Iatrogenic ureteral injury during colorectal surgery has a significant impact on patient outcomes: a French multicentric retrospective cohort study

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Abstract

Aim: The long-term urological sequelae after iatrogenic ureteral injury (IUI) during colo-rectal surgery are not clearly known. The aims of this work were to report the incidence of IUI and to analyse the long-term consequences of urological late complications and their impact on oncological results of IUI occurring during colorectal surgery through a French multicentric experience (GRECCAR group).

Method: All the patients who presented with IUI during colorectal surgery between 2010 and 2019 were retrospectively included. Patients with ureteral involvement needing *en bloc* resection, delayed ureteral stricture or noncolorectal surgery were not considered.

Results: A total of 202 patients (93 men, mean age 63 ± 14 years) were identified in 29 cen-tres, corresponding to 0.32% of colorectal surgeries ($n = 63\,562$). Index colorectal surgery was mainly oncological ($n = 130$, 64%). IUI was diagnosed postoperatively in 112 patients (55%) after a mean delay of 11 ± 9 days. Intraoperative diagnosis of IUI was significantly associated with shorter length of stay (21 ± 22 days vs. 34 ± 22 days, $p < 0.0001$), lower rates of postoperative hydronephrosis (2% vs. 10%, $p = 0.04$), anastomotic complication (7% vs. 22.5%, $p = 0.002$) and thromboembolic event (0% vs. 6%, $p = 0.02$) than postop-erative diagnosis of IUI. Delayed chemotherapy because of IUI was reported in 27% of patients. At the end of the follow-up [3 ± 2.6 years (1 month–13 years)], 72 patients pre-sented with urological sequalae (36%). Six patients (3%) required a nephrectomy.

Conclusion: IUI during colorectal surgery has few consequences for the patients if rec-ognized early. Long-term urological sequelae can occur in a third of patients. IUI may affect oncological outcomes in colorectal surgery by delaying adjuvant chemotherapy, especially when the ureteral injury is not diagnosed peroperatively.

KEYWORDS
chemotherapy, colorectal surgery, ureteral stent, ureteral injury

INTRODUCTION

What does this paper add to the literature?

Iatrogenic ureteral injury (IUI) occurs in 0.3% of colorectal surgeries. Patients with colorectal cancer are the most frequently exposed. Long-term urological sequelae can occur in a third of patients. IUI seems to have an impact on oncological outcomes, as delayed chemotherapy was reported in 27% of patients.

Iatrogenic ureteral injury (IUI) is considered by colorectal surgeons as a dreaded complication, regardless of the surgeon's experience. In their Swiss national survey, Douissard et al. [1] reported that 61.8% of colorectal surgeons had encountered at least one IUI in their career. Yet the incidence remains low in colorectal surgery, and lower than in gynaecological surgery: during gynaecological surgery IUI occurs in 1.70% of cases [2, 3], whereas during colorectal surgery the rate of IUI is less than 1%. In the largest cohort of 2 165 848 patients undergoing colorectal surgery, IUI was reported in 0.28% of cases [4]. Similarly, a Danish nationwide study of 18 474 patients undergoing colorectal surgery reported an IUI rate of 0.44% [5]. Nonetheless, even if IUI is a rare complication, it is associated with increased postoperative morbidity, prolonged length of stay and increased healthcare costs [6]. Furthermore, when IUI is diagnosed postoperatively, its management and the postoperative course are more difficult and longer than in the case of intraoperative diagnosis [7]. Selzman et al. [8] reported a significant difference between intraoperative and postoperative diagnosis of IUI in terms of the mean number of urological procedures (1.2 vs. 1.8, $p < 0.0006$). In addition, the hospital stay was reported to be shorter when IUI was repaired

within 1 week postoperatively (4.8 days) than in the presence of delayed diagnosis (10.1 days) [9]. With regards to postoperative diagnosis of IUI, even after optimal management, up to 20% of patients require prolonged urinary drainage or complex iterative reconstructive surgeries [10].

Some predictive factors of IUI during colorectal surgery have been identified, including previous pelvic radiation [11] or history of pelvic surgery [12], oncological rectal surgery [4] and left-sided location [13]. The impact of laparoscopy on IUI is controversial between series. In their cohort of 5729 colectomies, Palaniappa et al. [14] identified 14 IUIs (0.24%) and showed a significant increase in IUI during laparoscopic procedures compared with open procedures (0.66% vs. 0.15%, $p = 0.007$). The Danish nationwide study identified the laparoscopic approach as an independent predictive factor of IUI [odds ratio = 1.64 (1.02–2.63), $p = 0.04$] [5]. On the other hand, Sawkar et al. [15] reported that the IUI rate was significantly lower during laparoscopic procedures than open procedures (0.06% vs. 0.34%, $p < 0.0001$). A few authors did not identify any association between laparoscopy and IUI [4, 6].

Besides the risk factors and the type of diagnosis, the long-term consequences of IUI during colorectal surgery have been poorly studied. Palaniappa et al. [14] reported that 2 of 14 patients who underwent IUI required nephrectomy after 1 year. Selzman et al. [8] reported urological sequelae in 14% of IUI patients, including nephrectomy in five of them, after a mean follow-up of 9.5 years. However, no data about the oncological impact of IUI have been reported so far.

The aims of the current study were thus to describe IUI occurring during colorectal surgery through a French multicentric experience and to analyse the long-term consequences regarding urological late complications and their impact on oncological results.

