Risk factors and outcomes of bile leak after laparoscopic surgery for congenital biliary dilatation

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Author contribution:

YT and HU contributed to the conception and design of this study. YT, TT, AK, CS, WS, KY, KO, SM, HA, AT, and YK performed data acquisition. YT and TT performed statistical analysis and interpretation, and YT drafted the manuscript. HU critically reviewed the manuscript and supervised the entire study process. All authors read and approved the final manuscript.

Abstract

Purpose: One of the main causes of stricture at hepaticojejunostomy site after surgery for congenital biliary dilatation is inflammation or infection associated with bile leak. The aim of this study was to determine the risk factors and outcomes of bile leak after laparoscopic surgery.

Methods: We retrospectively reviewed the demographics and outcomes of patients who underwent laparoscopic surgery for congenital biliary dilatation between September 2013 and December 2019. Data from patients with bile leak were compared to data from patients without bile leak.

Results: Fourteen of 78 patients had bile leak. Hepatic duct diameter at anastomosis was the only risk factor of bile leak. Patients with the diameter ≤10 mm had higher incidence of bile leak than in patients with the diameter >10 mm (P = 0.0023). Among them, bile leak occurred more frequently in patients operated on by non-qualified surgeons based on the Japan Society for Endoscopic Surgery endoscopic surgical skill qualification system than by qualified surgeons (P = 0.027). However, none of the patients with bile leak developed anastomotic stricture afterwards.

Conclusion: Although good technical skill is necessary to avoid bile leak in narrow hepatic duct cases (≤10 mm), slight bile leak may not result in anastomotic stricture.

Keywords: laparoscopic surgery, congenital biliary dilatation, early complication, bile leak

Introduction

Stricture of hepaticojejunostomy is one of the complications of laparoscopic surgery for congenital biliary dilatation that should be prevented. Its main causes, as reported in studies, include small anastomosis, excessive tension, insufficient blood supply, and inflammation or infection associated with bile leak [1-4].

In our surgical approach, the common hepatic duct is cut 0.5 cm below the confluence point of the right and left hepatic ducts, paying attention not to impair blood supply to the remainder of the hepatic duct. Besides, in patients with narrow hepatic ducts, the lateral wall of the hepatic duct is cut to perform a wide hilar hepaticojejunostomy [5-8]. Hepaticojejunostomy is performed with 5–0 absorbable monofilament sutures in a single-layer interrupted manner also paying attention not to impair blood supply to the hepatic duct at the anastomotic site. However, bile leak occurs sometimes.

To the best of our knowledge, no earlier study has investigated bile leak after laparoscopic surgery for congenital biliary dilatation, in detail. The aim of this study was to determine the risk factors and outcomes of bile leak at the hepaticojejunostomy site after laparoscopic surgery.

Patients and Methods

This study was approved by the ethics committee of our hospital (#2019-0467) and conforms to the provisions of the Declaration of Helsinki. We retrospectively reviewed the demographics and

outcomes of patients who underwent laparoscopic surgery for congenital biliary dilatation with Roux-en-Y hepaticojejunostomy between September 2013 and December 2019. All the surgical operations were performed or supervised by one qualified surgeon without open conversion. The data of patients with postoperative bile leak were compared to those of patients without postoperative bile leak.

In this study, bile leak was defined as obvious bilious discharge from the drainage tube at the hepaticojejunostomy site, or as discharge from the drainage tube of total bilirubin level more than 3 times the serum total bilirubin level on postoperative day (POD) 3 as defined by the International Study Group of Liver Surgery (ISGLS) [9].

Laparoscopic surgery for congenital biliary dilatation was performed as described in our previous report [10]. The common hepatic duct was usually cut 0.5 cm below the confluence point of the right and left hepatic ducts and 0.5 cm above the point of connection to the pancreatic duct. In cases of stenosis or narrow hepatic duct, the lateral wall of the hepatic duct was incised to make a wide hilar anastomosis (Lilly's technique) [1,11,12]. In cases of stenosis in the hepatic or intrahepatic ducts, the membrane or septum that caused the stenosis was meticulously probed and resected [10]. The proximal jejunum was then exteriorized through the umbilical incision to form a 25 cm Roux loop. The Roux limb further introduced to the hilum via the retrocolic route, and Roux-en-Y hepaticojejunostomy in an end-to-side manner was performed with 5–0 absorbable interrupted monofilament sutures in a

single-layer. Anastomotic stricture and dilatation of intrahepatic bile ducts were regularly assessed using ultrasonography and magnetic resonance cholangiopancreatography in the outpatient office.

