Intracorporeal urinary diversion during robot-assisted radical cystectomy using indocyanine green

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Introduction: *To describe the feasibility of total intracorporeal urinary diversion during robotic assisted radical cystectomy using indocyanine green (ICG) and the Firefly system of the da Vinci Xi robot and to evaluate the digestive and urinary outcomes of this technique.*

Materials and methods: *After approval by the Institutional Review Board, we studied all consecutive patients who underwent robotic assisted radical cystectomy (RARC) and intracorporeal urinary derivation (ICUD) with the da Vinci Xi robot using ICG and the Firefly system, in our institution from January 1st 2018 to September 15th 2018. Pre, intra and postoperative data were analyzed with a follow up of at least 1 month.*

Results: *We included 25 patients. Preoperative data were the following: 92 % were men, median age was 74 years (IQR 69-76), 64% of patients had an ASA score ≥ 3. Median operative time was 390 min (IQR 360-460). Median return to bowel function was 3 days for gas (IQR 2-5) and 5 days for stool (IQR 3-6). Median length of hospital stay was 8 days (IQR 7-10). After a median follow up of 9.6 months (IQR 8.3-12.5), only one patient (4%) presented with postoperative obstructive syndrome. There were 2 (8%) urinary leaks and 1 (4%) uretrero-enteric stricture. There were no digestive fistulas recorded. Eleven patients (44%) were readmitted within 90 days for complications.*

Conclusions: *Total intracorporeal urinary diversion during robotic assisted radical cystectomy using ICG is a feasible technique that might reduce return of bowel function and with low urinary and digestive complications.*

Key Words: radical cystectomy, robotics, intracorporeal urinary diversion, ICG, indocyanine green

Introduction

Robot-assisted radical cystectomy (RARC) with intracorporeal urinary diversion (ICUD) is a challenging procedure.[1] Most complications that occur after radical cystectomy (robotic or open) are related to urinary diversion, rather than the extirpative step of the procedure.[2,3] Adequate arterial perfusion is a recognized prerequisite for an optimized healing of a gastrointestinal anastomosis.[4] Near-infrared (NIR) fluorescence technology using indocyanine green (ICG) is a promising method that provides a real-time assessment of intestinal perfusion; thus, leading to fewer anastomotic leaks in digestive surgery.[4–6] Since 2010, ICG has gained rapid popularity in urology.[7] The Firefly system uses ICG to visualize vessel perfusion under NIR visualization.[8] ICG allows identification of the superior mesenteric artery; therefore, allowing a safe, controlled perfused intestinal resection.[1] The authors chose to determine ischemia-related complications to evaluate the use of

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Figure 1. Demonstration of ICG usage. **1a)** Initial mesenteric angiography using ICG.

the Firefly system in intracorporeal urinary diversion (urinary stenosis and leak, small bowel stenosis and leak).

The objective of this study was to describe the feasibility of total intracorporeal urinary diversion during RARC using ICG and the Firefly system of da Vinci Xi, and to evaluate digestive and urinary outcomes of this technique in a preliminary series of patients.

Materials and methods

After approval had been obtained from our institutional review board, we included all consecutive patients who underwent RARC and ICUD with the da Vinci Xi robot using ICG and the Firefly system, from January 2018 to September 2018. Patients who received a follow up of less than 3 months were excluded. We also excluded patients who underwent cystectomy for neurologic bladder.

Patient demographics

At baseline, the following information was recorded: gender, age, body mass index (BMI), ASA score, Charlson Comorbidity Index, history of constipation, history of diabetes mellitus, history of abdominal

