Expert Consensus Guidelines on Minimally Invasive Donor Hepatectomy for Living Donor Liver Transplantation From Innovation to Implementation

A Joint Initiative From the International Laparoscopic Liver Society (ILLS) and the Asian-Pacific Hepato-Pancreato-Biliary Association (A-PHPBA)

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Objective: The Expert Consensus Guidelines initiative on MIDH for LDLT was organized with the goal of safe implementation and development of these complex techniques with donor safety as the main priority.

Background: Following the development of minimally invasive liver surgery, techniques of MIDH were developed with the aim of reducing the short- and long-term consequences of the procedure on liver donors. These techniques, although increasingly performed, lack clinical guidelines.

Methods: A group of 12 international MIDH experts, 1 research coordinator, and 8 junior faculty was assembled. Comprehensive literature search was made and studies classified using the SIGN method. Based on literature review and experts opinions, tentative recommendations were made by experts subgroups and submitted to the whole experts group using on-line Delphi Rounds with the goal of obtaining >90% Consensus. Pre-conference meeting formulated final recommendations that were presented during the plenary conference held in Seoul on September 7, 2019 in front of a Validation Committee composed of LDLT experts not practicing MIDH and an international audience.

Results: Eighteen Clinical Questions were addressed resulting in 44 recommendations. All recommendations reached at least a 90% consensus among experts and were afterward endorsed by the validation committee.

Conclusions: The Expert Consensus on MIDH has produced a set of clinical guidelines based on available evidence and clinical expertise. These guidelines are presented for a safe implementation and development of MIDH in LDLT Centers with the goal of optimizing donor safety, donor care, and recipient outcomes.

Keywords: guidelines, laparoscopic, living donor hepatectomy, living donor liver transplantation, minimally invasive, robotic

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Living donor liver transplantation (LDLT) is currently an accepted procedure that is used on a large scale in countries with low deceased donor availability, mainly Asian countries, and to a lesser extent in Western countries with higher access to deceased donors.

The use of minimally invasive techniques in living donor surgery started with laparoscopic donor nephrectomy. First reported in 1994,[1,2] it rapidly became a standard practice worldwide, validated by several Randomized Controlled Trials, and the vast majority of kidney transplant centers now offer laparoscopic donor nephrectomy.[3,4] Donor hepatectomy is generally considered to carry a higher risk than donor nephrectomy due to larger organ size, higher anatomical complexity, and the need for splitting the highly vascularized liver. Recent developments of minimally invasive liver surgery and the evidence of its advantages over the open approach, have logically led to consider its application to donor hepatectomy with the goal of improving short and long term consequences of the procedure.[5–7] Minimally invasive donor hepatectomy (MIDH) appears to be a highly complex procedure. It was first reported in 2002 with the pure laparoscopic procurement of left lateral grafts for pediatric recipients[8] and followed by the development of laparoscopic assisted procedures, also known as hybrid techniques, for the procurement of larger grafts.[9,10] In 2013, first cases of pure laparoscopic full right and full left donor hepatectomies were reported.[11–14] The recent development of MIDH occurred mainly in Asia where LDLT accounts for over 80% of liver transplantation cases. Particularly, teams in Seoul, account for the vast majority of pure laparoscopic donor right hepatectomy cases with over 500 cases performed since 2015.[15–19] A limited number of European surgeons have continued to use MIDH in their liver transplant programs and new programs were implemented in the USA but numbers are small. Recently, a few teams have also reported robotic assisted MIDH (RADH).

Although laparoscopic liver resections are now well settled, the real status of MIDH was left unclear and only superficially addressed in previous consensus conferences and guidelines on laparoscopic liver surgery.[5,7] Therefore, the time had come to organize the development of MIDH and propose guidelines about how this technique can safely expand. This manuscript reports the preparatory work and the proceedings of the Expert Consensus Guidelines meeting on MIDH for LDLT, held in Seoul on September 7, 2019.

METHODS

The project was initiated in September 2018 on behalf of the International Laparoscopic Liver Society (ILLS) and the Asian-Pacific HepatoPancreatoBiliary Association. The development of the current guidelines is summarized in Figure 1 and followed 3 main steps including, (a) selection of experts and working groups, and identification of clinical questions (CQ), (b) formulating recommendations and developing agreement, and (c) finalize guidelines during a meeting in the presence of a validation committee and an international audience (Table 1).

Selection of Experts, Working Groups, and Identification of Items

Twelve senior surgeons were selected on the grounds of their clinical expertise, publications and scientific knowledge on MIDH and composed the ‘‘Expert panel.’’ Their tasks were to identify relevant topics and inherent CQ, propose scientific recommendations, and participate in final voting for agreement. A set of 8 junior surgeons dedicated to liver surgery and led by a scientific coordinator were selected as the ‘‘Research team.’’ Their tasks were to perform a systematic literature review, analyze selected manuscripts, and assist the Experts Panel in assessing Level of Evidence and developing specific recommendations. The Expert Panel was divided into Working Groups. Each Working Group was assigned 1 or more CQ(s) to be addressed with the aid of 1 member of the Research Team. A total of 18 CQs were allocated to 4 sessions: Rationale and Donor outcomes, Recipient outcomes, Techniques, and Training/Certification

Formulating Recommendations and Developing Agreement

The process to provide evidence-based recommendations were as follows:

(a) Systematic literature review: PubMed, Embase, and Cochrane databases were screened, and systematic reviews, comparative

