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A PROSPECTIVE STUDY OF CONTRASTING PERFORMANCE OF MITOMYCIN-C INSTILLATION IN A SINGLE SESSION TO THAT OF SIX SESSIONS IN PATIENTS WITH LOW-RISK, NON-MUSCLE-INVASIVE BLADDER CANCER

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ABSTRACT

Background:

The effectiveness of intravesical instillation in preventing recurrence and development of non-muscle-invasive bladder cancer was demonstrated following transurethral excision of low-grade and low-stage tumors. Methods and patients: A prospective randomized controlled trial included 48 individuals with low-risk non-muscle-invasive bladder cancer. All patients were considered as long as their tumors were single papillary and 3 cm or smaller; those with muscle invasion, G3 tumors, bladder carcinoma in situ, or tumors that had been surgically removed with perforation were prohibited. After the tumor was fully removed, patients were randomly

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assigned to one of two groups. One group received 40 mg of mitomycin C instilled into the urinary bladder after hematuria stopped (typically within 6 hours). The other group received six sessions of mitomycin C instillation. The median follow-up for this group was 24 months. Progress, length of hospital stay, and catheterization period were among the events examined, along with recurrence-free rate, recurrence rate per year, and number of new tumors growing per year. Results: As of the 24-month follow-up, the recurrence-free rate was 93.4% in group B after six sessions of mitomycin C instillation, compared to 80.1% in group A after a single session. Group B, which received mitomycin C instillation for six sessions, had a lower recurrence rate (9.1% vs. 4.5%) and recurrence per year rate (9.85% vs. 3.3%). Group A, which had mitomycin C instillation for one session, had no such advantage. The rate of new tumors each year was marginally lower in Group B, which received six sessions of mitomycin C instillation, compared to Group A, which received one session. The advancement rate was 4.5%, and there was no statistically significant difference between the two groups. The other results were also comparable. Compared to six sessions of mitomycin C instillation, one session (Group A) was associated with a shorter hospital stay, a shorter catheterization length, a lower level of local symptoms, and a lower cost. Conclusions After surgery or within six hours of resection, a single dose of mitomycin C may be just as effective as a six-dose regimen. The six-session plan may save money by avoiding unnecessary hospitalization and catheterization. Hence, this method can be used instead of the six sessions of mytomycin C instillations or observation. Immediate mitomycin C instillation, often within 6 hours following TURBT, may restrict cell implantation as a mechanism of early recurrence, according to this study. Aim of the study: The purpose of this study is to evaluate the effects of mitomycin C given once versus six times after transurethral removal of a bladder tumor on the rates of recurrence and progression in patients with low-risk, non-muscle-invasive bladder cancer.

Keywords Mitomycin C, bladder cancer, Transurethral resection, patients with low-risk.

Introduction

When it comes to tumors of the urinary system, bladder cancer ranks second (1). It ranks fourth among male cancers, behind colorectal, lung, and prostate cancers, and 6.6% of all cancer cases are attributed to this disease. It accounts for 2.4% of all cancers in women and ranks tenth overall (2). Urothelial bladder cancer (UBC) is responsible for over 145,000 annual deaths and over 357,000 new cases globally (1). Tobacco use is considered the leading cause of UBC, accounting for a third of all cases. The risk of developing UBC is three to four times higher in

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men than in women. Men's higher smoking rate (1) partly explains the disparity. There are around 70% non-muscle-invasive UBC cases, 30% with muscle-invasive UBC (cT2 or higher), 20% with pT1 disease, and 10% with carcinoma in situ (CIS), as shown in Table 1. (2).
Treatment options and the course of non-muscle-invasive UBC can vary greatly. But some people have disease progression and die, while others don't (3). There is a 47% chance of disease recurrence and a 9% chance of progression to muscle-invasive disease within 5 years of diagnosis for patients with non-muscle-invasive UBC who do not receive intravesical treatment (4).Patients dealing with non-muscle-invasive UBC have limited access to risk-based tools and evidence to aid with decision-making, which can hinder their ability to make informed choices about their treatment options and may lead to poorer health outcomes. Molecular markers like cytology, NMP22, and FISH, as well as clinical and pathologic characteristics, are factors that can predict the outcome, but their effectiveness in guiding treatment decisions for patients with non-muscle-invasive UBC remains to be fully established. The optimal course of treatment for individuals suffering from high-grade cTa, CIS, or cT1 UBC remains unknown, in contrast to the generally non-controversial care of cTa low-grade UBC (5). Effective intravesical therapies for non-muscle-invasive UBC are currently in the early stages of development and testing. To this day, the indication, kind, and course of intravesical therapy are all hotly debated topics. Criteria for treatment success or failure and choices between radical cystectomy and secondary intravesical therapy are two more contentious topics. Here, we take a look at the various intrathecal treatment options and evaluate and contrast their oncologic effectiveness (6, 7).

Cancer of the bladder surface:
According to the World Health Organization's (WHO) collapsed grading system for urothelial carcinoma of the urinary bladder, non-muscle invasive bladder cancers are categorized as either low grade or high grade (4), with well, moderately, or poorly differentiated (G1, G2, or G3, respectively) (7). The histological patterns of non-muscle invasive tumors range from visible exophytic lesions, typically of low or intermediate grade, to the invisible, generally aggressive CIS (8). These tumors can also occur at multiple sites of the bladder epithelium at the same time or in a sequential fashion. Considering the natural history or therapy of non-muscle-invasive lesions requires greater differentiation than the imprecise general term of superficial bladder cancer (9), due to the fact that the recurrence rate and potential for advancement are different among these lesions. The most common symptom in 85% of patients with a new bladder tumor is gross, painless hemoturia; in virtually all cases, microscopic hemoturia is present as well (4). Since the hematuria is often intermittent and may be associated with Valsalva maneuvers, it is important to investigate any episode of gross hematuria even if further urinalysis comes up negative. Of those patients with gross hemoturia, 50% will have a clear cause, 20% will have a urologic malignancy, and 12% will have a bladder tumor (4). In more

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advanced tumors, patients may experience symptoms such as dysuria, frequency, pelvic discomfort, and urgency, all of which are associated with urinary tract blockage (10).

Table 1 displays the urinary bladder urothelial carcinoma staging system.