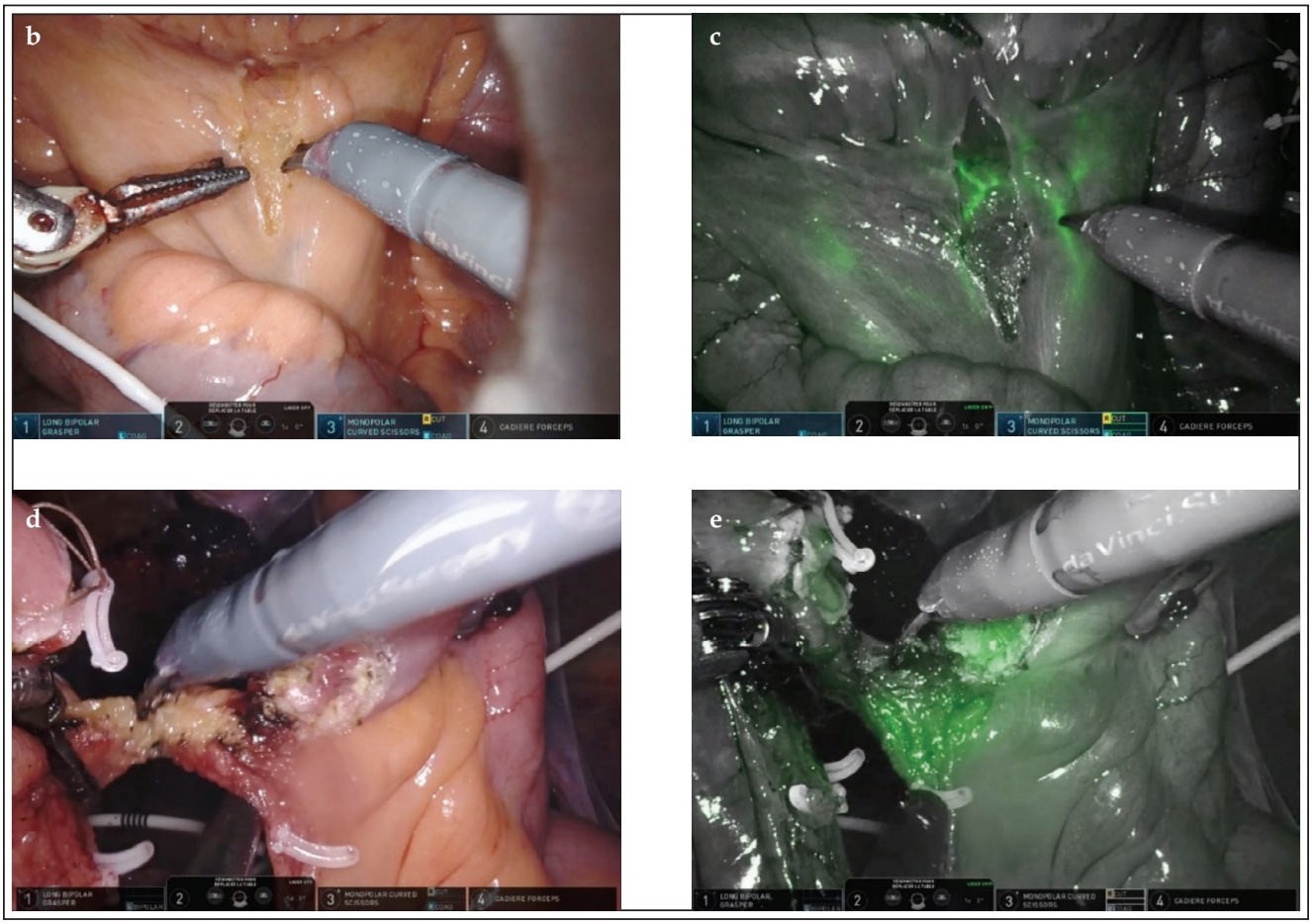

Figure 1b, 1c, 1d, 1e. Mesentery division guided by ICG and the Firefly system.

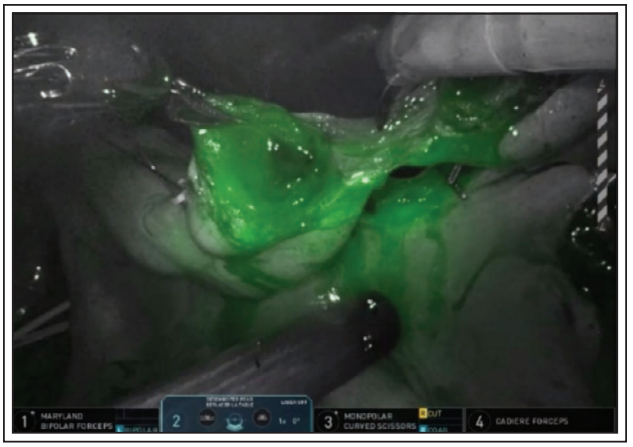

Figure 1f. ICG aspect of each bowel end post resection.

surgery, pathology of the last transurethral resection of bladder tumor (TURBT), and history of neoadjuvant chemotherapy.

