Visual Internal Urethrotomy With Intralesional Mitomycin C and Short-term Clean Intermittent Catheterization for the Management of Recurrent Urethral Strictures and Bladder Neck Contractures

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OBJECTIVE To evaluate our longitudinal experience using visual internal urethrotomy (VIU) with intralesional mitomycin C (MMC) and short-term clean intermittent catheterization (CIC) for urethral strictures and bladder neck contractures (BNC) after failure of endoscopic management.

MATERIALS AND METHODS This case series involved review of our prospectively developed database of all men who underwent VIU with MMC and CIC in a standardized fashion for urethral stricture or BNC between 2010 and 2013 at our tertiary care medical center. Etiology was identified as radiation-induced stricture (RIS) or non-RIS and analyzed by stricture location. Cold knife incisions were made in a tri or quadrant fashion followed by intralesional injection of MMC and 1 month of once daily CIC.

RESULTS All 37 patients previously underwent at least 1 intervention for urethral stricture or BNC before VIU with MMC and CIC. Mean stricture length was 2.0 cm (range, 1-6 cm; standard deviation, 1.0 cm). Over the median follow-up period of 23 months (range, 12-39 months), 75.7% of patients required no additional surgical intervention (RIS, 54.5%; non-RIS, 84.6%; $P = .051$). In those that did recur, median time to stricture recurrence was 8 months (range, 2-28 months). One patient with recurrence required urethroplasty.

CONCLUSION VIU with MMC followed by short-term CIC provides a minimally invasive and widely available tool to manage complex recurrent urethral strictures (<3 cm) and BNC without significant morbidity. This approach may be most attractive for patients who are poor candidates for open surgery. UROLOGY 85: 1494−1500, 2015.

Urethral strictures arise from a process of fibrosis within the urethral mucosa that can be initiated by a variety of insults. Although urethral strictures may be idiopathic, many are iatrogenic and result from a history of urethral catheterization, cystoscopy, transurethral resection of the prostate, prostatectomy, prostate radiation therapy, or hypospadias repair. Other notable causes of urethral strictures include pelvic trauma, urethritis, and lichen sclerosus.[1]

Radiation-induced urethral strictures (RIS) are uncommon, but when they do occur, they are often complex and traditionally have been difficult to manage. Previous investigation of stricture occurrence after radiation therapy for prostate cancer has been described with a reported incidence of 1.8% after brachytherapy, 1.7% after external beam radiotherapy (EBRT), and 5.2% after combination radiation therapy.[2] Additional studies report urethral stricture development in 2.4%-8.2% of patients after prostate brachytherapy, which typically occur at the bulbomembranous urethra or the bladder neck.[3,4]

Multiple modalities are available for the treatment of urethral strictures including self-catheterization, urethral dilation, laser incision, urethral stent placement, visual internal urethrotomy (VIU), and open repair. Endoscopic internal urethrotomy has been promoted as the standard initial treatment for bulbar urethral strictures.[5] However, after a

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single VIU, the long-term cure rates for non—radiation-associated strictures are as low as 30%-40%.[6]

In an effort to decrease the rate of urethral stricture recurrence after VIU, supplemental injection of mitomycin C (MMC) has been proposed owing to its ability to mitigate scar formation via inhibition of fibroblast proliferation.[7,8]

In the present study, we aim to describe a safe and widely available endoscopic alternative to open surgical reconstruction that is more durable than VIU alone in patients with recalcitrant urethral strictures and bladder neck contractures (BNC) of various etiologies. We propose that VIU with MMC and short-term clean intermittent catheterization (CIC) may be a particularly attractive option for patients who are not candidates for definitive open urethroplasty. Although previous studies of VIU with MMC focused specifically on anterior urethral strictures or BNC with a small population undergoing radiation therapy, we include all stricture loci in one of the largest reported cohorts with the longest postoperative follow-up to date.[7,8] Furthermore, given the unique and traditionally problematic nature of strictures owing to radiation, we compare our findings from RIS with nonradiation etiologies.

MATERIALS AND METHODS

This study was designed as a case series involving review of a prospectively developed database of all men presenting for reconstructive urethral surgery between 2010 and 2013 to our tertiary care medical center. Men included in this study had symptoms of urinary obstruction, had urethral stricture or BNC confirmed via office cystoscopy, and were poor surgical candidates for open surgery or refused open repair. Selected patients subsequently underwent VIU with MMC followed by a short period of CIC. Retrospective analysis was conducted, and complete data were available for all included subjects. Informed consent was obtained from all subjects in this study at the time of initial patient visit.

