ORIGINAL PAPER

UROLOGICAL ONCOLOGY

Identification of potential prognostic factors for absence of residual disease in the second resection of T1 bladder cancer

Anna Katarzyna Czech[1], Katarzyna Gronostaj[1], Jakub Frydrych[1], Jakub Fronczek[2], Mikołaj Przydacz[1], Tomasz Wiatr[1], Łukasz Curyło[1], Przemysław Dudek[1], Jerzy Gąsowski[3], Piotr L. Chłosta[1]

[1]*Department of Urology, Jagiellonian University Medical College, Cracow, Poland*
[2]*Department of Intensive Care and Perioperative Medicine, Jagiellonian University Medical College, Cracow, Poland*
[3]*Department of Internal Medicine and Gerontology, Jagiellonian University Medical College, Cracow, Poland*

Citation: Czech AK, Gronostaj K, Frydrych J, et al. Identification of potential prognostic factors for absence of residual disease in the second resection of T1 bladder cance. Cent European J Urol. 2019; 72: 252-257.

Article history
Submitted: April 26, 2019
Accepted: Sept. 2, 2019
Published online: Sept. 16, 2019

Corresponding author
Anna Katarzyna Czech
Department of Urology
Jagiellonian University Medical College
18 Grzegórzecka Street
31-531 Cracow, Poland
phone: +48 12 424 79 50
anna.czech@gmail.com

Introduction The aim of this single centre retrospective study was to analyse the results of second resection (repeat transurethral resection of bladder tumour – reTURBT) after a macroscopically complete resection of T1 urothelial bladder tumour and to identify prognostic factors for absence of residual disease (T0) in the second resection of T1 bladder cancer.

Material and methods Patients with T1 bladder cancer diagnosed in a macroscopically complete initial resection who underwent second resection within 12 weeks were included into the retrospective analysis. Based on the presence or absence of residual disease, patients were grouped for further analysis. Univariate and multivariable logistic regressions were performed to identify potential prognostic factors.

Results Among the 139 patients who met the inclusion criteria, 96 (69.1%) had no residual disease (T0) and 43 (30.9%) had residual disease in the second resection (including muscle invasive bladder cancer in 2.2%). Adjusted odds ratios (OR) of T0 status obtained from the final model were as follows: detrusor muscle presence in the first resection (OR 3.05; 95% CI 1.12-8.35, p = 0.03), immediate post-operative intravesical mitomycin C administration after the first TURBT (OR 2.52, 95% CI 1.12–5.68; p = 0.03) and primary bladder cancer setting (OR 2.45, 95% CI 1.10–5.47; p = 0.03).

Conclusions Our results add evidence regarding the importance of detrusor muscle presence in the first TURBT. Identification of predictors of T0 status at second resection could help design prospective studies assessing the possibility to avoid re-resection in selected patients with T1 bladder cancer without compromising oncological outcomes.

Key Words: non-muscle invasive bladder cancer ‹› second look ‹› second TURBT ‹› transurethral resection

INTRODUCTION

Second resection (repeat transurethral resection of bladder tumour – reTURBT) in urothelial bladder cancer is advocated by major uro-oncological guidelines which recommend reTURBT in all T1 tumours [1, 2, 3]. The reasons for second resection include risk of residual disease and risk of upstaging to muscle invasive bladder cancer (MIBC) [1]. Moreover, some studies suggest improved outcomes regarding recurrences, progression and/or survival in patients undergoing reTURBT vs. no reTURBT, but these are not universal findings and strong evidence is lacking [4]. Despite the relative safety of reTURBT, additional surgery poses risk of complications, may delay adjuvant treatment and is associated with costs. A Ta high-grade (HG) tumour is no longer an indication for reTURBT in the European

Association of Urology (EAU) Guidelines [1], although some authors suggest that lack of clinical utility of reTURBT in this group should be revised [5]. The necessity of reTURBT in patients with T1 high-grade (HG)/grade 3 (G3) bladder cancer when detrusor muscle is present in the specimen from first TURBT has been questioned [6]. A few studies evaluated the prognostic value of tumour-free status in repeat resection and found that absence of residual tumour was associated with improved recurrence and progression outcomes in patients with high risk non-muscle invasive bladder cancer (NMIBC) [7, 8, 9].

