

Assessment of the infiltrative character of bladder cancer at the time of transurethral resection: a single center study

Paweł Grzególkowski, Krystian Kaczmarek, Artur Lemiński, Michał Soczawa, Adam Gołąb, Marcin Słojewski

Department of Urology and Urological Oncology, Pomeranian Medical University, Szczecin, Poland

Citation: Grzególkowski P, Kaczmarek K, Lemiński A, Soczawa M, Gołąb A, Słojewski M. Assessment of the infiltrative character of bladder cancer at the time of transurethral resection: a single center study. Cent European J Urol. 2017; 70: 22-26.

Article history

Submitted: Jan. 6, 2016

Accepted: Dec. 4, 2016

Published online: Dec. 30, 2016

Corresponding author

Paweł Grzególkowski
Pomeranian Medical
University
Department of Urology
72, Powstańców
Wielkopolskich
70-111 Szczecin, Poland
phone: +48 607 445 859
lekpawelgrzegolkowski@gmail.com

Introduction Determining the clinical stage of bladder carcinoma before radical cystectomy is characterized by a high inaccuracy rate. The discrepancy in some reports reaches up to 48%. Therefore intraoperative clinical staging of bladder carcinoma is not recommended before radical treatment as it is for prostate cancer. However, the accuracy of clinical assessment of the muscle invasive character of the tumors at the time of transurethral resection has not been studied. In our study we estimate the accuracy of clinical staging during endoscopic treatment.

Material and methods 332 patients who had undergone transurethral resection of bladder cancer were studied in this retrospective analysis. Data such as age, gender, presence of hydronephrosis, operator, the results of bimanual bladder examination, TURB report and pathologic report, were collected from each patient. Intraoperative prediction of the muscle invasive nature of the tumor was compared with pathological reports. A logistic regression analysis was used to evaluate the influence of particular variables on upstaging and downstaging.

Results Overall accuracy between clinical and histopathology staging was 87.8%. Discrepancy was observed only in 36 patients. Patients with pTa stage were the most numerous group among patients with accurate prediction of the muscle invasiveness character of the tumor. Univariable logistic regression indicated that the presence of a palpable mass in the bimanual examination was a predictor of upstaging, with an OR 11.75 CI95% [2.49–55.32].

Conclusions The study indicated the high accuracy between clinical and pathological reports. Intraoperative evaluation of tumor character should be an indispensable part of treatment, which can be useful for planning in advance the further stages of treatment.

Key Words: bladder carcinoma <> cancer staging <> transurethral resection

INTRODUCTION

Urinary bladder carcinomas are among the most principal aspects of urological oncology. Bladder cancer is diagnosed in men aged mostly over 45 years (98% of cases). The most frequent symptom is asymptomatic hematuria. Statistically, tumors are found three times more commonly in men than in women. Epidemiological data shows a strong relationship with smoking cigarettes and exposure to industrial carcinogens [1]. The most common histological type of bladder cancers are transitional cell carcinomas (TCC).

These bladder carcinomas show a wide spectrum of morphological forms, from a single polyp to solid and infiltrating masses. According to the data, in 70% of cases the bladder tumors are superficial, non-muscle invasive (NMIBC) [2]. In this group the golden standard of treatment is transurethral electroresection (TURB). In case of muscle invasive tumors (MIBC) radical treatment such as cystectomy is strongly recommended. The radical treatment of MIBC should be done with the least possible delay [3]. Furthermore, radical treatment should be planned in advance particularly during an endoscopic

procedure, which can also minimize the delay. In particular, we should consider such methods when there is a suspicion of muscle invasive character of a tumor. Therefore, the goal of our study was to evaluate the value of the clinical evaluation of the bladder tumors at the time of TURB procedure performed before histopathologic evaluation.

MATERIAL AND METHODS

From January 2014 to December 2014, a retrospective analysis of 332 patients who underwent the TURB procedure was conducted. All procedures were performed in a single academic urological center. During transurethral resection surgeons tried to predict the muscle invasive character of the tumors based on clinical aspects. After transurethral resection, clinical assessment was compared with pathological evaluation of samples acquired during TURB. Patients with advanced tumors in whom only partial resection was performed were excluded from the study. Cases of radical resection and an absence of muscle in TURB specimens were also excluded. The final study population consisted of 272 cases. One hundred and twenty-seven patients had primary tumors and 145 had recurrent tumors. Primary tumors were mostly diagnosed using ultrasonography (90 cases), 32 during cystoscopy and 5 after computer tomography. All recurrent tumors were diagnosed during cystoscopy. The surgeons were not blinded by previous diagnoses in cases of recurrent tumors.

