

# Management of Urethral Recurrences

## Urothelial and Nonurothelial



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### KEYWORDS

- Urethra • Urothelial carcinoma • Squamous cell carcinoma • Recurrence • Organ preservation
- Therapy

### KEY POINTS

- Urethral carcinoma is a rare disease and may present as primary cancer or be associated with disease of the bladder at the time of cystectomy.
- There are relatively more data on management of urethral recurrence following cystectomy for urothelial carcinoma of the bladder.
- Urethral metachronous relapses have been managed with both urethra preserving as well as urethrectomy.
- There are minimal data on management of relapse following primary urethral carcinoma. The management options are similar to those seen with primary urethral cancer.
- Multimodal therapies with chemotherapy and radiation should be considered in more advanced disease.

### INTRODUCTION

Urethral carcinoma can be encountered in the settings of primary urethral cancer, synchronous presentation with other genitourinary (GU) malignancies, relapse following primary urethral cancer, or metachronous recurrence after treatment of other GU malignancies. Regardless of clinical situation and presentation, there are comparatively few data on treatment options for primary and recurrent urethral cancer. There are no prospective studies in the management of urethral carcinoma, and the current information is largely based on retrospective experience, often from single institutions.<sup>1</sup>

This article will review some of the reported therapeutic strategies in the management of recurrent urethral carcinoma. It describes treatment options in recurrences encountered following cystectomy

as well as relapse following treatment for primary urethral cancer.

### URETHRAL RECURRENCE AFTER CYSTECTOMY

Prophylactic urethrectomy at the time of radical cystectomy for urothelial carcinoma is often performed in patients who are considered to be at high risk for urethral recurrence. Certain contemporary indications for prophylactic urethrectomy in men include cystectomy for nonmuscle invasive bladder cancer (NMIBC), history of recurrent NMIBC, involvement of the prostatic urethra by urothelial cancer, or microscopic involvement of the urethra based on positive intraoperative urethral frozen sections.<sup>2</sup> In female patients, cancer at the bladder neck or cancer involving the anterior

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vaginal wall is associated with an increased risk of urethral recurrence.<sup>3,4</sup>

It is reported that following radical cystectomy, new urethral tumors occur in 1.5% to 6% of men and 6% to 11% of women. Some have suggested that the incidence of urothelial recurrence in the female urethra may be lower, possibly related to prominence of squamous mucosa in the female urethra.<sup>5</sup> Furthermore, the incidence of urethral recurrence is reportedly also lower in both men and women treated with neobladder reconstruction (1%–4%).<sup>6–8</sup> Most urethral recurrences occur within 24 months after surgery, with reported median time to relapse of 8 to 28 months.<sup>9</sup> In a report that included 7 patients with neobladder substitution who had initial negative intraoperative frozen sections but positive urethral margins at final pathology, only 1 patient subsequently developed recurrence in the urethra.<sup>1</sup> Similarly, of 136 patients with moderate-to-severe atypia or positive urethral margins, only 5 patients (3.7%) subsequently developed urethral recurrence.<sup>10</sup>

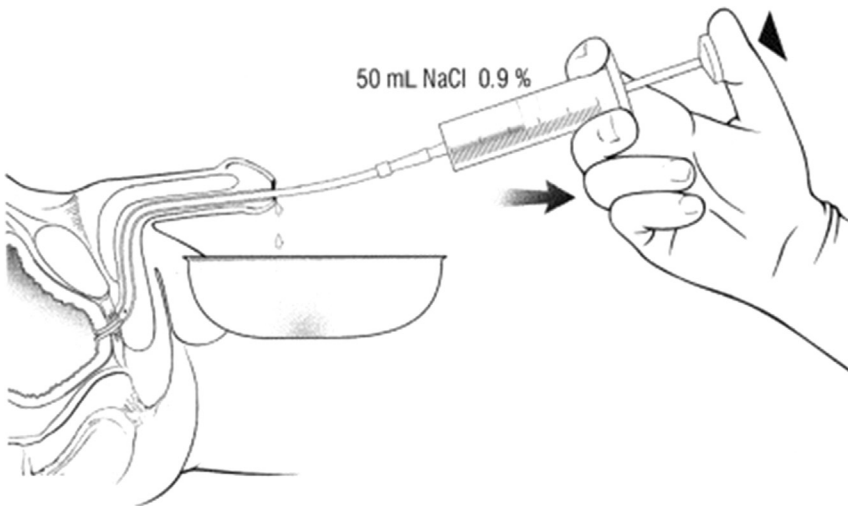
Lower incidence of urethral recurrence in patients with neobladders may to some extent relate to selection bias, with lower-risk patients or those with negative bladder neck or prostatic urethral margins being selected for neobladder diversion. However, some authors have suggested that even after controlling for potential risk factors such as tumor grade and multifocality, carcinoma in situ, and pathologic stage, as well as prostatic involvement, patients with neobladder diversions may still have lower adjusted rates for urethral recurrence compared with cutaneous diversions.<sup>11,12</sup> Others have suggested urine remaining

in contact with the urothelium may be protective or that juxtaposition of the ilium to the urethra may provide a degree of protection, although none of these purported mechanisms has been proven.<sup>6</sup>

The detection and diagnosis of urethral recurrence following radical cystectomy can be secondary to symptomatic presentation or detection through routine surveillance with urethral wash cytology or endoscopic examination.

One reported technique for performing a urethral wash involves the insertion of a minimally lubricated 14 French (Fr) catheter into the proximal penile urethra, followed by irrigation of 100 mL of normal saline solution and collection of all extruded solution at the level of the urethral meatus. The catheter should be withdrawn gradually and removed while flushing continues (Fig. 1).<sup>13</sup>

The value of routine surveillance, however, is questioned by some, as there is evidence that positive urethral wash cytology may not improve survival. In several case series, patients experienced similar survival rates, regardless of whether they received treatment following diagnosis based on symptoms (bleeding, urethral discharge, pain, or palpable mass) or based primarily on positive urethral cytology.<sup>14–16</sup> It has also been suggested that while asymptomatic patients diagnosed by cytology might have a higher chance of harboring noninvasive disease, overall survival may not be significantly better than survival in symptomatic patients with invasive (pT1–pT4) cancer.<sup>17</sup> On the contrary, others have demonstrated that noninvasive recurrences have a favorable prognosis when detected early,<sup>18</sup> and there is evidence that patients who present with symptomatic urethral



**Fig. 1.** Technique for performing a urethral wash for cytology. (From Varol C, Thalmann GN, Burkhard FC, et al. Treatment of urethral recurrence following radical cystectomy and ileal bladder substitution. *J Urol* 2004;172(3):937–42; with permission.)

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