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World J Gastroenterol 2018 July 7; 24(25): 2647-2784



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World Journal of Gastroenterology (*WJG*) is now indexed in Current Contents[®]/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch[®]), Journal Citation Reports[®], Index Medicus, MEDLINE, PubMed, PubMed Central and Directory of Open Access Journals. The 2018 edition of Journal Citation Reports[®] cites the 2017 impact factor for *WJG* as 3.300 (5-year impact factor: 3.387), ranking *WJG* as 35th among 80 journals in gastroenterology and hepatology (quartile in category Q2).

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NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
 ISSN 1007-9327 (print)
 ISSN 2219-2840 (online)

LAUNCH DATE
 October 1, 1995

FREQUENCY
 Weekly

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 7901 Stoneridge Drive, Suite 501,
 Pleasanton, CA 94588, USA
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PUBLICATION DATE
 July 7, 2018

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Minimally invasive donor hepatectomy, are we ready for prime time?

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Conflict-of-interest statement: None of the authors has any conflict of interest.

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Manuscript source: Invited manuscript

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Received: March 29, 2018

Peer-review started: March 30, 2018

First decision: May 17, 2018

Revised: May 25, 2018

Accepted: June 9, 2018

Article in press: June 9, 2018

Published online: July 7, 2018

Abstract

Minimally invasive surgery potentially reduces operative morbidities. However, pure laparoscopic approaches to donor hepatectomy have been limited by technical complexity and concerns over donor safety. Reduced-wound donor hepatectomy, either in the form of a laparoscopic-assisted technique or by utilizing a mini-laparotomy wound, *i.e.*, hybrid approach, has been developed to bridge the transition to pure laparoscopic donor hepatectomy, offering some advantages of minimally invasive surgery. To date, pure laparoscopic donor left lateral sectionectomy has been validated for its safety and advantages and has become the standard in experienced centres. Pure laparoscopic approaches to major left and right liver donation have been reported for their technical feasibility in expert hands. Robotic-assisted donor hepatectomy also appears to be a valuable alternative to pure laparoscopic donor hepatectomy, providing additional ergonomic advantages to the surgeon. Existing reports derive from centres with tremendous experience in both laparoscopic hepatectomy and donor hepatectomy. The complexity of these procedures means an arduous transition from technical feasibility to reproducibility. Donor safety is paramount in living donor liver transplantation. Careful donor selection and adopting standardized techniques allow experienced transplant surgeons to safely accumulate experience and acquire proficiency. An international prospective registry will advance the understanding for the role and safety of pure laparoscopic donor hepatectomy.

Key words: Laparoscopic donor hepatectomy; Living donor liver transplantation; Minimally invasive surgery

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Core tip: Reduced-wound donor hepatectomy has been developed to bridge the transition to pure laparoscopic

donor hepatectomy, offering some advantages of minimally invasive surgery. To date, pure laparoscopic donor left lateral sectionectomy has been validated for its safety and advantages, while pure laparoscopic approaches to major left and right liver donation have been reported for their feasibility in expert hands. Careful donor selection and adopting standardized techniques allow experienced transplant surgeons to accumulate experience in this complex procedure. An international prospective registry will advance the understanding for the role and safety of pure laparoscopic donor hepatectomy.

Au KP, Chok KS. Minimally invasive donor hepatectomy, are we ready for prime time? *World J Gastroenterol* 2018; 24(25): 2698-2709 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v24/i25/2698.htm> DOI: <http://dx.doi.org/10.3748/wjg.v24.i25.2698>

INTRODUCTION

Liver transplantation is the most effective treatment for end-stage liver disease. Shortage of cadaveric grafts has encouraged the rapid development of living donor liver transplantation (LDLT). However, donor morbidity remains the primary concern and the major bottleneck for LDLT. Donor operation poses a 25%-35% morbidity^[1,2] to a healthy individual, and half of morbidities are related to abdominal wall trauma, including hernia, intestinal obstruction and chronic wound pain^[2]. Permanent large incision brings physical and mental stress to young women.

On the other hand, the minimally invasive approach to liver resection has gained wide acceptance for oncological indications^[3]. Laparoscopic hepatectomy has been carried out for liver tumours with minimal mortality and morbidity^[4]. Various reviews and meta-analyses have validated the benefits of this technique, which include reduced blood loss, less postoperative pain and hastened recovery^[5-11]. Considering the advantages of laparoscopic hepatectomy, it appears legitimate to transfer these benefits to liver donors. To such an end, minimally invasive donor hepatectomy was introduced to reduce the morbidity of open hepatectomy^[12]. However, the development of minimally invasive donor hepatectomy has advanced at a slow and arduous pace. The first pure laparoscopic right liver donation^[13] was reported only 15 years after the first laparoscopic right hepatectomy^[14]. Concerns still exist regarding the safety and outcomes for minimally invasive donor hepatectomy. To provide insights into wider application this technique, we performed a comprehensive literature review to appreciate the existing challenges and current status of minimally invasive donor hepatectomy.

A literature search was performed on PubMed (US National Library of Medicine, National Institutes of Health, United States) for relevant English articles with a

combination of keywords: "LDLT" with "laparoscopy" and/or "laparoscopic assisted" and/or "hand assisted" and/or "subcostal incision" and/or "upper midline incision" and/or "robotic assisted". The references of the selected papers were reviewed for additional relevant articles.

