Risk factors associated with positive surgical margins' location at radical cystectomy and their impact on bladder cancer survival

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Abstract

Purpose To evaluate the risk factors associated with positive surgical margins' (PSMs) location and their impact on disease-specific survival (DSS) in patients with bladder cancer (BCa) undergoing radical cystectomy (RC).

Methods We analyzed a large multi-institutional cohort of patients treated with upfront RC for non-metastatic (cT1-4aN0M0) BCa. Multivariable binomial logistic regression analyses were used to assess the risk of PSMs at RC for each location after adjusting for clinicopathological covariates. The Kaplan–Meier method was used to estimate DSS stratified by margins' status and location. Log-rank statistics and Cox' regression models were used to determine significance.

Results A total of 1058 patients were included and 108 (10.2%) patients had PSMs. PSMs were located at soft-tissue, ureter(s), and urethra in 57 (5.4%), 30 (2.8%) and 21 (2.0%) patients, respectively. At multivariable analysis, soft-tissue PSMs were independently associated with pathological stage T4 (pT4) (Odds ratio (OR) 6.20, $p < 0.001$) and lymph-node metastases (OR 1.86, $p = 0.04$). Concomitant carcinoma-in-situ (CIS) was an independent risk factor for ureteric PSMs (OR 6.31, $p = 0.003$). Finally, urethral PSMs were independently correlated with pT4-stage (OR 5.10, $p = 0.01$). The estimated 3-years DSS rates were 58.2%, 32.4%, 50.1%, and 40.3% for negative SMs, soft-tissue-, ureteric- and urethral PSMs, respectively (log-rank; $p < 0.001$).

Conclusions PSMs' location represents distinct risk factors' patterns. Concomitant CIS was associated with ureteric PSMs. Urethral and soft-tissue PSM showed worse DSS rates. Our results suggest that clinical decision-making paradigms on adjuvant treatment and surveillance might be adapted based on PSM and their location.

Keywords Bladder · Cancer · Urothelial carcinoma · Cystectomy · Margin · Ureter · Urethra · Soft tissue

Introduction

Urothelial carcinoma (UC), which encompasses bladder cancer (BCa) and upper tract urothelial carcinoma (UTUC) represents the sixth most commonly diagnosed cancer in Western Countries [1]. The bladder is the most predominant site of origin. BCa is a heterogeneous disease comprising both non-muscle-invasive (NMIBC) and muscle-invasive (MIBC) with different oncological outcomes [2]. Radical cystectomy (RC) with pelvic lymph node dissection (PLND) represents a mainstay in the treatment of MIBC providing both pelvic cancer control and survival [3].

The reported rate of positive surgical margins (PSMs) at RC ranges from 4 to 15% in the literature [4–6]. PSMs are impacted by the quality of surgical excision and are related to several factors such as timely diagnosis, centralization of procedures, surgeon's volume and administration of neoadjuvant chemotherapy [7, 8]. Although the presence of PSMs intuitively will result in worse clinical outcome, it still is a question whether their prognostic influence differs if stratified according to their location. To date, only sparse data

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are available on this question. Ureteric and urethral PSMs increased the risk by seven-fold of developing urothelial recurrence [9], with often challenging decision-making regarding both diagnosis and treatment [10]. Soft-tissue PSMs proved strong predictors of both local recurrence and worse disease-specific outcomes either in overall and/or stage-based analyses [4, 6, 11–13].

The objective of our study was to comprehensively evaluate risk factors associated with PSMs at RC stratified by different locations and the impact of each PSMs site on survival outcomes using individual patients' data (IPD) from a large multi-institutional dataset.

Materials and methods

Patients selection and data collection

Demographic, clinicopathological and outcome data were retrospectively collected from medical records of 1058 patients who underwent RC and bilateral PLND without neoadjuvant treatment(s) for cT1-4aN0M0 urothelial BCa between October 1986 and October 2015. A total of eight tertiary referral centers provided the IPD (Fig. 1). Ethical approval was obtained at each site according to national regulations and the principles of the Declaration of Helsinki in accordance with Good Clinical Practice guidelines.

