Published in final edited form as:

Urol Oncol. 2017 October ; 35(10): 603.e1–603.e5. doi:10.1016/j.urolonc.2017.06.042.

Is restaging transurethral resection (TUR) necessary in patients with non-muscle invasive bladder cancer (NMIBC) and limited lamina propria invasion?

François Audenet^{a,*}, Caitlyn Retinger^{a,*}, Christine Chien^b, Nicole E. Benfante^a, Bernard H. Bochner^a, S. Machele Donat^a, Harry W. Herr^a, and Guido Dalbagni^a

^aUrology Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, USA

^bDepartment of Epidemiology - Biostatistics, Memorial Sloan Kettering Cancer Center, New York, USA

Abstract

Objectives—To evaluate the influence of lamina propria invasion type at initial transurethral resection (TUR) on re-staging pathology.

Materials and Methods—We reviewed prospectively-maintained records of all patients with a high-grade pT1 non-muscle invasive bladder cancer (NMIBC) who underwent both initial and restaging TUR within 6 weeks at our center between 2001 and 2016. The pathology of second TUR specimens was analyzed with regard to the characteristics of lamina propria invasion found at initial resection.

Results—We included 198 patients, with a median age of 70 years (interquartile range: 63–79). Muscle was present in the initial TUR specimen in 107 patients (54%). Pathology restaging was pT0 in 73 patients (37%), pTis in 44 (22%), pTa in 27 (14%), pT1 in 50 (25%) and pT2 in 4 (2%). Eighty-seven patients (44%) had tumors with minimal lamina propria invasion at initial TUR: 53 specimens (27%) had focal invasion (few malignant cells in the lamina propria); 15 specimens (7.6%) had superficial invasion (invasion of the lamina propria to the level of the muscularis mucosae (T1a)); and 19 specimens (10%) had multifocal superficial invasion (multiple areas of T1a). Of the patients with minimal lamina propria invasion, residual disease was found in 54 patients (62%). However, none of those patients had T2 disease.

Corresponding author: Guido DALBAGNI, MD, Urology Service, Department of Surgery, Kimmel Center for Prostate and Urologic Cancers, Memorial Sloan Kettering Cancer Center, 353 E. 68th Street – New York, NY 10065 – USA, Tel: +1-646-422-4394, Fax: +1-212-988-0760, dalbagni@mskcc.org.

*François Audenet and Caitlyn Retinger contributed equally to this manuscript

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflicts of interest: none

Conclusions—A significant number of patients with T1 tumors have residual disease at restaging TUR as do patients with minimal lamina propria invasion. The extent of T1 invasion doesn't eliminate the need for repeat TUR.

Keywords

bladder cancer; urothelial carcinoma; transurethral resection; diagnosis; prognosis

Introduction

Urothelial carcinoma of the bladder affects more than 430,000 people worldwide each year, of which 75% have non-muscle invasive bladder cancer (NMIBC) confined to the mucosa (Ta or carcinoma in situ (CIS)) or lamina propria (T1) but not involving the muscularis propria [1]. Although these tumors are grouped under the heading of NMIBC, nearly all T1 tumors are high grade and have the potential to progress to muscle invasion and extravesical dissemination [2]. These high-risk NMIBC are often understaged by initial resection, with a risk of muscle-invasive disease detected by second resection from 4% to 25% [3]. It has been demonstrated that a second transurethral resection (TUR) plays a role in diagnosis, prognosis and treatment [4]. For these reasons, both the American Urological Association (AUA) and the European Association of Urology (EAU) guidelines recommend performing a second TUR for high-risk NMIBC [4,5].

Substaging of T1 tumors has been investigated to improve prognostic classification. In a recent meta-analysis, the depth of lamina propria invasion was shown to be the most prognostic factor in T1 NMIBC [6]. In this study, tumors with lamina propria invasion beyond the muscularis mucosae had an increased hazard for progression three-times greater than tumors with minimal involvement of the lamina propria. However, the influence on the re-staging pathology of lamina propria invasion type found at initial TUR has never been evaluated. In order to assess the benefit of a systematic second look, this study analyzed the results of a second TUR for T1 NMIBC with regard to the characteristics of lamina propria involvement at the time of the initial resection.

