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Biliary reconstruction using non-penetrating, tissue everting clips versus conventional sewn biliary anastomosis in liver transplantation

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Abstract

Background. Biliary complications occur following approximately 25% of liver transplantations. Efforts to decrease biliary complications include methods designed to diminish tissue ischemia. Previously, we reported excellent short-term results and decreased biliary anastomosis time in a porcine liver transplant model using non-penetrating, tissue everting clips (NTEC), specifically VCS® clips. *Methods.* We examined the incidence of biliary anastomotic complications in a group of patients in whom orthotopic liver transplantation was performed with biliary reconstruction using NTEC and compared that group to a matched group treated with biliary reconstruction via conventional end-to-end sewn choledochocholedochostomy. Patients were matched in a 1:2 fashion by age at transplantation, disease etiology, Child-Turcot-Pugh scores, MELD score or UNOS status (prior to 1998), cold and warm ischemia times, organ donor age, and date of transplantation. *Results.* Seventeen patients had clipped anastomosis and 34 comparison patients had conventional sewn anastomosis. There were no differences between groups in terms of baseline clinical or demographic data. The median time from completion of the hepatic artery anastomosis to completion of clipped versus conventional sewn biliary anastomosis was 45 (interquartile range = 20 min) versus 47 min (interquartile range = 23 min), respectively ($p = 0.12$). Patients were followed for a mean of 29 months. Biliary anastomotic complications, including leak or anastomotic stricture, were observed in 18% of the clipped group and 24% of the conventional sewn group. *Conclusions.* Biliary reconstruction can be performed clinically using NTEC as an alternative to conventional sewn biliary anastomoses with good results.

Introduction

Liver transplantation remains a complex procedure with potential for significant patient morbidity, not only in the perioperative period, but also over the life of the graft. Biliary complications occur in 10–30% of recipients after liver transplantation [1–4]. Prevention of biliary complications has focused on efforts to diminish tissue ischemia. Techniques such as the cholecystocholedochostomy, side-to-side choledochocholedochostomy popularized by Neuhaus [5], and end-to-end choledochocholedochostomy with shortened ducts have been used to ameliorate the risk of biliary ischemia and resultant complications such as leak or stricture.

In order to decrease tissue ischemia and reaction, we and others have examined the use of non-crushing clips or staples to approximate tissue. Geevarghese *et al.* [6] of our group described the use of one such device in a porcine model. This device approximates everted tissue edges without penetrating the mucosa. Using a porcine orthotopic liver transplant model, the authors showed less ischemic injury and shorter times for anastomosis when the clipping device was compared with standard sewn biliary anastomoses. In the 4 years since publication of this report, we have used the Autosuture VCS® device in selected patients undergoing orthotopic liver transplantation at Vanderbilt University Medical Center. This paper describes the demographic, operative and postoperative data for that group of patients and compares that group to a matched cohort of patients who received conventional end-to-end sewn choledochocholedochostomy.

Methods

Patients

Prior to implementing this case control study, approval was granted by our Institutional Review Board. We performed the biliary anastomoses in 17 patients undergoing orthotopic liver transplantation using the Autosuture VCS® clip device. Patients were selected if the donor and recipient bile ducts were similar in size and the operation was otherwise routine. These patients comprise the study group.

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A comparison patient cohort was matched in a 2: 1 fashion to the clipped group of patients using the following criteria: gender, age at transplantation, date of transplant, disease etiology, Child classification, MELD score, UNOS status, cold and warm ischemia times, and organ donor age. Any transplant recipient was excluded from consideration in whom other types of biliary anastomoses, such as choledochojejenostomy or hepaticojejenostomy, were created.

Surgical technique

For patients undergoing clipped anastomosis, stay sutures were place at 3, 6, 9, and 12 o'clock positions. Arcuate-legged clips were then applied in the four quadrants of the anastomosis. For patients undergoing sutured anastomosis, two 5–0 polydioxanone stay sutures were placed and then interrupted single sutures circumferentially.

