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Intraoperative Ultrasonography as a Guidance for Dividing Bile Duct During Laparoscopic Living Donor Hepatectomy

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Manuscript Preparation E
Literature Search F
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Background: The purpose of this study was to investigate the feasibility of using intraoperative ultrasonography as a guidance in dividing bile duct during laparoscopic donor hepatectomy.

Material/Methods: Cases of living liver donors who underwent laparoscopic living donor hepatectomy from May 2013 to December 2017 were reviewed. Operative and postoperative data were compared between donors with intraoperative ultrasonography and donors with intraoperative cholangiography. For analyzing whether bile duct division was performed successfully, anatomical type and number of bile duct openings were reviewed. When the number of bile ducts were achieved as expected, it was considered "successful".

Results: Intraoperative cholangiography was used in 67 donors (62.6%) while intraoperative ultrasonography was used in 36 donors (33.6%). Mean operation time was 405.0±76.2 minutes versus 275.1±37.5 minutes, $P<0.001$, respectively, and was longer in donors who had a cholangiography. There was no difference in the success rate of bile duct division between donors who had a cholangiography (92.5%) and donors who had an ultrasonography (88.9%, $P=0.716$). The mean hospital stay after operation was longer in donors who had a cholangiography (11.6±4.3 days versus 9.0±2.7 days, $P<0.001$). There was no difference in biliary complication rate between donors who had a cholangiography (11.9%) and donors who had an ultrasonography (8.3%, $P=0.743$).

Conclusions: Intraoperative ultrasonography can be used safely in dividing bile duct during laparoscopic living donor hepatectomy with similar outcomes to intraoperative cholangiography.

MeSH Keywords: Laparoscopy • Liver Transplantation • Living Donors • Ultrasonography, Doppler, Color

Abbreviations: CT – computed tomographic; MRCP – magnetic resonance cholangiopancreatography

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Background

Laparoscopy has been widely used throughout the field of liver surgery. Living donor hepatectomy, which requires perfection in every step by step procedure, is now performed by laparoscopy in certain institutions that are specialized in minimal invasive surgery. In 2002, Cherqui et al. and Soubrane et al. reported the first laparoscopic living donor hepatectomy for a pediatric patient [1,2]. After this successful start, left hemihepatectomy and right hemihepatectomy also showed feasible results when performed in living donors [3,4]. For precise transection of liver parenchyme and division of hilar structures, procedures such as indocyanine green camera or intraoperative cholangiography have been used in those centers that perform laparoscopic living donor hepatectomy [5,6].

Our center has published a number of reports on laparoscopic liver resection, and performed more than 100 cases of laparoscopic living donor hepatectomy [3,7–12]. While intraoperative cholangiography has been initially used for preventing biliary complications, intraoperative ultrasonography has been used for bile duct visualization since December 2016. The purpose of this study was to analyze the feasibility of intraoperative ultrasonography compared to cholangiography especially in bile duct division during laparoscopic living donor hepatectomy.

Material and Methods

Patients and data

Living donors who underwent living donor right hemihepatectomy, extended right hemihepatectomy, left hemihepatectomy, and extended left hemihepatectomy, during the period of May 2013 to December 2017 were reviewed for study inclusion. Donors who underwent left lateral sectionectomy and donors who underwent open conversion during laparoscopy were excluded from the study. Demographic data and anatomical, clinical, and surgical data were collected from a prospectively maintained database. Anatomical variations of the donors were reviewed based on computed tomographic (CT) angiography, magnetic resonance cholangiopancreatography (MRCP), intraoperative cholangiography, and operative records. Postoperative complications of donors were categorized based on Clavien-Dindo classification.

Donor evaluation

Donors were evaluated for their eligibility for living donation by complete ethical, psychological, medical, and anatomical evaluation. Anatomical variations were assessed using CT angiography and MRCP. All donors 1) should not have combined comorbidity, 2) should be less than 65 years old, 3) should have

no fatty change with a macrosteatosis of less than 30%, and 4) should have an expected remnant liver of more than 30%. At first, only patients with simple anatomical variations were selected for laparoscopic living donor hepatectomy. However, as our experience accumulated, patients with anatomical variations also had laparoscopic living donor hepatectomy.

