



A systematic approach for successful repair of radiated and non-radiated ureteral injuries

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Background: Successful ureteral reconstruction is challenging, particularly in radiated fields. We characterize and directly compare surgical outcomes in modern cohorts of radiated and non-radiated patients undergoing ureteral reconstruction utilizing a systematic approach to pre-operative assessment. We hypothesize that radiated patients will undergo more complex ureteral reconstructions and experience higher rates of surgical failure and complications compared to nonradiated patients.

Methods: Consecutive cases of ureteral reconstruction for acquired ureteral injury performed by a single surgeon from 2010–2018 were retrospectively reviewed. Clinical data were collected including pre-operative bladder capacity, ureteral injury characteristics, and surgical technique. Ileal ureter and autotransplantation were classified as “complex” ureteral repairs, and surgical success was defined as freedom from surgical revision of the ureteral anastomosis and/or ureteral stenting.

Results: There were 47 ureteral reconstructions performed including 17 (36%) radiated patients. Radiated patients had lower pre-operative bladder capacity and were more likely to undergo complex repairs compared to non-radiated patients (35% vs. 7%, $P=0.01$). Overall surgical success was high (98%) and similar between radiated (94%) and non-radiated groups (100%) at median follow up of 30 months. Clavien grade 3–4 complications occurred in 18% of radiated and 10% of non-radiated patients ($P=0.48$).

Conclusions: Careful pre-operative evaluation and appropriate selection of surgical technique facilitates high and similar success of ureteral reconstruction in radiated and non-radiated patients. Complex ureteral repairs were more common in radiated patients, however the majority of radiated ureteral injuries (65%) were reconstructed without tissue transfer. Radiated patients had lower pre-operative bladder capacities, but similar surgical morbidity, renal function, and persistent urge incontinence compared to non-radiated patients.

Keywords: Disease; ureteral; radiation injury; reconstructive surgical procedure

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Introduction

Ureteral injury presents a heterogeneous and challenging surgical problem for the urologist. In the modern era, the majority of ureteral injuries are iatrogenic occurring in 0.24–5% of colorectal and 0.02–0.04% of gynecologic operations (1–4). Surgical reconstruction of these injuries can be difficult, but alternatives are poor as endoscopic management is rarely definitive and chronic ureteral stenting or percutaneous nephrostomy (PCN) drainage is associated with significant morbidity and decline of renal function (5). The mainstays of ureteral reconstruction include ureteroneocystostomy with either psoas hitch or Boari flap for injuries of the distal and mid ureter, and ileal ureter or renal autotransplantation for more proximal injuries.

As treatments for pelvic organ malignancies continue to improve and cancer survivorship years prolong, more ureteral reconstructions are performed in radiated fields. Pelvic radiotherapy has two main effects relevant to ureteral reconstruction: (I) microvascular injury to the ureter which may increase risk of surgical failure; and (II) decreased compliance, functional capacity, and mobility of the bladder (6–8). While prior studies identify radiation as a risk factor for surgical failure few studies compare surgical outcomes of radiated and non-radiated ureteral repairs (9,10).

This study directly compares patient characteristics and surgical outcomes in modern cohorts of radiated and non-radiated patients undergoing ureteral reconstruction. The study will test two hypotheses. First, that patients with history of pelvic radiation will require more complex ureteral reconstructions than non-radiated patients. Second, that patients with history of pelvic radiation are more likely to experience post-operative complications and surgical failure. We present the following article in accordance with the STROBE reporting checklist (available at <https://tau.amegroups.com/article/view/10.21037/tau-21-574/rc>).

Methods

Consecutive patients undergoing ureteral surgery by a fellowship trained reconstructive urologist at a tertiary referral center from January 2010–October 2018 were identified via review of hospital administrative data (n=115). Patients who underwent concurrent cystectomy, revision of uretero-enteric anastomoses, repair of a ureteropelvic junction (UPJ) injury, and pediatric patients were excluded (n=68), leaving 47 patients who underwent ureteral

reconstruction for analysis. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the University of Iowa (Nos. FWA000003007, IORG0000070, IRB00000099) and individual consent for this retrospective analysis was waived.