DEFINITIONS

The minimally invasive approaches include reduced-wound (RW), pure laparoscopic (PL) and robotic-assisted (RA) procedures. In RW donor hepatectomy, resection is facilitated by a mini-laparotomy incision. RW approaches comprise hand-assisted laparoscopy^[3], where resection is effected through laparoscopy but expedited by a hand port; the laparoscopic-assisted or hybrid approach^[3], where laparoscopic mobilization (with or without hand assistance) is followed by open parenchymal transection; and mini-laparotomy, where resection is performed with an open technique via a reduced-length upper midline wound. In PL donor hepatectomy, liver resection is completed through laparoscopic ports. An auxiliary incision, usually suprapubic, is used only for graft retrieval. When a robotic system is involved, the procedure is considered an RA donor hepatectomy.

CHALLENGES

Limited role of LDLT in the West

LDLT expanded the donor pool and has become the predominant form of liver transplantation in the East due to the critical shortage of cadaveric donors. In the West, where deceased grafts are more widely available, LDLT is less desirable considering additional risks on the healthy live donor. In the United States, LDLT constitutes less than 5% of liver transplants^[15]. None of the centres performed more than 30 live donor operations last year^[15]. Limited volumes and experience have restricted the possibility of technical innovation. Although pioneered in Europe^[12], minimally invasive donor hepatectomy has only been readily reproduced in Asia, where LDLT continued to flourish.

Albeit unpopular, LDLT continues to play a unique role in the West. When waitlist mortality is considered, recipients with access to a living donor have survival benefits^[16]. In a cohort of patients listed for a liver graft in the United States, the risk of death of LDLT recipients was 50% less than those waiting for a cadaveric liver graft^[17]. LDLT is most beneficial for transplant candidates with low priority to a cadaveric graft but at high risk of death while waiting for one^[18]. These patients include those with low Model for End-stage Liver Disease scores but significant complications from portal hypertension, as well as patients with more advanced hepatocellular carcinoma, *i.e.*, at high risk to progress beyond criteria. In fact, with continuing efforts to foster live donation, the numbers of LDLTs have been growing in Canada^[19]. Toronto has established the largest LDLT centre in the West, with LDLT accounting

for 30% of total liver transplants^[20]. Their enthusiasm for promoting LDLT will promote ongoing technical advancements for the procedure.

Technical complexity

Laparoscopy revolutionized abdominal surgery, promoting the advantages of reduced morbidity and hastened recovery, and offering long-term outcomes comparable to those of open surgery^[21-23]. While laparoscopy has become standard in gastric and colorectal surgery^[22,23], its application in liver surgery has developed at a much slower pace. Complex vascular and biliary variations and potential major bleeding during parenchymal transection have made laparoscopic liver resection technically challenging. Reports indicate an average learning curve of 30-60 laparoscopic hepatectomies is required before operating time and blood loss can be optimized^[24,25].

Donor hepatectomy entails additional technical demands. Precise transection of the bile duct is crucial to reduce biliary complications in both donor and recipient. Maintaining the correct parenchymal transection plane minimizes liver congestion and preserves graft function. Presence of vascular and biliary variations poses extra challenges. With respect to laparoscopic donor hepatectomy, parallel expertise in laparoscopic liver surgery and donor hepatectomy are required^[26]. Laparoscopic left lateral sectionectomy, when performed for liver donation, requires approximately 20 procedures for an experienced transplant surgeon to achieve optimized blood loss and warm ischaemic time^[27,28]. A precipitous learning curve is encountered before one can perpetuate proficiency in this complex procedure.

Donor safety

Donor safety is paramount in LDLT. Donor hepatectomy imposes 0.1%-0.2% mortality^[29] and 25%-35% morbidity^[1,2] to an healthy individual. As such, safety has been the primary obstacle to a wider application of minimally invasive approaches in the donor arena. During the early development of laparoscopic hepatectomy, management of venous haemorrhage during hepatic transection has been particularly problematic. High-flow venous tributaries within the liver parenchyma make laparoscopic transection technically challenging. However, through accumulation of experience, technical refinements have paved the way for safer approaches to liver resection. Surprisingly, lower blood loss has been achieved with laparoscopic hepatectomy^[5-11], thanks to improved visualization and positive pressure from the pneumoperitoneum.

Biliary complications occur after 10% of donor hepatectomies^[1], the majority of which require intervention. The most common site of a bile leak is the transection surface, from caudate branches or from the hilar plate^[30]. Parenchymal transection in laparoscopic hepatectomy is expedited with energy devices, while small bile duct tributaries are usually controlled with clips instead of ligatures. The initial concern for more bile leaks after

laparoscopic hepatectomy was unfounded after a meta-analysis revealed a lower leak rate of less than 2% in minimally invasive hepatectomy^[4]. It is believed that laparoscopic magnification provides superior visibility for identifying tributary branches and minor leakages.

Meanwhile, laparoscopic management of bile duct division remains a topic of debate. Determining the site of bile duct transection is a unique and critical step in donor hepatectomy. Dividing too close to graft produces multiple bile duct openings, while keeping too flush to donor poses risk of biliary stricture. Presence of anatomical variations imposes additional technical challenges. An aberrant right hepatic duct occurs in 15% of the population, and 6% of the right posterior duct drains into left hepatic duct^[31]. In the setting of donor hepatectomy, laparoscopy has to prove at least equivalent performance in managing bile duct transection before its application can be expanded.

Recipient outcomes

In PL and RA donor hepatectomy, the liver graft is retrieved through a small wound after enveloping in a plastic bag. The initial fear of a longer warm ischaemic time and its undesirable consequences has deprived acceptance for more innovative approaches. From the reported series, the donor warm ischaemic time varied from 3-12 min for PL approaches^[13,32-37] to 8-15 min for RA approaches^[38,39], which were not prolonged when compared with open procurement. More importantly, initial experiences in from left lateral sectionectomy showed that graft survivals were not different from the open approach^[40].