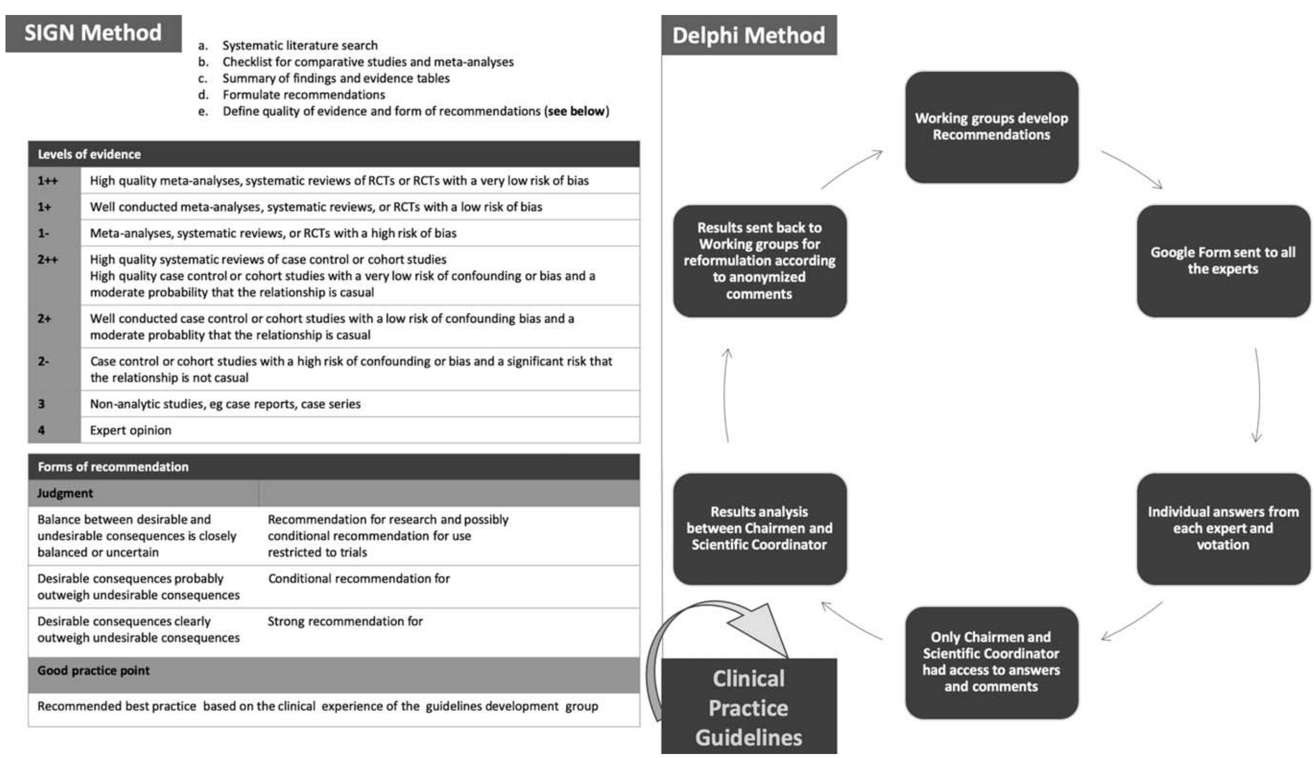

FIGURE 1. Guidelines process.

TABLE 1. Members of the Expert Consensus Guidelines Meeting on Minimally Invasive Donor Hepatectomy (MIDH) Sorted by Alphabetical Order

Experts		Research Team		Validation Committee	
Daniel Cherqui (Chairman)	France	Ruben Ciria (Scientific Coordinator)	Spain	Hiroto Egawa	Japan
Kyung-Suk Suh (Chairman)	Korea	Felipe Alconchel	Spain	Jan Lerut	Belgium
Javier Briceño	Spain	María Dolores Ayllón	Spain	Chung-Mao Lo	Hong Kong
Dieter Broering	Saudi Arabia	Giammauro Berardi	Italy	Mohamed Rela	India
Ho Seong Han	Korea	François Cauchy	France	Gonzalo Sapisochin	Canada
KH Kim	Korea	Irene Gómez-Luque	Spain		
CH David Kwon	USA	Suk Kyun Hong	Korea		
Fernando Rotellar	Spain	Young In Yoon	Korea		
Benjamin Samstein	USA				
Oliver Soubrane	France				
Roberto Troisi	Italy				
Go Wakabayashi	Japan				

studies, observational manuscripts, and case-series were included and analyzed. A wide literature search including pure laparoscopic, laparoscopic-assisted, hand-assisted, hybrid, and robotic procedures in the context of living donor hepatectomy was done. Manuscripts published in English, and available in full text were collected and SIGN methodology was used to assess the quality of the evidence.[20] Quality of evidence was scored from 1++ (best evidence) until 4 (lowest evidence) (Fig. 1). All manuscripts were included into a summary of findings proforma according to SIGN methodology (network SIGN). Only comparative studies, systematic reviews and trials underwent a full checklist form.

(b) Summary of findings: A summary of available literature including evidence tables were created for each CQ. These summaries and all the tables and checklists were supplied to experts to propose recommendations.

(c) Recommendations. A set of recommendations were formulated by the Expert Panel based on the available evidence analyzed by the research teams. All recommendations included the level of evidence and were ranked as strong, conditional or recommendation for research. A special recommendation entitled " good practice point" was considered when it was based on the clinical experience of the Expert Panel while not formally supported by literature.

(d) Developing agreement. Each working group submitted the recommendations for each CQ to the chairmen and the scientific coordinator. A synthesis of the work from different groups was completed in July 2019. The synthesis of the work was then distributed to all experts, for a first on line Delphi vote and comments.[21] The results of the Delphi vote were kept anonymous and reviewed by the chairmen and the scientific coordinator. Recommendations were approved if an agreement rate of >90% was achieved (at least 11/12 experts). If the predefined rate of 90% was not reached, the recommendation, including feedback comments, was returned to the expert review group to amend accordingly. Subsequently, the amended recommendations that had not passed on the first Delphi round were sent to all experts for a second Delphi vote. The same approval process was followed. Delphi rounds were performed on the 3rd of August, 2nd of September and 6th of September 2019.

Guidelines Meeting + Quality Appraisal

A plenary pre-meeting session including chairmen, experts, scientific coordinator, and available research team was held in Seoul on the 6th of September 2019 on the day before the Validation Conference. During this session, the few remaining recommendations that had not passed the second Delphi round, were subjected to a third a third Delphi round on site. After that, all recommendations were discussed and finalized before Public Validation Conference. On September 7, 2019 the evidence and expert based recommendations were presented and discussed during the abovementioned Public Validation Conference in which the Validation Committee participated. This committee consisted of 5 members consisting of international expert surgeons with recognized experience in LT and LDLT but with no experience in MIDH (Table 1). To avoid bias, the members of the validation committee had no prior knowledge of the guidelines until the day of this public presentation. The validation committee was invited to comment freely during the proceedings and during a final panel discussion that included all its members. This session was part of the official Asian-Pacific HepatoPancreatoBiliary Association meeting program and open to all meeting delegates. All attendees could participate and share opinions which were considered by working teams and the experts before the final version of these guidelines.