METHOD

Study population

All the patients with IUI occurring during colorectal surgery in 29 tertiary referral colorectal centres from the French Research Group of Rectal Cancer Surgery (GRECCAR) between 2010 and 2019 were retrospectively included. Benign and malignant colorectal surgeries were considered, including resections of the colon and rectum but also other colorectal surgeries such as ventral rectopexy and adhesiolysis for bowel obstruction. Patients with IUI were identified using the French coding system, with the following codes: S371 for 'iatrogenic ureteral injury', S3710 for 'without any intra-abdominal injury' and S3711 for 'with an intra-abdominal injury'. Only patients undergoing colorectal surgery with these codes were included. We defined IUI by partial or complete section, or thermic injury. Patients with ureteral stricture were not included in our study because this injury frequently occurs late and one of our objectives was to describe the acute management of IUI. Patients with ureteral involvement needing *en bloc* resection or those undergoing noncolorectal surgery were not considered.

Data collection

All collected data were provided by surgeons from each centre after institutional approval, using patient files. Demographic information included age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, comorbidities, previous abdominal surgery or pelvic radiation. Characteristics of the index colorectal procedure included indication, surgical approach (open, laparoscopic or robotic assisted; conversion to open surgery), type of dissection energy [monopolar electrosurgery, bipolar electrosurgery, Ultracision® (Ethicon Endosurgery), LigaSure Impact® (LS, Medtronic), Thunderbeat® (Olympus Medical Systems Corp.)], concomitant anastomosis or stoma creation. Characteristics of IUI included side location, type of lesion, time for diagnosis (intra- or postoperatively), method of diagnosis if postoperative and management of IUI.

Outcome measures

Postoperative morbidity was defined as any complication occurring during the hospital stay or within 90 days after surgery. The IUI was not considered as a postoperative complication. Medical morbidity included renal, cardiovascular, pulmonary, septic and thromboembolic complications. Surgical morbidity included ileus (defined by abdominal distension and pain, and vomiting in the postoperative period), anastomotic complications (leakage, deep abscess, peritonitis and stricture), bleeding, wound complications, stoma-related complications and pelvic abscess (i.e. deep abscess occurring without anastomosis). We distinguished the urological complications, such as urinary tract infection, urinoma, urodigestive fistula, hydronephrosis, haematuria or bladder clot, ureteral necrosis and stenosis. The severity of surgical morbidity was classified according to that described by Dindo et al. [16]. Major complications were defined as those requiring surgical or radiological intervention (Dindo III) and life-threatening complications requiring intensive care management (Dindo IV). Unplanned surgery (excluding redo for postoperative diagnosis of IUI) and length of stay were reported. Delayed chemotherapy (over two postoperative months) because of IUI, among patients with an indication of adjuvant chemotherapy, was reported.

Long-term results were retrieved. They concerned urological sequelae, iterative urological surgeries (including ureteral stent removal or changing, renal drainage, nephrectomy) and survival in the case of cancer. Overall survival was defined as the period between the date of surgery (index colorectal procedure) and the date of death whatever the cause. Disease-free survival was defined as the period between the date of surgery (index colorectal procedure) and the date of the first relapse of the disease or death.

Patients alive with no evidence of disease at the last follow-up were censored.

Statistical analysis

Quantitative data are reported as mean and standard deviation (and range) and categorical data are reported as absolute numbers and percentages. Pre-, intra- and postoperative data were compared between patients with an intraoperative diagnosis of IUI and those with a postoperative diagnosis of IUI. Quantitative data were compared with Student's *t*-test. Categorical data were compared using Pearson's chi-square test or Fisher's exact test, as appropriate. All tests were two-sided, with a level of significance set at $p < 0.05$. Survival curves were only calculated in patients with primary cancer (excluding locoregional recurrence and peritoneal carcinomatosis). The curves were plotted according to the method of Kaplan and Meier and differences between survival distributions were assessed by the log-rank test. Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS Inc., version 24.0) software. This study was conducted according to the ethical standards of the Committee on Human Experimentation of our institution and reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [17].

RESULTS

Patients' characteristics

Between 2010 and 2019, 202 patients with IUI during colorectal surgery were identified in 29 centres, corresponding to 0.32% of colorectal surgeries ($n = 63\,562$; Figure 1). Women comprised 54% of these patients ($n = 109$), and the mean age was 63 ± 14 years (range 20–93 years). A total of 45% and 26% of these patients had previous abdominal surgery ($n = 92$) and pelvic radiation ($n = 53$), respectively. Demographic data are reported in Table 1. No difference was observed between the two groups of IUI diagnosis.

Intraoperative characteristics

IUI occurred during scheduled colorectal surgery in 86% of cases. The index colorectal surgery was mainly represented by oncological surgery ($n = 130$, 64%) and less frequently by diverticulitis ($n = 22$, 11%), Hartmann reversal ($n = 11$, 5.5%), redo surgery for anastomotic complication ($n = 10$, 5%), inflammatory bowel disease ($n = 8$, 4%), endometriosis ($n = 5$, 2.5%), colonic ischaemia ($n = 5$, 2.5%) and various others ($n = 11$, 5.5%). The different surgical procedures are detailed in Table 2, and were not significantly different between the two groups except for proctectomy which was more frequently performed in patients with a postoperative diagnosis of IUI (36% vs. 22%, $p = 0.03$). Index colorectal surgery was performed through an open ($n = 139$, 69%), conventional laparoscopic ($n = 60$, 30%) or robotic approach ($n = 3$, 1%). A conversion to open surgery before IUI occurred in 19 patients (9%). A preoperative ureteral catheter was placed in 14 patients (7%) and was palpated during surgery in two patients. Ureters were most frequently identified by ureteral contraction visualization ($n = 123$, 61%). Intravesical methylene blue injection was performed in two cases (1%). Ureters were not identified in 52 patients (26%).