Data collection

A prepared data extraction sheet was used to identify patient gender, disease etiology, date of transplant, Child-Turcot-Pugh score [7], model of end-stage liver disease (MELD) score [8], United Network of Organ Sharing (UNOS) status (prior to implementation of MELD), preoperative liver function studies, international normalized ratio, serum creatinine, and donor age. Cold ischemia time, warm ischemia time, total operative time, and time from completion of hepatic artery anastomosis to biliary anastomosis were calculated from the standard operative note. This note routinely records the times involved with the organ procurement (cross clamp time, time organ taken off ice) as well as the times when events occur during the course of the transplantation. Use of venovenous bypass, type of biliary and arterial anastomosis, use and type of stenting for bile duct anastomoses, and transfusion requirements were all recorded. Duration of intensive care unit (ICU) stay as well as hospital stay was recorded. Clinical and laboratory markers were collected from postoperative day 3 and 7 as well as routine scheduled follow-up visits after hospital discharge at 1, 3, 6, and 12 months as well as the most recent follow-up visit.

Outcomes

The primary outcome was development of a documented biliary complication, either in the form of anastomotic leak or anastomotic stricture. This was recorded if there was definitive evidence from either radiographic studies or at the time of re-exploration. Instances of bile leak after removal of t-tubes were not further considered as these were all self-limited and unrelated to type of anastomoses. Instances of ischemic biliary lesions not associated with anastomotic strictures were also not included in this analysis. Arterial anastomotic problems were recorded, as these are known to predispose biliary complications.

Statistical analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS, Inc.). Summary data are presented as the median and percentages. Variability around the median is expressed as the interquartile range (75th percentile minus 25th percentile). Comparisons between treatment groups were performed using the Mann-Whitney U test and Pearson's chi square test of proportion, with the alpha level set at 0.05.

Results

During the period from July 1, 1996 to March 31, 2004, 420 liver transplants were performed at our institution. The Autosuture VCS® clip device was used in 17 patients and the hand-sewn cohort consisted of 34 matched patients transplanted from this time period. Demographic characteristics and preoperative laboratory values are presented in Table I. There were no statistically significant differences between the two groups on any of these baseline measures or etiology of end-stage liver disease.

Postoperative and outcome data are shown in Table II. There were no statistically significant differences between the two groups in cold ischemia time, warm ischemia time, or total duration of operation. The median time between completion of the hepatic artery anastomosis and completion of the biliary anastomosis was 45 min for the clipped group versus 47 min for the sewn group ($p = 0.12$). There were no differences between groups in transfusion of blood products, days spent in the ICU, or days spent in the hospital.

Table I. Demographic characteristics and preoperative liver function tests of liver transplant recipients by anastomosis type.

Parameter	Clipped ($n = 17$)	Sewn ($n = 34$)	p value
Age (years)	54 (14)	52 (8)	0.48
Male (%)	11 (65%)	22 (65%)	1.00
CTP	9 (3)	10 (3)	0.29
MELD	16 (10)	18 (7)	0.23
Donor age (years)	32.5 (23)	33.0 (25)	0.78
Albumin (g/dl)	2.8 (0.5)	2.6 (0.6)	0.15
Total bilirubin (mg/dl)	3.0 (3.2)	3.7 (3.2)	0.49
Serum Cr (mg/dl)	1.1 (0.6)	0.9 (0.6)	0.84
INR	1.4 (0.6)	1.5 (0.6)	0.22
SGOT (U/L)	78 (63)	69 (60)	0.37
SGPT (U/L)	58 (72)	45 (36)	0.24
Alkaline phosphatase (U/L)	166 (102)	143 (114)	0.09

Data are presented as median (and associated interquartile range) or as percentages. CTP, Child-Turcot-Pugh score; MELD, model of end-stage liver disease score; INR, international normalized ratio.

Table II. Operative variables by anastomosis type.

Variable	Clipped ($n=17$)	Sewn ($n=34$)	p value
Cold ischemia time (hour:min)	7:24 (4:55)	6:16 (4:39)	0.80
Warm ischemia time (min)	0:40 (0:12)	0:39 (0:10)	0.84
Operative time (hour:min)	6:20 (1:30)	6:00 (1:40)	0.61
HA to biliary anastomosis time (min)*	0:45 (0:20)	0:47 (0:23)	0.12
RBC transfusion (units)	7 (7)	8 (7)	0.58
FFP transfusion (units)	10 (13)	14 (15)	0.50
Cryoprecipitate transfusion (units)	0 (0)	0 (0)	0.36
Platelet transfusion (6 packs)	8 (10)	8 (6)	0.36
Hospital stay (days)	7 (7)	8 (16)	0.52
ICU stay (days)	2 (2)	3 (3)	0.21

Data are presented as median (and associated interquartile range). HA, hepatic artery; RBC, red blood cell; FFP, fresh frozen plasma; ICU, intensive care unit.
*Denotes time from completion of hepatic artery (HA) anastomosis to completion of biliary anastomosis.

