Optimal Bile Duct Division Using Real-Time Indocyanine Green Near-Infrared Fluorescence Cholangiography During Laparoscopic Donor Hepatectomy

TO THE EDITOR:

Despite advances in living donor liver transplantation (LDLT), biliary complications remain common during donor hepatectomy. These complications may be avoided by determining optimal bile duct division points. Intraoperative cholangiography and preoperative magnetic resonance cholangiopancreatography (MRCP) have been shown to be helpful in determining optimal division points. Alternatively, dissection around the bile ducts and exploration through the cystic ducts can help localize division points accurately.

Recently, indocyanine green (ICG) near-infrared fluorescence cholangiography has been applied to various hepatobiliary and pancreatic operations. To test its real-time applicability to laparoscopic donor hepatectomy, we used this technique to precisely determine the adequate dissection lines for bile ducts. Following an initial case report in 2010 describing ICG cholangiography in open living donor hepatectomy,[1] few studies have described the application of this technique to laparoscopic living donor hepatectomy. To our knowledge, these previous studies are limited to case reports or case series and to laparoscopic left living donor hepatectomy. Here we report our initial experiences with ICG near-infrared fluorescence cholangiography in various types of laparoscopic donor hepatectomy.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; B1, segment 1 bile duct; B2, segment 2 bile duct; B6, segment 6 bile duct; CT, computed tomography; ICG, indocyanine green; LBD, left bile duct; LDLT, living donor liver transplantation; MRCP, magnetic resonance cholangiopancreatography; OPC, outpatient clinic; RABD, right anterior bile duct; RAPD, right posterior bile duct; RBD, right bile duct; SD, standard deviation.

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Patients and Methods

The institutional review board of Seoul National University Hospital approved this study (institutional review board number H-1603-010-746). Written informed consent was obtained from all patients before their participation. This prospective study included all consecutive living donors who underwent pure 3-dimensional laparoscopic hepatectomy between April 29 and June 10, 2016. Patients were excluded only if the fluorescent imaging system was not available on the day of surgery.

PREOPERATIVE EVALUATION

All donors underwent a complete medical and anatomical evaluation, including liver dynamic computed tomography (CT), CT volumetry (Dr. Liver, Humanopia Ltd., Pohang, Gyungbuk, South Korea), and MRCP. Intraoperative cholangiography has not been routinely performed in our center since 2009, at which time it was replaced by MRCP.[2]

ADMINISTRATION OF ICG

All donors were assessed preoperatively for history of iodine allergy and anaphylactic reactions to any other drugs. ICG (0.05 mg/kg) was injected intravenously 30-60 minutes before exposure of the hilar plate, taking into consideration the time of bile excretion.[3]

FLUORESCENT IMAGING SYSTEM

The Pinpoint (Novadaq, Ontario, Canada) or LuxEndoBright (Korea Electrotechnology Research Institute, Seoul, South Korea) system was used for near-infrared imaging, depending on the availability of each system on the day of surgery.

REAL-TIME FLUORESCENT CHOLANGIOGRAPHY TECHNIQUES

After isolating and temporarily clamping the right portal vein and hepatic artery in patients undergoing right hepatectomy or the left portal vein and hepatic artery in patients undergoing left hepatectomy, the ischemic demarcation line on the liver surface was marked with an electric cauterizer. The liver parenchyma was resected along this demarcation line using a laparoscopic cavitron ultrasonic surgical aspirator. After exposing the anterior surface of the hilar plate, the distal bile duct was temporarily clamped with a laparoscopic bulldog clamp to congest the bile and eventually visualize the bile duct clearly through the fluorescent imaging system. After comparing real-time ICG fluorescence cholangiography and preoperative MRCP imaging results, the areas around the right and left hepatic ducts were carefully dissected. When the right or left hepatic duct and the caudate or aberrant bile duct were clearly visualized, the appropriate cutting lines of the bile ducts for both donor and recipient were determined. This point was marked with temporary clips based on real-time imaging which enabled ICG fluorescence images to be displayed instantaneously on the laparoscopic screen. After rechecking the patency of each side of the bile ducts and the common hepatic duct, cutting was performed along the marked line.

