

# The Southampton Consensus Guidelines for Laparoscopic Liver Surgery

## From Indication to Implementation

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**Objective:** The European Guidelines Meeting on Laparoscopic Liver Surgery was held in Southampton on February 10 and 11, 2017 with the aim of presenting and validating clinical practice guidelines for laparoscopic liver surgery.

**Background:** The exponential growth of laparoscopic liver surgery in recent years mandates the development of clinical practice guidelines to direct the speciality's continued safe progression and dissemination.

**Methods:** A unique approach to the development of clinical guidelines was adopted. Three well-validated methods were integrated: the Scottish Intercollegiate Guidelines Network methodology for the assessment of evidence and development of guideline statements; the Delphi method of establishing expert consensus, and the AGREE II-GRS Instrument for the assessment of the methodological quality and external validation of the final statements.

**Results:** Along with the committee chairman, 22 European experts; 7 junior experts and an independent validation committee of 11 international surgeons produced 67 guideline statements for the safe progression and dissemination of laparoscopic liver surgery. Each of the statements reached at least a 95% consensus among the experts and were endorsed by the independent validation committee.

**Conclusion:** The European Guidelines Meeting for Laparoscopic Liver Surgery has produced a set of clinical practice guidelines that have been independently validated for the safe development and progression of laparoscopic liver surgery. The Southampton Guidelines have amalgamated the available evidence and a wealth of experts' knowledge taking in consideration the relevant stakeholders' opinions and complying with the international methodology standards.

**Keywords:** clinical practice, consensus, guidelines, implementation, indication, laparoscopic liver surgery, patient selection, procedures, Southampton, technique

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The first European Guidelines Meeting on Laparoscopic Liver Surgery (EGMLLS) was held in Southampton on February 10 and 11, 2017, with the specific aim of presenting and validating guidelines for laparoscopic liver surgery (LLS).

Previously, the consensus meeting in Louisville (2008)<sup>1</sup> reviewed the feasibility of LLS, whereas that of Morioka (2014)<sup>2</sup> focused on a comparison with open resections, then the current standard of practice, demonstrating a clear role for the laparoscopic approach in the modern era of liver surgery. While the laparoscopic approach must continue to demonstrate a lack of inferiority compared with the open approach, the future must be directed at its potential advantages, development, and safe progression.<sup>3</sup> Building on the foundation laid by the 2 previous meetings, this manuscript represents clinical practice guidelines designed specifically to direct the safe future development of laparoscopic liver surgery. The Southampton Guidelines aim to provide both experienced and training surgeons, and centers, guidance as to the appropriateness of care, to reduce variations in practice and to facilitate the safe expansion of LLS with the goal of improving patient care.<sup>4</sup>

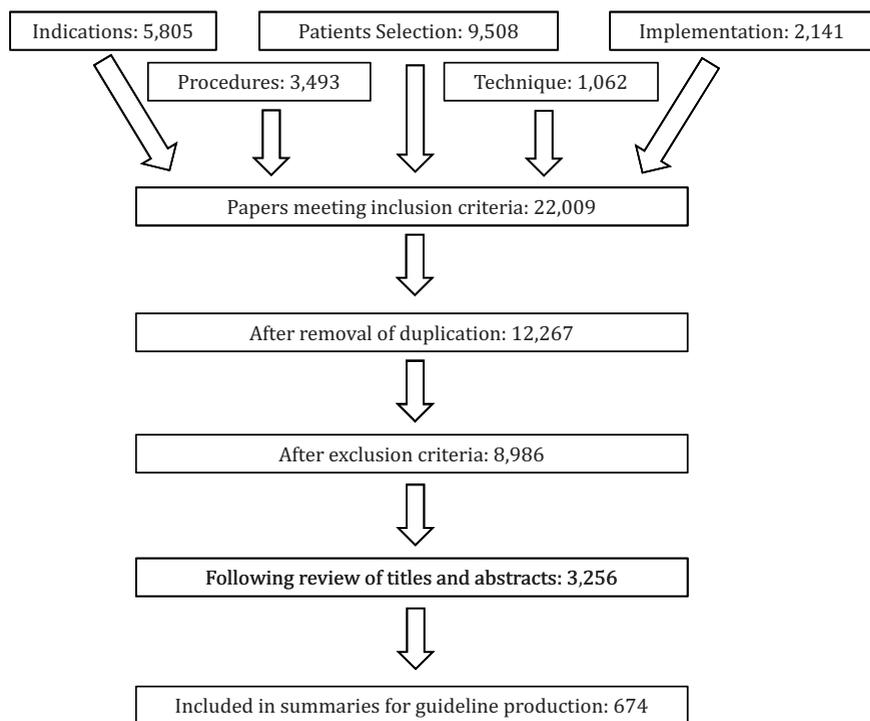
**METHODS**

The members of the steering committee and the expert panel were selected by the committee chairman for their wealth of experience and their significant contributions to the development of laparoscopic liver surgery. Of the 11 members of the international validation committee, 7 surgeons only perform open resections, whereas the remaining 4 surgeons perform both open and laparoscopic liver surgery. To provide clear clinical practice guidelines on LLS and its safe expansion, 5 key domains were identified by the Steering Committee: Indications, Patient selection, Procedures, Techniques, and Implementation. Each domain was further subdivided into topics, for example, the “*Indication*” domain was separated into: resections for “*Colorectal Liver Metastases*,” “*Hepatocellular Carcinoma*,” and “*Benign and Other Rare Liver Metastases*.” In addition to the 5 members of the steering committee, a further 18 liver surgeons, all with recognized expertise in LLS, were selected to form the Expert Panel. The expert panel was divided

into working groups, and each was assigned a number of topics to develop specific guidelines. An independent validation committee of 11 experts and 2 patient representatives was involved throughout the process of statement production.

