LLR has now entered the exploration and assessment phases of surgical innovation, particularly at highly specialized centers. <sup>29</sup> For new surgical procedures to become widely adopted as standard operations, they should first be compared with established procedures and shown to be superior in at least some respects. <sup>30</sup> However, acquiring surgical mastery in LLR is difficult and requires specific training. Furthermore, additional instruments are required, and these can add costs beyond those associated with open liver resection (OLR). Enthusiasm for new surgical technologies such as LLR should not stand in the way of proper comparative evaluation. <sup>31</sup>

The Second International Consensus Conference on LLR (IC-CLLR) was held from October 4 to 6, 2014, in Morioka, Iwate Prefecture, Japan, with the dual goal of defining the current role of LLR and developing recommendations and guidelines. This goal was to be achieved through analysis of the available literature and through expert presentations including videos in front of an independent Jury. The organizing committee invited 43 respected surgeons, that is, 34 expert panel members with demonstrated experience in LLR, plus 9 jury members, from 18 countries, to provide evidence and draw recommendations. The organizing committee formulated 17 questions in 2 categories—benefits and risks, and techniques of LLR. Each question was assigned a specific working group, composed of 3 to 7 expert panel members who were selected on the basis of their scientific and clinical activities. A search of the English language literature was performed through MEDLINE, EMBASE, and the Cochrane Library for articles published on LLR between 1991 and August 2014. The expert panel members were asked to add any missing relevant articles according to the questions, prepare reviews of the evidence, and draft recommendations in response to the questions. The jury provided recommendations on questions 1 to 7, which were related to benefits and risks of LLR. Basically, this part of the consensus meeting followed the independent jury-based consensus model (Zurich-Danish model).<sup>32</sup> However, the experts provided recommendations on questions 8 to 17, which were related to technical aspects of LLR.

Approximately 240 individuals from 5 continents attended the ICCLLR. The audience consisted largely of surgeons involved or interested in LLR. State-of-the-art invited and competitive videos were presented that demonstrated many advanced LLR techniques. A member of each working group gave a 15-minute presentation covering their specific question, and each presentation was followed by questions from the jury, the expert panel, and the audience. Final statements and recommendations were presented by the primary author of each of the 17 working groups. The paper will be presented in 2 sections, the jury section followed by the expert technical section.

# DESCRIPTION AND RECOMMENDATIONS REGARDING QUESTIONS (Q1–Q7) CONSIDERED BY THE JURY

The jury consisted of 9 surgeons with expertise in liver surgery including transplantation (Table 1). The members were also selected

**TABLE 1.** Consensus Conference Jury Members United States Steven Strasberg\* Jeffrey Barkun Canada Pierre Clavien Switzerland Palepu Jagannath India William Jarnagin United States Japan Norihiro Kokudo Chung Mao Lo China Russell Strong Australia Masakazu Yamamoto Japan \*Chairman

by Drs Strasberg and Wakabayashi for expertise in clinical research methodology, innovative procedures, surgical safety, stratification of adverse events, and experience with consensus conference methods. Members of the jury had not written papers advocating for or against major laparoscopic liver surgery. The jury considered questions in seven clinical areas (Q1-7). Evidence was evaluated using GRADE<sup>33</sup> and recommendations made according to the Zurich-Danish consensus conference model.<sup>32</sup> In addition, procedures were assessed as to their stage of development according to the Balliol classification of IDEAL.34 The experts reviewed the literature and prepared summaries. The extensive reports provide valuable literature information, and comments and recommendations of the experts were reviewed by the jury and taken into account in their recommendations. This information can be found as Supplemental data files to this paper available at http://links.lww.com/SLA/A754. The jury was divided into 2-person teams to lead the discussion on particular questions. This information can be found as Supplemental data files to this paper available at http://links.lww.com/SLA/A754. All jury members made recommendations on all 7 questions and these recommendations are unanimous.

#### **BACKGROUND**

# **Definition and Rating of Comparators**

As per GRADE, comparators were selected pre hoc to evaluate OLRs and LLRs (Table 2). For some outcomes, the jury sought to determine if the evidence indicated that the results of LLR were clinically equal or at least not inferior to OLR (Table 2). For other outcomes, the jury evaluated whether the outcome after LLR was superior to OLR (Table 2). In the case of postoperative complications, the jury evaluated evidence for equality or superiority depending on the complication. Some complications like wound complications and pulmonary complications might be expected to be decreased by LLR (superiority of laparoscopic surgery) while others such as bile leaks are potentially greater and needed to be evaluated for equality. The list of comparators was accepted by the experts and the jury before the conference. The jury opinion of the relative importance of the comparators was determined before the meeting using a utility scale of 1 to 10. Scores were highest for postoperative mortality, complications, and margin negativity.

# Rating of Quality of Evidence by GRADE

GRADE rates quality of evidence by a 2-step process.<sup>33</sup> First, the study is given a preliminary rating based on methodology used.

