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The utility of radiopharmaceutical uptake in the bladder neck and prostate on preoperative FDG PET/CT in determining urethral surgical margin positivity in patients undergoing radical cystoprostatectomy for bladder cancer

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Abstract

Background Bladder cancer is the most common malignancy of the urinary system. It is a heterogeneous type of cancer with a high potential for metastasis, approximately 25% of which occurs as muscle invasive. As with other malignancies, accurate and precise staging of bladder cancer is one of the mainstays for choosing the most appropriate treatment for the patient. Detection of metastasis is extremely important in choosing the treatment strategy. FDG PET/CT is widely used in the clinical management of various malignancies and is increasingly used in the primary staging of muscle-invasive bladder cancer and detection of recurrence after radical cystectomy. We aimed to determine the role of radiopharmaceutical uptake in the bladder neck and prostate region in preoperative FDG PET/CT in patients with muscle-invasive bladder tumors in determining the positivity of prostatic urethra surgical margins in the final pathology after cystectomy and its effect in determining the type of diversion to be chosen.

Methods The data of male patients who underwent FDG PET/CT before radical cystectomy due to MIBC between January 2009 and January 2023 in the Department of Urology at Istanbul Faculty of Medicine were retrospectively analyzed. The correlations between the presence of radiopharmaceutical uptake in the bladder neck or prostate in FDG PET CT and the positivity of the prostatic urethra surgical margin in the postoperative final pathology of these patients and the invasion of urothelial carcinoma in the prostate were analyzed.

Results Prostatic urethra surgical margin positivity was detected in 8 of 50 male patients who had FDG PET CT in the preoperative period. Prostatic urethra surgical margin positivity was detected in 5 of 19 patients with bladder neck and prostate region involvement on FDG ($p=0.2554$). Prostate involvement was seen on FDG in 6 of 9 patients

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with urothelial carcinoma invasion into the prostate ($p=0.1492$). Prostate adenocarcinoma was observed in the final pathology of 12 patients, and 8 of these patients had FDG uptake ($p=0.106$). While no statistically significant relationship was found between the presence of bladder neck and prostate region involvement on FDG and prostatic urethra surgical margin, urothelial carcinoma invasion into the prostate and prostate adenocarcinoma, a statistically significant relationship was observed between the presence of malignancy in the prostate (urothelial carcinoma and/or adenocarcinoma) ($p=0.0189$).

Conclusions While no statistically significant relationship was found between radiopharmaceutical uptake in the bladder neck and prostate region on preoperative FDG PET CT in CIBC and prostatic urethra surgical margin positivity, urothelial carcinoma invasion into the prostate and the presence of prostate adenocarcinoma; It was found valuable in detecting the presence of malignancy in the prostate (adenocarcinoma/urothelial carcinoma).

Keywords Muscle-invasive bladder cancer (MIBC), FDG PET/CT, Bladder neck and prostate uptake, Prostatic urethral surgical margin, Urothelial carcinoma invasion, Radical cystoprostatectomy

Background

Bladder cancer is the most common malignancy of the urinary system. It is a heterogeneous type of cancer with a high potential for metastasis, with approximately 25% of cases occurring as muscle invasive. As with other malignancies, accurate and precise staging of bladder cancer is one of the fundamental bases for selecting the most appropriate treatment for the patient. Detection of metastasis is extremely important in determining the treatment strategy.

It is known that bladder tumors can involve the prostatic urethra and ducts in men. Primary transitional cell carcinoma (TCC) of the prostate is rare, while the incidence of secondary transitional cell carcinoma of the prostate and prostate is higher, with a reported incidence of 12%–48% [1]. Bladder tumors can spread to the prostatic urethra, prostatic ducts, and prostate stroma in two different ways: extravesical and intraurethral. Preoperative transurethral loop biopsies from the prostatic urethra have been used to detect urothelial carcinoma in the prostatic urethra. However, the diagnostic value of such biopsies is controversial; one study reported only a 53% sensitivity for prostatic stromal invasion [2]. Since transurethral loop biopsies sample only the prostatic urethral mucosa and/or prostate tissue close to the urethral lumen, they may lead to the possibility of missing urothelial carcinoma invasion in deeper prostate tissue.