Characterisation of patients without residual disease in the second resection could potentially help select the group in which this additional procedure could be avoided without compromising oncological outcomes. That would require building of a model based on predictive factors able to reliably select such group of patients and validation in studies focusing on long-term oncological outcomes.

In this single institution retrospective study, we aimed to analyse the results of second resection after macroscopically complete resection of T1 urothelial bladder tumours and to identify prognostic factors for absence of residual disease (T0) in the second resection of T1 bladder cancer.

MATERIAL AND METHODS

Patients

All patients with T1 urothelial bladder cancer operated between December 2012 and October 2018 in a single institution were included into retrospective analysis if they met the following criteria: 1) T1 urothelial bladder cancer diagnosed in a macroscopically complete transurethral resection of bladder tumour (TURBT) 2) second resection within 12 weeks. Exclusion criteria were: clinical suspicion of incomplete TURBT or suspicion of muscle invasive disease in the first TURBT (e.g. equivocal pathology).

Demographic, clinical and pathological data from the first TURBT together with timing and pathology results of the second resection were recorded.

Table 1. *Clinical and pathological characteristics of 139 patients with T1 bladder cancer*

Characteristic or finding	n (%)
Number of patients	139 (100%)
Age (median, interquartile range)	67 (61-75)
Gender	
Male	117 (84.2%)
Female	22 (15.8%)
Bladder cancer setting	
Primary	91 (65.5%)
Recurrent	48 (34.5%)
First TURBT performed by	
Resident	101 (72.7%)
Senior	38 (27.3%)
Tumor focality	
Solitary	68 (48.9%)
Multiple (>1)	66 (47.5%)
Unknown	5 (3.6%)
Tumor size (largest tumour diameter)	
<3 cm	67 (48.2%)
≥3 cm	56 (40.3%)
Unknown	16 (11.5%)
Immediate postoperative intravesical mitomycin C administration	
Yes	44 (31.7%)
No	95 (68.3%)
ISUP grade	
ISUP LG	74 (53.2%)
ISUP HG	64 (46.1%)
Unknown (G2)	1 (0.7%)
Lamina propria invasion	
Minimal	44 (31.7%)
Non-minimal	95 (68.3%)
Detrusor muscle presence in first TURBT	
DM present	96 (69.1%)
DM absent	43 (30.9%)
Carcinoma in situ	
CIS present	11 (7.9%)
Lymphovascular invasion	
LVI present	7 (5%)
Prostatic urethra involvement	
PUI present	10 (7.2%)
Time to second resection in weeks (median, interquartile range)	9 (7–12)
Time to second resection	
2–6 weeks	30 (21.6%)
7–12 weeks	109 (78.4%)

TURBT – transurethral resection of bladder tumor; ISUP – International Society of Urological Pathology; LG – low grade; HG – high grade; DM – detrusor muscle; CIS – carcinoma in situ; LVI – lymphovascular invasion; PUI – prostatic urethra involvement

Transurethral resection of bladder tumour

All TURBTs were performed in white light by senior urologists or by residents under senior's surveillance. Technique of TURBT and indications for random and prostatic urethral biopsies were consistent with the EAU Guidelines [1]. Data on tumour focality (solitary vs. multiple), tumour size (<3 cm vs. ≥3 cm) and information regarding completeness of resection were collected from the operative reports. Following TURBT, patients had continuous bladder irrigation with 0.9% saline until the next morning after surgery which is a routine practice in our Department, unless there was suspicion of bladder perforation. Immediate post-operative intravesical mitomycin C (40 mg) was administered

Table 2. *Pathological results of the second resection in 139 patients with T1 bladder cancer*

Residual disease	n (%)	Stage	n (%)	Residual tumours summary	n (%)	Residual disease summary	n (%)
No residual disease (T0)	96 (69.1%)	T0	96 (69.1%)	T0	96 (69.1%)	T0	96 (69.1%)
MIBC HG	3 (2.2%)	MIBC	3 (2.2%)	Residual tumours (MIBC/ T1/Ta/Tx)	40 (28.7%)	Residual disease (MIBC/ T1/Ta/Tx/ CIS)	43 (30.9%)
T1HG	10 (7.2%)	T1	20 (14.4%)				
T1HG+CIS	2 (1.4%)						
T1LG	8 (5.8%)						
TaHG	1 (0.7%)	Ta	10 (7.1%)				
TaHG+CIS	1 (0.7%)						
TaLG	7 (5.0%)						
Ta PUNLMP	1 (0.7%)						
TxHG NMI	2 (1.4%)	Tx	7 (5.0%)				
TxLG NMI	3 (2.2%)						
TxGx NMI	2 (1.4%)						
CIS alone	3 (2.2%)	CIS	3 (2.2%)	CIS	3 (2.2%)		