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Ta	Noninvasive papillary carcinoma
Tis	Carcinoma in situ" flat tumor"
T1	Tumor invades subepithelial connective tissue .
T2	Tumor invades muscularis propria .
PT2a	Tumor invades superficial muscularis properia (inner half)
PT2b	Tumor invades deep muscularis properia (outer half)
T3	Tumor invades perivesical tissue
PT3a	Microscopically
PT3b	Macroscopically (extravesical mass)
T4	Tumor invades any of the following: prostatic stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall
T4a	Tumor invades prostatic stroma, uterus, vagina
T4b	Tumor invades pelvic wall, abdominal wall
Regional lymph nodes (N):	
Regional lymph nodes include both primary and secondary drainage region. All nodes above the aortic bifurcation are distant lymph nodes.	
NX	Lymph nodes cannot be assessed
N0	No lymph node metastasis
N1	Single regional lymph node metastasis in the true pelvis (hypogastric, obturator, external iliac , or presacral lymph nodes metastasis.
N2	Multiple regional lymph node metastasis, in the true pelvis (hypogastric, obturator, external iliac , or presacral lymph nodes metastasis)
N3	Lymph nodes metastasis to the common iliac lymph nodes
Distant Metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis

Evaluation of bladder cancer patients:

Patients with microscopic hematuria require a full evaluation, but low-risk patients do not require repeated evaluations. A full evaluation for bladder cancer includes urine cytology,

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cystoscopy, upper tract imaging (mainly a CT scan of the pelvis and abdomen), and a prostate specific antigen (PSA) blood test. Patients with a history of smoking, occupational exposure, being over the age of 40, having undergone prior urologic surgery, experiencing painful voiding symptoms, a history of UTI, abuse of analgesics such as phenacetin, a history of pelvic radiation, or previous cyclophosphamide treatment should be evaluated every six months (4). Although blue light cystoscopy could be used as an auxiliary to white light cystoscopy and random bladder samples, the former is considered the gold standard for tumor detection. Even though there are several urine markers for urothelial cancer diagnosis, such as BTA Stat, BTA Trak, telomerase, and cytokeratin 20, none of them have been shown to be as sensitive or specific as office cystoscopy (11). On the one hand, there are several markers that have been approved by the FDA; on the other, there are markers that are less specific than cytology, leading to a higher rate of false-positive results, and finally, there are markers that seem more sensitive than urine cytology, particularly for the detection of low-grade Ta tumors (11, 12).

The treatment for bladder cancer that does not invade the muscles involves completely removing the tumor through transurethral resection.The first stage in the treatment of non-invasive procedures that target muscles in bladder cancer is that the tumor is completely removed with transurethral resection. However, even after the initial visual ablation of the main tumor, a significant number of patients may experience tumor recurrences within five years, ranging from forty percent to eighty percent (12). Figure 1 shows that a biphasic recurrence curve, with a first peak within 3-6 months and a second peak between 1.5 and 2.5 years, was demonstrated by Akaza et al. (13) by examining the hazard curve of recurrences following TURBT. Areas of dysplastic urothelium, insufficient resection, or implanted tumor cells can give rise to these new tumors. After TUR, bladder carcinogenesis typically progresses through a complex cascade of events. (14)

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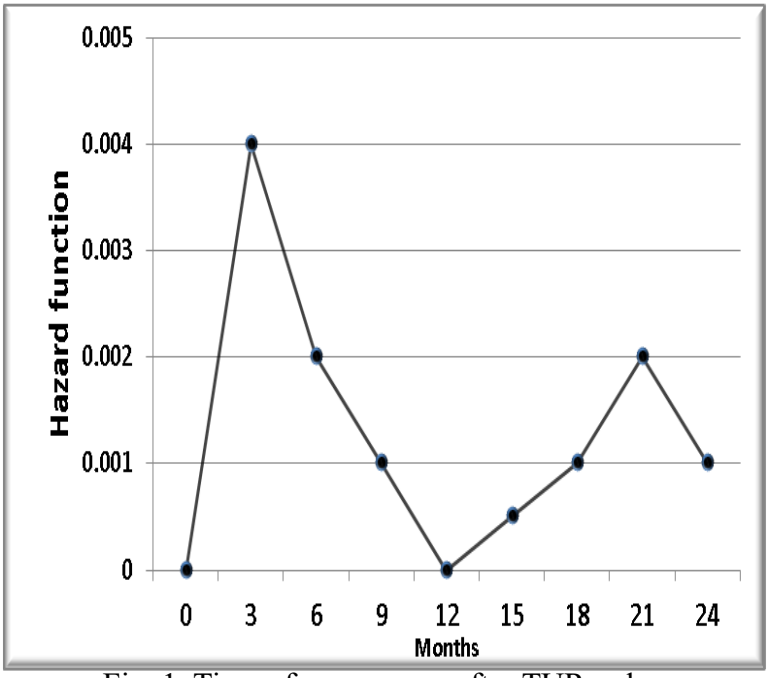

Fig. 1. Time of recurrence- after TUR only
(adapted from Akaza et al., Urol Oncol 1998 ; 4:121-9)

Inadequate resection or implanted tumor cells are the main causes of early recurrences, while dysplastic urothelium areas that seemed normal after the first TUR are the main causes of late recurrences connected to tumors. (15-16) A significant risk of recurrence and invasive disease progression is associated with high-grade tumors, in contrast to low-grade lesions (17–18). A flat, epithelial-confined, high-grade tumor is called a carcinoma in situ. About half of individuals with carcinoma in situ that goes untreated will develop invasive bladder cancer within five years, making this lesion crucial (19). Although TUR is effective, many urologists feel that it will not be enough to treat all cases of non-muscle-invasive urothelial carcinoma on its own due to concerns about field change and the potential residual tumor cells from implantation or incomplete resection. Intravesical chemotherapy is effective in treating non-muscle-invasive urothelial carcinoma in this manner. It follows that a combination of medicinal therapy and surgical excision permits a more rigorous course of treatment (20). Treatment for bladder cancers that have not spread to muscles has a triple purpose:

