New technical development for pure laparoscopic donor hepatectomy: indocyanine green cholangiography and three-dimensional laparoscopy

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Abstract: In addition to the accumulation of experience, improvements in laparoscopic imaging systems, devices, and introduction of new techniques have been reported to overcome limitations in pure laparoscopic donor surgery. Major limitations of conventional laparoscopy are the lack of depth perception and tactile feedback. As a possible solution for the limitations, the successful application of three-dimensional (3D) visualization has been reported; 3D laparoscopy can provide depth perception and also excellent hand-eye coordination. Optimal intraoperative visualization of the biliary duct anatomy and an appropriate cutting point were considered major issues during pure laparoscopic donor hepatectomy. Recently, real-time intraoperative imaging using indocyanine green (ICG) has been reported as a reliable method that may replace conventional intraoperative cholangiography in pure laparoscopic donor hepatectomy. In this review, we describe the current status of ICG cholangiography and 3D laparoscopy in laparoscopic donor hepatectomy.

Keywords: Living donor liver transplantation; laparoscopic liver resection; indocyanine green (ICG); three-dimensional laparoscopy (3D laparoscopy); intraoperative cholangiogram

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Introduction

Laparoscopic donor hepatectomy is becoming increasingly common. However, pure laparoscopic donor hemihepatectomy is currently performed only at centers that are highly experienced in both donor surgery and laparoscopic hepatectomy. In addition to the accumulation of experience, improvements in laparoscopic imaging systems, devices, and introduction of new techniques have been reported to overcome the limitations associated with pure laparoscopic donor surgery.

One of the major limitations of laparoscopy are the lack of depth perception and tactile feedback (1). Recent advances in laparoscopic imaging systems have increased the performance of pure laparoscopic donor hepatectomy. For example, three-dimensional (3D) visualization can provide depth perception as well as excellent hand-eye coordination (2). The successful application of 3D laparoscopy for increasing the application of laparoscopic donor hepatectomy has recently been reported (3).

Although an intraoperative cholangiogram with contrast injection via the cystic duct has been established as a standard technique in the conventional open procedure and even hybrid donor hepatectomy (4-6), that procedure can be cumbersome in pure laparoscopic surgery. As a result, optimal intraoperative visualization of the biliary duct anatomy and establishment of an appropriate cutting point have been considered major problematic issues associated with laparoscopic donor hepatectomy (7). The introduction of intraoperative imaging using indocyanine green (ICG) has been reported in laparoscopic hepatobiliary surgery (8,9). In pure laparoscopic donor surgery as well, ICG cholangiography has recently been reported as a reliable method (10).

We herein report the current status of ICG cholangiography and 3D laparoscopy in laparoscopic donor hepatectomy.

ICG near-infrared fluorescence cholangiography (NIFC)

The establishment of an appropriate point of the bile duct division of the graft liver is the most important point for preventing biliary complications of both donors and recipients. Since donor safety should be the top priority in living donor liver transplantation, the bile duct must be divided with great caution.

In living donor hepatectomy, intraoperative cholangiography has been considered the standard procedure in most centers, with bile duct division performed under the guidance of a C-arm fluoroscope with a radiopaque marker (11,12). However, a standard cholangiogram is not always easy to perform in pure laparoscopic donor hepatectomy. Even at highly experienced centers, in their initial experience, the application of pure laparoscopic donor hepatectomy has been limited to donors with a simple biliary anatomy (2,13,14).

Troisi *et al.* mentioned the potential utility of ICG NIFC in laparoscopic donor hepatectomy in their report on their initial experience with laparoscopic donor hepatectomy (7). ICG has been used clinically to estimate the cardiac output and liver function since its approval by the U.S. Food and Drug Administration (FDA) in 1954 (9). Protein-bound ICG was found to emit fluorescence, peaking at about 840 nm under illumination with near-infrared light (750–810 nm) (15). Because little light at 840 nm is absorbed by hemoglobin or water, the fluorescence signals emitted by protein-bound ICG can be visualized.

In the field of hepatobiliary surgery, in the late 2000s, some Japanese groups reported methods of intraoperatively visualizing the hepatobiliary structures using ICG-fluorescence imaging (8,16,17). For an intraoperative cholangiogram with ICG-fluorescence imaging, intrabiliary injection and intravenous injection have been reported as the route of ICG. Ishizawa *et al.* reported fluorescent cholangiography with ICG excreted into bile following preoperative intravenous injection (8). Cholangiography with the injection of 2.5 mg of ICG diluted into 1 mL solution was first reported by Ishizawa *et al.*; according to that report, ICG fluorescence in the extrahepatic bile ducts continues up to 6 h after the injection (8).

Mizuno *et al.* reported the application of intraoperative ICG cholangiography in conventional open donor left hepatectomy in 2010 as the first report of this concept (18). In that case report, ICG (0.025 mg/mL) was injected through a transcystic tube. Following this report, several case reports and case series have been published (19,20) (*Table 1*).