Procedure for bile duct visualization

For safe bile duct division, our center started to perform intraoperative cholangiography during laparoscopic living donor hepatectomy as a routine procedure. However, we started using intraoperative ultrasonography instead of intraoperative cholangiography starting from December 2016. The reason why we shifted from intraoperative cholangiography to intraoperative ultrasonography was due to its relative simplicity in procedure with no radiation exposure.

For intraoperative cholangiography, the cystic duct was temporarily ligated but later cannulated for radiocontrast infusion. Usually, intraoperative cholangiography was taken initially for identification of biliary anatomy (Figure 1A). After the inspection of anatomy, a marker thread visible on x-ray or a laparoscopic bull-dog clamp (Aesculap, Center Valley, PA) is placed on the right bile hepatic duct at the level of the presumed site of transection (Figure 1B). When the cholangiography shows adequate safety margin, the bile duct is ligated either by polymer clip or suture. An additional intraoperative cholangiography is taken later for confirming secure ligation with no leakage.

For intraoperative ultrasonography, a laparoscopic probe is used. Even in cases where intraoperative cholangiography was used for bile duct visualization, intraoperative ultrasonography was used for identifying the hepatic vein and its V5 and V8 branches. At first, dissection of the surrounding tissues should be made (Figure 2A). For better visualization of bile duct in the ultrasonography, laparoscopic bull-dog clamp is placed on the common bile duct for bile congestion of the proximal biliary tree (Figure 2B). A laparoscopic probe is placed to visualize the bile duct and is moved horizontally to identify the right hepatic duct and its confluence with left hepatic duct and common hepatic duct (Figure 2Ca, 2Da). In the intraoperative ultrasonography, the bile duct is visualized on the top of the screen with the portal vein lying beneath with absence of color flow in color doppler mode (Figure 2Cb, 2Db). The right hepatic duct is ligated using polymer clip (Figure 2E), and cut with a laparoscopic scissor (Figure 2F). In the case of a wide right hepatic duct, it can be close using a suture.

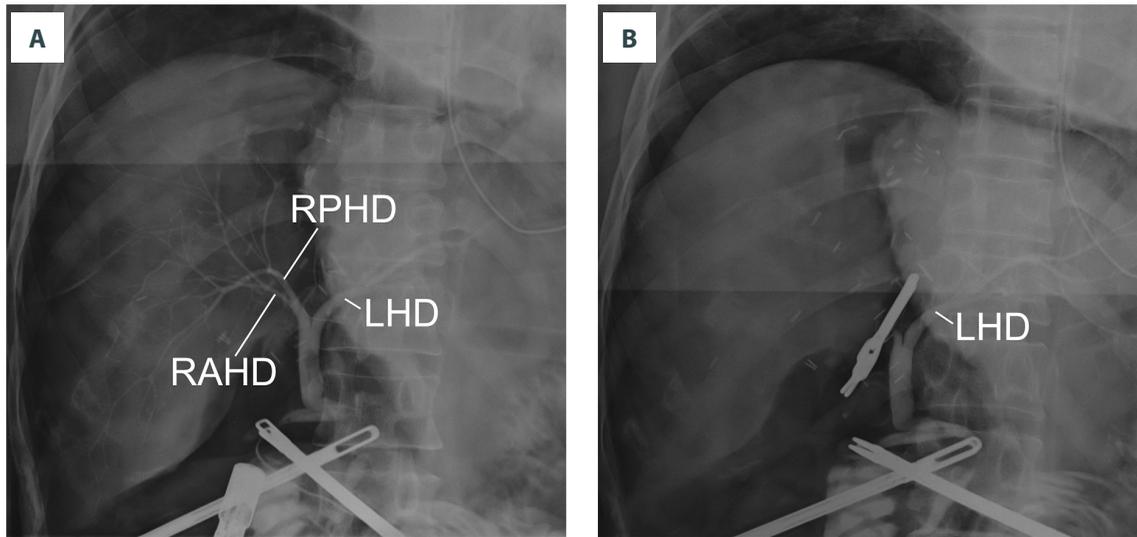


Figure 1. (A) 47-year-old female donor was found with a type I biliary anatomy during operative cholangiography. (B) After confirming adequate free margin of bile duct division with temporarily clamping the right hepatic duct, the duct was ligated. RPHD – right posterior hepatic duct; RAHD – right anterior hepatic duct; LHD – left hepatic duct.