Management of IUI

The left ureter was the most frequently injured ($n = 138$, 68%), and bilateral injury was observed in 11 patients (6%). IUI was diagnosed intraoperatively in 91 patients (45%), and postoperatively in 112 patients (55%); one patient underwent a bilateral IUI, which was diagnosed intraoperatively for the right side and postoperatively for the left side.

In case of intraoperative diagnosis, uretero-ureterostomy was the ureteral repair most frequently performed ($n = 68/91$, 75%). The other IUI repairs are detailed in Table 3.

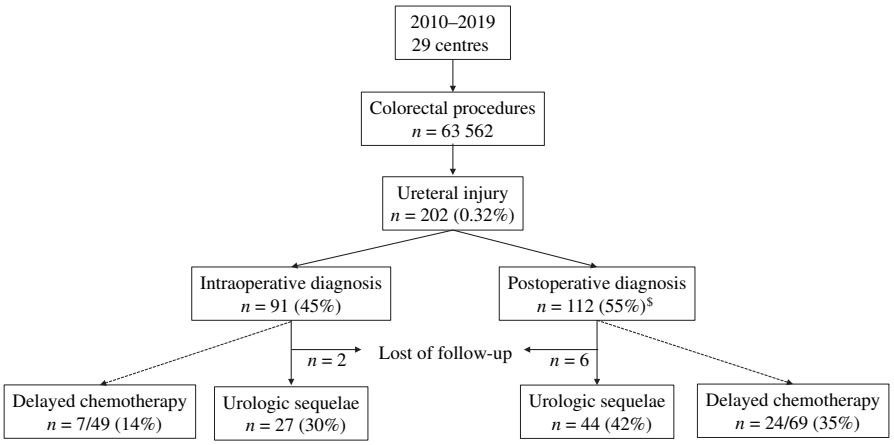

FIGURE 1 Flowchart of the study population. $^{\$}$There is one patient with bilateral iatrogenic ureteral injury diagnosed intraoperatively for the right side and postoperatively for the left side.

TABLE 1 Demographic characteristics of 202 patients with ureteral injury during colorectal surgery.

	Overall population ($n=202$)	Intraoperative diagnosis ($n=90$)[c]	Postoperative diagnosis ($n=111$)[c]	p-value
Gender				0.2
Male	93 (46)[a]	37 (41)	56 (51)	
Female	109 (54)	53 (59)	55 (49)	
Mean age (years)	63 ± 14 [20–93][b]	65 ± 14	62 ± 13	0.09
Mean BMI (kg/m^2)	26 ± 6 [17–59]	26 ± 5	27 ± 6	0.2
ASA score				0.2
1–2	124 (61)	53 (59)	71 (64)	
3–4	67 (33)	35 (39)	31 (28)	
NA	11 (6)	2	9	
Medical comorbidities				
Cardiovascular disease	111 (55)	50 (56)	60 (54)	0.9
Active smoking	30 (15)	13 (14)	17 (15)	0.8
Diabetes	30 (15)	12 (13)	18 (16)	0.8
Pulmonary disease	24 (12)	13 (14)	9 (9)	0.2
Urological history	19 (9)	8 (9)	11 (10)	0.8
Chronic renal insufficiency	5 (2.5)	2 (2)	2 (2)	0.96
Previous abdominal surgery	92 (45)	44 (49)	48 (43)	0.3
Previous pelvic radiation	53 (26)	17 (19)	36 (32)	0.09

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; NA, not available.

[a]Number (percentage).

[b]Mean ± standard deviation [range].

[c]The patient with bilateral ureteral injury diagnosed intraoperatively for the right side and postoperatively for the left side was excluded.

Postoperative diagnosis occurred after a mean delay of 11 ± 9 days (range 2–43 days), using imaging and measurement of the drain fluid creatinine level in 79.5% ($n=89$) and 28% ($n=31$) of cases, respectively. Among these 112 patients, a reoperation was necessary to repair the IUI in 62 patients (55%) and was mainly represented by reimplantation into the bladder with psoas hitch ($n=14/112$, 12.5%). The other IUI repairs are detailed in Table 3. Of the patients with postoperative diagnosis of IUI, 45% did not require surgery but only urine drainage, based on ureteral stent and/or percutaneous nephrostomy and/or urinary catheter.

Postoperative outcomes

Overall morbidity occurred in 71% of patients ($n=144$), including surgical morbidity in 129 patients (64%) and medical morbidity in 60 patients (30%). We identified urological complications in 35% of patients ($n=71$), represented mainly by urinary tract infection ($n=27$), urinoma ($n=23$), urodigestive fistula ($n=14$), hydronephrosis ($n=13$), haematuria or bladder clot ($n=6$) and acute urinary retention ($n=4$). The most frequent nonurological surgical complications were ileus ($n=40$, 20%), anastomotic complications ($n=32/136$ patients with anastomosis, 23.5%) and wound complications ($n=31$, 15%). Details of complications are reported in Table 4.

Unplanned surgery was necessary in 66 patients (33%) for digestive indications ($n=40$), urological indications ($n=22$) or both ($n=4$). The mean length of stay was 28 ± 23 days (range 2–145 days). Postoperative mortality within 90 days after surgery occurred in six patients (3%) due to multiple organ failure ($n=4$), septic shock ($n=1$) and acute pulmonary oedema ($n=1$).

Intraoperative diagnosis of IUI was significantly associated with a shorter length of stay (21 ± 22 days vs. 34 ± 22 days, $p<0.0001$) and lower rates of postoperative hydronephrosis [$n=2/90$ (2%) vs. $n=11/111$ (10%), $p=0.04$], anastomotic complication [$n=6/90$ (7%) vs. $n=25/111$ (22.5%), $p=0.002$] and thromboembolic event [$n=0$ vs. $n=7/111$ (6%), $p=0.02$] than postoperative diagnosis of IUI. The other surgical, urological and medical complications were similar

TABLE 2 Intraoperative characteristics of index colorectal surgery in 202 patients with ureteral injury.

