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Review – Bladder Cancer

Repeat Transurethral Resection in Non–muscle-invasive Bladder Cancer: A Systematic Review

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Abstract

Context: Initial treatment for most bladder cancers (BCs) involves transurethral resection (TUR) or tumours. Often more cancer is found after the initial treatment in around half of patients, requiring a second resection. Repeat transurethral resection (reTUR) is recommended for high-risk, non–muscle-invasive bladder cancer (NMIBC) to remove any residual disease and improve cancer outcomes.
Objective: To systematically review the practice and therapeutic benefit of an early reTUR for high-risk NMIBC.
Evidence acquisition: A systematic review of original articles was performed using PubMed/Medline and Web of Science databases in December 2016 (initial) and October 2017 (final). We searched the references of included papers.
Evidence synthesis: We screened 15 209 manuscripts and selected 31 detailing 8409 persons with high-grade Ta and T1BC for inclusion. Detrusor muscle was found at initial TUR histology in 30–100% of cases. Residual tumour at reTUR was found in 17–67% of patients following Ta and in 20–71% following T1 cancer. Most residual tumours (36–86%) were found at the original resection site. Upstaging occurred in 0–8% (Ta to ≥T1) and 0–32% (T1 to ≥T2) of cases. Conflicting data report the impact of reTUR on subsequent recurrence and cancer-specific mortality. Recurrence for Ta was 16% in the reTUR group versus 58% in the non-reTUR group. For T1, recurrence ranged from 18% to 56%, but no clear trend was identified between reTUR and control. No clear relationship between reTUR and progression was found for Ta, although for T1 rates were higher in the non-reTUR group in series with control populations (5/6 studies). Overall mortality was slightly reduced in the reTUR group in two studies with controls (22–30% vs 26–36% [no reTUR]).
Conclusions: Residual tumour is common after TUR for high-risk NMIBC. The reTUR helps in the diagnosis of this residual cancer and may improve outcomes for cancers initially staged as T1.
Patient summary: Some bladder cancers (BCs) are aggressive but confined to the bladder surface. Initial treatment includes endoscopic resection. More cancer is found after the initial treatment in approximately half of patients. In the aggressive but confined group of BC, a second resection, a few weeks after the first, may help find this residual cancer and improve outcomes, although the evidence quality for this is weak.

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1. Introduction

Bladder cancer (BC) is the fourth commonest male malignancy worldwide [1] and one of the most expensive cancers to manage [2]. Initial treatment for most BCs involves transurethral resection (TUR) of tumours to remove all possible tumours and obtain material for histological examination. Following resection, patients are started on treatment pathways that reflect the nature and potential of their disease (typically determined by histological grade and tumour-node-metastasis stage). Treatment for primary high-risk non–muscle-invasive BCs (NMIBC), such as high-grade (HG) or grade 3, Ta, or T1 cancers, often commences with a repeat TUR (reTUR) of bladder tumours within 2–6 wk of initial resection [3]. A reTUR is recommended by the European Association of Urology (EAU) guidelines if the first resection was incomplete, if detrusor muscle was not present in the initial specimen, if the clinical suspicion is of worse disease than reported by the pathologist, or to ensure the absence of muscle invasion [4]. These scenarios are in consensus across the major international guideline panels (Table 1). The reTUR should remove any residual disease and resample the initial resection area. Residual tumour at reTUR has been described in up to 75% of Ta and T1 patients [5,6]. Even more profound is the rate of upstaging from Ta to ≥T1 or T1 to ≥T2 at reTUR, which has been observed in up to 28% of initial T1 [5,7] and 9.5% of initial Ta-HG tumours [8], respectively. This is even more striking in cases where muscularis propria is missing in the first transurethral resection of bladder tumour (TURBT) specimens; here, upstaging to muscle-invasive disease has been reported in up to 45% of T1 patients undergoing a reTUR [9]. The reTUR may also have a therapeutic role. It may increase recurrence-free (RFS) [10,11], progression-free (PFS) [10], cancer-specific (CSS), and overall (OS) survival [10] after intravesical Bacillus Calmette-Guérin (BCG) immunotherapy and provide valuable prognostic information [8].

However, recent studies have questioned the benefit of reTUR. These reports, including patients with T1BC treated with/without BCG (according to study), did not show any improvement in PFS and CSS of patients undergoing a reTUR when detrusor muscle was included in the primary TURBT [12,13]. These authors suggest that reTUR may not be necessary for this group of patients, if muscle was present in the primary TURBT.

The aim of this systematic review (SR) was two-fold. Patient Intervention Comparator Outcome (PICO) 1 was to evaluate the surgical practice of reTUR (including the presence of detrusor muscle in the primary resection), percentage of residual tumours found at reTUR (same site, different site, any site), and upstaging of disease pathology at reTUR. PICO 2 was to assess the therapeutic benefit of reTUR regarding disease recurrence, progression, OS, and CSS.

2. Evidence acquisition

2.1. Systematic review

We searched PubMed/Medline and Web of Science in December 2016 and again in October 2017, for all original articles, with no language or time limits applied. We used string terms “re”, “second”, “restaging”, “repeat”, “early” AND “transurethral resection”, “TUR”, “TURB”, “reTUR” AND “bladder” AND “cancer”, “tumor”, “tumour”, “neoplasm”, and “carcinoma” (Fig. 1). Manuscripts included were original articles investigating the role of reTUR and disease

Table 1 – Figure 1 ReTUR recommendations across guideline panels

Guideline body	Recommendation on suitable reTUR candidates	Level of evidence given	Major differences
EAU (European Association of Urology)	1. Incomplete initial TUR 2. No muscle in specimen with the exception of LG-Ta/Gl and primary CIS 3. T1 tumors.	All Grade A (Strong)	*Used as the reference standard*
AUA (American Urological Association)	1. Incomplete initial TUR 2. HG-Ta tumours 3. T1 tumours	1. Grade B (strong) 2. Grade C (moderate) 3. Grade B (strong)	No comment is made that HG-Ta tumours do not need reTUR if muscle is present in the initial TUR
NCCN (National Comprehensive Cancer Network)	1. Incomplete initial TUR 2. No muscle in initial TUR for HG disease 3. Large or multi-focal lesions 4. T1 tumours 5. Select HG-Ta especially if no muscle in initial TUR	All Strong	Include large or multi-focal lesions as a reason to re-resect. Doesn’t specifically mention CIS
CUA (Canadian Urology Association)	1. Incomplete initial TUR 2. T1 tumour in absence of muscle 3. Any HG or T1 tumour with benign muscle	1. Grade A 2. Grade A 3. Grade C	Recommend reTUR in T1 or HG-Ta where muscle is present and not malignant.
NICE (Natioanl Institue for Clinical Excellence)	1. All high-risk non-muscle invasive bladder cancer	1. Low	Does not specify whether presence of muscle changes the approach.
ICUD (International Consultation on Bladder Cancer) 2012	1. T1 tumours (regardless of the presence of muscle)	1.Strong	Does not specify whether presence of muscle changes the approach. Does not discuss HG-Ta tumours.

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