Results

Thirteen consecutive living donors underwent pure 3-dimensional laparoscopic hepatectomy between April 29 and June 10, 2016. The fluorescence imaging system was not available for 3 of these donors, resulting in their exclusion. Of the remaining 10 donors, 6 were male and 4 were female. Their mean age was 32.6 ± 10.9 years, and their mean body mass index was 23.9 ± 1.4 kg/m^2. Most donors underwent right hemihepatectomy; however, 1 underwent an extended right hemihepatectomy, based on the adequacy of the volume of the remnant donor liver and the relatively small expected graft volume. In addition, 1 donor to a pediatric recipient underwent left lateral sectionectomy and in vivo reduction. Mean time to liver removal was 250.6 ± 50.2 minutes, mean estimated blood loss during the operation was 420.0 ± 182.9 cc, and mean postoperative hospital stay was 7.9 ± 0.7 days (Table 1).

TABLE 1. Patient Demographics

Variable	Total (n = 10)
Age, years	32.6 ± 10.9
Sex	
Male	6 (60.0)
Female	4 (40.0)
Body mass index, kg/m^2	23.9 ± 1.4
Type of operation	
Right hemihepatectomy	8 (80.0)
Extended right hemihepatectomy	1 (10.0)
Left lateral sectionectomy and in vivo reduction	1 (10.0)
Time to liver out, minutes	250.6 ± 50.2
Operation time, minutes	344.2 ± 62.7
Estimated blood loss, cc	420.0 ± 182.9
Hospital stay, days	7.9 ± 0.7

NOTE: Data are given as mean ± SD or n (%).

All donors underwent preoperative MRCP, with the image displayed beside the laparoscopic view monitor and ICG fluorescence cholangiography image, thereby allowing surgeons to refer to or compare the images whenever needed. The biliary system around the hilar plate, including any aberrant hepatic ducts, could be delineated in all 10 donors. Real-time viewing facilitated determination of the bile duct division points after marking, as well as the patency after clipping the bile duct (Figs. 1 and 2).

All donors underwent protocol CT scans on postoperative day 6 or 7, with all having patent hepatic vessels and no evidence of bile duct dilatation. Two donors showed small amounts of postoperative fluid collection along the resection margin, but without evidence of complications. One donor, who underwent extended right hemihepatectomy, showed evidence of suspected parenchymal congestion in the area of the middle hepatic vein. All patients were discharged between postoperative day 6 and 9 with no complications. Figure 3 presents a schematic graph of early liver function tests until discharge day and on the first evaluation in the outpatient clinic. All recipients were discharged on postoperative days 13-24, except for 1 recipient who died 74 days after liver transplantation due to primary nonfunction. Two patients experienced complications within 3 months, including 1 with severe depression and 1 with biliary anastomosis site