Materials and Methods

An institutional board-approved, retrospective review of the institutional database was performed to identify patients with clinical T1 (cT1) urothelial carcinoma of the bladder and no prior history of urothelial carcinoma, who underwent both an initial TUR and a re-staging TUR at our center. Diagnosis of cT1 disease was based on cystoscopy, bimanual examination, radiographic tests and pathologic evaluation. All tumors were staged according to the TNM 2009 system of the International Union Against Cancer and graded according to the World Health Organization / International Society of Urological Pathology 2004 grading system.

All pathology specimens were initially reviewed by a dedicated uro-pathologist. The characteristics of lamina propria invasion were assessed to distinguish minimal invasion from non-minimal invasion of the lamina propria. Minimal invasion of the lamina propria included: focal invasion, defined as few malignant cells in the lamina propria; superficial

invasion, defined as invasion of the lamina propria to the level of the muscularis mucosae (T1a); and multifocal superficial invasion, defined as multiple areas of T1a. All other types of invasions into or beyond the muscularis mucosae were categorized as non-minimal.

Intravesical therapy was not administered after the first TUR. The second TUR was performed within 6 weeks after the first one. During the second TUR, all visible tumors and previous resection scars were resected. Residual tumor was defined as restaging higher than pT0. The pathology of the second TUR was analyzed with regard to the characteristics of the initial resection.

We used Fisher's exact and chi-squared tests to examine the relationship between depth of tumor invasion at initial TUR and presence of residual disease, with $p < 0.05$ considered to be significant. We also used chi-squared tests to study the association between residual disease and presence of muscle tissue in the initial TURB. All analyses were performed using Stata 13 (StataCorp, College Station, TX).

Results

We identified 198 patients with initial cT1 disease who underwent a re-staging TUR within 6 weeks of their initial surgery from 2001 to 2016 (Table 1). The patients' median age was 70 years (interquartile range: 63 – 79 years) and 74% of the sample was male. Initial TUR was macroscopically complete in all cases. All pT1 tumors were high grade and muscle was present in the initial TUR specimen in 107 patients (54%). Eighty-seven patients (44%) had tumors with minimal lamina propria invasion at initial TUR: 53 specimens (27%) contained focal invasion, 15 specimens (7.6%) had superficial invasion and 19 specimens (10%) had multifocal superficial invasion.

Pathology restaging was pT0 in 73 patients (37%), pTis in 44 (22%), pTa in 27 (14%), pT1 in 50 (25%) and pT2 in 4 (2%). Muscle was identified in 168 specimens (85%). Overall, 125 patients (63%) had residual disease. Of those with minimal lamina propria invasion, residual disease was found in 54 patients (62%); however, none of those patients had T2 disease (Table 2). There was no significant difference in the risk of residual disease according to lamina propria invasion type at initial TUR (Table 3). The presence of muscle in the initial staging specimens was significantly associated with fewer incidences of residual disease (Table 3). However, 21 patients (52%) with minimal lamina propria invasion and presence of muscle at initial TUR still had residual disease at restaging, including 6 patients (15%) whose tumors were pT1 at restaging.

Discussion

TUR is a crucial procedure in the diagnosis and treatment of NMIBC. A complete and correctly performed TUR is essential to achieve good prognosis: a significant risk for residual tumor after initial TUR of T1 lesions has been demonstrated [7]. In our study, we found that only 37% of the patients were pT0 at restaging and 27% had pT1 or above residual disease, including 2% who had muscle-invasive disease. These patients with unexpected residual disease would have risked progression while on BCG. Many studies have reported that around 50% of patients newly diagnosed with cT1 tumors presented with

residual tumor at restaging TUR within 6 weeks after initial resection (Table 4) [8–20]. According to a meta-analysis conducted by Vianello et al, the residual rate at second TUR is 47% (95% CI = 0.41–0.53) [21]. Furthermore, the likelihood that muscle-invasive disease is detected by repeat resection of an initially T1 tumor ranges from 4% to 25%; if no muscle is present in the initial resection, the risk increases to 45% [3]. This risk increased to 50% in some radical cystectomy series, although these studies only enrolled selected patients [22]. Based on these findings, various guidelines strongly recommend a second TUR for patients newly diagnosed with cT1 tumors [4,5]. A restaging TUR has 4 objectives: diagnostic, therapeutic, prognostic and predictive. Indeed, it has been demonstrated that a second TUR can increase recurrence-free survival, provide prognostic information, and predict outcomes after BCG treatment [23,24].