F-18 fluoro-2-deoxy-glucose positron emission tomography (FDG PET/CT) is widely used in the clinical management of various malignancies and is increasingly being used in the primary staging of muscle-invasive bladder cancer and in the detection of recurrence after radical cystectomy.

It is thought that if the preoperative FDG-PET CT detects involvement in these regions of the prostate, it will contribute to the clinical and surgical management. Diagnosis of urethral tumor before cystectomy may lead to urethrectomy, which may be a contraindication for orthotopic diversion. It is recommended that orthotopic

diversion should not be abandoned based on positive preoperative biopsy findings alone in this patient group and that frozen section examination should be a part of radical cystectomy operation, especially in male patients [3, 4]. A significant portion of male patients with MIBC have a request for orthotopic diversion when making the decision for surgery. Positive urethral surgical margins may be a contraindication for orthotopic urinary diversion, and the fact that this decision can only be determined with intraoperative frozen section may be confusing for patients before surgery. If the positive predictive value of involvement in the bladder neck and prostate region in preoperative FDG PET/CT is found to be high in showing positive urethral surgical margins, it will make preoperative planning easier.

In this study, we aimed to determine the role of radiopharmaceutical uptake in the bladder neck and prostate region in FDG PET/CT performed preoperatively in patients with muscle-invasive bladder tumors in determining the positive prostatic urethral surgical margins in the final pathology after cystectomy and its effect in determining the type of diversion to be selected.

Methods

Following the approval of the local ethics committee, the data of patients who underwent radical cystectomy due to bladder cancer between January 2009 and January 2023 at Istanbul University School of Medicine Department of Urology were retrospectively reviewed. Patient demographics, FDG uptake patterns in the prostate gland, mean SUVmax value of uptake in the bladder neck and prostate, status of preoperative BCG treatment and neoadjuvant chemotherapy, whether frozen section was sent from the urethra during the operation, and the selected diversion types, prostatic urethra surgical margin positivity, prostate pathologies, bladder tumor stage, location of the tumor in the bladder, lymph node positivity rate, presence of variant histology in the postoperative final pathology and status of recurrence in the

urethra during the follow-up were recorded. FDG PET/CT images of these patients were re-evaluated by an experienced nuclear medicine specialist in our hospital in order to prevent possible reporting errors. All patients who underwent radical cystectomy having FDG PET/CT for preoperative staging purposes were included the study. Patients who received radiotherapy to the pelvic region, and who had previously diagnosed with prostate cancer were excluded.

The study was approved by Istanbul University Clinical Research Ethics Committee protocol code E-29,624,016–050.99–1810738.99. All procedures performed in our study were in accordance with the ethical standards of the local research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The need for consent to participate was deemed unnecessary according to national regulations.

Statistical analysis

Statistical analysis was performed using IBM SPSS statistical package programme v.21 for Mac IL, USA. Quantitative variables were given as mean $\pm$ standard deviation and qualitative values are shown in numbers and percentages. Distribution of data was tested using Kolmogorov-Smirnov test. Comparison of variables between two groups was made by using Chi-Square and Mann-Whitney U tests. The one-way analysis of variance (ANOVA) was used to determine the difference between

three or more independent groups. $P < 0.05$ was considered statistically significant.

Results

A total of 50 patients were included the study. The mean age of the patients was 65 years. The selected urinary diversion type was orthotopic ileal neobladder in 12 patients, ileal loop in 35 patients and ureterocutaneostomy in one patient. Also, ureters were occluded, and nephrostomy tubes were inserted into the kidneys in two patients. Patient characteristics are given in Table 1.

Radiopharmaceutical uptake was detected in the bladder neck and prostate region in 19 (38%) of 50 patients. At the final pathologic examination prostatic urethra surgical margin positivity was detected in 8 (16%) patients. Among 8 patients, 7 (87.5%) patients had urothelial carcinoma invasion. Radiopharmaceutical uptake in the bladder neck and prostate region was detected in 5 (62.5%) of 8 patients with positive prostatic urethra surgical margins in preoperative FDG-PET (Fig. 1).