In the months after the conference, a document with all recommendations was created, which was circulated and edited by all the group leaders. In May 2020, the final draft of the manuscript and recommendations were reviewed and approved by all members of the expert and validation committees before submitting the manuscript for publication.

Definitions

Procedures were classified as pure laparoscopic donor hepatectomy (PLDH) when the whole procedure was performed under laparoscopic vision and action, using a remote incision for graft extraction only. Other procedures are listed under several denominations in the literature including laparoscopic assisted, hand assisted and hybrid techniques. For practical reasons these were grouped as laparoscopic assisted donor hepatectomy (LADH). The most commonly used LADH procedures include laparoscopic liver mobilization, with or without hand assistance, followed by liver transection under direct vision through a mini-laparotomy, usually an 8–12 cm midline or subcostal incision. Hilar dissection is variably performed during the laparoscopic stage or through the mini-laparotomy. Finally, procedures including robotic surgery were classified as RADH.

RESULTS

The initial search identified a first set of 154 manuscripts from which a final set of 105 manuscripts[8–14,16–19,22–115] was used to the development of these guidelines (Fig. 2). Recommendations along their respective Level of evidence, form of recommendation and number of Delphi round agreement are displayed in Tables 2–4.

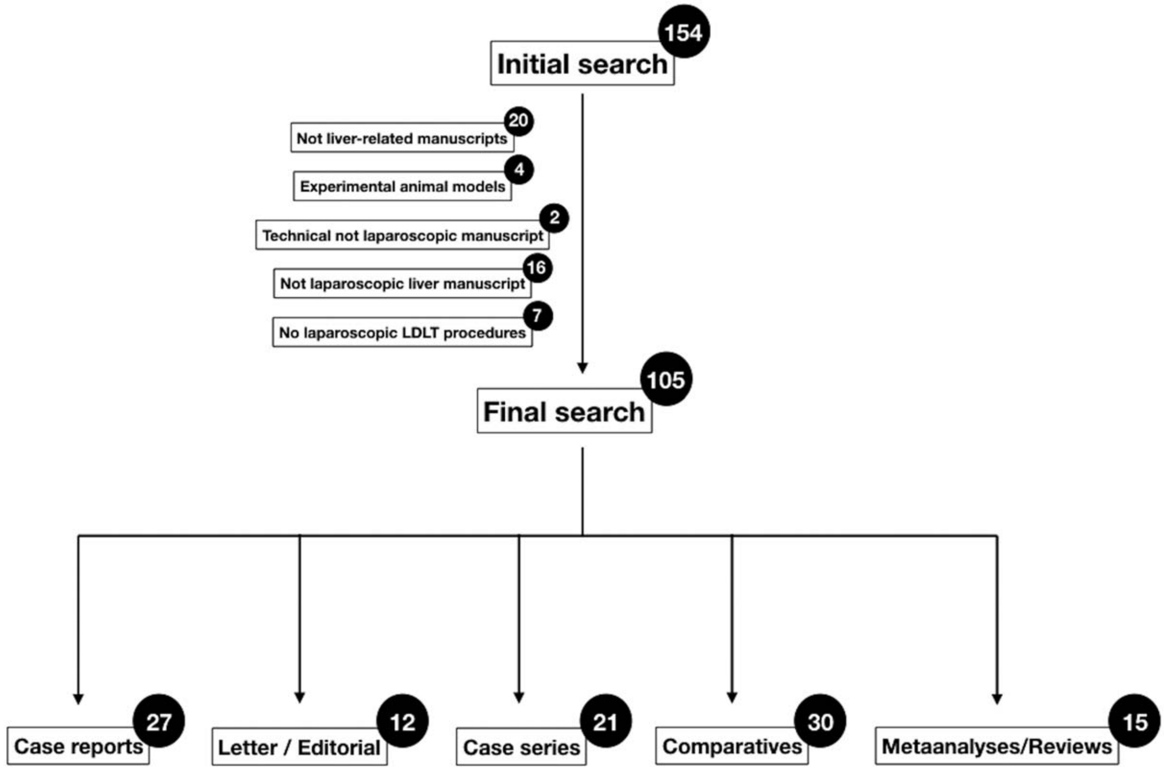

FIGURE 2. Flow chart of systematic literature review.

Section 1: Rationale and Donor Outcomes (Table 2)

CQs 1, Recommendations 1–3: Transferability of MIS Advantages to MIDH

An adequate evidence level could be obtained from 5 meta-analyses comparing MIDH versus open techniques that had been reported to date. All were scored as 1-, as they were based on retrospective cohorts which may have some inherent of bias.[40,43,62,75,78] The most recent one reported a reduction in blood loss, shorter hospital stay, lower morbidity, and shorter operative time in LADH versus open procedures.[40] No differences were observed between PLDH and open surgeries. The other 4 meta-analyses were based on mixed MIDH groups (PLDH and LADH) versus conventional approach. Mixed results (but never unfavorable to MIS approach) were observed regarding blood loss, hospital stay, operative time, and complications rate. A recent propensity score study of pure laparoscopic versus open LLS has reported reduced rates of blood loss and minor complications in MIDH.[41]

CQ2–3, Recommendations 4–7: Donor Death and Complications

There is no evidence supporting an increased risk of donor death related to MIDH. Two meta-analyses have reported similar donor complications without differences in both approaches.[62,78] Two other meta-analyses reported fewer complications rates in MIDH.[43,75] One of those also reported fewer complications related to wound-infection and discomfort.[43] Regarding comparative studies, similar results have been reported, including lower incidence of minor and major complications.[34,41] Individual data from 1 pioneering group suggested a possible increased risk of technical complications at the beginning of experience.[19] There are reports of certain complications related to laparoscopic approach (liver surface damage, hematoma) and a possible higher transaminase peak during the early learning curve.[18,39]

CQ 4–5, Recommendations 8–13: Short Term Rehabilitation and Quality of Life

Assessment of incision related complications (pain, discomfort, and incisional hernia) showed a significant decrease in incision discomfort in patients undergoing laparoscopy assisted donor hepatectomy versus open donor hepatectomy.[49] Decreased rates of sensory deficit, scar numbness, scar tightness and late morphine requirement in laparoscopy assisted donor right hepatectomy versus open donor right hepatectomy have also been reported.[83] A manuscript focusing on left-sided grafts reported a lower incidence of wound issues after PLDH (the LADH/open group had a 15% hernia rate versus 5% for the PLDH group) and fewer days off work after PLDH (33 vs 63 days, $P = 0.01$).[77] Assessment of QOL using standardized questionnaires (IQOLA SF-8/SF-36/dedicated questionnaire) has been reported in 2 studies.[61,83] One study did not show any significant difference between LADH and open hepatectomy using upper midline incision,[61] regarding body image. The other one showed significant improvements in IQOLA SF-8 items at 4 weeks in laparoscopy assisted versus open donor right hepatectomy.[83]

