Morbidity and predictors of delayed recognition of iatrogenic ureteric injuries

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Abstract

Introduction: Although intraoperative iatrogenic ureteric injuries (IUI) are rare, significant consequences can occur if they are unrecognized at the time. The focus of our study is to characterize the associated morbidity and identify predictors of delayed recognition of IUI.
Methods: Sunnybrook Health Sciences Centre Research Ethics Board approved the study. Patients with a diagnosis of IUI between 2002 and 2020 were identified through an institutional electronic medical record system. Data pertaining to the demographic characteristics, diagnosis, and management of IUI and overall outcomes were collected retrospectively.
Results: Of the 103 patients identified, 83% were female, 52% had previous abdominal surgery, and 18% had previous radiation. The median age was 67 (21–88) years. Twenty percent were not recognized at the time of surgery. Although delayed recognition was not a significant predictor for poor outcome after subsequent repair (i.e., hydronephrosis, ureteric stricture/obstruction), it was associated with substantial morbidity to the patient (i.e., additional procedures) and increased cost to the healthcare system (i.e., longer hospital stay, readmission to hospital). Patients who underwent laparoscopic surgery had an 11 times more likely chance of having an unrecognized IUI as compared to those who underwent open surgery (odds ratio 11.515, p=0.0001).
Conclusions: Delayed recognition of IUI may be associated with considerable adverse effects. In this retrospective case series, we identified laparoscopic surgery as a

significant predictor for delayed recognition of IUI. This information underscores the need for future studies to facilitate intraoperative identification of ureteric injuries, particularly during laparoscopic procedures.

Introduction

Although iatrogenic ureteric injuries (IUI) are rare with an incidence of 0.5-10%(1), intra-operatively unrecognized IUI can have significant consequences (2). In a population based study of 1,753 hysterectomy-associated IUI, the IUI that went unrecognized at the time of injury had higher rates of 90-day readmission (67% vs. 13%), sepsis (OR 2.0, 95% confidence interval (CI) 1.2-3.5 and 11.9, 95% CI 9.9-14.3), urinary fistula (OR 5.9, 95% CI 2.2-16 and 124, 95% CI 95.7-16), acute renal insufficiency (OR 23.8, 95% CI 20.1-28.2) and death (OR 1.4, 95% CI 1.03-1.9, p = 0032) as compared to those recognized at the time of injury (3). In a study by Hove *et al.* evaluating insurance claims in a Danish database the authors noted that the majority of claims (88%) were associated with delayed recognition of IUI and that presentations included flank pain, febrile postoperative course, ileus, urinary leakage and a transient rise in serum creatinine (4). Unrecognized IUI can have substantial consequences for the patient, increased costs for the health care system and may result in litigation. Intra-operative recognition of IUI is therefore important.

Surgical techniques to repair IUI include uretero-neocystotomy, uretero-ureterostomy, suture repair, ureteric stent placement and nephrostomy tube placement (1, 5-7). Various case series (maximum 164 patients) have evaluated the outcomes of IUI repair and found very high success rates if recognized at the time of injury regardless of technique (8-14). However, the management of IUIs recognized after a delay has not been as well studied. In a retrospective study of IUIs after delayed recognition 11/21 (52.5%) had successful ureteral stenting but only 3/11 (27.3%) had resolution requiring no further intervention (15). The outcome of reconstructive surgery was not mentioned (15). In a case series of 82 IUIs Al-Awadi *et al.* found that when an IUI was recognized and repaired within one week of the initial surgery, where the type of repair not specified, mean hospital stay was shorter (4.8 vs. 10.1 days) and there were fewer complications compared to those repaired after one week (16).

The aims of our study are to characterize the associated morbidity, outcomes, and identify predictors of delayed recognition of IUI.