In Japan, an endoscopic surgical skill qualification system is provided by the Japan Society for Endoscopic Surgery (JSES). To become a qualified pediatric surgeon, extensive experience of advanced endoscopic surgery in small children is needed. In this study, the outcomes of qualified surgeons, as indicated by the JSES endoscopic surgical skill qualification system, were compared to the outcomes of non-qualified surgeons to assess differences that may be attributed to operator skill level.

Fisher's exact test and Mann-Whitney U test were used to compare clinical data. *P*-values <0.05 were considered statistically significant.

Results

In total, 78 patients underwent laparoscopic repair of congenital biliary dilatation during the study period. The median age at operation was 3.12 years, and the median operative time was 389 minutes. There was no conversion to open surgery. Fourteen patients had bile leak, and one of them needed reoperation, while the rest were treated conservatively.

We compared the demographic data and outcomes of patients with bile leak to those of patients without bile leak after laparoscopic surgery for congenital biliary dilatation (Table 1). There were no differences in the age at operation, sex, body weight at operation, type of disease, operative time,

intraoperative blood loss volume, incision of the side wall of the hepatic duct for wide hilar anastomosis, and resection of membrane or septum in hepatic or intrahepatic duct to remove stenosis. In contrast, demographic data showed that hepatic duct diameter at anastomosis was significantly shorter in patients with bile leak than in patients without bile leak (P = 0.0032). The distribution of bile leak cases by hepatic duct diameter at anastomosis is shown in Fig.1. Considering physical differences, we compared the value obtained by dividing the diameter of the hepatic duct at anastomosis by the average diameter of the hepatic duct of healthy subjects of the same age. The average diameter of the hepatic duct by ages has been investigated in a multicentered study in Japan [13]. This value was also smaller in patients with bile leak than in patients without bile leak (P = 0.018). The duration of hospital stay after surgery was also significantly longer in patients with bile leak than in patients without bile leak (P = 0.016). The median period of drainage tube placement in patients with bile leak was 9.5 days. The median amount of maximal discharge per day was 93.5 ml and the median of peak discharge was on the second day after surgery.

It has been reported that in order to prevent stricture of hepaticojejunostomy, the diameter of the hepatic duct in non-neonates should be at least 1 cm [1-4]. Further, we compared the rate of bile leak between patients with hepatic duct diameter at anastomosis ≤10 mm and patients with hepatic duct diameter at anastomosis >10 mm (Table 2). Bile leak occurred more frequently in patients with hepatic duct diameter at anastomosis ≤10 mm than in patients with hepatic duct diameter at anastomosis >10 mm (P = 0.0023). To assess the influence of operator skill level, we compared outcomes between qualified

and non-qualified surgeons according to the JSES endoscopic surgical skill qualification system. Although there was no difference in the total bile leak rate between the two groups (Table 1), for patients with hepatic duct diameter at anastomosis ≤10 mm, the rate of bile leak was lower in patients operated on by qualified surgeons than in patients operated on by non-qualified surgeons (P = 0.027) (Table 2). This highlights the technical difficulty of operating on patients with narrow hepatic ducts. On the other hand, incision of the side wall of the hepatic duct did not increase or decrease the rate of bile leak even in cases with hepatic duct diameter at anastomosis ≤10 mm (Table 2). To further study the influence of the diameter of the hepatic duct at anastomosis, we analyzed bile leak using the value obtained by dividing the diameter of the hepatic duct at anastomosis by the average diameter of the hepatic duct of healthy subjects of the same age (Table 3). As a reference, the median value of the fusiform type in our series was 3.9. Patients with values ≥5 had significantly less bile leak than patients with values <5 (P = 0.043). This implies that a narrow hepatic duct at anastomosis corrected by patient body size is also a risk factor of bile leak. Although the number of patients is small, in patients operated on by qualified surgeons, bile leak occurred only in patients with values <4.

