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ScienceDirect

Journal of the Chinese Medical Association 78 (2015) 283–286

www.jcma-online.com

Original Article

Measurement of peritoneal fluid urea nitrogen and creatinine levels is useful to detect iatrogenic urinary tract leakage in colorectal surgery

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Received September 2, 2014; accepted November 4, 2014

Abstract

Background: Increased peritoneal drainage after colorectal surgery is a common problem. Measurement of peritoneal fluid urea nitrogen (UN) and creatinine (Cr) is a diagnostic tool to detect the urinary tract leakage (UTL). We evaluated its application in colorectal surgery.
Methods: We conducted a retrospective chart review study. We enrolled patients with iatrogenic UTL, and measured their UN and Cr levels in peritoneal fluid and compared them with those in blood and urine. Meanwhile, we assigned patients without UTL to a control group and compared clinical parameters of both groups.
Results: Twenty-three patients with iatrogenic UTL were recruited. The overall incidence was 0.5%. UN level in peritoneal fluid (322 ± 56 mg/dL) was significantly higher than that in blood (18.7 ± 4.0 mg/dL, $p < 0.001$); Cr level in peritoneal fluid (69.7 ± 14.3 mg/dL) was also significantly higher than that in blood (1.5 ± 0.5 mg/dL, $p < 0.001$). UN level in peritoneal fluid was significantly higher in the iatrogenic UTL group than in the control group (322 mL/dL vs. 9.3 mL/dL, $p < 0.001$); Cr level in peritoneal fluid was also significantly higher (69.7 mg/dL vs. 0.98 mg/dL, $p < 0.001$).
Conclusion: When increased peritoneal drainage is found postoperatively in colorectal surgery, measurement of UN and Cr levels in peritoneal fluid can be a useful diagnostic tool to determine intraperitoneal iatrogenic UTL.

Keywords: creatinine; peritoneal fluid; urea nitrogen; urinary tract leakage

1. Introduction

A common problem after major colorectal surgery is increased clear peritoneal drainage during the postoperative period (>500 mL/d).[1] The major differential diagnosis is between simple peritoneal drainage and iatrogenic urinary tract leakage (UTL), especially the ureteral injury. The incidence of operative ureteral injury with open or laparoscopic surgery ranges from <1% to 8%.[2–4] Bladder injuries are rare (<1%) during colorectal surgery.[2] Some iatrogenic UTLs are detected intraoperatively, and repair of the injury can be undertaken immediately. However, most of the injuries may remain undetected intraoperatively and be detected during the postoperative period.[2,5]

When increased clear peritoneal drainage (>500 mL/d) is detected postoperatively, iatrogenic UTL should be first considered. Traditionally, abdominal computed tomography scan, cystography, intravenous pyelography, or uroendoscopy is performed to confirm the diagnosis.[5] The concept of urea nitrogen (UN)–creatinine (Cr) disproportion in intraperitoneal extravasation of urine was first proposed in 1972.[6] Measured levels of UN and Cr in peritoneal fluid have been compared to their levels in blood, and peritoneal fluid UN and Cr levels

Conflicts of interest: The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

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http://dx.doi.org/10.1016/j.jcma.2015.01.006

similar to the levels in blood are believed to be diagnostic of simple peritoneal drainage rather than UTL.[7] This diagnostic tool is not routinely utilized and is mainly applied in patients with major abdominal trauma[8] or complicated urological surgery and hysterectomy.[9] Although this diagnostic tool could also be used to detect iatrogenic UTL after major colorectal surgery, little literature was found through a search of MEDLINE and PubMed. Therefore, in this study, we retrospectively analyzed patients with iatrogenic UTL and evaluated this diagnostic tool for its possible application in colorectal surgery.

2. Methods

At Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, we reviewed the medical records and operation notes for all patients receiving colorectal surgery during 2000–2013. We used this database for our study, which was a retrospective case–control analysis with prospective collection.

In our hospital, we place at least one Jackson–Pratt drain intraperitoneally in all patients receiving colorectal surgery. When massive peritoneal fluid (500 mL/d) from Jackson–Pratt drain is detected postoperatively, we send it for measurement of UN and Cr levels to exclude UTL. Meanwhile, we collect blood and urine samples and measure their UN and Cr levels for comparison. If iatrogenic UTL is highly suspected by the analysis result, we perform sonography, abdominal computed tomography scan, cystography, intravenous pyelography, or uroendoscopy to confirm the diagnosis.

