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A New Approach to Accomplish Intraoperative Cholangiography in Left Lateral Segmentectomy of Living Liver Donation

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEFG 1 **Lin Wei**
ADF 2 **Zhong-tao Zhang**
ADG 1 **Zhi-jun Zhu**
ADF 1 **Li-ying Sun**
B 1 **Zhi-gui Zeng**
B 1 **Wei Qu**
B 3 **Liang Zhang**
B 4 **En-hui He**
B 4 **Rui-fang Xu**
BC 1 **Guang-peng Zhou**

1 Liver Transplantation Center, Beijing Friendship Hospital, Capital Medical University and National Clinical Research Center for Digestive Diseases, Beijing, P.R. China
2 Department of General Surgery, Beijing Friendship Hospital, Capital Medical University and National Clinical Research Center for Digestive Diseases, Beijing, P.R .China
3 Department of Anesthesia, Beijing Friendship Hospital, Capital Medical University, Beijing, P.R.China
4 Department of Ultrasound, Beijing Friendship Hospital, Capital Medical University, Beijing, P.R. China

Corresponding Author: Zhong-tao Zhang, e-mail: zhangzht@ccmu.edu.cn
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Background: There are 2 main methods of bile duct division in harvesting left lateral segment of a living donor: 1) by intraoperative cholangiography through cystic duct with cholecystectomy, or 2) by direct vision with preoperative magnetic resonance cholangiopancreatography. Here, we present a new approach to cholangiography by using the bile duct stump of the fourth liver segment (B4 stump) to achieve left lateral segmentectomy in pediatric living donor liver transplantation.

Material/Methods: This was a prospective study of 221 living donors who had undergone intraoperative cholangiography via the B4 stump in the course of left lateral segmentectomy. We collected and analyzed the clinical data, including the success rate of cholangiography by catheterizing the B4 stump; the associated time cost; the classification of the donor liver's biliary anatomy; the number of bile duct orifices on the graft side; and postoperative complications involving the biliary tract.

Results: We were successful in catheterizing B4 stumps in all 221 patients. The mean time cost of these procedures was 7.21±3.62 minutes. Variations in the confluence of the right and left lobes were found in 58 patients (26.24%). Overall, sludge was detected in 18 cases (8.14%), gallstones were found in 3 patients (1.36%), and a polypoid gallbladder lesion was found in 1 patient (0.45%). There were 11 cases (4.98%) of bile leakage; no biliary strictures were found in the donors.

Conclusions: Intraoperative cholangiography via the B4 stump is an alternative procedure for living donors who undergoes left lateral segmentectomy.

MeSH Keywords: **Biliary Tract • Gallbladder Diseases • Liver Transplantation • Living Donors • Pediatrics**

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Background

Pediatric living donor liver transplantation emerged in 1989 in efforts to solve the severe scarcity of grafts [1,2]. Since then, this technique has spread widely, especially in Asia [3–5]. In the past 10 years, there was a rapid development of pediatric living donor liver transplantation in China [6]. In all such cases, the safety of the donor is the top priority. In the present study, we present a new approach to cholangiography via the bile duct stump of the fourth liver segment (B4 stump) during left lateral segmentectomy in pediatric living donor liver transplantation. To our knowledge, this is the first such report. Cholangiography by the B4 stump approach can preserve the donor's gallbladder while also providing clear images of the biliary anatomy, thus guiding the surgical division of the biliary tract. This approach can effectively avoid injury to the biliary on the donor side while also providing a suitable biliary duct orifice on the graft side.

Material and Methods

Study design

This study enrolled living donors who underwent intraoperative cholangiography via the B4 stump during hepatectomy between June 2013 and December 2017 at our center. All donors donated the left lateral segments of their livers to pediatric recipients. We prospectively collected the clinical data, including whether the cholangiography and catheterization of the B4 stump was successful, the time cost of this procedure, whether the cholangiographic image was legible, classification of the biliary anatomy, and the number of orifices on the graft side. The clinical data also included routine blood tests, tests of liver and kidney function, as well as abdominal ultrasound examinations. All of these tests were performed at 1, 3, 5, 7, and 14 days; at 1, 3, 6, and 12 months; and at 24 months after the operations. Postoperative biliary tract complications (such as bile leakage, biliary tract stenosis, and cholecystitis or cholecystolithiasis) occurring postoperatively were recorded. All 221 patients were followed until December 2018.