Methods

Sunnybrook Health Sciences Centre Research Ethics Board approved the study. Patients with a diagnosis of IUI between 2002 and 2020 were identified through an institutional

electronic medical record system. Collected data in this retrospective chart review included demographic variables (age, gender and comorbidities), previous radiation/abdominal surgery, initial diagnosis and surgery, time of diagnosis (immediate or delayed), type of surgery (laparoscopic or open), location of IUI (distal, middle or upper ureter) and type of repair (uretero-neocystotomy, uretero-ureterostomy, suture repair, stent only or no treatment). The outcomes evaluated included presence of new or worsening hydronephrosis on follow-up imaging (ultrasound or computed tomography (CT) scan), presence of stricture as defined as hydronephrosis proximally to a narrowing of the ureter at the site of previous repair on follow-up imaging and most importantly, the presence of ureteric obstruction as defined as presence of hydronephrosis proximally, narrowing of the ureter at the site of previous repair with reflux not being the etiology of the hydronephrosis.

Logistic regression analysis was used to determine if there was any significant relationship between demographic variables, patient and operative factors (previous radiation, previous surgery, initial diagnosis, initial procedure type) and delayed presentation of IUI. Logistic regression analysis was also used to determine if there was any significant relationship between delayed recognition of IUI and outcomes (hydronephrosis, ureteric stricture and ureteric obstruction). Statistical significance was defined as $p<0.05$. Data analysis was done with IBM® SPSS software.

Results

Demographics

Between 2002 and 2020 103 patients with IUI were identified at our institution. The average age of the patients was 58 (SD=14) and range of ages was 21 to 88 (median=67). Eighty-three percent of the patients were female. Evaluating comorbidities we found 57% had previous surgery, 31% had hypertension (HTN) and 11% had diabetes (DM). Fifty-two percent had previous abdominal surgery and 18% had previous radiation (Table 1).

Eighty percent of the injuries were recognized at time of the initial surgery. The remainder had delayed recognition (defined as repair not on same day as initial surgery) (Table 1). Of the 21 patients who had delayed recognition of IUI median time to presentation was 7 days (range 1-270 days). Eight of twenty-one presented to outside hospitals other than our institution. Presenting symptoms included nausea/vomiting, fever and flank pain while presenting signs included ileus, incisional infection, increased drain output, sepsis, hydronephrosis, urinary incontinence/leakage per vagina or rectum and recurrent urinary tract infections (Table 2).

Overall outcomes

For IUI location, 65% were distal, 33% were mid- and 2% were upper ureter (Table 1). The majority was repaired by uretero-neocystotomy +/- psoas hitch +/- boari flap (52%) followed by uretero-ureterostomy (29%), suture repair (14%), stent only (3%), nephrostomy tube drainage (1%) and no treatment (1%; patient was palliative). Of the 103 patients in the study 10 (10%) developed new or worsening hydronephrosis, 5 (5%) had ureteric stricture and 4 (4%) had ureteric obstruction after repair of IUI. There were no statistical differences in hydronephrosis, ureteric stricture and ureteric obstruction based on repair type or any other variables recorded in the study.

Predictors for delayed recognition of IUI

Univariate logistic regressions were performed to ascertain the effects of previous radiation, previous surgery, initial diagnosis, type of surgery and initial procedure type individually on the likelihood that patients had a delayed presentation of IUI. The logistic regression model for type of surgery (laparoscopic vs. open) was statistically significant $p<0.005$. The model explained 24% (Nagelkerke R^2) of the variance in time of diagnosis and correctly classified 84% of cases. Patients who underwent laparoscopic surgery had an 11 times more likely chance of delayed presentation of IUI as compared to patients who underwent open surgery (OR=11.515, p=0.0001). No other factors evaluated were associated with a delayed presentation of IUI (Table 3).

Delayed recognition of IUI and outcomes

In the 21 patients whose IUI was discovered after a delay, there were no statistically significant differences in hydronephrosis, ureteric stricture and ureteric obstruction after treatment compared with those recognized immediately (Table 3), regardless of repair type (uretero-neocystotomy +/- psoas hitch +/- boari flap (81%), uretero-ureterostomy (9%), stent only (5%) or nephrostomy tube drainage (5%)) (Table 1).