In this study, we included patients with iatrogenic UTL detected postoperatively. During the same period, we also assigned all patients with simple increased peritoneal fluid (500 mL/d) but without iatrogenic UTL (confirmed by sonography, abdominal computed tomography scan, cystography, intravenous pyelography, or uroendoscopy) to the control group. Patients with congestive heart disease, chronic liver disease with impaired liver function, and chronic renal disease with impaired renal function were excluded due to possible interference of UN and Cr levels.[10] The clinical parameters included age, sex, procedure name, site and mechanism of UTL, peritoneal fluid amount, and UN and Cr levels of peritoneal fluid, blood, and urine. We also calculated the ratios of UN and Cr levels in peritoneal fluid and blood in each group of patients for comparison. Prevention and management of UTL were not evaluated in this study.

All quantitative data were expressed as mean ± standard deviation. Analysis of variance with *post hoc* test and two independent sample *t* test were used for group comparisons of quantitative data. Statistical analysis was performed using SPSS version 12.0 for Windows (SPSS Inc., Chicago, IL, USA). Significance was defined as $p < 0.05$.

3. Results

In 2000–2013, 4493 patients receiving major colorectal surgery were registered in our medical record database. Twenty-three patients had definite diagnosis of iatrogenic UTL, and the overall incidence rate was 0.5%. Due to the retrospective nature of the study, parts of the data were missing. The clinical characteristics are shown in Table 1. Seventeen patients (74%) had open surgery, and six patients (26%) had laparoscopic surgery. The most common procedures were low anterior resection ($n = 7$) and anterior resection ($n = 6$). Most of the injuries occurred over the left ureter (82.6%), especially over the left middle third (M/3) and lower third. Two patients had bladder injury. One patient had ureteral injury over the right middle third and one patient had urethral injury. The common mechanisms were laceration ($n = 8$), ligation ($n = 6$), and thermal injury (including those caused during electrocautery and by vessel-sealing device, $n = 5$). Two patients had ureteroureterostomy leakage, and two patients had leakage from bladder repair.

UN and Cr levels in the peritoneal fluid, blood, and urine of 23 patients with iatrogenic UTL are shown in Table 2. UN/Cr levels in peritoneal fluid (322.1/69.7 mg/dL) were significantly higher than those in blood (18.7/1.5 mg/dL, $p < 0.001$) and significantly lower than those in urine (392.6/127.3 mg/dL, $p < 0.001$). Comparisons between patients with iatrogenic UTL and those of the control group are shown in Table 3. Peritoneal fluid amount and the levels of peritoneal UN, peritoneal Cr, blood UN, and blood Cr were significantly higher in the iatrogenic UTL group than in the control group, especially peritoneal UN and peritoneal Cr (322 mL vs. 9.3 mL for UN, and 69.7 mg/dL vs. 0.98 mg/dL for Cr; $p < 0.001$). The ratio of UN levels in peritoneal fluid and blood was 17.9 ± 5.1 (ranged from 10 to 29), and the ratio of

Table 1
Clinical characteristics of 23 patients with urinary tract leakage.

Clinical characteristics	$n = 23$
Age (y)	60.2 ± 14 (38–78)
Female/male	10/13
Procedure	
Low anterior resection	7
Anterior resection	6
Abdominoperineal resection	3
Right hemicolectomy	1
Laparoscopic anterior resection	3
Laparoscopic low anterior resection	2
Laparoscopic abdominoperineal resection	1
Site of urinary tract injury	
Left M/3 ureter	12
Left L/3 ureter	7
Bladder dome	2
Urethra	1
Right M/3 ureter	1
Cause of urinary tract leakage	
Laceration	8
Ligation	6
Thermal injury (including electrocautery and vessel-sealing device)	5
Ureteroureterostomy leakage	2
Leakage of bladder repair	2

Quantitative data are expressed as mean ± standard deviation (range of the value).
L/3 = lower third; M/3 = middle third.