**TABLE 2.** Comparators Considered by Jury and Their Relative Importance as Rated by the Jury

Comparator	Mean	SD
Mortality*	8.9	0.4
Complications*†	8.5	0.5
Margin negativity*	7.3	1.3
Overall survival*	6.9	1.5
Parenchymal sparing*	6.3	1.8
Cost*	5.6	1.0
Indication (benign vs malignant)*	5.4	2.5
Blood loss†	6.0	2.5
LOS†	5.1	1.4
Recovery†	6.4	1.0
Pain†	5.5	1.8
Cosmesist	4.0	1.6
Quality of life†	4.9	1.7
Incisional sequelaet	4.8	2.6

†Evaluated for superiority.

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RCTs are given a HIGH rating; observational studies, such as cohort and case control studies, receive a LOW rating; and case series a VERY LOW rating. In the second step, the studies are examined in detail to determine whether the rating should be moved up or down on the basis of 7 factors, which gauge the evidence by criteria other than study type. Three of these permit raising the rating of a study (see below).33

All available studies on LLR are observational studies—cohort studies, case series, or case reports. There are no published RCTs. According to GRADE, the quality rating of evidence in such studies is LOW. The jury determined whether any studies fulfilled criteria for raising or decreasing the rating. While there are 3 criteria for doing so, the one that was applicable in some of the available studies is "large treatment effect." A treatment effect of at least 50% permitted elevation of the rating from LOW to MODERATE. Because the studies were all observational, the criteria available in "MINORS," a validated method for rating surgical observational trials,35 were also used qualitatively to examine study quality. Note that the term "MI-NORS" is an acronym unrelated to the term "MINOR" used in this paper in reference to the extent of a liver resection.

# Determination of Strength of Recommendation

The jury made 2 types of recommendations: Type A and Type B. Type A are based on (1) the quality of the body of evidence, (2) the benefit/risk ratio, (3) the benefit/cost ratio, and (4) the preferences and values of patients. Type A recommendations may be STRONG, WEAK, or NONE; the jury preferred the term MODER-ATE to WEAK. Type B are recommendations for future steps that would improve the level of evidence for the comparator. The strength is based on a judgment of the prioritization of the effort that is required: Type B recommendations may be STRONG or MODERATE.

## MINOR and MAJOR Laparoscopic Resections

The classical definition was used. A MINOR resection is one in which 2 or fewer Couinaud segments are removed. A MAJOR resection is one in which 3 or more segments are removed. In actuality, most laparoscopic MINOR resections reported in the literature are left lateral sectionectomies or resections of segments 2, 3, 4b, 5, and 6, that is, mainly the anterior and inferior segments. The findings and recommendations of the jury under the term MINOR are based on this literature and therefore those types of resections and not more difficult resections involving posterior-superior segments.

Fortunately, the grading of complexity/difficulty of both OLRs and LLRs is in evolution. Currently, experts rate the complexity of various open 2-segment resections, that is, left lateral sectionectomy, right posterior sectionectomy, and right anterior sectionectomy very differently.<sup>36</sup> In fact, this was recognized in the Louisville consensus conference in which it was concluded that laparoscopic resections of posterior superior segments should be considered to be "major" resections. For the purposes of this report the important issue is that it be clear to the reader how the terms were used by the jury.

# Stage of Development According to the Balliol Classification of IDEAL

The stage of development of the various procedures, that is, minor LLR, major LLR, live donor LLR, and robotic LLR was categorized using the Balliol classification of IDEAL.34 Also taken into account were the conclusions and recommendations of the Belmont report in regard to oversight of innovative procedures.<sup>37</sup> These procedures fell into 1 of 3 categories: IDEAL stage 2a-"development in progress"; IDEAL stage 2b—"Exploration" stage; and IDEAL stage 3—"Assessment" phase. The first (IDEAL stage 2a—"development in progress) is the earliest phase of development of the three. Procedures in this category have the highest degree of risk due to novelty. Assignment to this category indicates the need for institutional ethical approval to perform the procedure as well as a reporting registry. The third (IDEAL stage 3-"Assessment" phase) covers procedures that have become standard practice. Risk due to novelty is low, but continuing assessment of outcomes is encouraged especially if high-level studies are lacking. IDEAL stage 2b is intermediate to the other 2 stages and is a stage in which considerable preliminary data supporting the safety of the procedure are present but in which it is judged that there is still risk associated with novelty. Such procedures should continue to be introduced in a cautious manner. The term "cautious" indicates first that surgeons undertaking these procedures are experienced both in liver surgery and advanced laparoscopy and second that outcomes are evaluated in registries and by RCTs where appropriate. An example of this is the National Surgical Quality Improvement Program registry in which serious morbidity and mortality of both open and laparoscopic procedures are recorded and reported.<sup>38</sup> Finally implicit in IDEAL 2b is that the patient should be provided with information regarding the status of the procedure namely that (a) the procedure is an innovative procedure which has not yet become standard practice, (b) that as an innovative procedure it may have unknown risks, and (c) that the procedure should be performed only by those who have expertise in advanced laparoscopic techniques and major open liver surgery. Again it should be noted that the jury used IDEAL as a guide but also used other sources such as the Belmont report in framing its recommendations regarding oversight of procedures.

# PRESENTATION OF FINDINGS

The outcomes under the questions 1 to 4 are presented separately for MINOR and MAJOR procedures, whenever the data allowed. Thus questions 1 and 2 are presented in 3 sections—MINOR, MAJOR and MINOR/MAJOR combined, the latter when the results of MAJOR and MINOR resections could not be distinguished. The questions covering the areas of robotic surgery, laparoscopic live donor surgery and the question whether RCTs are feasible are covered in separate sections.

