

Is the use of cold-cup biopsy necessary at the end of transurethral resection of bladder tumors?

Abstract

Objective: This study analysed the effects of cold-cup biopsy of resection base after TURBT on tumour staging and cancer outcome.

Methods: This was a retrospective study of newly diagnosed bladder cancer from January 2013 to August 2014 in a single institution, with a mean follow up of 18 months after initial cancer diagnosis. Exclusion criteria were known urothelial cancers or incomplete resection. We correlated clinic-pathological and tumour characteristics with rates of recurrence, progression and outcomes.

Results: Out of 75 patients, those with Ta, T1 and T2 urothelial carcinoma were 33, 30 and 12 respectively. During TURBT, detrusor muscle was seen in 31 main TURBT specimens and 47 separate deep cold-cup biopsy tissues. When deep cold-cup biopsy was performed, an additional 25.3% of patients (n=19) had detrusor muscle seen in the pathological report, 11 patients of the Ta/T1 cohort showed cancer in the biopsy and 1 of 75 patients was upstaged clinically from T1 to T2 disease.

Of the 11 patients in the Ta/T1 group with cancer seen in the deep specimen 4 had early recurrence or persistent tumor. Out of 48 negative cold-cup biopsy specimens, 5 had early recurrence on surveillance cystoscopy or persistent tumor during a relook TURBT. (p=0.042). Tumor size was not related to outcomes in this study.

Conclusion: Deep cold-cup biopsy improved availability and presence of detrusor muscle for pathological assessment. In the Ta and T1 patients, cancer found in the deep cold-cup biopsy increased rates of finding residual tumour and early tumour recurrence.

Keywords: bladder cancer, cup biopsy, deep biopsy, urothelial carcinoma; intravesical mitomycin, radical cystectomy, muscularis propria, muscularis mucosa

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Jegathesan Thiruchelvam, Kian Tai Chong
Department of Urology, Tan Tock Seng Hospital, Singapore

Correspondence: Jegathesan Thiruchelvam, Department of Urology, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore, 308433, Tel +65 62566011, Email thiruchelvam.jegathesan@mohh.com.sg

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Abbreviations: TURBT, transurethral resection of bladder tumor; TURIS, trans urethral resection in saline

Introduction

Bladder cancer is a significant cause of morbidity and mortality today. Histopathological staging^{1,2} and adequate tumor clearance is critical in prognosticating and assessing adequacy of treatment. Obtaining detrusor muscles during transurethral resection of bladder tumors (TURBT) is vital for cancer staging.³ Deep cold-cup biopsy at transurethral resection of bladder tumors (TURBT) is not a routine evidence-based practise, and its ability to obtain more accurate pathological staging is not conclusive. Superficial bladder cancer is now routinely treated with bladder preserving endourological surgery. Transurethral resection of bladder tumor (TURBT) is now the accepted modality of treating most forms of superficial bladder tumors. TURBT specimens are sent to the histopathologist piecemeal and staging and adequacy of tumor clearance is based upon this. Bladder cancers are often understaged or found to have persistent tumor during a first endoscopic resection of bladder tumors and hence a relook TURBT is recommended in higher risk bladder tumors.⁴ Various techniques have been described to obtain adequate depth of resection during a TURBT.⁵ The use of smoothelin has been described to distinguish between muscularis mucosae and muscularis propria.⁶ Reports of fractional resection of the tumor base for separate histopathological assessment have also been described.⁴ This study aims to investigate the necessity of a cold cup biopsy after a TURBT. In addition, we also aim to assess the usefulness of cold cup bladder biopsies to further

aid in the adequacy of TURBT, prognostication and staging of bladder cancers. Finally, we also aim to assess the safety of a bladder biopsy and assess for any complications that may arise due to the biopsy.

Methods

TURBTs in our institution are done by a specialist urology consultant or by a senior resident under the supervision of a consultant. Routine TURBT is conducted using a loop electrode with the TURIS resectoscope (Olympus) using bipolar energy. Patients are routinely paralysed or receive obturator blocks by the anaesthetist if the tumors are found to be located at the lateral wall. After resection of the tumor bulk is deemed to be adequate as judged by the surgeon a cold cup biopsy forceps is then used to take a sample representative of the base of the tumor. Haemostasis is then achieved by using a roller ball to diathermize the resected portion and surrounding area. Patients receive a dose of intravesical mitomycin C within 24 hours at a dose of 40mg diluted in 40ml of saline if resection is deemed complete and there are no complications such as perforation or excessive bleeding.