PRESENT STATUS

Reduced wound donor hepatectomy

In the first decade of this century, application of PL donor hepatectomy was greatly limited by technical difficulties. Transplant surgeons refrained from PL donor hepatectomy in fear of damaging vital vascular pedicles and potential catastrophic bleeding. Alternative strategies were developed to reduce wound length while retaining the reliability of conventional hepatectomy. In the hand-assisted technique, a hand port allowed for versatile liver traction to facilitate exposure and haemostasis during transection^[41]. Two hand-assisted right lobe donor hepatectomies were reported in a small series^[42]. Reduced wound was more often utilized, as in the hybrid technique^[43], where parenchymal transection was performed as an open procedure, after the liver was laparoscopically mobilized then retracted into the upper midline wound. The need for subcostal incision was avoided, while the safety of open transection was preserved. The hybrid technique gained popularity with multiple series reported for both right^[42-52] and left lobe donation^[44,47,49,52]. Over 200 hybrid donor hepatectomies have been performed worldwide with zero mortality and morbidities at least comparable to those of conventional

open surgery.

Transplant surgeons' passion for minimally invasive donor hepatectomy has not been limited by laparoscopy. Experienced centres advocated open right lobe donation through a 10-14 cm upper midline wound without laparoscopic assistance^[46,53-56]. This mini-laparotomy approach represents a philosophy distinct from that of minimally invasive surgery. Laparoscopy provides improved visualization and laparoscopic instruments minimize tissue manipulation, both of which contribute to the potential benefits of minimally invasive surgery. Mini-laparotomy is the pure pursuit of wound reduction while preserving the essence of open surgery. The technique became the standard practice in high-volume LDLT centres in South Korea^[54].

Donor and recipient outcomes of hybrid and mini-laparotomy approaches are summarized in Tables 1 and 2, respectively. Although inconsistently reported in case series, the benefits of reduced blood loss, wound pain and overall morbidity have been concluded in a meta-analysis comparing RW donor hepatectomy and open donor hepatectomy^[57]. Types of complications were not specified. Neither was there a clarification of different types of RW donor hepatectomy. As hybrid and mini-laparotomy represented distinct approaches towards minimally invasive surgery, it is appealing to investigate whether the benefit of RW donor hepatectomy is a result of improved visualization or reduced abdominal wall trauma or a combination of the two.

Another meta-analysis by Berardi *et al.*^[58] might provide information regarding the performance of hybrid donor hepatectomy. The minimally invasive donor hepatectomy group in the study comprised mostly hybrid left or right donor hepatectomy ($n = 227$, 89%) and a few pure laparoscopic left lateral sectionectomies ($n = 27$, 11%). No mini-laparotomy patients were included. Based on the pooled data, hybrid hepatectomy and PL donor hepatectomy were associated with fewer wound-related (OR = 0.41, $P = 0.04$) but similar biliary complications when compared with open donor hepatectomy. Reduction in analgesia requirement (MD = -0.54, $P = 0.04$) and hospital stay (MD = -1.6, $P = 0.004$) was observed. Hybrid donor hepatectomies have validated its safety and potential benefits to the donor. This technique allows transplant surgeons to accumulate experience before converting to pure laparoscopic approaches. The only question that remains is likely that of long-term graft outcomes. Nevertheless, the contributions of hybrid donor hepatectomy to the evolution of minimally invasive donor hepatectomy cannot be overemphasized.

Pure laparoscopic donor Hepatectomy

Left lateral sectionectomy: Laparoscopic approaches to donor hepatectomy become least controversial with respect to left lateral section donation. The Falciform ligament, where the vertical portion of the left portal vein is situated, provides a well-defined surface landmark for left lateral sectionectomy^[59]. A

transection plane along its right side exposes the hilar plate for left portal vein and bile duct transection. The constant anatomy and a small parenchymal transection surface offer technical advantages. Indeed, left lateral section was the first living donor liver graft harvested conventionally^[60] and laparoscopically^[12].

Since its feasibility was reported in 2002^[12], PL donor left lateral sectionectomy has been validated subsequently in several centres^[28,40,61-64]. The results of these studies are summarized in Table 3. According to case-control studies, the PL approach is associated with reduced blood loss, shortened length of stay and comparable donor morbidity over open surgery^[28,40,61]. To date, over 120 PL donor left lateral sectionectomies have been performed throughout the world^[63], and the approach is regarded as the standard procedure in specialized centres. PL donor left lateral sectionectomy appears to be a safe and reproducible approach to LDLT.

Right hepatectomy: The right liver graft is the main form of LDLT providing adequate functional liver to the recipient^[65]. The first PL donor right hepatectomy represented another quantum leap for minimally invasive donor hepatectomy. The procedure was first reported by Soubrane *et al.*^[13] in 2013, followed by several small-volume case series^[32-37,66,67] (Table 4). The pioneering surgeons' achievement had not been readily reproduced until a larger series became available earlier this year^[37].

Suh *et al.*'s series of 45 PL donor right hepatectomies derived from the work of a single surgeon, who had tremendous experience encompassing over 1000 open donor hepatectomies as well as 200 laparoscopic hepatectomies. In the early phase, donors with single right portal vein and right hepatic ducts were selected. After sufficient experience, additional selection criteria were no longer applied, and the PL approach was performed in 90% of right lobe donors in the later phase. Biliary imaging was a combination of preoperative magnetic resonance cholangiopancreatography and intraoperative indocyanine green (ICG) cholangiography, abbreviating the need for conventional operative cholangiogram. Compared with historical controls who had undergone open right lobe donation by the same surgeon, PL donor right hepatectomy took longer (331 ± 50 min vs 280 ± 40 min, $P < 0.001$), had more blood loss (436 ± 170 mL vs 338 ± 188 mL, $P = 0.013$) and longer warm ischaemic time (12.6 ± 4.4 mL vs 5.4 ± 3.6 mL, $P < 0.001$). Incidences of donor (8.9% vs 11.9%, $P = 0.73$) and recipient complications (24.4% vs 26.2%, $P = 0.85$) were similar.

