Short term complications from transurethral resection of bladder tumor

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Introduction: The diagnosis and subsequent management of bladder cancer often involves transurethral resection of bladder tumor (TURBT). Risks of TURBT include perioperative complications such as bleeding, pain and perforation. We aimed to determine TURBT complication rates and risk factors in a contemporary series.

Materials and methods: From 2002 to 2011, 505 patients underwent TURBT either for suspected bladder cancer or during follow up at a single institution. Baseline patient characteristics and complications within 2 weeks of surgery were extracted from the electronic medical record for all TURBTs. Patient and tumor characteristics were evaluated for associations with complication using univariate analysis. A multivariable logistic regression was fit to further examine associations between TURBT related characteristics and complication.

Results: A total of 910 TURBTs were performed on 505 patients. Overall complication rate was 8.1%. The most common complications were pain or spasm (3.0%), retention (2.8%), and infection (2.1%), and 0.5% of TURBTs had perforation. Over 85% of complications were Clavien-Dindo grade I or II. Forty-three patients had a complication after their first TURBT, while 25 had complications after subsequent TURBTs. Prior complication and single tumor, but not other patient or tumor-related characteristics, were associated with complication. Only prior complication (p < 0.01) was associated with subsequent complication after TURBT on multivariable analysis.

Conclusions: Complication rate after TURBT is 8.1% and complications are generally not severe in nature. Prior short term complication is likely associated with subsequent complication. Further studies are needed to validate these results and determine patient groups most at risk for intraoperative and post TURBT complications.

Key Words: postoperative complications, urinary bladder neoplasms

Introduction

Bladder cancer is the sixth most common cancer amongst US men and women.¹ An estimated 70% of

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new bladder cancer diagnoses are not invasive into the detrusor muscle (NMIBC) and are commonly managed using transurethral resection of bladder tumor (TURBT). After treatment, disease recurrence is common, and subsequent management often involves repeat TURBT if a new tumor or suspicious lesions are identified. While necessary for disease control, TURBT exposes patients to risks of intraoperative and perioperative complications.

Historically, reported rates of complication from TURBT ranged from 9.9%² to well over 25%.³ More recent series have shown complication rates of 4%-6%%, with lower rates of perforation and bleeding.^{4,5} Other common complications after TURBT include urinary retention and bladder pain or spasm. Data are limited

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regarding complications detected in the weeks following TURBT, as most prior series examine intraoperative and early complications following resection.

In terms of post TURBT complication prediction, tumor size and multifocality have previously been identified as risk factors.⁴ Additionally, analyses of large databases have shown that preoperative factors such as disseminated disease, weight loss, serum albumin, creatinine and functional status may be associated with complications.⁶ Improved knowledge of complication risk factors has the potential to impact preoperative counseling as well as intraoperative and postoperative decision making.

Therefore, using a retrospective cohort, our study aimed to determine rates of short term complications in a contemporary series. We examined both patient and tumor-related factors for associations with short term complications. We hypothesized that prior intervention may put patients at risk for additional complications.

Materials and methods

After obtaining IRB approval, we reviewed the charts of all patients who had an ICD-9 code related to bladder cancer or mass (57.33, 57.4, 188.0-188.9, 236.7, 233.7 or 223.3) or CPT code for bladder biopsy or TURBT (52204, 52224, 52234, 52235 or 52240) between January 1, 2002 and December 31, 2011. All patients who underwent TURBT were included in the study. In eligible patients, data was extracted related to patient and tumor characteristics, immediate perioperative intravesical treatment, and subsequent TURBT. We also extracted all data related to immediate complications and those that occurred within 2 weeks of surgery and defined these as "short term complications." Outside records scanned into the patient chart were also reviewed for the presence of prior complications. Patients were followed through January 1, 2013 and all subsequent TURBTs were recorded in a similar fashion. CPT codes from TURBT (52234, 52235, and 52240 for small, medium and large, respectively) were used to determine tumor size.

All complications were scored using the Clavien-Dindo system⁷ and included all scanned outside medical records and documented patient phone calls. A postoperative event had to fall within the Clavien-Dindo scoring system to count as a complication. For example, patients with bleeding may have simply called to inform their provider that bleeding was present; however, if no action was undertaken this was not counted as a complication. If a patient required a blood transfusion, it would be a grade II complication. A patient requiring both blood transfusion and operative intervention for clot evacuation would have

two complications and be graded as IIIb (indicative of their highest Clavien score).