ICG protocol for intracorporeal urinary diversion

All procedures were conducted using the da Vinci Xi robot equipped with the Firefly system (Novadaq Technologies, Mississauga, ON, Canada). The extirpative portion of cystectomy was performed in a standard fashion with extended pelvic lymph node dissection (ePLND) up to the aortic bifurcation. Before each bowel division, an anesthesiologist injected 0.2 mg/kg of ICG (Infracyanine, Laboratoire Serb, Paris, France). Firefly mode was turned on to visualize mesenteric vessels 30 seconds after injection. Division of the mesentery was performed using the Firefly mode to preserve an optimal perfusion for the

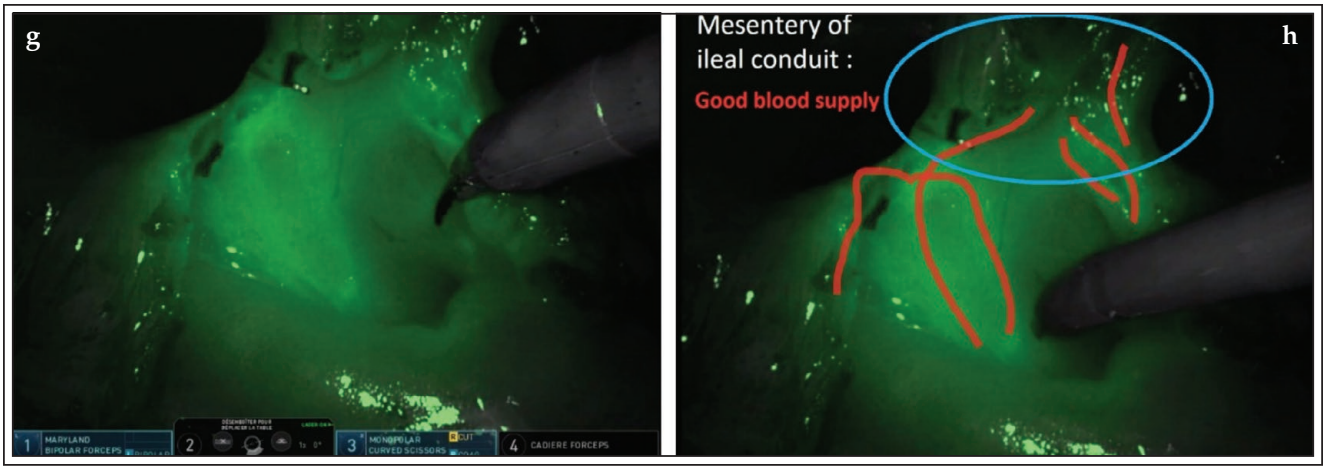

Figure 1g and 1h. Verification of the vascularization of the ileal conduit mesentery post division.

Figure 1i and 1j. Vascularization of ileal conduit prior to ileo-cutaneous anastomis.

future ileal graft and the remaining ileum. An ileal graft (10 cm, if the diversion was an ileal conduit, or 50 cm, if the diversion was a Studer neobladder) was taken out of continuity from the rest of the bowel using the da Vinci Xi EndoWrist 45 Stapler (Intuitive Surgical, Sunnyvale, CA, USA). Following bowel division, the Firefly system was used to ascertain whether the bowel segments were well-vascularized, Figure 1. If the vascularization was insufficient, complementary resection of the ischemic segment was performed. Bowel continuity was achieved via side-to-side ileoileal anastomosis using the da Vinci Xi EndoWrist 45 Stapler. The Firefly system was used to inspect the vascularization of the ileoileal anastomosis. Where inadequate perfusion was present, the surgeon resected the graft and repeated the anastomosis. If it was an ileal conduit, the Firefly system was used to check the vascularization of the proximal and distal ends of the conduit before the cutaneomucosal anastomosis. Similarly, where inadequate perfusion was present, the ischemic part of the graft was resected to obtain a final well-vascularized graft. For Studer neobladder, the Firefly system was used in the same fashion to ensure well-vascularized distal and proximal parts. Urinary diversion was then performed (ileal conduit [IC] or orthotopic neobladder [ONB]) in a similar fashion, as described by Goh (ONB) and Azzouni (IC).[9,10] For urinary drainage, we used JJ stents for ONB and Mono J stents for IC. We also tried to use the Firefly system to assess the ureteral vascularization but it was impossible because of the small diameter of the ureteral vessels.

