | 1 (6.7) | |
| **Ureteral positive surgical margin, n (%)** | | | 0.292[c] |
| No | 13 (92.9) | 15 (100) | |
| Yes | 1 (7.1) | 0 | |

[a,b]: Bonferroni adjustment, [c]: Chi-square analysis, [T]: Student's t-test, [M]: Mann-Whitney U test, SD: Standard deviation, pT: Pathological tumor, pN: Pathological node

## Univariate and Multivariate Analysis of the Factors Influencing Survival of Patients

Both DFS and OS were worse in the non-T-regressed group (Figures 1 and 2). Length of hospitalization, smoking status, T2 pathology to RC time, cystectomy pathological tumor (pT) stage, cystectomy pathological node (pN) stage, cystectomy lymphovascular invasion, and number of positive lymph nodes were the factors affecting DFS in the univariate analysis. T2 pathology to RC time (hazard ratio=1.620, 95% CI, 1.004-2.613, p<0.048) was the only independent predictor for DFS following RC in the multivariate analysis, as shown in Table 2.

Kaplan-Meier analysis showed better DFS in the T regression group at 5 years (100% vs. 64.3%, p=0.019) (Figure 1). Also, Kaplan-Meier analysis showed better OS in the T regression group at 5 years (100% vs. 59.1%, p=0.008) (Figure 2).

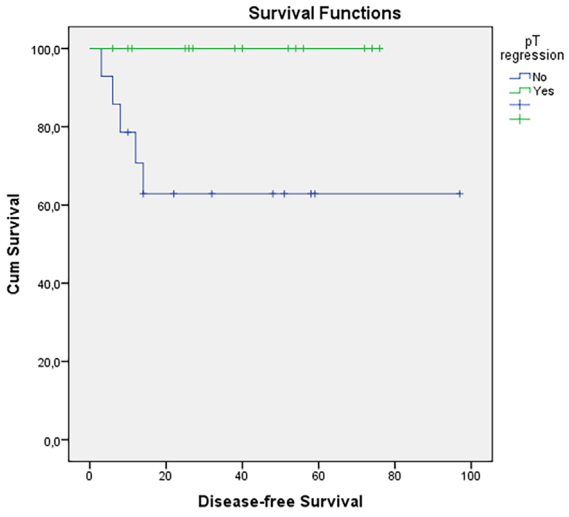


**Figure 1.** Kaplan-Meier curve for disease-free survival according to presence of pathological T-stage regression. The p-value of the log-rank method was 0.019 and the chi-square value was 5.487
pT: Pathological tumor

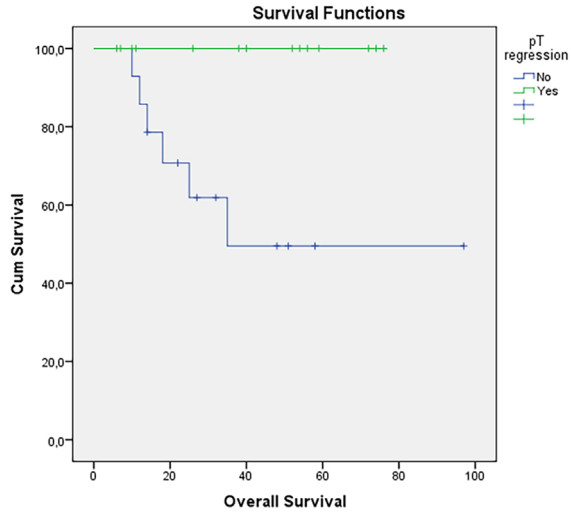


**Figure 2.** Kaplan-Meier curve for overall survival according to presence of pathological T-stage regression. The p-value of the log-rank method was 0.008 and the chi-square value was 6.945
pT: Pathological tumor

**Table 2. Univariate and multivariate cox proportional hazards regression models for patient survival**

| Variable | Univariate model | | Multivariate model | |
|---|---|---|---|---|
| | HR (95% CI) | p-value | HR (95% CI) | p-value |
| Diagnosis-radical cystectomy time (years) | 1.029 (0.998-1.061) | 0.070 | | |
| T2 pathology-radical cystectomy time | 1.522 (1.061-2.182) | **0.022** | 1.620 (1.004-2.613) | **0.048** |
| Age at RC | 1.009 (0.892-1.142) | 0.886 | | |
| Gender | 29.82 (0.004-243.3) | 0.460 | | |
| Smoking | 7.512 (1.360-41.476) | **0.021** | | |
| Charlson comorbidity index | 0.033 (<0.1-1220.4) | 0.526 | | |
| Primary pT-staging | 0.570 (0.154-2.109) | 0.400 | | |
| Primary carcinoma *in situ* | 0.038 (<0.1-1168.3) | 0.535 | | |
| Tumor size (Ref:<3cm) | 36.991 (0.14-99784.0) | 0.370 | | |
| Bacillus Calmette-Guérin (BCG) | 5.368 (0.596-48.36) | 0.134 | | |
| Mitomycin-C (MMC) | 7.311 (0.802-66.61) | 0.078 | | |
| Pre-cystectomy carcinoma in situ status | 0.038 (<0.1-1168.3) | 0.535 | | |
| Pre-cystectomy lymphovascular invasion | 4.776 (0.492-46.32) | 0.177 | | |
| Operation time (min.) | 1.006 (0.983-1.029) | 0.612 | | |
| Peroperative blood loss (mL) | 0.999 (0.991-1.006) | 0.704 | | |
| Length of hospitalization | 1.218 (1.062-1.396) | **0.005** | | |
| Cystectomy pT-staging | 1.953 (1.071-3.564) | **0.029** | | |
| Cystectomy pN staging | 4.344 (1.378-13.688) | **0.012** | | |
| Cystectomy lymphovascular Invasion | 15.732 (1.735-142.6) | **0.014** | 9.243 (0.862-99.094) | 0.066 |
| Removed lymph node number | 0.865 (0.691-1.084) | 0.208 | | |
| Number of positive lymph nodes | 2.319 (1.026-5.237) | **0.043** | | |

pT: Pathological tumor, pN: Pathological node, HR: Hazard ratio, CI: Confidence interval

## Discussion

Yin et al. (4) showed an 8% absolute improvement in 5-year survival with NAC. Also, our study found that, following NAC, detecting a pT regression in cystectomy pathology is associated with better DFS and OS.

Our study findings indicate that the cystectomy pT0 and pN0 rate in patients with T regression were significantly higher than those in the other group. Similar findings were observed in the previous study. Møller et al. (6) found that NAC increased pathological downstaging of the tumor and was indirectly associated with OS benefit. Grossman et al. (2) found that pathological downstaging and response was detected in patients who received NAC treatment (21.7%). When our study findings were compared with those in the literature, similar outcomes were observed. NAC prior to RC demonstrated a significant survival benefit. These studies have shown an additional 5% improvement in OS when NAC is administered before RC (7-8). Furthermore, a study reported a 5% increase in OS and a 9% increase in DFS when RC was preceded by platinum-based NAC compared to RC alone (9). Mazza et al. (10) observed 5-year DFS and OS rates of 90% and 86%, respectively, following NAC. Our study findings are that DFS and OS in the T regression group at 5-years are 64.3% and 59.1%, respectively. Compared to the literature, the lower rate of DFS and OS in our study is a result of the delay in RC time.