Clinical assessment was based on ultrasonography of the urinary system performed one day before endoscopic surgery and intraoperative evaluation. Ultrasonographic examination was performed in order to confirm the presence of hydronephrosis as a predicting factor of MIBC. The intraoperative assessment consisted of evaluation of the macroscopic appearance of the tumor and underlying layers of the bladder. Moreover, bimanual palpation (BP) was performed in all cases. BP of the bladder was used to detect any palpable extravescicular masses and was performed under anesthesia before and after resection. All resections were performed under white light. Pathological assessment was made according to the 2009 TNM pathological classification. All specimens were histologically confirmed to be urothelial carcinoma.

The following data was collected from each patient: age, gender, presence of hydronephrosis, operator, the results of bimanual bladder examination, TURB report and pathologic report. Operators were divided into two groups consisting of both urology specialists and urology residents. The first group consisted of 7 surgeons and the second group was made up of 8 surgeons.

We estimated the accuracy between clinical and pathological assessment. Logistic regression was performed to assess the influence of particular variables on downstaging and overstaging. Statistical analyses were performed using Statistica 12 software.

RESULTS

The study population was 19.5% female and 80.5% male, with an overall average age of 68 years (range: 37 to 93 years old). Overall accuracy between clinical and histopathology staging was 87.8%. Discrepancy was observed only in 36 patients. Pathologists identified muscle invasive tumors in 25 patients, whereas surgeons in 51 patients. Among patients with accurate staging, those with pTa stage were the most numerous. In the majority of patients with discrepancy, upstaging was observed (86.1%). The highest difference in assessment of the muscle invasive character of the tumor was in patients with pT1 stage and es-

Table 1. Baseline characteristics of the total study population

Variable	Accurate staging	Upstaging	Downstaging
n	236	31	5
Age, years			
Mean	68.0	69.9	64.2
SD	10.4	9.9	11.9
Gender			
Female	48	5	0
Male	188	26	5
Bladder cancer history			
Primary	104	18	5
Recurrent	132	13	0
Number of tumors			
Solitary	193	31	5
Multiple	43	0	0
Hydronephrosis			
No	230	30	5
Yes	6	1	0
Bimanual examination			
Not palpable	233	27	5
Palpable	3	4	0
T-stage TURB specimen			
T0	26	1	0
Tis	1	0	0
Ta	154	7	0
T1	35	23	0
T2	20	0	5
Tumor grade			
G0	26	1	0
G1	64	6	1
G2	127	19	2
G3	19	5	2
Surgeon			
Urologist	175	26	3
Resident	61	5	2

SD – standard deviation

estimated to be 58.4%. All of those patients were overstaged. Every patient with downstaging had primary, solitary, not palpable tumor. Moreover, all of those patients had confirmed pT2 stage. Total discrepancy in patients with MIBC was 25.0%. The baseline characteristics of the total study population are shown in Table 1.

The number of procedures per surgeon was different between urologists and residents. The average number of performed procedures per year was 30.1 and 7.6, respectively ($p < 0.05$). However, univariable logistic regression did not indicate any particular variable as a predicting factor for downstaging. The analysis only showed that a palpable mass found during bimanual examination was a predictor of upstaging, with an OR 11.75 CI95% [2.49–55.32] (Table 2).

DISCUSSION

In bladder cancer, careful staging is indispensable for patient counseling and decision-making. Therefore, many authors tried to assess the discrepancy between clinical and pathological staging of bladder tumors. In previous reports, clinical staging usually consisted of bimanual examination, CT scan findings, previous TURB pathologic reports and was compared with the pathological evaluation of cystectomy specimens. The authors emphasized that discrepancies between cT-stage and pT-stage can have consequences for disease management and prognosis. Many of those studies included patients who received neoadjuvant treatment before cystectomy, which might have been the cause of discrepancy in staging [4, 5].