Notably, the PL approach produced more liver grafts with multiple bile duct openings (53% vs 26%, $P < 0.001$). The surgeon might err on the safe side to divide the bile duct close to the graft side. However, more bile duct openings made recipient biliary anastomosis more challenging, potentially compromising this outcome. In this series, donor bile duct was initially closed with intra-

Table 1 Outcomes of hand-assisted and laparoscopic-assisted donor hepatectomy

	LLS	Left	Right	OT (min)	Blood loss (mL)	WIT (min)	HS (d)	Donor Cx	Recipient Cx
Hand-assisted									
Suh <i>et al</i> ^[42] , 2009			2	765-898	-	-	10-14	2 (100%) ^a	2 (100%) ^b
Hybrid									
Comparative study									
Kurosaki <i>et al</i> ^[44] , 2006 ^c		10/12	3/1	363 ± 33/320 ± 68	302 ± 191/283 ± 371	3	11.0 ± 2.7/12.8 ± 4.9	-	^d
Baker <i>et al</i> ^[45] , 2009			33/33	265 ± 58 ¹ /316 ± 61	417 ± 217/550 ± 305	-	4.3/3.9	7 (21.2%) ^e	-
Thenappan <i>et al</i> ^[46] , 2011 ^f	8/7			312 ± 68/324 ± 106	1033 ± 1096/733 ± 457	-	6.0 ± 2.0/6.4 ± 3.7	2 (13.3%) ^g	7 (46.7%) ^h
Choi <i>et al</i> ^[48] , 2012 ⁱ			40/20/90	279 ± 72/384 ± 42 ¹ /303 ± 61	450 ± 316/870 ± 653 ¹ /532 ± 323	-	11.8 ± 4.5/12.1 ± 2.8/12.0 ± 3.6	5 (12.5%)/6 (30.0%) ^k	-
Marubashi <i>et al</i> ^[49] , 2013 ¹	17/32	14/47		435 ± 103 ¹ /383 ± 73	353 ± 396/456 ± 347		10.3 ± 3.3 ¹ /18.3 ± 16.7	3 (9.7%) ^m	-
Nagai <i>et al</i> ^[55] , 2012 ⁿ			19/30	371 ± 52/363 ± 53	212 ± 114 ¹ /316 ± 121	-	5.9 ± 1.2 ¹ /7.8 ± 2.3	7 (25.0%) ^o	10 (35.7%) ^p
Makki <i>et al</i> ^[50] , 2014			26/24	703 ± 124/675 ± 118	337 ± 89/396 ± 126	-	-	4 (15.4%) ^q	2 (7.8%) ^r
Shen <i>et al</i> ^[51] , 2016 ^s			28/20	386 ± 49/366 ± 45	384 ± 180/416 ± 164	3.0 ± 1.6/2.9 ± 1.5	7.4 ± 2.5/7.3 ± 1.6	5 (17.9%) ^t	-
Kitajima <i>et al</i> ^[52] , 2017		35/38		459 (310-633) ¹ /403 (256-597)	245 (22-1840)/400 (20-1638)	-	12 (7-50)/12 (8-31)	8 (22.9%) ^u	13 (17.1%) ^v
			41/39	431 (310-651)/402 (315-588)	201 (10-1559) ¹ /313 (55-2165)	-	12 (8-27)/ 12 (7-40)	9 (22.0%) ^w	
Case series									
Koffron <i>et al</i> ^[43] , 2006			1	235	150	-	3	0	0
Suh <i>et al</i> ^[42] , 2009			7	310-575	-	-	8-17	4 (57.1%) ^x	5 (71.4%) ^y
Soyama <i>et al</i> ^[47] , 2012		9	6	456 (328-581)	520 (230-1000)	-	-	1 (6.7%) ^z	-

¹Statistically significant; ^aIntra-abdominal collection and pleural effusion in both patients; ^bBiliary stricture and stroke in one patient and bile leak and biliary stricture in the other patient; ^cCombined results of left and right hepatectomy; ^dThree (23%) early graft loss within 2 mo; ^eSmall bowel injury (*n* = 1), biloma (*n* = 1) and other complications (*n* = 3); ^fCombined results of 15 hybrid and mini-laparotomy compared with 15 open operations, types of graft other than left lateral section not specified; ^gBile leak (*n* = 1) and incisional hernia (*n* = 1); ^hBile leak (*n* = 2), vascular complications (*n* = 3), intra-abdominal collection (*n* = 1) and chylous ascites (*n* = 1); ⁱSingle-port laparoscopic-assisted (*n* = 40) vs laparoscopic-assisted (*n* = 20) vs open (*n* = 90); ^jIntra-abdominal bleeding (*n* = 2), bile leak (*n* = 3) and pleural effusion (*n* = 1); ^kWound complication (*n* = 2), diaphragmatic hernia (*n* = 1), pleural effusion (*n* = 2) and biliary stricture (*n* = 1); ^lCombined results of donor left lateral sectionectomy and left hepatectomy; ^mDelayed gastric emptying requiring endoscopy (*n* = 2) and grade I complication (*n* = 1); ⁿCombined results of 19 hybrid and 9 mini-laparotomies compared with 30 open operations; ^oIntra-abdominal bleeding (*n* = 1), bile leak (*n* = 1), intra-abdominal collection (*n* = 1), ileus (*n* = 2), deep vein thrombosis (*n* = 1) and phlebitis (*n* = 1); ^pBile leak (*n* = 2), biliary stricture (*n* = 2), hepatic artery stricture (*n* = 2), hepatic vein stricture (*n* = 2) and intra-abdominal collection (*n* = 2); ^qPleural effusion requiring tapping (*n* = 1) and grade I complications (*n* = 3); ^rBile leak (*n* = 1) and biliary stricture (*n* = 1); ^sLaparoscopic-assisted (*n* = 28) compared against mini-laparotomy (*n* = 20); ^tIntra-abdominal bleeding (*n* = 1), ileus (*n* = 1), pneumonia (*n* = 1) and pleural effusion (*n* = 2); ^uBile leak (*n* = 3), intra-abdominal collection (*n* = 1), pneumonia (*n* = 1) and grade I complications (*n* = 3); ^vCombined results of left and right hepatectomy; bile leak (*n* = 5), biliary stricture (*n* = 5), portal vein thrombosis (*n* = 2), arterial complication (*n* = 1); ^wFever of unknown origin (*n* = 2), renal failure (*n* = 1), small bowel obstruction (*n* = 1) and grade I complications (*n* = 5); ^xBile leak (*n* = 1), intra-abdominal collection (*n* = 1) and pleural effusion (*n* = 3); ^yBile leak (*n* = 1), portal vein thrombosis (*n* = 1) and biliary stricture (*n* = 3); ^zPortal vein thrombosis. Cx: Complications; HS: Hospital stay; LLS: Left lateral section; OT: Operating time; WIT: Warm ischaemic time.