1. Obtain rid of that sickness that's already there.
2. Recurrence prevention,
3. Stopping tumors from getting worse.

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It is crucial to aim for recurrence prevention, and patients with non-muscle invasive bladder cancer have shown that intravenous chemotherapy is effective at this (21). Many patients may be overtreated, even though these medicines are beneficial for those at low risk of recurrence and progression (22), which can lead to unnecessary side effects and increased healthcare costs for patients who may not need such aggressive treatment. However, it is incorrect to assume that low-grade cancers cannot invade. At the outset, 25% of patients with muscle-invasive illness have grade I, stage Ta, or Tl disease (23). Furthermore, with just one round of mitomycin C, the recurrence rate in this low-risk group has varied from 4% to 44%. The National Bladder Cancer Cooperative Group A (NBCCGA) recently identified 36% of bladder cancers at the Ta stage. Stage of the tumor is one of the variables that can influence the likelihood of disease recurrence; for example, patients with tumors in stage Ta had around a 4% chance of developing invasive illness and about a 50% chance of tumor recurrence following TUR. However, there is a 30% likelihood of invasive disease and a 70% chance of recurrence within 5 years for patients whose tumors have invaded the lamina propria (Tl) (24-25). Grade significantly affects the likelihood of progression. For example, patients with grade 1 cancer have a 3% chance of progression and a 48% chance of tumor recurrence. Those with grade 2 neoplasms have an 11% chance of progression, and those with grade 3 tumors have a 44% chance of disease progression and a 59% and 80% recurrence rate, respectively (25). Recurrence and advancement can be predicted by the number of lesions. Solitary neoplasms occur in 22% to 46% of patients, while multifocal lesions occur in 48% to 75%. Patients with a single tumor have a lower likelihood of recurrence compared to those with many lesions (26). Patients with primary tumors had a recurrence rate around half that of subjects with previous recurrence; however, the likelihood of advancement increases with numerous recurrences. Recurrence and progression rates are further affected by multiple concurrent prognosticators: patients with grade 1 tumors in stage Tl progress in 21% to 48% of cases, whereas patients with grade 2 or 3 tumors in stage Ta progress in 6% and 25% of cases, respectively (26). Both patients and urologists are troubled by the psychological impact of these recurrence and progression rates (3, 7), as they can lead to increased anxiety, fear of treatment failure, and a diminished quality of life for those affected. For both curative and preventative (adjuvant) reasons, a number of cytotoxic and immune-modifying drugs have been administered intravenously. However, some studies have shown that endovesical chemotherapy, when administered early, reduces recurrence rates, which implies that chemotherapy drugs can control tumor cells floating free within the bladder (27-28). Additionally, animal studies and

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clinical trials have provided support for the idea of cell implantation during transurethral resection of bladder cancer that is not muscle-invasive as a mechanism for recurrence (29-32). Mitomycin C inhibits DNA synthesis and is an alkylating agent, antibiotic, and antitumor. The medicine is typically administered intravenously, once weekly for 6–8 weeks, at a dosage ranging from 20 to 60 mg. Some studies have shown that by optimizing mitomycin c delivery, the recurrence rate can be cut in half. To accomplish this goal, you need to fast for at least one night, use sodium bicarbonate to slow the drug's breakdown, and increase the concentration to 40 mg in 20 ml of solution. In a multicenter experiment, the recurrence rate was reduced from 57.5% to 17.1% when local microwave therapy was used in conjunction with mitomycin C (20 mg/50 ml). The recurrence-free rate at 2 years was 75% in a study that used microwaves with greater doses (40 to 80 mg) for 6 to 8 weeks to treat high-grade bladder cancer. Numbers 33–35. Drug transport into bladder tissue appears to be improved by electromotive intravenous mitomycin c (4). In 15% of patients, mitomycin C causes temporary filling symptoms (LUTS), and in rare cases, it causes dermatitis of the external genitalia or the palms of the hands, which necessitates stopping treatment. The enormous size of the molecule, which is 329 daltons (6), makes systemic toxicity unusual. Mitomycin C reduces recurrence in 2 to 33 percent of patients and produces a complete response in 39% to 78% of patients with remaining tumors (36).

Methods and Patients

The Gazi Al-Hariry Teaching Center participated in a prospective randomized controlled trial from 2012 to 2014 that included 65 patients with newly diagnosed Ta or Tl non-muscle-invasive urothelial carcinoma of the bladder. The patients had a 3 cm or smaller primary tumor (first tumor without intervention), and they were categorized as either single or papillary. As far as excretory urography could tell, every single patient's upper urinary tract was fine. The following patients were not eligible to participate: those with a history of invasive or G3 tumors, bladder cancer in situ, age greater than 80 years, uncontrolled urinary infections, or mental disorders such as schizophrenia or depression. Both the TNM and WHO reference center systems were used for the stage and grading of bladder tumors, respectively. In order to establish a consistent T category and grade, all histology exams were conducted. Each patient was assigned at random to receive 40 mg once after a full transurethral resection of the bladder tumor. The patients were divided into two groups: one that received mitomycin C diluted in 50 ml of saline (Group A) and was administered when hematuria stopped, typically within 6 hours of transurethral resection, and another that received 40 mg of mitomycin C six times weekly (Group B). After each instillation, the catheter was clamped for 1 hour, and the bladder was

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washed with saline. Tests including cystoscopy, urine cytology, and ultrasonography were performed on patients at 3, 6, 9, 12, 15, 18, 21, and 24 months. Every time a cystoscopy was performed, the doctor would remove any tumors or aberrant urothelium and send the tissue to a reference pathologist for recurrence confirmation. It is the time that passes between the first transurethral resection and the first recurrence that is known as the recurrence-free interval. According to histological criteria, cancer verified by biopsy was considered a recurrence. By dividing the total number of positive cystoscopies by the number of years of follow-up, we can get the recurrence rate per year, which is a statistical measure of the proportion of patients who experienced recurrence throughout the follow-up period. The annual tumor detection rate (NURR) is calculated by dividing the total number of tumors found during positive cystoscopies by the number of years of follow-up. The progression rate is defined as the percentage of cases of invasive bladder tumors or metastases. After determining the recurrence-free rate using the Kaplan-Meier method, the log-rank test was used for comparison (33). Just before and one week following the transurethral resection, a full blood count, serum creatinine, urinalysis, and urine culture were conducted.

Data Management and Statistical Analysis

For this data, we consulted SPSS, Inc.'s 2013 Statistical Package for the Social Sciences, version 21.0. The distribution of all variables was checked for normality, and descriptive statistics were given as frequency (No.), proportions, and mean ± standard deviation (SD).

We compared means using a Student's t-test and analysis of variances (ANOVA) tests and frequencies and proportions using a chi-square test, and where the chi-square test wasn't appropriate, we utilized Fisher's exact test. For a P-value to be deemed significant, it had to be less than or equal to 0.05.

