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Process Improvements Positively Impact the Use of Intravesical Mitomycin C after Transurethral Resection of Nonmuscle Invasive Bladder Cancer in a Large, Urban Urology Practice

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Abstract

Introduction: We assessed the rate of intravesical mitomycin C therapy in patients with nonmuscle invasive bladder cancer who underwent transurethral resection of the bladder, as well as the impact of procedural changes governing its use.

Methods: A retrospective review of our bladder cancer database identified patients who underwent transurethral resection of the bladder with mitomycin C therapy during January 2008 to July 2014. Since our mitomycin C protocols were revised during 2013, patients were stratified based on date of service. Patient demographics and data describing mitomycin C use were tabulated.

Results: During January 2008 to May 2013, 276 of 737 (37.5%) ideal patients received mitomycin C (not accounting for patients in whom mitomycin C was contraindicated). Conversely 461 of 737 patients (62.5%) did not receive mitomycin C. Shortages of mitomycin C were responsible for nonuse in 18.4% of cases while no specified reason for nonuse was given in 59%. When cases in which mitomycin C use was contraindicated were taken into account, mitomycin C was used in 51.6% overall. After the implementation of new mitomycin C operating procedures, mitomycin C use increased significantly to 76.0% ($p < 0.001$) (accounting for appropriate nonuse). During this period mitomycin C shortages were not responsible for any case in which mitomycin C was not used.

Conclusions: During 2008 to 2013 mitomycin C was not used in a significant proportion of patients who underwent transurethral resection of the bladder. The implementation of a revised protocol governing mitomycin C use significantly and positively impacted mitomycin C use. Importantly, pharmacy shortages no longer contribute to the nonuse of mitomycin C in patients with bladder cancer. These data highlight the impact of continual improvement initiatives on standard clinical practice.

Key Words: mitomycin, urinary bladder neoplasms

Abbreviations and Acronyms

MMC = mitomycin C

NMIBC = nonmuscle invasive bladder cancer

TURB = transurethral resection of the bladder

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Bladder cancer is a serious public health issue, with more than 70,000 new cases of bladder cancer and more than 15,000 bladder cancer related deaths in the United States in 2013.[1] Transurethral resection of the bladder is a standard approach in the management of nonmuscle invasive bladder tumors.[2] The primary aims of TURB are to completely remove papillary nonmuscle invasive tumor tissue, to establish the histological diagnosis of the tumor, to determine its clinical stage and to define clinically relevant prognostic factors (eg tumor grade, number, size and configuration as well as the presence of carcinoma in situ).[2] However, the efficacy of the procedure is suboptimal, with early recurrences often related to persistent tumors that were not identified during the initial resection, reimplantation of seeded tumor cells[3] and under staging (related to the nonvisualization of muscle invasive cells on resection specimen histology).

An important adjunct to TURB is the use of intravesical immunotherapeutic or chemotherapeutic agents. Mitomycin C is a commonly used adjuvant therapy after TURB for nonmuscle invasive bladder cancer, and it is used therapeutically (treatment of carcinoma in situ or residual nonvisible tumor), prophylactically (prevention of recurrence and progression in superficial bladder cancer) or as an adjuvant in the immediate postoperative setting.[4] In a meta-analysis of patients with stage Ta-T1 tumors, MMC instillation immediately after TURB was associated with a 39% decrease in recurrence.[5] American Urological Association guidelines recommend MMC use or specify MMC as a treatment option depending on the case presentation.[6] An initial single dose of MMC is recommended postoperatively in cases of abnormal growths on the urothelium; small volume, low grade Ta cancers; and multifocal and/or large volume, low grade Ta or recurrent Ta cancers. For high grade Ta/T1 and Tis (including recurrences) MMC is recommended after repeat resection.[5,6]

The beneficial effects of mitomycin on disease recurrence in patients with NMIBC after TURB are well established and supported by a large body of clinical data. As such, best practice guidelines from the National Comprehensive Cancer Network®, American Urological Association and European Association of Urology recommend MMC instillation after TURB to minimize the morbidity and mortality associated with the recurrence and progression of NMIBC.[7] However, paradoxically, studies of administrative data sets show suboptimal rates of use in clinical practice.[8,9] Reasons for this may include local or national shortages of MMC, or surgeon belief that MMC is not efficacious or that NMIBC is associated with a low risk of recurrence.

As part of a continual improvement program at our large, urban clinical urology center, we conducted a retrospective vigilance study to assess post-TURB MMC use and barriers to its use. Furthermore, we assessed the impact of implementing revised TURB-MMC operating procedures on post-TURB MMC use.

Materials and Methods

We performed a retrospective analysis of our institutional review board approved bladder cancer database to identify patients who underwent single or multiple transurethral resections of bladder tumors, with or without perioperative intravesical neoadjuvant treatment with MMC, during a 7-year contemporary period (January 2008 to July 2014) at our large, urban clinical urology center. As part of a process improvement strategy to drive optimal rates of MMC use, a revised TURB-MMC operating procedure was implemented in June 2013. This initiative included 1) distributing educational material to all providers and patients with bladder tumors, 2) combining consent forms for TURB and MMC instillation into a single form, 3) holding weekly planning meetings with our institutional pharmacy to ensure the availability of an uninterrupted MMC supply and 4) incorporating MMC use in every surgical time-out checklist. We assessed the impact of these revised procedures on MMC use 12 months immediately after their implementation. Surgeons were unaware that details describing MMC use were being tracked. All surgeons who contributed data to the study were fully aware of the contraindications for MMC instillation (eg bladder perforation, stent insertion at TURB and excessive bleeding).

Patients were stratified into 2 groups based on date of service (January 2008 to May 2013 and June 2013 to July 2014). Patients were further classified according to whether they received MMC therapy after TURB. In all patients in both periods studied, MMC was given within 60 minutes of completing the resection. In addition, the dwell time was consistently 60 minutes.

Patient demographics, histological pathology, and tumor grade and stage at TURB were collected. The date of service and data describing perioperative MMC instillation were also retrieved. Patients with muscle invasive tumors were excluded from the study. Continuous variables were compared using the independent samples t-test or Wilcoxon ranked sum test depending on whether assumptions concerning the underlying distributions were met. Chi-square tests of proportion were used to compare data for dichotomous and categorical variables.

Results

A total of 945 patients underwent TURB with adjunct MMC therapy during January 2008 to July 2014. Patients were