# Results for Comparators in Q1 to Q4 for MINOR LLRs

Data accumulated since 2008 confirm and add weight to the recommendation of the first consensus conference that MINOR liver resections should be considered to be a standard practice (IDEAL 3). Although the evidence level remains LOW, the benefit/risk ratio in available studies and the treatment effect for certain comparators is high. These allow a STRONG recommendation. This does not indicate that performance of these procedures by OLR is not also acceptable practice or that higher levels of evidence are still not desirable.

#### Q1. Short-term Outcomes

(Supplemental data, available at http://links.lww.com/SLA/

Comparator: Operative mortality (MINOR resections) Result of Literature Studies: Laparoscopic outcomes are not inferior.

Quality of Evidence: LOW (cohort studies, case series)

Comment: Multiple underpowered studies. Large number of patients studied

Recommendation Type A: IDEAL stage 3

Strength of recommendation: STRONG

Recommendations Type B: Serious underreporting of mortality rates may occur if only 30-day mortality rates are provided. Report 30- and 90-day mortality rates in studies (STRONG recommendation). It is unlikely that high-level studies can be done because

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of low frequency of the event for MINOR resections but 90-day mortality rates are needed. Best possibility for evaluation through large registry studies of LLRs and OLRs (MODERATE recommendation)

Comparator: Postoperative complications (MINOR Resections)

Result of Literature Studies: Laparoscopic outcomes are superior in some areas and do not appear different in other areas

Quality of Evidence: LOW (cohort studies, case series)

Comments: Multiple complication-reporting schemas have been used making comparisons difficult. Results in cirrhotic livers, especially as pertains to possible reduction in postoperative ascites after laparoscopic surgery, show interesting treatment effect but unable to determine if treatment effect is more than 50%. As a result, adjustment to MODERATE quality of evidence was not possible.

Recommendation Type A: IDEAL stage 3 Strength of Recommendation: STRONG

Recommendations Type B: To perform higher quality studies to definitively determine whether morbidity of LLR is decreased compared to OLR in some areas. This effect is likely to be observed at low sample size in cirrhotics (MODERATE). Also improve consistency of reporting of complications based on available standard classification systems<sup>39-41</sup> (STRONG).

Comparator: Margin negativity in malignant diseases (MI-NOR resections)

Result of Literature Studies: Laparoscopic outcomes are not inferior

Quality of Evidence: LOW (cohort studies, case series)

Recommendation Type A: IDEAL stage 3

Strength of Recommendation: STRONG

Recommendations Type B: To perform higher quality studies to definitively determine whether margin negativity rates of LLR are noninferior (MODERATE). This is particularly an issue when a lesion is located near a vascular structure.

Comparator: Length of stay (MINOR resections)

Result of Literature Studies: Laparoscopic outcomes are superior

Quality of Evidence: LOW (cohort studies, case series)

Adjustment of level by criteria: Data show effect size more than 50% and justify elevation of the evidence grade to MODERATE.

Recommendation Type A: IDEAL stage 3

Strength of recommendation: STRONG

Recommendation Type B: To include LOS in future studies of LLR to confirm findings at a higher level of evidence (MODERATE), and with consistently objective criteria for discharge.

# Q2. Long-term Outcomes

(Supplemental data, available at http://links.lww.com/SLA/

Comparator: Overall survival (MINOR resections)

Result of Literature Studies: Laparoscopic outcomes are not

Quality of Evidence: LOW (cohort studies, case series).

Comment: Multiple underpowered studies. Large number of patients studied

Recommendation Type A: IDEAL stage 3 Strength of recommendation: STRONG

Recommendation type B: The question whether overall survival of LLR is not inferior to OLR could only be definitively answered by an RCT with a very large sample size. It is unlikely that such a study would ever be performed. The recommendation is for a registry of LLRs and OLRs, in which possible differences in overall survival might be detected. The recommendation strength is MOD-ERATE.

# Results for Comparators in Q1 to Q4 for MAJOR LLRs

#### Q1. Short-term outcomes

Comparator: Operative mortality (MAJOR resections) Result of Literature Studies: Laparoscopic outcomes are not inferior

Quality of Evidence: LOW (cohort studies, case series)

Recommendation Type A: IDEAL stage 2b

Strength of recommendation: STRONG

Recommendations Type B: Report 30- and 90-day mortality rates in studies (STRONG recommendation). It is unlikely that highlevel studies can be done because of low frequency of the event. Best possibility for evaluation through registry studies (both LLR and OLR cases) especially as MAJOR LLR diffuses into more general use (STRONG recommendation).

Comparator: Postoperative complications (MAJOR resections)

Result of Literature Studies: Laparoscopic outcomes are not inferior. Liver-related outcomes such as liver failure are much more related to volume of liver resected than surgical approach. Suggestion that some laparoscopic outcomes are superior. Great variability in how individual complications are collected and reported including failure to report severity

Quality of Evidence: LOW (cohort studies, case series)

Recommendation Type A: IDEAL stage 2b

Strength of recommendation: STRONG

Recommendations Type B: To perform higher quality studies to definitively determine whether morbidity of LLR is noninferior/superior. The need to use of standardized classification of complications and their severity<sup>39–41</sup> is mandatory. The recommendation strength is STRONG.