In the EORTC risk tables, the T1 high-grade tumors do poorly, with 1- and 5-year disease progression rates of 11.4% and 19.8%, respectively [2]. However, cT1 tumors are heterogeneous with respect to recurrence and prognosis. Some tumors have the potential to progress to muscle-invasive or metastatic disease and these patients should be identified as candidates for aggressive treatment with early cystectomy. Additional prognostic factors have been described in selected patient populations. Female sex, age, tumor size, concomitant CIS and CIS in the prostatic urethra are important prognostic factors in T1 patients treated with BCG [25]. In a recently published international, multicentric, retrospective study, re-TUR in the presence of muscle in the primary specimen didn't improve the outcomes, and re-TUR in the absence of muscle had a borderline significant positive impact on time to recurrence, time to progression, overall survival and cancer specific survival [20]. However, in a randomized study, patients with T1 disease at first TUR had a two-fold increased risk of recurrence and a four-fold increased risk of progression when re-TUR was not done [23].

Aiming to risk stratify T1 bladder cancers, several substaging systems have been proposed. In particular, the extent of the lamina propria invasion has been investigated. Several reports have explored the utility of examining invasion of the muscularis mucosae (MM) layer to substage pT1 tumors. The T1a/T1b/T1c system holds prognostic value for progression and disease-specific survival. T1a indicates invasion up to the MM; T1b, invasion into the MM; and T1c, invasion beyond the MM. The meta-analysis performed by Martin-Doyle et al based on 1,431 patients identified depth of invasion into lamina propria (T1b/c) as the risk factor with the highest impact: they found a progression hazard ratio [HR] = 3.34 ($p < 0.001$) and a cancer-specific survival HR = 2.02 ($p < 0.001$) [6]. In a prospective study, pT1 substaging was used to determine the indication of re-TUR after BCG [26] and in multivariate analysis, substaging, CIS and tumor size were significant predictors of progression. Recent evidence suggests that histopathologic classification into T1a and T1b can be translated into a molecular signature, reflecting progressive dysregulation and resulting in more invasive stages [27]. However, the main problem with this system is the lack of consensus regarding identification of the MM at the point of invasion of the tumor, causing a variable substaging rate (58–100%). Reasons for the variation may include the difference in quality of TUR, damage to the lamina propria by previous TUR, and intravesical treatment.

However, even when minimal invasion of the lamina propria is identified, residual tumor is frequently discovered at restaging TUR. In our series, residual disease was found in 60% of patients who had focal invasion at initial TUR, which is similar to findings in tumors with superficial invasion (60%), multifocal superficial invasion (69%) or non-minimal invasion (64%). Different patterns of T1 tumors may affect margins of resection and consequently residual tumor left behind after initial TUR [3]. Some tumors have broad-front invasion whereas other present tentacular invasion, requiring removal of not only the visible epithelial portion of tumors, but also the invisible microscopic mucosal or invasive tumor, including deep muscle [3]. Therefore, because the type of lamina propria invasion remains unpredictable during TUR, we suggest that all T1 tumors should undergo restaging TUR, even if the initial specimen presents with minimal invasion.

In order to optimize TUR, photodynamic diagnosis (PDD) including fluorescence cystoscopy and narrow-band imaging has demonstrated a better sensitivity than conventional procedures for the detection of tumors [28]. A meta-analysis by Burger et al reported an increase in detection of tumor lesions and an absolute reduction of 11% in recurrence rates within 12 months [29]. However, the benefit on progression rate and survival remains to be demonstrated and no data is available regarding the rate of residual tumor at restaging within 6 weeks.

A potential limitation of this study is its retrospective design. We focused our study on limited invasion of the lamina propria, including focal invasion, superficial invasion, and multifocal superficial invasion. We didn't specifically analyze other prognostic factors such as multifocality, tumor size, CIS or smoking status, nor the effects on long-term recurrence and progression rate. Although all the specimens were reviewed by a dedicated uro-pathologist, the description of the type of lamina propria invasion didn't use the previously published substaging systems. Furthermore, the presence of muscle reported at initial TUR was surprisingly low (54%) and may have multifactorial explanations, including perioperative visibility, surgical technique and pathological analysis. However, the low rate of pT2 at restaging (2%) with good muscle representation (85%) can be considered a marker of the quality of the initial resection. Finally, the aim of this study was to answer to a simple, clinically-relevant question: does limited invasion of the lamina propria reduce the need for restaging TUR? The answer is no, and a second resection should be performed every time an invasive tumor is diagnosed, due to the high risk of residual disease.