With respect to techniques for the administration of ICG, the intravenous injection of ICG compared to the conventional direct injection of contrast into the bile duct may be associated with saving time. Also, the intravenous injection may ignore the difficulty and avoid bile duct injury caused by the catheterization into the bile ducts for injecting contrasts, especially in laparoscopic surgery.

Hong *et al.* first reported the use of ICG NIFC with intravenous injection during various types of laparoscopic donor hepatectomy (10) (*Table 1*). In their prospective study of ten cases (right hemihepatectomy in eight donors, extended right hemihepatectomy in 1 donor, left lateral sectionectomy with *in vivo* reduction in 1), the history of iodine allergy was preoperatively checked in all donors. ICG (0.05 mg/kg) was injected intravenously 30–60 minutes before exposure of the hilar plate with considering the timing of bile excretion (21). After exposing the anterior surface of the hilar plate, the distal bile duct was temporarily clamped to congest the bile and eventually visualize the bile duct. In all donors, the biliary system around the hilar plate, including any aberrant hepatic ducts, was visualized (10). Concerning the safety of ICG cholangiography, Hong *et al.* mentioned that the risk of an adverse reaction to ICG injection is negligible because the amount of ICG injected at a dosage of 0.05 mg/kg is approximately 0.003% at doses exceeding 0.5 mg/kg (10). The amount of ICG injected for the liver function estimation is 0.5 mg/kg (22,23). Furthermore, ICG cholangiography does not require consideration of the risk of radiation exposure for donors or operating room personnel.

Recently, a single-blind, randomized, 2-arm trial comparing the efficacy of ICG NIFC versus white light (WL) alone during laparoscopic cholecystectomy was reported (24). In that study, the detection rates for seven

Table 1 Summary of findings of previous studies about ICG cholangiography in donor hepatectomy

Authors	Year	Journal	Summary
Mizuno *et al*.	2010	*Am J Transplant*	A case report. ICG (0.025 mg/mL) was administered through a transcystic tube in open donor hepatectomy. The left hepatic duct, anterior and posterior branch of the right hepatic duct were clearly visualized
Mizuno *et al*.	2014	*Transplant Proc*	Eighteen donors underwent ICG cholangiography for open donor hepatectomy. Since the introduction of ICG cholangiography, the authors had not encountered any biliary complication in either donors or recipients
Tomassini *et al*.	2015	*Acta Chir Belg*	ICG cholangiography was conducted in 11 fully laparoscopic left donor hepatectomy using five different protocols. ICG cholangiography is an additional method to visualize the lobar ducts, but still insufficient for the segmental ducts
Hong *et al*.	2017	*Liver Transpl*	ICG (0.05 mg/kg) was injected intravenously 30–60 minutes before exposure of the hilar plate during laparoscopic hepatectomy in ten donors. The biliary system around the hilar plate, including any aberrant hepatic ducts, could be delineated in all 10 donors
Hong *et al*.	2017	*Surg Endosc*	Using a 3D view and ICG cholangiography, pure 3D laparoscopic living donor right hemihepatectomy is feasible in a donor with separate right posterior and right anterior hepatic ducts
Suh *et al*.	2018	*Am J Transplant*	The proportion of grafts with multiple bile duct orifices was significantly higher in the pure laparoscopic donor hepatectomy with ICG cholangiography group than in the conventional donor hepatectomy group (53.3% *vs*. 26.2%; P=0.010)

ICG, indocyanine green; 3D, three-dimensional.

biliary structures before and after surgical dissection were evaluated. The detection rates before dissection were significantly higher in the NIFC group for all seven biliary structures than in WL group. In addition, an increased body mass index was reported to be associated with a reduced detection rates in both groups, especially before dissection.

For wide application of ICG cholangiography into the field of donor hepatectomy, we should pay attention to the limitations associated with ICG cholangiography performed by presently available devices. For example, ICG fluorescence can penetrate approximately 5–10 mm into the tissue, and it cannot easily visualize bile ducts surrounded with thick connective tissue (21). The importance of preserving the surrounding tissue of the bile duct to maintain optimal vascularization and prevent biliary complication has been well recognized (4). Therefore, we should not compromise the vascularization of the bile duct for better visualization when using ICG cholangiography.

Suh *et al.* retrospectively evaluated the outcomes of donors who underwent pure laparoscopic donor right hepatectomy with ICG cholangiography (n=45) compared with those who underwent conventional donor right hepatectomy (n=42) (25). While both groups had a comparable length of postoperative hospital stay and rates of complications and re-hospitalization, the proportion of grafts with multiple bile duct orifices was significantly higher in the pure laparoscopic donor hepatectomy with ICG cholangiography group than in the conventional donor hepatectomy group (53.3% *vs*. 26.2%; P=0.010) (25) (*Table 1*). Suh *et al.* hypothesized that this might be because surgeons may still lack confidence in determining the point of bile duct division and move to the right side more naturally, despite preoperative magnetic resonance cholangiopancreatography (MRCP) images and ICG cholangiography. Whereas, in the conventional open procedure, Takatsuki *et al.* reported the efficacy of encircling the bile duct using a radiopaque marker filament for determining the precise point of bile duct division under real-time C-arm cholangiography to reduce the incidence of multiple bile ducts (4). In addition to confirming the quality of visualization achieved by ICG cholangiography, the optimal procedure for determining the appropriate cutting line of the bile duct should be discussed in future studies.