Delayed recognition of IUI and morbidity

In addition to requiring an operation to repair the IUI most patients with delayed recognition of IUI experienced significant morbidity. Eighteen required nephrostomy tube (15) or ureteric stent (3) with a median time to first intervention of 7 days (range 1-9 days). Approximately half went on to have multiple interventions (i.e. nephrostomy tube changes, ureteric stent changes) prior to definitive repair of the IUI. Average hospitalization time was longer in the delayed recognition group (21 +/- 40 days versus immediate 12 +/- 10 days, p=0.0001) and 6/21 patients required readmission to hospital for symptoms related to the delayed diagnosis of IUI, imposing a cost burden to the health care system. Lastly, 1 patient had persistent wound drainage for 3 months following his/her initial surgery before the IUI was recognized and another patient had

ureteric stent changes for over 10 years to manage the non-healing IUI before being referred for definitive repair.

Discussion

One of the objectives of this retrospective study was to identify predictors for delayed recognition of IUI. Previous radiation, previous surgery, initial diagnosis, type of surgery, initial procedure type and demographics were not found to be predictors. We did find that laparoscopic surgery had a higher likelihood of delayed presentation of IUI than open surgery (OR 11.515, p=0.000). The other objective of this retrospective study was to characterize associated morbidity with delayed presentation of IUI. We found that delayed recognition of IUI was associated with substantial patient morbidity in addition to requiring another operation to repair the IUI. Most patients required diversion of urine via nephrostomy tube or ureteric stent and approximately half required multiple procedures until definitive management was completed. Patients experienced prolonged admissions to hospital and readmissions, increasing the cost to the health care system. In other larger studies delayed recognition of IUI has also been shown to have negative consequences to the patient and increased costs for the health care system (3, 4, 16, 17).

Fortunately, in our series of 103 patients we did not identify a direct relationship between delayed recognition of IUI and hydronephrosis, ureteric stricture and ureteric obstruction after definitive treatment. This is likely because the majority of the patients in our study had good outcomes regardless of when the injury was recognized; only 10% had new or worsening hydronephrosis, 5% had ureteric stricture and 4% had ureteric obstruction. In a series of 82 IUIs Al-Awadi *et al.* also found a high success rate of repair (93.9%) regardless of the timing of diagnosis or type of repair (16).

In general, gynecological and general surgical procedures are being done more frequently with minimally invasive techniques (i.e. laparoscopic or robotic) (18, 19). We also noted this in our series. In the first half of the study period 5.8% of procedures were done laparoscopically while in the second half of the study period 25.5% of procedures were done laparoscopically. Using the Danish National Colorectal Cancer database of 18,474 patients Andersen *et al.* found a higher rate of IUI in surgeries conducted laparoscopically as compared to an open approach (0.6% vs. 0.4%, p=0.03) (13). Over time in our series, where the majority of the laparoscopic procedures were done in the latter half of the study period, we noted a higher proportion of the IUIs being recognized in a delayed manner (25.5% 2011 onwards versus 13.5% before 2011). Patients who underwent laparoscopic surgery had an 11 times more likely chance of having an unrecognized IUI as compared to those who underwent open surgery (OR=11.515, p=0.0001). As the number of laparoscopic surgeries increases, we may see a higher incidence of IUI in the future, in particular those recognized in a delayed manner.