The collected variables were age at RC, sex, pathological tumor (pT) stage and grade, the presence of concomitant carcinoma-in-situ (CIS), pathological nodal (pN) status, number of lymph-nodes (LNs) removed, presence of lympho-vascular invasion (LVI) and adjuvant treatment(s). The patients underwent laboratory tests, physical examination, computed tomography (CT) of the abdomen/pelvis and at least a chest X-ray to rule out the presence of (distant) metastases. Follow-up was performed according to institutional protocols. Disease-related death was determined by the treating physicians following chart review or corroborated by death certificates. Survival was defined as the time-interval between RC and the date of last imaging and/or clinical visit (censored), or of documented (disease-related) death.

Pathological evaluation

The RC specimens were processed according to institutional pathological procedures and were (locally) reviewed by a dedicated pathologist. Pathological stage was based on the Tumor Nodes Metastasis (TNM) classification system (2002 classification, 6th edition), while tumor grade was based on the 2004/2016 World Health Organization (WHO) system. Surgical margins' status and locations were reported. A PSM was defined as the presence of microscopic or macroscopic tumor both invasive carcinoma as well as CIS at inked areas of soft-tissue, ureteric and urethral margins of the RC-specimen. In case of multiple PSM, the site with the largest PSM was recorded. Microscopic and macroscopic PSMs were considered together in the current analysis.

Statistical analysis

Descriptive analysis included frequencies and proportions for categorical variables. Medians and interquartile range (IQR) were reported for continuous coded variables. The Mann–Whitney *U* test or Kruskal–Wallis test were used for comparison of the continuous data and the Chi-squared or Fisher's exact test for categorical data. All tests were two-sided with a level of significance set at $p < 0.05$. Multivariable binomial logistic regression models were used to assess

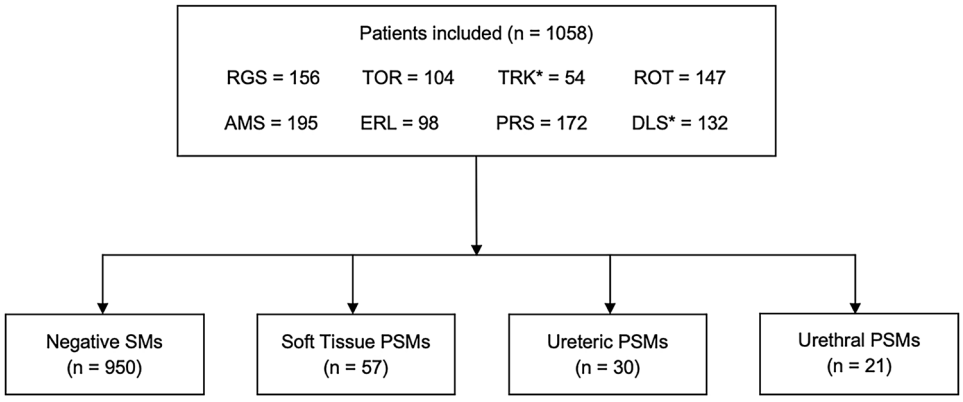

Fig. 1 Consort flow diagram. A total of 1058 patients were included in the current analysis, 950 with negative SMs and 57, 30, 21 with soft-tissue-, ureteric- and urethral PSMs, respectively. The breakdown of patients from each center is shown: RGS = Regensburg (Germany); TOR = Toronto, ON (Canada); TRK = Turku (Finland); ROT = Rotterdam (The Netherlands); AMS = Amsterdam (The Netherlands); ERL = Erlangen (Germany); PRS = Paris (France); DLS = Dallas, TX (United States). *Pathology review of the cases from Turku and Dallas were done by TvdK (Toronto). *PSMs* positive surgical margins, *SMs* surgical margins

the odds ratio (OR) with 95% confidence intervals (CI) testing the risk of PSMs at RC for each location after adjusting for clinico-pathological covariates. The area under the curve (AUC) for each model was calculated. The Kaplan–Meier method was used to estimate disease-specific survival (DSS) stratified by margins' status and location and the log-rank method was used to determine significance. Univariable Cox regression models were used to assess the Hazard Ratio (HR) with 95% CI testing the relationship between the PSMs' location with DSS. Statistical analyses were performed using RStudio Version 1.2.5001 (RStudio: Integrated Development for R. RStudio, Inc., Boston, MA URL http://www.rstudio.com/).