According to the literature, 20% of patients have primary tumors of muscle invasive nature ($\geq pT2$). Furthermore, more than 30% patients with recurrent bladder cancer can have progression to higher stage and approximately 10% of these recurrent tumor progress to MIBC [6, 7]. Therefore, early staging of bladder cancer invasiveness is very important for making further clinical decisions. In our study, the overall discrepancy between surgeon prediction and pathologic finding was only 12.2%. Nevertheless, most patients had superficial papillary tumors (pTa), which was 59%. Among patients with confirmed MIBC, the discrepancy in assessment increased to 25%. Furthermore, it is important to note that pathologic findings after radical cystectomy often do not correlate with staging based on TURB, which suggests that the discrepancy between clinical assessment performed at the time of TURB and pathological findings after radical treatment is much higher [4]. Despite these, potential differences in the final evaluation of patients with MIBC, we consider early clinical staging as a worthy and necessary part of BC

Table 2. Logistic regression analysis predictors of upstaging and downstaging

Variable	Upstaging		Downstaging	
	OR	p	OR	p
Age. Years	1.02	0.32	0.96	0.40
Gender: female vs. male	0.77	0.62	1.00	0.00
Bladder cancer history recurrent vs. primary	0.60	0.18	0.00	1.00
Number of tumors multiple vs. solitary	0.00	1.00	0.00	1.00
Hydronephrosis yes vs. no	1.31	0.81	0.00	1.00
Bimanual examination palpable vs. not palpable	11.75	0.00	0.00	1.00
Surgeon resident vs. urologist	0.54	0.23	2.03	0.44

OR – odds ratio

management. It might have influence on prognosis by planning in advance further treatment and shorten a delay to radical cystectomy. Many authors emphasized that the delay below three months significantly improved survival [8, 9, 10]. The best time for cystectomy is achieved more easily when the decision is made at the time of transurethral resection. Poletajew et al. showed that in provincial centres, the median time to cystectomy is shorter than in both university and regional centres [11]. It suggested that clinical assessment can be especially helpful in centres where a large number of patients were treated.

In our study most patients with discrepancy were overstaged (86.1%). Among patients with palpable masses, the percentage of overstaging was higher than in patients without palpable masses and estimated at 57% and 10.1% respectively. The European Urology Association recommends BP as an indispensable part of TURB [3]. Ploeg et al. studied the accuracy of clinical staging through BP. In this large study, which included 1409 patients with diagnosed MIBC, the authors found that pT-stage after cystectomy does not correlate with preoperative cT-stage based on BP. Total discrepancy was observed in 42% of patients. The authors indicated that downstaging was more frequent (31%), which is in contrast to our results [12]. This could be due to the timing of BP and the fact that in our study surgeons predicted only the muscle invasive character of the tumor, whereas Ploeg et al. considered their clinical assessment based on TNM classification. Furthermore, in our study overstaging of palpable masses was mainly observed in male patients. In this group of patients the bladder is more difficult to examine, particularly when the prostate is enlarged. Nonetheless, the dif-

ference in results between both studies suggests some caution in interpreting the outcome of BP. In another study performed by Mehrsai et al. the specificity of BP was 82%, although the sensitivity was only 46%. The authors examined 32 patients and in all cases BP was performed before radical treatment [13]. For a better estimation of the value of BP, more prospective studies should be performed.

We did not find a correlation between the presence of hydronephrosis and staging discrepancy. Odds ratio for overstaging and hydronephrosis was 1.31. This suggests a tendency to upstage when urinary obstruction was observed, although this was not statistically significant. Many previous publications indicated that hydronephrosis is associated with the muscle invasive character of the tumor. For instance Bartsch et al. or Haleblan et al. have proven that preoperative hydronephrosis is an independent prognostic factor for a high probability of advanced bladder tumours. Additionally, Bartsch et al. determined hydronephrosis as an independent prognostic marker for recurrence-free survival besides the pT classification and lymph node status in patients who underwent cystectomy [14, 15]. In our study, a lack of correlation between hydronephrosis and staging discrepancy suggests it as a valuable predictor factor at the time of TURB. In our study there was no difference in accuracy of clinical staging between urologists and urologists in training. A proper staging was observed in 90% of cases performed by residents. On the other hand, residents marked clinical staging only in 25% of all analyzed cases. These good results could be due to a proper clinical education system and following guidelines' advice. However, Ploeg et al. indicated the accuracy of clinical staging based on BP seems to be 5% higher in non-teaching hospitals compared with teaching hospitals. This was explained by the fact

that BP in the non-teaching hospitals was performed only by urologists instead of residents. Furthermore, in teaching hospitals, it is not certain that every outcome of BP performed by a resident is checked by a urologist [9].