Conclusions

A significant number of patients with T1 tumors have residual disease at restaging TUR. This is not any different among patients with minimal lamina propria invasion. We suggest that the extent of T1 invasion doesn't eliminate the need for repeat TUR, for diagnostic, therapeutic, prognostic and predictive purposes. Subsequent treatments depend on the quality of the information provided by re-staging TUR. Molecular profiling of NMIBC for tailored treatment would then be the next step forward.

References

1. Burger M, Catto JWF, Dalbagni G, Grossman HB, Herr H, Karakiewicz P, et al. Epidemiology and risk factors of urothelial bladder cancer. *Eur Urol.* 2013; 63:234–41. DOI: 10.1016/j.eururo.2012.07.033 [PubMed: 22877502]
2. Cambier S, Sylvester RJ, Collette L, Gontero P, Brausi MA, van Andel G, et al. EORTC Nomograms and Risk Groups for Predicting Recurrence, Progression, and Disease-specific and Overall Survival in Non-Muscle-invasive Stage Ta-T1 Urothelial Bladder Cancer Patients Treated with 1–3 Years of Maintenance Bacillus Calmette-Guérin. *Eur Urol.* 2016; 69:60–9. DOI: 10.1016/j.eururo.2015.06.045 [PubMed: 26210894]
3. Herr HW, Donat SM. Quality control in transurethral resection of bladder tumours. *BJU Int.* 2008; 102:1242–6. DOI: 10.1111/j.1464-410X.2008.07966.x [PubMed: 19035888]
4. Babjuk M, Böhle A, Burger M, Capoun O, Cohen D, Compérat EM, et al. EAU Guidelines on Non-Muscle-invasive Urothelial Carcinoma of the Bladder: Update 2016. *Eur Urol.* 2016; :1–15. DOI: 10.1016/j.eururo.2016.05.041
5. Chang SS, Boorjian SA, Chou R, Clark PE, Daneshmand S, Konety BR, et al. Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline. *J Urol.* 2016; 196:1021–9. DOI: 10.1016/j.juro.2016.06.049 [PubMed: 27317986]
6. Martin-Doyle W, Leow JJ, Orsola A, Chang SL, Bellmunt J. Improving selection criteria for early cystectomy in high-grade t1 bladder cancer: a meta-analysis of 15,215 patients. *J Clin Oncol.* 2015; 33:643–50. DOI: 10.1200/JCO.2014.57.6967 [PubMed: 25559810]
7. Brausi M, Collette L, Kurth K, van der Meijden AP, Oosterlinck W, Witjes JA, et al. Variability in the recurrence rate at first follow-up cystoscopy after TUR in stage Ta T1 transitional cell carcinoma of the bladder: a combined analysis of seven EORTC studies. *Eur Urol.* 2002; 41:523–31. [PubMed: 12074794]
8. Klän R, Loy V, Huland H. Residual tumor discovered in routine second transurethral resection in patients with stage T1 transitional cell carcinoma of the bladder. *J Urol.* 1991; 146:316–8. [PubMed: 1856924]
9. Herr HW. The value of a second transurethral resection in evaluating patients with bladder tumors. *J Urol.* 1999; 162:74–6. DOI: 10.1097/00005392-199907000-00018 [PubMed: 10379743]
10. Brauers A, Buettner R, Jakse G. Second resection and prognosis of primary high risk superficial bladder cancer: is cystectomy often too early? *J Urol.* 2001; 165:808–10. [PubMed: 11176474]
11. Schips L, Augustin H, Zigeuner RE, Gallé G, Habermann H, Trummer H, et al. Is repeated transurethral resection justified in patients with newly diagnosed superficial bladder cancer? *Urology.* 2002; 59:220–3. [PubMed: 11834389]
12. Schwaibold HE, Sivalingam S, May F, Hartung R. The value of a second transurethral resection for T1 bladder cancer. *BJU Int.* 2006; 97:1199–201. DOI: 10.1111/j.1464-410X.2006.06144.x [PubMed: 16566814]
13. 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; 58:185–90. DOI: 10.1016/j.eururo.2010.03.007 [PubMed: 20303646]
14. Ali MH, Ismail IY, Eltobgy A, Gobeish A. Evaluation of second-look transurethral resection in restaging of patients with nonmuscle-invasive bladder cancer. *J Endourol.* 2010; 24:2047–50. DOI: 10.1089/end.2010.0319 [PubMed: 20929433]
15. Yucel M, Hatipoglu NK, Atakanli C, Yalcinkaya S, Dedekarginoglu G, Saracoglu U, et al. Is repeat transurethral resection effective and necessary in patients with T1 bladder carcinoma? *Urol Int.* 2010; 85:276–80. DOI: 10.1159/000316073 [PubMed: 20733272]
16. Katumalla FS, Devasia A, Kumar R, Kumar S, Chacko N, Kekre N. Second transurethral resection in T1G3 bladder tumors - Selectively avoidable? *Indian J Urol.* 2011; 27:176–9. DOI: 10.4103/0970-1591.82833 [PubMed: 21814305]