Institutional review board approval was obtained. This is a retrospective study conducted in a single centre. Patients who were newly diagnosed with primary urothelial carcinoma of the bladder between January 2013 to August 2014 with a mean follow up of 18 months after initial diagnosis were included in this study. Records were followed up until February 2016. Patients with pre-existing urothelial carcinoma, gross incomplete resection after the 1st TURBT and concurrent upper urothelial carcinoma were excluded from the study. Patient factors assessed were age, gender and duration of

follow up. Tumor factors studied included size of tumor, location of tumor, stage, grade, tumor recurrence and time to recurrence. Other histopathological factors studied relevant to this study include presence of both detrusor muscle and cancer in both the TURBT specimen and cup biopsy specimen. Intraoperative bladder perforation and the use of postoperative intravesical mitomycin were also documented. Primary outcome measured was the presence of detrusor muscle seen in the deep biopsy which was suggestive of the adequacy of the depth of the primary resection.¹ Secondary outcomes included assessment of the number of specimens which have been upstaged due to the deep biopsy, presence of tumor in the deep biopsy despite having nil tumor left behind visually during primary resection and recurrent rates in tumors. An early recurrence rate was defined as recurrence within 3 months from the initial TURBT. Statistical analysis was done using Fisher's test to analyse the difference between the groups using $p < 0.05$ as a cut off.

Histopathology of TURBT specimens were reported as per TNM staging by the pathologist. Histopathology for adequate muscle in the base was reported as present, absent or inconclusive. In this study

patients reported to have absent or inconclusive for muscularis propria in the base were categorized as not having muscle in the base.

Results

During the period of January 2013 to August 2014 75 cases of newly diagnosed primary urothelial bladder carcinoma were identified. Mean follow up duration was 18 months. Another 70 cases of TURBT were not included as they had a prior history of urothelial carcinoma. Table 1 shows the statistical breakdown of the cohort studied.

33, 30, and 12 patients were identified with Ta, T1, T2 urothelial carcinoma respectively by the histopathologist. During TURBT, detrusor muscle was reported present in 31 main TURBT specimens and 47 separate deep cold-cup biopsy specimens (Figure 1). When deep cold cup biopsy was performed an additional 25.3% of patients had detrusor muscle seen in the pathological report (Figure 2), 11 patients of the Ta/T1 cohort showed cancer in the deep biopsy and 1 of 75 patients was upstaged clinically from T1 to T2 disease. 6 patients in the Ta/ T1 group did not have follow up data and tumor follow up was not possible.

Table 1 The statistical breakdown of the cohort studied

	Average patient age(years)	Gender (%female)	% of High grade tumor	Size >3cm (%)	TURBT Specimen Presence of detrusor muscle (%)	Deep biopsy Presence of detrusor muscle (%)	Presence of tumor (%)
Ta	69.7	3	42.4	3	24	66.7	6
T1	71.2	16.7	100	40	40	50	23.3
T2	72.6	50	100	66.7	-	-	-

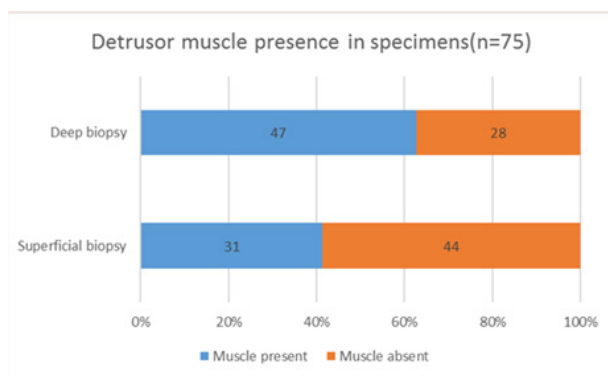


Figure 1 Comparison of presence of detrusor muscle.