Some factors may affect the RC time: patient's comorbidities, tumor and surgeon-related factors. The time from the decision to undergo surgery to the actual procedure is a crucial factor. Delaying RC for more than 12 weeks is associated with advanced cancer stage and reduced survival (11-14). Also, our study found that length of hospitalization, smoking status, T2 pathology to RC time, cystectomy pT stage, cystectomy pN stage, and cystectomy lymphovascular invasion were factors affecting DFS in the univariate analysis. On the other hand, multivariate analysis showed that time from T2 pathology to RC was the only independent predictor for DFS. Kulkarni et al. (15) reported a significant increase in mortality risk: a surgical delay of more than 40 days between TUR-BT and RC, and an increased risk of mortality. Additionally, a moderate delay in RC does not compromise patient outcomes. Nielsen et al. (16) found that a moderate delay between the last TUR-BT and RC did not independently impact disease progression or patient survival outcomes. Similarly, Bruins et al. (17) reported that a surgical delay exceeding 3 months had no effect on tumor stage or OS. As a result, our study found that T2 pathology to RC is an important predictor for DFS. On the other hand, our study results show that the time between T2 pathology and RC has no impact on pT regression.

Fleischmann et al. (18) demonstrated the importance of integrating tumor regression grade with TNM classification. The objective of this research was to verify the influence of tumor regression grade, when integrated with TNM classification, on survival rates within an independent patient cohort with MIBC, all of whom underwent NAC and RC.

### Study Limitations

This study was limited by its retrospective design, non-randomized nature, incomplete data on treatment-related side effects, and a relatively small sample size. On the other hand, usage of only one NAC regimen, a homogeneous group, and inclusion of only urothelial carcinoma were the strengths of the study.

## Conclusion

Detection of pT regression in cystectomy pathology after NAC is associated with better DFS and OS. T2 pathology to RC time was an independent predictor of DFS.

### Ethics

**Ethics Committee Approval:** Ethics committee approval, numbered 2025/0081, was secured on 31.07.2025 from İstanbul provincial health directorate, Göztepe Prof. Dr. Süleyman Yalçın City Hospital.

**Informed Consent:** This study retrospective case-control study.

### Acknowledgements

**Publication:** The results of the study were not published in full or in part in form of abstracts.

**Contribution:** There is not any contributors who may not be listed as authors.

### Footnotes

### Authorship Contributions

Surgical and Medical Practices İ.H.Z., Ö.A., Ö.K., M.Ç.Ç., A.Y., Concept: İ.H.Z., Ö.A., Ö.K., M.Ç.Ç., A.Y., Design: Ö.A., Ö.K., M.Ç.Ç., Data Collection or Processing: İ.H.Z., Ö.A., Ö.K., Analysis or Interpretation: İ.H.Z., A.Y., Literature Search: İ.H.Z., Ö.K., M.Ç.Ç., Writing: İ.H.Z., M.Ç.Ç., A.Y.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

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*Original Article*

DOI: 10.4274/uob.galenos.2025.2025.6.2

*Bull Urooncol 2025;24(4):109-116*

# *Predictive Value of the Mayo Adhesive Probability Score for Outcomes in Open and Laparoscopic Partial Nephrectomy*

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## Abstract

**Objective:** The Mayo adhesive probability (MAP) score is used to predict the presence of adherent perinephric fat. The study aimed to assess the impact of MAP score on intra- and postoperative outcomes in partial nephrectomy (PN).
**Materials and Methods:** This retrospective analysis encompassed 130 patients treated with either open or laparoscopic PN. MAP scores were calculated, and their relevance to intra- and postoperative characteristics was evaluated.
**Results:** Cases were seperated into 2 groups according to MAP scores [group 1: MAP score ≤2 (n=86 (66.15%) and group 2: MAP score ≥3 (n=44 (33.85%)]. No significant differences were observed in age, tumor size, body mass index, PN laterality, or radius, exophytic/endophytic, nearness, anterior/posterior location, and preoperative aspects and dimensions used for an anatomical nephrometry scores. Male patients, as well as those with higher American Society of Anesthesiologists scores (≥2) and Charlson comorbidity index (≥4), demonstrated significantly elevated MAP scores ($p<0.001$, $p=0.046$, $p=0.022$). Median operation time was longer [135 (interquartile range (IQR): 120-180) vs 160 (IQR: 140-180) min] in group 2 ($p=0.014$). Although duration of WIT [28 (IQR: 19.5-37.5) vs 33.5 (IQR: 21.75-41.25) min] and intraoperative bleeding [400 (IQR: 200-700) vs 500 (IQR: 200-900) mL] were higher in group 2, no statistically significant difference was observed ($p=0.262$, $p=0.352$). No significant differences were observed regarding intra- and postoperative transfusion requirements or hospital length of stay.
**Conclusion:** Elevated MAP scores are linked to longer operative times, while having a minimal effect on intra- and postoperative complications and outcomes.
**Keywords:** Complications, partial nephrectomy, laparoscopic surgery, renal cell carcinoma

## Introduction

Partial nephrectomy (PN) is commonly selected for managing small renal masses in suitable patients, as it offers notable benefits regarding oncologic control, preservation of renal function, and overall quality of life (1,2). Various nephrometry scoring systems (NSS) are used to assess surgical complexity of PN for many years, such as preoperative aspects and dimensions used for an anatomical (PADUA) and radius, exophytic/endophytic, nearness, anterior/posterior location (RENAL) (3,4). These scoring systems were designed to standardize the measurement of renal tumor size, location, and depth. The scores obtained from these systems aim to provide objective results for decision-making regarding PN and assess the risks of complications. These imaging-based NSS are beneficial in terms of PN complexity, complication risk assessment and functional outcome prediction (4).

Not only tumor-specific but also patient-related factors may influence PN outcomes. Among them, the structure of perinephric adipose tissue plays an important role. Adherent perinephric fat (APF), characterized by tenacious visceral fat situated between Gerota's fascia and the renal parenchyma, has been linked to prolonged operation time (OT), higher intraoperative blood loss, and an increased likelihood of conversion to an open approach (5,6). The Mayo adhesive probability (MAP) score was created to estimate the likelihood of APF by incorporating two radiologic parameters: posterior perinephric fat thickness (PNFT) and the

**Cite this article as:** Özgür G, Çimşit C, Altuntaş T, et al. Predictive value of the mayo adhesive probability score for outcomes in open and laparoscopic partial nephrectomy. Bull Urooncol. 2025;24(4):109-116.

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**Received:** 23.06.2025 **Accepted:** 13.10.2025 **Publication Date:** 24.12.2025

extent of perinephric stranding (PNS) (7). High MAP value was associated with both APF and various intra- and postoperative characteristics in PN (5).

With this study we aimed to assess the potential clinical efficacy of the MAP score in patients who underwent open PN (OPN) or laparoscopic PN (LPN), through identifying factors affecting the MAP score and evaluating intra- and postoperative parameters of PN patients according to their MAP scores.

## Materials and Methods

### Patient Selection and Study Design

This study conducted retrospectively at a single center for participant enrollment. It was performed in accordance with the established protocol and Good Clinical Practice (GCP) guidelines, as outlined in: ICH harmonized tripartite guidelines for GCP (1996) and the Declaration of Helsinki on medical research involving human participants (originally adopted in Helsinki, 1964; amended in Tokyo, 1975; Venice, 1983; Hong Kong, 1989; and Somerset West, 1996). The study was authorized by the Institutional Review Board and approved by the Institutional Ethics Committee of Marmara University (protocol no: 09.2025.25-0149, date: 11.03.2025).

Patients treated with PN for a renal mass between December 2021 and December 2024 were consecutively enrolled in the study. The data of the patients whose abdominal imaging studies were obtained were evaluated retrospectively. PN was performed OPN or LPN. Patient's age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, Charlson comorbidity index were recorded. Tumor characteristics (tumor size, RENAL and PADUA score) detected by imaging methods and results reported in postoperative tumor pathology (T stage, Fuhrman grade, surgical margin, etc.) were collected. In addition, complications, OT, warm ischemia time (WIT), estimated blood loss (EBL) etc. and postoperative characteristics (hospitalization time, transfusion requirement, renal function, etc.) were recorded for statistical analysis.