Results

Patients and pathological characteristics

Descriptive clinicopathological features of the 1058 patients included in the current analysis and stratified by margins' status and location are presented in Table 1. A total of 108 (10.2%) patients with PSMs were identified (Fig. 1). PSMs were located at soft-tissue, ureter, and urethra in 57 (5.4%), 30 (2.8%) and 21 (2.0%) patients, respectively. Median age at RC was 67 years (IQR 58–74 years). No differences were found regarding to PSMs' occurrence or location and year of RC ($p = 0.36$).

PSMs were significantly associated with advanced pT-stage and presence of lymph-node metastases. Overall, the proportion of PSMs increased with advancing pT-stage (Table 1). In patients who received RC for NMIBC, no soft-tissue PSMs were reported whereas ureteric and urethral PSMs were found in 13.4% and 14.3% of cases, respectively (Table 1). Lymph-node metastasis were significantly correlated with PSMs, irrespective of the PSMs' location ($p < 0.001$; Table 1). Concomitant CIS was significantly more frequent in patients with PSMs, especially in the ureteric PSM sub-group. Adjuvant treatment(s), i.e., radiation and/or chemotherapy, were administered more often to patients with PSMs ($p = 0.03$ and $p = 0.01$, respectively). We found no significant differences for sex, tumor-grade, number of LNs removed, LVI and margins' status and locations (all, $p > 0.05$).

Risk factors associated with PSMs' location

Multivariable binomial logistic regression analysis adjusted for the effect of clinicopathological covariates is presented in Table 2. Soft-tissue PSMs were independently associated with pT4-stage (OR 6.20, 95% CI 2.54–17.5, $p < 0.001$) and pN-positive disease (OR 1.86, 95% CI 1.03–3.41, $p = 0.04$), respectively. Concomitant CIS was an independent risk factor associated with ureteric PSMs (OR 6.31, 95% CI 1.54–7.61, $p = 0.003$). Finally, urethral PSMs were independently correlated with pT4 stage (OR 5.10, 95% CI 1.61–19.6, $p = 0.01$). No associations were found for age, sex, tumor-grade and LVI in the prediction of PSMs' location. The AUC of the models for soft-tissue, ureteric and urethral PSMs were 0.73 (95% CI, 0.71–0.75), 0.72 (95% CI, 0.71–0.75) and 0.76 (95% CI, 0.74–0.78), respectively (Table 2).

Comparison of survival estimates in soft-tissue, ureteric, and urethral PSMs

Within a median follow-up of 2.3 years (IQR 1.0–5.0 years), 520 (49.2%) disease-related deaths occurred. Of these, 43 (75.4%), 14 (46.7%) and 13 (61.9%) occurred in the soft-tissue, ureteric and urethral PSMs groups, respectively ($p < 0.001$). Median follow-up of the survivors was 4.5 years (IQR 2.2–7.5 years). We found no difference according to disease-specific events and year of RC stratified by margins' status and location ($p = 0.15$; Table 1). At Cox-regression analysis, the soft-tissue PSM was correlated with worse DSS (HR 2.00, 95% CI 1.46–2.73, $p < 0.001$). Figure 2 shows the Kaplan–Meier curves of the four investigated SM-groups for DSS with follow-up truncated at 10 years. The estimated 3-year DSS probabilities were 58.2% (95% CI, 55.0–61.6), 32.4% (95% CI, 22.0–47.7), 50.7% (95% CI, 32.7–78.5), 40.3% (95% CI, 23.7–68.8) for negative SMs, soft-tissue-, ureteric- and urethral PSMs, respectively (log-rank, $p < 0.0001$).

Discussion

In this retrospective, multi-institutional analysis, we evaluated risk factors associated with PSMs' location and their impact on DSS in a large cohort of patients undergoing RC for non-metastatic BCa. We found specific associations for PSMs' location risk, even after adjusting for known clinicopathological variables. Furthermore, we described the influence of PSMs' location on disease-specific outcomes. The present study represents one of the very few studies that comprehensively evaluated such distinct margin patterns using IPD from a large multi-institutional collaboration.