Inclusion criteria

All donations involved the left lateral segment of the donor liver and all were voluntary. All of the procedures met the ethical requirements for living-donor liver transplantation in China. Signed informed consent to participate in the study was obtained from all of the patients, and all passed the routine medical evaluation; including that abdominal ultrasound showed that the size and shape of the donor gallbladder were normal and that the gallbladder emptying fraction was greater than 35% [7].

Exclusion criteria

Exclusion criteria included: stones or other organic diseases in the gallbladder, lesions within the gallbladder, or rare variations in the biliary tract, as indicated by magnetic resonance cholangiopancreatography (MRCP); history of cholecystectomy; variations in the anatomy of the gallbladder, such as a left-sided organ; and refusal to participate in the study.

Before approaching the porta hepatis, the biliary division point was roughly marked according to both preoperative MRCP images and visual observation during the procedure, thus we were able to draw a preliminarily line showing where the liver parenchyma could be divided. Then, as described in the literature [8,9], the porta hepatis of the donor liver was dissected in order to expose the artery and portal vein of the left lobe. In the early stage (June 2013–October 2015) of this study, the ligamentum hepatogastricum was divided and the proper hepatic artery was also partially dissociated. In the late stage (November 2015–December 2017) of this study, the ligamentum hepatogastricum was preserved and only the left hepatic and middle hepatic arteries were dissociated.

During the process of splitting the liver parenchyma, it was gradually divided from shallow to deep. When the relatively large 4-segment Glisson structure was encountered, about 1 cm of the Glisson branch was fully dissociated, the residual liver side was sutured, and the graft side was clamped with a thin straight bulldog. Then the Glisson branch was divided in the middle. The portal vein as well as the arterial and biliary orifices were carefully identified on the cut surface of the graft side. After that the portal and arterial orifices were closed with continuous 6-0 Prolene suture. After the bulldog clamp was removed and the B4 orifice detected, an intravenous catheter (BD Intravenous Catheters, Becton Dickinson Infusion Therapy Systems Inc., Sandy, UT, USA) was inserted into the bile duct (Figure 1).

When the orifice of B4 was too small, fine scissors were used to split the anterior wall of the bile duct lengthwise in order to facilitate insertion of the catheter, which was then fixed in place. We routinely placed a purse string suture around the opening of the bile duct using 6-0 Prolene suture. After the B4 stump had been catheterized, the patient was repositioned with the head low and feet high. Intraoperative cholangiography was then initiated using C-arm fluoroscopy (GE Medical Systems) and a contrast agent (meglumine diatrizoate) was slowly injected through the catheter. The resulting images portrayed the anatomy of the left and right hepatic ducts as well as biliary segments 2, 3, and 4 (B2, B3, and B4). Then the division marker (small straight bulldog) was adjusted according to the cholangiographic images until the ideal position was achieved. In the early stage (June 2013–October 2015) of this study, the cystic duct was untreated. In the late

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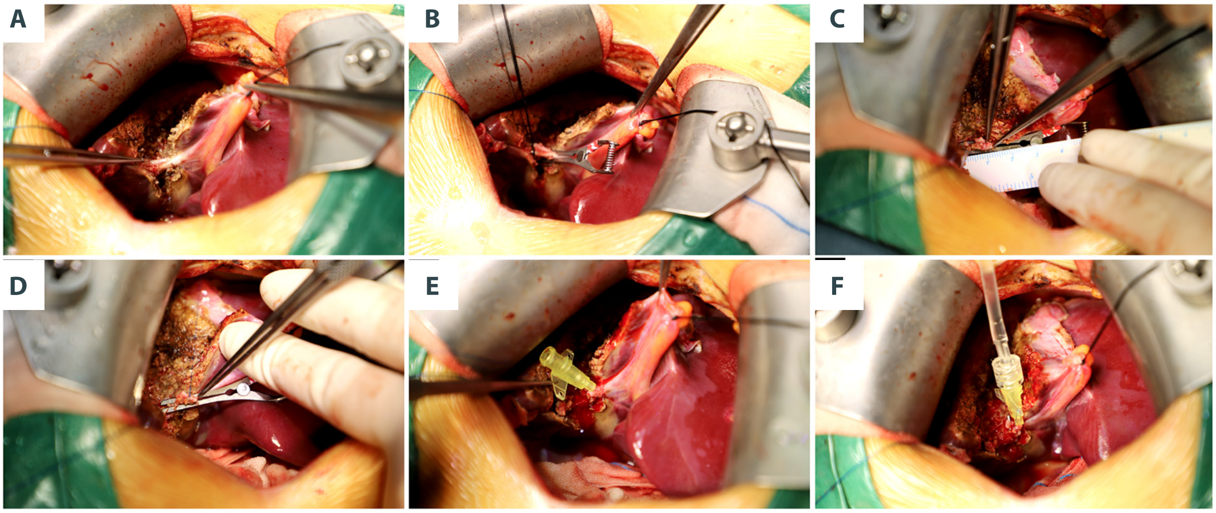