### Radiologic Evaluation and Image Interpretation

Perinephric fat thickness and PNS grade were assessed using preoperative contrast-enhanced computed tomography (CT) or T1-weighted magnetic resonance imaging (MRI). CT evaluations were performed using a 256-slice scanner (Brilliance ICT-256, Philips Healthcare, Eindhoven, the Netherlands), whereas MRI examinations were obtained with a 3T Philips Ingenia system (Philips Healthcare, Eindhoven, Netherlands). All measurements were taken from axial CT sections at the axial level corresponding to the renal vein side scheduled for PN (7,8). The lateral PNFT was defined as the distance from the renal capsule to the posterolateral abdominal wall measured parallel to the renal vein, while the posterior PNFT was assessed as the straight-line distance from the renal capsule to the posterior abdominal wall (7,8). Perirenal stranding, defined as a linear area of soft tissue density within the perinephric space, was documented for each kidney on MRI or CT scans when present and categorized according to its severity. Stranding was graded according to the MAP Score as 0 (absent), type 1 (mild, thin rim of stranding), or type 2 (severe, diffuse, thick stranding) (7). MAP score was calculated by summing the posterior PNFT and PNS scores (Figure 1).

All patient data were reviewed using two PACS systems (Novapacs, Novarad Corporation, United States of America) by two radiologists with 2 and 27 years of experience, respectively. Each radiologist independently evaluated the imaging studies while blinded to clinical outcomes, and recorded their findings. The data were then cross-checked, and any discrepancies (n=2) were reassessed together to reach a consensus. Subsequent comparisons were made between patients who underwent open versus LPN in terms of measurements and postoperative complications.

### Surgical Technique

All procedures were conducted at a single institution. LPN was carried out through a transperitoneal route using three or four trocars with the patient positioned in lateral decubitus. OPN was performed retroperitoneally in the same position, utilizing a flank incision with a median length of 14 cm (range 12-15 cm). All operations were undertaken by surgeons who had a minimum of ten years of clinical experience in this field. Both LPN and OPN patients, the collecting system was closed if necessary and renorrhaphy was performed. In all patients, hemostatic agent was placed in the surgical field after tumor removal and hemostatic management.

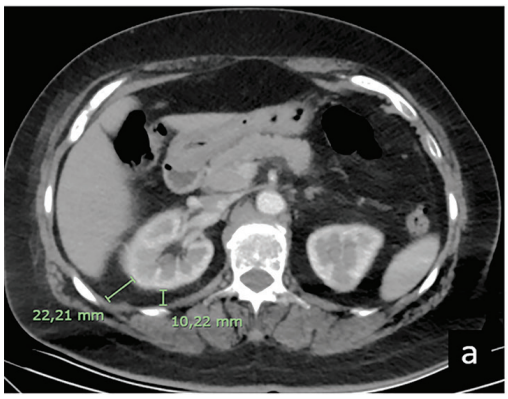
### Statistical Analysis

Statistical analyses were performed using IBM SPSS version 25.0. Normality tests were initially applied to evaluate the distribution of the data. Continuous variables are presented as median, mean, minimum, and maximum values, whereas categorical variables are expressed as counts and percentages. The chi-square test was used for categorical variables. The Mann-Whitney U test was applied to compare the patient and control groups due to non-normal distribution of the data. For normally distributed parameters, the independent samples t-test was utilized. A p-value of $<0.05$ was considered statistically significant.

## Results

The study comprised 130 cases with available CT or MRI images. Among them, 78% (n=101) underwent CT scans, while 22% (n=29) had MRI scans, all of which were retrospectively evaluated. Clear renal cell carcinoma (RCC) was the most frequent pathological subtype identified in the surgical specimens (n=85, 66.2%). Fourteen (11%) patients had chromophobe RCC and 6 (4.7%) had papillary RCC. Nine (7.1%) patients had oncocytoma and 10 (7.9%) had angiomyolipoma. Regarding staging of the tumors, 88 (87.1%) were stage T1, 6 (5.9%) were T2 and 7 (6.9%) were T3. Majority of the patients had Fuhrman grade 1 (12.6%) and Fuhrman grade 2 (66.3%) RCC on pathology. Positive surgical margins were observed in only 2 patients (1.6%).

Demographic, preoperative, and postoperative characteristics of the patients are summarized in Table 1. The mean age was 57.57±12.12 years, with 86 patients (63.2%) being male and 50 (36.8%) female. The median BMI of the patients was




| | | Scoring |
|---|---|---|
| Posterior Perinephric Fat Thickness (PNFT) (mm) | <10 | 0 |
| | 10-19 | 1 |
| | ≥20 | 2 |
| Perinephric Stranding (PNS) (Grade) | None | 0 |
| | Type 1 | 2 |
| | Type 2 | 3 |
| Mayo Adhesive Probability Score = posterior PNFT + PNS | | |

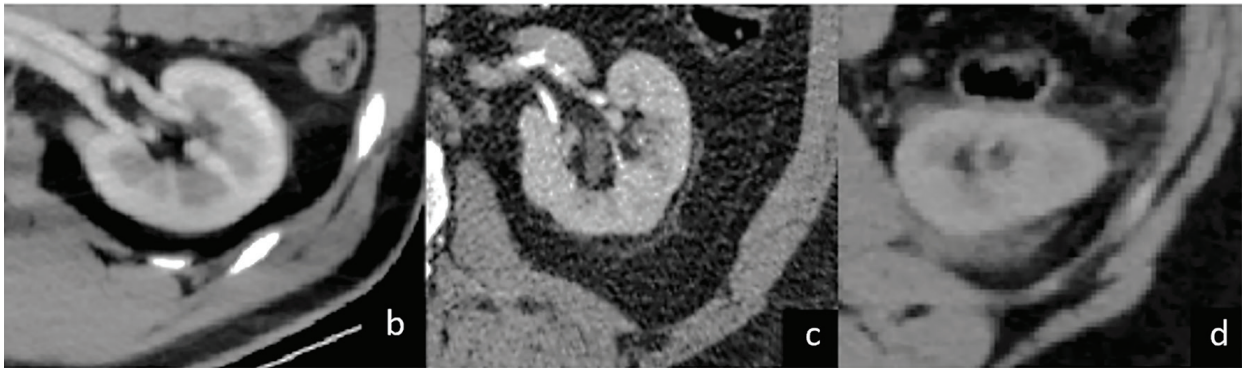



**Figure 1.** The scoring of perinephritic fat thickness and perinephritic stranding

a: Lateral PNFT was measured from the renal capsule to posterolateral abdominal wall in parallel to the renal vein and posterior PNFT was measured from the renal capsule to the posterior abdominal wall as a direct line. Stranding was graded as 0 (b: no stranding), type 1 (c: thin rimlike mild stranding), or type 2 (d: diffuse, thick banded severe stranding). The Mayo adhesion probability (MAP) score was obtained by summing the posterior PNFT and PNS scores

PNFT: Perinephritic fat thickness, PNS: Perinephritic stranding

28.72 [interquartile range (IQR): 25.85-31.135)]. Seventy-three (53.7%) patients underwent right sided PN while 63 (46.3%) underwent left PN. Off-clamp PN was performed for 61 patient. Remaining 69 patients' WIT time was 37 minutes (IQR: 28-42) for laparoscopic cases and 23.5 minutes (IQR: 16.25-33.5) for open cases. Patients had a median ASA score of 2 (IQR: 1-2) and median Charlson comorbidity index of 3 (IQR: 2-4). The median tumor size was 31 mm (IQR: 23-44.75). The median RENAL nephrometry score was 5 (IQR: 4-6), and the median PADUA nephrometry score was 7 (IQR: 6-8). The median OT was 140 (IQR: 120-180) minutes. Median intraoperative EBL was 400 mL (IQR: 200-800) and the median hospital stay was 5 (IQR: 3-6) days. The median measured posterior PNFT was 14 mm (IQR: 9-21) and posterolateral PNFT was 17 mm (IQR: 12-25). Median MAP score was calculated as 2 (IQR: 1-3) in patients whose PNS scores were summed with posterior PNFT.