MIBC – muscle invasive bladder cancer; HG – high-grade; LG – low-grade; CIS – carcinoma in situ; PUNLMP – papillary urothelial neoplasm of low malignant potential; TxHG NMI – high-grade non-muscle invasive bladder cancer (lamina propria invasion not reported, no detrusor muscle invasion); TxLG – low-grade non-muscle invasive bladder cancer (lamina propria invasion not reported, no detrusor muscle invasion); TxGx NMI – papillary urothelial cancer with grade and lamina propria invasion not reported, no detrusor muscle invasion

at the discretion of the surgeon performing TURBT (based on clinical assessment of the tumour and past bladder cancer history, in patients without bladder perforation and without severe haematuria).

Pathology

Pathological assessment of the specimens was performed in the local pathology department using the 2009 and 2017 Tumour Node Metastasis (TNM) classification and the 2004 World Health Organization (WHO) / International Society of Urological Pathology (ISUP) classification (1973 WHO grading system was used additionally in some patients). No formal T1 substaging was applied. However, based on the description of lamina propria invasion, T1 tumours were categorised as either minimal (focal and/or superficial) lamina propria invasion T1 or non-minimal lamina propria invasion T1 tumours.

Second resection

Based on the time interval between first and second resection, patients were categorised as undergoing a re-TURBT within 2–6 weeks (time frame recommended by the EAU Guidelines) or 7–12 weeks after first resection. Second resection included any visible suspicious lesions and deep resection of the scar. Presence and type (stage, grade) of residual disease was recorded. On this basis, patients were grouped for further analysis.

Statistical analysis

To identify potential prognostic factors, patients were divided in two groups: no residual disease (T0) vs. residual tumours (MIBC, T1, Ta, unspecified NMIBC). Patients with carcinoma in situ (CIS) alone in the second resection who had CIS as a concomitant finding with T1 tumour in the first resection were excluded from further analysis, as CIS alone neither represents T0, nor residual tumour, but persistent disease which is considered non-resectable. We selected 3 variables for inclusion in the final multivariable logistic regression model based on clinical expertise and literature review after investigating univariate relations between each variable and the outcome.

Analyses were performed using Statistica software version 13 (TIBCO Software Inc. Palo Alto CA, USA). A p value <0.05 was considered statistically significant.

RESULTS

One hundred thirty-nine patients met the inclusion criteria of T1 bladder cancer diagnosed in a macroscopically complete TURBT and second resection within 12 weeks. Clinical and pathological characteristics of the entire cohort are presented in Table 1.

Detailed pathology results of the second resection are presented in Table 2. Overall, 96 (69.1%) patients had no residual disease and 43 (30.9%) had

Table 3. *Comparison of patients according to the absence or presence of residual tumours in the second resection and results of univariate analyses*

Second resection outcome in 136 patients (CIS alone in re-resection excluded)	T0	Ta / T1 / Tx NMI	MIBC	
	96 (70.6%)	37 (27.2%)	3 (2.2%)	
	No residual disease 96 (70.6%)	Residual tumours 40 (29.4%)		Univariate logistic regression
Age mean (SD) Median (IQR)	67 (9.9) 67 (61–75)	67.4 (10.1) 67 (62–74.5)		p = 0.8
Gender: male	80 (83.3%)	34 (85%)		p = 0.8
First TURBT primary (no bladder cancer history)	70 (72.9%)	19 (47.5%)		p = 0.005
Senior surgeon Resident	27 (28.1%) 69 (71.9%)	10 (25%) 30 (75%)		p = 0.7
Solitary tumour Multiple (>1) (5 unknown)	53 (57%) 40 (43%)	14 (36.8%) 24 (63.2%)		p = 0.04
Tumour size <3 cm ≥3 cm (16 unknown)	 51 (58.6%) 36 (41.4%)	 14 (42.4%) 19 (57.6%)		p = 0.1
Mitomycin C postoperative administration	38 (39.6%)	6 (15%)		p = 0.007
ISUP LG ISUP HG (1 unknown – G2)	56 (58.9%) 39 (41.1%)	18 (45%) 22 (55%)		p = 0.1
Minimal lamina propria invasion	30 (31.3%)	13 (32.5%)		p = 0.9
Detrusor muscle present in first TURBT	74 (77.1%)	20 (50%)		p = 0.002
CIS present	5 (5.2%)	3 (7.5%)		p = 0.6
LVI present	6 (5.3%)	1 (2.5%)		p = 0.4
Prostatic urethra involvement	4 (4.2%)	6 (15%)		p = 0.04
Time to second resection Median (IQR)	 9 (7–11)	 9 (7–11)		p >0.9
Time to second resection 2–6 weeks 6–12 weeks	 22 (22.9%) 74 (77.1%)	 7 (17.5%) 33 (82.5%)		p = 0.5