Baseline patient characteristics and tumor characteristics were analyzed for univariate association with short term complication using the Wilcoxon test for continuous variables and Pearson chi squared test for categorical. Next, TURBT was isolated as a separate event and similar statistical tests were used to determine if tumor characteristics and/or previous complication was associated with complication after TURBT. A multivariable logistic regression was then fit to evaluate the independent effect of tumor number, grade, stage, size, prior complication and use of perioperative chemotherapy on complication risk.

Results

Out of 936 consecutive patients with the above-listed billing codes, 505 patients met the inclusion criteria and had at least one TURBT. Baseline patient characteristics and complication data are shown in Table 1. The median age was 69 years (IQR 60-74). Overall complication rate after individual TURBT was 8.1%. Forty-three patients (7.1%) within the cohort had a complication after their initial TURBT at our institution, while 25 (1.6%) had a short term complication after subsequent TURBT. Having a

TABLE 1. Baseline characteristics

Characteristic	Whole cohort
Patient age (median (IQR))	67 (60-74)
Sex (n) Male Female	392 (78%) 113 (22%)
Race (n) White Non-White	468 (94%) 31 (6%)
ASA class (n) 1 2 3 4	3 (1%) 103 (26%) 255 (65%) 30 (8%)
Smoking status (n) Ever smoker Never smoker	253 (70%) 152 (30%)
Complication (n) Yes No	43 (9%) 453 (91%)

TABLE 2. Individual transurethral resection of bladder tumors (TURBTs) characteristics by complication

Characteristic	All TURBTs	No complication	Complication	p value
Grade (n)				0.29
Low	409 (54%)	379 (55%)	30 (48%)	
High	348 (46%)	315 (45%)	33 (52%)	
Tumor number				< 0.01
Single	521 (58%)	466 (56%)	55 (74%)	
Multiple	385 (42%)	366 (44%)	19 (26%)	
Tumor stage				0.66
T0	106 (12%)	98 (12%)	8 (11%)	
Ta	593 (67%)	546 (67%)	47 (64%)	
Tis	17 (2%)	14 (2%)	3 (4%)	
T1	115 (13%)	106 (13%)	9 (12%)	
T2+	59 (7%)	52 (6%)	7 (9%)	
Tumor size				0.94
Small	181 (22%)	16 (22%)	15 (22%)	
Medium	450 (54%)	414 (54%)	36 (52%)	
Large	205 (22%)	187 (24%)	18 (26%)	
CIS				0.37
Yes	57 (9%)	50 (8%)	7 (12%)	
No	598 (91%)	546 (92%)	52 (88%)	
Perioperative intrave	esical chemotherapy			0.38
Yes	221 (37%)	203 (38%)	18 (32%)	
No	377 (63%)	338 (62%)	39 (68%)	
Resection within 8 w	eeks of prior TURBT			0.89
Yes	46 (5%)	42 (5%)	4 (5%)	
No	864 (95%)	794 (5%)	70 (95%)	
Complication prior t	o TURBT			< 0.01
Yes	91 (11%)	40 (5%)	57 (77%)	
No	813 (89%)	796 (95%)	17 (23%)	

complication with initial TURBT at our institution was associated with subsequent complication (p < 0.01).

Table 2 shows the characteristics of individual TURBT based on whether or not a short term

complication occurred. There were 910 total TURBTs on the 505 patients. Seventy-four (8.1%) of TURBTs resulted in at least one complication. Prior complication (p < 0.01) and single tumor (p < 0.01) were associated

TABLE 3. Multivariable logistic regression of post-transurethral resection of bladder tumor (TURBT) complications

Characteristic	Odds ratio	95% CI	p value
Tumor number (other:single)	0.78	0.27-2.27	0.65
Tumor grade (high:low)	0.93	0.29-2.96	0.90
Tumor stage (>Ta:Ta or lower)	0.89	0.20-4.03	0.88
Tumor size (small:med)	0.92	0.23-3.67	0.83
Tumor size (med:large)	0.68	0.19-2.35	0.83
Perioperative chemo (yes:no)	1.11	0.36-3.45	0.47
Prior complication	234.94	82.38-670.01	< 0.01

TABLE 4. Complication type (A) and severity (B)