Patients were divided into group 1 [MAP score ≤2 points, n=86 (66.15%)] and group 2 [MAP score ≥3 points, n=44 (33.85%)] (Table 2). No statistically significant difference was observed in age [(56.43 (±12.26) vs 60.68 (±1.36)], BMI [28.12 (25.4-31.25) vs 29.31 (26.41-31.45)] and PN side [right side 50 (58.1%) vs 21 (47.7%)] (p=0.1, p=0.14, p=0.259 respectively). Tumor size, RENAL and PADUA nephrometry score were similar between the groups (p=0.275, p=0.296, p=0.181 respectively). Male patients [42 (48.8%) vs 39 (88.6%)] had significantly higher MAP scores (p<0.001). Patients in group 2 had a higher ASA score [1 (1-2) vs 2 (1-2)] and higher Charlson comorbidity index confidence interval [3 (2-4) vs 4 (3-5)] (p=0.046, p=0.022, respectively).

Median OT was significantly higher [135 (IQR: 120-180) min vs 160 (IQR: 140-180) min] in group 2 (p=0.014). According to the MAP score, although the duration of WIT [28 (IQR: 19.5-37.5) vs 33.5 (IQR: 21.75-41.25) min] and the intraoperative EBL [400 (IQR: 200-700) vs. 500 (IQR: 200-900) mL] were higher in group 2 patients, no statistically significant difference was observed (p=0.262, p=0.352 respectively). There was no difference between group 1 and 2 in terms of peri- and postoperative transfusion requirements and length of hospital stay (p=0.906, p=0.876, p=0.533 respectively). Effect size analysis showed a small but significant effect size for OT (r=0.216), while other parameters (WIT: r=-0.151, EBL: r=-0.083, hospital stay: r=-0.055) demonstrated negligible effects without statistical significance (Figure 2).

Fifty-four of the patients (41.54%) underwent LPN and 76 (58.46%) underwent OPN. Patients who underwent OPN and LPN were evaluated separately according to MAP score and their surgical characteristics are shown in Table 3. In OPN patients, OT was significantly longer in those with higher MAP scores (p=0.013). Although OT was also higher in LPN patients with elevated MAP scores, the difference was not statistically significant (p=0.275). WIT and EBL tended to be higher in both OPN and LPN patients with MAP scores ≥3, but these differences

| Table 1. Demographic, preoperative and postoperative characteristics of patients | | |
|---|---|---|
| | | PN patients (n=130) |
| Age (year) mean ± SD | | 57.57±12.12 |
| BMI (kg/m$^2$) median (IQR) | | 28.72 (25.85-31.135) |
| PN side n (%) | Right | 73 (53.7) |
| | Left | 63 (46.3) |
| Gender n (%) | Male | 86 (63.2) |
| | Female | 50 (36.8) |
| Surgery type n (%) | Laparoscopic | 54 (41.54) |
| | Open | 76 (58.46) |
| ASA score median (IQR) | | 2 (1-2) |
| Charlson comorbidity index median (IQR) | | 3 (2-4) |
| Tumor size (mm) median (IQR) | | 31 (23-44.75) |
| RENAL score median (IQR) | | 5 (4-6) |
| PADUA score median (IQR) | | 7 (6-8) |
| Operation time (min) median (IQR) | | 140 (120-180) |
| WIT median (IQR) | | 30 (19.25-38.75) |
| Perioperative bleeding amount (mL) median (IQR) | | 400 (200-800) |
| Perioperative transfusion requirement n (%) | | 21 (15.4) |
| Postoperative transfusion requirement (n) % | | 17 (12.5) |
| Number of hospitalization day median (IQR) | | 5 (3-6) |
| Posterior PNFT median (IQR) | | 14 (9-21) |
| Posterolateral PNFT median (IQR) | | 17 (12-25) |
| Posterior PNFT score n (%) | <10 mm | 33 (25.2) |
| | 10-19 mm | 61 (46.6) |
| | >20 mm | 37 (28.2) |
| PNS (n) % | No | 80 (61.1) |
| | Type 1 | 49 (37.4) |
| | Type 2 | 2 (1.5) |
| MAP score median (IQR) | | 2 (1-3) |

BMI: Body mass index, PN: Partial nephrectomy, RENAL: Radius, Exophtic/endophtic, nearest, anterior/posterior, location, PADUA: Preoperative aspects and dimensions used for an anatomical, ASA: American Society of Anaesthesiologists, WIT: Warm ischemia time, PNFT: Perinephric fat thickness, PNS: Perinephric stranding, MAP: Mayo adhesive probability, IQR: Interquartile range, SD: Standard deviation

did not reach statistical significance (p>0.05). No significant differences were observed in peri- or postoperative transfusion requirements or hospital length of stay.

## Discussion

PN is the preferred approach for T1 renal tumors and may also be appropriate for certain larger tumors if technically achievable (1). Both laparoscopic and OPN are commonly used for appropriate renal masses, with comparable functional and oncologic outcomes (9). In our study, tumor features, surgical parameters, and pathological outcomes were consistent with previous reports (9,10). The majority of our patients were male (11,12). The most tumors were classified as T1a or T1b (87.6%). Additionally, the majority of lesions were Fuhrman grade 1 or 2, in line with similar cohorts (12-14). OT and WIT in our study were also comparable to previously published data, where OT typically approaches 2 hours and WIT remains below 30 minutes (5,14).

There are some imaging-based nephrometry scores (RENAL, PADUA) used to assess PN complexity, which usually include anatomical information such as tumor size, tumor location, and tumor depth. However, patient-related characteristics such as APF, PNFT, PNS have also been reported to affect some intraoperative and postoperative outcomes (6,15). The clinical significance of various measurements obtained from imaging methods such as PNFT and PNS has been evaluated in various studies (8). There was a correlation in the posterior and posterolateral measurements of PNFT (8). We measured not only posterior PNFT but also posterolateral PNFT in our study to evaluate this relation. Posterolateral PNFT measurement had similar clinical features as the posterior PFNT. MAP score was found to be consistent with both posterior PNFT and posterolateral PNFT in our study (16).

Davidiuk et al. (7) employed the MAP score, which combines posterior PNFT and PNS, to anticipate the occurrence of APF in patients. The MAP score is linked to APF and various operative characteristics (6,7,17). Perirenal adipose tissue was found to be thicker in men compared to women (8). Therefore, as supported by our study, MAP score ≥3 was significantly more frequently observed in men (16,18). Studies have reported that older age and high BMI are also associated with high MAP score (7,16,18). However, there may be a weak relationship between BMI and perirenal fat (8). In our study, although patients in group 2 were older and had higher BMI compared with group 1, these differences were not statistically significant. Nonetheless, despite the lack of statistical significance, these trends may still be clinically relevant, as increased age and BMI could potentially complicate perioperative management and surgical planning.

Hypertension and diabetes may be considered as risk factors for high APF and MAP scores (6,16). When patient comorbidities are considered, MAP score was higher in our patients with high ASA score and high Charlson comorbidity index. However, tumor-related factors do not seem to be correlated with the MAP score. There was no apparent relation between tumor size, stage, grade, pathology (benign or malignant) or histology of the malignancy and MAP score (16,18). In the present study, according to the MAP scores, there was no difference in tumor size, tumor pathology, PADUA and RENAL nephrometry scores between the groups.