CIS – carcinoma in situ; Tx NMI – papillary urothelial cancer with lamina propria invasion not reported, no detrusor muscle invasion; MIBC – muscle invasive bladder cancer; SD – standard deviation; IQR – interquartile range; ISUP – International Society of Urological Pathology; HG – high-grade; LG – low-grade; CIS – carcinoma in situ; LVI – lymphovascular invasion

residual disease in the second resection, including MIBC in 3 (2.2%) and CIS alone in 3 (2.2%).

Patients with CIS alone in the second resection (all of whom had CIS as a concomitant finding with T1 tumour in the first resection) were excluded from further analysis leaving a total of 136 patients. Comparison of groups without residual disease (outcome of interest = T0, n = 96, 70.6%) and with residual tumours (n = 40, 29.4%; CIS alone excluded), as well as results of univariate regression analyses are presented in Table 3. Factors significantly associated with T0 status in univariate analyses were: first TURBT primary (no previous bladder cancer history, odds ratio [OR] 2.98; 95% confidence interval [CI] 1.38–6.41, p = 0.005), solitary tumour (vs. multiple, OR 2.27; 95% CI 1.05–4.94, p = 0.04), immediate post-operative intravesical mitomycin C administration after initial TURBT (OR 3.71; 95% CI 1.42–9.69, p = 0.007), detrusor muscle presence in first TURBT (OR 3.36; 95% CI 1.54–7.35, p = 0.002), and prostatic urethra involvement (PUI) presence (vs. PUI absence, OR 0.25; 95% CI 0.07–0.93, p = 0.04).

Adjusted estimates of effect of three variables selected for the final multivariable logistic regression model on T0 status were as follows: detrusor muscle presence in first resection (OR 3.05; 95% CI 1.12–8.35, p = 0.03), immediate intravesical mitomycin C administration after initial TURBT (OR 2.52, 95% CI 1.12–5.68; p = 0.03) and primary bladder cancer setting (OR 2.45, 95% CI 1.10–5.47; p = 0.03). Results of univariate and multivariable logistic regressions are presented in Table 4.

Table 4. *Results of univariate and multivariable logistic regression analyses (T0 status at second resection as the outcome of interest)*

Variable	Univariate analysis		Multivariable analysis	
	OR (95% CI)	p value	OR (95% CI)	p value
Detrusor muscle present in first TURBT (vs. muscle absent = reference)	3.36 (1.54–7.35)	0.002	3.05 (1.12–8.35)	0.03
Mitomycin C administration after first TURBT (vs. no mitomycin = reference)	3.71 (1.42–9.69)	0.007	2.52 (1.12–5.68)	0.03
Primary bladder cancer setting (vs. recurrent = reference)	2.98 (1.38–6.41)	0.005	2.45 (1.10–5.47)	0.03

OR – odds ratio; CI – confidence interval; TURBT – transurethral resection of bladder tumour

DISCUSSION

The main reasons for a second resection in T1 bladder cancer include risk of residual disease and risk of upstaging to MIBC [1]. Residual tumour and upstaging rates in our series are within ranges reported in the recent systematic review [4].