Venovenous bypass was used in one patient with clipped anastomosis and in two patients with sewn anastomoses. Two patients in the clipped group had arterial conduits from the aorta to the donor vessel; the remainder of the anastomoses were created by direct end-to-end anastomosis of native and donor vessels. During the early part of this review, t-tubes were used routinely; none were used after September 2002 when we transitioned to use of internal biliary stents. T-tubes were used in 11 of 17 patients (65%) in the clipped group and in 25 of 34 (74%) in the hand-sewn cohort. Intraoperative cholangiograms (IOC) were performed in 4 of the 11 patients (36%) with t-tubes in the clipped group and 15 of 25 (60%) in the sewn group. In each instance when an IOC was obtained, findings were normal with no evidence of anastomotic stricture or leak. In the remainder of patients with t-tubes, saline infusion was routinely used to test the patency and integrity of the biliary anastomosis prior to completion of the operation. Internal stents using variable sized pediatric silastic feeding tubes were used in 5 of 17 patients (29%) in the clipped group compared with 9 of 34 (26%) in the sewn group.

There was no difference in median follow-up between groups (37 months for clipped group vs 30 months for the sewn group, $p=0.72$). Two patients in the clipped group died, one at 3.3 years and another at 5.6 years after transplantation. Six patients in the hand-sewn cohort died after a mean of 286 days. No long-term arterial problems were documented in patients from either group; short-term arterial concerns were identified in two patients in the sewn group, both in the early postoperative period. In one patient, Doppler examination revealed elevated resistance in the hepatic artery at separate examinations but overall flow was felt to be suitable and no intervention was necessary as liver function studies remained satisfactory. In the other patient, sluggish flow was noted on Doppler examination; the patient underwent arteriogram with intra-arterial papaverine infusion and subsequent Doppler studies revealed normal flow.

Anastomotic bile duct leaks were observed in two patients (12%) in the clipped group and five patients (15%) in the sewn group ($p=0.77$). Anastomotic strictures of the bile duct were observed in three patients (18%) in the clipped group and seven patients (21%) in the sewn group ($p=0.80$)

Table III. Details of procedures required for patients with leak or anastomotic stricture.

Patient	Anastomosis type	Date of first leak	Date of first stricture	Total ERCP	Total IR procedures	Duct revision required
1	Clipped	POD 3	POD 3	4	1	No
2	Clipped	N/A	Month 1	2	0	No
3	Clipped	Month 1	Month 3	6	1	Yes
1	Sewn	POD 7	Month 3	7	0	Yes
2	Sewn	Month 1	Month 3	1	0	No
3	Sewn	Month 1	Month 3	0	5 (after revision)	Yes
4	Sewn	Month 1	Month 1	2	0	No
5	Sewn	Month 1	N/A	1	0	No
6	Sewn	N/A	Month 6	0	1	Yes
7	Sewn	N/A	Month 6	0	0	No
8	Sewn	N/A	Month 6	3	0	No

ERCP, endoscopic retrograde cholangiopancreatography; IR, interventional radiology drain placement; POD, postoperative day; N/A, not applicable.

(see Table III). Overall, there was no difference in presence of either anastomotic leak or anastomotic strictures between the two groups, with $p = 0.63$. Non-operative intervention (either ERCP or percutaneous dilation by interventional radiologists) was successful in management of biliary complications in all but one patient in the clipped group and three patients in the hand-sewn cohort. These patients required operative revision of their biliary anastomosis with enteric anastomoses.

Discussion

Calne *et al.* described the biliary anastomosis as the "technical Achilles' heel" of liver transplantation [9]. The reported complication rates from biliary reconstruction after orthotopic liver transplantation range from 10% to as high as 50%, although most recent studies cite instances closer to 25% [1–4]. Complications may be divided into early or late. Early complications frequently present as leaks, although strictures of the anastomosis may rarely be present due to technical error. Late complications usually present as strictures resulting in cholangitis or biliary obstruction.