In other words, while 5 out of 19 patients with bladder neck and prostate involvement detected on FDG-PET CT had positive prostatic urethra surgical margins, 3 out of 31 patients without involvement detected on FDG-PET CT had positive prostatic urethra surgical margins. No statistically significant relationship was found between bladder neck and prostate involvement on FDG PET CT and positive prostatic urethra surgical margins ($p = 0.2554$).

The sensitivity, specificity, positive predictive value and negative predictive value of FDG PET/CT in determining prostatic urethra surgical margin positivity were 62.50%, 56.25%, 26.32% and 85.71%, respectively. (Supplementary Table 1).

Among 8 patients with positive prostatic urethral surgical margins: two received Neoadjuvant chemotherapy (NAC), three received intravesical BCG treatment, and 5 patients were found to have variant histology in their final pathology. No statistically significant relationship was found between prostatic urethral surgical margin positivity and history of neoadjuvant chemotherapy, intravesical BCG application, and presence of variant histology. ($p = 1$, $p = 0.4$, $p = 0.7547$, respectively).

Urothelial carcinoma invasion of the prostate was detected in 9 (18%) patients in the final pathology, involvement in the bladder neck and prostate region was detected in 6 (66.6%) of these patients at FDG-PET, while 3 patients had no involvement. In other words, urothelial carcinoma invasion of the prostate was detected via FDG PET CT in 6 of 19 patients with involvement in the bladder neck and prostate region. On the other hand, urothelial carcinoma invasion of the prostate was detected in 3 of 31 patients who had involvement in FDG PET CT. (Figure) The relationship between involvement

Table 1 Patient characteristics

	FDG BN/P+* (n:19)	FDG BN/P-* (n:31)	Total (n:50)
Mean Age (years)	66,5	64	65
Diversion Type			
Ileal Loop	15	20	35
Orthotopic bladder	3	9	12
Ureterocutaneostomy	0	1	1
Percutaneous nephrostomy	1	1	2
Tumor location in bladder			
Trigone	2	4	6
Dome	2	2	4
Bladder neck	3	1	4
Lateral, Anterior, Posterior wall	5	17	22
Multiple	4	6	10
No tumor	3	1	4
Bladder Tumor T Stage			
pT0	3	3	6
pTa	0	2	2
pT1	1	3	4
pT2	3	6	9
pT3	8	12	20
pT4	6	3	9