Like previous reports on soft-tissue PSMs [4, 6, 13], our findings based on a large number of patients and surgeons, confirmed a solid association between soft-tissue PSMs with both increasing pT-stage and pN-positive disease. Furthermore, patients who harbored soft-tissue PSMs showed worse disease-specific outcomes. As such, neoadjuvant chemotherapy to shrink the primary tumor and especially adjuvant treatment(s) in case of a soft-tissue PSM could be considered for either to pathological downstaging and local

Table 1 Patients and tumor characteristics of the 1058 patients with non-metastatic bladder cancer (cT1-4aN0M0) who underwent radical cystectomy and urinary diversion, stratified according to their margins' status and the location of the margin if positive

Variable	Overall	Negative SMs	Soft tissue PSMs	Ureteric PSMs	Urethral PSMs	*p*
Patients, *n* (%)	1058 (100.0)	950 (89.8)	57 (5.4)	30 (2.8)	21 (2.0)	
Age (years), median (IQR)	67 (58–74)	67 (58–74)	67 (59–73)	67 (59–72)	65 (70–53)	0.97
Year of RC, *n* (%)						
1986–2000	354 (33.5)	324 (34.1)	14 (24.6)	11 (36.7)	5 (23.8)	0.36
2001–2015	704 (66.5)	626 (65.9)	43 (75.4)	19 (63.3)	16 (76.2)	
Sex, *n* (%)						
Male	836 (79.0)	753 (79.3)	40 (70.2)	27 (90.0)	16 (76.2)	0.17
Female	222 (21.0)	197 (20.7)	17 (29.8)	3 (10.0)	5 (23.8)	
pT-stage, *n* (%)						
NMIBC (pTa/is/1)	80 (7.6)	73 (7.7)	0 (0.0)	4 (13.4)	3 (14.3)	< 0.001
pT2	266 (25.1)	253 (26.6)	6 (10.5)	6 (20.0)	1 (4.8)	
pT3	513 (48.5)	472 (49.7)	26 (45.6)	10 (33.3)	5 (23.8)	
pT4	199 (18.8)	152 (16.0)	25 (43.9)	10 (33.3)	12 (57.1)	
Grade (WHO 2004), *n* (%)						
Low grade	41 (3.9)	40 (4.2)	0 (0.0)	1 (3.3)	0 (0.0)	0.33
High grade	1017 (96.1)	910 (95.8)	57 (100.0)	29 (96.7)	21 (100.0)	
pN-stage, *n* (%)						
pN0	648 (61.3)	600 (63.2)	23 (40.4)	15 (50.0)	10 (47.6)	< 0.001
pN1	151 (14.3)	129 (13.6)	10 (17.5)	10 (33.3)	2 (9.5)	
pN2-N3[a]	259 (24.5)	221 (23.3)	24 (42.1)	5 (16.7)	9 (42.9)	
LNs removed, median (IQR)	13 (8–18)	13 (8–18)	13 (8–17)	10 (7–13)	14 (8–18)	0.19
Concomitant CIS, *n* (%)						
Absence	655 (61.9)	598 (63.0)	35 (61.4)	10 (33.3)	12 (57.1)	0.01
Presence	403 (38.1)	352 (37.1)	22 (38.6)	20 (66.7)	9 (42.9)	
LVI, *n* (%)						
Absence	560 (52.9)	513 (54.0)	22 (38.6)	15 (50.0)	10 (47.6)	0.14
Presence	498 (47.1)	437 (36.0)	35 (61.4)	15 (50.0)	11 (52.4)	
Adjuvant radiotherapy, *n* (%)	69 (6.5)	56 (5.9)	9 (15.8)	2 (6.7)	2 (9.5)	0.03
Adjuvant chemotherapy, *n* (%)	293 (27.7)	251 (26.4)	26 (45.6)	8 (26.7)	8 (38.1)	0.01
Disease-specific events, *n* (%)	520 (49.2)	450 (47.4)	43 (75.4)	14 (46.7)	13 (61.9)	< 0.001
Disease-specific events per year of RC, *n* (%)						
1986–2000	169 (16.0)	152 (16.0)	8 (14.0)	6 (20.0)	3 (14.3)	0.15
2001–2015	351 (33.2)	298 (31.4)	35 (61.4)	8 (26.7)	10 (47.6)	
Follow-up (years), median (IQR)	2.3 (1.0–5.0)	2.5 (1.0–5.2)	1.5 (0.7–3.6)	1.6 (1.0–3.0)	1.4 (0.5–3.8)	0.01
Survivors' follow-up (years), median (IQR)	4.5 (2.2–7.5)	4.6 (2.3–7.5)	4.9 (2.6–10.3)	1.7 (1.1–4.0)	4.5 (3.6–8.3)	0.01

