ORIGINAL ARTICLE

The use of indocyanine green during robotic ureteroenteric reimplantation for the management of benign anastomotic strictures

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Abstract

Purpose We describe our technique for using intraureteral and intraurinary diversion indocyanine green (ICG) during robotic ureteroenteric reimplantation and report our outcomes.

Methods We retrospectively reviewed eight patients who underwent ten robotic ureteroenteric reimplantations between August 2013 and July 2017. ICG was injected antegrade and/or retrograde into the lumen of the ureter, and retrograde into the lumen of the urinary diversion. All patients consented to off-label use of ICG. Postoperatively, all patients were assessed for: clinical success: the absence of flank pain; and radiological success: the absence of obstruction on renal scan and/or loopogram.

Results Visualization of ICG under near-infrared fluorescence allowed for precise identification of the strictured ureter and urinary diversion, which fluoresced green; and localization the ureteroenteric stricture margins, which poorly fluoresced green. The median operative time was 208 min (IQR 191–299), estimated blood loss was 125 ml (IQR 69–150), and length of stay was 6 days (IQR 1–8). Three of eight (37.5%) patients suffered a minor (Clavien ≤ 2), and 2/8 (25.0%) patients suffered a major (Clavien > 2) post-operative complication. There were no complications related to ICG use. At a median follow-up of 29 months (IQR 21–38), 8/10 (80.0%) ureteroenteric reimplantations were clinically and radiologically successful.

Conclusions Intraureteral and intraurinary diversion ICG may be utilized as a real-time contrast agent during robotic ureteroenteric reimplantation to assist with identification of the strictured ureter and urinary diversion, and delineation of the ureteroenteric stricture margins. Despite this, RUER remains a technically difficult and morbid procedure.

Keywords Fluorescence · Indocyanine green · Robotics · Ureteroenteric stricture

Introduction

Benign ureteroenteric stricture (UES) formation after radical cystectomy and urinary diversion is relatively common [1–3], and may cause irreversible loss of kidney function. However, definitive management of UES is challenging [3]. Although endoscopic treatments are often used first-line, they are associated with poor long-term success rates [4–7]. While open ureteroenteric reimplantation is considered the gold-standard treatment [3], it generally requires a midline laparotomy incision and is associated with considerable morbidity [8]. Also, given the re-operative setting, patients often have dense adhesions and peri-ureteral fibrosis, which makes identification of the ureters and urinary diversion, and localization of the UES margins difficult [3, 8, 9].

The robotic modality is well suited for ureteral reconstruction as it maintains the benefits of minimally invasive surgery and provides the surgeon with magnified three-dimensional vision, tremor filtering, and the ability to suture with precision [10–12]. In addition, the integration of near-infrared fluorescence (NIRF) to the robotic platform allows surgeons to utilize indocyanine green (ICG) as a real-time intraoperative contrast agent to facilitate identification of the ureter, and localization of UES margins [12, 13]. Despite this, robotic ureteroenteric reimplantation (RUER) remains technically challenging and such reports are limited [9, 14–16]. Furthermore, the use of ICG during RUER has yet to be described.

We hypothesize that ICG may assist with RUER, especially in the setting of a reconstructed urinary tract and

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re-operative surgical field. Herein, we describe our technique for using intraureteral and intraurinary diversion ICG during RUER.

Materials and methods

Patient cohort

We performed an Institutional Review Board-approved retrospective review of all patients who underwent RUER with intraureteral and intraurinary diversion ICG between 2013 and 2017. The indication for surgery was a benign UES that developed after radical cystectomy and urinary diversion. If recurrent malignancy was suspected based on clinical history and/or imaging, biopsies were performed. All procedures were performed by a single surgeon (DDE) using the da Vinci® Si or Xi Surgical Systems (Intuitive Surgical, Sunnyvale, USA) with integrated Firefly™ (Intuitive Surgical, Sunnyvale, USA) NIRF imaging capability. All patients consented to off-labeled intraureteral and intraurinary diversion ICG administration after full disclosure. Descriptive statistics were used to report patient characteristics and peri-operative outcomes.

ICG preparation and administration

ICG was prepared by dissolving 25 mg of IC-Green™ (©Akorn Inc, Lake Forest, USA) into 10 ml of water, and was administered at the start of each case. With regards to intraureteral ICG, those with a percutaneous nephrostomy tube had 10 ml injected antegrade, while those with a nephroureteral stent had 10 ml injected retrograde into the lumen of the ureter. With regards to intraurinary diversion ICG, an 18 French Foley catheter was used to inject 20 ml retrograde into the lumen of the urinary diversion.

