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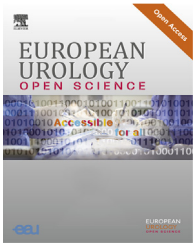

European Association of Urology

Brief Correspondence

Implementing a Checklist for Transurethral Resection of Bladder Tumor to Standardize Outcome Reporting: When High-quality Resection Could Influence Oncological Outcomes

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Article info

Article history:
Accepted September 6, 2022

Associate Editor:
M. Carmen Mir

Keywords:
Urothelial cancer
Endoscopy
Resection
Diagnosis
Treatment

Abstract

Several randomized controlled trials (RCTs) comparing en bloc resection of bladder tumor (ERBT) to conventional transurethral resection of bladder tumor (cTURBT) have reported controversial results. In particular, the 1-yr recurrence rate ranged from 5% to 40% for ERBT and from 11% to 31% for cTURBT. We provide an updated analysis of an RCT comparing the 1-yr recurrence rate for ERBT versus cTURBT for a cohort of 219 patients comprising 123 (56.2%) in the ERBT group and 96 (43.8%) in the cTURBT group. At 1 yr, 11 patients in the ERBT group and 12 in the cTURBT group experienced recurrence. The heterogeneity in recurrence observed in other RCTs could be explained by the scarce and heterogeneous adoption of tools and techniques that have been proved to lower the recurrence rate, supporting the need for implementation of a TURBT checklist. This prompted us to create a checklist of items for RCTs to standardize how TURBT is performed in trials, facilitate comparison between studies, assess the applicability of results in real-life practice, and provide a push towards high-quality resections to improve oncological outcomes. The checklist could have utility as a user-friendly guide for reporting TURBT procedures to improve our understanding of trials involving this procedure.

Patient summary: We compared the recurrence rate at 1 year for bladder cancer treated with two different approaches to remove bladder tumors in our center. The rates were comparable for the two groups. Other studies have found widely differing recurrence rates, so we propose use of a checklist to standardize these procedures and provide more consistent outcomes for patients.

Transurethral resection of bladder tumor (TURBT) is crucial in the management of non–muscle-invasive bladder cancer (NMIBC) as it defines the ideal postoperative management tailored according to the patient's risk group [1]. En bloc resection of bladder tumor (ERBT) was introduced in an attempt to provide higher-quality specimens, lower complication rates, and better oncological outcomes in comparison to conventional TURBT (cTURBT) [2]. Several randomized

https://doi.org/10.1016/j.euros.2022.09.025

controlled trials (RCTs) have reported controversial results; in particular, the 1-yr recurrence rate ranges from 5% to 40% for ERBT and from 11% to 31% for cTURBT (Table 1). BC recurrence after TURBT is a complex and multifactorial event, driven mainly by patient and tumor characteristics, but is significantly influenced by the strategy for care, and in particular the quality of the resection and the approaches used to reduce the risk of recurrence. In our recently published RCT comparing ERBT versus cTURBT [3], we found very high rates of detrusor muscle (DM) presence in specimens from both ERBT (95%) and cTURBT (94%). Subanalyses showed similar results in terms of oncological outcomes (3-mo recurrence-free survival) [3]. Here we update the oncologic outcomes for our series by providing 1-yr results for the EBRT and cTURBT groups.

This is an updated analysis of a single-center, prospective, noninferiority RCT of patients undergoing ERBT or cTURBT for BC [3]. Participants were enrolled between April 2018 and June 2021. Kaplan-Meier curves were used to illustrate recurrence-free survival. The log-rank test was used to assess univariable differences in recurrence-free survival according to the resection technique used. Statistical analyses were performed using R v4.1.3 (R Foundation for Statistical Computing, Vienna, Austria). All tests were two-sided, with the significance level set at $p < 0.05$.