Comparator: Margin negativity (MAJOR resections) Result of Literature Studies: Laparoscopic outcomes are not inferior.

Quality of Evidence: LOW (cohort studies, case series)

Note: There is a concern that the patients being compared between open and laparoscopic major resection may not be identical, in particular, that resections of lesions close to vessels, may be overrepresented in some open series.

Recommendation Type A: IDEAL stage 2b

Strength of recommendation: STRONG

Recommendations Type B: Continue to evaluate procedure as an ongoing trial. To perform higher quality studies to definitively determine whether margin negativity rates of LLR are noninferior. The recommendation strength is STRONG, especially as this is thought to be an important determinant of recurrence-free survival for many cancers.

Comparator: Length of stay (MAJOR resections)

Result of Literature Studies: Laparoscopic outcomes are superior.

Quality of Evidence: LOW (cohort studies, case series)

Adjustment of level by criteria: Data very consistently show effect size more than 50% and justify elevation of the grade to MOD-ERATE.

Recommendation Type A: IDEAL stage 2b Strength of recommendation: STRONG

Recommendation Type B: To include LOS in future studies of LLR to confirm findings at a higher level of evidence and with consistently objective criteria for discharge. Recommendation is STRONG.

Comparator: Parenchymal sparing (MAJOR resections) Recommendations can be found in addenda.

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## Q2. Long-term outcomes

Comparator: Overall survival (MAJOR resections)

Result of Literature Studies: Laparoscopic outcomes are not inferior.

Quality of Evidence: LOW (cohort studies, case series)

Comment: Multiple significantly underpowered studies

Recommendation Type A: IDEAL stage 2b Strength of recommendation: STRONG

Recommendation Type B: The question whether overall survival of LLR is not inferior to OLR could only be definitively answered by an RCT with a large sample size. It is unlikely that such a study would ever be performed given the annual volumes of liver resections performed per indication. The recommendation is thus registry of laparoscopic and open procedures in which large differences in overall survival might be detected. The recommendation strength is STRONG.

# Results for Comparators in Q1 to Q4 in Which Results of Comparators for MINOR and MAJOR Resections Cannot Be Evaluated Separately

#### Q1. Short-term outcomes

Comparator: Transfusion/Blood loss (MINOR and MAJOR resections)

Comment: Transfusion is an especially important outcome measure in patients with malignancies as transfusion avoidance has been associated with delayed/decreased postoperative tumor recurrence.

Result of Literature Studies: Estimated blood loss was considered by the jury to be an unreliable metric, and this is supported by the literature. Comments are based on results of transfusions received during surgery or in the postoperative period. Many studies were conducted in a manner, which does not allow differentiation between major and minor procedures. However, blood transfusions are rarely given to patients having MINOR resections. Therefore, the results are taken to mainly refer to MAJOR procedures. Some studies report intraoperative transfusion only. Those also reporting postoperative transfusion do not do so over a uniform postoperative period.

Result of Literature Studies: Laparoscopic outcomes are superior

Quality of Evidence: LOW (cohort studies, case series)

Recommendations Type A: For MINOR: IDEAL stage 3, For MAJOR: IDEAL stage 2b

Recommendations Type B: To perform higher quality studies to definitively determine whether transfusion rates of LLR are superior—STRONG. Consider performing studies to standardize method of blood loss measurement—STRONG

Comparator: Short-term recovery (MINOR and MAJOR resections)

Result of Literature Studies. The variable is poorly defined and outcomes cannot be evaluated.

Quality of Evidence: LOW (cohort studies, case series)

Recommendation Type B: Continue to evaluate procedure as is ongoing trial. Extract data from higher quality studies that examine this variable, which has been poorly addressed. STRONG because it is one of the main rationale for procedures to be done laparoscopically.

# Q2. Long-term Outcomes

Recommendations on Incisional Hernia and Cosmesis can be found in addenda.

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# Q3. COST

(Supplemental data, available at http://links.lww.com/SLA/A757.)

Comparator: Cost (MINOR and MAJOR resections)

Result of Literature Studies: Laparoscopic outcomes are not inferior though there may be a difference between MINOR and MA-JOR resections (see later).

Quality of Evidence: LOW (cohort studies, case series)

Adjustment of level by criteria: The level of evidence is based on cohort or case control studies (rating LOW EVIDENCE), but the data show effect size more than 50% for MINOR resections and justify elevation of the grade to MODERATE. There is a reasonable possibility that results are health care system specific

Recommendation Type A: IDEAL stage 2b for MAJOR and IDEAL stage 3 for MINOR

Strength of recommendation: STRONG

Recommendations Type B: To perform additional studies targeting MAJOR resections while taking different health care systems into account as well as possibly indirect costs. MODERATE

# Q4. Pain and Quality of Life

(Supplemental data, available at http://links.lww.com/SLA/A758.)

Comparator: Pain (MINOR and MAJOR resections)

Result: The studies indicate an improvement in this variable. Evaluation is hampered by measurement methodology.