Ureteral injury characteristics and management

Ureteral injury etiology was classified as either external trauma, surgical injury, radiotherapy, endoscopic stone treatment, or other. Surgical ureteral injuries were those recognized intraoperatively or diagnosed radiographically in the immediate postoperative period. Injuries in a previously radiated patient without another identified cause were classified as radiotherapy induced. All patients undergoing delayed reconstruction had a PCN tube placed and ureteral stent removed, if present. Pre-operative antegrade and retrograde pyelograms were obtained to characterize the ureteral injury with simultaneous cystogram +/- videourodynamics to determine bladder capacity. Bothersome lower urinary tract symptoms (LUTS) were assessed in all patients at least 4 weeks following ureteral stent removal and defined as bothersome urinary frequency, urgency, and/or persistent urge incontinence requiring more than one pad per day and/or pharmacologic treatment. Injuries extending cephalad to the iliac vessels were classified as proximal and those entirely caudal to the iliac vessels were classified as distal. Ureteral reconstructions were classified as either ureteral reimplant, reimplant with psoas hitch, reimplant with psoas hitch and Boari flap, ureteral replacement with bowel (e.g., ileal ureter), or autotransplant. Ileal ureter and autotransplantation were classified as “complex” ureteral repairs.

Postoperatively, all patients were managed with ureteral stent, foley catheter, and pelvic drain. Catheters were removed after the 7–10-day cystogram revealed no leak, and the ureteral stent was removed around one month. Clinical follow up included assessment of voiding function and flank pain after the stent had been removed, bothersome LUTS (as defined above) requiring more than one pad and/or pharmacologic treatment more than three months after ureteral stent removal, worsening renal function (relative to pre-operative values), and worsening hydronephrosis (relative to the pre-operative appearance) assessed on renal ultrasound at three months and then annually.

Our approach to evaluation and surgical management of radiated ureteral injuries is summarized in *Figure 1*. In

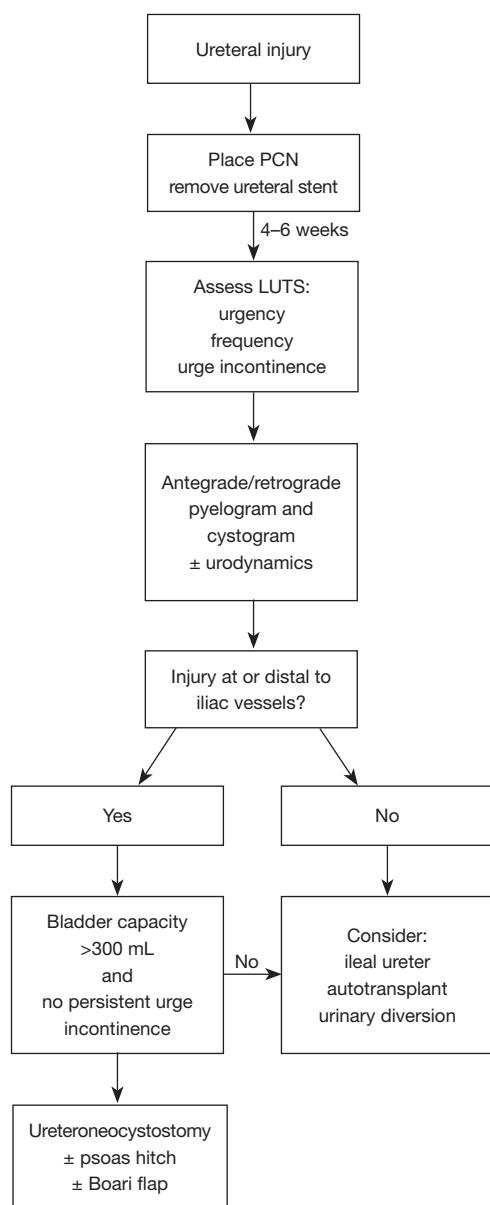


Figure 1 Our suggested approach to evaluation and management of ureteral injuries in both radiated and non-radiated patients. This approach centers on preoperative evaluation of the location of the injury, assessment of bothersome lower urinary tract symptoms at least four weeks after ureteral stent removal, and measurement of anatomic bladder capacity. We propose most radiated distal ureteral injuries with bladder capacity >300 mL can be reconstructed using ureteroneocystostomy techniques with psoas hitch and/or Boari flap. More proximal injuries and/or distal injuries in radiated patients with minimal bladder capacity or persistent incontinence should be considered for bowel interposition with ileal ureter, renal autotransplantation, or urinary diversion. PCN, percutaneous nephrostomy tube; LUTS, lower urinary tract symptoms.