Biliary leaks and anastomotic strictures may cause significant morbidity for the patient and are often due to inadequate technical detail in creation of the anastomosis, prolonged cold ischemia time, or to ischemia of the distal aspects of donor and recipient ducts [10], especially with hepatic artery thrombosis. The vasa vasori are thought to be important for viable donor duct tissue; attempts at decreasing the incidence of biliary anastomotic complications have focused on attempts to decrease tissue ischemia at the distal ends of the donor duct. Some authors have advocated cholecystocholedochotomy or end-to-side choledochocholedochostomy in order to prevent excessive tissue dissection and theoretically diminish ductal ischemia and resultant biliary complications. However, Davidson *et al.* showed no difference in rates of biliary complications between end-to-end and side-to-side anastomoses in a well conducted randomized trial [11]. Hence, most transplant surgeons use the end-to-end anastomosis, given its relative ease and ability to use shorter duct length.

However, the end-to-end anastomosis is still subject to ischemia at the distal duct margins and this may represent the major cause of early bile leak and anastomotic stricture. To lessen tissue ischemia at sites already predisposed to poor blood flow, techniques of non-penetrating tissue approximation have been studied. There are extensive data on vascular anastomoses comparing intimal injury and anastomotic stricture in tissues approximated with non-penetrating clips [12–14]. The concept of tissue approximation without penetration was later applied to longitudinal incisions in pig ureter and common bile ducts [15].

We previously applied this technology to the vascular and biliary anastomosis in eight pigs undergoing orthotopic liver transplantation and reported less smooth muscle injury under histologic examination on postoperative day 1 in the group with biliary anastomosis created with non-penetrating, tissue everting clips. An additional benefit was shorter times for anastomosis compared with interrupted sutured anastomosis [6]. This finding was echoed by Birth *et al.* [16] in 18 pigs undergoing either choledochal excision or transection repaired with VCS® clips. Using a laser Doppler flow meter, they reported better perfusion at the anastomotic site in the clipped group. Additionally, there was less fibrosis and wall thickness of the anastomosis at histologic examination 6 months after transplantation.

To our knowledge, this is the first report describing the use of non-penetrating, tissue everting VCS® clips in patients undergoing liver transplantation. We applied this technique to a group of patients with end-stage liver disease undergoing liver transplantation. The 17 patients in the index group represent a diverse population of patients from the most commonly observed etiologies including viral hepatitis, alcohol-induced hepatitis, idiopathic causes, and autoimmune disease. This group was compared to a cohort of patients that were matched as closely as possible in a two to one ratio. As designed, there were no differences between groups using our pre-established criteria of gender, age at transplant, CTP or MELD scores, cold/warm ischemia times, and donor age. The operative variables were similar as well, with no difference observed in total duration of the transplant or the time from completion of the hepatic artery anastomosis to completion of the biliary anastomosis. Although the latter showed a trend for significance, it is only a surrogate marker of the true time required for biliary anastomosis. Our recorded time included time spent verifying hemostasis or documenting flows through the portal and arterial anastomoses with Doppler ultrasound. Despite this caveat, our groups were well matched with no differences in transfusion requirements or total operative time; these findings indicate that the difference in time for anastomoses spent on hemostasis should not account for the difference between groups.

In this series, the incidence of anastomotic leak or anastomotic stricture was 18% and 24% for the clipped and sewn groups, respectively. Few leaks progressed to anastomotic strictures that required operative intervention. Only 6% of the clipped group and 9% of the sewn group required operative biliary revision. This is similar to the findings by Davidson *et al.* [17] in a group of 477 transplant procedures. They found that 16% of their patients developed a biliary complication that required treatment; of those, 9% required conversion to choledochojejenostomy. The remaining patients with either leak or anastomotic stricture were managed successfully with either ERCP or percutaneous intervention by radiologists. Rerknimitr *et al.* [18] found that 91% of biliary strictures and all leaks discovered in 367 orthotopic liver transplant recipients could be successfully managed with ERCP.

In summary, we found that the use of non-penetrating, tissue everting approximating clips (Autosuture VCS®) produced a similar incidence of biliary leak and anastomotic stricture in a group of 17 patients who had similarly sized donor and recipient ducts and 34 matched comparison subjects undergoing orthotopic liver transplantation.

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References

[1] Wise PE, Pinson CW. Biliary complications of liver transplantation. In: Clavien PA, Baillie J, editors. Diseases of the gallbladder and bile ducts: diagnosis and treatment. Malden, MA: Blackwell Science; 2001:245–57.