Quality of Evidence: LOW (cohort studies, case series)

Adjustment of level by criteria: The studies indicate an improvement in this variable over time but the effect size is less than 50% and therefore do not justify an increase in the rating of the evidence to MODERATE.

Recommendation Type A: IDEAL stage 2b for MAJOR and IDEAL stage 3 for MINOR

Recommendation Type B: To perform higher quality studies to definitively determine whether lower pain scores after LLR using are superior.

Comparator: Quality of life (MINOR and MAJOR resections)

Result: Few studies. Not different from open surgery

Quality of Evidence: LOW (cohort studies, case series)

Adjustment of Level by Criteria. None

Recommendation Type A: IDEAL stage 2b for MAJOR and IDEAL stage 3 for MINOR

Recommendation Type B: To perform higher quality studies to definitively determine whether Quality of Life scores after LLR using are superior.

# **Results for Other Questions**

## Q5. Robotic Liver Resection

(Supplemental data, available at http://links.lww.com/SLA/A759.)

Result: A small number of studies report that outcomes of robotic liver resections are superior or not inferior to other techniques. There are also claims that learning minimally invasive liver surgery is easier with the robotic approach. Possible need for 2 trained surgeons to perform procedures especially for MAJOR liver surgery. Note that the range of instruments available for robotic liver surgery is currently much smaller than for laparoscopic or open techniques. At present this type of surgery is considered to be IDEAL stage 2a (Development)—especially in regard to instrumentation.

Quality of Evidence: LOW (cohort studies, case series) and sparse

Recommendation Type A: IDEAL 2a

Recommendation Type B: Requires both ongoing institutional ethical approval and a reporting registry of all cases in place before beginning to perform this procedure. Close evaluation of results by registry and comparative studies using higher quality methodology. Cost/benefit (value) studies particularly desirable given the cost of robotic technology. More rigorous evaluation of claims re learning minimally invasive surgery (see Result). Clarify level of personnel required for MAJOR liver surgery. Recommendation is STRONG.

# Q6. Laparoscopic Donor Hepatectomy PEDIATRIC

(Supplemental data, available at http://links.lww.com/SLA/A760.)

Result: Not different from open surgery in safety in highly specialized centers. Has advantages of minimally invasive surgery.

Quality of Evidence: LOW (cohort studies, case series)

Recommendation Type A and B: Procedure is classified as IDEAL 2b. In this case, the procedure requires institutional oversight and a registry to determine short and long term outcomes in both donor and recipient. Rationale: Essential to determine benefit/risk ratio ("Balance of harms") The recommendation is STRONG.

# Q6. Laparoscopic Donor Hepatectomy ADULT To ADULT

Result: Insufficient evidence from few centers Quality of Evidence: LOW (cohort studies, case series) Recommendation Type A and B: Procedure is classified as IDEAL 2a.

Requires both ongoing institutional ethical approval and a reporting registry of all cases in place before beginning to perform this procedure. Long-term outcomes in donors and recipient needed. On the basis of potential and unknown risk to donor and level of surgical skills required, this procedure cannot be recommended for wide introduction at this time. Rationale: Essential to determine benefit/risk ratio ("Balance of harms"). The recommendation is STRONG.

# Q7. Randomized Controlled Trials

Result. None currently available but 2 trials in progress. At the time of writing, 2 RCTs are in accrual comparing laparoscopic to OLRs, that is, the ORANGE II Plus trial (http://clinicaltrials.gov/ct2/show/record/NCT01441856) and the OSLO CoMet Trial (http://clinicaltrials.gov/ct2/show/NCT01516710). These trials are testing a number of the comparators evaluated at the consensus conference, but at this time no results are available.

Recommendation: The Jury strongly encourages launching and participation in such trials. The recommendation is STRONG.

# Additional JURY Recommendations Regarding Major Resections

- MAJOR laparoscopic liver surgery requires a high level of technical skill and has a steep learning curve. How skills should be acquired by trainees and surgeons already in practice should be the subject of an urgent focused effort by the leaders in this field. The future of laparoscopic liver surgery is dependent on this issue. STRONG recommendation.
- A scoring system is being proposed to grade the technical difficulty of laparoscopic liver surgery to guide the development of expertise safely. Validation and application of this process is STRONGLY recommended.

# **EXPERT PANEL SECTION**

#### Introduction

The technique-related questions were discussed among the expert panel members, who reviewed the literature and shared their experiences and knowledge. The quality of the evidence was LOW. STRONG recommendations reflect unanimity or near unanimity among experts. These recommendations are based upon the literature review and the expert opinions.

The statements and recommendations are presented in Table 3.