RC radical cystectomy, *SMs* surgical margins, *PSMs* positive surgical margins, *pT-stage* pathological tumor stage, *NMIBC* non-muscle invasive bladder cancer, *WHO* World Health Organization, *pN-stage* pathological nodal stage, *LNs* lymph nodes, *CIS* carcinoma-in-situ, *UC* urothelial carcinoma, *LVI* lympho-vascular Invasion

[a]Two patients had pN3 disease, both of them in the negative SMs group

cancer control [14, 15]. In our series, both adjuvant radiation and chemotherapy were related to the presence of soft-tissue PSMs. It must be pointed out that our study cohort did not receive any neoadjuvant treatment. In addition, we also found a considerably higher incidence of LVI in patients with soft-tissue PSMs. The prognostic role of LVI has been well-established among patients undergoing RC [16]. LVI was shown to be associated with disease-specific outcomes within each pathological stage [17] and our data reflected by survival analysis endorsed this assumption picturing LVI as a crucial feature in the decision-making process. In conclusion, we confirmed the adverse prognostics attached to soft-tissue PSMs, which are a sign of locally advanced BCa at RC [11].

Regarding ureteric PSMs, we found these in 30 (2.8%) patients and concomitant CIS was an independent risk factor associated with ureteric PSMs. Several studies reported CIS as a key predictor of ureteric PSMs at RC and demonstrated

Table 2 Multivariable binomial logistic regression analyses for the prediction of PSMs according to its location among the 1058 patients with non-metastatic bladder cancer (cT1-4aN0M0) treated with radical cystectomy

Variable	Soft tissue PSMs		Ureteric PSMs		Urethral PSMs	
	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
Age (years) as cont.	1.01 (0.98–1.03)	0.70	0.98 (0.95–1.02)	0.4	1.00 (0.96–1.05)	0.8
Sex						
Female	1.00 (Ref.)	–	1.00 (Ref.)	–	1.00 (Ref.)	–
Male	0.59 (0.33–1.12)	0.09	2.18 (0.75–9.3)	0.2	0.75 (0.28–2.35)	0.59
pT-stage						
Organ-confined (NMIBC, pT2)	1.00 (Ref.)	–	1.00 (Ref.)	–	1.00 (Ref.)	–
pT3	2.33 (0.98–6.44)	0.07	0.74 (0.29–1.94)	0.5	0.77 (0.19–3.23)	0.7
pT4	6.20 (2.54–17.5)	<0.001	1.79 (0.67–4.76)	0.2	5.10 (1.61–19.6)	0.01
Grade (WHO 2004)						
Low grade	1.00 (Ref.)	–	1.00 (Ref.)	–	1.00 (Ref.)	–
High grade	0.69 (0.64–17.6)	0.98	1.52 (0.7–8.31)	0.7	0.52 (0.24–2.94)	0.99
pN-stage						
Negative	1.00 (Ref.)	–	1.00 (Ref.)	–	1.00 (Ref.)	–
Positive	1.86 (1.03–3.41)	0.04	1.55 (0.68–3.56)	0.3	1.47 (0.56–3.89)	0.44
Concomitant CIS						
Absence	1.00 (Ref.)	–	1.00 (Ref.)	–	1.00 (Ref.)	–
Presence	1.01 (0.58–1.77)	0.97	3.31 (1.54–7.61)	0.003	1.17 (0.46–2.84)	0.73
LVI						
Absence	1.00 (Ref.)	–	1.00 (Ref.)	–	1.00 (Ref.)	–
Presence	1.00 (0.54–1.85)	0.97	0.79 (0.34–1.86)	0.6	0.73 (0.28–1.96)	0.53
AUC of the model (95% CI)	0.73 (0.71–0.75)		0.72 (0.71–0.74)		0.76 (0.74–0.78)	