[2] Fleck A, Zanotelli ML, Meine M, Brandao A, Leipnitz I, Schlindwein E, et al. Biliary tract complications after orthotopic liver transplantation in adult patients. Transplant Proc 2002;34:519–20.

[3] Krawczyk M, Nyckowski P, Zieniewicz K, Pawlak J, Michalowicz B, Malkowski P, et al. Biliary complications following liver transplantation. Transplant Proc 2000;32:1429–31.

[4] Hernandez Q, Ramirez P, Munitiz V, Pinero A, Robles R, Sanchez-Bueno F, et al. Incidence and management of biliary tract complications following 300 consecutive orthotopic liver transplants. Transplant Proc 1999;31:2407–8.

[5] Neuhaus P, Blumhardt G, Bechstein WO, Steffen R, Platz KP, Keck H. Technique and results of biliary reconstruction using side-to-side choledochocholedochostomy in 300 orthotopic liver transplants. Ann Surg 1994;219:426–34.

[6] Geevarghese SK, Bradley AL, Atkinson J, Wright JK, Chapman WC, Van Buren DH, et al. Comparison of arcuate-legged clipped versus sutured hepatic artery, portal vein, and bile duct anastomoses. Am Surg 1999;65:311–6.

[7] Campbell DA Jr, Magee JC, Rudich SM, Punch JD. Transplantation and immunology: hepatic transplantation. In: Greenfield LJ, Mulholland MW, editors. Surgery: scientific principles and practice. Philadelphia: Lippincott Williams & Wilkins; 2001:577.

[8] Wiesner R, Edwards E, Freeman R, Harper A, Kim R, Kamath P, et al. United Network for Organ Sharing Liver Disease Severity Score Committee. Model for end-stage liver disease (MELD) and allocation of donor livers. Gastroenterology 2003;124:91–6.

[9] Calne RY, McMaster P, Portmann B, Wall WJ, Williams R. Observations on preservation, bile drainage and rejection in 64 human orthotopic liver allografts. Ann Surg 1977;186:282–90.

[10] Moser MA, Wall WJ. Management of biliary problems after liver transplantation. Liver Transpl 2001;7:S46–52.

[11] Davidson BR, Rai R, Kurzawinski TR, Selves L, Farouk M, Dooley JS, et al. Prospective randomized trial of end-to-end versus side-to-side biliary reconstruction after orthotopic liver transplantation. Br J Surg 1999;86:447–52.

[12] Pikoulis E, Burris D, Rhee P, Nishibe T, Leppaniemi A, Wherry D, et al. Rapid arterial anastomosis with titanium clips. Am J Surg 1998;175:494–6.

[13] Kirsch WM, Zhu YH, Hardesty RA, Chapolini R. A new method for microvascular anastomosis: report of experimental and clinical research. Am Surg 1992;58:722–7.

[14] Matsumoto K, Obara H, Hayashi S, Harada H, Morisue A, Kitajima M. A new technique of vascular anastomosis with VCS clip applier system. XXX World Congress of the International College of Surgeons, Bologna, Italy: Monduzzi Editore SpA, 1996:1837–40.

[15] Leppaniemi AK, Wherry DC, Soltero RG, Pikoulis E, Hufnagel HV, Fishback N, et al. A quick and simple method to close vascular, biliary, and urinary tract incisions using the new Vascular Closure Staples: a preliminary report. Surg Endosc 1996;10:771–4.

[16] Birth M, Markert U, Strik M, Wohlschlager C, Brugmans F, Gerberding J, et al. Vascular closure staples-a new technique for biliary reconstruction: prospective randomized comparison with manual suture in an animal model. Transplantation 2002;73:31–8.

[17] Davidson BR, Rai R, Nandy A, Doctor N, Burroughs A, Rolles K. Results of choledochojejunostomy in the treatment of biliary complications after liver transplantation in the era of nonsurgical therapies. Liver Transpl 2000;6:201–6.

[18] Rerknimitr R, Sherman S, Fogel EL, Kalayci C, Lumeng L, Chalasani N, et al. Biliary tract complications after orthotopic liver transplantation with choledochocholedochostomy anastomosis: endoscopic findings and results of therapy. Gastrointest Endosc 2002;55:224–31.