*BN Bladder Neck, P Prostate

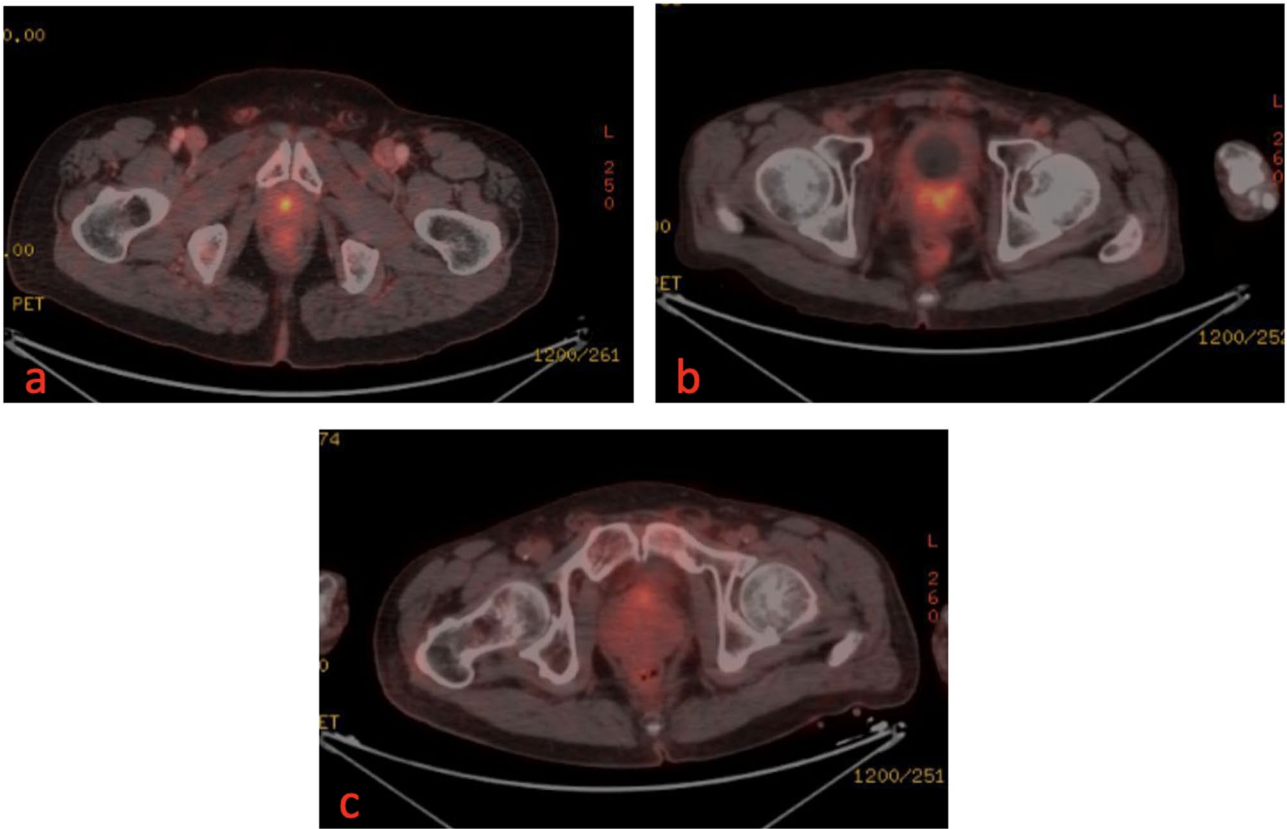


Fig. 1 **a** Prostatic urethra surgical margin positivity **b** urothelial carcinoma invasion in the prostate **c** Prostate adenocarcinoma

in the bladder neck and prostate region in FDG PET CT and urothelial carcinoma invasion of the prostate was not found to be statistically significant ($p=0.1492$).

The sensitivity, specificity, positive predictive value and negative predictive value of FDG PET/CT in determining urothelial carcinoma invasion in the prostate were 66.67%, 68.29%, 31.58% and 90.32%, respectively. (Supplementary Table 1)

Concomitant prostate adenocarcinoma was detected in 12 (24%) of 50 patients. Six (50%) patients had Gleason score 6 (3+3); five (42%) patients had Gleason score 7 [4 patients had G (3+4), 1 patient had G (4+3)] and one patient had Gleason score 8 (4+4) adenocarcinoma. One patient had urothelial carcinoma and adenocarcinoma infiltration of the prostate. Prostate involvement was detected in 8 (66.6%) of 12 patients with prostate adenocarcinoma on FDG-PET CT, while no prostate involvement was detected in four patients. In other words, prostate adenocarcinoma was detected in 8 of 19 patients with prostate involvement on FDG PET CT (Figure); while prostate adenocarcinoma was detected in 4 of 31 patients without prostate involvement on FDG PET CT. No statistically significant relationship was found between prostate involvement and the presence

Table 2 Relationship between radiopharmaceutical uptake in the bladder neck and prostate region and pathology Results, neoadjuvant KT

	FDG BN/P + (n:19)	FDG BN/P- (n:31)	Total (n:50)	P
Prostatic Urethra Surgical Margin +	5 (63)	3 (37)	8	0.2554
Prostate Pathology				
Urothelial Carcinoma Invasion	6 (67)	3 (33)	9	0.1492
Prostate Adenocarcinoma	8 (67)	4 (33)	12	0.106
Urothelial Ca/P. Adenoca	14 (67)	7 (33)	21	0.0189
PIN, BPH	6 (20)	24 (80)	30	
Lymph Node Metastasis	4 (25)	12 (75)	16	0.3859
Presence of variant histology	11 (39)	17 (61)	28	>0,05
History of Neoadjuvant chemotherapy	5 (33)	10 (67)	15	>0,05

urothelial carcinoma invasion in the prostate of prostate adenocarcinoma in FDG PET CT ($p=0.106$). (Table 2)