Postoperative care

Following surgery, all patients were managed with the intent of enhanced recovery after surgery. This included immediate removal of the nasogastric tube and administration of clear liquids, which were initiated on the day of the surgery, and their diet was advanced with the return of bowel function. Starting from the day 1, irrigation of the pouch and rinsing of the Mono J stents in IC were performed twice daily. The abdominal drain was removed when the output was < 100 mL/day and fluid biochemistry excluded urine. Early ambulation was instituted in all patients. As soon as patients could tolerate oral intake, the use of oral pain medication was started. Patients were discharged after the recovery of normal bowel movements, apyrexia, minimal pain controlled by oral medication, and appropriate use of the stoma of the ileal conduit. Concerning ONB, cystoscopy was performed under local anesthesia 3 weeks postoperatively in the outpatient clinic for JJ stent removal. Regarding the ileal conduit, the Mono J stents were removed 2 to 3 weeks postoperatively in the outpatient clinic via direct traction on the stent. A post-removal ultrasound scan was performed to check for upper urinary tract dilation.

Intraoperative and postoperative data

The following intraoperative data were collected: extent of pelvic lymph node dissection, type of intracorporeal diversion, pathology of the specimen, and status of the surgical margins. The following postoperative data were collected: length of follow up, length of stay, 90-day readmission rate, early (0-30 days) and late (31-90 days) complications, classified as the highest Clavien grade per patient. The main endpoints of the study were recorded: ischemia-related complications (urine leak, uretero-enteric stricture, and digestive stenosis and leak) and return of bowel function evaluated by the time to regular diet and the passage of gas and stool.

Statistical analysis

Categorical variables are described using frequency tables. For the descriptive analysis, quantitative variables are expressed as mean and standard deviations or as median and interquartile range; qualitative variables are expressed as percentages. We used SPSS software, version 12.0 (IBM Corp.) to perform the statistical analysis.

Results

Patient cohort

Fluorescence-enhanced robotic radical cystectomy was successfully performed in 25 patients (23 men and 2 women) with a median age of 74 years (interquartile range (IQR), 69-76). All patients had total robotic intracorporeal urinary reconstruction, Figure 2.

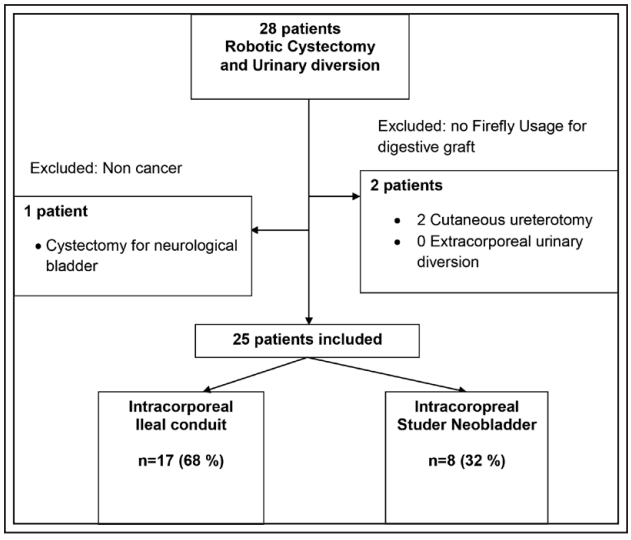

Figure 2. Patient flow chart.

TABLE 1. **Patient demographics**

Parameters	
Number of patients (n)	25
Gender, n (%)	
Male	23 (92)
Female	2 (8)
Age, yr. median (IQR)	74 (69-76)
Comorbidities, median (Charlson Comorbidity Index) (IQR)	6 (5.0-6.0)
ASA score, n (%)	
1-2	9 (36)
3-4	16 (64)
BMI, kg/m^2, median (IQR)	26.0 (23.0-28.4)
Previous abdominal surgery, n (%)	8 (32)
History of constipation, n (%)	1 (4)
Diabetes mellitus, n (%)	6 (24)
Neoadjuvant chemotherapy, n (%)	7 (28)
Clinical stage, n (%)	
≤ cT1	8 (32)
≥ cT2	17 (68)

ASA = American Society of Anesthesiologists;
IQR = interquartile range; BMI = body mass index; yr. = year

Preoperative data

ASA score was 3-4 in 64% of cases, median Charlson score was 6 (IQR 5.0-6.0), and median BMI was 26.0 (23.0-28.4). One patient (4%) had constipation prior to surgery, six patients (24%) had diabetes mellitus, and seven patients (28%) underwent neoadjuvant chemotherapy. Ten preoperative pT2 patients were unable to receive neoadjuvant chemotherapy because of Poor Performance Status or altered renal function. Eight patients (32%) had non-muscle-invasive bladder cancer and 17 patients (68 %) had muscle-invasive bladder cancer on the last TURBT, Table 1.