A. Overall complication rate	n (9/)
Overall complication rate	n (%)
Infection	17 (2.1%)
Bleeding	8 (1.1%)
Perforation	4 (0.5%)
Pain/spasm	24 (3.0%)
Retention	22 (2.8%)
Other	14 (1.8%)
R	
B. Clavien-Dindo score	n (%)
2.	n (%) 33 (45.8%)
Clavien-Dindo score	, ,
Clavien-Dindo score	33 (45.8%)
Clavien-Dindo score I II	33 (45.8%) 30 (41.7%)
Clavien-Dindo score I II	33 (45.8%) 30 (41.7%) 0 (0%)
Clavien-Dindo score I II IIIa IIIIb	33 (45.8%) 30 (41.7%) 0 (0%) 6 (8.3%)

with complication after TURBT while tumor grade, stage, CIS, the use of perioperative chemotherapy and re-resection TURBT were not. Multivariable logistic regression accounting for tumor number, grade, stage and size, the use of perioperative intravesical chemotherapy, and the presence of prior complication showed that only prior complication (OR 234.94, 95% CI 82.38-670.01-, p < 0.01) was associated with short term complication, Table 3.

Table 4 shows complication types and Clavien-Dindo scoring of the highest complication present after TURBT. Complications were generally not severe in nature. The most common complications were pain or spasm (3.0%), retention (2.8%), and infection (2.1%). Four patients (0.5%) had a perforation, 87.5% of complications were Clavien-Dindo grade I or II. There were six grade III complications (8.3%), three grade IV complications (4.2%) and no grade V complications. Post TURBT complication management required only a phone call or prescription in 54.1% of the events.

Discussion

We analyzed a contemporary retrospective cohort to determine the incidence and severity of post TURBT complication. The complication rate was 8.1%, with the majority of them being Clavien-Dindo grade I or II.

We additionally examined TURBT related factors for association with short term complication. Having a prior short term complication after TURBT was found to be associated with short term complication after subsequent TURBT on both univariate and multivariate analysis. Additionally, individual patient complication occurring during the initial resection at our institution was associated with the same patient having a complication after subsequent TURBT. This suggests that prior complication, or some other patient or tumor related factor in patients who have previously suffered from a complication, may increase the risk of complication after TURBT.

It is encouraging that complications in this series, while somewhat common at 8.1% of TURBTs, are generally not severe in nature. Initial series examining post TURBT complications showed high rates of complication and increased severity. Dick et al examined 373 patients who underwent TURBT from 1931-1971, showing a 5% perforation rate and 24% rate of infection. There was also a 1.3% rate of perioperative mortality.3 Kondás and Szentgyörgyi reported on 1250 TURBTs at their institution from 1973-1990, showing a 9.9% complication rate, 3.8% perforation rate (0.4% intraperitoneal) and 0.8% mortality.² The series by Collado et al is the largest single institution cohort to date. They analyzed TURBTs completed in 2821 patients from 1979-1996 for superficial bladder cancer, 5.1% of patients had a complication, with a 2.8% rate of bleeding and a 1.3% rate of perforation.4 While our cohort showed a higher complication rate, their group did not include complications within 2 weeks of surgery. Additionally, our rates of significant bleeding were similarly low at 1.1%, and our rate of perforation was 0.5%. As such, these series represent gradual improvement in TURBT outcomes, which may be attributed to any number of factors, including equipment improvement, surgical education and evolution of technique. Our study may serve as a current benchmark of TURBT complications seen at an academic institution, from which further improvement may be measured. While complication rate determination is important, the ability to predict and potentially intervene on patients who are at highest risk of complication has greater potential to change daily clinical practice.

Multiple studies have identified risk factors for post TURBT complication. Collado et al found in their retrospective cohort that tumor size and number were associated with perioperative complication.⁴ Our study did not show a similar association with tumor size, though it did show that a lack of multifocality (ie. single tumor) was associated with short term

complication on univariate analysis. This may represent a new risk factor for complication; however, its lack of significance on multivariable analysis indicates that it is likely not associated. Regarding additional risk factors, studies using large databases have examined preoperative patient characteristics for association with post TURBT complications. Using the National Surgical Quality Improvement Program (NSQIP) database, Hollenbeck et al created a multivariable model of over 21,000 TURBTs which showed that disseminated disease, weight loss, low albumin, elevated creatinine, functional status and emergent case status were associated with complications (as well as 30 day and 90 day mortality).6 Furthermore, a recent study using the 2011 NSQIP database showed a close to 5% readmission rate after TURBT and higher rates of urinary tract infection and other complications in patients who were readmitted after urologic surgery.8 While our study is likely underpowered to detect many of the above risk factors, it is notable that, to our knowledge, previous complication has not been previously shown to be associated with short term TURBT related complication.