Finally, we investigated the systemic influence of bile leak by comparing serum C-reactive protein (CRP) levels. Patients with other complications (e.g., wound infection, pancreatic fistula, and ileus) were excluded from this comparison (Table 4). There was no difference between the serum CRP levels of patients with bile leak and of patients without bile leak on POD 1 or POD 3. Similarly, there was

no difference in the rate of change of serum CRP level from POD 1 to POD 3 between the two groups. None of the patients with bile leak developed anastomotic stricture from then until now. Further, neither of the two patients (2.6%) in our series, with stricture of hepaticojejunostomy, had bile leak after surgery.

Discussion

Our results showed that hepatic duct diameter at the anastomotic site is the only risk factor of bile leak at the hepaticojejunostomy site. Although patients with bile leak needed longer durations of hospital stay after surgery, none of them developed anastomotic stricture. Since the serum CRP levels of patients with bile leak did not increase compared to those of patients without complications, bile leak in our series may not cause inflammation or infection that can lead to anastomotic stricture. Nevertheless, bile-tight anastomosis is desirable as long as blood supply to the anastomotic site is not impaired.

The bile leak rate in our study was 17.9%, and this is higher than the 1.6–6.5% reported in previous studies on laparoscopic surgery [1,4,14]. This may have been due to the meticulous stenosis release performed on the bile ducts and even on the intrahepatic bile ducts that often led to further resection of the common hepatic ducts leaving narrow ducts for anastomosis [10,15-17]. In our series, the percentage of patients with hepatic duct diameter at anastomosis ≤10 mm was as high as 47% (37/78). Another explanation for this may be the difference in the criteria of bile leak because previous studies did not clearly show their criteria of bile leak. Discharge defined as bile leak according to the ISGLS criteria

sometimes looked light yellow and did not appear to be bile leak.

The main causes of bile leak in patients with narrow hepatic ducts include technical difficulty and high inner pressure of the bile duct at anastomosis. Although there has been no report that measured the inner pressure of bile duct at anastomosis after hepaticojejunostomy, the common bile duct pressure is known to decrease after endoscopic papillotomy along with the decrease of Oddi sphincter pressure [18]. This implies that the inner pressure of the bile duct at anastomosis would be higher in patients with narrow hepaticojejunostomy, especially at an early time after surgery with edematous tissues, when the liver size is constant. In fact, the incidence of bile leak was less in patients with high ratios of hepatic duct diameter at anastomosis to average hepatic duct diameter of healthy subjects of the same age (≥5) in our series (Table 3). Our results also show that the rate of bile leak in patients with hepatic duct diameter at anastomosis ≤10 mm and who were operated on by qualified surgeons according to the JSES endoscopic surgical skill qualification system, was less than that in the patients who were operated on by non-qualified surgeons. This suggests that technical skill should be considered in the laparoscopic treatment of patients with narrow hepatic ducts. However, Table 3 shows that in patients with a low ratio (<4) of hepatic duct diameter at anastomosis to average hepatic duct diameter of healthy subjects of the same age, there is some risk of bile leak even in patients operated on by qualified surgeons. Our study is limited by the small number of patients under study, and more data is needed to accurately assess the risk factor and the impact on outcomes of bile leak. Some studies have described new and sound anastomotic

techniques for the treatment of patients with narrow hepatic ducts [19,20]. These techniques may reduce the rate of bile leak in future patients.

Conclusion

The incidence of bile leak from the hepaticojejunostomy site in patients with hepatic duct diameter at anastomosis ≤10 mm was significantly high. The patients with the value ≥5, obtained by dividing the diameter of the hepatic duct at anastomosis by the average diameter of the hepatic duct of healthy subjects of the same age, had significantly less bile leak than patients with the value <5. This implies that a narrow hepatic duct at anastomosis corrected by patient body size is also a risk factor of bile leak. However, in our series, bile leak did not cause anastomotic stricture. Nevertheless, bile-tight anastomosis is desirable as long as blood supply to the anastomotic site is not impaired and the stenotic sites in the hepatic duct are maximally released. Good technical skill is necessary in the treatment of patients with narrow hepatic ducts, and novel techniques may be beneficial.

Compliance with ethical standards

Disclosure of potential conflicts of interest

The authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in this study.