	Overall population ($n = 202$)	Intraoperative diagnosis ($n = 90$)[g]	Postoperative diagnosis ($n = 111$)[g]	*p*-value
Admission type				0.5
Elective	174 (86)[a]	79 (88)	94 (85)	
Emergent	28 (14)	11 (12)	17 (15)	
Surgical approach				
Open	139 (69)	61 (68)	77 (69)	0.8
MIS	63 (31)	29 (32)	34 (31)	
Laparoscopy	60 (30)	29 (32)	31 (28)	
Robotic assisted	3 (1)	0	3 (3)	
Conversion into open before ureteral injury	19/63[f] (31)	9/29 (34)	9/34 (26)	0.7
Surgical indication				
Cancer	130 (64)	53 (59)	76 (69)	0.16
Primary segmental resection	88	43	44	
Locoregional recurrence	18	5	13	
Peritoneal carcinomatosis	14	3	11	
Recurrence and carcinomatosis	10	2	8	
Diverticulitis	22 (11)	13 (14)	9 (8)	0.2
Hartmann reversal	11 (5.5)	7 (8)	4 (4)	0.2
Redo surgery[b]	10 (5)	3 (3)	7 (6)	0.5
Inflammatory bowel disease	8 (4)	4 (4)	4 (4)	0.99
Endometriosis	5 (2.5)	2 (2)	3 (3)	0.99
Colonic ischaemia	5 (2.5)	2 (2)	3 (3)	0.99
Other[c]	11 (5.5)	6 (7)	5 (5)	0.5
Procedure type				
Proctectomy	61 (30)	20 (22)	40 (36)	**0.03**
Left colectomy	47 (23)	26 (29)	21 (19)	0.1
Abdominoperineal excision	20 (10)	8 (9)	12 (11)	0.7
Sigmoidectomy	15 (7.5)	9 (10)	6 (5)	0.3
Hartmann reversal	11 (5.5)	7 (8)	4 (4)	0.2
Multiple resection[d]	10 (5)	2 (2)	8 (7)	0.2
Right colectomy	7 (3.5)	5 (6)	2 (2)	0.2
Total coloproctectomy	4 (2)	1 (1)	3 (3)	0.6
Subtotal colectomy	3 (1.5)	2 (2)	1 (1)	0.6
Ileocaecal resection	3 (1.5)	3 (3)	0	0.09
Other[e]	21 (10.5)	7 (8)	14 (13)	0.3
Energy for dissection				0.2
LigaSure®	47 (23)	21 (37)	26 (39)	
Monopolar electrosurgery	30 (15)	19 (33)	10 (15)	
Multiple energy	19 (9)	7 (12)	12 (18)	
Ultracision®	16 (8)	5 (9)	11 (16)	
Bipolar electrosurgery	7 (3.5)	2 (3.5)	5 (7.5)	
Thunderbeat®	4 (2)	2 (3.5)	2 (3)	
NA	79 (39)	34	45	
Digestive continuity				
Concomitant anastomosis	136 (67)	61 (68)	74 (67)	0.9

TABLE 2 (Continued)

	Overall population ($n=202$)	Intraoperative diagnosis ($n=90$)[g]	Postoperative diagnosis ($n=111$)[g]	p-value
With stoma creation	69 /136	24 /61	41 /74	0.06
Without stoma creation	67 /136	37 /61	33 /74	
Stoma without anastomosis	54 (27)	26 (29)	29 (25)	0.6
NA	14 (7)	3	8	
Preoperative ureteral catheter placement	14 (7)	10 (11)	4 (4)	0.05

Note: $p<0.05$ (in bold) was considered as significant.

Abbreviations: MIS, minimally invasive surgery; NA: not available.

[a]Number (percentage).

[b]For anastomotic complications including anastomotic fistula or stricture.

[c]Includes rectal bleeding, rectal prolapse, colonic perforation during gynaecological surgery, radiation stenosis, diverticular stenosis, bowel obstruction.

[d]Defined by right colonic resection associated with left colonic resection for cancer or Crohn's disease.

[e]Includes Soave procedure, cytoreductive surgery without colorectal resection, anastomotic repair, ventral rectopexy and adhesiolysis for bowel obstruction.

[f]About patients with a MIS approach.

[g]The patient with bilateral ureteral injury diagnosed intraoperatively for the right side and postoperatively for the left side was excluded.

between groups, as well as unplanned reoperation and 90-day mortality (Table 4).

Long-term follow-up

At the end of follow-up, eight patients were lost to follow-up. After a mean delay of 3 ± 2.6 years (1 month–13 years), 72 patients presented with urological sequelae (36%), including ureteral stricture ($n=20$, 10%), chronic urinary fistula ($n=17$, 8%), recurrent urinary tract infections ($n=15$, 7%), chronic hydronephrosis ($n=7$, 3.5%), chronic urinary retention ($n=5$, 2.5%) and urinary incontinence ($n=2$, 1%). Six patients required nephrectomy (3%). Iterative urological reoperations were necessary in 57 patients (28%), mainly for iterative changes of ureteral stents or nephrostomy tubes ($n=35/57$, 61%). Long-term urological sequelae were more frequently reported after postoperative diagnosis ($n=44$, 42%) than intraoperative diagnosis ($n=27$, 30%), without a significant difference ($p=0.2$).