#### **EXPERT RECOMMENDATIONS**

# Spread, Difficulty, Alternatives

# Q8. Current Spread of LLR

The number of LLRs reported has steadily increased, especially since 2009, with the increase marked by greater proportions of major and anatomic LLRs, although minor resections still comprise the vast majority of procedures in clinical practice. East Asia, North America, and Europe seem to be witnessing the greatest diffusion of LLR. The number of hepatocellular carcinoma (HCC) cases to which LLR is applied has increased steeply over the past 5 years, especially in Asia and Europe, and the rate of conversion to OLR is gradually decreasing. 44,45

# Q9. A Difficulty Scoring System for LLR

In an effort to estimate the difficulty of LLR easily before surgery, a novel difficulty scoring system was created for discussion at the ICCLLR. <sup>46</sup> The difficulty of LLR is determined by various factors, such as the tumor size, the extent of liver resection, the tumor location, the proximity to major vessels, and the severity of fibrosis. <sup>46</sup> The difficulty scoring system can be used to predict the difficulty of LLR from preoperative variables and to appropriately select patients according to the surgeons' skill level, ranked as low, intermediate, advanced, or expert. In addition, to these factors, it was suggested that the use of hand-assisted laparoscopic surgery (HALS) and the hybrid method (in which the operation is begun laparoscopically and completed through a small open incision) are likely to reduce certain difficulties associated with pure LLR and should be taken into account in future difficulty scorings.

## Q10. The Role of HALS and Hybrid Procedures in LLR

Although pure laparoscopy is the most commonly used technique worldwide, there are geographical differences, and many centers use a combination of pure laparoscopic, HALS, and the hybrid technique in selected cases. <sup>2,47–49</sup> Although there are no data that suggest any of these 3 approaches is superior to the others, HALS and the hybrid method are claimed by their proponents to be beneficial for large lesions, <sup>50,51</sup> posterior lesions, <sup>52,53</sup> donor hepatectomy <sup>20,54–58</sup> and for the training of surgeons in major LLR techniques. <sup>44,47,59</sup> HALS and the hybrid method can be used to manage intraoperative difficulties that are encountered, and they can in theory decrease the frequency of conversion to a full open incision. <sup>47,59</sup>

# Techniques

## Q11. Conceptual Changes

The caudal approach is the main conceptual change in LLR. 30,60,61 The caudal approach, which relies on visual magnification, offers improved exposure around the right adrenal gland and the vena cava and greatly facilitates identification of the Laennec's capsule 2 and the Glissonian pedicle at the hilar plate. Furthermore, meticulous caudal-cranial transection of the hepatic parenchyma with magnification results in better identification of intraparenchymal structures for optimal transection of the liver. Compared to the anterior approach, which has been described for the resection of large tumors with liver parenchymal transection before right lobe mobilization, 63 the caudal approach can be applied efficiently to

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#### TABLE 3. EXPERT TECHNICAL Recommendations for LLR

#### Spread, difficulty, alternatives

Q8. What is the spread of LLR?

- 1. The number of LLRs has increased steeply worldwide over the past 5 years, and published conversion rates have gradually decreased.
- Q9. What determines the difficulty of LLR?
  - 1. The difficulty of LLR should be estimated by a combination of factors including the extent of liver resection, tumor location, tumor size, proximity to major vessels, and the severity of fibrosis.
  - 2. Preoperative estimation of the difficulty of LLR is useful in selecting appropriate patients according to the surgeon's experience and skill levels.
- Q10. What is the role of HALS and the hybrid method?
  - 1. Pure LLR, HALS, and the hybrid method appear equivalent and are a matter of the surgeon's preference.
  - 2. HALS and the hybrid method are used to manage intraoperative difficulties anticipated for pure LLR.

#### Techniques

Q11. What has changed in the concept of liver resection?

- 1. The "caudal" approach is the main conceptual change in LLR, in contrast to the "anterior" approach in OLR.
- 2. The "lateral approach" (left lateral decubitus) gives access to right posterior segments.
- Q12. What are the essentials of bleeding control in LLR?
  - 1. A temporary increase in CO<sub>2</sub> pneumoperitoneum pressure can be used to help control bleeding during LLR.
  - 2. Low central venous pressure (<5 mmHg) is recommended during LLR, as in OLR.
- 3. Laparoscopic suturing skills are essential for LLR.
- Q13. What is the best technique for parenchymal transection?
- 1. Currently, several techniques and devices are equivalent for parenchymal transection in LLR and should be left to the surgeon's preference, as in OLR.
- Q14. What kind of energy devices should be used for LLR?
  - 1. Various energy devices appear to be equivalent and should be left to the surgeon's preference and expertise, as in OLR.
- 2. An argon beam coagulator, if used for hemostasis, requires caution to avoid potential gas embolism.
- Q15. What is the best approach to the hilar structures (individual or Glissonian approach)?
- 1. Individual hilar dissection and the Glissonian approach appear equivalent and should be left to the surgeon's preference and expertise, as in OLR.
- Q16. Is anatomical resection preferable for LLR?
- 1. Anatomical resection for HCC and parenchyma-sparing strategy for CRLM are recommended as in the open approach and require continued evaluation of their application to LLR.

# Simulation, navigation

- Q17. What is the role of simulation and navigation in LLR?
  - 1. Preoperative simulation is useful for measuring the remnant liver volume, visualizing the anatomy and tumor location, and planning the resection plane in selected cases,
- All publications in this area are cohort or case series. Therefore the quality of the evidence is judged as LOW.
- All recommendations are STRONG by a group of experts.