References

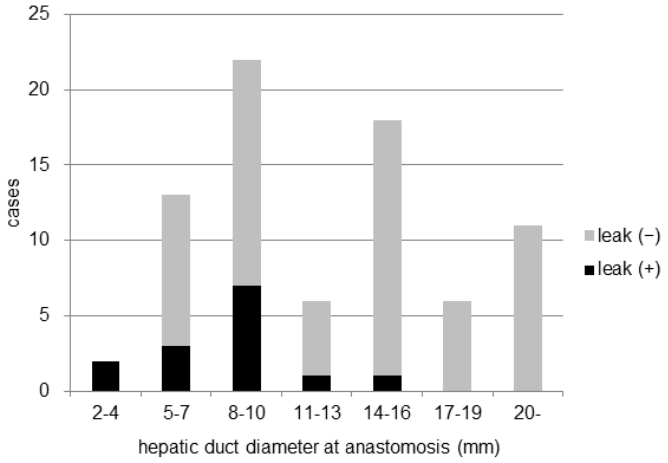
1. Tang ST, Yang Y, Wang Y, Mao YZ, Li SW, Tong QS, Cao GQ, Zhao ZX (2011) Laparoscopic choledochal cyst excision, hepaticojejunostomy, and extracorporeal Roux-en-Y anastomosis: a technical skill and intermediate-term report in 62 cases. Surg Endosc 25:416-422. doi:10.1007/s00464-010-1183-y
2. Diao M, Li L, Cheng W (2013) Role of laparoscopy in treatment of choledochal cysts in children. Pediatr Surg Int 29:317-326. doi:10.1007/s00383-013-3266-z
3. Diao M, Li L, Cheng W (2016) Laparoscopic redo hepaticojejunostomy for children with choledochal cysts. Surg Endosc 30:5513-5519. doi:10.1007/s00464-016-4915-9
4. Zhang B, Wu D, Fang Y, Bai J, Huang W, Liu M, Chen J, Li L (2019) Early complications after laparoscopic resection of choledochal cyst. Pediatr Surg Int 35:845-852. doi:10.1007/s00383-019-04489-y
5. Todani T, Watanabe Y, Urushihara N, Noda T, Morotomi Y (1995) Biliary complications after excisional procedure for choledochal cyst. J Pediatr Surg 30:478-481
6. Stringer MD (2007) Wide hilar hepaticojejunostomy: the optimum method of reconstruction after choledochal cyst excision. Pediatr Surg Int 23:529-532. doi:10.1007/s00383-007-1929-3
7. Urushihara N, Fukuzawa H, Fukumoto K, Sugiyama A, Nagae H, Watanabe K, Mitsunaga M, Miyake H (2011) Totally laparoscopic management of choledochal cyst: Roux-en-Y Jejunojejunostomy and wide hepaticojejunostomy with hilar ductoplasty. J Laparoendosc Adv Surg Tech A 21:361-366. doi:10.1089/lap.2010.0373
8. Urushihara N, Fukumoto K, Fukuzawa H, Mitsunaga M, Watanabe K, Aoba T, Yamoto M, Miyake H (2012) Long-term outcomes after excision of choledochal cysts in a single institution: operative procedures and late complications. J Pediatr Surg 47:2169-2174. doi:10.1016/j.jpedsurg.2012.09.001
9. Koch M, Garden OJ, Padbury R, Rahbari NN, Adam R, Capussotti L, Fan ST, Yokoyama Y, Crawford M, Makuuchi M, Christophi C, Banting S, Brooke-Smith M, Usatoff V, Nagino M, Maddern G, Hugh TJ, Vauthey JN, Greig P, Rees M, Nimura Y, Figueras J, DeMatteo RP, Buchler MW, Weitz J (2011) Bile leakage after hepatobiliary and pancreatic surgery: a definition and grading of severity by the International Study Group of Liver Surgery. Surgery 149:680-688. doi:10.1016/j.surg.2010.12.002
10. Tanaka Y, Tainaka T, Sumida W, Hinoki A, Shirota C, Murase N, Oshima K, Shirotsuki R, Chiba K, Uchida H (2018) Introduction of resection of intrahepatic bile duct stenosis-causing membrane or septum into laparoscopic choledochal cyst excision. Pediatr Surg Int 34:1087-1092. doi:10.1007/s00383-018-4320-7
11. Lilly JR (1978) Total excision of choledochal cyst. Surg Gynecol Obstet 146:254-256