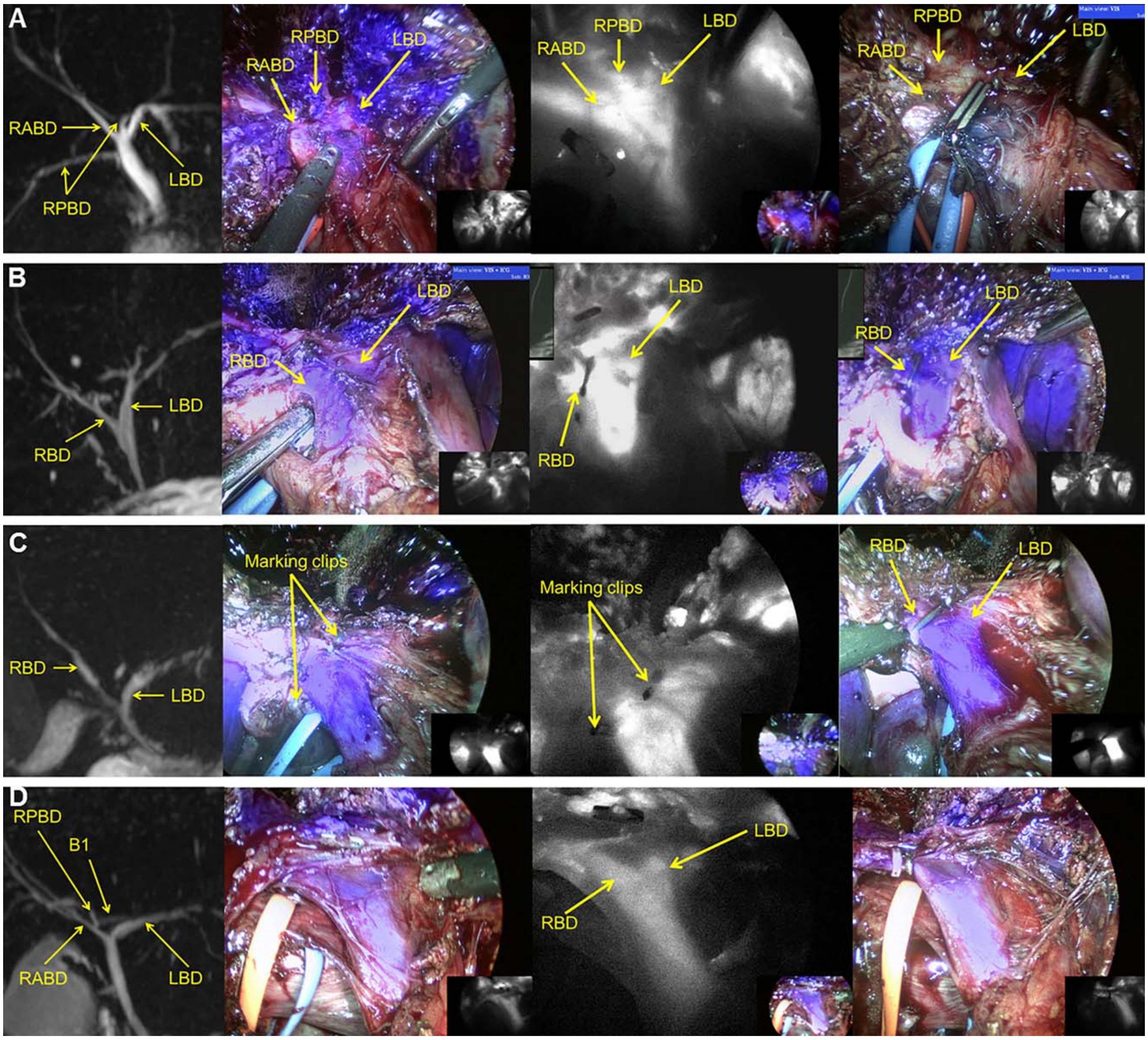

FIG. 1. Preoperative MRCP and ICG fluorescence cholangiography using the LuxEndoBright system in 4 patients: (A) MRCP showed a bile duct near trifurcation, color and monochromatic fluorescent images were consistent with those of MRCP, and actual background color images after clipping showed a patent left bile duct. (B) Fluorescent image showing a conventional bile duct, consistent with the results of MRCP. (C) MRCP and fluorescent images showing conventional bile duct anatomy, clips on soft tissue to mark the appropriate cutting line, and division by the clip with good patency. (D) MRCP showing conventional bile duct anatomy, except that the B1 duct drained into the right posterior bile duct. The bile duct was divided close to the right and left bifurcation without inducing strictures at the left bile duct using a clip and Hem-o-lok.

stricture; the latter patient underwent endoscopic biliary drainage.

Discussion

This study presents our initial experience and evaluates the use of ICG fluorescence cholangiography in laparoscopic donor hepatectomy. As the number of patients undergoing LDLT increases, surgical techniques continue to improve. Laparoscopic donor hepatectomy is increasingly performed, accompanied by increased cosmetic and functional demands by donors. Furthermore, the introduction of 3-dimensional imaging has increased the rates of pure 3-dimensional

