

Overnight continuous saline irrigation after transurethral resection for non-muscle-invasive bladder cancer is helpful in prevention of early recurrence

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Abstract

Introduction: It has been reported that many methods prevent recurrence after transurethral resection of bladder tumour (TURBT) for non-muscle-invasive bladder cancer (NMIBC), but it has rarely been reported that overnight continuous saline irrigation is effective in preventing recurrence. The purpose of this study was to evaluate the efficacy of overnight continuous saline irrigation in preventing recurrence after TURBT.

Methods: We retrospectively studied patients with NMIBC who underwent TURBT from January 2010 to May 2015 at our institution. Patients who underwent cystoscopy every 12 weeks during the first year after surgery were included. Patients with cancer stage \geq pT2, lymph node metastasis, or distant metastasis were excluded. The overnight continuous saline irrigation (OCSI) group and the no irrigation group were compared and analyzed.

Results: A total of 332 patients were included in the study. There were no differences in the basic characteristics of the patients between the two groups. In the OCSI group, the recurrence-free survival rate was higher than that in the no irrigation group, indicating that there was a significant difference between the two groups ($p=0.032$).

Conclusions: After TURBT surgery, OCSI may help prevent early recurrence of NMIBC.

Introduction

Approximately 70% of bladder cancers present as non-muscle invasive bladder cancer (NMIBC).¹ Transurethral resection (TUR) still remains the gold standard for the treatment of NMIBC. However, even if TUR completely removes tumours of Ta and T1 stages, 40% recur within one year.^{2,3} Therefore, intravesical chemotherapy or bacillus Calmette Guérin (BCG) immunotherapy is recommended after TUR

for prevention of recurrence and progression of high-risk NMIBC.^{4,5} However, intravesical chemotherapy and BCG immunotherapy have local or systemic side effects and they are difficult to apply in all patients. In addition, intravesical chemotherapy may have a problem of high cost due to the chemotherapeutic agent, proficiency of medical personnel dealing with the chemotherapeutic agent, and serious complications due to the chemotherapeutic agent if bladder perforation is suspected after surgery.^{6,7} Furthermore, BCG immunotherapy is problematic in terms of supply and demand due to global shortage.⁸

According to Soloway et al,⁹ one of the mechanisms of bladder tumour recurrence is implantation of floating tumour cells in the bladder wall after transurethral resection of bladder tumour (TURBT). Therefore, we think that it is possible to prevent early recurrence by removing tumour cells floating in the bladder and preventing implantation in the bladder wall by performing overnight continuous saline irrigation (OCSI) after TUR. We compared the OCSI group and the no irrigation group after TUR to determine whether this technique was effective in preventing early recurrence.

Methods

Subjects

We retrospectively reviewed patients diagnosed with NMIBC after TUR at our hospital from January 2010 to May 2015 and who were followed for 12 months postoperatively. In our hospital, since 2014, all TUR patients have undergone OCSI. Patients who had cancer stage \geq pT2, lymph node metastasis, or distant metastasis on computed tomography images after TUR, as well as those who underwent mitomycin-C (MMC) or epirubicin instillation after TUR or repeated TUR, were excluded.

Followup

Patients underwent cystoscopy every 12 weeks (± 2) during followup and they were followed up for 12 months. Recurrence of bladder cancer was confirmed by cystoscopy.

Comparison method

TUR was performed for removing the tumours completely, and a 22 Fr three-way Foley catheter was inserted and continuous irrigation was started by connecting a 3000 cc bag of normal saline to the Foley catheter in the OCSI group (using a total of 9000 cc of saline). But, after TUR was performed, a 16Fr Foley catheter was inserted and drainage was performed in the no irrigation group. The baseline characteristics and the recurrence-free survival rate of the OCSI group and the no irrigation group were compared.

Statistical analysis

The standard Chi-square test was used to compare the two groups, and the recurrence-free survival rate was calculated by the Kaplan-Meier method with log-rank test. The statistical program used was SPSS version 21.0 for Windows. A p value < 0.05 was considered statistically significant.