Figure 1. (**A**) About 1 cm of the Glisson branch's segment 4 is dissected. (**B**) The donor side of the Glisson branch is ligated, and the graft side clamped with a thin straight bulldog. (**C**) The orifices of the hepatic artery, portal vein, and bile duct are identified. (**D**) The orifice of the portal vein as well as the arterial orifice is sutured. (**E**) An intravenous catheter is inserted in the B4 stump. (**F**) The catheter is fixed in place.

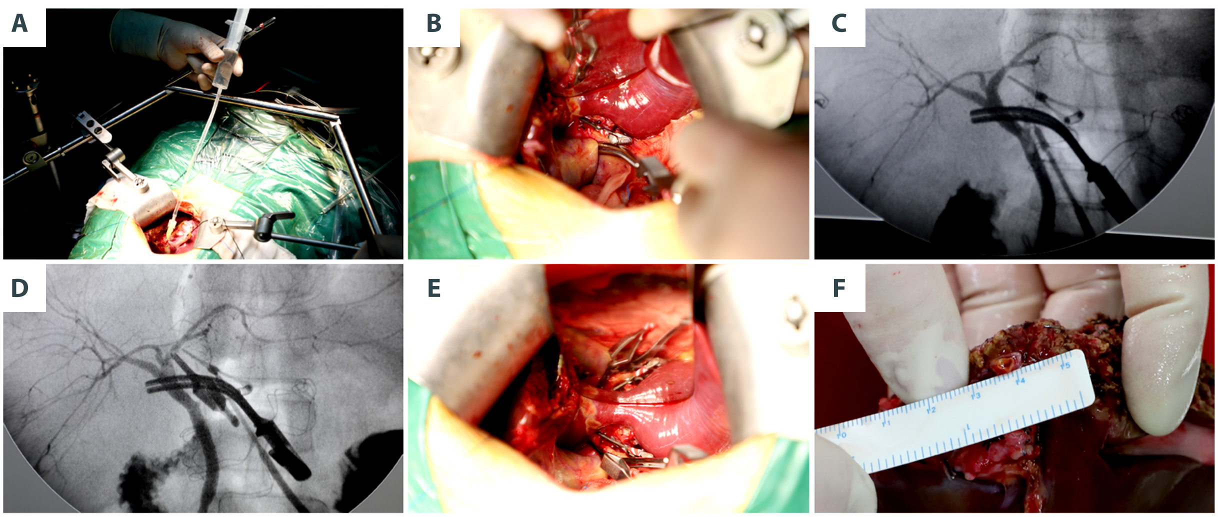

Figure 2. (**A**) Connection of extension tube and injection syringe. (**B**) Clamping of the cystic duct with a large bulldog and marking of the division point of the bile duct with a single small bulldog. (**C**) Image of the biliary tract with a single marker of the division point. (**D**) Image of the biliary tract with a double marker of the division point. (**E**) Marking of the division point of the bile duct with two small bulldogs. (**F**) Orifice of bile duct on the graft side.

stage (November 2015–December 2017) of this study, the cystic duct was clamped with a bulldog in order to block the retrograde entry of contrast agent into the gallbladder (Figure 2).

After cholangiography, the bulldog clamp was removed from the cystic duct. The intravenous catheter at B4 was also removed and the B4 orifice was closed. Finally, the last steps of the donor operation and back-table treatment of the graft were completed as described in the literature [8,9].