12. Li S, Wang W, Yu Z, Xu W (2014) Laparoscopically assisted extrahepatic bile duct excision with ductoplasty and a widened hepaticojejunostomy for complicated hepatobiliary dilatation. Pediatr Surg Int 30:593-598. doi:10.1007/s00383-014-3501-2
13. Hamada Y, Ando H, Kamisawa T, Itoi T, Urushihara N, Koshinaga T, Saito T, Fujii H, Morotomi Y (2016) Diagnostic criteria for congenital biliary dilatation 2015. J Hepatobiliary Pancreat Sci 23:342-346. doi:10.1002/jhbp.346
14. Li L, Feng W, Jing-Bo F, Qi-Zhi Y, Gang L, Liu-Ming H, Yu L, Jun J, Ping W (2004) Laparoscopic-assisted total cyst excision of choledochal cyst and Roux-en-Y hepatoenterostomy. J Pediatr Surg 39:1663-1666
15. Ando H, Ito T, Kaneko K, Seo T, Ito F (1996) Intrahepatic bile duct stenosis causing intrahepatic calculi formation following excision of a choledochal cyst. J Am Coll Surg 183:56-60
16. Ando H, Kaneko K, Ito F, Seo T, Ito T (1997) Operative treatment of congenital stenoses of the intrahepatic bile ducts in patients with choledochal cysts. Am J Surg 173:491-494
17. Tanaka Y, Tainaka T, Sumida W, Shirota C, Hinoki A, Murase N, Oshima K, Shirotsuki R, Chiba K, Uchida H (2017) The efficacy of resection of intrahepatic bile duct stenosis-causing membrane or septum for preventing hepatolithiasis after choledochal cyst excision. J Pediatr Surg 52:1930-1933. doi:10.1016/j.jpedsurg.2017.08.056
18. Funch-Jensen P, Csendes A, Kruse A, Oster MJ, Amdrup E (1979) Common bile duct and Oddi sphincter pressure before and after endoscopic papillotomy in patients with common bile duct stones. Ann Surg 190:176-178. doi:10.1097/00000658-197908000-00009
19. Urushihara N, Fukumoto K, Nouso H, Yamoto M, Miyake H, Kaneshiro M, Koyama M, Nakajima H (2015) Hepatic ductoplasty and hepaticojejunostomy to treat narrow common hepatic duct during laparoscopic surgery for choledochal cyst. Pediatr Surg Int 31:983-986. doi:10.1007/s00383-015-3779-8
20. Chang X, Zhang X, Xiong M, Yang L, Li S, Cao G, Zhou Y, Yang D, Tang ST (2019) Laparoscopic-assisted cyst excision and ductoplasty plus widened portoenterostomy for choledochal cysts with a narrow portal bile duct. Surg Endosc 33:1998-2007. doi:10.1007/s00464-018-06635-4

Figure legends

Fig. 1 Histogram of patients with and without bile leak by the hepatic duct diameter at anastomosis.

Fig. 1


25
20
15
10
5
0
cases
2-4
5-7
8-10
11-13
14-16
17-19
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hepatic duct diameter at anastomosis (mm)
leak (−)
leak (+)

Table 1. Demographic data and outcomes of patients with bile leak and of patients without bile leak after laparoscopic surgery for congenital biliary dilatation