Results

A total of 332 patients were included in the study. The no irrigation group included 212 patients and the OCSI group included 120 patients. No significant differences were seen between the groups in term of age, gender, hypertension, diabetes, stage, tumour grade, tumour size, number of tumours, or BCG immunotherapy. Regarding smoking, which is known as a very important risk factor, no significant differences were seen between groups of patients who are smokers, those who do not smoke, and those who quit smoking for more than one year (Table 1).

To evaluate the treatment efficacy of OCSI, we compared the duration of time to the initial recurrence, frequency of recurrence, and recurrence-free survival rate in the OCSI group to those of the no irrigation group.

The mean duration of time to the initial recurrence in the no irrigation group was 277.19 ± 7.39 days (95% confidence interval [CI] 262.70–291.68) and that in the OCSI group was 302.85 ± 8.11 days (95% CI 286.96–318.74). In the non-irrigation group, 131 patients (61.8%) had no recurrence, while 81 patients (38.2%) had recurrence. In the OCSI group, however, 88 patients (73.3%) had no recurrence, while 32 patients (26.4%) had recurrence.

The recurrence-free survival rate at 12 months after surgery was significantly higher in the OCSI group than in the no irrigation group (log-rank test $p = 0.032$) (Fig. 1).

Table 1. Baseline characteristics of patients

	No irrigation group (n=212)	OCSI group (n=120)	p
Age	66.80 \pm 12.28	67.56 \pm 12.14	0.586
Gender			0.881
Male	178 (84.0%)	100 (83.3%)	
Female	34 (16.0%)	20 (16.7%)	
Hypertension			0.535
Yes	56 (26.4%)	28 (23.3%)	
No	156 (73.6%)	92 (76.7%)	
Diabetes			0.650
Yes	28 (13.2%)	18 (15.0%)	
No	184 (86.8%)	102 (85.0%)	
Smoking history			0.468
Yes	81 (38.2%)	43 (35.8%)	
No	59 (27.8%)	32 (26.7%)	
Cessation (>1 yr)	72 (34.0%)	45 (37.5%)	
T stage			0.202
Ta	141 (66.5%)	68 (56.7%)	
T1	58 (27.4%)	42 (35.0%)	
CIS	13 (6.1%)	10 (8.3%)	
Grade			0.573
PUNLMP	29 (13.7%)	18 (15.0%)	
Low-grade	126 (59.4%)	73 (60.8%)	
High-grade	57 (26.9%)	29 (24.2%)	
Size			0.276
<3 cm	174 (82.1%)	104 (86.7%)	
≥ 3 cm	38 (17.9%)	16 (13.3%)	
Multiplicity			0.251
Single	149 (70.3%)	77 (64.2%)	
Multiple	63 (29.7%)	43 (35.8%)	
BCG			0.300
Yes	97 (45.8%)	62 (51.7%)	
No	115 (54.2%)	58 (48.3%)	

Values are presented as mean \pm standard deviation for continuous variables and number for categorical variables. BCG: bacillus Calmette-Guerin; OCSI: overnight continuous saline irrigation; PUNLMP: papillary urothelial neoplasm of low malignant potential.

Discussion

Recurrence of bladder cancer after TUR surgery may be caused by residual cancer due to incomplete resection, failure to identify a small lesion, and new implantation of floating tumour cells.¹⁰ These cancer recurrence mechanisms can be blocked to prevent recurrence. The existing BCG instillation destroys floating cancer cells, and intravesical chemotherapy is known to remove residual cancer cells at the resection site.^{4,11} However, intravesical chemotherapy is not completely safe for the patients. In some case studies, patients died due to successive complications caused by MMC and epirubicin instillation.¹²⁻¹⁴ BCG immunotherapy has also been recorded in patients who died of mild to severe complications.¹⁵⁻¹⁹

For those reasons, use of intravesical chemotherapy after TURBT in NMIBC is on the decline among urologists. According to the studies, 18% of European urologists responded that they always choose intravesical chemotherapy, while 28% responded that they never use it. Among

