



## Research Article

# Is there any Effect of Intracavitary Therapy for Superficial Bladder Tumors on Urethral Strictures?

 Mustafa Karabicak,<sup>1</sup>  Hakan Turk,<sup>2</sup>  Sitki Un,<sup>3</sup>  Erkan Arslan<sup>4</sup>

<sup>1</sup>Department of Urology, Batman Regional State Hospital, Batman, Turkey

<sup>2</sup>Department of Urology, Evliya Celebi Training and Research Hospital, Kutahya, Turkey

<sup>3</sup>Department of Urology, Denizli State of Hospital, Denizli, Turkey

<sup>4</sup>Department of Urology, Harran University Faculty of Medicine, Sanliurfa, Turkey

### Abstract

**Objectives:** In this study, we aimed to find the answer to the question of whether intracavitary therapy administered for bladder tumor has any effect on the development of urethral strictures.

**Methods:** The patients who underwent transurethral resection of the bladder with the diagnosis of bladder tumor in our clinic were divided into two as the group with urethral strictures and the group without urethral strictures. Intracavitary therapies, follow-up, and recurrence data of the patients of both groups were recorded.

**Results:** The mean age of the patients with and without urethral stricture was 67.8 and 68.4 years, respectively. There was no significant difference between the T staging and grading of patients in the two groups. There was no statistically significant difference between the patients with and without urethral stricture in terms of intracavitary therapy rates ( $p=0.943$ ).

**Conclusion:** Although we demonstrated that intracavitary therapy administered for bladder tumors had no effect on the development of urethral strictures, we believe we need randomized controlled trials with larger patient series.

**Keywords:** Intracavitary therapy, urethral stricture, transurethral bladder resection

**Cite This Article:** Karabicak M, Turk H, Un S, Arslan E. Is there any Effect of Intracavitary Therapy for Superficial Bladder Tumors on Urethral Strictures?. EJMO 2019;3(1):33-36.

Bladder tumor is the 7<sup>th</sup> most common cancer in men worldwide.<sup>[1]</sup> It is the most common cancer of the urinary system, with an incidence of 9/100.000 in men and 2/100.000 in women.<sup>[1]</sup> About 75% of all newly diagnosed bladder cancers are non-muscle-invasive bladder cancers. Although non-muscle-invasive bladder tumors can be treated totally by transurethral resection of bladder tumor (TUR-B), most of these tumors recur, unfortunately, and some will progress to muscle-invasive form.<sup>[2]</sup> Primary therapy for non-muscle-invasive bladder cancer is TUR-B followed by intravesical therapies.<sup>[3]</sup> Recurrence and progression rates of bladder cancer were shown to decrease by intravesical therapy.<sup>[4, 5]</sup>

In a study, the incidence of urethral stricture was found to be 4% in patients who underwent TUR-B.<sup>[6]</sup> Internal urethrotomy (IU) is the usual method to repair post-TUR-B urethral strictures. The risk of recurrence is high after urethral stricture operation, depending on the location and the patient. It was observed that using mitomycin C (MMC) to the area of strictures was very effective in the prevention of recurrence in urethral strictures as well as bladder neck contractures.<sup>[7, 8]</sup>

In this study, we aimed to find the answer to the question of whether the incidence of urethral stricture will decrease or not, in patients who receive intracavitary treatment for bladder tumor.

**Address for correspondence:** Hakan Turk, MD. Evliya Celebi Egitim ve Arastirma Hastanesi, Uroloji Klinigi, Kutahya, Turkey

**Phone:** +90 555 551 68 85 **E-mail:** hkntkrk000@hotmail.com

**Submitted Date:** October 01, 2018 **Accepted Date:** October 08, 2018 **Available Online Date:** January 04, 2019

©Copyright 2019 by Eurasian Journal of Medicine and Oncology - Available online at [www.ejmo.org](http://www.ejmo.org)



## Methods

The data of 237 patients underwent TUR-B and eventually diagnosed with bladder cancer in our clinic between May 2013 and May 2018 were retrospectively screened. Patients who underwent TUR-B due to primary bladder tumor and were followed-up at least for 1 year were included in the study. Those who underwent TUR-B in another center, or yielded T2 pathology of TUR-B, or those without follow-up data were excluded from the study.

All of the patients included were primary bladder cancer and they were diagnosed with TUR-B. In the follow-up, they were divided into two groups as the patients with urethral strictures and the patients without urethral strictures. Patients' ages, T stages, and grades were recorded. The type and the number of intracavitary therapies administered were recorded. Tumor recurrences developed during the follow-up period were recorded. Urethral strictures were treated with IU or dilatation.

## Statistical Analysis

IBM Statistical Package for the Social Sciences, Chicago, IL v20 program was used for statistical analysis. Differences between the groups were assessed by Chi-square test for categorical variables, by t-test or Mann–Whitney U-test for continuous variables.  $P < 0.05$  was considered statistically significant.