corporeal suturing. After a bile leak was encountered, suturing was replaced by applying two metal clips on the donor side, which might have shifted the division point to the graft side. Nevertheless, recipient biliary complications were kept minimal (*n* = 1, 2.2%), reflecting the technical excellence of the implant surgeon. The occurrence of one hepatic artery thrombosis and two intra-operatively detected intimal dissections prompted the surgeon of a potential problem for PL donor hepatectomy. The author attributed the issue to intimal damage during intra-corporeal ligation (reduced tactile feedback) and retraction during caudate transection. From this series, it was concluded that PL donor right hepatectomy was a feasible procedure for experienced transplant surgeons. However, further evaluation is needed to standardize the techniques for better operative outcomes.

Left hepatectomy: Although a right liver graft is usually preferred for higher graft volume, donor right hepatectomy is associated with more morbidity than is left hepatectomy^[68-70]. Considering that donor risk is essentially related to the proportion of the liver resected, the left liver graft is selected when graft volumes are deemed adequate. The first PL donor left hepatectomy was performed in 2012^[71], followed by a small series followed^[37,40,71-73]; currently, approximately 20 cases have been reported in the literature (Table 5). There was no donor death or major complications. However, with limited experience, no conclusions can be arrived at, apart from the technical feasibility of this procedure in selected donors in expert hands.

Recipient safety remained the primary concern of using a left lobe graft^[74]. Smaller grafts put the recipient

Table 2 Outcomes of donor hepatectomy with mini-laparotomy

	LLS	Left	Right	OT (min)	Blood loss (mL)	WIT (min)	HS (d)	Donor Cx	Recipient Cx
Comparative study									
Kim <i>et al</i> ^[53] , 2009			23/23	232 ± 29 ¹ /269 ± 37	186 ± 59/218 ± 67	-	10 ± 3/12 ± 4	3 (13.0%) ^a	1 (4.3%) ^b
Thenappan <i>et al</i> ^[46] , 2011 ^c	8/7	-	-	312 ± 68/324 ± 106	1033 ± 1096/733 ± 457	-	6.0 ± 2.0/6.4 ± 3.7	2 (13.3%) ^d	7 (46.7%) ^e
Nagai <i>et al</i> ^[55] , 2012 ^f			9/30	371 ± 52/363 ± 53	212 ± 114 ¹ /316 ± 121	-	5.9 ± 1.2 ¹ /7.8 ± 2.3	7 (25.0%) ^g	10 (35.7%) ^h
Shen <i>et al</i> ^[51] , 2016 ⁱ			20/28	366 ± 45/386 ± 50	416 ± 164/383 ± 180	2.9 ± 1.5/3.0 ± 1.6	7.3 ± 1.6/7.4 ± 2.5	1 (5.0%) ^j	
Case series									
Lee <i>et al</i> ^[54] , 2011			141	254 ± 47	352 ± 144	-	10 ± 3	25 (17.7%) ^k	51 (36.2%) ^l

¹Statistically significant; ^aIntra-abdominal bleeding (*n* = 2) and pleural effusion (*n* = 1); ^bBile leak requiring laparotomy (*n* = 1); ^cCombined results of 15 hybrid and mini-laparotomy compared with 15 open operations, types of graft other than left lateral section not specified; ^dBile leak (*n*=1) and incisional hernia (*n* = 1); ^eBile leak (*n* = 2), vascular complications (*n* = 3), intra-abdominal collection (*n* = 1) and chylous ascites (*n* = 1); ^fCombined results of 19 hybrid and 9 mini-laparotomies compared with 30 open operations; ^gIntra-abdominal bleeding (*n* = 1), bile leak (*n* = 1), intra-abdominal collection (*n* = 1), ileus (*n* = 2), deep vein thrombosis (*n* = 1) and phlebitis (*n* = 1); ^hBile leak (*n* = 2), biliary stricture (*n* = 2), hepatic artery stricture (*n* = 2), hepatic vein stricture (*n* = 2) and intra-abdominal collection (*n* = 2); ⁱMini-laparotomy (*n* = 20) compared against laparoscopic-assisted (*n* = 28); ^jPneumonia; ^kRhabdomyolysis (*n* = 1), intra-abdominal bleeding (*n* = 4), bile leak (*n* = 4), ileus (*n* = 2) and grade I complications (*n* = 14); ^lBiliary complications (*n* = 36), intra-abdominal bleeding (*n* = 5) and vascular complications (*n* = 6). Cx: Complications; HS: Hospital stay; LLS: Left lateral section; OT: Operating time; WIT: Warm ischaemic time.