Results

The following reasons were given for the exclusion of 17 individuals from the study: out of 65 patients initially enrolled, 5 had muscle-invasive tumors, 4 had G3 tumors, 1 had bladder CIS, 1 had no histological evidence of tumor, and 6 were lost during follow-up. So, 24 patients were considered for Group A, which received mitomycin C in a single session, and 24 patients were considered for Group B, which received mitomycin C across six sessions. The study included 48 patients, with a mean age of 57.5 ± 8.1 years, and 4 women and 44 males participated. Both groups had similar clinical and pathological features, and both groups were followed for 24 months (table 2). Two patients (9.1%) in Group A, which received mitomycin C in a single

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session, had recurring tumors, whereas just one patient (4.5%) in Group B had this problem. There was a statistically negligible difference between the groups after one and six sessions of mitomycin C; nevertheless, the recurrence rate was reduced in the six-session group (table 3). Table 3 shows that, from an alternative perspective, there was no statistically significant progression in either of the two groups (two patients, or 4.5% of the total) (P=0.98). The recurrence-free rates are displayed in table 4 and shown in figure 2. The results showed that the rates decreased with the passage of time in both groups, with the six-session mitomycin C group having a longer recurrence-free interval than the one-session group. However, the difference between the two groups was not statistically significant (P = 0.18, Figure 2). In addition, figure 3 shows that the two-year recurrence-free rates for the groups treated with one session of mitomycin C and six sessions of mitomycin C were 80.1% and 93.4%, respectively. Recurrence rates were 3.3% in group B after six sessions of mitomycin C, compared to 9.85% in group A (P = 0.08), and tumor per year rates were lower in the six-session mitomycin C group than in the one-session mitomycin C group (table 4). Table 5 shows that, when comparing the two groups, group A had 16.6% new tumors each year and group B had 12.5%, with a p-value of 0.63. Recurrence of multiple tumors was also reported in 5 patients in group A and 1 patient in group B.

When trying to figure out how a single early instillation of mitomycin C could affect cell implantation and thereby cause early recurrence, many cutoff points for recurrence timing were investigated. There was no statistically significant difference between the two groups (p = 0.11) when it came to early recurrence in the first 12 months; however, in the second year, 3 patients in each group experienced recurrence, and again, there was no statistically significant difference (p = 0.87) between the two groups (figure 4). At the 24-month follow-up, the six-session mitomycin C group had a longer hospital stay and more catheterization time than the one-session mitomycin C group. Patients in group A stayed in the hospital for 51.3 hours, while patients in group B stayed for 60.5 hours. Additionally, patients in group A spent 29 hours catheterizing, while patients in group B spent 36.3 hours. Table 6 shows that neither comparison yielded statistically significant differences (P > 0.05). While no hematological alterations were detected, three patients in the six-session mitomycin C group did experience chemical cystitis and mild allergic skin reactions, but these side effects were not considered serious.

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Table 2. Patient characteristics

Variable		0ne session MMC Group A	six sessions MMC Group B	Overall
Patients number		24	24	48
Age (year) mean ± SD		56.3 ± 9.7	58.6 ± 10.1	57.5 ± 8.1
Gender	Male	22 (91.7%)	22 (91.7%)	44 (91.7%)
	Female	2 (8.3%)	2 (8.3%)	4 (8.3%)
Mean tumor size (cm)		2.0	2.2	2.1
Pathological stage and grade (%)	Ta	10 (41.7%)	9 (37.5%)	19 (39.6%)
	T1	14 (58.3%)	15 (62.5%)	29 (60.4%)
	G1	15 (62.5%)	16 (66.7%)	31 (64.6%)
	G2	9 (37.5%)	8 (33.3%)	17 (35.4%)
	Follow up (month)	24	24	24

Table 3. Recurrence &progression

Variable	**One session MMC (Group A) N = 24**	**Six sessions MMC (Group B) N = 24**	**P value**
Recurrence	**2 (9.1%)**	**1 (4.5%)**	**0.67 *(NS)***
Progression	**1 (4.5%)**	**1 (4.5%)**	**0.98 *(NS)***

Table 4. Recurrence-free rates for 24 months follow-up

	Recurrence free rates								P.value
Group	3 month	6 month	9 month	12 month	15 month	18 month	21 month	24 month	
One session MMC(Group A)	91.7	90.3	85.1	82.9	75.1	73.4	73.5	68.3	0.39 *(NS)*
Six sessions MMC(Group B)	100.0	100.0	100.0	96.20	92.30	91.1	89.3	78.1	0.57 *(NS)*

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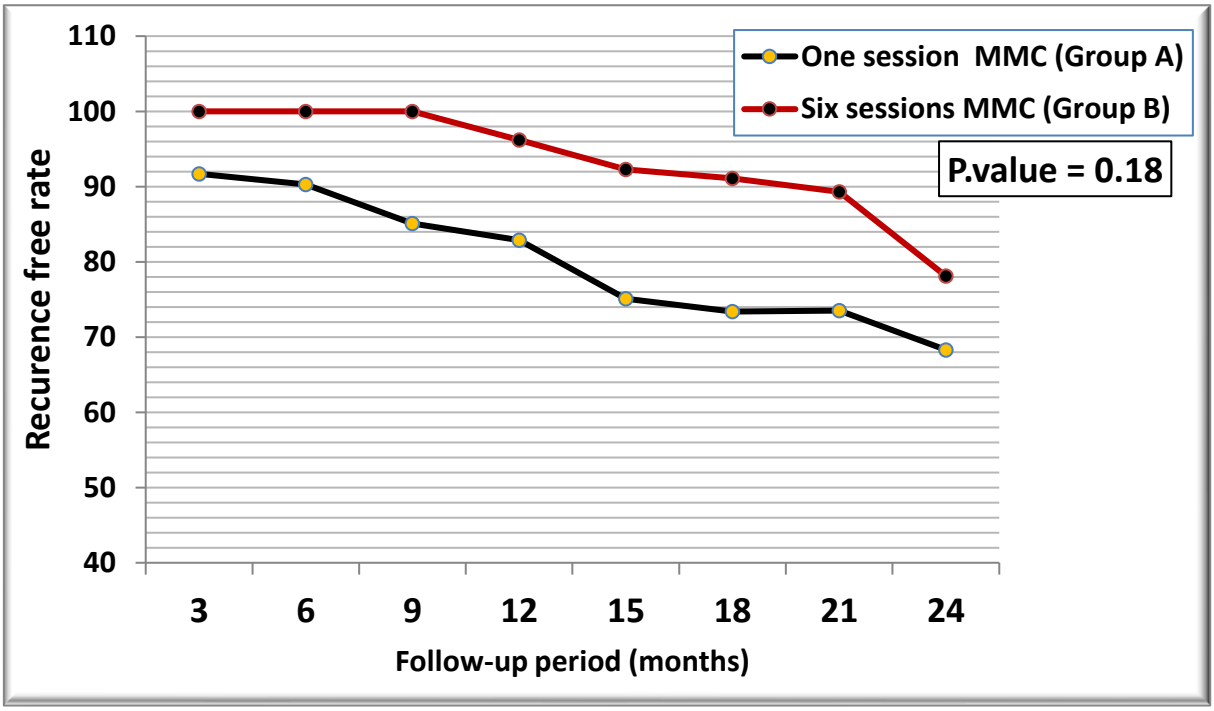

Figure 2. Recurrence-free rates for 24 months follow-up.