Intraoperative data

The median operative time was 390 minutes (360-460), median blood loss was 200 mL (100-300). Extended pelvic lymph node dissection up to the aortic bifurcation was performed in all patients. No patient had super extended pelvic lymph node dissection up to the inferior mesenteric artery. Seventeen patients (68%) had an ileal conduit and 8 patients (32%) had a Studer neobladder. Specimen pathology showed 36% pT0, 4% pTa, 4% pT1, 8% pT2, 28% pT3, and 20% pT4. Four patients (16%) had positive lymph nodes and no patient had positive surgical margins. Mesenteric angiography using ICG successfully identified mesenteric vessels in all patients who underwent intracorporeal diversion (25 of 25). For one patient, both ends of the bowel prior to digestive anastomosis seemed hypo perfused under infrared light; we therefore resected those ischemic ends. Firefly then confirmed that the new extremities were well perfused. Thereafter, a well perfused digestive anastomosis was performed.

Postoperative data

Median follow up duration was 9.6 months (IQR, 8.3-12.5), median length of stay was 8 days (IQR 7-10). Eleven patients (44%) were readmitted within the first 3 months. Within the first month, 15 patients (60%) presented minor complications (Clavien 1-2), and 4 patients (16%) presented severe complications (Clavien 3-4). The following 2 months six patients (24%) presented minor complications (Clavien 1-2), and two patients (8%) presented major complications (Clavien 3-4). No patient died in our cohort. Two patients had an uretero-neobladder fistula with urinary peritonitis on day 6 and 7, respectively, and had to undergo reoperation comprising open resection of the neobladder, bilateral ureterostomies, and postoperative intensive care. One of those two patients also had a mechanical obstruction of the ileo-ileal anastomosis and had anastomosis redone during the same surgery. Two patients presented with obstructive pyelonephritis on the day 15 after Mono J removal, requiring a nephrostomy tube and an antegrade Mono J stent placement. One of the two patients required intensive care for septic shock. Because Mono J removal was performed successfully 2 weeks later for both patients, we concluded that the cause of the obstructive pyelonephritis was an anastomotic inflammation rather than ureteral stenosis. One patient presented a uretero-enteric stricture 75 days after the initial surgery requiring a nephrostomy tube and uretero-neobladder reimplantation. One patient presented a myocardial infarction 2 months after the surgery requiring intensive cardiologic care. Seven of the readmitted patients within 3 months had Clavien I-II complications. Four of the readmitted patients within 3 months presented Clavien III-IV complications.

Recovery of bowel function was as follows: the median time for passage of gas was 3.0 days (2.0-5.0), the median time for passage of stool was 5.0 days (3.0-6.0), and the median time to regular diet was 4.0 days (3.0-6.0), Table 2.

TABLE 2. **Postoperative parameters**

Parameters	
Follow up in mo, median (IQR)	9.6 (8.3-12.5)
LOS in days, median (IQR)	8 (7-10)
30 day readmission, n (%)	11 (44)
Early complications (0-30 day)* n (%)	
Clavien 1-2	15 (60)
Clavien 3-4	4 (16)
Clavien 5	0 (0)
All (Clavien 1-4)	19 (76)
Late complications (31-90 day)* n (%)	
Clavien 1-2	6 (24)
Clavien 3-4	2 (8)
Clavien 5	(0)
All (Clavien 1-4)	9 (36)
Ischemia-related complications (0-90 day) n (%)	
Urinary leak	2 (8)
Uretero-enteric stricture	1 (4)
Digestive leak	0 (0)
Mechanical digestive obstruction	1 (4)
Return of bowel function, day, median (IQR)	
Passage of gas	3.0 (2.0-5.0)
Passage of stool	5.0 (3.0-6.0)
Time to regular diet	4.0 (3.0-6.0)