17. Takaoka E-I, Matsui Y, Inoue T, Miyazaki J, Nakashima M, Kimura T, et al. Risk factors for intravesical recurrence in patients with high-grade T1 bladder cancer in the second TUR era. *Jpn J Clin Oncol*. 2013; 43:404–9. DOI: 10.1093/jjco/hyt016 [PubMed: 23444116]
18. Lazica DA, Böttcher S, Degener S, Rundstedt von F-C, Brandt AS, Roth S, et al. [T1 high-grade bladder cancer - value of second operation with prognostic parameters of first operation: analysis of 167 cases]. *Aktuelle Urol*. 2013; 44:124–8. DOI: 10.1055/s-0033-1334962 [PubMed: 23580383]
19. Shim JS, Choi H, Noh TI, Tae JH, Yoon SG, Kang SH, et al. The clinical significance of a second transurethral resection for T1 high-grade bladder cancer: Results of a prospective study. *Korean J Urol*. 2015; 56:429–34. DOI: 10.4111/kju.2015.56.6.429 [PubMed: 26078839]
20. Gontero P, Sylvester R, Pisano F, Joniau S, Oderda M, Serretta V, et al. The impact of retransurethral resection on clinical outcomes in a large multicentre cohort of patients with T1 high-grade/Grade 3 bladder cancer treated with bacille Calmette-Guérin. *BJU Int*. 2016; 118:44–52. DOI: 10.1111/bju.13354 [PubMed: 26469362]
21. Vianello A, Costantini E, Del Zingaro M, Bini V, Herr HW, Porena M. Repeated white light transurethral resection of the bladder in nonmuscle-invasive urothelial bladder cancers: systematic review and meta-analysis. *J Endourol*. 2011; 25:1703–12. DOI: 10.1089/end.2011.0081 [PubMed: 21936670]
22. Fritsche H-M, Burger M, Svatek RS, Jeldres C, Karakiewicz PI, Novara G, et al. Characteristics and outcomes of patients with clinical T1 grade 3 urothelial carcinoma treated with radical cystectomy: results from an international cohort. *Eur Urol*. 2010; 57:300–9. DOI: 10.1016/j.eururo.2009.09.024 [PubMed: 19766384]
23. Divrik RT, Yildirim U, Zorlu F, Ozen H. The effect of repeat transurethral resection on recurrence and progression rates in patients with T1 tumors of the bladder who received intravesical mitomycin: a prospective, randomized clinical trial. *J Urol*. 2006; 175:1641–4. DOI: 10.1016/S0022-5347(05)01002-5 [PubMed: 16600720]
24. Sfakianos JP, Kim PH, Hakimi AA, Herr HW. The effect of restaging transurethral resection on recurrence and progression rates in patients with nonmuscle invasive bladder cancer treated with intravesical bacillus Calmette-Guérin. *J Urol*. 2014; 191:341–5. DOI: 10.1016/j.juro.2013.08.022 [PubMed: 23973518]
25. Gontero P, Sylvester R, Pisano F, Joniau S, Vander Eeck K, Serretta V, et al. Prognostic factors and risk groups in T1G3 non-muscle-invasive bladder cancer patients initially treated with Bacillus Calmette-Guérin: results of a retrospective multicenter study of 2451 patients. *Eur Urol*. 2015; 67:74–82. DOI: 10.1016/j.eururo.2014.06.040 [PubMed: 25043942]
26. Orsola A, Werner L, De Torres I, Martin-Doyle W, Raventós CX, Lozano F, et al. Reexamining treatment of high-grade T1 bladder cancer according to depth of lamina propria invasion: a prospective trial of 200 patients. *Br J Cancer*. 2015; 112:468–74. DOI: 10.1038/bjc.2014.633 [PubMed: 25535728]
27. Descotes F, Dessen P, Bringuier PP, Decaussin M, Martin PM, Adams M, et al. Microarray gene expression profiling and analysis of bladder cancer supports the subclassification of T1 tumours into T1a and T1b stages. *BJU Int*. 2014; 113:333–42. DOI: 10.1111/bju.12364 [PubMed: 24053469]
28. Mowatt G, N'dow J, Vale L, Nabi G, Boachie C, Cook JA, et al. Photodynamic diagnosis of bladder cancer compared with white light cystoscopy: Systematic review and meta-analysis. *Int J Technol Assess Health Care*. 2011; 27:3–10. DOI: 10.1017/S0266462310001364 [PubMed: 21262078]
29. Burger M, Grossman HB, Droller M, Schmidbauer J, Hermann G, Dr goescu O, et al. Photodynamic diagnosis of non-muscle-invasive bladder cancer with hexaminolevulinate cystoscopy: a meta-analysis of detection and recurrence based on raw data. *Eur Urol*. 2013; 64:846–54. DOI: 10.1016/j.eururo.2013.03.059 [PubMed: 23602406]