Statistical analysis

Variables in normal distribution are depicted as means ± standard deviation. Variables in non-normal distribution are presented as the median (first quartile, third quartile). All of the statistical analyses were performed using SPSS 22.0 software (IBM, SPSS, Chicago, IL, USA). $P<0.05$ was considered to be statistically significant.

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Table 1. Clinical features of 221 living donors for pediatric liver transplantation.

Gender	
Male	96
Female	125
Relationship to recipient	
Father	95
Mother	121
Other relatives	5
Age (years)	31.50±5.29
Body mass index (kg/m²)	22.44±2.98
GRWR (graft to recipient weight radio	2.92±0.99%
Gallbladder emptying fraction before operation	70.65±22.34%
Blood lose (mL)	152.91±103.04
Postoperative hospital stay (days)	7.70±1.84
Mean follow-up (months)	33.61±16.84

Results

Between June 2013 and December 2017, a total of 278 pediatric living-donor liver transplantations were completed at our center. Of these, 221 cases were eligible for inclusion in the present study. Their general characteristics are presented in Table 1.

The surgical procedures in all 221 donors were successful in that it was possible to place a catheter into the B4 stump and acquire clear biliary images by cholangiography. The mean time for these procedures was 7.21±3.62 minutes. The classification of biliary anatomy (according to the Ohkubo criteria for classification [10]) and the number of bile duct orifices on the graft are shown in Table 2.

We divided our study into 2 stages because small adjustments were applied in the procedures: the early stage ranged from June 2013–October 2015 and late stage from November 2015–December 2017. There were 91 cases in the early stage and 130 in the late stage. Complications involving the gallbladder are listed in Table 3.

Overall, sludge was detected in 18 cases; it disappeared within 6 months. Gallbladder stones were found in 3 cases and a polypoid gallbladder lesion was found in 1 case, but the patients were asymptomatic.

There were 11 cases (4.98%) of bile leakage, and all 11 donors recovered within 14 days having been treated with ultrasound-guided puncture and percutaneous drainage. An abdominal incisional hernia emerged in 2 cases and was successfully treated with herniorrhaphy. The donors' mean postoperative hospitalization time was 7.70±1.84 days. The median postoperative recovery time of liver function was 5 days (range, 3–31 days). No biliary strictures appeared in any of the donors postoperatively, and none of the patients suffered from diarrhea, changes in bowel habits, or colitis during a mean follow-up of 33.61 months.

Table 2. Classification of biliary anatomy and number of bile duct orifices on graft.

	N (%)	N (%) 1 orifice	N (%) 2 orifices	N (%) 3 orifices
A	112 (50.68)			
B	11 (4.98)			
C	25 (11.31)			
D	29 (13.12)			
E	19 (8.60)			
F	7 (3.17)			
G	3 (1.36)			
Classification not applicable	15 (6.79)			
H	176 (79.64)	166 (75.11)	10 (4.52)	0
I	9 (4.07)	9 (4.07)	0	0
J	27 (12.22)	24 (10.86)	3 (1.36)	0
K	5 (2.26)	0	5 (2.26)	0
Classification not applicable	4 (1.81)	0	2 (0.90)	2 (0.90)

Biliary classification followed the Ohkubo criteria [10]. For left lateral segmentectomy, the orifices of bile duct were mainly decided by the biliary anatomy of the left lobe; therefore, no orifices were described in the biliary anatomy of the right lobe (in the first 8 lines).

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Table 3. Postoperative gallbladder complications.

	N (%) Entire study	N (%) Early stage	N (%) Late stage	*P* value Early stage *vs.* late stage
Biliary sludge	18 (8.10)	9 (9.89)	9 (6.90)	0.461
Gallstone	3 (1.36)	3 (3.30)	0	0.068
Polypoid lesion	1 (0.45)	1 (1.10)	0	0.291

Early stage: 91 cases between June 2013–October 2015. Late stage: 130 cases between November 2015–December 2017.

Discussion

In living-donor liver transplantation, the safety of the donor is the primary concern. The ultimate goal is to simultaneously take into account the recipient's needs as well as the health of the donor [11,12]. For a surgeon who performs the donor surgery, how to accurately divide the biliary tract is a key problem. As reported in the literature [13–15], anatomic variations in the right hepatobiliary tract as it joins the biliary tract of the left lobe are not uncommon. Although such variations can be recognized via MRCP before surgery, an intraoperative direct view of the hepatic hilum is not sufficient in bile duct division without some risk of injury to the biliary tract.