A total of 248 patients were assessed for eligibility. Exclusion of patients diagnosed with cT0 ($n = 11$) or cT2 ($n = 11$) tumors or benign features ($n = 5$) and those with variant histology ($n = 2$) left a cohort of 219 patients, 123 (56.2%) in the ERBT group and 96 (43.8%) in the cTURBT group. Patients presenting with low-grade, high-grade, and CIS were 70 (56.9%), 49 (39.8%), and four (3.3%) versus 56 (58.3%), 37 (38.5%), and three (3.1%) for ERBT versus cTURBT, respectively. A total of 201 patients reached at least 1 yr of follow-up. The median follow-up for patients without recurrence was 19 mo (interquartile range 14–35). Fifty patients (29 in the ERBT group and 21 in the cTURBT group) experienced BC recurrence, of which 11 for ERBT and 12 for cTURBT occurred during the first year of follow-up. Kaplan-Meier analysis revealed 1-yr recurrence-free survival rates of 90.9% (95% confidence interval 0.859–0.962) for EBRT and 87% (95% confidence interval 0.804–0.942) for cTURBT ($p = 0.88$; Supplementary Fig. 1).

Since a low recurrence rate was observed for both techniques, we investigated what quality criteria could explain these results. The presence of DM is widely recognized as the main marker of resection quality and has the potential to independently predict early BC recurrence [4]. In the TURBT setting, several other factors decrease the risk of recurrence: photodynamic diagnosis [5], narrow band imaging [6], continuous saline bladder irrigation [7], postoperative single-shot instillation of mitomycin C (MMC) [8], and restaging TURBT [9]. Although there has been no clear demonstration to date, use of one, two, or more of these strategies could potentially provide the highest benefit in terms of recurrence-free survival. Limitations to underline, however, include the difficulty in accessing certain technologies (eg, no reimbursement for hexaminolaevulinic acid) and low surgeon adherence to recommendations (eg, low adoption of postoperative single-shot MMC instillation).

Considering the RCTs on EBRT published to date, adoption of these tools and approaches is poorly reported (Table 2). Thus, a possible reason for the heterogeneity in

Table 1 – Oncologic outcomes and inclusion/exclusion criteria for randomized controlled trials comparing ERBT versus cTURBT

Study	Patients		High grade, *n* (%)		RR at 12 mo (*n*)		Inclusion/exclusion criteria
	ERBT	cTURBT	ERBT	cTURBT	ERBT	cTURBT	
Liu 2013	64	56	7 (10.9)	5 (8.9)	7	6	Inclusion: papillary BC at cystoscopy with no extravesical extension, lymphatic metastasis, or invasion of adjacent organs apparent on imaging. Exclusion: urothelial papillomas, MIBC, CIS, or UTUC.
Zhang 2015	149	143	G2: 8 (5.4)	[G2] 8 (5.6)	46	45	Inclusion: primary single or multiple papillary BCs in the bladder with no UTUC abnormalities and absence of extravesical extension, lymph node metastasis, and adjacent organ invasion. Exclusion: biopsy-proven inverted papilloma.
Cheng 2018	95	98	40 (42.1)	48 (48.9)	3	15	Inclusion: primary NMIBC and ECOG score 0–1. Exclusion: recurrent NMIBC, MIBC, CIS, and pregnancy.
Balan 2018	45	45	–	–	7/41	11/40	Inclusion: papillary BC between 1 and 3 cm in diameter. Exclusion: solid sessile tumors, lesions located in the bladder neck area, and tumors involving the ureteral orifice.
Gakis 2020	56	59	G2: 25 (44.6)	G2: 23 (38.9)	19/48	11/49	Inclusion: newly diagnosed or recurrent BC on cystoscopy.
			G3: 9 (16)	G3: 17 (28.8)			Exclusion: tumor diameter ≤0.5 cm; clinically apparent MIBC; >5 tumor lesions; instillation therapy within the last 8 wk; tumors too extensive to resect and retrieve in one piece.
Razzaghi 2021	40	39	5 (12.5)	6 (15.4)	7	6	Inclusion: suspicious lesion on imaging. Exclusion: hydronephrosis and/or stage T3–4 BC on imaging; presence of CIS on cold-cup biopsy; UTUC; untreated urinary infection; recurrent BC; and tumor diameter >3 cm on cystoscopy.
Present series	123	96	53 (43.1)	40 (41.6)	11	12	Inclusion: primary or recurrent BC located anywhere in the bladder, with a maximum of three separated lesions and/or maximum size of 3 cm for each. Exclusion: preoperative evidence of MIBC, ureteral involvement, and/or nodal/metastatic extension of the disease.