*highest Clavien complication per patient
mo = months, LOS = length of stay

Discussion

Large studies have shown that although RARC is increasing in popularity, more than 80% of urinary diversions are still performed extracorporeally.[3] Conversely, many surgeons have questioned the point of performing RARC first, followed by open diversion, as this eliminates most of the advantages, such as smaller wound incision and reduced bowel exposure.[11] A retrospective comparison involving open diversion in the framework of the International Robotic Cystectomy Consortium, which included 935 patients, further confirmed the safety of intracorporeal diversion by showing a lower risk of postoperative complications, including gastrointestinal complications in these patients.[11,12] Nevertheless, extracorporeal diversion has the advantage of easy visualization of the mesenteric vasculature using back-table transillumination; therefore, preventing unnecessary vessel injury. Bowel and mesentery division represents one of the most challenging steps in intracorporeal urinary diversion.[13] A potential solution to this issue might be the use of ICG and the Firefly system during RARC, since it was shown to be safe and feasible for mesenteric angiography during intracorporeal urinary diversion.[14] The use of ICG for mesenteric angiography for robotic intracorporeal urinary diversion has been studied by Manny et al in eight patients and Goh et al in 17 patients.[9,14] However, in the paper by Manny et al, authors only included a limited number of patients, only ileal conduits, did not focus on mesenteric angiography alone, and did not perform comparative analysis with other intracorporeal series.[14] Goh et al series also had a limited number of patients.[9] We present here, to the best of our knowledge, the largest retrospective study with a prospectively maintained database, which focused on short term digestive and urinary outcomes of total intracorporeal urinary derivation using ICG and the da Vinci Xi robot.

Several studies have suggested different dosages for ICG.[8,14,15] Our anesthesiologists injected a bolus of 0.2 mg/kg before each bowel division. ICG enabled us to identify the mesenteric vasculature in 100% of patients. This result is similar to that of Manny et al where the mesenteric vasculature was identified in eight out of eight patients.[14] Goh et al confirmed that fluorescence imaging can readily highlight bowel vascularization and may serve as an excellent adjunct for the identification of important arterial supply.[9] In our series, no ICG-related side effect was observed. Moreover, operative time was not affected by ICG usage. Indeed, since ICG fluorescence of the mesentery occurs 30-60 seconds after intravenous injection, the operative time is almost the same, even if Firefly vision is used multiple of times during the surgery. Our median operative time of 390 min (360-460) is similar to that in previous published series, Table 3.

Wada et al found that the maximum fluorescence of ICG in colorectal surgery is correlated with better recovery of bowel function.[4] Our series corroborated that finding since we found a relatively quick recovery of bowel function (first passage of stool at 5 days and regular diet at 4 days). The only intracorporeal urinary diversion series that used the Firefly system and evaluated bowel recovery function, found a median time for passage of stool of 6 days, which corroborates our results that return to bowel function is relatively quick. Return of bowel function was only evaluated by one series of intracorporeal diversion without Firefly and found a median time for passage of stool at 6.5 days.[16] Although no statistical comparative analysis was performed between the Firefly series (Goh's series and ours) and the ones not using Firefly (Canda's series) in