The sensitivity, specificity, positive predictive value and negative predictive value of FDG PET/CT for prostate adenocarcinoma were determined as 66.6%, 71.05%, 42.11% and 87.10%, respectively.(Supplementary Table 1) No statistically significant relationship was found

between bladder neck and prostate region involvement in FDG PET/CT and prostatic urethra surgical margin positivity, urothelial carcinoma invasion in the prostate and the presence of prostate adenocarcinoma.

Bladder neck and prostate involvement was detected on FDG PET CT in 6 out of 9 patients with urothelial carcinoma invasion in the prostate and in 8 out of 12 patients with prostate adenocarcinoma. A statistically significant relationship was found between the presence of any malignancy in the prostate (urothelial carcinoma invasion and/or prostate adenocarcinoma) and bladder neck and prostate involvement on FDG PET/CT ($p = 0.0189$).

The sensitivity, specificity, positive predictive value and negative predictive value of FDG PET/CT in showing the presence of a malignancy in the prostate gland (urothelial carcinoma invasion or prostate adenocarcinoma) were determined as 68.42%, 80.65%, 68.42% and 80.65%, respectively. (Supplementary Table 1).

Discussion

Urothelial carcinoma is a frequent disease with 549,393 new cases worldwide in 2018. About one of four patients present with muscle invasive bladder cancer (MIBC) which treatment is usually radical cystectomy with pelvic lymph node dissection. In case of metastatic disease, the first line therapy is usually chemotherapy. To decide appropriate treatment accurate staging is crucial. Either contrast enhanced computed tomography or magnetic resonance imaging is recommended for staging in current guidelines. However, radical cystectomy reveals upstaging in 40% of patients and downstaging in 20% [5]. This phenomenon highlights the limitations of the current staging of MIBC.

In men undergoing radical cystoprostatectomy (RCP) for urothelial carcinoma (UC), prostatic

involvement is detected on final pathology in 15–48% of cases. The American Joint Committee.

on Cancer Staging (AJCC) categorized prostatic involvement as T4 disease, regardless of the degree of prostatic involvement. However, researchers have found differences in outcomes based on the depth of prostatic invasion (superficial ductal or stromal) and in some cases the site of origin (bladder or prostatic urethra) [6].

In a study, prostatic involvement was found to be an independent predictor of urethral recurrence in men following radical cystectomy for urothelial carcinoma. Surprisingly the incidence of urethral recurrence was lower in patient with orthotopic diversion which might be a consequence of patient selection [7]. In our study, the sensitivity of FDG PET/CT in determining urothelial carcinoma invasion in the prostate were 66.67%; however no statistically significant relationship was found between

bladder neck and prostate region involvement in FDG PET/CT and prostatic urethra surgical margin positivity.

In a study by Barocas et al. [6] both bladder tumor stage and prostatic stromal involvement found to lead unfavorable outcomes. The authors concluded that although prostatic involvement originating from the bladder appears to be locally aggressive in nature and is associated with higher rates of positive LNs, patients have similar survival outcomes compared to those with stromal involvement originating from the prostatic urethra.

In another study by Bruins et al. [8] authors reported that more than 51% of the 1476 patients who underwent radical cystoprostatectomy had cancer involving the prostate and those who had prostatic urothelial carcinoma, especially with prostatic stromal involvement, had worse prognosis. The researchers concluded that there are no reliable preoperative clinical and histopathological risk factors to predict clinically significant prostatic adenocarcinoma/urothelial carcinoma.