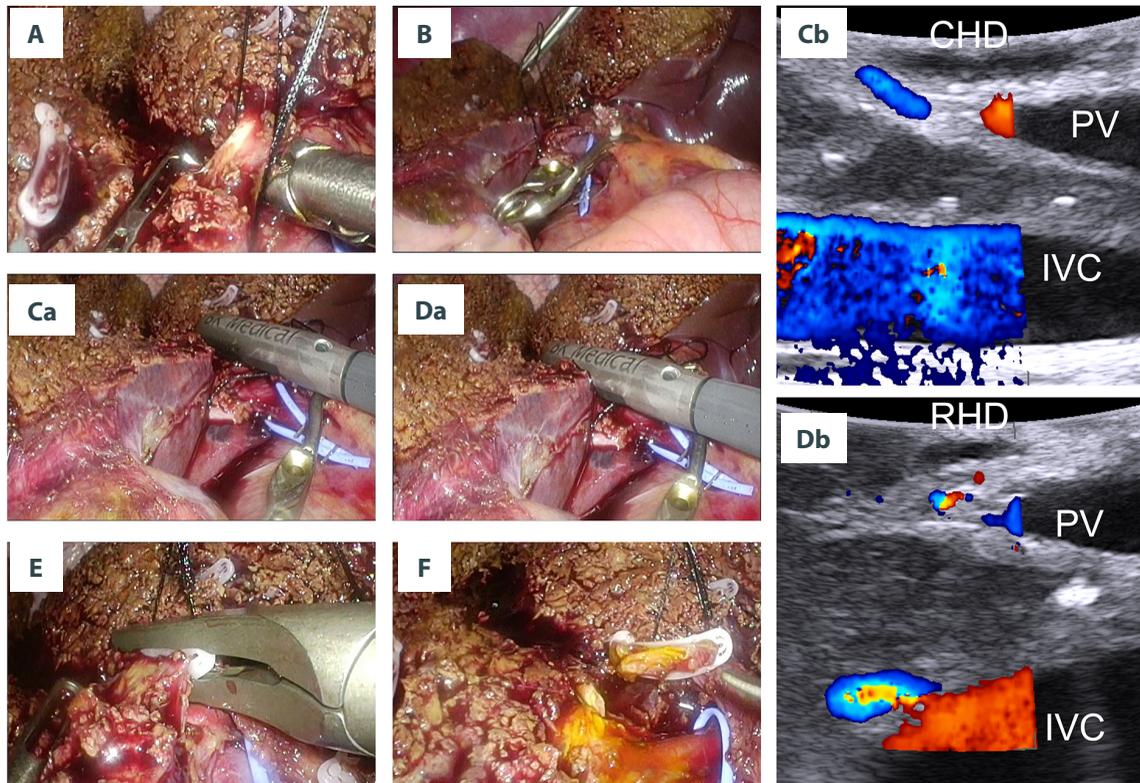


Figure 2. For safe bile duct division: (A) right hepatic duct should be completely isolated with adequate dissection of surrounding tissues. (B) By temporarily clamping the common bile duct and waiting for certain amount of time, the duct is filled with bile for better visualization. (Ca) Intraoperative ultrasonography performed on the left side of the exposed right hepatic duct shows (Cb) clearly appearing common hepatic duct on the top of the ultrasonography. (Da) As the probe moves to the right, (Db) ultrasonography reveals right hepatic duct. (E) Right hepatic duct is ligated with adequate free margin from the hilar duct, (F) and bile duct is divided caut-intraoperative ultrasonography using laparoscopic scissor. CHD – common hepatic duct; RHD – right hepatic duct; PV – portal vein; IVC – inferior vena cava.