general, selection of surgical technique was similar for radiated and non-radiated repairs other than (I) Boari flaps were not utilized in radiated patients with persistent urge incontinence requiring more than one pad per day 4–6 weeks after ureteral stent removal and/or when bladder volumes were less than 300 mL; and (II) when performing the ureteral anastomoses to the bladder/bowel, we relied on visual confirmation of active bleeding from the transected ureteral stump (not only ureteral lumen size) before performing the anastomosis.

Outcomes and statistical analysis

The primary outcome was surgical success as defined by freedom from operative revision of the ureteral anastomosis. Secondary outcomes included unplanned need for upper tract drainage (e.g., ureteral stent/PCN) within 90 days of surgery, worsening renal function [glomerular filtration rate (GFR)] relative to pre-operative values, persistent urge incontinence, and persistent hydronephrosis after ureteral stent removal. Notably, asymptomatic post-operative hydronephrosis with stable renal function was attributed to ureteral reflux and not routinely investigated unless the hydronephrosis was progressive, symptomatic, or associated with worsening renal function. Postoperative complications within 90 days of surgery were classified according to the Clavien-Dindo system and those \geq grade 3 designated as severe (11). Patients with radiated versus non-radiated ureteral reconstructions were compared with respect to patient characteristics, ureteral injury characteristics and management, surgical outcomes, and post-operative complications using the Student's *t*-test for continuous variables and Chi-square analysis for categorical variables. A *P* value of <0.05 constituted statistical significance.

Results

We analyzed 47 consecutive cases of ureteral reconstruction performed by a single surgeon between January 2010–October 2018. *Table 1* provides a summary of patient characteristics, ureteral injury characteristics, and ureteral injury management. Notably, 36% of ureteral injuries were in a radiated field. Seven patients (15%) underwent immediate ureteral repair at the time of either recognized surgical injury (6 patients) or external trauma (1 patient). Ureteral reconstruction techniques included simple reimplant in 10 (21%), reimplant with psoas hitch in 23 (49%), reimplant with psoas hitch and Boari flap in

Table 1 Comparison of patient characteristics, ureteral injury characteristics, surgical repair techniques, and outcomes of radiated versus non-radiated ureteral repairs

Variables	Total (n=47)	Non-radiated (n=30)	Radiated (n=17)	P
Patient characteristics				
Gender, No. [%]				0.16
Male	11 [23]	9 [30]	2 [12]	
Female	36 [77]	21 [70]	15 [88]	
Age, mean ± SD (years)	54±15	55±17	54±13	0.83
BMI, mean ± SD (kg/m ²)	29±7.4	29±7.3	30±7.7	0.66
Tobacco use, No. [%]				0.68
Current	13 [28]	7 [23]	6 [35]	
Former	12 [25]	8 [27]	4 [24]	
Never	22 [47]	15 [50]	7 [41]	
Diabetes, No. [%]	8 [17]	4 [13]	4 [24]	0.37
Preoperative bladder capacity, mean ± SD (mL)	398±181	500±189	311±124	0.001
Preoperative GFR, mean ± SD (mL/min)	67±25	69±27	65±24	0.61
Ureteral injury characteristics and management				
Laterality, No. [%]				0.15
Left	21 [45]	16 [53]	5 [29]	
Right	18 [38]	11 [37]	7 [42]	
Bilateral	8 [17]	3 [10]	5 [29]	
Etiology, No. [%]				0
External trauma	2 [4]	2 [7]	0	
Surgical injury	27 [58]	24 [80]	3 [18]	
Radiotherapy	13 [28]	0	13 [76]	
Endoscopic stone treatment	2 [4]	1 [3]	1 [6]	
Other	3 [6]	3 [10]	0	
Proximal extent of injury, No. [%]				0.1
Superior to external iliac vessels	23 [49]	12 [40]	11 [65]	
Inferior to external iliac vessels	24 [51]	18 [60]	6 [35]	
Management prior to reconstruction, No. [%]				0.22
Ureteral stent	11 [23]	5 [17]	6 [35]	
Nephrostomy	15 [32]	8 [27]	7 [41]	
Ureteral dilation	6 [13]	4 [13]	2 [12]	
Ureteral reconstruction	8 [17]	7 [23]	1 [6]	
Immediate repair	7 [15]	6 [20]	1 [6]	