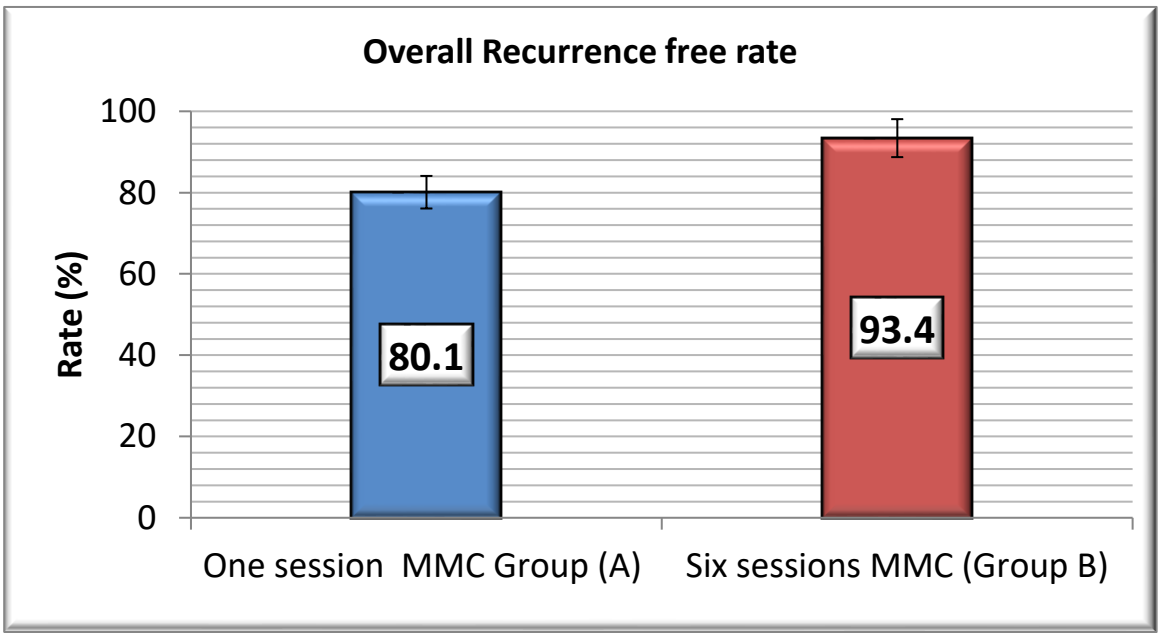

Figure 3. Overall recurrence free rates of both studied groups

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Table 5. Recurrence and new tumor per Year rates

	One session MMC (Group A) N = 24	Six sessions MMC (Group B) N = 24	P. value
Recurrence per year	9.85%	3.30%	0.08 *(NS)*
New tumor per year	16.60%	12.5%	0.63 *(NS)*

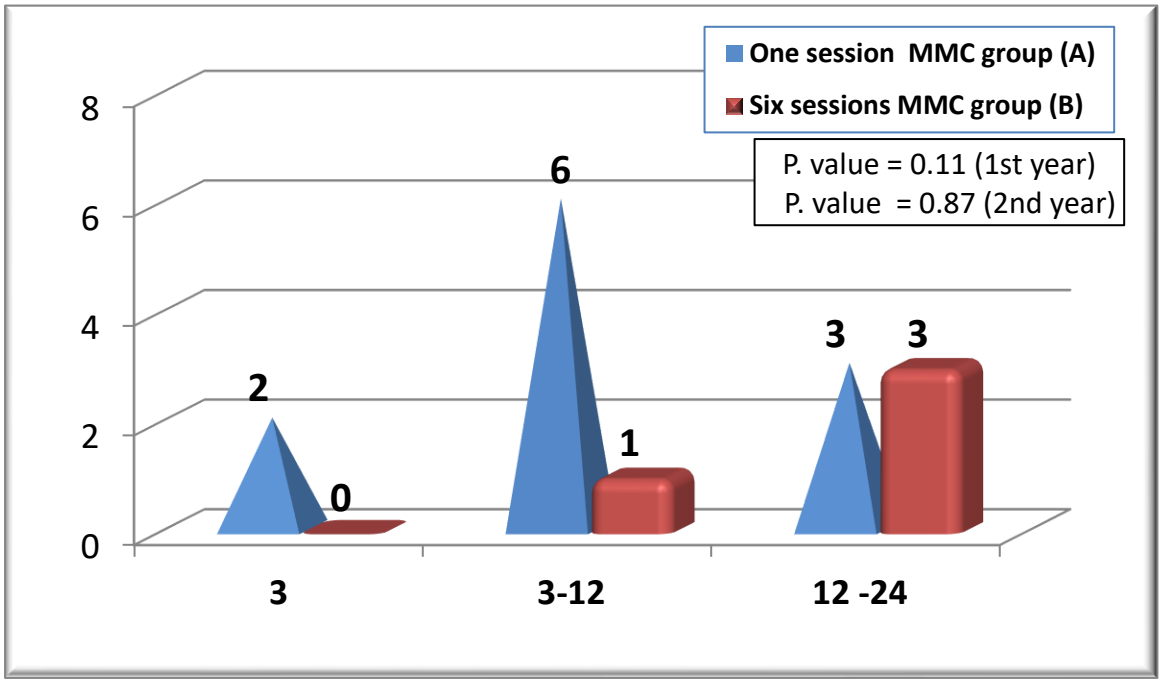

Table 6. Hospital stay and catheterization period during the 24 months

Variable		One session MMC (Group A) N = 24	Six sessions MMC (Group B) N = 24	P value
Hospital stay:	Total hours	**1231**	**1452**	**0.67 *(NS)***
	Hours/patient	**51.3**	**60.5**	
Catheterization period	Total hours	**696**	**872**	**0.98 *(NS)***
	Hours/patient	**29**	**36.3**	

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Discussion

For the treatment of non-muscle-invasive UBC, various antineoplastic drugs have been investigated. So far, the intravesical chemotherapeutic drug most often employed is mitomycin C (MMC). The other options include epirubicin, doxorubicin, and gemcitabine. By blocking the production of new DNA, MMC is able to combat tumors. When compared to TUR alone, utilizing intravesical MMC following TUR had a statistically significant advantage, according to a meta-analysis of randomized studies (n = 1,774). Recurrence rates were 32% in the group who had TUR in addition to MMC, compared to 54% in the group that received TUR alone (37). The most prevalent adverse effects, experienced by 41% of the individuals (38), were dysuria and frequency. Dissimilarities in MMC preparation and technique contribute to the large variation in response rates observed among studies. A recent study by Gao et al. showed that the level of medication concentration was directly correlated with tumor uptake and, by extension, the oncologic efficacy of intravesical MMC (39). The goal of this multi-institutional phase III trial was to determine the optimal method of administering 40 mg of MMC in 20 mL of sterile water, along with other optimizations such as methods to decrease urine production and alkalinization of urine. Patients were randomly assigned to either the regular regimen or the optimized regimen. By the end of the fifth year, the optimized regimen had reduced the recurrence rate from 75% with the standard regimen to 49%. Additionally, there was a delay of 12–29 months in the median time to recurrence (40). Urinary pH elevation, volume reduction, and intravesical content buffering are the three main components of MMC-optimized intravesical chemotherapy. To do this procedure, one must follow these steps: limit fluid intake for 8 hours before and during the treatment; begin taking oral sodium bicarbonate 12 hours before instillation; and empty the bladder with a urethral catheter just before instillation (40).