Recently, some centers have reported successful pure laparoscopic right donor hepatectomy in donors with variant biliary anatomy (26,27) (*Table 1*). Although these reports support the wider spread of laparoscopic donor surgery, liver transplant surgeons should be reminded that these successful cases have been reported from highly experienced transplant teams with expertise in performing laparoscopic donor surgery.

Table 2 Summary of findings of previous studies about 3D laparoscopy in hepatectomy

Authors	Year	Journal	Summary
Velayutham *et al.*	2016	*Surg Endosc*	Twenty patients undergoing laparoscopic liver resection by high-definition 3D laparoscope between were matched to a retrospective control group of patients who underwent LLR by 2D laparoscope. The operative time was significantly shorter in the 3D group when compared to 2D group
Suh *et al.*	2016	*Liver Transpl*	The first report of two cases of pure laparoscopic extended right hepatectomy, purely using 3D laparoscopy
Hong *et al.*	2017	*Surg Endosc*	Using a 3D view and ICG cholangiography, pure 3D laparoscopic living donor right hemihepatectomy is feasible in a donor with separate right posterior and right anterior portal veins
Lee *et al.*	2018	*Transplantation*	As a single center experience, results of 115 cases of pure laparoscopic living donor hepatectomy with 3D laparoscopy were reported. No donors developed complications during the recent period. The operative time (293.6 *vs*. 344.4 minutes; P<0.001) and hospital stay (7.3 *vs*. 8.3 days; P=0.002) were significantly shorter during the most recent period
Hong *et al.*	2018	*J Gastrointest Surg*	Left lateral sectionectomy with in situ reduction to obtain a monosegment graft was successfully conducted by a pure 3D laparoscopic procedure in a case of pediatric living donor liver transplantation
Park *et al.*	2019	*Ann Hepatobiliry Pancreat Surg*	Pure living donor right hepatectomy with 3D laparoscopy safe and feasible in six donors with type II and III portal vein variations

LLR, laparoscopic liver resection; ICG, indocyanine green; 2D, two-dimensional; 3D, three-dimensional.

3D laparoscopy

Compared to the conventional two-dimensional (2D) video-assisted system, the 3D video-assisted system was reported to provide depth perception and precise measurement of the anatomical space (28). In addition, it provides excellent hand-eye coordination (1). The clinical benefit of 3D displays during laparoscopic/thoracoscopic surgery has been reported in various types of surgery, including gastrectomy, esophagectomy, rectal surgery, etc. (28-31). For example, a significantly shortened operative time was reported in gastrectomy, esophagectomy, radical resection for rectal cancer, and thoracoscopic lobectomy. In addition, in the field of liver surgery, Velayutham *et al.* reported a reduced operating time by 3D visualization compared to 2D visualization in laparoscopic liver resection (1).

Suh *et al.* noted that the introduction of a 3D laparoscopy for liver surgery in 2015 resulted in the more frequent use of the laparoscopic-assisted procedure for donor hepatectomy; thereafter, the first pure laparoscopic donor extended right hepatectomy using 3D laparoscopy was performed (2). Recently, Lee *et al.* reported their experiences with pure laparoscopic donor right hepatectomy with the largest number of donors (n=115) from a single center (3). At present, further experiences with 3D laparoscopy and ICG cholangiography are being accumulated without any selection criteria, such as cases with anatomical variance for pure laparoscopic donor hepatectomy (25). Findings of previous studies are summarized in *Table 2*.

The successful application of 3D laparoscopy accompanied with ICG cholangiography in laparoscopic donor hepatectomy has been reported in cases demanding complex procedures. Hong *et al.* reported a successful case of left lateral sectionectomy by a pure 3D laparoscopic procedure with *in situ* reduction to obtain a monosegment graft in a case of pediatric living donor liver transplantation (32). Park *et al.* recently reported successful pure laparoscopic donor right hepatectomy with 3D laparoscopy and ICG cholangiography in donors with type II and III portal vein variations with a comparison between pure laparoscopic donor right hepatectomy and the conventional open procedure (33).

Concerning scientific evidence, as shown in other types of surgery, although 3D laparoscopy may offer clinically quantitative benefits, such as a shorter operative time, comparative studies between laparoscopic donor hepatectomy with 3D laparoscopy and 2D laparoscopy with a sufficient number of cases have not yet been published.

Conclusions

It is apparent that advances in surgical device and techniques such as ICG cholangiography and 3D laparoscopy have offered benefits for the application of pure laparoscopic surgery to living donor hepatectomy. Furthermore, in highly skilled teams or centers, these techniques have been successfully used to expand the indication of pure laparoscopic donor hepatectomy. Thus far, however, the benefits of these techniques have been reported mostly from expert teams. The accumulation of more experiences will bring new information on not only the benefits but also the obstacles that should be considered in order to expand the application of these techniques for safe laparoscopic donor hepatectomy.

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