Oncological results

Delayed chemotherapy because of IUI was reported in 32 patients among 119 patients with indicated chemotherapy (27%). Delayed chemotherapy occurred less frequently in the case of intraoperative diagnosis [$n=7/49$ (14%) vs. $n=24/69$ (35%), $p=0.01$].

Regarding patients with primary cancer (excluding locoregional recurrence and peritoneal carcinomatosis), 1-, 3- and 5-year overall survival rates were 97%, 92% and 92% for colon cancer and 95%, 80% and 69% for rectal cancer, respectively ($p=0.1$); 1-, 3- and 5-year disease-free survival rates were 92%, 66% and 66% for colon cancer and 86%, 73% and 58% for rectal cancer, respectively ($p=0.9$).

No difference was observed between intraoperative and postoperative diagnosis of IUI, in terms of 1-, 3- and 5-year overall survival rates (94%, 85% and 85% vs. 98%, 86% and 74%, respectively, $p=0.88$; Figure 2A) nor 1-, 3- and 5-year disease-free survival rates (93%, 68% and 63% vs. 87%, 70% and 61%, respectively, $p=0.88$; Figure 2B).

The 1-, 3- and 5-year overall survival rates were decreased in the case of delayed chemotherapy (including primary and metastatic colorectal cancer or locoregional colorectal recurrence) when compared with on-time chemotherapy (95%, 54% and 54% vs. 98%, 88% and 81%, $p=0.06$), without significant difference (Figure 3A). The 1-, 3- and 5-year disease-free survival rates were significantly decreased in the case of delayed chemotherapy (68%, 30% and 30% vs. 90%, 67% and 55%, $p=0.009$; Figure 3B). In the presence of colon cancer, median survival was significantly decreased in the case of delayed chemotherapy (17 vs. 66 months, $p=0.005$) whereas the difference was not significant for rectal cancer (28 vs. 68 months, $p=0.15$).

DISCUSSION

We have reported here the largest French multicentre study on IUI during colorectal surgery, with 202 patients, corresponding to 0.32% of colorectal surgeries. Most IUIs occurred during scheduled colorectal surgery (86%). When IUI was diagnosed postoperatively (55%), surgical outcomes were worse than after an intraoperative diagnosis of IUI. Among patients who required adjuvant chemotherapy, more than a quarter underwent delayed chemotherapy because of IUI. At the end of the follow-up, 36% of patients presented with urological sequalae, six of whom required nephrectomy (3%).

Our IUI incidence (0.32%) is in accordance with the other large series, such as the American one (0.28%) [4] or the Danish one

TABLE 3 Management of ureteral injury in 202 patients.

	Overall population ($n = 202$)	Intraoperative diagnosis ($n = 90$)[d]	Postoperative diagnosis ($n = 111$)[d]	*p*-value
UI location				0.4
Left	138 (68)[a]	66 (73)	72 (65)	
Right	53 (26)	20 (22)	33 (30)	
Bilateral	11 (6)	4 (4)	6 (10)	
Type of injury				0.09
Partial section	85 (42)	40 (44)	45 (58)	
Complete section	77 (38)	48 (53)	29 (37)	
Burn	6 (3)	2 (2)	4 (5)	
NA	34 (17)	0	33	
Time for diagnosis (days)	–	–	11 ± 9 [2–43][b]	–
Diagnosis[e]				
Imaging	–	–	89 (79.5)	–
Creatinine into the drain	–	–	31 (28)	–
Other[c]	–	–	8 (7)	–
Surgical redo for UI	–	–	62 (55)	–
Surgical approach				
Abdominal surgery	–	–	43/62 (69)	–
Open			38	
Laparoscopy			5	
Transurethral surgery	–	–	18/62 (29)	–
Abdominal ureteral repair		89 (98)	43 (38)	
Uretero-ureterostomy	73 (36)	68 (75)	5 (4.5)	**<0.0001**
Uretero-neocystostomy	18 (9)	11 (13)	7 (6)	0.8
Vesico-psoas hitch	19 (9)	5 (5)	14 (12.5)	**0.005**
Ileal interposition graft	1 (0.5)	1 (1)	0	0.99
Cutaneous ureterostomy	2 (2)	0	0[d]	–
Bricker ileal conduit urinary diversion	3 (1)	1 (1)	2 (2)	0.6
Renal autotransplantation	1 (0.5)	0	0[d]	–
NA	14 (7)	2	12	
Urine drainage[f]	199 (99)	90 (100)	108 (96)	0.2
Ureteral catheter		82 (90)	54 (48)	
Percutaneous nephrostomy		0	43 (38)	
Urinary catheter		85 (93)	17 (15)	
Suprapubic catheter		1 (1)	7 (6)	

Note: $p < 0.05$ (in bold) was considered as significant.

Abbreviations: NA, not available; UI, ureteral injury.

[a]Number (percentage).

[b]Mean ± standard deviation [range].

[c]Intraoperative diagnosis during unplanned surgery ($n = 4$), leakage of urine from laparotomy scar or from vagina ($n = 2$), pneumaturia ($n = 1$) and ureteral tissue on pathological analysis ($n = 1$).

[d]The patient with bilateral ureteral injury diagnosed intraoperatively for the right side and postoperatively for the left side was excluded from statistical analysis.

[e]Some patients were diagnosed with several options.

[f]Some patients underwent several drains.

(0.44%) [5]. Regarding the index colorectal procedure, our IUI occurred more frequently during oncological surgery (64%), followed by diverticulitis (11%), similar to others [4, 5, 18]. We report that the left ureter was the most frequently injured (68%), which is usually described [5], mainly due to its close contact with the descending mesocolon and thus the inferior mesenteric artery.

TABLE 4 Postoperative outcomes of 202 patients with ureteral injury during colorectal surgery.