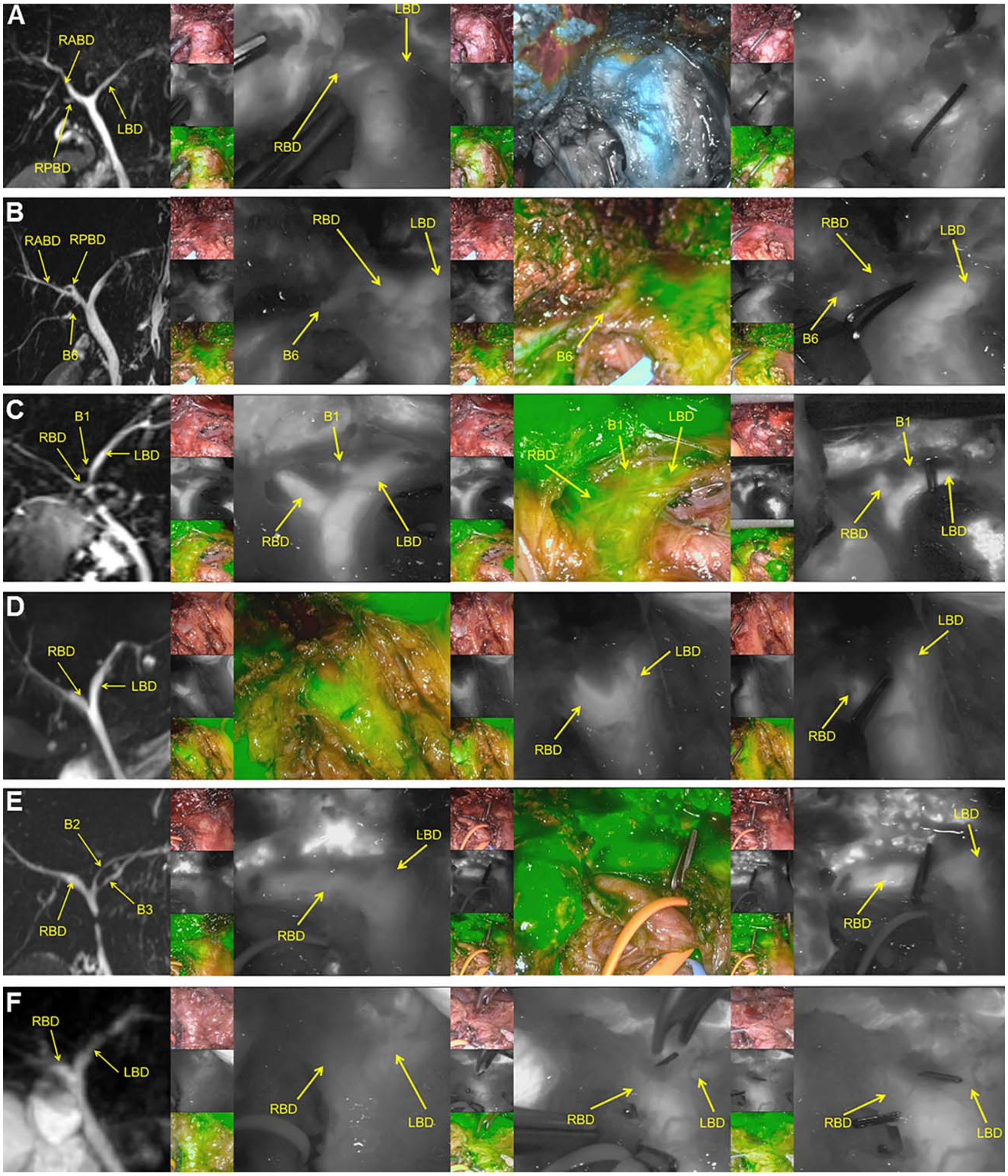

FIG. 2. Preoperative MRCP and ICG fluorescence cholangiography by the Pinpoint system of 6 patients: (A) MRCP and fluorescent images showed conventional bile duct anatomy. The bile duct was clipped after its patency was checked. (B) Fluorescent image consistent with that of MRCP, showing the B6 duct draining separately into the right duct. The bile duct was divided without injuring B6 and the left bile duct. (C) Fluorescent image consistent with that of MRCP, showing the B1 duct draining into the left duct, with clipping more to the left side of the B1 duct for left lateral sectionectomy. (D) MRCP and fluorescent image showed conventional bile duct anatomy. (E) MRCP showing trifurcation of the B2, B3, and right bile ducts and a clipped right bile duct preserving the left bile duct. (F) MRCP and fluorescent images showing conventional bile duct anatomy, marked with clips for appropriate cutting under real-time viewing.

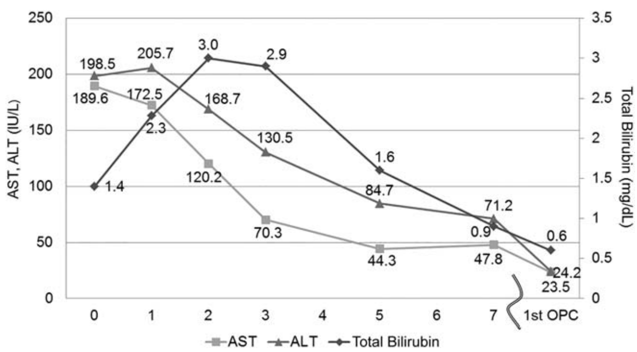

FIG. 3. Schematic graph showing postoperative reductions in liver function test results. Each number represents the mean of 10 patients.

laparoscopic donor hepatectomy because this method results in excellent depth perception and hand-eye coordination.[4] In the absence of definitive anomalies of the bile duct or portal vein, most donor hepatectomies performed at our center since November 2015 have been performed using pure 3-dimensional laparoscopy. However, identifying an appropriate bile duct division point, especially during laparoscopic donor hepatectomy, remains a major issue, because it can prevent biliary complications in both donor and recipient.