CQ 6, Recommendations 14–15: Comparison of MIDH and Donor Nephrectomy

One study compared the outcomes of patients undergoing laparoscopic donor hepatectomy and those undergoing laparoscopic

TABLE 2. Summary of Recommendations Part 1

		Level of Evidence	Form of Recommendation	Delphi Round Agreement
SESSION 1. RATIONALE AND DONOR OUTCOMES				
CQ1 ARE THE ADVANTAGES OF MIS LIVER RESECTION TRANSFERABLE TO MIDH?				
1	Laparoscopic Liver Resection for tumors, including major hepatectomy, has been showed to be associated with reduced pain, blood loss, transfusion, complications and hospital stay when compared with open resection. These advantages have been confirmed for MIDH in left-lateral grafts and only partially in right grafts	1−	Strong	First
2	A major advantage of MIDH is the avoidance of large incisions and their long term consequences (discomfort/pain, keloids, hernias and cosmesis) and complications	2++	Strong	First
3	Cosmesis may be less important in cancer patients but is very important for living donors. In this regard, pure laparoscopy/robotic is associated with the best cosmetic results	4	GPP	First
CQ2 DOES MIDH INCREASE THE RISK OF DONOR DEATH?				
4	No donor death has been reported after PLDH so there is no evidence that this procedure increases donor death.	1−	Strong	First
5	Considering that 1 possible case of death due to torrential bleeding has been reported in a mini-incision case, this approach should be handled cautiously	4	Conditional	First
CQ3 DOES MIDH INCREASE DONOR COMPLICATION RATE?				
6	In view of global data, MIDH is not associated with increased donor complications	1−	Strong	First
7	Special care must be taken during the initial implementation of PLDH, since some groups have reported increased donor complications in early experience.	2++	Conditional	Third
CQ4 DOES MIDH IMPROVE SHORT TERM REHABILITATION? HOSPITAL STAY/LEAVE FROM WORK				
8	The need for analgesics is reduced when MIDH is performed against standard open procedures.	1−	Strong	First
9	Globally, for left lateral, full left, and full right grafts procurement, meta-analyses, including PLDH and LADH, suggest a trend towards shorter hospital stay with MIDH.	1−	Strong	First
10	Leave from work may be reduced for left sided graft procured by pure laparoscopic approach compared to open	2+	Conditional	First
CQ5 DOES MIDH IMPROVE LONG TERM QUALITY OF LIFE? PAIN AND DISCOMFORT/HERNIA/BODY IMAGE				
11	Quality of life after LADH is improved compared to conventional open approaches. This should be the same for PLDH approach although it has not been formally studied with standardized questionnaires	2+	Strong	Second
12	Short and long-term incision related pain, discomfort and complications are decreased in LADH compared to conventional open approaches	2+	Strong	Second
13	Studies addressing quality of life from different techniques of MIDH and using standardized questionnaires should be encouraged	4	Conditional	First
CQ6 IS MIDH COMPARABLE TO LAPAROSCOPIC DONOR NEPHRECTOMY?				
14	Pure laparoscopic left-lateral sectionectomy for adult to child living donor liver transplantation is associated with at least similar short-term outcomes as minimally invasive donor nephrectomy	2+	Strong	First
15	The comparable short-term results of these 2 procedures should be used for promoting implementation of pure laparoscopic left-lateral sectionectomy as standard practice for adult to child living donor liver transplantation	4	Strong	First
SESSION 2. RECIPIENT OUTCOMES				
CQ7 DOES MIDH COMPROMISE RECIPIENT OUTCOMES? FOR PEDIATRICS/FOR ADULTS				
16	Recipient outcomes are probably not inferior when MIDH is used compared to open approach for both pediatric and adult patients	2++	Conditional	First
17	Caution should be taken during initial experience with PLDH as increased grade IIIa-b adult recipient biliary complications have been reported in one study	2−	Conditional	Second

CQ indicates clinical question; GPP, good practice point; LADH, laparoscopic assisted donor hepatectomy; MIDH, minimally invasive living donor hepatectomy; MIS, minimally invasive surgery; PLDH, pure laparoscopic donor hepatectomy; RADH, robotic assisted donor hepatectomy.

