Histology at transurethral resection of bladder tumor and radical cystectomy for bladder cancer: Insights from population-based data

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Introduction

Transurethral resection of bladder tumour (TURBT) is the definitive diagnostic procedure for bladder cancer. Pathological findings, including extent of disease (T stage), grade, and histology, dictate subsequent steps in management. Pathological review at TURBT is, therefore, crucial to guide management.[1]

Like any diagnostic biopsy, TURBT provides a limited pathological sample to characterize the extent and biological risk of bladder cancer. There is little published data about quality of reporting and concordance between TURBT and radical cystectomy (RC) in routine clinical practice. In this study, we compare pathological findings at TURBT with subsequent findings at RC among all patients treated in Ontario from 2009–2013.

Methods

This retrospective, population-based study reports timing and pathological concordance of TURBT and RC among all patients treated with RC in Ontario from 2009–2013. This is a substudy of a population-based, retrospective cohort study to describe management and outcome of urothelial carcinoma of the urinary bladder in the Canadian province of Ontario. Primary study results and methodology are reported elsewhere.[2,3] All incident cases of bladder cancer in Ontario in patients who underwent cystectomy from 2009–2013 were identified using the Ontario Cancer Registry (OCR) and linked to treatment records. Stage of disease was not routinely available in the existing data sources; for this reason, we obtained surgical pathology reports for all cystectomy cases. The study was approved by the research ethics board of Queen's University.

The OCR is a passive, population-based cancer registry that captures diagnostic and demographic information on at least 98% of all incident cases of cancer diagnosed in the province of Ontario (approximate population 13 500 000).[4,5] Records from the Canadian Institute for Health Information were used to identify those patients treated with RC. Surgical pathology reports were obtained from the OCR. A team of trained data abstractors reviewed the pathology reports and entered pathological variables into an electronic database, capturing stage as assigned by the pathologist. To be eligible for the current study, patients with RC were required to have a preceding TURBT pathology report available for review.

Results

Study population

From our database, we identified pathology reports for 1647 patients treated with RC. Among these cases, we were able to identify a preceding TURBT pathology report for 1580 (96%); this represents the study population. The characteristics of the study population are shown in Table 1. Two-thirds (1039/1580, 66%) of patients had muscle-invasive disease at TURBT immediately preceding RC.

At time of TURBT, 541 (34%) of patients had no evidence of invasion of muscularis propria and presumably received RC for high-risk pathological or clinical features. Among these 541 cases, at time of RC, 303 (56%) were upstaged to T2+ disease. Among 132 patients with carcinoma in situ (CIS) only at TURBT immediately prior to RC, 90 (68%) were found to have invasive carcinoma at RC. Similarly, 244 of 369 (66%) of cT1 cases were upstaged to >pT2 disease. Conversely, among the 1039 cases with T2+ disease at TURBT, 106 (10%) were down-staged to <T2 at time of RC.

Table 1. Demographic characteristics and pathologic findings at time of TURBT among patients with bladder cancer treated with cystectomy in Ontario from 2009–2013 (n=1580)

	n (%)**
Age (years)	
<50	52 (3)
50–60	252 (16)
61–70	480 (30)
70+	796 (50)
Gender	
Male	1209 (77)
Female	371 (24)
Histology	
Urothelial	1485 (94)
Squamous cell	40 (3)
Adenocarcinoma	23 (1)
Other histology*	32 (2)
LVI	
Yes	631 (40)
No	768 (49)
Unstated	181 (12)
Stage at TURBT	
TX	8 (<1)
Ta	92 (6)
Tis	72 (5)
T1	369 (23)
T2+***	1039 (66)

*Other includes sarcomatoid transitional cell carcinoma, carcinoma not otherwise specified (NOS), squamous cell carcinoma sarcomatoid, small cell carcinoma NOS, signet ring adenocarcinoma. **% may not add to 100% due to rounding. ***T2+ denotes T2, T3, and T4. LVI: lymphovascular invasion; TURBT: transurethral resection of bladder tumor.