Definition of successful bile duct division

For comparing the successful bile duct division, both the biliary anatomy of each donor and the actual number of the bile duct opening in graft liver were reviewed. During right hemihepatectomy, only type I bile ducts are the potential candidates that are expected to achieve single bile duct in graft liver. Other anatomical variations are expected to yield 2 or more bile ducts in graft liver. On the other hand, during left hemihepatectomy, anatomical variations other than type I bile ducts are also potential candidates for achieving single bile duct in graft liver. We categorized the results “as expected” and “more ducts than expected”.

Statistical analysis

Comparisons of baseline characteristics, anatomical variations, operative and postoperative recovery between intraoperative cholangiography and intraoperative ultrasonography were performed using appropriate statistical analyses. Numerical variables were expressed as mean \pm standard deviation or median and range and were analyzed using Student's *t*-test or Mann-Whitney test, respectively. Categorical variables were compared using chi-square test, Fisher's exact test, or linear-to-linear association.

Two-sided *P*-values <0.05 were used to indicate statistical significance. Statistical analyses were performed with SPSS 20.0 (SPSS Inc., Chicago, IL, USA). This study was approved by the Institutional Review Board of Samsung Medical Center (IRB No. 2018-01-073).

Results

During the study period, 118 donors underwent laparoscopic living donor hepatectomy. Five donors who underwent laparoscopic left lateral sectionectomy and 6 donors who underwent open conversion during laparoscopy were excluded. A total of 107 donors, 57 males and 50 females were included to the study (Table 1). A total of 89 donors (83.2%) underwent right hemihepatectomy while 12 donors (11.2%) underwent extended right hemihepatectomy, 2 donors with left hemihepatectomy (1.9%), and 4 donors (3.7%) with extended left hemihepatectomy. Ninety-nine donors (92.5%) had type I portal vein, and 88 donors (82.2%) had type I bile duct.

While 4 donors underwent bile duct division without bile duct visualization, 67 living donors (62.6%) and 36 living donors (33.6%) underwent bile duct division using intraoperative cholangiography and intraoperative ultrasonography, respectively. Donor with intraoperative cholangiography underwent mean number of 3.4 ± 1.5 cholangiography.

Table 1. Demographical, clinical and operative characteristics of the patient group.

Factors	No. of patients	%
Sex (Male)	57/50	53.3
Age, mean (years)	31.1 \pm 11.1	
Body mass index, mean (kg/m ²)	23.2 \pm 2.7	
Operation		
Right hemihepatectomy	89	83.2
Extended right hemihepatectomy	12	11.2
Left hemihepatectomy	2	1.9
Extended left hemihepatectomy	4	3.7
Portal vein type		
I	99	92.5
II	6	5.6
III	2	1.9
Bile duct type		
I	88	82.2
II	11	10.3
IIIa	2	1.9
IIIb	4	3.7
IIIc	1	0.9
IV	1	0.9
Right inferior hepatic vein	49	45.8
Bile duct visualization		
No visualization	4	3.7
Intraoperative cholangiography	67	62.6
Intraoperative ultrasonography	36	33.6
Number of cholangiography performed, mean	3.4 \pm 1.5	

Comparison of operative data according to the method of bile duct visualization

Table 2 summarizes the results comparing operative data between the intraoperative cholangiography group and the intraoperative ultrasonography group. There was a difference in operation year between the intraoperative cholangiography group (91.0% before 2017) and the intraoperative ultrasonography group (97.2% since 2017, *P*<0.001). Although there were 2 left hemihepatectomies and 4 extended left hemihepatectomies in the intraoperative cholangiography group whereas all patients in the intraoperative ultrasonography group had right hemihepatectomy, the difference was not statistically significant (*P*=0.089).

Mean operation time (405.0 \pm 76.2 minutes versus 275.1 \pm 37.5 minutes, *P*<0.001) and median warm ischemic time group (median 360 seconds, range 100–1860 versus median 179.5, range 127–423, *P*<0.001) was longer in the intraoperative cholangiography group.