The generally observed tendency towards upstaging in this study might be due to urologists' concern of mismatching the intraoperative staging, especially in muscle invasive tumor. In our analysis, surgeons preferred to upstage the assessment, especially when there was no suspicion of invasive or advanced tumor. There is no doubt that this study has several limitations such as retrospective analysis, a heterogenous group of surgeons, patients with different tumor history. Furthermore, bladder tumor resection was performed under white-light cystoscopy, when the usage of fluorescent cystoscopy enables the detection of non-visible cancers. However, in our point of view the study strongly suggests that the clinical assessment of the muscle invasive character of the tumor should be an obligatory part of endoscopic resection.

CONCLUSIONS

The study emphasized the high accuracy between clinical assessment at the time of transurethral resection and pathological report. This suggests that operator evaluation is useful for planning in advance the further stages of treatment. However, discrepancy was mostly observed in patients with pT1 and pT2 stage, therefore the choice of treatment has to be reevaluated after pathological examination. For surgeons the prediction of the character of the tumor was the easiest in patients with papillary tumors.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

References

1. Fradet Y. Screening for bladder cancer: the best opportunity to reduce mortality. *Can Urol Assoc J.* 2009; 3: S180-183.
2. Eble JN, Young RH. Carcinoma of the urinary bladder: a review of its diverse morphology. *Semin Diagn Pathol.* 1997; 14: 98-108.
3. Babjuk M, Böhle A, Burger M, et al. EAU Guidelines on Non-Muscle-invasive Urothelial Carcinoma of the Bladder: Update 2016. *Eur Urol.* 2017; 71: 447-461.
4. van Dijk PR, Ploeg M, Aben KK, et al. Downstaging of TURBT-Based Muscle-Invasive Bladder Cancer by Radical Cystectomy Predicts Better Survival. *ISRN Urol.* 2011; 2011: 458930.
5. McLaughlin S, Shephard J, Wallen E, Maygarden S, Carson CC, Pruthi RS. Comparison of the clinical and pathologic staging in patients undergoing radical cystectomy for bladder cancer. *Int Braz J Urol.* 2007; 33: 25-31.
6. Skinner DG, Lieskovsky G. Management of invasive and high-grade bladder cancer. In Skinner DG, Lieskovsky G, eds. *Diagnosis and Management of Genitourinary Cancer.* Philadelphia: Saunders, 1998; Chapt 16, pp. 295-312.
7. Kurth KH, Denis L, Bouffieux C, et al. Factors affecting recurrence and progression in superficial bladder tumours. *Eur J Cancer.* 1995; 31a: 1840-1846.
8. Gore JL, Lai J, Setodji CM, Litwin MS, Saigal CS. Mortality increases when radical cystectomy is delayed more than 12 weeks: results from a Surveillance, Epidemiology, and End Results-Medicare analysis. *Cancer.* 2009; 115: 988-996.
9. Chang SS, Hassan JM, Cookson MS, Wells N, Smith JA, Jr. Delaying radical cystectomy for muscle invasive bladder cancer results in worse pathological stage. *J Urol.* 2003; 170: 1085-1087.

10. Fahmy N, Aprikian A, Al-Otaibi M, et al. Impact of treatment delay in patients with bladder cancer managed with partial cystectomy in Quebec: a population-based study. *Can Urol Assoc J.* 2009; 3: 131-135.
11. Poletajew S, Lisinski J, Moskal K, et al. The time from diagnosis of bladder cancer to radical cystectomy in Polish urological centres- results of CysTiming Poland study. *Cent European J Urol.* 2014; 67: 329-332.
12. Ploeg M, Kiemeny LA, Smits GA, et al. Discrepancy between clinical staging through bimanual palpation and pathological staging after cystectomy. *Urol Oncol.* 2012; 30: 247-251.
13. Mehrsai A, Mansoori D, Taheri Mahmoudi M, Sina A, Seraji A, Pourmand GH. A comparison between clinical and pathologic staging in patients with bladder cancer. *Urol J.* 2004; 1: 85-89.
14. Bartsch GC, Kuefer R, Gschwend JE, de Petriconi R, Hautmann RE, Volkmer BG. Hydronephrosis as a prognostic marker in bladder cancer in a cystectomy-only series. *Eur Urol.* 2007; 51: 690-697.
15. Haleblan GE, Skinner EC, Dickinson MG, Lieskovsky G, Boyd SD, Skinner DG. Hydronephrosis as a prognostic indicator in bladder cancer patients. *J Urol.* 1998; 160: 2011-2014. ■