CRLM indicates colorectal liver metastasis.

expose the inferior vena cava from caudal to cranial with division of the short hepatic veins before parenchymal transection. <sup>61,64</sup> In addition, CO<sub>2</sub> pneumoperitoneum is likely to reduce bleeding from hepatic veins. <sup>30</sup> Placement of the patient in the reverse Trendelenburg position should help decrease the venous pressure and improve exposure by gravitationally shifting visceral structures away from the liver hilum. Other conceptual changes include the superior and lateral approaches with or without the use of intercostal or transthoracic trocars. <sup>22,65</sup> For these approaches, the patient is placed in the left lateral decubitus position. The left lateral decubitus position or even the prone position <sup>66</sup> offers better exposure of the right posterior segments and lifts the right hepatic vein higher than the vena cava to reduce hepatic venous bleeding. <sup>30</sup> However, there are some inherent drawbacks to LLR, such as lack of tactile sensation and restricted maneuvers that can lead to challenges in treating bleeding.

### Q12. Essentials in Bleeding Control

The CO<sub>2</sub> pneumoperitoneum is generally established at 10 to 14 mm Hg, <sup>67-72</sup> and this provides for fairly good control of back-bleeding during liver transection. <sup>30,69</sup> Low central venous pressure (<5 mm Hg) should be used during LLR, as in open surgery. <sup>71,72</sup> Selective control of the inflow during laparoscopy may be more efficient than during open surgery (possible effect of the pneumoperitoneum). In cases of severe bleeding, increasing the pneumoperitoneum pressure <sup>30</sup> and decreasing the airway pressure by a brief pause in the artificial ventilation <sup>72</sup> are maneuvers that can be used to decrease back-bleeding. Although there were no data as to what pneumoperitoneum pressure should be used to decrease back-bleeding when encountered, the range used by some members of the expert

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technical panel was 16 to 20 mm Hg. Careful inspection after decreasing the pneumoperitoneum pressure should be performed routinely, along with selective bipolar coagulation or suture at the bleeding point.  $^{73}$  Suturing skills are needed for all LLR.

# Q13. Parenchymal Transection

Transection of the superficial layer of the liver parenchyma can be done with an energy device. Deeper transection should be performed meticulously by exposing intraparenchymal structures with an ultrasonic aspirator (Cavitron ultrasonic surgical aspirator or equivalent), the clamp-crushing technique, or similar parenchymal dissection technique. 74 Hemostasis is usually achieved with bipolar cautery for vessels of 2 mm or less, and with vessel sealing devices or clips for vessels of 3 to 7 mm. Locked clips or staplers are used for vessels of more than 7 mm. As in open surgery, some authors recommend the use of staplers for parenchymal transection. 75 This is an efficient and expeditious technique. However, many consider it lacks precision and identification of divided structures. Almost all authors have reported using staplers to secure and divide major vessels such as the main hepatic veins or portal vein branches as well as the segmental Glissonian pedicles. Therefore, multiple surgical implements are frequently chosen and, as in OLR, it is difficult to specify the best technique and device for laparoscopic hepatic parenchymal transection, which is mainly dependent on surgeon's preference.

## Q14. Energy Device

Unlike open surgery in which liver resection can be performed without any specific technology outside of regular cautery (eg, the crush-clamp technique), LLR typically involves the use of some kind

of energy device. No specific energy device has emerged as superior over another,  $^{76}$  The argon beam coagulator is not generally recommended due to the risk of gas embolism.  $^{77}$ 

# Q15. Hilar Approach

In the case of right or left hepatectomy, hilar dissection with individual vessel preparation is a standard practice. It requires caution and planning by preoperative imaging to identify anatomical variations. Hilar dissection cannot be performed distal to the first bifurcation of the portal branch (ie, the right anterior and posterior sectional branches). The Glissonian approach serves as an important alternative if it is applied appropriately. <sup>13–15,78–80</sup> A discussion ensued about the potential "pitfalls" of stapling the right or left hilar pedicle via Glissonian approach with potential risk of injury or stenosis to the contralateral hepatic duct. It was agreed that only surgeons experienced with this technique should use it.

# Q16. Anatomical Resection

Remnant liver volume and tumor clearance are important issues in LLR, as they are in OLR. Two basic surgical techniques are commonly used to reduce disease recurrences: anatomical resection for HCC and margin-negative parenchyma-sparing resection for colorectal cancer liver metastasis. Anatomical resection refers to parenchymal preserving resections of portal territories including sectionectomy, segmentectomy, and subsegmentectomy. 13-15,22,72 These are complex resections that require identification of anatomical boundaries. These boundaries rely on external landmarks, intraoperative ultrasound, and selective clamping using the Glissonian approach. Superficial resection can be performed nonanatomically according to a parenchyma-sparing strategy, 81,82 but care must be taken to secure an adequate resection margin due to the lack of tactile sensation during LLR. The use of intraoperative ultrasound either for accuracy of clear margins or to avoid injuries of major pedicles is recommended during LLR.

# Simulation, Navigation

# Q17. Simulation, Navigation

Preoperative simulation is useful for measuring the remnant liver volume, visualizing the anatomy and tumor location, and defining the resection plane.<sup>83,84</sup> Further study is needed to evaluate the effect of simulation and navigation on clinical outcomes in terms of both short-term and long-term results.