In the retrospective study by Bizzarri et al., the diagnostic performance of FDG PET/CT in detecting lymph node metastases in patients with variant histology (VH) bladder cancer was compared to conventional imaging modalities such as CT and MRI. Among 29 patients who underwent radical cystectomy, FDG PET/CT demonstrated superior sensitivity (87.5%), specificity (90.5%), and overall accuracy (89.7%) compared to CT and MRI. Notably, CT failed to identify any nodal metastases, while PET/CT showed high concordance with pathological findings [9]. In our study, we specifically investigated FDG PET/CT uptake in the bladder neck and prostate region and found a statistically significant association between FDG uptake in this area and the presence of malignancy in the prostate (urothelial carcinoma and/or adenocarcinoma) ($p = 0.0189$). These findings suggest that FDG PET/CT may be valuable not only for lymph node staging but also for detecting extravesical extension, particularly in regions such as the prostate and bladder neck.

The findings of our study have important implications for surgical planning and patient counseling in the setting of muscle-invasive bladder cancer (MIBC). Although FDG PET/CT showed limited accuracy in predicting prostatic urethral surgical margin positivity, its high negative predictive value (NPV: 85.71%) suggests that a negative finding may provide reassurance regarding the absence of extensive prostate involvement. In patients being considered for orthotopic urinary diversion—a procedure contraindicated in the presence of urethral or prostatic involvement—this may aid in preoperative decision-making and patient counseling. Conversely, a positive FDG uptake in the bladder neck and prostate region, despite its relatively low positive predictive value (PPV: 26.32%), should prompt more careful intraoperative

assessment, possibly including extended apical dissection or frozen section analysis. Furthermore, when any malignancy (urothelial carcinoma and/or adenocarcinoma) is suspected based on PET/CT (PPV: 68.42%, NPV: 80.65%), surgeons may choose to avoid orthotopic diversion or consider a more extensive prostate resection, even in the absence of biopsy-proven prostate involvement. Thus, FDG PET/CT can support individualized surgical planning and improve patient-specific risk communication prior to radical cystectomy.

Several diagnostic tools are used preoperatively to assess prostate involvement in patients undergoing radical cystoprostatectomy. Transurethral loop biopsy of the prostatic urethra is frequently performed to detect urothelial carcinoma invasion; however, its positive predictive value is limited (12.5%) because it samples only the mucosa and periurethral tissue [10]. MRI, particularly multiparametric MRI, offers excellent soft tissue contrast and can help visualize extravesical spread and prostate involvement; however, its accuracy depends on reader expertise and standardized interpretation. Cystoscopy allows direct visualization of bladder neck and prostatic urethral abnormalities, but its ability to assess deeper stromal invasion is inherently limited. In contrast, FDG PET/CT provides functional imaging and systemic evaluation, which can detect metabolically active lesions in the bladder neck and prostate. While its positive predictive value for specific outcomes (e.g., margin positivity or prostate invasion) remains modest, its high negative predictive value supports its use as a complementary tool in ruling out extensive disease.

^{18}F -FDG PET/CT has a limited role in evaluating the local extension of bladder cancer due to interference of radioactive urine. Some researchers requested to take images after ^{18}F -FDG washout, urination, bladder catheterization or bladder irrigation. To take very early images might also be useful [11]. Based on the results of another study authors concluded that diuretic ^{18}F -FDG PET/CT has a higher diagnostic value compared to contrast-enhanced CT in detecting primary urinary bladder cancer and evaluating locoregional staging, (sensitivity 96% vs. 92% and sensitivity 78% vs. 44%, respectively) [12].

PSMA PET/CT has emerged as the gold standard molecular imaging modality in prostate adenocarcinoma, showing superior sensitivity and specificity in detecting both primary and metastatic lesions [13, 14]. However, its utility depends on sufficient PSMA expression, which can be low or absent in certain aggressive histologic subtypes, such as neuroendocrine-differentiated prostate cancer and urothelial carcinoma. In such scenarios, ^{18}F -FDG PET/CT can provide complementary diagnostic value, as it highlights tumors with high glycolytic activity regardless of PSMA expression. This distinction is particularly relevant for patients with castration-resistant prostate

cancer or those with bladder cancer and concomitant aggressive prostate involvement, where ^{18}F -FDG PET/CT may outperform PSMA PET/CT in lesion detection [15]. Thus, ^{18}F -FDG PET/CT and PSMA PET/CT should not be seen as competing techniques but as complementary modalities, each with distinct advantages depending on the underlying tumor biology.

