African Journal of Urology (2016) **22**, 67–70

African Journal of Urology

Official journal of the Pan African Urological Surgeon's Association
web page of the journal

www.ees.elsevier.com/afju
www.sciencedirect.com

Uro-oncology
Original research

Factors that predict residual tumors in re-TUR patients

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Received 9 April 2015; received in revised form 9 June 2015; accepted 2 July 2015
Available online 30 November 2015

KEYWORDS
Bladder tumor;
Transurethral resection;
Complete resection;
Multifocal

Abstract
Introduction: The first and foremost rule in the treatment of superficial bladder cancer is correct and complete resection of the tumor. Histopathological analysis of the resected tumor will help to define the correct tumor stage, thus delaying or, ideally, avoiding tumor recurrence and progression.
Objectives: To examine the prognostic factors for residual tumors in the tumor base or in another area of the bladder in patients subjected to repeat transurethral resection (re-TUR).
Patients and methods: Between September 2009 and August 2014, 188/221 patients advised to undergo re-TUR for stage T1 tumors were subjected to the procedure. The following data were collected for this retrospective study: patients' age and sex, information on whether initial TUR was carried out for a primary tumor/primary tumors, tumor number, tumor size and tumor grade, as well as information on whether muscularis propria was found in the resected specimens of initial TUR, whether there was carcinoma in situ and whether single-dose intracavitary chemotherapy was administered following initial TUR.
Results: On re-TUR, new tumors outside of the previous resection area were found in 34 (18%) and residual tumors in the initial resection area in 48 (25.5%) patients. 61.7% of the patients diagnosed with new tumors outside of the previous tumor area and 62.5% of those with residual tumors in the initial resection area had initially undergone TUR for multifocal tumors. Both univariate and multivariate analysis revealed a significant relationship between male sex, multifocal primary tumors and the detection of residual tumors in the previous resection area during re-TUR.

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Peer review under responsibility of Pan African Urological Surgeons' Association (PAUSA).

http://dx.doi.org/10.1016/j.afju.2015.07.004

Conclusion: For the reasons mentioned above, we believe that re-TUR will influence the treatment strategies and have an impact on T1-tumor progression, especially with regard to multifocal tumors.

Introduction

The gold standard in the diagnosis and treatment of bladder cancer is transurethral resection (TUR). The first and the foremost rule in the treatment of superficial bladder cancer is the correct and complete resection of the tumor [1,2]. Histopathological analysis of the resected tumor will help to correctly define the tumor stage, and therefore delay and even avoid tumor recurrence and progression. Guidelines published by the European Association of Urology (EAU 2014) suggest repeat TUR (re-TUR) in all high-grade T1 and selected high-grade Ta tumors [3–5]. During re-TUR, microscopic and/or macroscopic residual tumors can be identified in the initial resection area or new areas. For the detection of residual tumors, the grade, stage, size and number of the initial tumor(s) is important [4–7]. It is known that residual tumors diagnosed during re-TUR may be due to technical insufficiency or to the fact that they have been overlooked during initial TUR [5,8–12]. Another important factor is the grade of tumor invasion [5,8–12]. In this study, we aimed to examine the prognostic factors for residual tumor detection in the tumor base or in another area in patients subjected to re-TUR.

Patients and methods

In this retrospective study, we reviewed the data of 1021 patients who underwent TUR for superficial bladder tumors between 2009 and 2014. As a routine practice in our clinic we perform a second TUR in patients with T1 tumors, regardless of the pathological grade, multiplicity or recurrence factor. 221 patients were advised to have re-TUR for T1 tumors. Of these, 18 refused re-TUR, 8 were subjected to radical cystectomy due to widespread tumors, 3 had a high anesthesia risk and 4 were lost to follow-up after initial TUR. Thus, 33 patients were excluded from the study, leaving a total of 188 patients subjected to re-TUR.

Initial TUR was done using standard 30° and 70° optic lenses for cystoscopy. Using a hot loop, all the visible tumors were excised with either en-bloc or graded resection, depending on the tumor size. The resected tumors as well as the tumor bases were sent for histopathological assessment. Patients with T1 pathology results were scheduled for re-TUR within a 4–6 week period from initial TUR. 96 patients scheduled for re-TUR received single-dose intracavitary chemotherapy following the initial operation. 92 patients with postoperative hematuria were not eligible for single-dose intracavitary chemotherapy. The patients were called 2 weeks after initial TUR to review their histopathological results and to discuss further treatment which was planned according to the pathology results.

During re-TUR, all visible tumors were resected. Afterwards, the areas of initial TUR were also resected and sent in different containers for histopathological analysis.

For statistical analysis, the following data were collected: patients' age and sex, information on whether initial TUR was carried out for a primary tumor/primary tumors, tumor number, tumor size and tumor grade, as well as information on whether muscularis propria was found in the resected specimens of initial TUR, whether there was carcinoma in situ (CIS) and whether single-dose intracavitary chemotherapy was administered following initial TUR.

SPSS 20.0 for Windows was used for statistical analysis. The logistic regression analysis and chi-square analysis were used for the data review.

Results

168 male and 20 female patients aged between 31 and 78 (mean 67.3) years received re-TUR. 157 (83.5%) patients had primary and 31 (16.5%) had recurrent tumors. Initial TUR was performed on 106 (56.3%) patients with a single tumor and 82 (43.7%) patients with multifocal tumors. 106 (56.3%) patients had high-grade and 82 (43.7%) low-grade T1 tumors. In 20 (10.6%) patients, additional CIS was detected. 96 (51%) patients received single-dose intracavitary chemotherapy, while 92 (49%) patients were not eligible for single-dose intracavitary chemotherapy due to hematuria.

On re-TUR, 34 (18%) patients were diagnosed with new tumors outside of the resection area, while 48 (25.5%) had residual tumors within the initial resection area. In 61.7% of the patients diagnosed with residual tumors outside of the initial resection area, initial TUR had been performed for multifocal tumors (Table 1). The tumor stage and grade were found to be increased in 5 (2%) and 6 (3%) patients, respectively. Radical cystectomy was performed on the patients with increased tumor stage. The other patients were treated with BCG immunotherapy.

Both univariate and multivariate analysis revealed a significant relationship between male sex, multifocal primary tumors and the detection of residual tumors in the previous resection area during re-TUR. (Table 2) ($p < 0.05$). A new tumor in a new area detected during re-TUR was found to be significantly related to multifocal primary tumors only (Table 3) ($p < 0.0001$). No morbidity or mortality was seen in the patients subjected to re-TUR in connection with this procedure.

Discussion

70–75% of newly diagnosed bladder tumors are non-muscle invasive bladder tumors (NMIBC). About 1–10% of those tumors are CIS, 70–80% of them are Ta and 20% of them are T1 tumors [13–15]. NMIBC type tumors are a heterogeneous disease group and cover a wide range in terms of recurrence, progression and survival rates. Stage pT1 tumors are usually high-grade tumors with a high risk for progression [16,17]. Those tumors tend to progress in 29–74% of the patients over a 5-year period [18]. The shift of superficial