# **Summary of JURY Recommendations**

- MINOR LLR is confirmed to be a standard practice in surgery but is still in an assessment phase (IDEAL 3) as it is adopted by an increasing proportion of surgeons. Judged as a whole available literature studies indicated that some outcomes such as certain postoperative complications and length of stay were superior to open procedures and no outcomes were inferior. Unfortunately, the quality of studies is generally designated as LOW. Thus, additional higher quality studies are suggested to define its role and benefits in relation to open surgery.
- MAJOR LLR is an innovative procedure. It is still in an exploration or learning phase (IDEAL 2b) and has incompletely defined risks. It should continue to be introduced cautiously. Judged as a whole available literature studies indicated that length of stay is superior to open procedures and other outcomes were not inferior. Blood loss is also reported to be less but questions remain regarding the methodology used. Again the quality of studies is generally designated as LOW. Therefore, there are strong recommendations for additional higher quality studies includ-

- ing registries to define its role and benefits in relation to open surgery.
- METHODOLOGIC PROBLEMS resulted in a number of additional recommendations including the reporting of 90-day mortality, reporting of complications based on available standard classification systems, and standardization of methods of evaluating blood loss
- MAJOR ROBOTIC SURGERY: Very little data available for evaluation. Thus at this time the procedure fits IDEAL 2a best. Advisable to be done within institutional review board—approved registry.
- LAPAROSCOPIC DONOR SURGERY: Pediatric donor surgery: as for major laparoscopic liver surgery is IDEAL 2b. Adult to adult donor surgery is an innovative procedure in a development phase (IDEAL 2a). At this time, the recommendation is that it be performed under institutional ethical approval and reporting registry.
- EDUCATION: A major focused effort is required to determine how the laparoscopic skills needed for MAJOR LLR should be obtained by trainees and hepatopancreatobiliary surgeons in practice.

# **Summary of Expert Technical Recommendations**

- GENERAL AGREEMENT is achieved that experience in both open liver surgery and advanced laparoscopy is mandatory and surgeons must begin with minor laparoscopic resections.
- A GLOBAL SPREAD of LLR has occurred after the first international consensus conference in 2008. Overall, LLR is utilized in a small percentage of liver resections (range: 5%–30%), although some groups have reported higher rates, reaching 50% to 80%. The vast majority of data arise from minor resections but the proportion of major resections is increasing.
- THE SCORING SYSTEM is proposed for estimating the difficulty of LLR preoperatively.
- HALS AND HYBRID TECHNIQUE can help overcome certain difficulties associated with pure LLR and may be useful in minimizing conversions.
- CONCEPTUAL CHANGES include
  - The caudal approach that optimizes hilar dissection and transection of the liver parenchyma for major and/or anterior resections.
  - The lateral approach (left lateral decubitus position) that optimizes access to posterior segments.
- A CO<sub>2</sub> PNEUMOPERITONEUM of 10 to 14 mm Hg is generally used along with low central venous pressure and allows a good control of the bleeding during LLR.
- LAPAROSCOPIC PARENCHYMAL TRANSECTION requires specific instruments. Several are available including a variety of energy devices and staplers. It is essential that the surgeons have a concrete understanding of the advantages and limitations of available instruments to conduct safe and effective LLR.
- ENERGY DEVICES are efficient and reliable but cannot replace
  the acquisition of basic skills of hepatic surgery such as meticulous dissection, direct visualization, and sealing of the vascular
  structures. Caution should be made with the use of argon beam
  coagulator.
- HILAR APPROACH includes individual hilar dissection and Glissonian approach. Although individual hilar dissection is the standard technique, Glissonian approach is feasible and can be useful for anatomical liver resection, especially hemihepatectomy, sectionectomy, or less. It can reduce the operative time but needs expertise, skills, and knowledge of liver anatomy.
- ANATOMICAL RESECTION for HCC and margin-negative parenchyma-sparing resection for colorectal cancer liver metastasis are standard of care procedures, but the laparoscopic versions of these techniques need to be standardized to increase propagation.

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• PREOPERATIVE SIMULATION seems accurate in measuring volumetrics and surgical margins. Current studies lack intraoperative real-time navigation.

## **ADDENDA**

## Q1. Short-term Outcomes

Comparator: Parenchymal sparing (MAJOR resections) Result of Literature Studies: Insufficient evidence

Comment: The jury notes the concern that larger procedures resecting more liver parenchyma are sometimes favored if the procedure is done laparoscopically because a smaller parenchyma-sparing operation may be more complex laparoscopically. The magnitude of this issue is unknown.

Quality of Evidence: LOW (cohort studies, case series) Recommendation Type A: none

Recommendation Type B: Continue to evaluate procedure as is ongoing trial. Extract data from higher quality studies that examine this variable, which has been poorly addressed. STRONG because the possibility of sparing parenchyma through magnified visualization is stated as a rationale for procedures to be done laparoscopically.

# Q2. Long-term Outcomes

Comparator: Incisional hernia (MINOR and MAJOR resections)

Result of Literature Studies: Insufficient evidence

Recommendations: None

Comparator: Cosmetic result (MINOR and MAJOR Resections)

Result of Literature Studies: The level of evidence is based on cohort or case control studies evaluating single port approach. Although the available evidence is limited, cosmetic advantage in lap liver resection is apparent, as is the case with other laparoscopic

Quality of Evidence: LOW (cohort studies, case series) Recommendations: None

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Details of members of the expert panels can be found in Supplemental data files available at http://links.lww.com/SLA/A754.

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