Identification of urinary diversion and ureter

An extensive lysis of adhesions was often necessary to expose the junction between the strictured ureter(s) and urinary diversion. NIRF was utilized to identify the course of the strictured ureter(s) and urinary diversion and subsequently guide our dissection. Under NIRF, the urinary diversion and strictured ureter(s) fluoresced green, while the surrounding tissue did not fluoresce (Fig. 1).

Ureterolysis, excision of stricture

Upon identification of the strictured ureter(s), ureterolysis was performed circumferentially towards the urinary diversion. NIRF was utilized to delineate the UES. Under NIRF, healthy ureter fluoresced green, while strictured
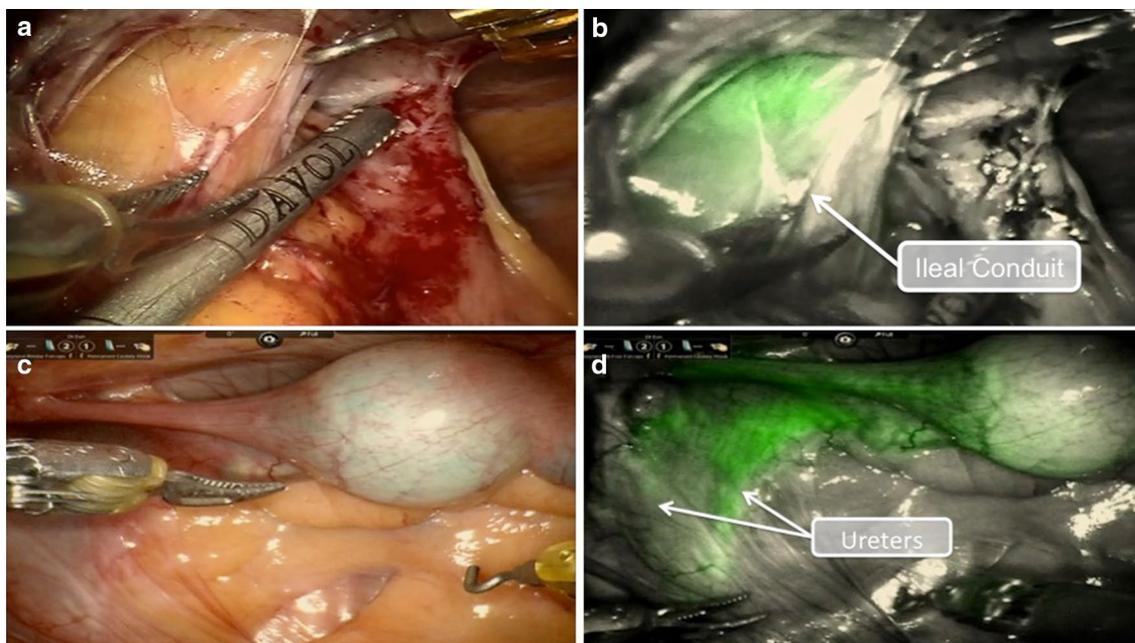

Fig. 1 Urinary diversion identification in absence (**a**) and presence (**b**) of NIRF. Identification of strictured ureters in absence (**c**) and presence (**d**) of NIRF

ureter fluoresced poorly or did not fluoresce at all (Fig. 2). The proximal extent of the UES was sharply excised and a healthy, well-perfused edge of ureter was confirmed. The distal extent of the UES was sharply excised and the resulting defect in the urinary diversion was repaired in a running fashion using a 5–0 monofilament absorbable suture.

Reimplantation

Although all reimplantations were performed in a tension-free fashion, the type of reimplantation performed depended on the number of strictured ureters and the UES length. For a unilateral, short-segment UES, a Bricker anastomosis was utilized [17]. The urinary diversion was incised distal to the prior ureteroenteric junction. The ureter was spatulated and anastomosed to the urinary diversion using two running 5–0 monofilament absorbable sutures. For bilateral, short-segment UES, a Wallace anastomosis was utilized [18]. A proximal cuff of the urinary diversion was excised. The bilateral ureters were spatulated and their medial walls were anastomosed together using a running 3–0 monofilament absorbable suture. The free edges of the newly conjoined ureters were then anastomosed to the urinary diversion using a running 3–0 monofilament absorbable suture.