The primary concern with the treatment of individuals with non-muscle-invasive UBC is whether MMC slows tumor growth and death, even though it has been demonstrated to lower the likelihood of disease recurrence (by around 14%). By focusing on primary TUR and omitting patients with recurrent disease, Huncharek et al. meta-analyzed eleven randomized studies that compared patients treated with intravesical chemotherapy after TUR vs TUR alone (42). The authors found that a 44% reduction in the likelihood of tumor recurrence at one year was achieved when chemotherapy was added to TUR. Recurrence rates were lowest among patients whose chemotherapy treatment lasted two years or more. After analyzing eight trials that focused on patients with recurrent cancers and administered chemotherapy, Huncharek et al. discovered that the probability of disease recurrence decreased by 38% after one year; furthermore, this rate improved with treatment durations beyond two years (43). According to

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this research, MMC (mitomycin C) was more effective than doxorubicin, which is another chemotherapy drug. Despite claims to the contrary, multiple investigations have shown that adjuvant intravesical chemotherapy has long-lasting benefits. The recurrence rate was found to be lower after a median follow-up of seven years in a trial that compared TUR alone with one or five instillations of MMC (42). Recurrence rates were also found to be lower at five years for the optimized dose of MMC in a phase III trial that compared it to a standard dose (40). It is not yet known what function maintenance chemotherapy and sequential chemo-immunotherapy play. Cancer patients at high risk of tumor recurrence or progression are the most prevalent candidates for adjuvant intravesical chemotherapy instillations. It is crucial to categorize patients according to their risk to enhance outcomes, even though there is no convincing proof that chemotherapy reduces progression rates. Intravesical chemotherapy is an option for patients with moderate or high risk of tumor recurrence, tumor size greater than 3 cm, tumor grade T1 or above, or central nervous system involvement (CIS). The absence of evidence supporting the efficacy of chemotherapy in this scenario (42, 43) means that patients at high risk of progression should definitely explore intravesical immunotherapy. Although this study only looks at single instillations, there is some evidence that chemo given immediately after surgery lowers the recurrence rate compared to TUR alone. A single instillation of MMC after surgery is routinely recommended for Ta low-risk patients (44) due to the authors' demonstrated recurrence risk reductions of 50% at 2 years and 15% at 5 years.

Prior research using a large meta-analysis of randomized clinical trials determined that instillation within the first twenty-four hours following TUR was adequate (45). Unless bladder perforation occurs, complications are extremely rare (44). Patients who have had a single tiny tumor surgically removed have the greatest outcomes (45). Nevertheless, the urological community has exhibited a lack of enthusiasm for its regular usage in clinical practice, possibly due to concerns about the long-term effectiveness and the need for more robust clinical trial data to support its routine application. A phase II prospective trial was recently conducted by Dalbagni et al. to evaluate the effectiveness of intravesical gemcitabine in patients with high-risk non-muscle-invasive bladder cancer who had BCG-refractory disease. Half of the patients had a full recovery, and 21 percent were disease-free after one year (46). Although mitomycin C instillation in multiple sessions does reduce recurrence and progression, this study found that single-dose instillation given immediately or within 6 hours after TURBT achieved comparable results, suggesting that both methods are equally effective in treating low-grade non-muscle-invasive bladder cancer. The risk of side effects is higher with repeated instillations of mitomycin C (35). For high-grade tumors, six rounds of mitomycin C or BCG instillations are

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preferable, despite the cost and risk of frequent hospital visits associated with this group (36-39). Multiple studies have shown that certain characteristics of non-muscle invasive bladder cancer, such as tumor size, shape, disease-free interval, grade, stage, and bladder carcinoma in situ, can be used as valid indicators for recurrence and progression (36-39). Patients with a solitary, papillary, primary, or recurrent tumor measuring 3 cm or less and who have been free of disease for over a year can be considered to have a low risk of advancement based on these clinical characteristics. The inclusion criteria for this study were derived from these findings, and the low risk status of this group was further supported by the fact that both groups, which received either one or six sessions of mitomycine C, had a median follow-up of 24 months. Because mitomycin-C does not produce myelosuppression and sepsis like BCG and thiotepa do, it was chosen for this investigation (40). Additionally, unlike doxorubicin, which can cause tissue damage via extravasation (40), intravesical mitomycin C appears to have a substantially higher response rate than other chemotherapeutic medicines (47-48). Comparable to results obtained in controlled trials of a six-session instillation of epirubicin or mitomycin C with short-term follow-up (38, 41, 42), this study found that recurrence of tumor per year rates were slightly decreased and the recurrence-free interval was slightly increased in the six-session mitomycin C group compared to the one-session mitomycin C group during the 24-month follow-up. This clinical outcome showed that patients treated with six sessions of Mitomycin C had a lower rate of transurethral resection. The six-session Mitomycin C group required more time in the hospital and more catheterizations than the one-session Mitomycin C group at the 24-month follow-up. In this trial, side effects occurred at an extremely low rate. However, mitomycin C instillation is a costly procedure that can cause both local and systemic side effects, and it requires six sessions (49). Another perk of mitomycin C instillation in a single session is that patients won't have any extra pain if a local regional anesthetic is administered, and almost all patients already have a catheter after TUR. Nevertheless, a prompt instillation should not be administered in the event of a ruptured bladder or a protracted TUR. There was a significant psychological advantage to this method as well, since many patients were worried about recurrence too soon, even though they had been told they were low risk to begin with.

It is highly probable that cell implantation is a recurrence mechanism, given the substantial decrease in early recurrence following a single session of mitomycine instillation. This data reveals that early recurrences in controls are mostly associated with cell implantation, which is unrelated to tumor natural history (36). One study found that high-risk non-muscle-invasive bladder cancer patients treated with BCG had a significantly lower recurrence rate when they had direct post-TUR MMC instillation rather than pre-instillation mitomycine. However, the

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stage and grade at recurrence were unaffected (50). Combining microwave-induced local hyperthermia with intravesical mitomycin-C (MMC) seems to be a safe and effective therapy strategy for both ablative and prophylactic patients, according to certain research that studies the effects of this combination. Recurrence prevention of superficial bladder cancer, especially in cases when other treatments have been unsuccessful, is an additional area where the technology may be useful (51).