Several strategies are available to determine an optimal bile duct division point during living donor hepatectomy. Intraoperative cholangiography has been considered the gold standard in most centers, with bile duct division performed dynamically under the guidance of a C-arm fluoroscope or using the rubber band tagging method.[5] However, intraoperative cholangiography has not been routinely performed at our center since 2009, when it was replaced by preoperative MRCP. Biliary complication rates were lower after than before this switch, with recent MRCPs being regarded as equal in quality to intraoperative cholangiography, providing equally precise and accurate results.[2] If a short division point is expected, the areas around the bile ducts should be carefully dissected, followed by probing through the divided bile duct or cystic duct opening. Intraoperative cholangiography is quite cumbersome, with both the patient and operating room personnel being at risk of radiation exposure. Injecting contrast fluid through the cystic duct is quite difficult and may unwittingly injure the bile duct, especially during laparoscopic surgery. Moreover, probing through the cystic duct is also difficult during laparoscopic surgery.

Real-time ICG near-infrared fluorescence cholangiography may overcome some of these limitations of laparoscopic surgery. First used in ophthalmologic surgery, ICG fluorescent imaging has been used to assess lymphatic flow in patients undergoing surgery for breast and gastric cancer. Because of its fluorescent properties, ICG is being used in hepatobiliary and pancreatic surgery; for example, it is used in cholangiography and in identifying hepatic segments, liver cancer, and lymphatic drainage. To date, this modality has been little used for donor hepatectomy. To our knowledge, this is the first report to describe the use of ICG near-infrared fluorescence cholangiography during various types of laparoscopic donor hepatectomy.

This novel technique enabled intraoperative determination of biliary anatomy and real-time identification of optimal bile duct division points after dissection of the hilar plate. Its correlation with preoperative MRCP was also adequate. This technique identified right and left hepatic duct bifurcation and aberrant hepatic ducts simultaneously during the operation. The bile duct division point could be precisely determined and marked by temporarily clipping soft tissue adjacent to it. Moreover, this imaging technique could assess bile duct patency or strictures after clamping or clipping the division point, with bile ducts finally divided after double clipping.

ICG fluorescence cholangiography has several advantages. First, it is easier and more convenient to perform than conventional radiologic intraoperative cholangiography. Cannulation, which may be cumbersome in laparoscopic surgery, is not necessary for the injection of dye. Second, ICG fluorescence cholangiography is safe. It does not involve radiation, which is unavoidable in conventional cholangiography. The amount of ICG injected (0.05 mg/kg) is very small, and the risk of adverse reactions to ICG injection is negligible because it is approximately 0.003% at doses exceeding 0.5 mg/kg.[3] Third, fluorescent imaging is superior to conventional cholangiography in showing biliary anatomy from various angles at any point during surgery. Fluorescent imaging can help in understanding 3-dimensional spatial direction and relationships of structures around the hilar plate. Fourth, in contrast to conventional cholangiography which is available only in monochromatic images, ICG fluorescence cholangiography results can be displayed as both monochromatic and color images. Overlaying fluorescent color images on actual background color images enhanced the ability to determine exact locations.

These advantages resulted in ICG near-infrared fluorescence cholangiography having additional value over the current standard of care. It increased comfort, improved surgeon's confidence in the bile duct division point, enabled rapid and efficient dissection, and ultimately enabled efficient operation.

ICG near-infrared fluorescence cholangiography has limitations. It can penetrate only approximately 5-10 mm into tissue,[3] and it cannot easily delineate bile ducts covered with thick connective tissue. Transecting the parenchyma and dissecting around the hilar plate are essential to clearly visualize these bile ducts. Because patients with high body mass index are more at risk of having fatty hilum, which requires additional dissection to clearly visualize the bile ducts, this technique may be limited in patients with high body mass index. The patients in our study had a mean body mass index of $23.9 \pm 1.4\,kg/m^2$, which is relatively low. However, we recently used this technique successfully in donors with higher body mass index, up to $30.3\,kg/m^2$, without any complications. These patients required additional dissection around the hilar plate to clearly visualize the bile ducts, and preoperative MRCP images were helpful for further dissection.

This study had several limitations. First, the number of patients was small and the follow-up period was short. In addition, quantitative comparisons between conventional radiologic intraoperative cholangiography or MRCP and ICG fluorescence cholangiography were not easy and required the participation of 3 or 4 doctors in the operating room. Further experience with longer-term follow-up of both donors and recipients is required to develop a standardized, safe, and feasible procedure.

In conclusion, ICG fluorescence cholangiography was successful in delineating the biliary system around the hilar plate and in determining optimal bile duct division points during laparoscopic donor hepatectomy. This technique may be particularly useful in laparoscopic surgery, during which intraoperative cholangiography and probing through the divided bile duct opening or cystic duct opening is relatively difficult. Real-time ICG fluorescence cholangiography may serve as an excellent adjunct to preoperative MRCP.

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