For a unilateral, long-segment UES an appendiceal interposition was preferentially utilized. Prior to excising the appendix and cecal cuff, a 2–0 monofilament absorbable suture was used to ligate the appendix and cecal cuff in a running fashion. This suture line was excluded using a 3–0 monofilament absorbable suture in an interrupted Lembert fashion. After spatulating the appendix and the ureter, the appendiceal cap was anastomosed to the urinary diversion, while the cecal cap was anastomosed to the ureter. Each anastomosis was performed using two running 5–0 monofilament absorbable sutures.

If the appendix was not available or not suitable for use, a transureteroureterostomy was utilized. This involved completely mobilizing the affected ureter and minimally mobilizing the recipient ureter. After widely spatulating the affected ureter and creating a 1.5 cm ureterotomy on the recipient ureter, an end–side anastomosis was performed using two running 5–0 monofilament absorbable sutures.

Stent placement

Nephroureteral stents were transabdominally placed after completing the posterior half of the anastomosis. A guide-wire was introduced intracorporeally through the assistant port and used to deploy the proximal end of the stent into the renal pelvis. The distal end of the stent was inserted into the urinary diversion under direct visualization.

Post-operative evaluation

At 6 weeks post-operatively, all patients underwent a loopogram. In the absence of a leak, the nephroureteral stent(s) was/were removed. Subsequently, all patients were assessed for: clinical success, the absence of flank pain; and
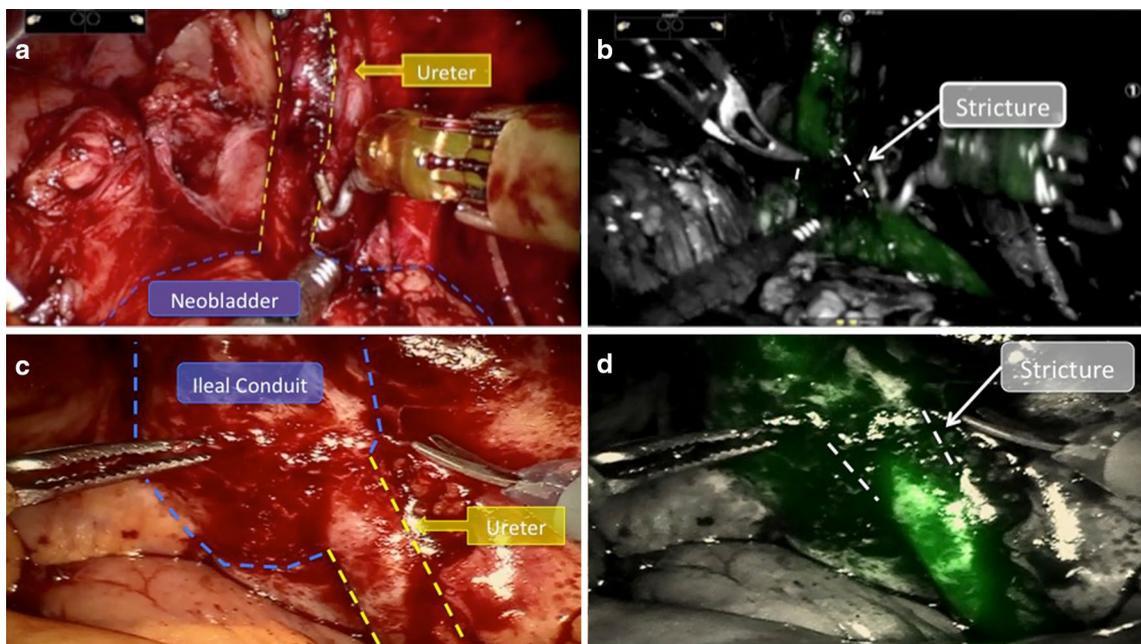

Fig. 2 Localization of healthy versus strictured ureter in absence (**a**) and presence (**b**) of NIRF in neobladder. Localization of healthy versus strictured ureter in the absence (**c**) and the presence (**d**) of NIRF in ileal conduit

radiological success, the absence of obstruction on mercaptoactetyl-triglycine renal scans and/or the presence of reflux on loopograms depending on the patient's renal function. Imaging was obtained at 2 and 6 months post-operatively, and then at 1-year interval thereafter.