Several studies have explored the association between APF and high MAP scores, suggesting that a higher MAP score may serve as a predictor of APF and influence surgical decision-making, particularly the choice between open and robotic approaches. For example, Walach et al. (18) found that patients with MAP scores ≥3 had a higher likelihood of undergo OPN (53%), while those with MAP scores ≤2 were more commonly treated with robotic surgery (58%). While a high MAP score has been suggested to affect the selection of surgical approach, our analysis found no significant difference in MAP scores between cases undergoing open versus LPN (18).

| Table 2. Comparison of Patients based on the Mayo adhesive probability score | | | | |
|---|---|---|---|---|
| | | **Group 1 (MAP score ≤2) n=86 (66.15%)** | **Group 2 (MAP score ≥3) n=44 (33.85%)** | **p-value** |
| **Age (year) mean ± SD** | | 56.43±12.26 | 60.68±11.36 | 0.1 |
| **BMI (kg/m²) median (IQR)** | | 28.12 (25.4-31.25) | 29.31 (26.41-31.45) | 0.14 |
| **PN Side n (%)** | **Right** | 50 (58.1) | 21 (47.7) | 0.259 |
| | **Left** | 36 (41.9) | 23 (52.3) | |
| **Sex n (%)** | **Male** | 42 (48.8) | 39 (88.6) | **<0.001** |
| | **Female** | 44 (51.2) | 5 (11.4) | |
| **Surgery type n (%)** | **Laparoscopic** | 37(43) | 17(38.6) | 0.631 |
| | **Open** | 49 (57) | 27 (61.4) | |
| **ASA score median (IQR)** | | 1 (1-2) | 2 (1-2) | **0.046** |
| **Charlson comorbidity index median (IQR)** | | 3 (2-4) | 4 (3-5) | **0.022** |
| **Tumor size (mm) median (IQR)** | | 30 (23-41.25) | 35.5 (22.5-64.25) | 0.275 |
| **RENAL score median (IQR)** | | 5 (4-6) | 5 (4-6) | 0.296 |
| **PADUA score median (IQR)** | | 7 (6-8) | 7 (6-8) | 0.181 |
| **Operation time (min) median (IQR)** | | 135 (120-180) | 160 (140-180) | **0.014** |
| **WIT median (IQR)** | | 28 (19.5-37.5) | 31.5 (21.75-41.25) | 0.262 |
| **Peroperative EBL (mL) median (IQR)** | | 400 (200-700) | 500 (200-900) | 0.352 |
| **Perioperative transfusion requirement n (%)** | | 13 (15.1) | 7 (15.9) | 0.906 |
| **Postioperative transfusion requirement (n) %** | | 9 (10.5) | 5 (11.5) | 0.876 |
| **Number of hospitalization day, days median (IQR)** | | 5 (3.25-6) | 5 (3-6) | 0.533 |
| **Posterior PNFT, mm median (IQR)** | | 11 (7-17) | 19 (14-24.75) | **<0.001** |
| **Posterolateral PNFT, mm median (IQR)** | | 15 (9.75-20) | 23 (19-30.75) | **<0.001** |
| **Posterior PNFT score n (%)** | **<10 mm** | 32 (37.2) | 1 (2.3) | **<0.001** |
| | **10-19 mm** | 38 (44.2) | 22 (50) | |
| | **>20 mm** | 16 (18.6) | 21 (56.8) | |
| **PNS (n) %** | **No** | 79 (91.9) | 0 | **<0.001** |
| | **Type 1** | 7 (8.1) | 42 (95.5) | |
| | **Type 2** | 0 | 2 (4.5) | |

BMI: Body mass index, PN: Partial nephrectomy, RENAL: Radius, exophtic/endophtic, nearest, anterior/posterior, location, PADUA: Preoperative aspects and dimensions used for an anatomical, ASA: American Society of Anaesthesiologists Score, WIT: Warm ischemia time, PNFT: Perinephric fat thickness, PNS: Perinephric stranding, MAP: Mayo adhesive probability score, EBL: Estimated blood loss, IQR: Interquartile range, SD: Standard deviation

Patients with high MAP scores have a statistically significant higher OT regardless of surgical technique (11-13,17,18). In our study, OT was significantly longer in group 2 compared with group 1 across all cases. When subgroup analyses were performed according to type of surgery, in patients who underwent LPN, although OT was higher in MAP score ≥3 patients, no significant differences were observed between the groups. Still, this finding may carry clinical relevance, as even modest increases in operative time can impact perioperative risk, anesthesia duration, and resource utilization. However, in patients who underwent OPN, the OT was again significantly high in MAP score ≥3 patients when compared with patients in MAP score ≤2 patients. Yao et al. (12) reported that increased dissection time due to APF prolonged the operation duration in LPN patients with high MAP score, but did not change the WIT time due to renal artery clamping after perirenal fat removal. APF occurrence may be linked to higher MAP scores and prolonged WIT (19). Patients with a MAP score ≥3 exhibited longer WIT in the OPN, LPN, and overall patient groups. However, consistent with previous studies, no significant differences in WIT were observed between groups based on MAP scores (12,18).

Elevated APF and MAP scores are linked to a greater risk of complications and perioperative bleeding (6,13). High MAP scores were associated with increased EBL across all surgical approaches, including open, laparoscopic, and robotic PN (6,12,17). EBL is found to be higher in patients with MAP score ≥3 (18). In our study, peroperative EBL was higher in OPN, LPN patients with MAP score ≥3, but no statistically significant difference was observed. Davidiuk et al. (20) suggested that while APF may lead to slightly longer OT, it does not appear to significantly impact clinically relevant outcomes such as complication rates, transfusion requirements, or length of

| Table 3. Operation characteristics of open and laparoscopic partial nephrectomy patients according to mayo adhesive probability score | | | |
|---|---|---|---|
| **Open PN patients (n=76)** | **MAP score ≤2 n=49 (64.5%)** | **MAP score ≥3 n=27 (35.5%)** | **p-value** |
| **Operation time (min) median (IQR)** | 130 (120-175) | 160 (140-180) | **0.013** |
| **WIT median (IQR)** | 24 (17-34) | 32.5 (15.75-34.75) | 0.632 |
| **Peroperative EBL (mL) median (IQR)** | 550 (300-850) | 750 (475-1075) | 0.114 |
| **Peroperative transfusion requirement n (%)** | 10 (20.4%) | 6 (22.2%) | 0.853 |
| **Postoperative transfusion requirement (n) %** | 8 (16.3%) | 4 (14.8%) | 0.863 |
| **Number of hospitalization day median (IQR)** | 5 (4-7) | 6 (4-9.25) | 0.38 |
| **Laparoscopic PN patients (n=54)** | **MAP score ≤2 n=37 (68.5%)** | **MAP score ≥3 n=17 (31.5%)** | **p-value** |
| **Operation time (min) median (IQR)** | 140 (112.5-180) | 150 (126-197.5) | 0.275 |
| **WIT median (IQR)** | 30 (26.2-39.25) | 42,5 (30.5-53.5) | 0.116 |
| **Perioperative EBL (mL) median (IQR)** | 125 (100-300) | 225 (150-300) | 0.176 |
| **Perioperative transfusion requirement n (%)** | 1 (5.9%) | 3 (8.1%) | 0.772 |
| **Postoperative transfusion requirement (n) %** | 1 (2.7%) | 1 (5.9%) | 0.566 |
| **Number of hospitalization day median (IQR)** | 5 (3-5) | 4 (3-6) | 0.798 |
| PN: Partial nephrectomy, WIT: Warm ischemia time, EBL: Estimated blood loss, MAP: Mayo adhesive probability, IQR: Interquartile range | | | |