Table 3 Outcomes of pure laparoscopic donor left lateral sectionectomy

	No.	OT (min)	Blood loss (mL)	WIT (min)	Conversion	HS (d)	Donor Cx	Recipient Cx
Comparative study								
Soubrane <i>et al</i> ^[28] , 2006	16/14	320 ± 67 ¹ /224 ± 15	19 ± 44 ¹ /99 ± 185	10 (6-12)/5(2-7)	1 (6.3%)	7.5 ± 2.3/8.1 ± 3.0	3 (18.7%) ^a /5 (35.7%)	6 (37.5%) ^b /6 (42.8%)
Kim <i>et al</i> ^[61] , 2011	11/11	330 ± 68/306 ± 29	396 ± 72/464 ± 78	6 ± 2/5 ± 1	0	6.9 ± 0.3 ¹ /9.8 ± 0.9	0/1 (9.1%)	2 (18.1%) ^c /2 (18.1%)
Samstein <i>et al</i> ^[40] , 2015 ^d	17/20	478 ± 68 ¹ /398 ± 42	177 ± 101 ¹ /375 ± 191	-	0	4.3 ± 1.5 ¹ /6.0 ± 1.5	2 (9.1%) ^e /5 (25%)	1 (4.5%) ^f /1 (4.5%)
Case series								
Cherqui <i>et al</i> ^[12] , 2012	2	360-420	150-450	4-10	0	5-7	0	1 (50.0%) ^g
Yu <i>et al</i> ^[92] , 2012	15	331 ± 63	410 ± 71	6 ± 2	0	7.1 ± 0.8	0	-
Scatton <i>et al</i> ^[62] , 2015 ^h	67	275 (175-520)	82 ± 79	9 ± 4	4 (5.7%)	6 (3-18)	17 (25.3%) ⁱ	
Soubrane <i>et al</i> ^[63] , 2015 ^j	124	308 (180-555)	50 (10-500)	8	5 (4.0%)	6.3 (2-18)	21 (16.9%) ^k	-
Troisi <i>et al</i> ^[64] , 2017	11	237 ± 99	70 ± 41	4	0%	4	2 (18.1%) ^l	5 (45.4%) ^m

¹Statistically significant; ^aBile leak requiring laparoscopy (*n* = 1) and wound haematoma (*n* = 2); ^bPortal vein thrombosis requiring re-transplant (*n* = 1), hepatic artery thrombosis (*n* = 2) and biliary stricture (*n* = 3); ^cPortal vein stenosis requiring stenting (*n* = 1) and biliary stricture (*n* = 1); ^dResults included 5 left hepatectomy and compared with mixed open and hybrid controls; ^eHernia (*n* = 1) and bile leak (*n* = 1); ^fPortal vein thrombosis requiring exploration (*n* = 1); ^gHepatic artery thrombosis (*n* = 1); ^hResults included 3 left hepatectomy; ⁱBile leak (*n* = 2), biliary stricture (*n* = 1), pulmonary complications (*n* = 2), bladder injury (*n* = 1), and complications (*n* = 5); ^jCombined results of 5 centres; ^kBile leak (*n* = 3), wound haematoma requiring drainage (*n* = 1), bladder injury requiring cystoscopy (*n* = 1), fluid collection requiring drainage (*n* = 1), others: grade I-II complications; ^lHepatic necrosis (*n* = 1) and collection (*n* = 1) ^mFungemia leading to death (*n* = 1) and biliary stricture (*n* = 4). Cx: Complications; HS: Hospital stay; LLS: Left lateral section; OT: Operating time; WIT: Warm ischaemic time.

at risk of small-for-size syndrome. Even when implanted with similarly sized grafts, left lobe recipients experienced more arduous recovery^[75]. In a sense, the current status of PL donor left hepatectomy is primarily limited by the inherent disadvantage of the graft type. However, with time and experience, the undesirable consequences of small-for-size liver grafts have been minimized with refined surgical techniques^[76-78]. A Japanese series of 200 left lobe recipients revealed long-term survivals comparable to those of right lobe recipients^[79]. This re-

emphasizes left lobe LDLT as a valuable option for LDLT, especially when donor remnant volume is marginal for right lobe donation.

Robotic-assisted donor hepatectomy

Interestingly, robotic surgery has taken the lead over laparoscopy regarding donor right hepatectomy. The first RA donor right hepatectomy was reported in 2012^[38], one year before the first PL approach to this surgery^[13]. Robotic systems offer a stable magnified field and

Table 4 Outcomes of pure laparoscopic donor right hepatectomy

	No.	OT (min)	Blood loss (mL)	WIT (min)	Conversion	HS (d)	Donor Cx	Recipient Cx
Comparative study								
Takahara <i>et al</i> ^[67] , 2015	5/25	480 ± 54 ¹ /380 ± 45	91 ± 69 ¹ /268 ± 194	9	0	9.4 ± 1.8/9.0 ± 2.2	1 (20%) ^a	-
Suh <i>et al</i> ^[37] , 2018	45/42	331 ± 50 ¹ /280 ± 40	436 ± 170 ¹ /338 ± 188	12.6 ± 4.4 ¹ /5.4 ± 3.6	0	8.2 ± 1.3/8.4 ± 1.0	5 (11.9%) ^b	11 (26.2%) ^c
Case series								
Soubrane <i>et al</i> ^[13] , 2013	1	480	100	12	0	7	0	0
Rotellar <i>et al</i> ^[32] , 2013	1	480	100	3	0	4	0	1 (100%) ^d
Han <i>et al</i> ^[33] , 2015 ^e	2	-	-	-	9	9 (8-10)	-	-
Chen <i>et al</i> ^[39] , 2015	1	415	150	6	0	6	1 (100%) ^f	1 (100%) ^g
Kim <i>et al</i> ^[36] , 2017	3	427-502	200-270	4.5-5.0	0	7-8	0	0