Conclusions

An immediate one-session instillation of mitomycin C is as effective as six sessions of mitomycin C in extending the disease-free interval and drastically lowering the rates of recurrence, progression, and recurrence of tumors per year in patients with low-risk non-muscle-invasive bladder cancer.

This risk-free method avoids many transurethral resections, shortens patients' stays in the hospital, and extends the time they spend catheterized, all while causing few or no side effects from the numerous instillations of mitomycine. Patients with low-risk, non-muscle-invasive bladder cancer may discover this method to be an alternative to either observation alone or six sessions of mitomycin C instillations.

Recommendation:

1.After completing a simple transurethral resection (T.U.R.) of a bladder tumor, our research team advised patients with low-risk, non-muscle-invasive bladder cancer to undergo a single session of mitomycin C instillation into their urinary bladder.

2. Mitomycin C delivery optimization was accomplished by removing extra volume from urine, fasting overnight, and increasing concentration to 40 mg in 20 mL by reducing drug degradation with sodium bicarbonate.

3. conduct additional research comparing the effects of immediately injecting mitomycin vs. waiting to administer BCG.

4. The duration of this study's follow-up is too short, requiring monitoring for over two years.

References:

1. Parkin DM: The global burden of urinary bladder cancer. Scand J Urol Nephrol Suppl. 2008; 218: 12-20. [Links]

2. Kirkali Z, Chan T, Manoharan M, Algaba F, Busch C, Cheng L, et al.: Bladder cancer: epidemiology, staging and grading, and diagnosis. Urology. 2005; 66: 4-34. [Links]

Eureka Open Access Journals
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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)

ISSN 2760-4942 (Online) Volume 2, Issue 5, May 2026

https://eurekaoa.com/index.php/5

3. Sylvester RJ: Natural history, recurrence, and progression in superficial bladder cancer. ScientificWorldJournal. 2006; 6: 2617-25. [Links]
4. Pawinski A, Sylvester R, Kurth KH, Bouffioux C, van der Meijden A, Parmar MK, et al.: A combined analysis of European Organization for Research and Treatment of Cancer, and Medical Research Council randomized clinical trials for the prophylactic treatment of stage TaT1 bladder cancer. European Organization for Research and Treatment of Cancer Genitourinary Tract Cancer Cooperative Group and the Medical Research Council Working Party on Superficial Bladder Cancer. J Urol. 1996; 156: 1934-40, discussion 1940-1. [Links]
5. Crispen R: History of BCG and its substrains. Prog Clin Biol Res. 1989; 310: 35-50. [Links]
6. Mathé G, Amiel JL, Schwarzenberg L, Schneider M, Cattan A, Schlumberger JR, et al.: Active immunotherapy for acute lymphoblastic leukaemia. Lancet. 1969; 1: 697-9.
7.Scher,H.I.;Shipley,W.U.;Herr,H.W. In cancer: principles and practice of oncology ;De Vita, V.T.J.: Philadelphia, (1997),pp 1300-22.
8.Torti,F.M. superficial bladder Cancer, Cancer chemo pharmaco.,(1987),20(supp), 563.
9. Abel PD: Follow-up of patients with "superficial" transitional cell carcinoma of the bladder: The case for a change policy. Br J Urol (1993);72:135-142
10 Asternzl (chairmon) , J.A. et al, Bladder cancer muscle-invasive and metastatic , European Association of Urology , 4, (2012), 16 .
11.Alexander kari, department of urology , school of medicine, university of calfornia – San Francisco , San Francisco CA, USA. Treatment of superficial bladder cancer, Evidence Based Urology, 31; (2010) , 311.
12. Borhan et al. Borhan A, Reeder JE, O' Connell MJ. et al: Grade porgession and regression in recurrent urothelial cancer. J Urol (2003)'169:2106 .
13. Akaza H, Kurth KH, Hinotsu S, et al. Intravesicle chemotherapy and immunotherapy for superficial tumors: basic mechanism of action and future direction. Urol Oncol (1998);4:121_ 9.
14. Klan R, Loy V, Huland H. Residual tumor discovered in routine second transurethral resection in patients with stage Tl transitional cell carcinoma of the bladder. J Urol (1991);146:316.
15. Levison VB, Curwen MP. The site of recurrence of noninfiltrating ; bladder tumors. Br J Urol (1978);50:237.
16. Oosterlinck W, Kurth KH, Schroder F, et al. A prospective European Organization for Research and Treatment of Cancer Genitourinary Group randomized trial comparing

Eureka Open Access Journals
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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)

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https://eurekaoa.com/index.php/5

transurethral resection followed by a single intravesical instillation of epirubicin or water in single Ta, Tl papillary carcinoma of the bladder. J Urol(1993);149:749_ 52.
17. Oosterlinck W, Lobel B, Jakse G et al. Guidelines on bladder cancer. European Association of Urology (EAU) Working Group on Oncological Urology. Eur Urol 2002; 41 (2): 105-12.
18. Freeman JA, Esrig DE, Stein JP, et al. Radical cystectomy for high risk patients with superficial bladder cancer in the era of orthotopic urinary reconstruction. Cancer (1995);76:833.
19. Konety BR, Williams RD. Superficial transitional (Ta/Tl/CIS) cell carcinoma of the bladder. BJU Int. (2004); 94 (1): 18-21.
20. Sylvester R J, Oosterlinck W, van der Meijden A P M, "A Single, 6 immediate post-operative instillation of chemotherapy decreases the risk of recurrence in patients with stage Ta Tl bladder cancer: A meta¬-analysis of published results of randomized clinical trials", J. Urol. (2004); 171: pp. 2,186-2,190.
21. Kamat A M, Lamm D L, "Intravesical therapy for bladder cancer' Urology (2000);55: pp. 161-168.
22. Crawford D E, "Intravesical therapy for superficial cancer: need for more options", J. Clin. Oncol. (2002);20: pp.3,185-3,186.
23. Bostwick D G, Natural History of Bladder Cancer", J. Cell. Biochem. (1991);161: pp. 31-38.
24. Lutzeyer, W.;Rubben, H.;Dahm, H. management of urinary bladder cancer J.Urol.,(l982), 127,250.
25. Holmang S, Johannson SL: Stage Ta-T2 bladder cancer: The relationship between findings at first follow-up cystoscopy and subsequent recurrence and prognosis. J Urol (2002); 167:1634-1637.
26. Lamma, D.L. recurrent bladder cancer Urol. Clin. North Am .(1992),19,573.
27. Ch. Bouffioux, K.H. Kurth, A. Bono, W. Oosterlinck, C. Boeken Kruger, M. de Pauw and R. Sylvester, the European Organization for Research and Treatment of Cancer Genito-urinary Group: Intravesical adjuvant chemotherapy for superficial transitional cell bladder carcinoma: results of 2 European Organization for Research and Treatment of Cancer randomized trials with mitomycin C and doxorubicin comparing early versus delayed instillations and short-term versus long-term treatment, J. Urol. (1995) 153, p. 934
28. Iborra, I., Solsona, E., Monros, J. L. and Ricos, J. V.: Double randomized trial between Adriamycin (ADM) and Mitomycin C (MMC) instilled immediately or delayed after resection