Table 1 (continued)

Table 1 (continued)

Variables	Total (n=47)	Non-radiated (n=30)	Radiated (n=17)	P
Surgical repair technique, No. [%]				0.11
Reimplant	10 [21]	8 [27]	2 [12]	
Reimplant with psoas hitch	23 [49]	16 [53]	7 [41]	
Reimplant with psoas hitch and Boari flap	6 [13]	4 [13]	2 [12]	
Ileal Ureter	6 [13]	1 [3]	5 [29]	
Autotransplant	2 [4]	1 [3]	1 [6]	
EBL, mean \pm SD (mL)	319 \pm 333	324 \pm 322	310 \pm 361	0.89
Length of stay, mean (days)	6.6 \pm 5.4	5.9 \pm 5.1	7.8 \pm 6.1	0.26
Outcomes				
Primary surgical success, No. [%]	46 [98]	30 [100]	16 [94]	0.18
Upper tract drainage within 90 days, No. [%]				0.16
Stent	1 [2]	1 [3]	0	
PCN	2 [4]	0	2 [12]	
Postoperative GFR, mean \pm SD (mL/min)	73 \pm 28	78 \pm 24	66 \pm 33	0.16
Change in postoperative GFR, mean \pm SD (mL/min)	5.7 \pm 24	8.4 \pm 23	0.97 \pm 25	0.31
Bothersome incontinence, No. [%]	5	3 [10]	2 [12]	0.9
Post-operative hydronephrosis, No. [%]	12	7 [23]	5 [29]	0.64
90-day complications, No. [%]				0.48
Clavien grade 3–4	5	2 [7]	3 [18]	
Clavien grade 1–2	13	9 [30]	4 [24]	
Follow up interval, median [IQR] (months)	30 [12–56]	27 [5–54]	37 [15–55]	0.45

No., number of patients; SD, standard deviation; BMI, body mass index; GFR, glomerular filtration rate; EBL, estimated blood loss; PCN, percutaneous nephrostomy tube; IQR, interquartile range.

6 (13%), ileal ureter in 6 (13%), and autotransplant in 2 (4%) patients. Representative pre- and post-operative images from three successfully managed radiated ureteral repairs are shown in *Figure 2*.

Comparison of radiated and non-radiated ureteral repairs

Radiated patients had lower preoperative bladder capacity (311 \pm 124 mL) compared to non-radiated patients (500 \pm 189 mL) (P=0.001) but were otherwise similar with regard to patient and ureteral injury characteristics (*Table 1*). Complex repairs (ileal ureter or autotransplant) were performed in 6/17 (35%) of radiated patients and 2/30 (7%) non-radiated patients (P=0.01) (*Table 1*). Primary surgical success was achieved in 30 (100%) non-radiated and 16 (94%) radiated

patients at median follow up of 30 months (P=0.45). One radiated patient underwent anastomotic revision in the immediate post-operative period (post-operative day 7) due to a malpositioned right ureteral stent causing urine leak after bilateral ileal ureter. Secondary outcome analysis showed that upper tract drainage within 90 days, change in postoperative GFR, persistent urge incontinence, and asymptomatic post-operative hydronephrosis were similar between non-radiated and radiated patients. Two radiated patients had PCN placed within 90 days of surgery. The first patient had worsening hydronephrosis and declining renal function which was ultimately found to be secondary to bladder outlet obstruction. The second patient had distal ureteral stent migration which was managed with temporary PCN placement. There was one ureteral stent placed in