¹Statistically significant; ^aBiliary complication; ^bLiver abscess (*n* = 1), Pneumonia (*n* = 1), upper respiratory tract infection (*n* = 1) and grade I complications (*n* = 2); ^cIntra-abdominal bleeding (*n* = 4), vascular complication (*n* = 4), biliary complication (*n* = 2) and others; ^dPneumonia; ^eVideo presentation; ^fWound haematoma; ^gPneumonia. Cx: Complications; HS: Hospital stay; OT: Operating time; WIT: Warm ischaemic time.

Table 5 Outcomes of pure laparoscopic donor left hepatectomy

	No.	OT (min)	Blood loss (mL)	WIT (min)	Conversion	HS (d)	Donor Cx	Recipient Cx
Comparative study								
Samstein <i>et al</i> ^[40] , 2015 ^a	5/20	478 ± 68 ¹ /398 ± 42	177 ± 101 ¹ /375 ± 191	-	0	4.3 ± 1.5 ¹ /6.0 ± 1.5	2 (9.1%) ^b /5 (25%)	1 (4.5%) ^c /1 (4.5%)
Case series								
Samstein <i>et al</i> ^[71] , 2013	2	358-379	125	-	0	4 ± 1	0	1 (50%) ^d
Troisi <i>et al</i> ^[72] , 2013	4	370-560	50-80	4-7	0	4-6	0	1 (25%) ^e
Almodhaiberi <i>et al</i> ^[73] , 2018	1	300	125	-	0	8	0	-

¹Statistically significant; ^aResults included 17 left lateral sectionectomies and compared with mixed open and hybrid controls; ^bHernia (*n* = 1) and bile leak (*n* = 1); ^cPortal vein thrombosis requiring exploration (*n* = 1); ^dBile leak (*n* = 1); ^eRecipient common hepatic artery dissection (*n* = 1). Cx: Complications; HS: Hospital stay; OT: Operating time; WIT: Warm ischaemic time.

provide ergonomic advantages beyond conventional laparoscopy, namely, improved range of motion and enhanced precision^[80]. Articulated instruments allow for proper plications of venous bleeding. In the setting of donor hepatectomy, robotic system facilitates closure of the hepatic duct stump with a running suture^[81]. Compared with clipping, suture closure requires a shorter bile duct length and potentially reduces the probability of multiple graft bile duct openings or donor biliary strictures.

RA donor right hepatectomy was reproduced in a series reported by Chen *et al*^[39] comparing 13 RA against 54 open procedures. The operating time in the RA group (596 min) was prolonged even when relative to that of PL approaches reported in the literature^[13,32-37]. Nevertheless, warm ischaemic time (10 min) did not appear to be an issue for graft retrieval with a robotic system. Compared with open hepatectomy, RA procedures had similar blood loss (169 mL vs 146 mL, *P* = 0.47) and overall morbidities (7.7% vs 9.3%, *P* = 0.68). With respect to donor benefits, reduction in analgesia (PCA/BW on D1 0.58 ng/kg vs 0.84 ng/kg, *P* = 0.03) and shorter returns to work (52.9 d vs 100 d, *P* = 0.02) and sex (100 d vs 156 d, *P* = 0.047) were reported. In the recipients, incidences of vascular and biliary complications were similar and liver functions

were comparable upon 1-year follow-up. With promising early results, the remaining issue is likely an exceedingly protracted learning curve. Expertise in robotic procedures is desired in addition to proficiency in laparoscopic hepatobiliary surgery and donor hepatectomy.

ARE WE READY FOR PRIME TIME?

Upon reviewing the literature, the benefits of PL approaches have been validated for more simple procedures in the case of left lateral sectionectomy. For lobar liver donation, technical feasibility has been demonstrated by experienced surgeons, yet reproducibility is likely limited by the precipitous learning curve as well as safety concerns. Limited evidence supports the potential advantages of adopting a PL approach. The subsequent section discusses strategies for overcoming these obstacles and ensuring a safe transition to minimally invasive donor hepatectomy.

Donor selection

The importance of cautious donor selection was demonstrated in Kim *et al*^[36]'s report on PL donor right hepatectomy. In the authors' series, 3 donors were selected among 92 candidates (4%), from a centre with tremendous experience encompassing over 3500 LDLT

operations. Strict selection criteria were applied, with emphasis on vascular and biliary anatomy. Donors with single and longer right hepatic artery, right portal vein and right hepatic duct were selected. The authors also excluded donors with larger estimated grafts, *i.e.*, more than 650 g. Similar criteria were applied in the early phase of Suh *et al.*^[37]'s series. Favourable anatomy allows for the acquisition of experience and standardization of techniques before more challenging anatomy can be safely handled. However, biliary variation *per se* should not be considered a contraindication to PL approaches, given the availability of surgical expertise. In fact, successful laparoscopic management of complicated biliary anatomy has been reported with no donor or recipient morbidity^[34,66].