Patient demographic data included age, history of prior stricture interventions, and stricture etiology. Stricture length was determined by retrograde urethrogram and/or intraoperatively under direct vision based on the length of the cold knife incision of the stricture. Preoperative postvoid residual (PVR), uroflow, and any history of incontinence were recorded. We further analyzed this database to identify stricture etiology as radiation vs non—radiation induced. The RIS group included patients with a history of prostate EBRT and/or brachytherapy. Non-RIS were analyzed as all other stricture etiologies.

Cystourethroscopy with a 22F rigid cystoscope was performed to allow for passage of a wire through the stricture site and into the urinary bladder. Direct VIU with cold knife incisions of the scar was made at the 12-, 3-, and 9-o'clock positions through the full thickness of the scar down to the level of healthy-appearing underlying tissue, if possible. Cold knife incisions at the 6-o'clock position were also performed when the bladder neck alone was involved. Using sharp cold knife incisions, we are able to directly visualize the change in tissue character from fibrosis to vascularized underlying tissue regardless of stricture location. Strictures with greater depth required a deeper incision down to the healthy-appearing tissue. This was followed by multiple injections of 0.4-mg/mL MMC in 0.2- to 0.4-mL aliquots at various points along the length of each incision for a total volume of 10 mL using a 23F Wolf (Vernon Hills, IL) injection or aspiration scope and a standard injection needle.

Patients were routinely discharged the same day with a 16-18F silastic Foley catheter, which was subsequently removed in the office in 5-7 days. CIC was performed by the patient once daily with a 16F straight or coude catheter after removal of the Foley catheter that was placed at the time of surgery.[9]

Longitudinal follow-up data were collected to investigate the relationship between stricture etiology and the success rate of VIU with MMC. Postoperative evaluation at 1, 3, 6, and 12 months, followed by further evaluation at 6-month intervals, thereafter, included urethral patency via cystoscopy, PVR, uroflowometry, and stricture recurrence requiring reoperation. Stricture recurrence was defined as the inability to pass a 16F flexible cystoscope through the stricture site.

Data analysis was conducted using PASW Statistics 18 software (SPSS, Inc., Chicago, IL). Continuous variables were reported as mean and standard deviation, with analyses conducted via a 2-sample *t* test. For continuous variables that did not follow a normal distribution, median and range were reported, with analysis conducted using a Mann-Whitney *U* test. Categorical data were shown as counts and percentages. Associations across categorical independent variables were evaluated using the Pearson chi-square univariate analysis. For all analyses, variables are considered significant predictors if the *P* value associated with the appropriate test statistic is $<.05$.

RESULTS

Thirty-seven patients underwent VIU with MMC and CIC for refractory urethral strictures and BNC. Stricture location included 5 pendulous, 15 bulbar, 6 posterior urethral stricture, and 11 BNC. There were no statistical differences in patient age, stricture length, and number of procedures before VIU with MMC and CIC when analyzed by stricture location ($P > .05$; Table 1).

Urethral stricture etiology was attributed to radiation in 11 patients, whereas 26 non-RIS patients were identified. Among RIS patients, 81.8% (n = 9) previously underwent brachytherapy alone and 18.2% (n = 2) had a history of both brachytherapy and EBRT. The most common stricture etiology among the non-RIS cohort was previous urethral instrumentation (34.6%) followed by radical prostatectomy (26.9%), infection (11.5%), hypospadias requiring pediatric repair (11.5%), idiopathic (11.5%), and external trauma to the urethra (7.7%). There were no differences in stricture length between RIS and non-RIS patients; however, RIS were subjectively noted to have deeper, full thickness spongiofibrosis (Table 1).

The mean age of men undergoing VIU with MMC was 59 years (range, 22-80 years). All patients had at least 1 failed intervention for urethral stricture before VIU with MMC and CIC (range, 1-6). The 22-year-old patient had recurrent strictures after previous repair of a urethral distraction injury that was associated with a pelvic fracture. As such, he had previously undergone and failed urethroplasty and subsequently preferred VIU with MMC. Overall, 29.7% patients (n = 11) failed previous