## Results

In the follow-up, patients were divided into two groups as 81 patients with urethral stricture and 156 patients without urethral stricture. The mean age of the patients with urethral stricture was 67.8 ( $\pm 9.1$ ) years while that of the other group was (68.4 $\pm 10.3$ ) years. There was no statistically significant difference between the distribution of T stages and grades of both groups. Those with a previous history of ureteral intervention such as IU and TUR-B before the diagnosis of bladder tumor constituted 27.1% of the group with stricture and 29.4% of the other group without stricture and there was no statistically significant difference between the groups ( $p = 0.429$ ). The incidence of intracavitary therapy was 56.7% and 46.7%, respectively, among the patients with and without urethral stricture and there was no statistically significant difference between the two groups ( $p = 0.943$ ). No statistically significant difference was found between the two groups when the patients were examined for the type of intracavitary therapy (Bacillus Calmette-Guérin [BCG], MMC), duration of treatment, and number of intracavitary therapies. The mean follow-up period was 31.1 ( $\pm 8.2$ ) months in the group with urethral stricture while 27.7 ( $\pm 8.7$ ) months in the group urethral stricture.

The mean number of interventions such as cystoscopy and TUR-B during the follow-up was 6.7 and 3.4 in the groups with and without urethral stricture, respectively. There was no statistically significant difference between the groups, despite the higher number in the group with stricture. Again, no significant difference was found in terms of recurrence between the two groups ( $p = 0.086$ ) (Table 1).

## Discussion

Incidence for T stage and grade determined in our patients was similar to the results of other studies reported in literature.<sup>[9, 10]</sup> In previous studies on TUR-B, the incidence rate of urethral stricture was between 4% and 29%, which is considerably decreased today due to the improvements in surgical instruments and techniques.<sup>[11–13]</sup> In our study, however, about one-third of patients had a urethral stricture. We attribute this to the factors that can affect the recurrence of urethral strictures, such as cystoscopy or TUR-B, that are applied during follow-up.

Urethral stricture recurrence within a short time is one of

**Table 1.** Patient demographic data and operation results

Variables	Urethral stricture (+) (n=81)	Urethral stricture (-) (n=156)	P
Age (average)	67.8	68.4	0.706
T stage n (%)			
TA	45 (55.5)	72 (46.1)	0.688
T1	36 (44.5)	84 (53.9)	0.504
Grade n (%)			
Low	59 (72.8)	116 (74.3)	0.188
High	22 (27.2)	40 (25.7)	0.188
Previous history of ureteral intervention n (%)			
Yes	22 (27.1)	46 (29.4)	0.429
No	59 (72.9)	120 (70.6)	0.429
Intracavitary therapy n (%)			
Yes	46 (56.7)	73 (46.7)	0.943
No	35 (43.3)	83 (53.3)	0.943
BCG	24 (52.1)	34 (46.5)	0.857
MMC	22 (47.9)	39 (53.5)	0.805
Induction	27 (58.6)	41 (56.1)	0.450
Induction + maintenance	19 (41.4)	32 (43.9)	0.521
Number of intracavitary therapies (average)	6.1	4.6	0.745
follow-up period (average)	31.1	27.7	0.666
Number of TURM (average)	3.4	2.4	0.780
Number of cystoscopy (average)	6.7	5.7	0.235
Bladder tumor recurrence n (%)			
Yes	55 (67.9)	105 (67.3)	0.086
No	26 (32.1)	51 (32.7)	0.086

the major issues after the treatment of strictures by IU. Various systemically or locally applied substances were used to increase the success of the IU. Besides transurethral injection of triamcinolone, proposed for the first time by Hebert in 1972, systemic steroid administration or use of triamcinolone ointment was also tried. In a study by Hosseini et al., patients who underwent clean intermittent catheterization with triamcinolone ointment for 6 months following IU were compared against those who used a water-based lubricant and the rate of developing urethral stricture after a 12-month follow-up was slightly lower in the triamcinolone group, though no statistically significant difference was noted.<sup>[14, 15]</sup> In this study, we aimed to find out the effect of intracavitary therapy on the recurrence of urethral stricture in the patients with a bladder tumor.

When we reviewed the other studies in literature with a view to improve the success of the IU, we saw that MMC was used for its anti-fibroblast and anti-collagen properties and for preventing scar tissue formation. In the follow-up of the patients who were treated with submucosal MMC to the stenotic area following IU, we observed that strictures were less in comparison to the non-treated patients.<sup>[7, 16, 17]</sup> In our study too, intracavitary MMC and BCG administration yielded no significant difference between the patients with and without urethral stricture. This can be the result of a failure in the administration of submucosal MMC to the region of stricture. Besides that, although there was no statistically significant difference, the number of TUR-B and cystoscopy was more in number among the patients with a urethral stricture in comparison to the patients without urethral stricture; hence, the incidence of strictures might be affected from this high number.

Intravesical administration of BCG executes its effect by a massive local immune response. BCG causes cytokine release in the bladder after it is adhered to urothelium and bladder cancer cells through fibronectin. The inflammatory process begins with the stimulation of the cellular immune response and continues. Immunological response activates cellular cytotoxic mechanisms, and tumor cells become the target of cellular immunity.<sup>[18]</sup> In this study, it was shown that the immunoreaction generated by BCG did not affect the development of urethral stricture.