	Total patients	Age	BMI	ASA 3-4, n (%)	Type of urinary diversion			Firefly used	Operative time, min	Complications (0-90d): possibly influenced by ICG						Time to regular diet, d	LOS, d
					Ileal conduit	Studer	Other			Urinary Leak, n (%)	Uretero-enteric stricture, n (%)	Ileus, n (%)	Small Bowel obstruction, n(%)	Neobladder-Bowel Fistula, n (%)	Digestive fistula, n (%)		
Jonsson et al 2011	45	65 (md)	26 (md)	NA	9	36	0	No	480 (md)	NA	NA	NA	1 (12.5)	NA	NA	NA	9 (md)
Canda et al 2011	27	61.4 (mn)	25.5 (mn)	9 (33.3)	0	27	0	No	594 (mn)	2 (7.4)	0	2 (7.4)	0	0	0	6.5 (mn)	10.5 (md)
Azzouni et al 2012	100	71 (md)	28.5 (md)	52 (52)	100	0	0	No	352 (md)	2 (2)	4 (4)	16 (16)	8 (8)	0	1 (1)	NA	9 (md)
Schwentner et al 2015	62	63.6 (mn)	25.5 (mn)	NA	0	62	0	No	477 (mn)	NA	NA	NA	NA	NA	NA	NA	16.7 (mn)
Collins et al 2014	80	64 (mn)	NA	NA	0	80	0	No	420 (mn)	NA	NA	NA	NA	NA	NA	NA	9 (mn)
Desai et al 2014	132	60 (mn)	26.8 (mn)	30 (32.6)	0	132	0	NA	456 (mn)	6 (4.5)	5 (3.8)	4 (3.0)	1 (0.7)	2 (1.4)	2 (1.4)	NA	10.6 (mn)
Manny et al 2014	8	71 (md)	NA	NA	8	0	0	Yes	NA	0	0	0	0	0	0	NA	NA
Goh et al 2012	15	68 (md)	27 (md)	11 (73)	7	8	0	Yes	450 (md)	1 (6.7)	1 (6.7)	3 (20.0)	0	0	0	6 (md)	9 (md)
Present series	25	74 (md)	26.1 (md)	16 (64)	18	7	0	Yes	390 (md)	2 (8)	1 (4)	4 (16)	1 (4)	0	0	4 (md)	8 (md)

Table 3. Major intracorporeal urinary diversion series; md = median; mn = mean; LOS = length of stay; BMI = body mass index; ASA = American Society of Anesthesiologists; NA = not available

terms of bowel function, the longer time for passage of stool in series without Firefly suggests that Firefly usage might help bowel function recovery, Table 3. This might be explained by the fact that preservation of a better bowel perfusion reduces ischemia and therefore helps bowel function recovery [4,14].

In our series, we only found two urinary leaks requiring reoperation, one mechanical digestive obstruction and 1 uretero-enteric stricture requiring reimplantation. This low ischemia-related complication rate is similar to the other available series using ICG in intracorporeal urinary diversion,[9,14] Table 3. Although a comparison with RARC series not using Firefly is not possible at this point because of the heterogeneity of the series, it seems plausible that use of Firefly might help prevent ischemia-specific complications, as suggested by Wada et al. for digestive surgery.[4] Furthermore, older and higher ASA risk patients have been shown to present higher complications following oncologic surgery.[17] In our series, patients are older and have a higher ASA score, Table 3. Our patients did not show higher ischemic complications compared to other series: this finding could probably be explained by the use of Firefly. There are two reasons why ICG might prevent ischemia. First, it helps guiding a better division of the mesentery by highlighting the arteries. Second, after the initial ileal division and anastomosis, ICG can be used to verify the good perfusion of the resected segments. We did not need to perform immediate intraoperative repair for any of the anastomosis neither of the urinary graft nor for the ileo-ileal anastomosis. This might be due to the fact that the surgeons carefully took the time to divide the mesentery in the optimal fashion between the main vessels which resulted in a lack of ischemia on both ileal segments. In conclusion, the Firefly technology is another tool enabling a safe controlled resection, with good vascular control.[1]

Several limitations in our study should be acknowledged. First and foremost, the retrospective design could affect selection bias and the median follow up of 9.6 months was short to draw definitive conclusions. Second, even though it is the largest Firefly series, the sample size remains relatively small and the follow up short, in comparison to other series without Firefly use.[10,18,19] We cannot state that the faster bowel function recovery found in the Firefly series (Goh's and ours) was statistically and

clinically significant compared to the series not using Firefly (Canda's), Table 3. Furthermore, even though the recovery of bowel function that we found was relatively quick, one must take into account that one of the confounding factors may be the use of the ERAS (Enhanced Recovery After Surgery) protocol in our institution, which was introduced at the same time as the Firefly system. The ERAS protocol is a factor itself for enhancing bowel function recovery. Without any doubt, the benefit of intraoperative ICG use can only be proven if compared to a control group. Further randomized controlled trials are therefore needed to assess the impact of ICG use on urinary and bowel function recovery.

Conclusions

Radical cystectomy with total intracorporeal urinary derivation using ICG and the Firefly system of the da Vinci robot is a reproducible technique, which allows accurate mesenteric angiography; therefore, facilitating the preservation of the vascularization of the bowel and graft. The technique is safe and feasible and might reduce ischemia-related complications and hasten the recovery of bowel function. Future high-powered randomized controlled trials with a longer follow up will be needed to confirm our findings. □

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