The percentage of patients with detrusor muscle present in the specimen from initial TURBT in our cohort was similar to contemporary series [4] suggesting comparable quality of resection, as muscle presence is considered a marker of quality in TURBT [10, 11]. Detrusor muscle presence in the first TURBT was an independent prognostic factor for the outcome of the second resection and was associated with 3 times higher odds of T0 status compared to the absence of detrusor muscle. In a large multicentre retrospective analysis of patients with T1HG/G3 tumours treated with Bacillus Calmette-Guérin (BCG), reTURBT had a positive impact on recurrence, progression, cancer-specific survival and overall survival only when muscle was not present in the specimen from the initial TURBT. The authors suggested that reTURBT could be avoided in patients with muscle present in the first TURBT [6].

Another independent prognostic factor for absence of residual disease was immediate post-operative intravesical mitomycin C administration. T1 bladder cancer is not an indication for single intravesical instillation; however, indications for immediate post-operative chemotherapy instillation are currently based on presumed oncological risk requiring clinical assessment of the tumour [1]. Our study reflects real life situations and our results underscore ablative effect of intravesical chemotherapy in T1 tumours.

Surprisingly, primary bladder cancer setting was another independent prognostic factor for T0 status. The intention of this study was to determine prognostic factors for a general T1 cohort. Hence, patients with recurrent bladder cancer were also included and represented one-third of the cohort. Our results suggest that if ever omitting reTURBT was to be considered, this should not be attempted in patients with recurrent T1 bladder cancer (history of any previous NMIBC).

In our study, one-third of patients had minimal lamina propria invasion, which is comparable to previously published data [12]. The prognostic importance of T1 substaging is currently investigated [13]. In our cohort, minimal lamina propria invasion was not associated with the second resection outcome, supporting previous findings [12].

Most patients underwent second resection beyond the time frame recommended by the EAU Guidelines and this may result in inferior oncological outcomes [14, 15]. Due to the retrospective study design, specific reasons for delayed reTURBT could not be determined. Nevertheless, in our analysis, we did not find sufficient evidence to conclude that the time to second resection was associated with the presence of residual tumour in re-resection.

Several studies assessed risk factors for residual disease in the second resection. Most of these studies focused on either unselected NMIBC populations (Ta and T1 [16, 17]) or on selected populations of patients with T1HG/G3 tumours [18, 19]. Moreover, studies differed in other inclusion criteria (e.g. completeness of first TUR and/or detrusor muscle presence) [20, 21]. Substantial variability in risk factors reported in different studies and lack of their reproducibility might reflect not only different populations and methodologies but also might be the effect of heterogeneous surgical techniques, and in general underline the complex nature of bladder cancer. Furthermore, studies assessing the influence of reTURBT on oncological outcomes give inconsistent results and prospective studies in this field are almost lacking [4, 22]. All these uncertainties, taken together, make potential selection of patients in which reTURBT could be safely avoided challenging.

Limitations of this study include its retrospective design and a small cohort. Most patients underwent second resection beyond the time frame recommended

by the EAU Guidelines. Other clinical outcomes (recurrence, progression and survival) were not assessed in the current analysis because of the immaturity of the data.

CONCLUSIONS

Our results add evidence regarding the importance of detrusor muscle presence in the first TURBT. Identification of predictors of T0 status at second resection could help design prospective studies assessing the possibility to avoid reTURBT in selected patients with T1 bladder cancer. These studies should take into consideration long term oncological outcomes.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

References

1. Babjuk M, Burger M, Compérat E, et al. EAU Guidelines on Non-muscle-invasive Bladder Cancer (TaTa and CIS). European Association of Urology Web site. https://uroweb.org/wp-content/uploads/EAU-Guidelines-Non-muscle-invasive-Bladder-Cancer-TaT1-CIS-2018.pdf. Accessed December 2018.

2. Chang SS, Boorjian SA, Chou R, et al. Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline. American Urological Association Web site. https://www.auanet.org/documents/education/clinical-guidance/Non-Muscle-Invasive-Bladder-Cancer.pdf. Accessed December 2018.

3. NCCN Clinical Practice Guidelines in Oncology. Bladder Cancer. v.1.2019. National Comprehensive Cancer Network Web site. https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed January 2019.

4. Cumberbatch MGK, Foerster B, Catto JWF, et al. Repeat transurethral resection in non-muscle-invasive bladder cancer: a systematic review. Eur Urol. 2018; 73: 925-933.

5. Dangi AD, Kumar RM, Kodiatte TA, et al. Is there a role for second transurethral resection in pTa high-grade urothelial bladder cancer. Cent European J Urol. 2018; 71: 287-294.