TABLE 3. Summary of Recommendations Part 2

		Level of Evidence	Form of Recommendation	Delphi Round Agreement
SESSION 3. TECHNIQUES				
CQ8 IS PURE LAPAROSCOPIC TECHNIQUE APPLICABLE FOR: LEFT LATERAL GRAFTS? FULL LEFT LIVER GRAFTS INCLUDING MHV? FULL RIGHT LIVER GRAFTS?				
18	PLDH is applicable to LLS and should be considered standard practice once the team has fulfilled the adequate learning	2++	Strong	Third
19	PLDH is applicable to full left liver grafts including middle hepatic vein	2−	Conditional	First
20	PLDH is applicable to selected right liver grafts	2++	Strong	Second
CQ9 IS LADH: AN ESTABLISHED TECHNIQUE ON ITS OWN? A FIRST STEP FROM OPEN TOWARDS PURE LAP? A WAY TO AVOID CONVERSION TO FULL OPEN?				
21	LADH should refer to the use of laparoscopy, with or without hand-assistance, to perform the initial parts of the procedure followed by completion of the under direct vision using a small incision, usually an upper mid-line one less than 15 cm long	2++	Strong	Third
22	LADH procedures are established techniques in their own right for MIS liver surgery. For MIDH they have similar outcomes to open, so at present, they could be considered established techniques on their own.	2+	Strong	First
23	LADH may be considered as a definitive procedure or as a transition before shifting to pure laparoscopy.	2++	Conditional	Second
24	Small incisions may be associated with exposure limitations, especially in large donors. Therefore, small incisions should be applied thoughtfully and extension of incision used liberally to ensure safety in case of difficulty.	4	GPP	Third
CQ10 ARE THERE ANATOMICAL CONTRA-INDICATIONS? MULTIPLE PORTAL BRANCHES? MULTIPLE ARTERIES? MULTIPLE BILE DUCTS? LARGE GRAFT?				
25	Institutions starting a new PLDH program should start with donors with favorable anatomy	3	Strong	First
26	Difficult anatomy in MIDH should only be considered in centers with a well-settled learning curve	4	Strong	Second
27	Few anatomical variations preclude the procurement of left lateral section grafts. They should be looked for and addressed carefully	4	GPP	Third
28	Large grafts and deviation from standard biliary and vascular anatomy may increase the difficulty of MIDH procedure in right-lobe donation	3	Strong	First
CQ11 WHAT IS THE RATIONALE FOR ROBOTIC ASSISTED TECHNIQUES? SURGEONS COMFORT? TECHNICAL ADVANTAGE? DONOR SAFETY?				
29	RADH is still in its early phase compared to PLDH. First studies suggest that robotic approach is as safe as the conventional open procedure, and offers the advantages inherent to minimally invasive techniques	2+	Strong	Third
CQ12 WHAT IS THE BEST LIVER TRANSECTION TECHNIQUE? ULTRASONIC ASPIRATOR (CUSA OR EQUIVALENT)? ENERGY DEVICE? CRUSH CLAMP?				
30	Parenchymal transection method is left to surgeon's preferences. The use of ultrasonic-aspirator is the most commonly used method; however, other techniques using energy devices or clamp crush have also been reported	4	GPP	First
31	It is recommended to avoid the blind use of energy devices deeper than the superficial part of the liver to avoid damage of large structures, particularly hepatic veins	4	GPP	First
CQ13 SHOULD WE USE PRINGLE MANEUVER? NEVER? ALWAYS? SELECTIVELY?				
32	There is no evidence that the use of intermittent Pringle maneuver has a detrimental effect on the graft and on the remnant in living donor hepatectomy.	3	Strong	First
33	Pringle maneuver can be used electively when deemed required by the surgeon as it may provide a drier surgical field leading to less operative time and reduced blood loss	4	GPP	First
34	Some kind of inflow control should be prepared in the event of necessity.	4	GPP	First
CQ14 WHAT IS THE BEST METHOD FOR BILE DUCT IDENTIFICATION AND CLOSURE? CHOLANGIOGRAM? ICG? BOTH?				
35	As in open surgery, excellent MRCP and planning are required to recognize anatomical variations and anticipate the optimal transection site	4	Strong	Third
36	Intraoperative cholangiogram and real-time ICG fluorescence are the available methods to identify the best location of bile duct division.	3	Strong	First
37	Clips and suturing are available methods for donor bile duct closure. Clips are easier but suturing is recommended in case of short bile duct on donor side	3	GPP	First
CQ15 WHAT ARE THE BEST METHODS OF VASCULAR DIVISION? ARTERY: CLIP, LIGATION, STAPLER/PORTAL VEIN: CLIP, UNILATERAL OR BILATERAL STAPLER/HEPATIC VEIN: UNILATERAL OR BILATERAL STAPLER				
38	The method for vascular division should be left to the surgeons' preference. As in open surgery, adequate length of vessel should be obtained on both the graft and the donor side	4	Strong	First
39	Staplers or clips can be used. Bilateral staplers require removal of the graft stapler line before implantation. This is avoided by the use of unilateral staplers	3	GPP	Second
40	For hepatic artery, clips are the recommended methods. For portal vein, staplers or clips can be safely used. For hepatic veins, staplers are recommended.	4	GPP	First

GPP indicates good practice point; ICG, indocyanin green; LADH, laparoscopic assisted donor hepatectomy; MIDH, minimally invasive living donor hepatectomy; PLDH, pure laparoscopic donor hepatectomy; RADH, robotic assisted donor hepatectomy; ICG, indocyanin green.

TABLE 4. Summary of Recommendations Part 3

		Level of Evidence	Form of Recommendation	Delphi Round Agreement
SESSION 4. TRAINING AND CERTIFICATION				
CQ16 WHO SHOULD DO IT? SURGEONS WITH PREVIOUS EXPERIENCE IN LAP LIVER SURGERY? LAPAROSCOPIC LIVER RESECTION EXPERIENCE WITHOUT TRANSPLANT EXPERIENCE? LIVER TRANSPLANT SURGEON?				
41	MIDH should be performed by surgeons with expertise in open and minimally invasive liver resection and living donor liver transplantation	4	Strong	First
CQ17 SELF TAUGHT VS PROCTORING? TRAVELING TO AN EXPERIENCED CENTER FOR ONE OR SEVERAL CASES? SPECIFIC FELLOWSHIP? VIDEOS AND SPECIFIC COURSES? PROCTORING PROGRAM?				
42	A proctored training is recommended to implement and standardize MIDH and to shorten the learning curve	3	Strong	First
CQ18 CERTIFICATION? NEED FOR INSTITUTIONAL APPROVAL? NEED FOR MANDATORY INTERNATIONAL REGISTRY?				
43	Institutional approval and commitment is required before starting an MIDH program	3	Strong	Third
44	International and Institutional registries are recommended to ensure safety and monitor quality of outcomes	3	Strong	First

GPP indicates good practice point; MIDH, minimally invasive living donor hepatectomy.

donor nephrectomy.[69] This study covered a period of 13 years and enrolled 124 donors undergoing full laparoscopic left lateral sectionectomy for adult to child LDLT and 300 donors undergoing laparoscopic donor nephrectomy. This study included a propensity score matching and showed a decreased complication rate and comprehensive complication index in left lateral liver donors compared to kidney donors, although a higher hospital stay was observed in liver donors.