Table 2. Comparisons of operative data of laparoscopic living donor hepatectomy according to the method of bile duct visualization before bile duct division.

	Intraoperative cholangiography (n=67)		Intraoperative ultrasonography (n=36)		P
Year of operation					<0.001
Before 2017	61	(91.0%)	1	(2.8%)	
Since 2017	6	(9.0%)	35	(97.2%)	
Operation (right vs. left)					0.089
Right hemihepatectomy	50	(74.6%)	36	(100.0%)	
Extended right hemihepatectomy	11	(16.4%)	–		
Left hemihepatectomy	2	(3.0%)	–		
Extended left hemihepatectomy	4	(6.0%)	–		
Operation time, mean (minutes)	405.0±76.2		275.1±37.5		<0.001
Warm ischemic time, median (seconds)	360 (100–1860)		179.5 (127–423)		<0.001
Estimated blood loss, mean (ml)	324.5±165.0		233.3±112.8		0.004
Transfusion	0		0		1.000
Portal vein type (Type I vs. others)					0.124
I	64	(95.5%)	31	(86.1%)	
II	3	(4.5%)	3	(8.3%)	
III	–		2	(5.6%)	
Bile duct type (Type I vs. others)					0.140
I	58	(86.6%)	27	(75.0%)	
II	5	(7.5%)	5	(13.9%)	
IIIa	–		1	(2.8%)	
IIIb	–		2	(5.6%)	
IIIc	4	(6.0%)	–		
IV	–		1	(2.8%)	
Right inferior hepatic vein	32	(47.8%)	16	(44.4%)	0.748
Number of bile ducts in graft					0.030
1	57	(85.1%)	24	(66.7%)	
2/3	10/0	(14.9%)	10/2	(33.3%)	
Successful achievement in bile duct division					0.716
As expected	62	(92.5%)	32	(88.9%)	
More ducts than expected*	5	(7.5%)	4	(11.1%)	

* During right hemihepatectomy, only type I bile ducts are the potential candidates that are expected to achieve single bile duct in graft liver. On the other hand, during left hemihepatectomy, anatomical variations other than type I bile ducts are also expected to achieve single bile duct in graft liver.

The intraoperative cholangiography group had more estimated blood loss (324.5±165.0 mL) compared to the intraoperative ultrasonography group (233.3±112.8 mL, $P=0.004$)

Although the intraoperative ultrasonography group had more variations in portal vein (type I, 95.5% in intraoperative cholangiography versus 86.1% in intraoperative ultrasonography, $P=0.124$) and bile duct (type I 86.6% in intraoperative cholangiography versus 75.0% in intraoperative ultrasonography, $P=0.140$) the difference was statistically insignificant. The intraoperative cholangiography group had higher proportion of liver graft with single bile duct (85.1%) compared to the intraoperative ultrasonography group (66.7%, $P=0.03$),

There was no difference in the success rate of bile duct division between the intraoperative cholangiography (92.5% were as expected) and the intraoperative ultrasonography group (88.9% were as expected, $P=0.716$). Only 5 patients (7.5%) in the intraoperative cholangiography group and 4 patients (11.1%) in the intraoperative ultrasonography group had more ducts than expected.

Comparisons of postoperative recovery according to the method of bile duct visualization

Table 3 summarizes the postoperative data according to the method of bile duct visualization. The intraoperative

Table 3. Comparisons of postoperative recovery after laparoscopic donor hepatectomy according to the method of bile duct visualization before bile duct division.