Eureka Open Access Journals
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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)

ISSN 2760-4942 (Online) Volume 2, Issue 5, May 2026

https://eurekaoa.com/index.php/5

of superficial bladder carcinoma. Proceedings of European Association of Urology Congress, abstract, (1988) p-241.
29. T. Weldon and M.S. Soloway, Susceptibility of urothelium to neoplastic cellular implantation, Urology(1975) 5, p. 824
30. P.H. Abrams, R.G. Choa, C.G. Gaches, M.H. Ashken and N.A. Green, A controlled trial of single dose intravesical adriamycin in superficial bladder tumors, Brit. J. Urol. (1981) 53, p. 585.
31. K.G. Burnand, P.J. Boyd, M.E. Mayo, K.E.D. Shuttleworth and R.W. Lloyd-Davies, Single dose intravesical thiotepa as an adjuvant to cystodiathermy in the treatment of transitional cell bladder carcinoma, Brit. J. Urol. (1976)48, p. 55.
32. H. Zincke, D.C. Utz, W.F. Taylor, R.P. Myers and F.J. Leary, Influence of thiotepa and doxorubicin instillation at time of transurethral surgical treatment of bladder cancer on tumor recurrence: a prospective, randomized, double-blind, controlled trial, J. Urol. (1983)129, p. 505.
33. Peto R, Pike MC, Armitage P,et al.Design and analysis of randomized clinical trials requiring prolonged observation of each patient .Part II ;analysis.Br.J.Cancer (1977);35;l-39.
34. P.-U. Malmstro'm / Critical Reviews in Oncology /Hematology 47 (2003) 109_ 126.
35.Shoenfeld Y, Aron-Maor A, Tanai A, Ehrenfeld M: BCG and autoimmunity: another two-edged sword. J Autoimmun. 2001; 16: 235-40.
36. Bouffioux, C: Intravesical adjuvant treatment in superficial lbladder cancer. A review of the question after 15 years of experience with the EORTC GU Group. Scand. J. Urol. Nephrol., suppl. (1991), 138: 167.
37.Nilsson S, Ragnhammar P, Glimelius B, Nygren P; SBU-group. Swedish Council of Technology Assessment in Health Care: A systematic overview of chemotherapy effects in urothelial bladder cancer. Acta Oncol. 2001; 40: 371-90.
38.Thrasher JB, Crawford ED: Complications of intravesical chemotherapy. Urol Clin North Am. 1992; 19: 529-39. [Links]
39.Gao X, Au JL, Badalament RA, Wientjes MG: Bladder tissue uptake of mitomycin C during intravesical therapy is linear with drug concentration in urine. Clin Cancer Res. 1998; 4: 139-43. [Links]
40. Au JL, Badalament RA, Wientjes MG, Young DC, Warner JA, Venema PL, et al.: Methods to improve efficacy of intravesical mitomycin C: results of a randomized phase III trial. J Natl Cancer Inst. 2001; 93: 597-604. [Links]

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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)

ISSN 2760-4942 (Online) Volume 2, Issue 5, May 2026

https://eurekaoa.com/index.php/5

41. Lamm DL, Riggs DR, Traynelis CL, Nseyo UO: Apparent failure of current intravesical chemotherapy prophylaxis to influence the long-term course of superficial transitional cell carcinoma of the bladder. J Urol. 1995; 153: 1444-50. [Links]

42.Huncharek M, Geschwind JF, Witherspoon B, McGarry R, Adcock D: Intravesical chemotherapy prophylaxis in primary superficial bladder cancer: a meta-analysis of 3703 patients from 11 randomized trials. J Clin Epidemiol. 2000; 53: 676-80. [Links]

43. Huncharek M, McGarry R, Kupelnick B: Impact of intravesical chemotherapy on recurrence rate of recurrent superficial transitional cell carcinoma of the bladder: results of a meta-analysis. Anticancer Res. 2001; 21: 765-9. [Links]

44. Witjes JA, Hendricksen K: Intravesical pharmacotherapy for non-muscle-invasive bladder cancer: a critical analysis of currently available drugs, treatment schedules, and long-term results. Eur Urol. 2008; 53: 45-52.

45. Sylvester RJ, Oosterlinck W, van der Meijden AP: A single immediate postoperative instillation of chemotherapy decreases the risk of recurrence in patients with stage Ta T1 bladder cancer: a meta-analysis of published results of randomized clinical trials. J Urol. 2004; 171: 2186-90.

46. Dalbagni G, Russo P, Bochner B, Ben-Porat L, Sheinfeld J, Sogani P, et al.: Phase II trial of intravesical gemcitabine in bacille Calmette-Guérin-refractory transitional cell carcinoma of the bladder. J Clin Oncol. 2006; 24: 2729-34.

47. Melekos MD,Moutzouris GD. Intravesical therapy of superficial bladder cancer .Current pharmaceutical design (2000);6:345-359.

48. Hayes MC, Birch BR, Cooper AJ ;et al. Cellular resistance to mitomycin c is associated with overexpression of MDR-1 in urothelial cancers cell line (MGH-UI). BJU international (2001);78(3):245-250.

49. Tolley, D. A., Hargrave, T. B., Smith, P. H., Williams, J. L., Grigor, K. M., Parmar, M. K. B., Freedman, L. D., Uscinska, B. M. and Urological Cancer Working Party.: Effect of intravesical mitomycin C on recurrence of newly diagnosed superficial bladder cancer: interim report from the Medical Research Council Subgroup on Superficial Bladder Cancer. Brit. Med. J. (1988); 296: 1759

50. J. Park, K. Song, M. Jo ; Efficacy of immediate post-TUR mitomycin-C (MMC) instillation in high-risk non-muscle-invasive bladder cancer treated with bacillus Calmette-Guerin (BCG). J Clin Oncol 29: 2011 (suppl 7; abstr 281).

51-B. Moskovitz*, G. Meyer, A. Kravtzov, M. Gross, A. Kastin, K. Biton & O. Nativ; Thermo-chemotherapy for intermediate or high-risk recurrent superficial bladder cancer patients. Annals of Oncology Advance Access published February 25, 2005.