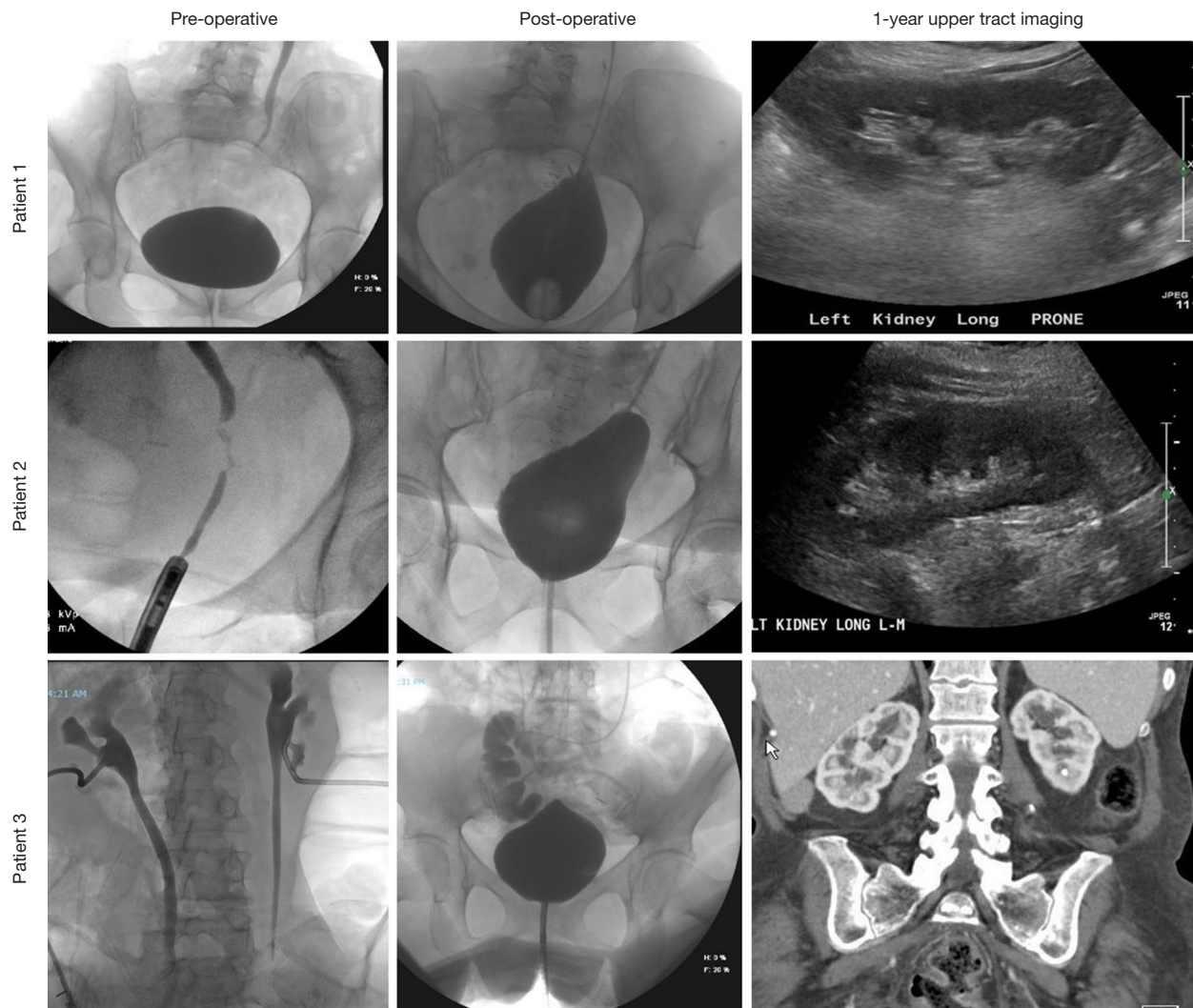


Figure 2 Representative preoperative, post-operative, and follow-up imaging in three radiated patients. Patients 1 and 2 both developed left ureteral strictures following radiotherapy for cervical cancer. Pre-operative urodynamics revealed bladder capacities above 300 mL without bladder instability and both were managed successfully with a ureteral reimplant augmented with a psoas hitch. Patient 3 had bilateral ureteral strictures from cervical radiotherapy and a 200 mL bladder capacity. Urinary diversion was offered, but patient elected bilateral ileal ureter (here shown as a reverse-7 repair).

a non-radiated patient at an outside facility for sepsis of presumed urinary origin which was later removed without sequelae. Clavien 3 and 4 complications occurred in 2 non-radiated and 3 radiated patients ($P=0.48$).