	Intraoperative cholangiography (n=67)	Intraoperative ultrasonography (n=36)	P
Total bilirubin, peak (mg/dL)	3.5±1.7	3.0±1.6	0.132
Aspartate aminotransferase, peak (U/L)	280.9±139.6	227.3±89.7	0.040
Alanine aminotransferase, peak (U/L)	283.7±120.4	235.8±118.3	0.055
Prothrombin time, peak (INR)	1.60±0.19	1.59±0.24	0.863
Hospital stay, mean (days)	11.6±4.3	9.0±2.7	<0.001
Complication of donor	17 (25.4%)	4 (11.1%)	0.124
Ileus	2 (3.0%)	–	0.541
Wound	1 (1.5%)	1 (2.8%)	1.000
Complicated fluid collection	2 (3.0%)	–	0.541
Biliary complication	8 (11.9%)	3 (8.3%)	0.743
Bile leakage	6 (9.0%)	2 (5.6%)	
Biliary stricture	2 (3.0%)	1 (2.8%)	
Bleeding	1 (1.5%)	–	1.000
Portal vein stricture/thrombosis	1 (1.5%)	–	1.000
Others	2 (3.0%)	–	0.541
Clavien-Dindo classification	50 (74.6%)	32 (88.9%)	0.084
None	6 (9.0%)	2 (5.6%)	
I	–	–	
II	11 (16.4%)	2 (5.6%)	
III	–	–	
IV/V	7 (10.4%)	0 (0.0%)	
Readmission due to complication			0.093

INR – international normalized ratio.

cholangiography group had significantly higher peak aspartate aminotransferase (280.9±139.6 U/L versus 227.3±89.7 U/L, $P=0.040$). Mean hospital stay after operation was longer in the intraoperative cholangiography group (11.6±4.3 days) than the intraoperative ultrasonography group (9.0±2.7 days, $P<0.001$).

Although complication rate seemed to be higher in the intraoperative cholangiography group (25.4%) compared to the intraoperative ultrasonography group (11.1%) there was no statistical significance ($P=0.124$). Biliary complication rates were 11.9% in the intraoperative cholangiography group (6 leakages and 2 strictures) and 8.3% in the intraoperative ultrasonography group (2 leakages and 1 stricture) and the difference was not statistically significant ($P=0.743$). Regarding the severity of complications, linear-by-linear association showed the difference was not statistically significant ($P=0.084$). There was no difference in the readmission rate ($P=0.093$).

Table 4 summarizes the cases with biliary complications. Two patients in the intraoperative cholangiography group had reoperation due to bile leakage. A 47-year-old female donor had bile leakage from the cut surface and was primarily repaired during laparoscopic exploration. A 55-year-old male donor had bile leakage from the cystic duct due to displacement of ligating clip. The donor's cystic duct was again ligated during

laparoscopic exploration. Other donors with bile leakage or biliary stricture had percutaneous drainage or endoscopic retrograde bile duct drainage while 1 donor was managed with delayed removal of the drainage tube that was inserted during laparoscopic living donor hepatectomy with no additional procedures. All the donors recovered with no additional complications and the drainage tubes are all removed.

Discussion

As laparoscopic living donor hepatectomy has begun to be performed in leading centers around the world, the main focus has been on its feasibility regarding the complications of donor and recipients [1,2,5,13–17]. To minimize the potential risk of surgical complications, especially for the donor, maximizing the safety is justified despite the increased procedural complexity and operative time. However, as the surgeons overcome the learning curve, efforts should be made to make the procedure simpler without jeopardizing the donor's safety.

Intraoperative cholangiography was initially used for identifying the exact biliary anatomy in addition to MRCP. Intraoperative cholangiography was performed by cannulating the cystic duct, deciding the site of bile duct division, and checking for secure

Table 4. Cases with biliary complications and the interventions that were performed.

	Sex/age	Complications	Intervention
Intraoperative cholangiography	F/47	Bile leakage on the cut surface of the graft	Primary repair during laparoscopic exploration
	M/55	Bile leakage from the cystic duct due to displacement of ligating clip	Ligation of cystic duct during laparoscopic exploration
	F/27	Bile leakage	PCD insertion
	M/31	Bile leakage	PCD and ERBD insertion
	M/22	Bile leakage	PCD and ERBD insertion
	M/19	Biliary stricture	ERBD insertion
	F/22	Bile leakage	PCD insertion
	M/34	Biliary stricture	ERBD insertion
Intraoperative ultrasonography	F/49	Biliary stricture	ERBD insertion
	M/37	Bile leakage	Delayed removal of drainage tube
	M/29	Bile leakage	PCD insertion

PCD – percutaneous drainage; ERBD – endoscopic retrograde biliary drainage.

division with no leakage or stricture. Intraoperative ultrasonography was used for identifying the middle hepatic vein and its V5 and V8 branches. However, intraoperative ultrasonography was adapted for visualizing the bile duct since December 2016.

