# Secondary Tumors After Urinary Diversion

Roger Li, MD, Janet E. Baack Kukreja, MD, MPH, Ashish M. Kamat, MD, MBBS*

**KEYWORDS**

• Urinary diversion • Secondary malignancy • Ureterosigmoidostomy • Cystoplasty • Neobladder • Urinary conduit

**KEY POINTS**

- Secondary malignancies are estimated to arise in 0.18% to 15.00% of patients undergoing various urinary diversions.
- Secondary malignancies occur most frequently after ureterosigmoidostomies and cystoplasties.
- Long-term vigilance is essential because reported latency period ranges from 2 to more than 30 years, with most lesions detected a decade after urinary diversion.
- Current surveillance protocols include patient history, imaging, urinalysis, and endoscopic evaluation, with biopsies reserved for suspicious lesions.

## INTRODUCTION

The development of secondary malignancies after interposition of urinary and bowel mucosa has been recognized since its first description by Hammer in 1929.[1] Altogether, more than 300 secondary tumors have been reported within various urinary diversion constructs.[2] The risk for cancer arising from the intestinal segments used for urinary diversion has been estimated to be between 8- and 477-fold higher.[3,4] Preclinical and clinical studies have been conducted to define the mechanism of carcinogenesis in this unique microenvironment with several interesting hypotheses. In this review, we summarize the current knowledge on the developmental patterns and carcinogenic mechanisms of secondary malignancy after urinary diversions. The pressing need for consensus guidelines pertaining to cancer screening after urinary diversion is also highlighted.

## URETEROSIGMOIDOSTOMY

Historically, ureterosigmoidostomy (**Table 1**) was the urinary diversion of choice in patients with nonfunctional bladders.[5] However, the propensity for neoplastic changes at the ureterosigmoid junction has been recognized since the early 1960s.[6] Although the development of junctional adenocarcinoma has been described as early as 2 years after ureterosigmoidostomy creation, the mean latency period ranges between 20 and 26 years.[7]

The incidence of adenocarcinoma has been found to be cumulative over the duration of the diversion.[8] Compared with other exstrophy patients, those having undergone ureterosigmoidostomy were 7000 times as likely to develop malignancies.[9] Described incidences range from 2% to 15%.[7] The majority of tumors follow the typical course of transforming from polyps to adenoma, and eventually to adenocarcinoma.[7,10]

The unacceptably high incidence of secondary malignancies has spelled the end to the routine use of ureterosigmoidostomies. In the unlikely event that diversion using the sigmoid colon is necessary, every effort must be made for its use as an isolated segment to prevent mixing urine with stool.[11–14] Owing to its limited usage, whether this alternative sigmoid diversion leads to reduced

Disclosure Statement: The authors have nothing they wish to disclose.
Department of Urology, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Unit 1373, Houston, TX 77030, USA
* Corresponding author.
*E-mail address:* akamat@mdanderson.org

Urol Clin N Am 45 (2018) 91–99
https://doi.org/10.1016/j.ucl.2017.09.010

**Table 1**
**Ureterosigmoidostomy series**

| | Number of Patients | Incidence (%) | Latency Period (y) | Histology |
|---|---|---|---|---|
| Azimuddin et al,[7] 1999 | — | 2–15 | 20–26 | Adenocarcinoma |
| Tollefson et al,[65] | 51 | 0 | 10–45 | — |
| Gobert et al, | 42 | 2.30 | — | Adenocarcinoma |
| Hurlstone et al, | 42 | 24 | 1–26 | Adenocarcinoma |

tumorigenesis remains relatively unknown. Instead, urologists have mainly used segments from elsewhere in the intestinal tract for the purpose of urinary diversion.

## URINARY DIVERSION USING ISOLATED GUT

### *Early Findings*

Owing to its rarity, early attempts to study the patterns of secondary malignancy after urinary diversion using isolated gut were limited to small single-center case reports and series. From a cohort of 645 patients after urinary reconstruction, Ali-El-Dein and colleagues[15] found 6 patients developing secondary malignancy at the uroinstestinal junction. Specifically, cancer was discovered in 3 of 54 patients (5.5%) after ileocystoplasty, 2 of 258 patients (0.8%) after ileal ureter, and 1 of 348 patients (0.3%) after ileal conduit. Unlike the prevalence of adenoma and adenocarcinoma subsequent to ureterosigmoidostomy, a wide range of pathologies including urothelial carcinoma, squamous cell carcinoma, mucinous adenoma and adenocarcinoma were found. Another pattern that emerged was the increased incidence subsequent to cystoplasties compared with other forms of intestinal diversion. However, the small sample size made it impossible to draw conclusions regarding secondary tumor incidence relative to the primary indication for urinary diversion, histologic makeup of the secondary tumors, origin of the diverting intestinal segment, or whether diversion was fashioned for urinary continence.

The analysis of an exhaustive list of 81 secondary tumors helped to shed light on some of these questions.[16] With regard to the primary indication for urinary diversion, secondary malignant tumors occurred much quicker after diversion for malignant disease at a median of 8 years versus 21.5 years for benign disease. In contrast, the latency period before developing benign and malignant secondary tumors were comparable in patients diverted for benign indications (median of 22.0 years vs 21.5 years, respectively). This is in contrast with the adenoma–adenocarcinoma sequence spanning 6 years observed after ureterosigmoidostomies.[4]

With regard to the origin of the diverting intestinal segment, 41.8% of the evaluable malignant tumors developed in isolated colonic segments, whereas 58.2% developed in ileal segments.[16] However, because the number of urinary diversions using each segment was unknown, no conclusions could be drawn regarding the relative incidence in the different intestinal segments. Nevertheless, it is clear that secondary malignancies can arise from diversion using either ileum or colon.

Of the evaluable tumors, 80.8% arose in continent urinary reservoirs versus 19.2% in conduits.[16] This finding corroborated with the observation made by Ali-El-Dein and associates that more secondary malignancies occurred in cystoplasties than conduits. Compounded with the lower usage rate of cystoplasties, the incidence of secondary malignancy seemed higher in this setting. However, the fact that conduits are frequently used for malignant indications has to be considered. These patients have a poor prognosis and may not outlive the latency period before developing secondary malignancies.

### *Focus on Cystoplasty*

Even with limited data, a trend toward a higher incidence of secondary cancer was evident after cystoplasty. Interestingly, cystoplasties from early studies were mostly performed in adults for contractile bladders secondary to genitourinary infections, most commonly tuberculosis and schistosomiasis.[15,16] Thus, in these patients, carcinogenesis may not be solely due to the urinary reconstruction, because it was suspected that the infections themselves could lead to cancer.[17,18] Furthermore, the patients' age and history of exposure to environmental carcinogens, such as tobacco smoke, can also confound the described incidences.

Beginning in the 1980s, augmentation cystoplasty was increasingly adopted for pediatric patients with nonfunctioning bladders owing to exstrophy, posterior urethral valves, or neuropathic etiologies. As these patients reached latency period for developing malignancies, they