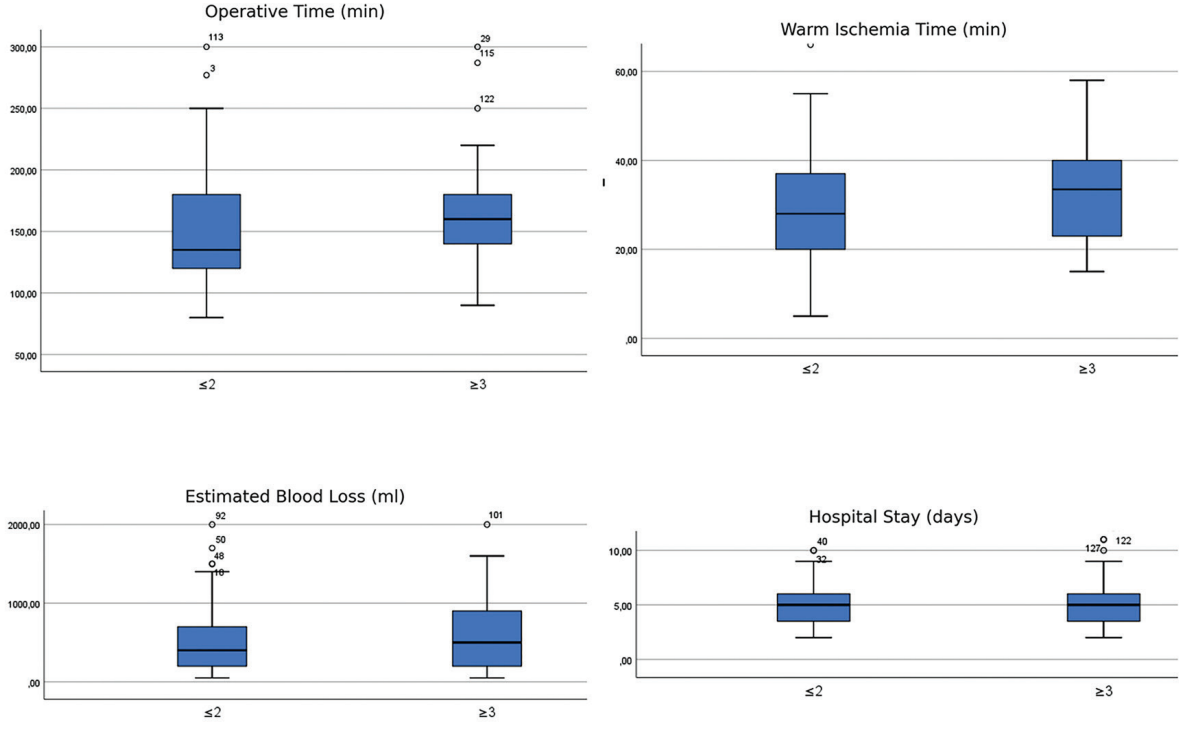



**Figure 2.** Comparison of surgical outcomes by MAP score group

Box plots show the operation time (OT), warm ischemia time (WIT), estimated blood loss (EBL), and length of hospital stay according to MAP score groups (≤2 and ≥3). Patients with higher MAP scores (≥3) had significantly longer OT (p=0.014). WIT and EBL showed higher median values in the MAP ≥3 group without a statistically significant difference (p=0.262 and p=0.352 respectively). Hospital stay was similar between groups (p=0.533)

MAP: Mayo adhesion probability

hospital stay hence, its effect is considered clinically insignificant. Fang et al. (19) reported that while APF may prolong operative time and increase EBL, it did not significantly affect the choice of surgical approach, transfusion rates, complication rates, or postoperative length of stay. Patients with a MAP score ≥3 showed marginally higher peri- and postoperative blood transfusion needs; however, no significant differences were observed between the groups. Hospital length of stay was also comparable.

Although parameters such as OT and EBL were not statistically significant, the trends observed in patients with higher MAP scores may still be clinically relevant. Factors such as sample size could have influenced statistical significance. Even modest increases in OT, WIT, or EBL can be clinically important, particularly in patients with comorbidities or reduced renal reserve. Therefore, the MAP score may serve as a practical preoperative warning tool, helping surgeons anticipate potential challenges and allocate resources accordingly.

### Study Limitations

Several limitations should be considered in interpreting the findings of this study. First, its retrospective design restricts the ability to draw causal conclusions and may introduce selection bias. Second, the relatively small sample size could have limited the statistical power to detect certain differences, particularly in postoperative outcomes. Moreover, intraoperative documentation of APF was not consistently recorded in operative reports, which constrains our capacity to validate the predictive utility of MAP scoring under real-time surgical conditions.

Despite these limitations, our results add to the expanding evidence on the utility of the MAP score in renal surgery. While higher MAP scores were associated with longer OT, they were not linked to an increased risk of intra- or postoperative complications. As such, although the MAP score may offer helpful preoperative information, it should not be the sole determinant guiding the surgical approach (open vs. laparoscopic) or the extent of resection (partial vs. radical). Rather, surgical decision-making should remain individualized, relying on a combination of imaging findings, tumor characteristics, and—importantly—the experience and judgment of the surgeon.

## Conclusion

Elevated MAP score calculated from PNFT and PNS was linked to certain intra- and postoperative outcomes in both open and LPN. Male patients, patients with high ASA score (≥2) and high Charlson comorbidity index (≥4) had significantly higher MAP scores. Patients with higher MAP scores experienced significantly longer OTs. Although the WIT and the intraoperative EBL were higher, no significant difference was observed. No significant differences were observed in peri- and postoperative transfusion requirements or hospital length of stay. In conclusion, our findings suggest an association between high MAP score and prolonged OT, while its effect on intraoperative and postoperative complications and outcomes appears limited.

### Ethics

**Ethics Committee Approval:** The study was authorized by the Institutional Review Board and approved by the Institutional Ethics Committee of Marmara University (protocol no: 09.2025.25-0149, date: 11.03.2025).

**Informed Consent:** Retrospective study.

### Acknowledgements

**Publication:** The results of the study were not published in full or in part in form of abstracts.

**Contribution:** There is not any contributors who may not be listed as authors.

### Footnotes

#### Authorship Contributions

Surgical and Medical Practices: G.Ö., Y.Ş., M.K., İ.T., T.E.Ş., Concept: G.Ö., T.A., M.Y.S., Y.Ş., T.E.Ş., Design: G.Ö., C.Ç., M.K., T.E.Ş., Data Collection or Processing: G.Ö., C.Ç., İ.B.A., M.Y.S., Analysis or Interpretation: G.Ö., T.A., M.Y.S., Literature Search: G.Ö., C.Ç., T.E.Ş., Writing: G.Ö., C.Ç., T.A., T.E.Ş.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

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*Case Report*

DOI: 10.4274/uob.galenos.2025.2025.3.4

*Bull Urooncol 2025;24(4):117-120*

# *A Rare Complication of Testicular Lymphoma: Fournier's Gangrene*

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**Abstract**

Testicular neoplasms represent an uncommon subset of urogenital malignancies, with lymphomatous involvement being an even more infrequent clinical presentation. Fournier's gangrene, a fulminant necrotizing fasciitis affecting the perineal region, is characterized by a polymicrobial pathogenesis. The therapeutic management of this condition is predicated upon three critical interventional strategies: Expeditious and comprehensive surgical debridement, targeted antimicrobial pharmacotherapy, and robust hemodynamic stabilization.We report a rare case of recurrent testicular diffuse large B-cell lymphoma in an 85-year-old diabetic man complicated by Fournier's gangrene, a severe infectious complication.
**Keywords:** DLBCL, Fournier's gangrene, necrotizing fasciitis, testicular lymphoma, testicular tumor

## Introduction

Testicular cancer is one of the rare malignancies of the male urogenital system and is typically diagnosed in younger age groups. However, it can also be encountered in elderly men, in whom it tends to follow a more aggressive course (1). The pathophysiology, histological subtypes, and prognosis of testicular cancers observed in elderly patients may differ from those in younger individuals. One such cancer is testicular lymphoma, which although rare, is the most common testicular malignancy in elderly men (2,3). The spread of local necrosis and infection to the perineal tissues can lead to Fournier's gangrene (FG), a severe and life-threatening condition (4). FG is a life-threatening, polymicrobial, necrotizing soft-tissue infection most commonly observed in men aged 60-70 years. It is characterized by a foul odor and primarily affects the perineum (5). On the other hand, these patients often have comorbidities such as diabetes mellitus, but the number of patients with hematological malignancies and FG is very low (6).