	Overall population ($n = 202$)	Intraoperative diagnosis ($n = 90$)[g]	Postoperative diagnosis ($n = 111$)[g]	*p*-value
Mean length of stay (days)	28 ± 23 [2–145][a]	21 ± 22	34 ± 22	**<0.0001**
Overall morbidity	144 (71)[b]	61 (68)	82 (74)	0.3
Surgical morbidity	129 (64)	52 (58)	76 (68)	0.1
Urological complication[h]	71 (35)	28 (31)	42 (38)	0.2
Urinary tract infection	27 (13)	8 (9)	19 (17)	0.08
Urinoma	23 (11)	11 (12)	11 (10)	0.7
Urodigestive fistula	14 (7)	5 (6)	9 (8)	0.6
Hydronephrosis	13 (6)	2 (2)	11 (10)	**0.04**
Haematuria or bladder clot	6 (3)	4 (4)	2 (2)	0.4
Acute urinary retention	4 (2)	2 (2)	2 (2)	0.99
Ureteral catheter migration	2 (1)	0	2 (2)	0.5
Ureteral stenosis	2 (1)	1 (1)	1 (1)	0.99
Ureteral necrosis	2 (1)	1 (1)	1 (1)	0.99
Vesico-cutaneous fistula	1 (0.5)	1 (1)	0	0.4
Ileus	40 (20)	18 (20)	22 (20)	0.3
Anastomotic complication	32/136 (23.5)[i]	6/61 (10)	25/74 (34)	**0.002**
Deep abscess	18 (13)	4 (7)	14 (19)	**0.049**
Asymptomatic leakage	11/136 (8)	2/61 (3)	8/74 (11)	0.2
Stricture	2 (1)	0	2 (3)	0.5
Peritonitis	1 (1)	0	1 (1)	0.99
Wound complication	31 (15)	16 (18)	15 (13)	0.2
Bleeding	11 (5)	3 (3)	8 (7)	0.3
Stoma-related complication	10 (5)	5 (6)	5 (4)	0.3
Pelvic abscess[j]	10 (5)	5 (6)	5 (4)	0.8
Colonic necrosis	1 (0.5)	0	1 (1)	0.99
Small bowel injury	1 (0.5)	0	1 (1)	0.99
Severity of surgical morbidity				0.1
Dindo I/II	40/129 (31)	20 (38)	20 (26)	
Dindo III/IV	89/129 (69)	32 (62)	56 (74)	
Unplanned reoperation	66 (33)	30 (33)	36 (32)	0.98
Digestive indication	40 (20)	17 (19)	23 (21)	
Urological indication	22 (11)	12 (13)	10 (9)	
Both	4 (2)	1 (1)	3 (3)	
Medical morbidity[h]	60 (30)	28 (31)	31 (28)	0.9
Acute renal failure	35 (17)	14 (16)	20 (18)	0.4
Pulmonary complication[c]	14 (7)	5 (6)	9 (8)	0.6
Cardiovascular complication[d]	9 (4)	7 (8)	2 (2)	0.08
Thromboembolic event[e]	7 (3.5)	0	7 (6)	**0.02**
Catheter-related sepsis	5 (2.5)	3 (3)	2 (2)	0.7
Other[f]	14 (7)	9 (10)	5 (4)	0.2
90-day mortality	6 (3)	3 (3)	3 (3)	0.25

Note: $p < 0.05$ (in bold) was considered as significant.

[a]Mean ± standard deviation [range].

[b]Number (percentage).

[c]Includes acute respiratory distress syndrome, pneumonia, pleural effusion, pneumothorax and haemothorax.

[d]Includes stroke, heart failure, acute pulmonary oedema, cardiac arrhythmia.

[e]Includes deep veinous thrombosis and pulmonary embolism.

[f]Includes multiple organ failure, blood transfusion, aplasia after hyperthermic intraperitoneal chemotherapy and anticoagulation-related bleeding.

[g]The patient with bilateral ureteral injury diagnosed intraoperatively for the right side and postoperatively for the left side was excluded.

[h]Some patients had several complications.

[i]The percentage was calculated among patients with anastomosis.

[j]Concerned patients without previous anastomosis.