Highlights

- Minimal lamina propria invasion doesn't reduce the risk of residual disease.
- Residual disease can be found even if muscle was present at initial specimen.
- The extent of T1 invasion doesn't eliminate the need for repeat TUR.

Table 1

Patient and TUR characteristics

Variables	N=198
Median age, years (interquartile range)	70 (63–79)
Male	146 (74%)
Muscle present in TUR 1	107 (54%)
<i>TUR 1 Lamina Propria Invasion:</i>	
Focal Invasion	53 (27%)
Superficial Invasion	15 (7%)
Multifocal Superficial Invasion	19 (10%)
Non-minimal invasion	111 (56%)
Muscle present in TUR 2	168 (85%)
<i>TUR 2 Pathology:</i>	
pT0	73 (37%)
pTis	44 (22%)
pTa	27 (14%)
pT1	50 (25%)
pT2	4 (2%)

Table 2

Pathology of repeat TUR specimens, stratified by invasion type at initial TUR

Pathology at repeat TUR	Invasion type at initial TUR			
	Non-minimal invasion N=111 (56%)	Minimal invasion		
		Focal Invasion N=53 (27%)	Superficial Invasion N=15 (7%)	Multifocal Superficial Invasion N=19 (10%)
pT0	40 (36%)	21 (40%)	6 (40%)	6 (31%)
pTis	22 (20%)	15 (28%)	4 (27%)	3 (16%)
pTa	15 (13%)	4 (8%)	1 (6%)	7 (37%)
pT1	30 (27%)	13 (24%)	4 (27%)	3 (16%)
pT2	4 (4%)	0 (0%)	0 (0%)	0 (0%)

Table 3

Presence of residual disease in the restaging specimen according to lamina propria invasion type and according to the presence of muscle at initial TUR

	Residual disease	No residual disease	<i>p</i>
Minimal lamina propria invasion	54 (62%)	33 (38%)	0.74
Non-minimal lamina propria invasion	71 (64%)	40 (36%)	
Presence of muscle	62 (57%)	47 (43%)	0.04
No muscle	63 (71%)	26 (29%)	

Table 4

Pathological results of restaging TUR for T1 NMIBC at initial resection

Study	N	Residual tumor	Muscle invasion	Delay after initial TUR (weeks)
Klän et al. 1991 ⁸	46	43%	2%	1–2
Herr et al. 1999 ⁹	58	78%	28%	4–6
Brauers et al. 2001 ¹⁰	42	64%	5%	4–6
Schips et al. 2002 ¹¹	76	33%	8%	4–6
Schwaibold et al. 2006 ¹²	136	52%	10%	4–6
Divrik et al. 2010 ¹³	105	33%	8%	2–6
Ali et al. 2010 ¹⁴	91	67%	26%	2–6
Yucel et al. 2010 ¹⁵	33	35%	11%	3–6
Katumalla et al. 2011 ¹⁶	50	36%	4%	4–6
Takaoka et al. 2013 ¹⁷	73	51%	4%	< 12
Lazica et al. 2013 ¹⁸	167	58%	7%	4–6
Shim et al. 2015 ¹⁹	29	76%	10%	3–8
Gontero et al. 2016 ²⁰	935	71%	Excluded	4–6
Present study	198	63%	2%	< 6