Section 2: Recipient Outcomes (Table 2)

CQ7, Recommendations 16–17: Recipient Outcomes

Results from a meta-analysis showed that overall recipient morbidity and 90-day mortality were not different between the minimally invasive and open approaches.[75] Evidence regarding the use of LLS for pediatric liver transplantation has 4 main comparative manuscripts, 2 of them with propensity score matching.[35,41,79,110] No significant differences in vascular or biliary complications nor overall mortality rates were found between the groups. No cases of primary graft non function were observed either. Regarding left sided grafts, a specific matched analysis of 31 LADH in a prospective cohort versus 79 open cases (historical control) was reported with equivalent graft survival rate was similar between groups either in LLS or left lobes.[93] There are 4 comparative studies in which right and left sided grafts are mixed.[49,56,102,112] In all of them, recipient's liver function tests on postoperative days 1, 2, and 3 were not significantly different between groups. The rate of vascular or biliary complications was similar, and 1-month and 3-month mortality rate. Regarding right liver grafts a recent propensity score matching manuscript reported no significant differences in occurrence of biliary, portal or arterial complications, 90-day mortality and 90-day allograft failure of recipients.[32] A higher percentage of hepatic vein stenosis was observed in the laparoscopic group. It was considered to be due to the use of bilateral vascular stapler to divide the hepatic vein. Some other series also compared PLDH versus open donor right hepatectomy, with 26, 45, and 5 cases, respectively.[18,39,65] Liver function tests and overall recipient outcomes were similar between groups. A recent study included 213 right lobe MIDH and 595 open cases and a propensity score matching of 198 cases in each group.[15] There were more early and late biliary complications in recipients of right grafts procured laparoscopically as compared to open (early 10% vs 4% and late 39% vs 21%, $P < 0.05$).

Section 3: Techniques (Table 3)

CQ8. Recommendation 18–20: Applicability of Pure Laparoscopic Techniques

Applicability of PLDH is proven by a large number of reports from different groups and countries. From the literature search, 11 comparative[32,34,39,41,56,64,65,77,79,110,114] and 10 case-series[14,16,17,19,25,33,57,72,86] manuscripts were analyzed. A set of 8 manuscripts focused on pure laparoscopic donor right hepatectomy[16,17,32,33,39,57,64,65] including 1 on robotic donor right hepatectomy.[64] Four were comparative manuscripts, from which 3 compared the outcomes of pure laparoscopic and open donor right hepatectomies and 1 compared the outcomes of pure laparoscopic, laparoscopic assisted and open donor right hepatectomies.[31,38,64,79] Nine studies focused on left-sided grafts, including pure laparoscopic donor left hepatectomy (n = 1), left lateral sectionectomy (n = 6) or both (n = 2), including 5 comparative studies.[41,77,79,110,114] Three manuscripts were identified concerning PLDLH with inclusion of the MHV in the graft.[14,19,34] All studies mentioned here confirmed the applicability of the pure laparoscopic approach to left lateral, full left, and full right grafts.

CQ9. Recommendation 21–24: Laparoscopic Assisted Techniques

Regarding left sided grafts, a study (including LLS) reported longer operative time than in open group, faster recovery of the physical component summary score and bodily pain score.[93] Regarding right liver grafts, 2 studies suggested that LADH was associated with less postoperative pain and fewer incision-related complications compared to open surgery.[83,115] Another study showed longer operative times and no differences regarding blood loss, postoperative increase in peak liver enzymes, total hospital stay, and incidence of postoperative complications.[91] One case-matched study compared right-lobe LADH with open procedures and reported similar donor and recipient complications, blood loss and operative times; hospital stay and analgesic use were shorter.[89] Another study reported lower blood loss in right lobe LADH versus open.[49] Evidence comparing LADH versus PLDH is limited. A Japanese group reported their evolution from LADH towards PLDH and compared the 2 approaches. Longer operative times, decreasing with experience, less blood loss and identical morbidity were observed.[9,55] All studies mentioned here confirmed the applicability laparoscopic assisted techniques to left lateral, full left, and full right grafts.

CQ10. Recommendation 25–28: Anatomical Contraindications

Some authors have recommended to consider only standard vascular anatomy with graft volume <240 mL and graft thickness <7 cm with no separate venous drainage of segments II and III as the only grafts to be considered, but these recommendations arose from early experience series which the experts have considered overcome.[35,96] In fact, few anatomical variations preclude the procurement of left lateral grafts.[79,96] The presence of a left hepatic artery originating from the left gastric artery does not represent a contraindication to MIDH and may instead be an advantage. Care should be taken in the case of a right posterior bile duct draining into the left hepatic duct.

Regarding pure laparoscopic donor right hepatectomy (PLRDH), there were mixed reports concerning anatomical contraindications. In an expert meeting held in Korea in 2016, it was stated that PLRDH should be performed in cases with standard bile duct and portal vein anatomy.[45] In a large pioneer study, the rate of major complications was significantly higher in nonstandard versus standard anatomy (9.3% vs 45.5%).[19] It has also been suggested that large grafts (>700 g) increase the difficulty of right lobe MIDH.[45,57] One group suggested that the donor criteria, especially in the early cases of PLRDH, should consist of the following: graft weight <700 g, graft recipient weight ratio >1% and favorable vascular and biliary anatomy.[38] However, the center with the most reported cases does not apply any selection different to open procedure.[17,18,32,39]

CQ11. Recommendation 29: Robotics

The first case of a minimally invasive donor right hepatectomy using robotic assistance was reported in 2012.[99] Two studies compared robotic versus open donor right hepatectomy; one included 13 robotic versus 54 open cases[64] and the other 35 robotic versus 70 propensity score matched open cases.[116] Both groups showed that donor safety is not compromised compared with the open procedure while presenting the established benefits of the minimal invasive approach. The first comparative study of pure laparoscopic versus robotic left lateral donor hepatectomy on 75 MIDH cases shows that both minimally invasive techniques are equally safe and effective in terms of donor benefits from the minimal invasive approach and suggested a possible shorter learning curve with robotics.[117]

CQ12–13. Recommendations 30–34: Transection and Inflow Control

Ultrasonic aspirators (CUSA Cavitron Ultrasonic Surgical Aspirator or equivalent) were the most commonly used instruments for parenchymal transection in 5 reviews.[26,37,46,55,95] Most teams use both an energy device for the superficial layer of liver parenchyma and an ultrasonic aspirator for deeper parenchymal transection. The use of intermittent Pringle maneuver is variable among teams. Previous reports on open donor hepatectomy showed no adverse effects of routine use of intermittent Pringle maneuver (15 minutes occlusion, 5 minutes reperfusion) and when compared with a control non Pringle group, a shorter transection time was noted.[118–120] The safe use of Pringle in MIDH has been reported (15–5 minutes) with a duration between 15 and 75 minutes by some groups.[12,26,64]