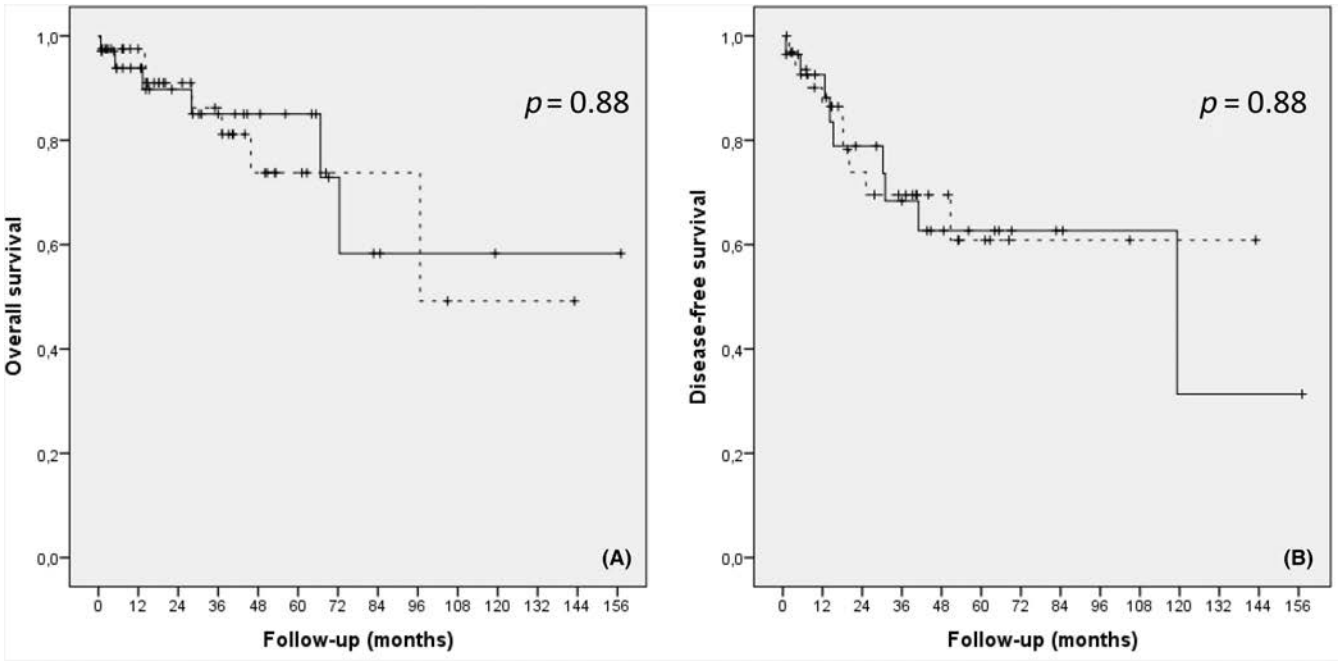

FIGURE 2 Overall (A) and disease-free (B) survivals of patients with iatrogenic ureteral injury occurring during colorectal surgery for primary cancer, according to the time of diagnosis: intraoperative (solid line) and postoperative (dotted line).

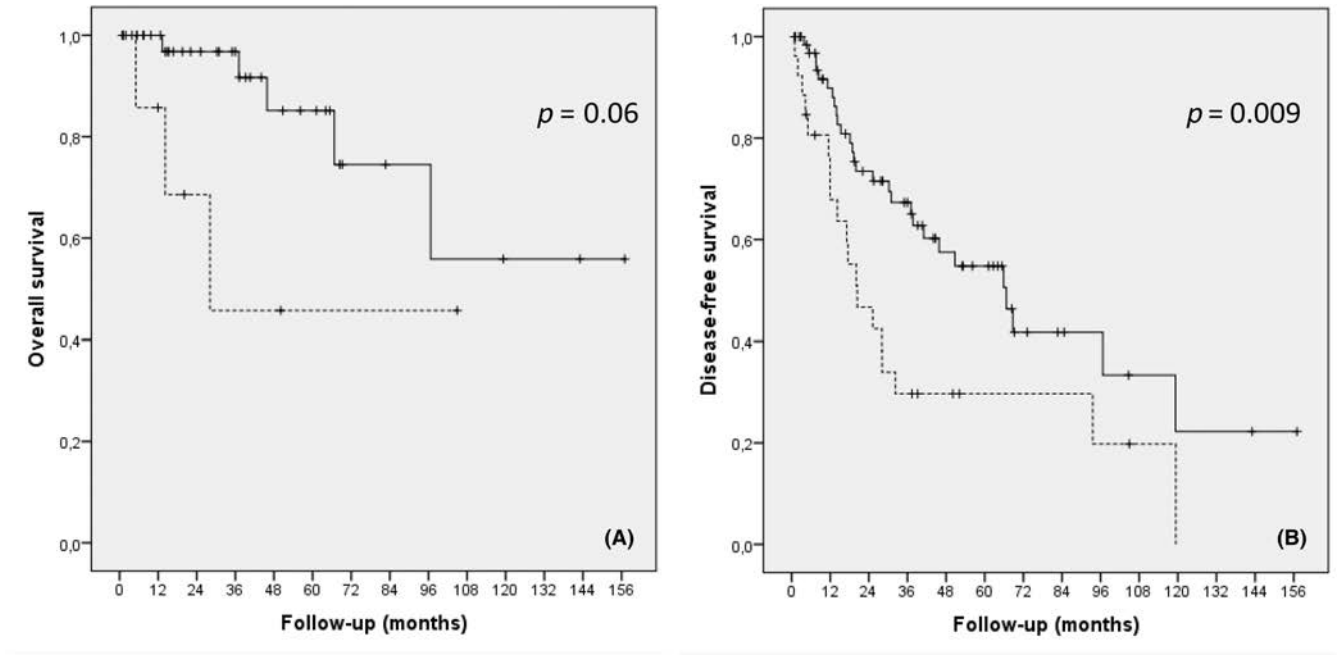

FIGURE 3 Overall (A) and disease-free (B) survivals of 94 patients with iatrogenic ureteral injury occurring during colorectal surgery for colorectal cancer according to on-time (solid line) or delayed chemotherapy (dotted line).

In terms of surgical approach, 69% of patients underwent open surgery, probably because of frequent complex procedures (i.e. locally advanced tumour, carcinomatosis, locoregional recurrence, redo surgery for anastomotic complication) or emergency procedures (i.e. colonic ischaemia). Our study did not analyse the impact of laparoscopy on IUI, unlike others [4, 6, 19].

Some measures to prevent IUI have been used. Preoperative placement of a ureteral stent was performed in 7% of our patients and was useful in only two patients. This low rate of prophylactic use of ureteral stenting is due to conflicting data. A few authors consider that preoperative ureteral stenting is associated with minor complications and is cost-effective [20], while others

report an increase in operating time, with new-onset urinary complications without a decrease in IUI rates [21]. A recent systematic review of 22 references and 869 603 patients reported that IUI occurred more frequently in patients with a prophylactic ureteral stent (1.49%) than in those without (0.17%) [odds ratio = 8.67 (95% CI 8.05–9.33), $p < 0.0001$]. Moreover, there was no significant difference between the two groups in terms of intraoperative diagnosis of IUI (62.5% vs. 52.94%, $p = 0.579$) [22]. It is thus difficult to make a conclusion about the usefulness of prophylactic ureteral stents in colorectal surgery. Other tools for identifying the ureter during surgery have been proposed, such as retrograde injection of methylene blue [23] and direct visualization of the dye or retrograde injection of indocyanine green using fluorescence-guided surgery, particularly during minimally invasive surgery (robotic for example) [24], with promising results, in combination with multispectral imaging [25]. Additional studies are necessary to validate the use of these new tools.