Table 2
UN and Cr levels of 23 patients with urinary tract leakage.

	Peritoneal fluid	Blood	Urine	p^a
UN (mg/dL)	322.1 ± 56 (200–403)	18.7 ± 4.0 (12–25)	392.6 ± 55 (290–500)	<0.001
Cr (mg/dL)	69.7 ± 14.3 (41–91)	1.5 ± 0.5 (0.77–2.67)	127.3 ± 24 (97–177)	<0.001

Quantitative data were expressed as mean ± standard deviation (range of the value).
ANOVA = analysis of variance; Cr = creatinine; UN = urea nitrogen.
[a] ANOVA was used.

Cr levels in peritoneal fluid and blood was 49.4 ± 17 (ranged from 29.7 to 89.8). Both were significantly higher in the iatrogenic UTL group than in the control group (Table 3).

4. Discussion

Increased postoperative peritoneal fluid is a common condition in patients with prolonged or complicated colorectal surgery. UN and Cr levels in peritoneal fluid can be collected from excessive postoperative peritoneal fluid to determine intraperitoneal urinary leakage. The concept that intraperitoneal urine can be detected by UN and Cr disproportion in peritoneal fluid was proposed in 1972[6] and has been applied for clinical practices for decades. The reference values of UN and Cr levels in postoperative peritoneal fluid should be equivalent to those in blood.[1] Increased drainage after abdominal surgery can be differentiated from peritoneal fluid by testing the drain contents for UN and Cr levels and comparing them with their blood levels. If fluid UN and Cr levels are equal to blood UN and Cr levels, the drainage is not urine.

This is the first study reporting the measurement of peritoneal fluid UN and Cr levels to detect iatrogenic UTL after colorectal surgery. We clearly demonstrated that levels of UN and Cr in peritoneal fluid were significantly greater than those in blood (10–29 times for UN, 29.7–89.8 times for Cr) in patients with UTL. Additionally, when compared with the control group, the levels of UN and Cr in peritoneal fluid were also significantly higher (322 mL vs. 9.3 mL for UN, 69.7 mg/dL vs. 0.98 mg/dL for Cr). Therefore, we propose that the measurement of UN and Cr levels in peritoneal fluid might be a valid initial test to determine intraperitoneal UTL. If peritoneal fluid levels are equal to blood levels, then one might follow the patients conservatively. Conversely, if peritoneal fluid levels are higher than blood levels, one might proceed with more extensive radiologic evaluation to detect possible urinary leakage.

In our study, the Cr ratio of peritoneal/blood was much higher than the corresponding UN ratio (49.4 vs. 17.9, Table 3). Actually, blood Cr is an important indicator of renal health because it is an easily measured byproduct of muscle metabolism that is excreted unchanged by the kidneys. Blood Cr can be measured by a simple test and is the most commonly used indicator of renal function.[11] Conversely, the range of UN in blood, urine, and peritoneal fluid is wide because of normal variations due to protein intake, endogenous protein catabolism, state of hydration, hepatic urea synthesis, and renal urea excretion.[12] Therefore, the Cr ratio of peritoneal fluid/blood is more sensitive to detect urinary tract injury. Besides, peritoneal fluid could be mixed with some postoperative exudates or fluid. Therefore, this could partially explain why, in the control group, the UN level in peritoneal fluid (9.3 ± 3.3 mg/dL) was much lower than that in blood (15.4 ± 3.5 mg/dL, Table 3). In Table 3, we can see the blood UN and Cr levels in the UTL group (18.7 mg/dL and 1.5 mg/dL, respectively) are slightly higher than those in the control group (15.4 mg/dL and

Table 3
Comparisons between patients with urinary tract leakage (n = 23) and control group (n = 20).