The down-staging at the time of RC may be attributed to the TURBT or use of neoadjuvant chemotherapy (NACT). We have previously reported that 19% of patients with muscle-invasive bladder cancer in Ontario treated with RC during this time period received NACT.[6]

Histology at time of TURBT and RC indicate that 94% of the pathology reports at TURBT prior to RC in Ontario describe a urothelial cancer, although 231 (16%) of these with concomitant squamous differentiation. The overall rate of variant or divergent pathology beyond squamous differentiation abstracted for the TURBT pathology reports was 6%, and that for the RC reports was 6.8%. Patients with variant histology at TURBT were commonly re-classified at RC; 30% of patients with pure squamous-cell histology and 25% with adenocarcinoma were re-classified as urothelial cancer at time of RC.

Discussion

In this study, we explore histopathological findings at time of TURBT and subsequent cystectomy among 1580 patients treated in Ontario from 2009–2013. Several important findings have emerged. First, we find that in routine clinical practice, one-third of patients undergoing cystectomy had high-risk, non-muscle-invasive disease and two-thirds had muscle-invasive disease at time of TURBT. Second, we observe substantial upstaging at time of RC; 56% of patients with <T2 disease at TURBT are found to have T2+ disease at time of RC. Third, the rate of down-staging T2+ at TURBT to <T2 disease at RC (10%) was lower than expected.

Finally, we find that variant histology at TURBT is often re-classified as urothelial cancer at time of RC in routine care.

A discrepancy between the initial clinical T stage at TURBT and the final pathological stage is common, with both frequent under-staging (40–49%) and over-staging (22–27%).[7-10] These discrepancies can have consequences for management and may be secondary to various factors, including incomplete TURBT, limitations of conventional imaging, and prolonged wait times between TURBT and RC. In the present study, the accuracy of the upstaging findings is limited without knowledge of other clinical parameters, such as imaging. However, the apparent down-staging of only 10% is remarkable. In a similar population-based study from Europe, excluding patients that received neoadjuvant therapies, the down-staging rates were approximately 26%.[7] Although an explanation for this disparity in Ontario is not answerable from this study, one could hypothesize differences in bladder cancer management — aggressivity of TURBT, delayed diagnosis leading to higher-volume disease, and prolonged wait times — may play a role.

The large variation in the reported incidence of divergent differentiation at TURBT (7–81%) is likely due to differences in sampling and enhanced recognition of its importance in more contemporary series.[11] The reporting of variant pathology beyond squamous differentiation in routine care in Ontario appeared to be less common than previous studies, suggesting inconsistent recognition or reporting. Interestingly, when we further look at the discrepancy between TURBT and RC for academic vs. community hospitals, we observed that the rates of variant pathology for TURBTs were academic 10% vs. community 5% (p=0.0001), and the rates of variant pathology for RC were academic 11% vs. community 5% (p<0.0001).

Limitations

Our results should be considered in light of methodological limitations. This is a retrospective study and the pathological reports were not reviewed by central pathologists. Thus, we are evaluating the histopathological reporting without confirming quality assurance. Although the pathology database used in this study describes general aspects of disease for patients in the province, the data source detailing information related to neoadjuvant and adjuvant chemotherapy,

radiation and immunotherapy treatment was not linked to the pathology data collected and limits our ability to examine and evaluate survival outcomes. Furthermore, not having access to non-muscle-invasive bladder cancer intravesical therapy data, we were unable to determine whether or not there was upstaging among those patients who received intravesical bacillus Calmette-Guerin compared to those who did not for patients who underwent RC for <cT2 disease. However, because this is a population-based study aimed at elucidating practice patterns and outcomes in "the real world," with all these inherent limitations, it still offers important insight into care and outcomes in routine practice.

Conclusions

These data illustrate that in a substantial proportion of patients, the extent of disease and dominant histology at time to TURBT will be re-classified at RC. We also observe that the rate of down-staging observed in routine practice is lower than expected. The extent to which these findings reflect a differential treatment effect or inconsistent reporting is not clear. The results of our study lend further to the premise that TURBT and RC specimens be reviewed by a pathologist with expertise in urological cancer and further lends to the premise that synoptic reporting may play a role in the assessment and a more accurate reporting of variant pathology. Further work is necessary to better understand these apparent inconsistencies in an effort to improve the quality of care delivered to patients with bladder cancer in the general population.

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