Besides the tools used to identify the ureter, the timing of IUI diagnosis is important. Very few authors have examined the outcomes of patients with IUI diagnosed intraoperatively compared with those diagnosed postoperatively. We found that intraoperative diagnosis was significantly associated with a shorter length of hospital stay, lower postoperative rates of hydronephrosis, anastomotic complications and thromboembolic events, and a lower rate of delayed chemotherapy (in the case of cancer) than postoperative diagnosis. Recently, Kominsky et al. [26] reported that delayed diagnosis of IUI was significantly associated with an increased number of procedures needed to manage the IUI: secondary or tertiary procedures in 56% and 19.3% of patients with postoperative diagnosis of IUI, in comparison with 16.7% ($p < 0.001$) and 3.3% ($p = 0.002$) of patients with early diagnosis of IUI, respectively. In accordance with others [7–10, 26], the early diagnosis of IUI is thereby associated with better surgical and oncological outcomes than postoperative diagnosis. Regarding the late postoperative diagnosis of IUI, we encourage an early measurement of the drain fluid creatinine level in the postoperative course in the case of difficult surgery. Otherwise, the observation of a large volume (into the drain) should indicate a measurement of creatinine level.

The strength of our study is the analysis of long-term urological and oncological results, exceptionally reported by others. After a mean delay of 3 ± 2.6 years, we have observed urological sequelae in more than a third of patients, requiring iterative urological surgery in 28%, with six nephrectomies (3%). These results are similar to those previously reported, with nephrectomy rates of between 2.4% [9] and 14% [14] of patients. The other long-term urological sequalae usually described are ureteral stenosis, chronic fistulas and urinoma [14], as in our series. Concerning oncological results, the different impact of IUI on disease-free survival rates according to colonic or rectal location may be explained by the delayed chemotherapy observed in 27% of patients. Indeed, it is well established that delayed adjuvant chemotherapy impairs patient survival, particularly after colonic cancer resection. In their meta-analysis of 15 410 patients with colorectal cancer (colonic location in the majority), Biagi et al. [27] demonstrated that a 4-week delay in adjuvant chemotherapy was associated with a significant decrease in both overall (hazard ratio 1.14, 95% CI 1.10–1.17) and disease-free (hazard ratio 1.14, 95% CI, 1.10–1.18) survival. Nevertheless, the small number of patients with delayed chemotherapy, and the absence of a control group in our study, do not allow us to conclude about the obvious impact of IUI on decreased survival.

Finally, our study is limited by its retrospective and multicentric nature, and the long inclusion period, leading to coding errors in the administrative database and/or missing data. It is possible that some patients with IUI were not diagnosed because of our coding system, which does not consider 'intraoperative complications of the genitourinary' or 'accidental puncture and laceration during a procedure' proposed by ICD 10. The real incidence of IUI is possibly underestimated because of some misdiagnosed cases. Yet the rarity of IUI does not allow us to perform any prospective study nor any retrospective study during a shorter period. Moreover, our study is limited by the absence of risk factor analysis, due to the absence of an adequate control group.

To conclude, iatrogenic ureteral injury during colorectal surgery has few consequences for patients if recognized early. Long-term urological sequelae can occur in a third of patients. Iatrogenic ureteral injury may affect the oncological outcome in colorectal surgery by delaying adjuvant chemotherapy, especially when the ureteral injury is not diagnosed peroperatively.

AUTHOR CONTRIBUTIONS

Diane Mege: Conceptualization; data curation; formal analysis; writing – original draft; methodology; investigation; supervision; validation; software; visualization; project administration. **Philippe Rouanet:** Methodology; data curation; validation. **Diane Charleux-Muller:** Data curation; methodology; validation. **Clarisse Eveno:** Data curation; methodology; validation. **Karine Poirot:** Data curation; methodology; validation. **Bertrand Trilling:** Data curation; methodology; validation. **Gilles Manceau:** Data curation; methodology; validation. **Yves Panis:** Data curation; methodology; validation. **Arnaud Alves:** Data curation; methodology; validation. **Alex Kartheuser:** Data curation; methodology; validation. **Marc Pocard:** Data curation; methodology; validation. **Charles Sabbagh:** Data curation; methodology; validation. **Anaïs Laforest:** Data curation; methodology; validation. **Zaher Lakkis:** Data curation; methodology; validation. **Bogdan Badic:** Data curation; methodology; validation. **Amélie Chau:** Data curation; methodology; validation. **Niki Christou:** Data curation; methodology; validation. **Adeline Germain:** Data curation; methodology; validation. **Alain Valverde:** Data curation; methodology; validation. **Emilie Duchalais:** Data curation; methodology; validation. **Mehdi Ouaissi:** Data curation; methodology; validation. **Leonor Benhaim:** Data curation; methodology; validation. **Maxime Collard:** Data curation; methodology; validation. **Jean-Jacques Tuech:** Data curation; methodology; validation. **Etienne Buscail:** Data curation; methodology; validation.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

None.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

This study was conducted according to the ethical standards of the Committee on Human Experimentation of our institution.

PATIENT CONSENT STATEMENT

Not necessary.

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APPENDIX

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