	Urinary tract leakage (n = 23)	Control group (n = 20)	p^a
Peritoneal fluid			
Fluid amount (mL/d)	1187 ± 616 (590–2900)	773 ± 178 (500–1100)	0.005
UN (mg/dL)	322 ± 56 (200–403)	9.3 ± 3.3 (4–16)	<0.001
Cr (mg/dL)	69.7 ± 14.3 (41–91)	0.98 ± 0.28 (0.48–1.64)	<0.001
Blood			
UN (mg/dL)	18.7 ± 4.0 (12–25)	15.4 ± 3.5 (10–22)	0.006
Cr (mg/dL)	1.5 ± 0.5 (0.77–2.67)	0.89 ± 0.33 (0.45–1.67)	<0.001
Urine			
UN (mg/dL)	392 ± 55 (290-500)	410 ± 89 (250–589)	0.44
Cr (mg/dL)	127 ± 24 (97-177)	138 ± 31 (98–200)	0.182
UN ratio			
Peritoneal/blood	17.9 ± 5.1 (10-29)	0.6 ± 0.1 (0.35–1.0)	<0.001
Cr ratio			
Peritoneal/blood	49.4 ± 17 (29.7-89.8)	1.1 ± 0.2 (0.54–1.69)	<0.001

Quantitative data were expressed as mean ± standard deviation (range of the value).
Cr = creatinine; UN = urea nitrogen.
[a] Two independent sample t test.

0.89 mg/dL), with a significant difference. We postulated that patients in the UTL group had more complicated situations, such as advanced cancer with adjacent urinary tract organ adhesion. As a result, during the operation, we had to manipulate the ureter, bladder, or even kidney, and we needed more time to complete the operation, which might have compromised partial renal function with slightly elevated blood UN and Cr levels.

In a retrospective review of >2.1 million colorectal procedures identified from a US nationwide database, the risk of ureteral injury was estimated to be 0.28%.[4] In our study, 23 patients had iatrogenic UTL among a total of 4493 patients reviewed during 2000−2013, including ureter, bladder, and urethral injury, and the overall incidence rate was 0.5%. Injury to the ureter usually occurs during high ligation of the inferior mesenteric artery; mobilization of the upper mesorectum near the sacral promontory; dissection deep in the pelvis in the plane between the lower rectum, pelvic sidewall, and bladder base; and dissection of the most cephalad portion of the perineal dissection in an abdominoperineal resection.[13] In this study, most injuries occurred over the left ureter (82.6%), especially over the left middle third (during the high ligation of inferior mesenteric artery) and the lower third (over pelvic sidewall and deep pelvic dissection). One patient had right ureteral injury caused by electrocautery during right hemicolectomy.

In 2012, Palaniappa et al[14] reported a significant increase in the incidence of iatrogenic ureteral injuries during laparoscopy compared with that during open colectomies. In our study, the incidence was also higher in laparoscopy (1.4%, 6/401) than in the open group (0.4%, 17/4092; $p = 0.01$). Two patients had total transection of the ureter by laparoscopic vessel-sealing device (LigaSure, 5 mm Blunt Tip 44 cm; Covidien Inc.). One had total transection of the left middle ureter during the high ligation of inferior mesenteric artery during laparoscopic anterior resection, and the other had bilateral ureteral transection during perineal dissection in laparoscopic abdominoperineal resection.

Bladder injury usually occurs when dissecting densely adherent rectosigmoid tumors or diverticular disease from the bladder wall.[2] Two patients in our study had bladder injury due to leakage from the repair. One of them had sigmoid cancer with invasion to the bladder dome, and the other was a case of sigmoid diverticulitis with colovesicle fistula formation. One patient with bulky lower rectal cancer undergoing neoadjuvant concurrent chemoradiation therapy had urethra injury during perineal dissection during an abdominoperineal resection. The failure rate of ureteroureterostomy was around 10% in most studies.[5] Two patients in our study had leakage following ureteroureterostomy, probably due to devascularization of the ureteral vessels.

There are some limitations of this study. First, this was a retrospective chart review study with limited case number ($n = 23$), and parts of the data were missing. Hence, the reliability and validity of this diagnostic tool could not be completely assessed. Second, some minor urinary tract injuries without obvious leakage and increased peritoneal drainage were not included in our study. There might be a selection bias.

In conclusion, when increased peritoneal fluid is found postoperatively in colorectal surgery, initial measurement of UN and Cr levels in peritoneal fluid could be a useful diagnostic tool to determine possible intraperitoneal iatrogenic UTL. Of course, this finding deserves further randomized controlled trials and their validation in large-scale studies.

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