CQ14. Recommendations 35–37: Bile Duct Identification and Closure

The method of bile duct identification was precisely reported in most of the manuscripts. Preoperative MRCP is mandatory but additional intraoperative method is recommended. For left lateral grafts, the use of cholangiography was limited to difficult cases. Regarding full right and full liver grafts, a form of biliary intraoperative mapping has been recommended. Although intraoperative cholangiography has been recommended as the reference method, Indocyanine green (ICG) near infrared fluorescence method is increasingly used. A combination of both has been proposed[65] but an experienced group now uses ICG as the only intraoperative visualization method.[16–18,36,39] The number of cases with multiple bile duct openings has been reported to be higher in laparoscopic approach compared to open but did not reach significance in none of the 2 manuscripts which reported this in detail.[121,122]

CQ 15. Recommendations 38–40: Vascular Division

The method of vascular division was also reported in most of the manuscripts. Hepatic artery was secured by locking clips in most reports. In the largest eastern series of right lobe liver grafts, right hepatic artery was divided using both a locking and a metal clip.[121] The portal vein was mostly cut after unilateral stapling, although some other groups reported using locking clips or bilateral staplers. Regarding hepatic veins, most manuscripts reported the use of unilateral staplers, although the use of bilateral staplers was occasionally reported. Two cases of donor portal vein stricture (Clavien3a and 3b) have been reported.[17–19] For left sided grafts, a similar pattern has been reported with clips for hepatic artery, and staplers for portal and hepatic veins. For hepatic veins, unilateral stapler is the most used, although a bilateral stapler was used for the common trunk of the left and middle hepatic veins in left lateral,[41] full left grafts,[14,77] and robotic right lobe.[116]

Section 4: Training and Certification (Table 4)

CQs 16–17. Recommendations 41–42: Training and Learning Curves

All manuscripts recommend that MIDH procedures should be performed by surgeons with experience in laparoscopic liver resections and LDLT. Regarding left lateral grafts, a reduction in the operative time with an increasing number of cases and experience has been reported.[34,36,72,86,110] Two manuscripts reported a decrease in the blood loss with learning curve.[41,86] The achievement of the learning curve for laparoscopic LLS has been settled between 20–25 cases.[36,41,72,86] For right lobes a decrease in operative time, blood loss, Asapartate Aminotransferase levels and hospital stay with progressive cases and experience has also been reported.[16–18,39] By risk adjusted CUSUM analysis, the learning curve for right lobe MIDH has been set at 65–70 cases.[16] The implementation of a MIDH program by Proctorship has been well defined in 2 manuscripts. In both cases, the proctor was an expert surgeon from a different institution, traveling to the center for the purpose of implementing an MIDH program.[34,36] The use of video sessions, review of surgical steps, standardization of procedures, and case by case discussion were all considered important parts of the training.

CQ 18. Recommendations 43–44: Certification and Registries

Five manuscripts discussed appropriately on certification and need for registries although no statistical analysis or results were provided. It is stated that the access to MIDH must be balanced with appropriate training and certification.[34] The authors also disclose that a separate certification process for LDLT is required by UNOS. Due to the difficulties in performing randomized controlled trials in the setting of MILDH, International Registries have been suggested as useful tools for monitoring and comparing results of minimally invasive versus open donor hepatectomies.[37,41,80] Recently, a panel recommended that MIDH should be submitted to the Institutional Review Board and reported in a registry.[45]

DISCUSSION

It must be emphasized that these guidelines are made for teams and individual surgeons with a prerequisite of expertise in LDLT and advanced laparoscopic liver surgery. MIDH is currently performed by a limited but growing number of expert centers and growing numbers are being published. It is not possible to provide a precise percentage of MIDH among LDLT, although it is certainly a minority at the moment. But this is a quickly moving field with growing application. As an example, in the center with the largest experience to date, the percentage of MIDH moved from less than 5% in 2007 (hand assisted) to less than 15% in 2014 (laparoscopic assisted) and 75% in 2016 (pure laparoscopic).[17] However, some of the largest LDLT Centers have not to this date adopted MIDH, and some of them have expressed significant skepticism. This mirrors the adoption of minimally invasive techniques for liver resection of liver tumors that has been slower than for other abdominal procedures.[123] Reasons included concerns about bleeding control and oncological adequacy and, probably, reluctance regarding a major change in practice requiring the acquisition of a whole new set of skills. Evidence concerning safety of MIS for liver resection has now been presented through 2 consensus meetings, 1 guideline report, 2 randomized controlled trials and numerous publications.[6,7,124–127] At the moment, the vast majority of HPB centers have included minimally invasive techniques in their regular practice for minor resections, and a smaller majority of them for major and complex resections.[128–131]

In the case of MIDH, the issue is even more complex than that of regular liver resection for tumor. Indeed, it deals with healthy donors, whose safety is paramount, and includes the additional obligation to provide grafts that should not be of lesser quality or associated with increased risks of complications. Evidence produced so far from expert centers have tempered these concerns by showing equivalent donor and recipient outcomes when compared with standard open procedure. MIDH is considered one of the most technically demanding procedures. It requires full expertise in MIS complex dissection, transection and suturing techniques and facility with novel technologies, including enhanced video equipment, laparoscopic ultrasonography, energy devices, laparoscopic ultrasonic aspirators, and staplers. For some experts, it includes full mastery of robotic surgery.

The presented guidelines are derived from comprehensive and critical review of the available literature. In addition, because of the highly specific nature of the procedure, expert opinion and consensus played a significant role on most technical recommendations. Eighteen CQs were studied and resulted in 44 recommendations.

Rationale and Donor Outcomes

It has been easily agreed that short term advantages observed with MIS liver resection were confirmed in living liver donors. This includes shorter hospital stay and reduced pain. Furthermore, it was emphasized that avoiding long abdominal incisions with muscle division were an even greater advantage in healthy living donors than in patients treated for liver tumors.