OR odds ratio, *CI* confidence interval, *PSMs* positive surgical margins, *pT stage* pathological tumor stage, *NMIBC* non-muscle invasive bladder cancer, *WHO* World Health Organization, *pN stage* pathological nodal stage, *CIS* carcinoma-in-situ, *UC* urothelial carcinoma, *LVI* lympho-vascular Invasion, *AUC* area under the curve

its direct link to UTUC recurrence [5, 18–21]. In a meta-analysis including 13,185 patients, these recurrence-rates ranged between 0.75 and 6.4% [9]. However, these reports probably underestimated this occurrence because of the small cohorts, lack of standardized surveillance protocols and/or competing mortality risks [22]. UC is often multifocal and the urothelial lining of the renal pelvis, the ureters and the urethra are also at risk after RC. When viewed as a whole pan-urothelial field defect characterized by metachronous tumors as a result of intra-luminal seeding and/or implants derived from an initial clone, it must be emphasized that not all patients harbor the same propensity for an urothelial recurrence [9, 18]. Such inclination might be partially elucidated by the unique features of CIS that, despite being part of the NMIBC category, can be characterized as MIBC at the molecular level by its high levels of genomic instability and mutations in TP53 [23]. Furthermore, a high concordance between history of CIS and its presence at RC specimen has been described [24]. Although not the main focus of the current study, our results of the multifocal nature of CIS and the higher associated risk for ureteric PSM in case of concomitant CIS highlighted the role of intraoperative frozen section analysis (FSA) as a critical crossroad of margins' management. However, concerns of FSA include the controversial performance compared to the permanent section analysis [5, 20], the related costs [25], the need for a longer operative and anesthesia time and even nephro-ureterectomy in some cases burdening the patients as well as the health-care systems [26]. Hence, (sequential) ureteric FSA remains matter of debate and its adoption is still mainly related to the daily routine in each hospital and/or surgeon's preference(s). Although our results showed comparable DSS at 3 years for patients with negative SM and ureteric PSM, a trend towards worse survival after 3 years can be appreciated in our study for patients with ureteric PSMs (Fig. 2). This might be explained by the fact that patients with CIS and/or ureteric PSMs are at life-long risk for late urothelial recurrence(s) [27]. In this context, Moschini et al. propagated the beneficial impact on disease-specific outcomes of sequential sectioning at intraoperative FSA [19]. Our findings corroborate those of others who also identified CIS as a prominent hallmark for patients who are candidates for FSA [20, 28]. As a consequence, we believe that it remains important to diagnose CIS before performing RC.