In our study, no statistically significant relationship was found between radiopharmaceutical uptake in the bladder neck and prostate region in FDG PET CT and prostate invasion of urothelial carcinoma, prostatic urethra surgical margin positivity and prostate adenocarcinoma; however, a statistically significant relationship was found with the presence of any malignancy in the prostate (urothelial carcinoma and/or adenocarcinoma) ($p=0.0189$). Especially in patients requesting orthotopic urinary diversion, predicting the possible presence of malignancy in the prostate (urothelial carcinoma and adenocarcinoma) without performing a prostate biopsy before the operation may be useful in determining the surgical strategy. In order to reduce surgical margin positivity in the presence of both urothelial carcinoma invasion and adenocarcinoma in the bladder neck and prostate, more distant control of the bladder and prostate pedicles; more careful apical dissection during prostate dorsal vein control are important in reducing surgical margin positivity in these regions. In patients undergoing surgery for prostate adenocarcinoma, the most common positive surgical margins and recurrence are detected in the apex region.

The retrospective, single-center nature of our study and the relatively small sample size limit the generalizability of our findings. Future research should focus on larger, prospective, multicenter studies to validate the diagnostic accuracy of FDG PET/CT in detecting prostatic urethral involvement and guiding surgical planning in MIBC patients. In addition, FDG PET/CT may provide additional value when combined with other diagnostic modalities, including multiparametric MRI, cystoscopic evaluation, and transurethral biopsy. While each method alone has certain limitations, their integration could improve diagnostic accuracy, guide patient selection, and optimize treatment planning. Integration of molecular biomarkers, such as genomic classifiers or circulating tumor DNA, with imaging results also holds promise for refining risk stratification and tailoring surgical approaches. Artificial intelligence-based radiomics applied to PET/CT images could further improve prediction of pathological outcomes. Such multimodal strategies may ultimately optimize patient selection for orthotopic urinary diversion and minimize the risk of positive surgical margins.

Conclusion

In our study, although no significant relationship was found between radiopharmaceutical uptake in the bladder neck/prostate region and prostatic urethra surgical margin positivity, prostate urothelial carcinoma invasion and prostate adenocarcinoma, a significant result was obtained in showing the presence of any malignancy in the prostate (adenocarcinoma and/or urothelial carcinoma invasion). In the presence of uptake in this region in FDG, surgical techniques aimed at reducing and preventing surgical margin positivity should be emphasized.

Abbreviations

FDG PET/CT	Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography
MIBC	Muscle-Invasive Bladder Cancer
RCP	Radical Cystoprostatectomy
UC	Urothelial Carcinoma
SUVmax	Maximum Standardized Uptake Value
BCG	Bacillus Calmette–Guérin
NAC	Neoadjuvant Chemotherapy

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12894-025-01962-w>.

Supplementary Material 1: Supplementary Table 1: Performance metrics of preoperative FDG PET/CT in predicting pathological outcomes after radical cystoprostatectomy.

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Authors' contributions

R.B.E. and R.A. conceived and designed the study. R.B.E. and A.T. collected the data. R.B.E., R.A., Y.Ş., and S.E. performed the data analysis. R.A., and Y.Ş. drafted the initial manuscript. M.Ö.S. and F.Ö. critically revised the manuscript for important intellectual content. All authors reviewed and approved the final version of the manuscript.

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Data availability

The datasets generated and/or analysed during the current study are available in the Zenodo repository at: <https://doi.org/10.5281/zenodo.15425614> (<https://doi.org/10.5281/zenodo.15425614>).

Declarations

Ethics approval and consent to participate

This study was approved by the Clinical Research Ethics Committee of Istanbul University (Protocol code: E-29624016–050.99-1810738). All procedures were conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments. The need for informed consent was waived due to the retrospective nature of the study and in accordance with national regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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