As for the limitations of the study, retrospective design and limited number of patients can be mentioned. To the best of our knowledge, this the first study conducted on this topic, which makes it valuable.

## Conclusion

We concluded that intracavitary therapy administered for bladder tumor did not affect the development of urethral

stricture. In the meantime, further randomized controlled studies are required to reach a more reliable result.

## Disclosures

**Ethics Committee Approval:** The study was approved by the Local Ethics Committee.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Concept – M.K.; Design – H.K., S.U., M.K.; Supervision – E.A.; Materials – E.A., S.U., H.T.; Data collection &/or processing – H.K., E.A.; Analysis and/or interpretation – S.U.; Literature search – S.U., M.K.; Writing – M.K.; Critical review – E.A.

## References

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. GLOBOCAN 2012 v1.0: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012. 2013. 2015. Geneva: World Health Organization; 2015.
2. American Cancer Society. Cancer Facts and Figures 2005, Atlanta: American Cancer Society; 2005.
3. Catalona WJ. Urothelial tumors of the urinary tract. In: Walsh P, Retik AB, Stamey TA, Vaughan ED, editors. Campbell's Urology. 6th ed. Philadelphia, PA: WB Saunders; 1992. p. 1094–136.
4. Tolley DA, Parmar MK, Grigor KM, Lallemand G, Benyon LL, Fellows J, et al. The effect of intravesical mitomycin C on recurrence of newly diagnosed superficial bladder cancer: A further report with 7 years of follow up. *J Urol* 1996;155:1233–8.
5. Böhle A, Bock PR. Intravesical bacille calmette-guérin versus mitomycin C in superficial bladder cancer: Formal meta-analysis of comparative studies on tumor progression. *Urology* 2004;63:682–6. [\[CrossRef\]](#)
6. Liu H, Wu J, Xue S, Zhang Q, Ruan Y, Sun X, et al. Comparison of the safety and efficacy of conventional monopolar and 2-micron laser transurethral resection in the management of multiple nonmuscle-invasive bladder cancer. *J Int Med Res* 2013;41:984–92. [\[CrossRef\]](#)
7. Liaqat Ali, Muhammad Shahzad, Nasir Orakzai, Ihsanullah Khan, Mubashira Ahmad. Efficacy of mitomycin C in reducing recurrence of anterior urethral stricture after internal optical urethrotomy. *Korean J Urol* 2015;56:650–5. [\[CrossRef\]](#)
8. Farrell MR, Sherer BA, Levine LA. Visual internal urethrotomy with intralesional mitomycin C and short-term clean intermittent catheterization for the management of recurrent urethral strictures and bladder neck contractures. *Urology* 2015;85:1494–9. [\[CrossRef\]](#)
9. Liem EIML, McCormack M, Chan ESY, Matsui Y, Geavlete P, Choi YD, et al. Monopolar vs. Bipolar transurethral resection for non-muscle invasive bladder carcinoma: A post-hoc analysis from a randomized controlled trial. *Urol Oncol* 2018;36:338. e1-0000000000. [\[CrossRef\]](#)
10. Rodríguez FM, Chéchile-Toniolo G, Salvador-Bayarri J, Palou J, Vicente-Rodríguez J. Multivariate analysis of the prognostic factors of primary superficial bladder cancer. *J Urol*

- 2000;163:73–8. [\[CrossRef\]](#)
11. Nielsen KK, Nordling J. Urethral stricture following transurethral prostatectomy. *Urology* 1990;35:18–24. [\[CrossRef\]](#)
  12. Hammarsten J, Lindqvist K, Sunzel H. Urethral strictures following transurethral resection of the prostate. The role of the catheter. *Br J Urol* 1989;63:397–400. [\[CrossRef\]](#)
  13. Hart AJ, Fowler JW. Incidence of urethral strictures following transurethral prostatectomy: Review of 2223 resections. *J Urol* 1997;117:194–201.
  14. Hebert PW. The treatment of urethral stricture: Transurethral injection of triamcinolone. *J Urol* 1972;108:745–7. [\[CrossRef\]](#)
  15. Hosseini J, Kaviani A, Golshan AR. Clean intermittent catheterization with triamcinolone ointment following internal urethrotomy. *Urol J* 2008;5:265–8.
  16. Mazdak H, Meshki I, Ghassami F. Effect of mitomycin C on anterior urethral stricture recurrence after internal urethrotomy. *Eur Urol* 2007;51:1089–92. [\[CrossRef\]](#)
  17. Vanni AJ. New frontiers in urethral reconstruction: Injectables and alternative grafts. *Transl Androl Urol* 2015;4:84–91.
  18. Donin NM, Lenis AT, Holden S, Drakaki A, Pantuck A, Belldegrun A, et al. Immunotherapy for the treatment of urothelial carcinoma. *J Urol* 2017;197:14–22. [\[CrossRef\]](#)