Discussion

This study characterizes and directly compares modern cohorts of radiated and non-radiated patients undergoing surgical ureteral reconstruction and tested two hypotheses.

We first hypothesized that patients with history of pelvic radiotherapy would require more complicated ureteral repair techniques. While radiated patients did require more complex reconstruction techniques compared to non-radiated patients, more than 50% of the radiated cohort was repaired with either reimplant alone or reimplant + psoas hitch. We speculate that decreased bladder capacity in the radiated cohort drove increased use of ileal ureter repairs accounting for this difference in selection of surgical technique. This conclusion is supported by the low average pre-operative

bladder capacity of ileal ureter repairs (196±22 mL) and rare utilization of Boari flaps in radiated patients (n=2, each with bladder capacity =350 mL).

Our second hypothesis was that patients in the radiated cohort would suffer more post-operative complications and higher rates of surgical failure. Here we found that while Grade 3 and 4 complications were not statistically different between the two cohorts, the overall high-grade complication rate was clinically significant at nearly 10%. Unlike primary ureteral reimplants in children, adult reimplants are nearly always performed in a re-operative field (91% in this cohort) and thus, one can and should expect these operations to be technically challenging. Still, surgical success was high and similar in both groups at a median follow-up of 30 months with only one patient in the radiated group requiring surgical revision. This leads us to reject our hypothesis that radiated patients experience higher rates of surgical complication and failure and conclude that equivalent success can be achieved with careful selection of repair technique in individual patients regardless of radiation history.

Radiated ureteral repairs

Our hypotheses were based primarily on smaller prior studies suggesting higher rates of complication and surgical failure in radiated ureteral reconstructions. The largest of these series reported on 23 radiated ureteral strictures noting a 100% anatomical success rate when defined by the absence of a recurrent ureteral (anastomotic) stricture (11). However, all of these repairs utilized bowel interposition (ileum), even for the 15 patients with distal ureteral strictures, and thus the results are not directly comparable to this series. Importantly, while the anatomic success rate reported with the ileal interposition surgery is admirable, post-operative bowel obstruction requiring surgery were reported in 13% including two patients requiring surgery for entero-urinary fistulas. Though utilization of non-native tissue for reconstructive procedures in radiated fields is often touted as a sound principle of reconstructive surgery, our series suggests that the majority of radiated ureteral injuries can be successfully repaired without bowel interposition, especially when only the distal ureter is diseased.

Studies reporting higher rates of surgical failure in radiated fields include a single center study of planned ureteral reconstruction during pelvic cancer surgery. This series revealed that radiated ureteral reconstructions

failed nearly 1/3 of the time and the relationship between radiation and failure appeared to be dose dependent (12). Another study evaluated the post-ureteroplasty “trifecta” of (I) freedom from hydronephrosis, (II) freedom from ureteral stent and (III) stable renal function. They report that radiated ureteral repairs failed to achieve the trifecta over 50% of the time (10 out of 19), which was significantly higher than non-radiated patients (OR 3.1; P=0.03) (9). Lastly, a study of 54 radiated patients undergoing urinary reconstruction, of which 18 (33%) were referred for isolated ureteral strictures, revealed that only two patients were reconstructed with native tissue alone (both Boari flaps), with the others requiring the utilization of ileum, the most common reason being the presence of a “contracted bladder”. Still, surgical success was achieved in only 67% of patients (13).

While we report a significantly higher overall success rate, we agree that Boari flap should be used cautiously in radiated patients—specifically avoiding use of Boari flap in radiated patients with diminished bladder capacity (<300 mL) or presence of urge incontinence requiring more than one pad/day and/or pharmacologic treatment. We based these criteria on prior urodynamic studies of men and women treated with radiotherapy for urothelial carcinoma in which median bladder capacity was 400 mL as well as our clinical experience in which creation of a well vascularized Boari flap is challenging in bladders <300 mL capacity and results in reduced functional bladder capacity (14). We performed only two Boari flap repairs in radiated patients. Both were successful, and both had bladder capacity >350 mL and no pre-operative urge incontinence. Therefore, we propose that consideration of these anatomic and functional aspects may aid appropriate patient selection.