In this case report, we present a patient who underwent right inguinal orchiectomy for a mass in the right testis and subsequently developed a recurrent mass in the right hemiscrotum two years later. Necrosis of this mass, followed by infection, resulted in FG. The case is discussed with respect to patient management, surgical and medical approaches, and complications, with the aim of contributing to the diagnostic and therapeutic process for this rare clinical condition.

## Case Reports

An 85-year-old male patient presented to the emergency department with systemic symptoms, including fatigue and fever, and a scrotal neoplastic mass. The patient's comprehensive medical history revealed a seven-year history of type 2 diabetes mellitus and a coronary artery bypass grafting procedure performed eight years earlier. His clinical profile indicated impaired self-management and a significant history of tobacco and alcohol use. Notably, the patient had undergone a right-sided inguinal orchiectomy two years prior, with histopathological examination confirming a diagnosis of diffuse large B-cell lymphoma (DLBCL). The initial surgical intervention demonstrated negative resection margins. However, the patient subsequently discontinued the recommended chemotherapeutic intervention. At the current medical evaluation, the patient's overall clinical status remained relatively stable, with a Glasgow coma scale score of 15, indicating full neurological responsiveness. Of particular clinical significance was the patient's report of a mass in the right hemiscrotum that had progressively enlarged over six months.

**Cite this article as:** Turhan A, Arıcı C, Çayan S. A rare complication of testicular lymphoma: Fournier's gangrene. Bull Urooncol. 2025;24(4):117-120.

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**Received:** 28.03.2025 **Accepted:** 20.07.2025 **Publication Date:** 24.12.2025

On physical examination, the patient was tachycardic, tachypneic, and normotensive (127/55 mmHg), with a subfebrile temperature (37.6 °C) and oxygen saturation of 97%. A purulent, foul-smelling persisting for two days was observed in the scrotal region. The scrotal skin exhibited hyperpigmentation with dry, black, necrotic desquamation. A mass was identified in the right hemiscrotum (Figure 1). Upon palpation, the mass was found to be fixed to the skin of the right hemiscrotum and exhibited crepitus. The left testis was palpated and found to be adherent to the mass. The proximal parts of the penis and urethra were not palpable, while the distal parts appeared normal. The anoscrotal region was also unremarkable. A 3×2 cm right inguinal lymph node was palpated.

Laboratory test results obtained in the emergency department are summarized in (Table 1). Tumor markers were negative. Abdominopelvic computed tomography revealed a 12×10 cm scrotal mass filling the right hemiscrotum, displacing the corpus cavernosum and urethra to the left. Pockets of air were observed within the mass, and an enlarged right inguinal lymph node was noted.

The clinical management protocol was initiated with empirical antibacterial therapy comprising a synergistic combination of broad-spectrum antibacterial agents (meropenem and teicoplanin). Concurrently, urgent surgical debridement was performed to address the infection and mitigate potential systemic complications. During the procedure, both a urethral catheter and a cystostomy catheter were placed. Scrotal exploration revealed that the mass was partially necrotic and infected, and a tissue culture was obtained. Right hemiscrotectomy and left orchiectomy were performed while the urethra was preserved

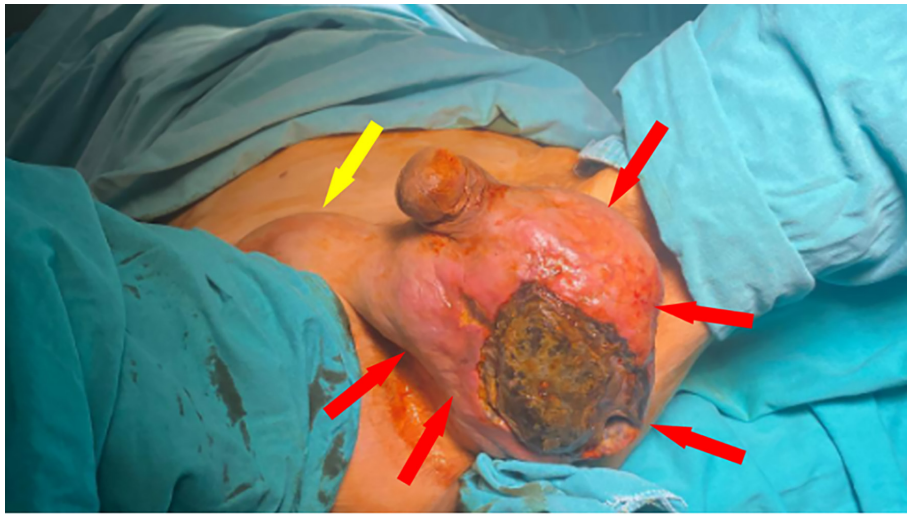

**Figure 1.** Preoperative image of the patient's testicular mass; the red arrow indicates the right hemiscrotal mass, and the yellow arrow indicates the right inguinal lymph node

**Table 1. Blood laboratory results**

| Parameter | Value | Reference range | Unit |
|---|---|---|---|
| Sodium (Na) | 135 | 135-145 | mEq/L |
| C-reactive protein (CRP) | 93.3 | 0-5 | mg/L |
| Creatinine | 1.18 | 0.6-1.2 | mg/dL |
| Fasting blood glucose | 360 | 70-100 | mg/dL |
| Hemoglobin (HGB) | 10.4 | 13.5-17.5 (male), 12.0-15.5 (female) | g/dL |
| White blood cells (WBC) | 10.31 | 4.5-11.0 | $\times 10^3/\mu L$ |
| Hematocrit (HCT) | 31 | 41-50 (male), 36-44 (female) | % |
| Lymphocytes (LYMPH) | 0.86 | 1.0-4.8 | $\times 10^3/\mu L$ |
| Monocytes (MONO) | 0.22 | 0.1-0.6 | $\times 10^3/\mu L$ |
| Neutrophils (NEUT) | 9.19 | 2.0-7.5 | $\times 10^3/\mu L$ |
| Eosinophils (EO) | 0.01 | 0.0-0.5 | $\times 10^3/\mu L$ |
| Platelets (PLT) | 264 | 150-450 | $\times 10^3/\mu L$ |
| Hemoglobin A1c (HbA1c) | 6.9 | <5.7 (normal), 5.7-6.4 (prediabetes), ≥6.5 (diabetes) | % |

Significantly elevated C-reactive protein levels suggest active inflammation. Severely elevated blood glucose levels indicate poor diabetes control. Low hemoglobin and hematocrit indicate anemia. Slightly elevated neutrophils may indicate infection or inflammation. Hemoglobin A1c is in the prediabetes/diabetes range
**Note:** Reference ranges can vary slightly between laboratories and may differ based on age, sex, and other individual factors. Always consult a healthcare professional for proper interpretation

with a catheter (Figure 2). To maintain urethral perfusion, the urethral catheter was removed postoperatively. Wound care was provided. The inguinal lymph node was left untreated.

Histopathological examination of the specimen confirmed. The tumor had infiltrated the testicular parenchyma, surrounding soft tissue, and scrotal structures, invading the rete testis, hilum, epididymis, and tunica. The surgical margins were intact, and no lymphovascular invasion was detected. Tissue cultures revealed growth of *Staphylococcus* and *Enterococcus* species.

In the postoperative period, daily wound care was performed, and no additional surgical debridement was required. After ten days follow-up, the patient was referred to plastic surgery for further management. The surgical site was left to heal by secondary intention. Systemic chemotherapy was planned following histopathological confirmation of DLBCL; however, it could not be initiated due to the patient's unexpected death in a traffic accident two months after the operation.