	Bile leak (+) (n = 14)	Bile leak (-) (n = 64)	*P*-value
Age at operation (years)	Median, 3.24 (range, 0.07–41.8)	Median, 3.12 (range, 0.08–55.6)	0.81
Sex (male/female)	2/12	14/50	0.72
Body weight at operation (kg)	Median, 12.5 (range, 3.88–58.4)	Median, 12.8 (range, 3.10–63.3)	0.79
Cystic type/fusiform type	7/7	48/16	0.10
Surgery performed by qualified pediatric surgeons based on the JSES endoscopic surgical skill qualification system (%)	14.3 (2/14)	34.4 (22/64)	0.20
Incision of the side wall of the hepatic duct for wide hilar anastomosis (%)	71.4 (10/14)	73.4 (47/64)	1
Resection of membrane or septum in hepatic or intrahepatic duct (%)	57.1 (8/14)	57.8 (37/64)	1
Diameter of hepatic duct at anastomosis (mm)	Median, 9 (range, 4–15)	Median, 14 (range, 5–25)	0.0032
Diameter of hepatic duct at anastomosis/ average diameter of the hepatic duct in healthy subjects of the same age	Median, 3.84 (range, 1.74–7.89)	Median, 6.0 (range, 1.43–16.7)	0.018
Operative time (minutes)	Median, 403 (range, 319–585)	Median, 389 (range, 234–852)	0.60
Intraoperative blood loss volume (mL)	Median, 44.5 (range, 5–153)	Median, 33 (range, 1–1216)	0.43
Duration of hospital stay after surgery (days)	Median, 13 (range, 7–20)	Median, 9.5 (range, 7–28)	0.016

JSES, Japan Society for Endoscopic Surgery

The *P*-value was calculated using Mann-Whitney U test and Fisher's exact test.

Table 2. Comparison of the rates of bile leak after laparoscopic surgery for congenital biliary dilatation between patients with hepatic duct diameter at anastomosis ≤10 mm and patients with hepatic duct diameter at anastomosis >10 mm

	Patients with hepatic duct diameter at anastomosis ≤10 mm (n = 37)	Patients with hepatic duct diameter at anastomosis >10 mm (n = 41)	*P*-value
Bile leak incidences(%)	32.4 (12/37)	4.9 (2/41)	0.0023
Surgery performed by qualified pediatric surgeons based on the JSES endoscopic surgical skill qualification system (%)	35.1 (13/37)	26.8 (11/41)	0.47
Bile leak rate after surgeries performed by qualified vs non-qualified pediatric surgeons based on the JSES endoscopic surgical skill qualification system (%)	7.7 (1/13) vs 45.8 (11/24) (*P* = 0.027)	9.1 (1/11) vs 3.3 (1/30) (*P* = 0.47)	
Incision of the side wall of the hepatic duct (%)	78.4 (29/37)	68.3 (28/41)	0.44
Bile leak rate after surgeries with vs without incision of the side wall of the hepatic duct (%)	31.0 (9/29) vs 37.5 (3/8) (*P* = 0.73)	3.6 (1/28) vs 7.7 (1/13) (*P* = 0.57)	

JSES, Japan Society for Endoscopic Surgery

The *P*-value was calculated using Fisher's exact test.

Table 3. Rate of bile leak after laparoscopic surgery for congenital biliary dilatation according to the value of diameter of hepatic duct at anastomosis/average diameter of the hepatic duct in healthy subjects of the same age

	Rate of bile leak	*P*-value	Rate of bile leak in patients operated on by qualified pediatric surgeons based on the JSES endoscopic surgical skill qualification system
Diameter of hepatic duct at anastomosis/average diameter of the hepatic duct in healthy subjects of the same age			
≥5	4/42	0.043	0/9
<5	10/36		2/15
≥4	7/55	0.10	0/15
<4	7/23		2/9

JSES, Japan Society for Endoscopic Surgery

The *P*-value was calculated using Fisher's exact test.

Table 4. Comparison of serum CRP levels between patients with bile leak and patients without bile leak after laparoscopic surgery for congenital biliary dilatation

	Bile leak (+) (n = 14)	Bile leak (-) (n = 51)	*P*-value
Serum CRP level on POD 1 (mg/dL)	Median, 4.65 (range, 1.74–13.7)	Median, 3.99 (range, 1.34–12.1)	0.12
Serum CRP level on POD 3 (mg/dL)	Median, 2.02 (range, 0.51–18.0)	Median, 1.67 (range, 0.12–7.98)	0.37
Serum CRP level at POD 3/POD 1	Median, 2.13 (range, 0.23–8.77)	Median, 2.08 (range, 0.55–17.4)	0.76

Patients with other complications (e.g., wound infection, pancreatic fistula, or ileus) are excluded from the analysis presented in this table.

CRP, C-reactive protein; POD, postoperative day

The *P*-value was calculated using Mann-Whitney U test.