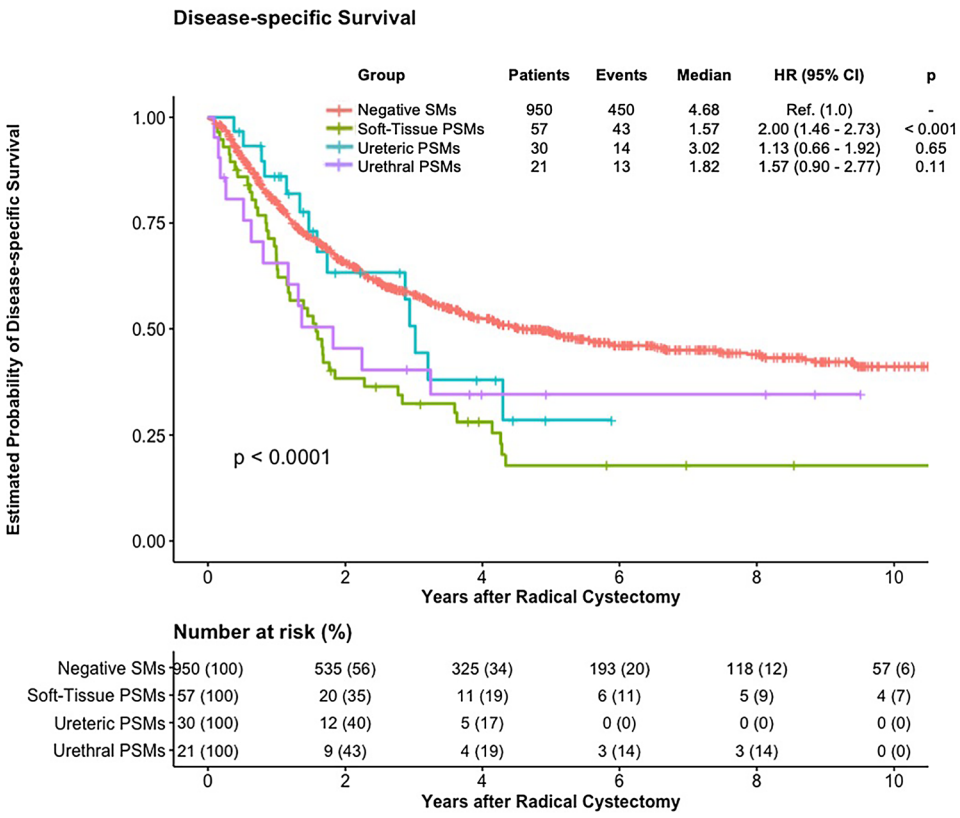

Fig. 2 Kaplan–Meier survival curves of disease-specific survival (log-rank, $p < 0.0001$) stratified by margins' status and location among 1058 patients with non-metastatic BCa undergoing RC are shown. Univariable Cox's regression analysis assessed the HRs with their 95% CI: negative SMs vs. soft-tissue PSMs (HR 2.00, 95% CI 1.46–2.73, $p < 0.001$), negative SMs vs. ureteric PSMs (HR 1.13, 95% CI 0.66–1.92, $p = 0.65$) and negative SMs vs. urethral PSMs (HR 1.57, 95% CI 0.90–2.77, $p = 0.11$), respectively. *PSMs* positive surgical margins, *SMs* surgical margins, *HR* hazard ratio, *CI* confidence interval, *DSS* disease-specific survival

The current European guidelines recommend negative FSA or a negative preoperative endoscopic urethral sampling prior to the decision to perform an orthotopic urinary diversion [3]. We found that advanced pathological stage was strongly associated with urethral PSMs. Recognizing such a remarkable link may have several implications. Since the methodology behind the studies addressing the reliability of urethral FSA were heterogeneous and limited by sample size [29, 30], tailoring the adoption of urethral FSA focusing on patients who would benefit the most from urethral FSA, such as those with a higher risk for pT4-disease, could enhance the performance of urethral FSA. On the other hand, these are the patients with worse DSS who ideally should have neoadjuvant treatment or even urethrectomy at time of RC. Indeed, urethral PSM indicated worse DSS than ureteric PSM in our study as was also shown by Neuzillet et al. [11]. Concerning the survival outcomes according to different location of PSMs, Neuzillet et al. described significant differences for the three different PSM locations in pN0-patients that mirror our own results [11]. Our cohort of urethral PSMs did only show the same trend. This may be explained by the different settings: a retrospective matched case-control design in the French study [11], which only focused on patients with pN0-diease and the higher rate of urethral PSMs compared to our study with IPD of a RC-cohort. Neuzillet et al. [11] suggested that both avoidance of urethral PSMs or performing primary urethrectomy in patients who are at higher risk for pT4-disease could translate into better survival outcomes. In general, urethral PSMs are an ominous sign as these are related to pT4-disease and have an unfavorable 3-year DSS, which is comparable to soft-tissue PSM.

Our study is not devoid of limitations that must be acknowledged. First, this study was limited by the retrospective design and is thereby subject to the shortcomings inherent to this type of analysis. Second, the study period spanned almost 30 years, in which different temporal practice patterns may have existed. Moreover, data about operative time and blood loss were not captured. Fourth, our cohort of patients did not receive NAC, which is the current standard of care treatment for MIBC. Other limitations include the absence of captured data on nephro-ureterectomy, urethrectomy and FSA at RC. We anticipate that with these data higher PSM rates might have been found. In addition, the shorter follow-up period of survivors in patients with ureteric PSM was remarkable. Strengths are the dedicated pathology review of the RC-specimens and the large set of IPD extracted from eight tertiary referral centers, which provided valuable comprehensive evidence for this understudied topic in BCa surgery.

Conclusions

PSMs' location represents distinct risk factors' patterns. CIS was associated with ureteric PSMs. Of note, 3-year DSS of ureteric PSMs was not different from negative SMs. Urethral and soft-tissue PSMs showed worse DSS rates. Our results suggest that clinical decision-making paradigms on adjuvant treatment for patients with soft-tissue and urethral PSMs and tailored surveillance for patients with ureteric PSMs might be accordingly adapted based on the PSM location.

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