To prevent complications associated with unrecognized IUI it is important to focus on intra-operative detection of IUI. Several published studies have explored methods to improve detection. The use of prophylactic ureteric stents has been reviewed in general surgery and gynecology. In a systematic review of 22 studies of general surgery cases Croghan *et al.* found a slightly higher incidence of IUI in prophylactically stented (1521/102,370; 1.49%) versus non stented (1333/767,233; 0.17%) patients but did not find a statistically significant difference in intra-operative recognition of IUI between prophylactically stented (10/16) and non-stented (9/17) patients (p=0.579) (20). Dumont *et al.* examined 155 pelvic surgery cases in a tertiary referral hospital and noted that the prophylactic ureteric stent significantly enhanced intra-operative diagnosis of IUI (OR=5.09; 95%CI =2.26-11.48) (21). However, prophylactic ureteric stent placement was not associated with reduced rates of IUI nor their complications. Thus, the benefit of prophylactic stenting to protect ureters is not clear. Cystoscopy to assess for lack of ureteric jet associated with IUI has also been reviewed in gynecologic procedures with conflicting results (22, 23). Lack of a ureteric jet on cystoscopy would normally trigger further work-up for the injury with a retrograde pyelogram. Because IUI are so rare in common gynecologic procedures Cadish *et al.* conducted a cost analysis and found that routine cystoscopy is not cost-effective in detecting IUI (24). However, selective cystoscopy in high risk cases where risk of IUI exceeds 3.96-8.95% is less expensive than no cystoscopy at all after weighing cost factors of diagnostic tests, treatments and complications. The results from our study highlight the need to identify cases defined as high risk. The incidence of IUI is low, approximately 0.244% (25) and less than 0.5% for laparoscopic colectomy and laparoscopic hysterectomy, respectively (26). Therefore, it is unlikely that selective cystoscopy to identify ureteric jets is financially justified for detection of IUIs with such a low incidence rate. The addition of an oral or intravenous agent to help detect ureteric jets has also been evaluated. Grimes *et al*. conducted a randomized clinical trial (n=130) that compared surgeon satisfaction in using 4 different ways of detecting IUI, preoperative oral phenazopyridine, or intraoperative intravenous sodium fluorescein, 20% mannitol, or normal saline immediately prior to the intraoperative cystoscopy (27). Surgeons in the study rated intravenous mannitol to be the most helpful in visualizing ureteric jets. There were no differences in cystoscopy length, time to surgeon confidence in visualization of ureteric jets and adverse events at 189-days follow-up. Future studies should continue to evaluate prophylactic stenting and other methods such as near-infrared fluorescence and experimental dyes (28, 29) for immediate identification of IUI.

There are limitations to this study. The data were collected retrospectively. Based on the identification of IUI through an institutional medical records system some injuries may have been missed. For example, a ureter that was injured by a urologist and repaired

by the same urologist intraoperatively may not have been recorded as an IUI. Our cohort was relatively small, especially for those with a delayed diagnosis of IUI (21/103). Thus, our ability to characterize morbidity and identify all predictors was limited by the availability of data and our adjustment for other factors such as comorbidities in the logistic regression analyses. Nonetheless, this is one of the largest case series to date evaluating IUI (8-14) and the only study, of which we are aware, that evaluates predictors for delayed recognition of IUI.

Conclusions

Although IUI are uncommon they may have significant consequences to the patient and health care system. In this retrospective case series we identified laparoscopic surgery as a predictor for delayed recognition of IUI. This information underscores the need for future studies to optimize intra-operative techniques to identify IUI, particularly in laparoscopic cases.

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Figures and Tables

Table 1. Demographic characteristics of the cohort.	
	Patient cohort n=103 (%)
Comorbidities	
Parkinson's	1 (1.0)
Hypertension (HTN)	32 (31.1)
Diabetes (DM)	11 (10.7)
High body mass index (BMI)	3 (2.9)
Liver disease	1 (1.0)
Coronary artery disease (CAD)	7 (6.8)
Previous surgery (any)	59 (57.3)
Patient and operative factors	
Previous abdominal surgery	
Yes	54 (52.4)
No	35 (34.0)
Unknown	14 (13.6)
Previous radiation	
Yes	18 (17.5)
No	85 (82.5)
Type of surgery	
Laparoscopic	16 (15.5)
Open	87 (84.5)
Timing of injury recognition	
Immediate	82 (79.6)
Delayed	21 (20.3)
Location of injury	
Distal	67 (65.0)
Mid	34 (33.0)
Proximal	2 (1.9)
Initial procedure type	
Total abdominal hysterectomy	57 (55.3)
Cystectomy*	3 (2.9)
Bowel resection	32 (31.1)
Pelvic exenteration*	2 (1.9)
Endoscopic ureteral surgery	1 (1.0)
Vascular surgery	4 (3.9)
Other	4 (3.9)