In our study, there were 58 individuals (26.24%) with variations in the confluence of the right and left lobes. These appeared in types B, C, E, and G of 11, 25, 19, and 3 cases, respectively, according to the Ohkubo classification. In harvesting the left liver from a donor, such variations increase the risk of injury unless surgery can be guided with the precise positioning provided by intraoperative cholangiography. Otherwise biliary leakage/obstruction in the donor can result. Variations in confluence involving segments 2, 3, and 4 of the bile duct as found in our study are shown in Table 2. Two orifices of the bile duct emerged in 20 grafts and 3 orifices in 2 grafts. Single orifices were found in the remaining 199 grafts. The 2 cases with 3 bile duct openings had rare variations in separated bile ducts (segment 2, 3, and 4) with confluence to the right and common hepatic duct as seen on cholangiography. Deka et al. measured the MRCPs of 287 patients and showed that the length of the left hepatic duct ranged from 1.2 mm to 30.36 mm with a median value of 6.83 mm [16]. This means that the length of the left hepatic duct in half of the patients ranged between 1.2 mm and 6.83 mm. Therefore, this can easily lead to division of the bile duct into 2 openings on the graft side without requiring intraoperative cholangiography to harvest the left lateral segment (although it could be harvested with a single orifice with the precise positioning provided by intraoperative cholangiography). Currently, some transplant centers do not perform intraoperative cholangiography when the prospective liver graft is in the left lateral segment. In such cases, division of the bile duct relies on preoperative MRCP and direct intraoperative vision. However, these procedures do not always suffice to determine the optimal cut point owing to the difficulty of identifying the left hepatic duct by direct vision and the impossibility of real-time positioning by preoperative MRCP. Therefore, the operator may inadvertently cut too far to the left in order to prevent biliary injury in the donor side, ending with a graft side that has multiple orifices. Such instances are reported to be associated with a more difficult biliary reconstruction as well as postoperative complications (mainly biliary leakage and biliary stricture). Therefore, we believe that intraoperative cholangiography is a better choice to ensure the safety of the donor while also taking into account the number of bile duct orifices required on the graft.

For intraoperative cholangiography, the traditional method is to remove the gallbladder and use the cystic duct for the procedure. Up to now, this has also been the first choice for intraoperative cholangiography in most liver transplant centers. Its advantages are a simple operation and clear biliary images. The downside is that the removal of a healthy gallbladder can have unintended consequences. According to reports in the literature, post-cholecystectomy syndrome (PCS) occurs in 5–47% of patients after cholecystectomy [17,18] and the incidence of gastrointestinal tumors is also increased [19,20].

Intraoperative cholangiography, including puncture of the common bile duct without cholecystectomy, has been described [21]. Testa et al. [22] reported a method of positioning and splitting of the right hepatobiliary tract in a living donor involving an incision of about 1 mm through the common hepatic duct. The location and splitting of the right hepatobiliary tract was performed with the help of incisional cholangiography and localization with a biliary probe. For a healthy donor, incision or puncture and subsequent suture of the common hepatic duct or common bile duct can lead to leakage of bile or biliary stenosis.

The method described in our paper – using catheterization and intraoperative cholangiography through the B4 stump – has not previously been reported. When a liver graft is obtained from the left lateral liver segment, dividing the Glisson structures of segment 4 while splitting the parenchyma cannot be avoided. Therefore, we routinely acquired the B4 stump during the procedure. Thus, the donor's reserved bile duct is not subjected to additional manipulation, and biliary tract complications can be avoided. Although the caliber of the B4 stump is usually small, our method enabled us to achieve a 100% success rate. Contrast-enhanced images can be used to clearly show the hilar anatomy of the liver and the secondary biliary branches; which is no different from the traditional cholecystectomy and cholangiography via the cystic duct and can guide precise division of the bile duct.