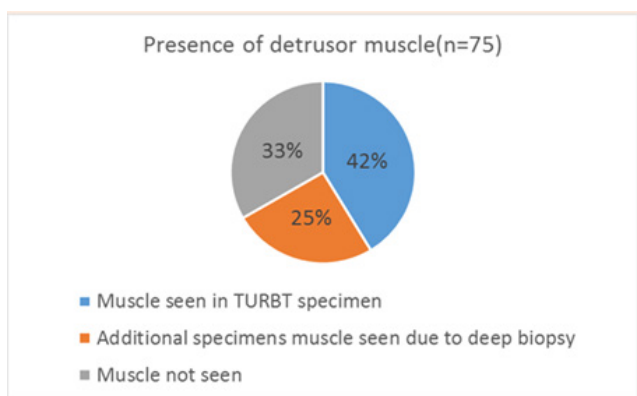


Figure 2 Additional benefit of cold cup biopsy in sampling detrusor muscle.

Of 9 patients in the Ta/T1 group with cancer seen in the deep specimen 4 had early recurrence. Out of 48 negative cold cup biopsy specimens 5 had early recurrence on surveillance cystoscopy or persistent tumor during a relook TURBT ($p = 0.027$) (Figure 3) Tumor size was not related to outcomes in this study.

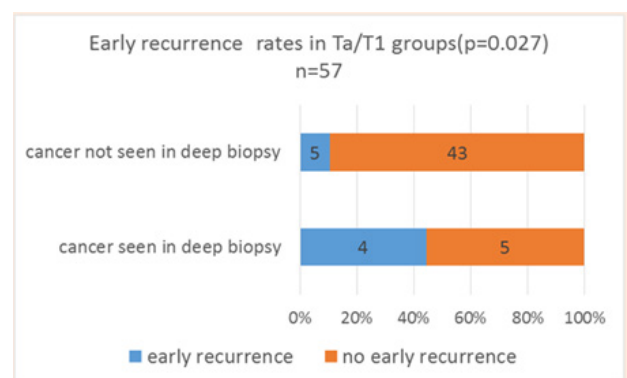


Figure 3 Early recurrence rates or persistence of disease in Ta/T1 groups.

Of the 12 patients with T2 disease 6 went on to have a radical cystectomy, 4 were diagnosed with metastases at diagnosis, 6 died during the follow up period of which 4 were due to metastases.

Of the 30 patients with T1 disease 3 had metastases at diagnosis. 1 patient underwent radical cystectomy, 6 died during the follow up period of which 4 were due to bladder cancer. 1 patient had an intraoperative perforation which was extraperitoneal and small and hence was managed with a catheter. This was not related to the deep cup biopsy and occurred during resection of the main tumor specimen.

Discussion

Cold cup biopsy of the base of the tumor is a routinely practised step in our institution at the end of the tumor resection. In this study we aimed to answer the few questions that were asked prior to the initiation of it. There are few studies which have documented and studied the use of a cold cup biopsy after the TURBT.

In our results we also encountered those who were inconclusive for muscle seen in the tumor base. There were 13 of such cases altogether. Perhaps use of different staining techniques may help to differentiate these specimens that truly lack detrusor muscle from those that do. In smaller specimens it may be technically challenging to differentiate muscularis propria from muscularis mucosa. Use of smoothelin has been described in the literature to aid in this.⁶

Also to note none of our cases of cold cup biopsy of the base were associated with thermal damage noted during histopathological review as compared to the other studies⁷ utilizing the loop electrode to take a sample which was noted in 20–40% of specimens. In the absence of use of electrical cutting energy for the deep biopsy the risk of bladder perforation remains low in our study due to the absence of the obturator jerk. In this study we were unable to assess for any benefit in survival or tumor progression in those with certain deep biopsy characteristics such as presence of detrusor muscle or absence of tumor in the deep biopsy due to the relatively short period of follow up and small numbers. Of significance this study has established that the use of a deep biopsy adds a valuable prognosticating factor which may help to predict the tumors with a higher risk of recurrence at 3 months as shown by those with tumor positivity at the base.

Conclusion

Deep cold cup biopsy improves the availability and presence of detrusor muscle for pathological assessment. In the Ta and T1 patients, cancer found in the deep cold cup biopsy increased rates of finding residual tumor and early tumor recurrence. It is also a safe procedure in our experience and we did not encounter any complications due to bladder biopsy in our centre. We would recommend that a deep cold cup biopsy is done at the end of TURBT to assess and prognosticate the tumor.

Disclosure

The above paper has been presented as a brief poster in the 14th Urological Association of Asia Congress 2016 Singapore, 20 - 24 July 2016 and the abstract for this poster has been published in the International Journal of Urology, Volume 23, Issue S1, July 2016.

Conflicts of interest

The author reports no other conflicts of interest in this work.

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