There is no evidence suggesting that MIDH is associated with an increased risk of donor death. Although there is always a possibility of under reporting, this is not specific to MIS and donor deaths are usually publicized. To date, no donor death or catastrophic event were reported during or after PLDH. There has been a report of a case of major bleeding and cardiac arrest occurring during donor right hepatectomy.[132] It seems that this procedure was performed using laparoscopic assistance for mobilization and midline incision for transection, but the event was not related to the size of the incision.[133] There is also no evidence of increased donor morbidity both with PLDH and LADH. However, there is a learning curve effect and complications are possible in early experience, a period that requires special care.[19]

Reasonably strong evidence supports that MIDH improves donor quality of life, body image, and obviously cosmesis. Significantly shorter leave from work has been well demonstrated in 1 US study.[77] This is a major point for donors who are family support and those at risk of losing their jobs. Long term incisional problems, including hernias and keloids, a significant issue after open donor hepatectomy, are obviously reduced. Hernias are not rare after open donor hepatectomy and they require repeat surgery including frequent need for a prosthetic reinforcement and a risk of recurrence.[77,134,135] Their suppression is a major advantage. Keloids, a non-rare complaint after open donor hepatectomy, are avoided or at least reduced in size.[136] Finally, abdominal discomfort, reported in up to 35% of cases after open donor hepatectomy, is also virtually suppressed.[135] Finally, 1 study showed that pure laparoscopic left lateral donor hepatectomy was associated with less minor complications and identical major ones than laparoscopic donor nephrectomy.[69] Laparoscopic donor nephrectomy being the current standard practice in donor nephrectomy, this should also apply to left lateral donor hepatectomy.

Recipient Outcomes

Reported recipient and graft survivals are identical with MIDH versus open donor hepatectomy for all types of grafts. Increased warm ischemic times inherent to graft extraction, (usually <10 minutes) have been reported with no clinical consequences and no cases of primary non function were reported. A recent study from the most experienced center comparing pure laparoscopic and open donor right hepatectomy reports an increased rate of recipient biliary complications in the laparoscopy group.[121] This study was not available at the time of the conference but we felt it should be added as this issue requires special attention. A previous trend towards a higher proportion of bile ducts opening in laparoscopic cases was confirmed, but this did not seem to be associated with increased complications in the recipient.[18] Technical precautions for bile duct division are discussed below. The role of the recipient surgeon should also be stressed. Biliary reconstruction is a critical part of the LDLT recipient operation and it requires particular attention and senior supervision.

Techniques

MIDH has been successfully reported for the retrieval of left lateral, full left, and full right grafts. Pure laparoscopic technique is currently largely dominant. However, laparoscopic assisted or hybrid procedures are considered very good techniques that can be used as a definitive procedure or as a bridge to pure laparoscopic techniques. There was concern at the conference that small incisions, with or without laparoscopic assistance, may be associated with exposure limitations, especially during right hepatectomy in large donors.[137] Therefore, small incisions should be applied thoughtfully and extension of incision used liberally to ensure donor safety in case of upcoming difficulties. Quality of exposure and vision is not considered a limitation during pure laparoscopic surgery.

Available data are limited regarding robotic approach, originating mainly from 2 groups.[64,116,117] Excellent outcomes are reported, comparable to fully laparoscopic MIDH for right grafts and to pure laparoscopy for left lateral grafts.[116,117] There is currently no evidence that RADH have a significant advantage over PLDH, but proponents highlight the stable magnified field, 3-D vision, enhanced instrument articulation, and a possibly quicker learning. At the moment, the use of robotics is mainly dependent on surgeon preference.

Although some centers offer MIDH to all their patients, most centers use a selective approach to donor anatomical variations, especially in the case of right liver grafts.[121] An increased number of donor complications has been suggested in the presence of multiple portal branches, multiple small arteries, and significant bile duct variations. It has also been suggested that large grafts (>700 g) the difficulty of right lobe MIDH.[26,57] It has been recommended that institutions starting a new MIDH program should select donors having favorable anatomy.[19]

Most authors recommend the use of ultrasonic aspirator (CUSA or equivalent) for liver transection as it allows precise identification of hepatic venous structures during transection and their safe management. However, other techniques may be used by surgeon's preference, including crush clamp and energy devices. They yield identical results provided they are precise and fully mastered. The use of stapler for parenchymal transection is considered inappropriate for MIDH. Intermittent Pringle maneuver is acceptable when required. Some teams use it routinely and the panel recommended to have it prepared in all cases.

Bile duct division in the donor is a highly critical part of the procedure. As in open donor hepatectomy, millimetric precision is required to avoid remnant bile duct complication in the donor and limit the number of cases with multiple bile ducts in the recipient, hence facilitating reconstruction in the recipient. Energy devices and electric cautery should be avoided in the vicinity of the bile duct during donor hepatectomy to avoid burn injuries and secondary stricture in both donor and recipient. Currently, intraoperative cholangiogram remains the standard for identification of the site of bile duct division. However, ICG real time fluorescence guidance is increasingly adopted and for several teams it has replaced cholangiography.[59,121]

Vascular divisions are the final steps of graft retrieval. They depend on surgeon preferences, but double clipping of arteries, clips, or linear stapler for the portal vein are possible options whereas linear stapling is required for main hepatic veins. Unilateral staplers have the advantage of saving precious millimeters.

Cost of laparoscopic surgery is initially higher (need for state of the art equipment, longer operative time) but this never stood against patient benefit. Randomized controlled trial on laparoscopic versus open liver surgery showed cost effectiveness with operating room costs being balanced by enhanced recovery.[125]

Training and Certification

The era of self-taught laparoscopic liver surgery is passed and specific training should nowadays be organized by new centers wishing to implement MIDH. This can only be done when a strong background of laparoscopic liver surgery has been acquired. Two mains ways were identified including having a designated member of the team spending time visiting an active center and/or inviting an outside expert to supervise and assist the first cases with the local team, referred to as proctoring. Finally, institutional approval and support should be required for a successful new program of MIDH.

Limitations of the Guidelines

Literature evidence is limited which precluded the possibility of a formal consensus conference with an independent jury. Rigorous methodology of available literature review was used but due to the highly technical nature of the subject, several recommendations based on practice and experience necessarily played an important role. The role of the validation committee of highly regarded international LDLT experts was paramount to the value of the final recommendations presented here.

CONCLUSIONS

MIDH was designed to improve the quality of life of individuals donating part of their liver to save someone else's life. Pure laparoscopic techniques are currently the most commonly used compared to laparoscopic assisted and robotic assisted ones. They allow the procurement of left lateral, full left, and full right liver grafts and have reached a high safety level in expert centers. With an increasingly informed and educated population, candidates to living liver donation will become aware of these techniques and will search for centers offering MIDH. We believe that the present guidelines will provide the foundation for a safe diffusion of this unavoidable technical advance in the field of liver transplantation with donor safety as the priority.

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