Repair type	All	Recognized (82)	Unrecognized (21)
Uretero-neocystotomy ± psoas hitch ± boari flap	54 (52.4%)	37 (45.1%)	17 (81.0%)
Uretero-ureterostomy	30 (29.1%)	28 (34.1%)	2 (9.5%)
Suture repair	14 (13.6%)	14 (17.1%)	0
Stent only	3 (2.9%)	2 (2.4%)	1 (4.8%)
No treatment	1 (1.0%)	1 (1.2%)	0
Nephrostomy drainage	1 (1.0%)	0	1 (4.8%)

*These procedures traditionally involve transection of the ureter at time of bladder removal. Therefore, in this series iatrogenic ureteric injuries was defined as unexpected injury to the ureter aside from the preoperatively planned transection of the ureter.

Table 2. Presentations and morbidity associated with delayed recognition of IUI (n=21)		
Presentation		
Symptoms	**n (%)**	
Nausea/vomiting	4 (19.0)	
Fever	7 (33.3)	
Flank pain	4 (19.0)	
Signs		
Ileus	3 (14.2)	
Incisional infection	1 (4.8)	
Increased drain output	4 (19.0)	
Sepsis	7 (33.3)	
Hydronephrosis	5 (23.4)	
Urinary incontinence/urine per vagina or rectum	4 (19.0)	
Recurrent urinary tract infection	1 (4.8)	
Unknown symptoms and signs	3 (14.2)	
Morbidity		
Nephrostomy tube (NT)	15 (71.4)	
Ureteric stent	3 (14.2)	
Time to first intervention (median (range))	7 days (1–9 days)	
Multiple procedures (i.e., NT, ureteric stent, nephrostogram, retrograde pyelogram)	10 (47.6)	
Hospitalization time (mean ± standard deviation)	Immediate 12±10 days	Delayed 21±40 days
Readmission to hospital	6 (28.4)	

IUI: iatrogenic ureteric injuries.

Table 3. Results from univariate logistic analyses to assess for predictors of delayed recognition of IUI					
Predictor	**B**	**Standard error**	**Odds ratio**	**95% CI**	**p**
Previous radiation					
Yes (ref)					
No	0.134	0.628	1.143	0.333–3.917	0.832
Previous surgery					
Unknown (ref)					
Yes	-0.249	.722	0.779	0.189–3.205	0.73
No	0.748	0.841	2.114	0.407–10.977	0.373
Initial diagnosis					
Other (ref)					
Endometrial/uterine cancer/cervical cancer/ovarian/adnexal sarcoma/benign gynaecology	0.021	1.164	1.021	0.104–9.985	0.986
Colorectal cancer/ diverticular disease/benign general surgery	-0.043	1.208	0.958	0.09–10.235	0.972
Vascular	0.223	1.565	1.25	0.058–26.869	0.887
Urologic cancer/benign urology	-1.386	1.803	0.25	0.007–8.56	0.442
Type of surgery					
Open (ref)					
Laparoscopic	**2.444**	**0.609**	**11.515**	**3.491–37.979**	**0.0001***
Initial procedure type					
Total abdominal hysterectomy/oophorectomy (ref)					
Bowel resection/upper gastrointestinal surgery/liver/pancreatic surgery	-0.177	0.72	0.838	0.204–3.438	0.806
Other	0.647	0.843	1.909	0.366–9.955	0.443

*Statistically significant difference. CI: confidence interval; IUI: iatrogenic ureteric injuries.