Technical standardization

Technical standardization may be the key to improving the safety and reproducibility of complex and sophisticated procedures. Based on experience in oncological liver resections, several basic skills are essential to laparoscopic liver resection^[82]. Liver resection is preceded by complete mobilization so that transection plane can be manipulated. After hilar dissection, the Glissonian pedicle is encircled. Surface parenchyma up to a depth of 2 cm is transected with energy devices, as there are no vital hepatic pedicles within superficial parenchyma. Deep parenchymal transection is effected through a Cavitron Ultrasonic Surgical Aspirator (CUSA™, Tyco Healthcare, Mansfield, MA, United States) because it is important not to damage intra-parenchymal hepatic structures. Small tributaries at the transection surface are controlled with a combination of clips and bipolar forceps.

The hanging manoeuvre has been demonstrated to be highly effective in open liver resections^[83]. Passage of a cotton tape along the avascular plane between the liver and the inferior vena cava allows for the liver to be suspended posteriorly. This manoeuvre reduces venous bleeding and guides transection along Cantlie's line. The lateral approach is a modification of this technique for laparoscopy^[84]. Instead of developing the avascular plane, the hanging tape is placed lateral to the inferior vena cava for right hepatectomy or between the inferior vena cava and ligamentum venosum for left hepatectomy. The need for dissection of the avascular plane, and hence the problematic bleeding from caudate branches, was abbreviated. This technique is simple, effective and applicable to different approaches of minimally invasive donor hepatectomy.

Intermittent inflow control with Pringle's manoeuvre^[85] also reduces blood loss during hepatic transection, but its use in the setting of LDLT is controversial. While detractors have raised the concern of potential ischaemic graft injury, routine intermittent inflow control has been adopted in several transplant units^[86-88]. In a randomized controlled trial, inflow control was performed with intermittent 15 min clamping and 5 min release cycles. The results confirmed no increase in recipient alanine

aminotransferase (peak 477 U/mL vs 345 U/mL, $P = 0.32$) or international normalized ratio (peak 2.6 vs 2.5, $P = 0.44$), while the donor blood loss was reduced (324 mL vs 486 mL, $P = 0.02$)^[88]. With evidence validating its safety, inflow occlusion remains an optional manoeuvre in LDLT without compromising graft function.

In donor hepatectomy, operative cholangiogram is essential to determining the site of bile duct division. Operative cholangiogram is usually performed after surgeons leave the surgical field. In the PL or RA approach, surgeons can remain the operative position during fluoroscopy^[32]. Real-time fluoroscopic guidance enhances precision and safety of bile duct division. Fluorescence imaging with ICG is a novel technique for intraoperative cholangiogram^[89]. ICG can be injected intravenously or directly into the biliary tree *via* the cystic duct stump^[90]. Intravenous ICG injection is the preferred technique given its simplicity. Instead of producing a separate plain image, the fluorescence of ICG is completely incorporated into the laparoscopic view. This approach provides real-time navigation with greatly enhanced accuracy. The largest series of RA donor right hepatectomy was performed with intravenous ICG cholangiography^[39]. One inherent limitation of ICG cholangiography is that the biliary tree can only be imaged when adequately exposed. An aberrant duct situated deeply in hepatic parenchyma may not be readily imaged. Perhaps a more effective approach is a combination of the two techniques. While a conventional cholangiogram remains essential to imaging any anatomical variation, fluorescence cholangiography might add precision in fine tuning the division point. In addition, ICG injection after temporary control of portal pedicles enhances visualization of ischaemic demarcation. Precise dissection along Cantlie's line minimizes blood loss and avoids leaving ischaemic parenchyma to graft and donor.

Prospective registry

Current studies on minimally invasive donor hepatectomies are primarily retrospective case control studies or case series, which can be limited by selection bias. With regard to donor safety, a prospective study with preoperative enrolment may be a better option. In donor operations, severe complications are the major concern. Due to limited sampling, uncommon but sinister complications may not be readily detected by a randomized controlled trial. In this setting, a prospective registry is an effective alternative. When laparoscopic cholecystectomy was introduced, bile duct injuries were more readily detected by a prospective registry than by randomized controlled trials^[91]. The Louisville statement emphasized the importance of a prospective registry to evaluate the safety of laparoscopic hepatectomy^[3]. As PL donor hepatectomy has not been evaluated in a randomized control trial, which can be logistically difficult, an international prospective registry can be initiated. Broad participation from transplant centres with available

expertise is encouraged so that the safety of donor procedures can be effectively evaluated.

CONCLUSION

Despite critics and challenges, minimally invasive donor hepatectomy has been performed with increasing frequency. Donor left lateral sectionectomy has provided most anatomical advantages for pure laparoscopic surgery. The technique has been well validated for its safety and advantages and has become the standard in experienced centres^[63]. RW donor hepatectomy, either in the form of a laparoscopic-assisted technique or utilizing a mini-laparotomy wound, has guided surgeons' transition from open donor hepatectomy to PL approaches. With accumulation of experience, PL donor right hepatectomy has been shown to be technically feasible. RA donor hepatectomy also appears to be a valuable alternative to PL donor hepatectomy.

Existing reports were derived from centres with tremendous experience in both laparoscopic hepatectomy and donor hepatectomy. The technical complexity associated with these procedures indicates an arduous transition from technical feasibility to reproducibility and disseminated application. Creation of an international prospective registry is awaited to centralize expert input for assessing the relevance of this approach. Moreover, careful donor selection and adopting standardized techniques should allow transplant surgeons to acquire technical proficiency in this procedure. A cautious approach is crucial, as one untoward event in donor surgery may significantly set back progress. After all, the ongoing successful evolution of PL donor hepatectomy will ultimately depend on donor safety.

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P- Reviewer: Kakaei F, Sugawara Y **S- Editor:** Gong ZM
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ISSN 1007-9327