6. Gontero P, Sylvester R, Pisano F, et al. The impact of re-transurethral resection on clinical outcomes in a large multicentre cohort of patients with T1 high-grade/Grade 3 bladder cancer treated with bacille Calmette-Guerin. BJU Int. 2016; 118: 44-52.

7. Guevara A, Salomon L, Allory Y, et al. The role of tumor-free status in repeat resection before intravesical bacillus Calmette-Guerin for high grade Ta, T1 and CIS bladder cancer. J Urol. 2010; 183: 2161-2164.

8. Bishr M, Lattouf JB, Latour M, Saad F. Tumour stage on re-staging transurethral resection predicts recurrence and progression-free survival of patients with high-risk non-muscle invasive bladder cancer. Can Urol Assoc J. 2014; 8: E306-E310.

9. Sanseverino R, Napodano G, Campitelli A, Addesso M. Prognostic impact of ReTURB in high grade T1 primary bladder cancer. Arch Ital Urol Androl. 2016; 88: 81-85.

10. Herr HW, Donat SM. Quality control in transurethral resection of bladder tumours. BJU Int. 2008; 102: 1242-1246.

11. Mariappan P, Zachou A, Grigor KM. Detrusor muscle in the first, apparently complete transurethral resection of bladder tumour specimen is a surrogate marker of resection quality, predicts risk of early recurrence, and is dependent on operator experience. Eur Urol. 2010; 57: 843-849.

12. Audenet F, Retinger C, Chien C, et al. Is restaging transurethral resection necessary in patients with non-muscle invasive bladder cancer and limited lamina propria invasion? Urol Oncol. 2017; 35: 603.e1-603.e5.

13. Fransen van de Putte EE, Otto W, Hartmann A, et al. Metric substage according to micro and extensive lamina propria invasion improves prognostics in T1 bladder cancer. Urol Oncol. 2018; 36: 361.e7-361.e13.

14. Baltaci S, Bozlu M, Yildirim A, et al. Significance of the interval between first and second transurethral resection on recurrence and progression rates in patients with high-risk non-muscle-invasive bladder cancer treated with maintenance intravesical Bacillus Calmette-Guerin. BJU Int. 2015; 116: 721-726.

15. Krajewski W, Zdrojowy R, Dembowski J et al. The optimal timing of restaging resection before introduction of Bacillus Calmette-Guerin immunotherapy in patients with high-risk non-muscle-invasive bladder cancer. Urol Int. 2019; 102: 60-68.

16. Kamiya N, Suzuki H, Suyama T, et al. Clinical outcomes of second transurethral resection in non-muscle invasive high-grade bladder cancer: a retrospective, multi-institutional, collaborative study. Int J Clin Oncol. 2017; 22: 353-358.

17. Zapała P, Dybowski B, Poletajew S, Białek L, Niewczas A, Radziszewski P. Clinical rationale and safety of restaging transurethral resection in indication-stratified patients with high-risk non-muscle-invasive bladder cancer. World J Surg Oncol. 2018; 16: 6.

18. Süer E, Özcan C, Baltaci S, et al. Time between first and second transurethral resection of bladder tumors in patients with high-grade T1 tumors: Is it a risk factor for residual tumor detection? Urol Int. 2013; 91: 182-186.

19. Ferro M, Di Lorenzo G, Buonerba C, et al. Predictors of residual T1 high grade on re-transurethral resection in a large multi-institutional cohort of patients with primary T1 high-grade/grade 3 bladder cancer. J Cancer. 2018; 9: 4250-4254.

20. Yucel M, Hatipoglu NK, Atakanli C, et al. Is repeat transurethral resection effective and necessary in patients with T1 bladder carcinoma? Urol Int. 2010; 85: 276-280.

21. Türk H, Ün S, Isoglu CS, et al. Factors that predict residual tumors in re-TUR patients. Afr J Urol. 2016; 22: 67-70.

22. Divrik RT, Sahin AF, Yildirim U, Altok M, Zorlu F. Impact of routine second transurethral resection on the long-term outcome of patients with newly diagnosed pT1 urothelial carcinoma with respect to recurrence, progression rate, and disease-specific survival: a prospective randomised clinical trial. Eur Urol. 2010; 58: 185-190.