About one-third of the donors included in this study underwent intraoperative ultrasonography for bile duct visualization while 62.6% of donors had intraoperative cholangiography. Since intraoperative ultrasonography was utilized in this study after we had accumulated certain amount of experiences, it is expected that most operative and postoperative data will be improved in the intraoperative ultrasonography group. As expected, length of operation time ($P<0.001$), warm ischemic time ($P<0.001$), and estimated blood loss ($P=0.004$) was favorable in the intraoperative ultrasonography group (Table 2). Although it lacked statistical significance, the intraoperative ultrasonography group had more donors with anatomical variations. The intraoperative cholangiography group had single bile duct in 85.1% of donors, while 66.7% of donors in the intraoperative ultrasonography group had single bile duct ($P=0.030$). By comparing the success rate in bile duct division, there was no statistically significant difference between the 2 groups ($P=0.716$). The reason why the difference in number of bile duct in a graft was significant while anatomical variation was not, is because of the 6 donors in the intraoperative cholangiography group who underwent left hepatectomy.

The key finding of this study was the similar success rate of bile duct division ($P=0.716$) and biliary complication rate ($P=0.743$) while changing the method of bile duct visualization.

We assumed that the improved operation time, warm ischemic time, estimated blood loss, and hospital stay was the overall result of improved technical experience in laparoscopic living donor hepatectomy with accumulating experience. Shorter operation time might have been partially derived from applying the intraoperative ultrasonography technique which only requires less than 1 minute, whereas intraoperative cholangiography takes significant amount of time with radiation exposure to the surgical team.

From these results, we suggest that shifting to intraoperative ultrasonography from intraoperative cholangiography by an experienced surgical team can be beneficial in reducing the time and effort, with no radiation exposure to the surgical staffs. Of course, this study does not guarantee safety for inexperienced surgical team outcomes who are under the learning curve of laparoscopic living donor hepatectomy. Intraoperative cholangiography provides actual visualization of the biliary anatomy when taken properly, while intraoperative ultrasonography is dependent on the examiner. Therefore, we do not deny that intraoperative cholangiography can provide more safety than intraoperative ultrasonography, and it still needs to be the first choice for beginning surgeons. Furthermore, intraoperative cholangiography can be used as a second option for bile duct visualization in case intraoperative ultrasonography fails to visualize the biliary structures.

Of course, this study has some limitations since it is a retrospective study. The background characteristics were significantly different between the 2 groups. Intraoperative cholangiography

was used in the earlier period, mostly before 2017, while intraoperative ultrasonography was mainly used since 2017. The improved operative and postoperative data should be interpreted as the consequence of overall improvement in the surgical experience, and not only from using intraoperative ultrasonography. Nevertheless, the fact that the successful bile duct division rate and biliary complication rate were similar shows the feasibility of intraoperative ultrasonography in substituting intraoperative cholangiography. As to our best knowledge, there is no published study that analyzed the feasibility of intraoperative ultrasonography for bile duct visualization during bile duct division, by comparing it to intraoperative cholangiography.

This study focused on utilizing intraoperative ultrasonography during laparoscopic living donor hepatectomy. It may be beneficial in reducing the operation time and effort along with

no risk of radiation exposure. As an option for surgical teams performing laparoscopic living donor hepatectomy, intraoperative ultrasonography should be considered as a substitute.

Conclusions

Intraoperative ultrasonography can be used as a guidance in dividing the bile duct during laparoscopic living donor hepatectomy with comparable outcome to intraoperative cholangiography. However, the utilization of technique should be performed by surgeons with enough experience in laparoscopic living donor hepatectomy.

Conflicts of interest

None.

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