Results

Eight patients underwent ten RUER. Baseline characteristics and peri-operative outcomes are shown in Table 1. Seven of 8 (87.5%) and 1/8 (12.5%) patients underwent RUER in an ileal conduit and Studer neobladder, respectively. Three of 8 (37.5%), 3/8 (37.5%), and 2/8 (25.0%) patients had left-sided, right-sided, and bilateral strictures, respectively. Five of 8 (62.5%) patients previously failed endoscopic management.

Intraureteral and intraurinary conduit ICG was utilized in all patients. Five of 8 (62.5%), 1/8 (12.5%), 1/8 (12.5%), and 1/8 (12.5%) patients underwent a Bricker anastomosis, Wallace anastomosis, appendiceal interposition, and left to right

Table 1 Baseline characteristics and peri-operative outcomes

Urinary conduit type	
Ileal conduit (%)	7 (87.5%)
Studer neobladder (%)	1 (12.5%)
UES laterality	
Right (%)	3 (37.5%)
Left (%)	3 (37.5%)
Bilateral (%)	2 (25.0%)
Median time to UES formation, months (IQR)	6.67 (4.10–42.5)
Median stricture length, (cm) (IQR)	2 (1–3)
Failed endoscopic treatment (%)	5 (62.5%)
Previous abdominal–pelvic radiation (%)	1 (12.5%)
Patients with ICG use	
Intraureteral	8 (100.0%)
Intraurinary diversion	8 (100.0%)
Anastomosis type	
Bricker	5 (62.5%)
Wallace	1 (12.5%)
Appendiceal interposition	1 (12.5%)
Transureteroureterostomy	1 (12.5%)
Median operative time, (min) (IQR)	205 (191–299)
Median estimated blood loss, (ml) (IQR)	150 (69–150)
Median length of stay, days (IQR)	6 (1–8)
Postoperative complications (%)	5 (62.5%)
Minor (%)	3 (37.5%)
Major (%)	2 (25.0%)
Median follow-up, months (IQR)	34 (21–38)
Clinical success (%)	8 (80.0%)
Radiological success (%)	8 (80.0%)

transureteroureterostomy, respectively. The median stricture length was 2 cm (IQR 1–3), operative time was 208 min (IQR 191–299), and length of stay (LOS) was 6 days (IQR 1–8). Five of 8 patients (62.5%) suffered a post-operative complication within 90 days of surgery; 3/8 (37.5%) suffered a minor (Clavien ≤ 2), and 2/8 (25.0%) suffered a major (Clavien > 2) complication. The minor complications included ileus managed with nasogastric tube, post-operative oxygen requirement managed with nasal cannula, and urinary leak managed with prolonged stenting. The major complications included bilateral pulmonary embolisms requiring anticoagulation and admission to the intensive care unit, and percutaneous nephroureteral stent placement after nephroureteral stent dislodgement. There were no complications related to ICG use.

At a median follow-up of 29 months (IQR 21–38), 8/10 (80.0%) ureteroenteric reimplantations were clinically and radiologically successful. One patient who underwent a right-sided Bricker anastomosis for a 3 cm UES developed a recurrence 2 months post-operatively. The recurrent UES was refractory to three endoscopic balloon dilations and is currently managed with chronic stenting. Another patient who had a history of abdominal–pelvic radiation who underwent a left-sided Bricker anastomosis for a 2 cm UES developed a recurrence 23 months post-operatively. The patient was managed with a chronic percutaneous nephrostomy tube, but eventually passed away due to metastatic lymphoma.

Discussion

Open ureteroenteric reimplantation is considered the gold-standard treatment of UES and is associated with excellent long-term success [3]. Reports of open ureteroenteric reimplantation with > 1-year follow-up have demonstrated success rates between 71.4 and 91.0% [8, 19–21]. Despite this, the procedure generally requires a midline laparotomy incision and is associated with high complication rates. In a single institutional report of 151 open ureteroenteric reimplantations, 48.0% of patients suffered a post-operative complication, with 12.1% of patients suffering a major (Clavien > 2) post-operative complication [8]. The major post-operative complications included death, bowel leaks and fascial dehiscence requiring reoperation, abdominal abscesses managed with percutaneous drainage, and urinary leaks managed with percutaneous nephrostomy tubes. Also, the average LOS after open ureteroenteric reimplantation has ranged from 6 to 10 days [8, 15, 20]. Furthermore, in the re-operative setting, patients often have dense adhesions and peri-ureteral fibrosis, which makes identification of the strictured ureter(s) and urinary diversion, and localization of UES margins difficult [3, 8, 9].