ERBT = en bloc resection of bladder tumor; cTURBT = conventional transurethral resection of bladder tumor; RR = recurrence rate; BC =bladder cancer; NMIBC = non–muscle-invasive BC; MIBC = muscle-invasive BC; CIS = carcinoma in situ; UTUC = upper tract urothelial carcinoma; ECOG = Eastern Cooperative Oncology Group; CT = computed tomography.

Table 2 – Critical assessment of checklist item reported in available randomized controlled trials comparing en bloc resection and conventional transurethral resection of bladder tumor

Study	Enhanced tumor visualization	Completeresection	DM presence	Single-shot Early instillation	Irrigation	Second resection
Liu 2013	NR	NR	NR	NR	Yes	NR
Zhang 2015	NR	Yes	Yes	No	Yes	Yes
Cheng 2018	Yes (NBI)	Yes	NR	NR	Yes	Yes
Balan 2018	NR	NR	NR	NR	–	NR
Gakis 2020	Yes (PDD)	Yes	Yes	Yes	–	Yes
Razzaghi 2021	NR	Yes	NR	Yes	Yes	NR
Present series	No	Yes	Yes	Yes	Yes	Yes
EAU grade of recommendation	Weak	Strong	Strong	Weak	Not graded	Strong

Yes = used; No = not used; NR =not reported; DM = detrusor muscle; NBI = narrow-band imaging; PDD = photodynamic diagnosis; EAU = European Association of Urology.

BC recurrence among RCTs is the use, or not, of validated tools/approaches that have been proven to influence BC recurrence. Therefore, standardization for TURBT reporting is warranted to overcome this limitation. To this end, we propose adoption of a checklist of items comprising all the strategies that have been reported to lower the recurrence rate in NMIBC (Table 2).

Excellence should be encouraged even for procedures that may be perceived as trivial, such as TURBT, which remains the cornerstone of NMIBC management [10]. This checklist would be part of a larger effort to improve the reporting of various types of health research, similar to the Consolidated Standards of Reporting Trials (CONSORT) statement, which already uses a 25-point checklist to improve the quality of research used in health care decision-making. In the past, surgical checklists have been used to prevent errors and complications that may occur during surgery. The aim of our suggested TURBT checklist is to provide a consistent list of items for RCTs to standardize how TURBT is performed, thereby facilitating comparison across studies, increasing the applicability of results to real-life clinical practice, and providing a push towards high-quality resections to improve oncologic outcomes for patients. The checklist should also be used alongside consideration of other parameters outside the perioperative period that could also significantly influence the risk of recurrence, such as adjuvant instillation therapies according to the European Association of Urology risk groups (MMC and bacillus Calmette-Guérin). We believe that our TURBT checklist is a user-friendly guide for reporting TURBT interventions that can be used alongside other checklists. We believe that its use will enhance the understanding of trials involving TURBT.

Author contributions: Pietro Diana had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Diana, Breda, Baboudjian.
Acquisition of data: Diana, Gallioli, Fontanet, Izquierdo.
Analysis and interpretation of data: Diana, Gallioli, Verri, Sanguedolce.
Drafting of the manuscript: Diana, Uleri, Baboudjian, Territo.
Critical revision of the manuscript for important intellectual content: Gallioli, Rodriguez-Faba, Gaya.
Statistical analysis: Diana.
Obtaining funding: None.
Administrative, technical, or material support: Breda, Palou.
Supervision: Breda.
Other: None.

Financial disclosures: Pietro Diana certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2022.09.025.

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