We did not utilize robotic assistance in any of our cases, but it seems likely that robotic assisted ureteral reimplantation will become more common as technology continues to improve and surgeons become more facile with difficult robotic cases (15). In the first series of robotic assisted repairs to focus on radiated ureters, four surgeons retrospectively reviewed 32 repairs over a seven-year period and found an overall success rate, defined as freedom from requiring a secondary ureteral procedure and/or ureteral stent, of 88% utilizing similar patient selection methodologies as our series (16). While it is unclear if the robotic repairs offer a true intraoperative surgical advantage, comparison of hospital stay and blood loss appear to favor the robotic repairs as is the case with most other robotic-assisted operations. However, robotic repairs will offer no

advantage, and do our patients no favors, if one is not able to follow the basic reconstructive principles of a tension-free anastomosis of well-vascularized tissue.

We reported several secondary outcomes that deserve mentioning. While post-operative hydronephrosis was not different between the cohorts, the overall rate of 26% should be considered when counselling patients perioperatively. We follow all renal units with renal ultrasound, GFR and patient reported symptoms post-operatively and will investigate any concerning findings with either retrograde pyelography or renal scan. Here, while the rate of persistent hydronephrosis is high, all were mild cases and likely represent permanent dilatatory changes of the obstructed ureter and/or post-operative reflux. *De novo* urge incontinence is of more concern, occurring in 11% of the overall cohort, though without difference between cohorts. While no patients to date have undergone secondary surgeries to ameliorate this problem, many women are treated with antimuscarinics post-operatively and this treatment should be expected in nearly all women with radiated bladders. Finally, mean post-operative GFR was stable in both cohorts, though patients with a history of radiation appear more likely to start with elements of renal insufficiency that should not be expected to recover post-operatively.

This study has several limitations. First, this is a retrospective analysis of surgical patients subject to inherent selection bias. Specifically, this study only includes patients referred to urology, deemed surgical candidates and whom elected surgical reconstruction. As such, we are unable to provide information on the total number of ureteral units that are not repaired—specifically those managed with nephrectomy or chronic renal drainage. Second, our median follow-up was only 30 months and it is possible that late recurrences, especially in the radiated group, may still occur. Third, our proposed algorithm for preoperative evaluation could not be universally applied in cases of need for immediate reconstruction at the time of recognized surgical injury. However, our algorithm was utilized in 86% of patients and we feel strongly that careful and accurate fluoroscopic assessment of the ureteral injury in conjunction with preoperative evaluation of the functional status of the bladder facilitates appropriate selection of surgical technique and improved patient counseling.

Finally, choice of ureteral reconstruction technique is complex and nuanced. We propose a systematic approach focused on anatomic and functional factors which we feel is applicable to most patients. However, this framework

fails to capture subtle, but often equally important, factors such as patient and surgeon preferences and impact of prior surgeries which may appropriately supersede an algorithmic approach. Further, our series does not include other forms of substitution ureteroplasty such as appendiceal interposition or buccal mucosa graft which may have been feasible alternatives to ileal ureter or autotransplant in our series. While we report high anatomical success rates in this series, a companion patient-reported outcomes analysis would provide a more complete picture, especially in the radiated cohort where bladder volumes were low.

Conclusions

Ureteral injuries in previously radiated operative fields can be successfully reconstructed with high, and similar success to non-radiated patients at medium term follow up. Careful patient selection, informed by pre-operative radiological and functional exams of the complete ureter and fully distended bladder, as well as meticulous operative techniques that obey the principles of reconstructive surgery, are the keys to achieving high anatomic and functional success in this difficult disease process.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://tau.amegroups.com/article/view/10.21037/tau-21-574/rc>

Data Sharing Statement: Available at <https://tau.amegroups.com/article/view/10.21037/tau-21-574/dss>

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Conflict of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://tau.amegroups.com/article/view/10.21037/tau-21-574/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work

are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the University of Iowa (Nos. FWA000003007, IORG0000070, IRB00000099) and individual consent for this retrospective analysis was waived.

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