The robotic platform is well suited for ureteral reconstruction [10–12] and may potentially decrease the morbidity of open ureteroenteric reimplantation. In a retrospective review of 41 patients who underwent 50 ureteroenteric reimplantations, Gin et al. found that RUER was associated with a shorter LOS compared to that of open ureteroenteric reimplantation (3.2 versus 6.4 days). However, there was no difference in the rate of post-operative complications [15].

Despite this, the literature regarding RUER is limited to a handful of small case series. In the first report of RUER, Dangle and Abaza described the technique in two patients with left-sided UES of 1 and 6 cm refractory to endoscopic management. Both patients were discharged on the first post-operative day without postoperative complications. At follow-up of nearly 2 and 3 years, there were no UES recurrences [9]. Tobis et al. described the technique in four patients who had failed endoscopic management. Two patients had left-sided, and two patients had right-sided UES. Intraoperatively, one patient sustained an injury to the left common iliac artery, which was repaired robotically. The mean LOS was 5.8 days, and there were no post-operative complications. At a mean follow-up of 16 months, there were no UES recurrences [14]. In a 10-year experience of reoperations following robotic radical cystectomy, Hussein et al. described RUER in 12 patients. Intraoperatively, there were two serosal tears, which were repaired robotically. The mean LOS was 5 days and there was one postoperative complication (Clavien > 2) that was not specified. At a mean follow-up of 13 months, 3/12 (25%) patients required further intervention, including ureteral stenting in two patients and repeat RUER in one patient [16].

ICG is well suited for use as a real-time contrast agent because it has a high signal–noise ratio, penetrates tissue, and has an excellent safety profile [22–24]. When activated by NIRF, ICG emits light that may be visualized with a charge-coupled device camera. Currently, the United States Food and Drug Administration has approved intravenous ICG for determining cardiac output, hepatic function and blood flow, and ophthalmic angiography. However, off-label intraureteral and intravenous ICG have shown significant utility during robotic ureteral reconstruction [12, 13, 25]. In our report, we utilized intraureteral and intraurinary diversion ICG as a real-time contrast agent to assist with RUER in two ways. First, intraureteral and intraurinary diversion ICG allowed for rapid identification of the strictured ureter and urinary diversion. This was particularly useful in guiding our dissection towards the UES in the setting of significant bowel adhesions and reconstructed anatomy. Second, intraureteral ICG allowed for clear delineation of the UES margins.

Furthermore, our report expands upon the existing literature in two additional ways. It has been suggested that the robotic platform, compared to the open approach, provides advantages in instrumentation and optics, which may allow for enhanced precision during ureteroenteric reimplantation [9]. While this may be the case, our findings, which are consistent with those of Hussein et al. [16], demonstrate that the procedure is associated with a significant failure rate as 2/10 (20%) procedures required additional interventions. Also, by nature of using smaller incisions, it makes intuitive sense that the robotic platform, compared to the open approach, may decrease the morbidity of ureteroenteric reimplantation. However, in contrast to prior RUER experiences that suggested limited post-operative morbidity, we found that 5/8 patients (62.5%) suffered a post-operative complication within 90 days of surgery, with 3/8 (37.5%) minor (Clavien ≤ 2), and 2/8 (25.0%) major (Clavien > 2) complications. These results suggest that ureteroenteric reimplantation is innately morbid, and is subject to significant post-operative complications regardless of operative approach. However, it should be noted that 3/8 (37.5%) patients in our series had a LOS of 1 day.

The results of our study must be taken in the context of its limitations. First, although our study is one of the largest reported RUER series to-date, it is limited by small patient numbers. However, as it is difficult to generate large single-institutional series, multi-institutional studies may be necessary to more adequately assess the utility of ICG in RUER. Second, although we believe that ICG may assist with RUER, the procedure remains technically difficult to perform. Caution must be exercised when performing RUER, regardless of expertise. Third, although we did not have any ICG-related complications, intraureteral and intraurinary diversion use remain off-label. Intravenous ICG has an excellent safety profile and has been associated with rare instances of anaphylactic shock and cardiorespiratory arrest [26]. While our technique minimizes systemic ICG exposure compared to intravenous administration, further studies are necessary to clearly define its ultimate safety profile.

Conclusions

Intraureteral and intraurinary diversion ICG may be utilized as a real-time contrast agent during RUER to assist with identification of the strictured ureter(s) and urinary diversion, and delineation of the UES margins. Despite this, RUER remains a technically difficult and morbid procedure.

Compliance with ethical standards

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