The mechanism explaining the association between prior complication and subsequent complication after TURBT is not clear. Patients may be at risk of complications due to their disease biology, inherent anatomy, underlying medical conditions or other unrelated factors. This observation may also be related to provider communication, counseling and patient understanding. As an example, it is known that health literacy plays a major role in healthcare disparities and cost⁹ and also can affect healthcare outcomes.¹⁰ Furthermore, our group previously found that poor health literacy is associated with minor, but not major, complications after radical cystectomy (unpublished data). Therefore, even though health literacy was not investigated in this cohort, it is feasible that patients with limited understanding of the disease, surgery, and/or expected post-operative course would have a heightened inclination to call or present due to pain, bleeding or other difficulties, especially since over 85% of the complications in our cohort were Clavien-Dindo grade I or II. Regardless of cause, if our finding is validated, prior complication may be an important predictor of subsequent post-operative events and has the potential to directly impact clinical care through modified pre-operative counseling, heightened operating room awareness or changes to postoperative monitoring.

Our study has several important limitations. First, it is a retrospective cohort and therefore represents the referral and practice patterns of a single institution and its respective faculty. Second, there is potential

selection bias in that patient complications were only detected if they re-presented to (or called) our institution within 2 weeks or if outside records were available in our system. This has potential to underestimate the complication rate, though likely does not underestimate the more severe complications that often require management at tertiary care facilities, regardless of their timing. Finally, our event rate is low, which may have led to a small sample size and a related inability to detect all important associations.

Strengths of our study include a large number of participants, thorough longitudinal data review to examine all subsequent complications and resections, and inclusion of patients who have had prior TURBT at an outside facility. We believe this serves to mirror "real world" practice patterns encountered at academic and large referral centers. Encouragingly, complication rates were relatively low including rates of infection, pain, bleeding and retention all at less than 3.0% and perforation less than 1%. While these rates may not be broadly applicable to all patients presenting for TURBT (particularly given our higher rate of complication with initial TURBT), they do represent a modern benchmark with which practicing clinicians and groups can compare personal outcomes. Finally, elucidation of prior complication as a risk factor for subsequent short term complication is a potentially important finding that has implications on subsequent patient management before, during and after TURBT.

Conclusions

In this study, we demonstrate that the short term complications rate within 2 weeks of TURBT is 8.1%. Complications were generally less severe than those seen in historical series. We also identified prior complication as a risk factor associated with subsequent short term TURBT related complication. Prospective studies are needed to validate this finding, though clinicians should be mindful of prior complication status when counseling and caring for patients in need of TURBT.

References

- Jemal A, Simard EP, Dorell C et al. Annual report to the nation on the status of cancer, 1975-2009, featuring the burden and trends in human papillomavirus (HPV)-associated cancers and HPV vaccination coverage levels. J Natl Cancer Inst 2013;105(3):175-201.
- Kondás J, Szentgyörgyi E. Transurethral resection of 1250 bladder tumours. Int Urol Nephrol 1992;24(1):35-42.

- 3. Dick A, Barnes R, Hadley H et al. Complications of transurethral resection of bladder tumors: prevention, recognition and treatment. *J Urol* 1980;124(6):810-811.
- Collado A, Chechile GE, Salvado J, Vincente J. Early complications of endoscopic treatment for superficial bladder tumors. *J Urol* 2000;164(5):1529-1532.
- Sugihara T, Yasunaga H, Horiguchi H et al. Comparison of perioperative outcomes including severe bladder injury between monopolar and bipolar transurethral resection of bladder tumors: a population-based comparison. *J Urol* 2014;192(5):1355-1359.
- Hollenbeck BK, Miller DC, Taub D et al. Risk factors for adverse outcomes after transurethral resection of bladder tumors. Cancer 2006;106(7):1527-1535.
- 7. Mitropoulos D, Artibani W, Graefen M et al. Reporting and grading of complications after urologic surgical procedures: an ad hoc EAU guidelines panel assessment and recommendations. *Eur Urol* 2012;61(2):341-349.
- 8. Rambachan A, Matulewicz RS, Pilecki M et al. Predictors of readmission following outpatient urological surgery. *J Urol* 2014;192(1):183-188.
- 9. Parker RM, Ratzan SC, Lurie N. Health literacy: a policy challenge for advancing high-quality health care. *Health Aff Proj Hope* 2003;22(4):147-153.
- 10. Schillinger D, Grumbach K, Piette J et al. Association of health literacy with diabetes outcomes. *JAMA* 2002;288(4):475-482.