This patient was treated according to standard urology protocol. The surgery was performed after obtaining the required written informed consent. As the patient's identity remained undisclosed, consent for publication was also obtained. Following the patient's death, additional consent for publication of all clinical information and images was explicitly obtained from the patient's next of kin/family.

## Discussion

Testicular cancer is among the rare malignancies of the urogenital system in men and is typically diagnosed in younger age groups. However, it can also occur in elderly men, in whom it tends to follow a more aggressive course (1). The pathophysiology, histological subtypes, and prognosis of testicular cancer in elderly patients may differ from those in younger individuals. While the distribution of seminomatous and non-seminomatous tumors may vary, elderly individuals have been reported to exhibit higher rates of metastatic spread (4). Additionally, although rare, testicular lymphoma is the most common testicular malignancy in elderly men. This disease typically manifests as the DLBCL subtype and accounts for approximately 5-7% of testicular malignancies in the elderly population (2,3). Patients with primary testicular lymphoma have a high risk of metastasis, with frequent spread to the central nervous system, contralateral testis, and lymph nodes (1,4). The local necrosis and infection of these masses can extend to the perineal tissues, leading to FG, a severe and life-threatening condition (4).

FG is a life-threatening necrotizing soft tissue infection, usually of polymicrobial etiology, that primarily affects the perineal region. In male patients, scrotal involvement is common, while testicular involvement is relatively rare. Anatomically, testicular blood flow originates directly from the aorta, whereas perineal blood flow is supplied by the pudendal artery. The infection typically spreads through Colles' fascia (superficial perineal fascia), extending into Buck's and dartos fasciae, allowing further progression into the scrotal and penile tissues (5). In the pathogenesis of FG, dermatological defects in the perineal, anal, or urogenital regions typically play a significant role, while idiopathic cases are less frequently encountered (7).

The necrotizing process in FG involves complex pathological mechanisms characterized by the infiltration of polymorphonuclear cells and fibrinoid coagulation within the feeding arterioles, occurring in the presence of multiple microorganisms (8). Epidemiologically, FG predominantly affects men and is rarely reported in women and the pediatric population (9). The average age at diagnosis is 60-70 years, and these patients often have comorbid conditions (10).

Clinically, severe genital pain, rapidly progressive cellulitis, and signs of systemic toxicity are characteristic (5,7). Prodromal symptoms such as fever and lethargy may appear up to seven days before the onset of perineal edema and severe pain. As the disease progresses, affected genital skin tissue may exhibit darkening, purulent discharge, and subcutaneous crepitus, while pain may decrease due to necrosis of nerve tissue. Despite the presence of a characteristic foul odor, cutaneous manifestations may not fully reflect the severity of the underlying tissue damage. To prevent the rapid progression of the infection, urgent and aggressive surgical debridement of all necrotic tissue, hemodynamic stabilization, and initiation of broad-

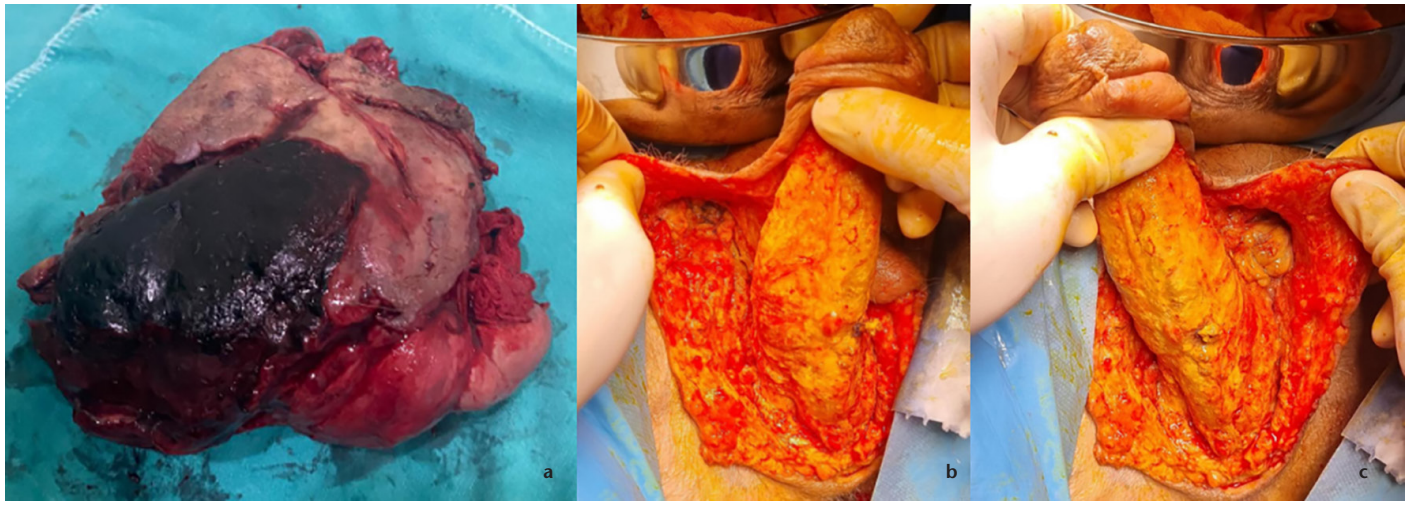


**Figure 2.** Postoperative excised testicular mass and surgical site; **a)** Excised testicular mass; **b)** Post-excision view of the right side of the scrotum and penis; **c)** Post-excision view of the left side of the scrotum and penis

spectrum prophylactic antibiotic therapy are crucial (5). Despite advancements in modern medical approaches, mortality rates associated with FG have remained relatively stable over the past 25 years, with recent epidemiological studies reporting rates between 7.5% and 19.8% (10).

Only a few cases reporting the coexistence of B-cell lymphoma and FG have been described. To date, 44 cases of FG associated with oncohematological malignancies have been described (6), with DLBCL identified in only four. In most cases, FG developed as a complication of an existing hematologic malignancy, due to neutropenia (11,12) or post-biopsy infection (13), or it was diagnosed incidentally during surgery (14). Uniquely, our patient developed FG due to necrosis of a scrotal mass. Unlike previous reports, FG in our case resulted from direct tumor necrosis rather than from immunosuppression or invasive procedures, highlighting the importance of considering lymphoproliferative disorders in patients presenting with scrotal FG.

Primary testicular lymphoma is a malignancy with a substantial risk of recurrence. In cases of relapse, chemotherapy and radiotherapy are the recommended therapeutic modalities (2). However, lymph node dissection and excision of recurrent masses are generally not preferred interventions. Consequently, in our case, the infected mass was surgically excised. Following FG management, the patient was scheduled for oncological follow-up and monitoring, but he died.

## Conclusion

Testicular masses may result in severe infectious complications, such as FG. Timely and appropriate recognition and management of infectious complications are paramount, as are the comprehensive evaluation and treatment of the underlying pathological condition.

### Ethics

**Informed Consent:** This patient was treated according to standard urology protocol. The surgery was performed after obtaining the required written informed consent. As the patient's identity remained undisclosed, consent for publication was also obtained. Following the patient's death, additional consent for publication of all clinical information and images was explicitly obtained from the patient's next of kin/family.

### Acknowledgements

**Publication:** The results of the study were not published in full or in part in form of abstracts.

**Contribution:** There is not any contributors who may not be listed as authors.

### Footnotes

### Authorship Contributions

Surgical and Medical Practices: S.Ç., Concept: A.T., C.A., S.Ç., Desing: A.T., C.A., S.Ç., Data Collection or Processing: A.T., C.A., S.Ç., Literature Search: A.T., C.A., S.Ç., Writing: A.T., C.A., S.Ç.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

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İsmail Önder Yılmaz
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Özer Ural Çakıcı
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