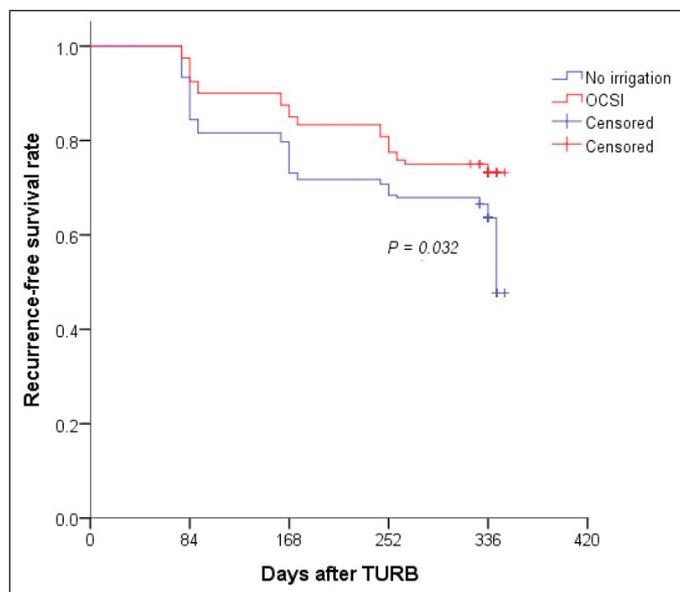


Fig. 1. Recurrence-free survival rate in the overnight continuous saline irrigation (OCSI) group and the no irrigation group. TURB: transurethral resection of bladder.

American urologists, 2% always performed intravesical chemotherapy, while 66% never chose to perform.^{6,7}

One study showed that osmotic cytolysis by irrigation with sterile water can be used to destroy tumour cells,²⁰ and another study suggested sterile water irrigation after TUR surgery as an alternative to intravesical chemotherapy.²¹ However, there are reports suggesting that distilled water can cause electrolyte imbalance and serious complications, such as intravascular hemolysis and death.^{22,23}

In rectal cancer, the main cause of local recurrence after curative operation has been found to be implantation of viable shed cancer cells. Local recurrence did not occur when saline irrigation was performed 20 times with a 30 ml enema syringe before anastomosis of the remnant rectum, but recurrence was observed in 11% of patients without irrigation.²⁴

In another rectal cancer meta-analysis study, normal saline washout showed better reduction in local recurrence than cetrimide, povidone-iodine, and formalin solution washout and irrigation volume of 1500 ml had better results than volume of less than 1500 ml, indicating efficacy of saline irrigation.²⁵

Originally, the purpose of physiological saline perfusion was to achieve hemostasis and clot removal in bladder hemorrhage. However, the authors speculated that continuous saline irrigation after TUR surgery could safely reduce the recurrence rate compared to the other methods if it can remove floating tumour cells and prevent implantation in the bladder wall, although continuous saline irrigation cannot destroy cancer cells or remove residual cancer cells.

Onishi et al²⁶ stated that recurrence-free rates at one, three, and five years were 76.7%, 67.3%, and 61.3%, respectively, in the continuous saline irrigation group (n=123) and 81%, 58%, and 58%, respectively, in the MMC instillation group

(n=115), indicating that there was no significant difference between the two groups. Thus, the study insisted that saline irrigation is not inferior to MMC in terms of efficacy in reducing recurrence in bladder cancer.

In a recently published study, Onishi et al²⁷ reconfirmed that there was no significant difference in the five-year recurrence-free rates of 62.6% and 70.4% (log-rank test p=0.53) between the continuous saline irrigation group (n=114) and the MMC instillation group (n=113) through a randomized controlled trial.

In this study, we assessed the effects of continuous saline irrigation in the OCSI group and compared this group with the no irrigation group. The results showed that continuous saline irrigation was effective in preventing early recurrence.

This study was performed at a single institution, the number of patients included was small, and the followup period was short; therefore, only early recurrence was observed up to one year after surgery, and there was a limitation that it was performed retrospectively. Prospective, multicentre, long-term followup studies with more patients are needed in the future.

Conclusion

After TURBT surgery, OCSI could reduce early recurrence of NMIBC. OCSI is expected to be more widely used because it is an economical, safe, and easy-to-perform technique.

Competing interests: The authors report no competing personal or financial interests.

This paper has been peer-reviewed.

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