The following points summarize the specific factors that may contribute to the success of our procedure. 1) Select a relatively bulky B4 stump for catheterization. 2) Select the intravenous indwelling needle matching the B4 stump for catheterization. 3) Close the portal and arterial orifices on the cut surface of segment 4's Glisson. 4) Use a purse string suture with 6-0 Prolene at the biliary end of the B4 stump to fix the catheter. 5) If the B4 stump is of very small caliber, fine scissors were used to split the anterior wall of the bile duct lengthwise; this can increase the success rate and convenience of catheterization. 6) Clamping the root of the cystic duct with a large bulldog clamp can prevent the contrast agent from entering the gallbladder during cholangiography. 7) Two small straight metal bulldog clamps are used to mark the biliary split point; thus, bile duct division between the 2 clamps will be more precise. 8) Directly split the biliary tract with sharp scissors; avoid excessive blunt dissection of the tissue surrounding the biliary tract.

It has been reported [23–25] that 17–35.6% of patients who have undergone cholecystectomy will develop dyspeptic post-cholecystectomy syndrome, and some 10% of the latter will develop chronic post-cholecystectomy syndrome. In addition, it has been reported that cholecystectomy increases the long-term risk of colonic tumors [26]. In our center, almost 80% of pediatric living-donor liver transplantations involved the use of left lateral segment as grafts, and 97.7% of the donors were parents of the recipients. Their average age (31.48 years) was young. It is important to protect healthy young donors, to preserve the gallbladder, and avoid the possibility of post-cholecystectomy syndrome. Another consideration is avoiding the risk of digestive tract cancer due to gallbladder removal. The new method described in this paper has been successfully performed with intraoperative catheterization and cholangiography in 221 patients. Some scholars have pointed out that in the course of procuring liver grafts, injury to the liver branch of the vagus nerve is inevitable, and it is possible to cause depression in gallbladder motor activity and induce secondary cholecystolithiasis and cholecystitis. Therefore, they recommended resection of the donor's gallbladder [9]. There has as yet been no systematic study of whether the function of the preserved gallbladder following left lateral segmentectomy is compromised and therefore must be removed. On the contrary, some centers do not routinely perform cholangiography and cholecystectomy in harvesting a left lateral segment graft from a living donor, and there have been no reports of adverse reactions related to preservation of the donor's gallbladder [8,27]. Su et al. [28] reported ultrasonic follow-up for the changes in live liver donor's gallbladders. Between 2013 and 2015 at our center, a total of 91 living donors were followed for an average of 21 months; all had accepted cholangiography using the B4 stump and all retained their gallbladders during left lateral segmentectomy. Biliary sludge was found after surgery in 9 patients (9.89%); it disappeared in 6 patients within 3 months. The other 3 patients developed gallbladder stones. One donor was found to have gallbladder polyposis at 505 days post-surgery. We continued our observation and follow-up of additional 130 cases from November 2015 to December 2017. Two adjustments to the procedure, applied from November 2015 onward, involved clamping the cystic duct with a large bulldog before cholangiography in order to avoid contrast agent refluxing into the gallbladder as well as to limit its distention after cholangiography. The second adjustment was made in order to enhance protection of the hepatic branch of the vagus nerve by preserving the hepatogastric ligament and limiting dissecting of the hepatic hilum. Therefore, we divided our cohort into 2 groups, as shown in Table 3, which compares the gallbladder complications among these 2 groups. We found that the postoperative sludge in the gallbladders of donors decreased from 9 out of 91 (9.89%) to 9 out of 130 (6.90%), and that all of the sludge disappeared within 6 months without the appearance of gallbladder stones in the late stage group. Although there were no statistically significance differences in morbidities of sludge, gallstones, and polypoid lesions between the early and late stages of our study, all morbidities showed downward trend in the later stage. We believe low morbidity and inadequate sample size contributed to our negative statistical results. Finally, there were 3 cases of gallbladder stones and 1 case of gallbladder polyposis among our 221 liver donors, none of which led to clinical symptoms. The donors in this group did not develop diarrhea, changes in bowel habits, or colitis within the average 33.61 months of follow-up.

Conclusions

A 100% success rate can be achieved with catheterization of the B4 stump in order to enable intraoperative cholangiography and guide division of the biliary tract. The complications of preserved gallbladder in donors was relatively low. Therefore, intraoperative cholangiography using catheterization of the B4 stump is an alternative approach to left lateral segmentectomy in living-donor liver transplantation.

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