The methodology for the production of the Southampton Guidelines was developed in collaboration with an independent methodologist. A unique approach to the production was adopted by integrating 3 validated methods: the SIGN (Scottish Intercollegiate Guidelines Network) methodology for the assessment of evidence and development of guideline statements<sup>5</sup>; the Delphi method (for establishing expert consensus)<sup>6</sup>; and the AGREE II-GRS (Global Rating Scale) Instrument<sup>7</sup> for the assessment of the methodological quality and external validation of the final statements.

A systematic review using Ovid Medline and Pubmed was undertaken in July 2016 and repeated in January 2017 to review all the existing literature for each topic. All manuscripts meeting the inclusion criteria were evaluated using the SIGN methodology to establish the Study Quality and assigned an Evidence Level (supplementary Appendix S1; <http://links.lww.com/SLA/B340> and Fig. 1; Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram). Through the use of Considered Judgement Forms (as per the SIGN methodology), the findings of the systematic review and the opinions of the experts in each working group were combined to form the provisional statements. A form of recommendation (ie, strength), based upon the level of evidence from the systematic review, was assigned to each statement (supplementary Appendix S2; <http://links.lww.com/SLA/B340>). All the statements were amalgamated and disseminated to the entire expert panel for voting in accordance with the Delphi methodology. This methodology allows each expert to either agree or disagree with a given statement, and make recommendations for changes to that statement should they feel it necessary. If a statement reached greater than or equal to a 95% agreement in the first Delphi round, it was accepted



**FIGURE 1.** PRISMA diagram. A graphical representation of the included publications within the systematic review. Searches were performed in July 2016 and repeated in January 2017 using OVID Medline and Pubmed searches. Inclusion criteria: any publication relating to laparoscopic liver surgery; exclusion criteria: nonhuman studies, comparative studies with less than 10 cases, case reports, non-English and full-text unavailable. Each search contains: [Laparosco\* OR minimally-invasive OR Keyhole] AND [Liver OR Hepat\* OR Liver Surgery OR Liver Resection], With the addition of searches specific to topic for example in “Bleeding”: AND [blood OR bleeding OR haemorrhage OR Haemosta\*].

into the guidelines for presentation at the meeting and removed from further Delphi rounds. Statements failing to reach a 95% agreement were returned to the original working group, along with their respective anonymized comments, for revision, and were entered into the subsequent Delphi round. After 3 Delphi rounds, 66 statements had reached at least a 95% agreement and 3 had not. The identities of those producing the provisional statements and those providing feedback remained anonymous except to the guideline's chairman.

At the pre-meeting assembly, a fourth Delphi round was held with the intent to review the guideline statements and reach a consensus on the 3 outstanding statements. In addition, the form of recommendations assigned to each statement was reviewed, assessed, and modified to ensure the evidence level provided neither over nor under-represented the statement. This was performed taking into consideration factors such as the clinical importance of the topic, the relevance of implications to the clinical setting, and the consistency of the body of evidence. At this point, 2 statements were removed as they failed to reach agreement; hence 67 statements were accepted for the meeting. The Validation Committee reviewed the literature searches and the subsequent summaries used for the production of the guideline statements, specifically examining the methodological techniques underpinning the production of each statement as per the AGREE II-GRS tool.<sup>8</sup>

In addition to the expert panel and validation committee, the 2-day conference was attended by over 190 specialists, from 23 different countries, all sharing an interest in liver surgery. During the conference, the highest-level evidence supporting each statement was presented along with the form of recommendation. In addition, all in attendance voted electronically, demonstrating their additional support, or otherwise, for each statement. The validation committee considered the outcomes of these votes, the opinions of the patient representatives, and proposed a number of recommendations before granting endorsement. The expert panel accepted all the recommendations from the validation committee. A detailed description of this novel methodology for the development of surgical guidelines will be published separately, as will the detailed systematic reviews for the core topics.

## GUIDELINES

The Southampton Guidelines were derived from the aforementioned methodology and thus are based on published evidence and expert opinion. It is of critical importance to note that the majority of the evidence originates from surgeons experienced in both liver surgery and advanced laparoscopic techniques working in specialist liver centers. Therefore, the guidelines should not be misconstrued as an endorsement for surgeons to perform LLS without the necessary experience and training or in an institution without the proficiency and support to practice liver surgery. It is also noteworthy that LLS accounts for 30% to 60% of liver resections in these specialist centers, and therefore there are implicit selection criteria to assess which patients are deemed appropriate candidates for a laparoscopic approach. The criteria vary among institutions and surgeons in accordance with proficiency and expertise; and will evolve with time.

### Section 1: Indications

#### Topic 1: Colorectal Liver Metastases (CRLM)

*Are Laparoscopic Liver Resections (LLR) Indicated for the Management of CRLM?* The literature suggests improved short-term outcomes for LLR of CRLM compared with open liver resection (OLR) with similar long-term outcomes. A recent meta-analysis found a reduced blood loss and need for transfusion with comparable

operative times and length of hospital stay in the laparoscopic group. Overall survival and disease-free survival were similar between the groups, and a lower incidence of R1 resections was observed in the laparoscopic group.<sup>9</sup> Preliminary results from the first large-scale prospective randomized control trial (COMET)<sup>10</sup> comparing laparoscopic and OLRs for CRLM have shown improved short-term outcomes for the laparoscopic approach, which is supported by previous propensity score-matched studies.<sup>11</sup> Other studies report similar benefits in those aged over 70.<sup>12</sup> Increasing margin width in R0 resections did not significantly correlate with better overall survival,<sup>13</sup> and as such, the guidelines confirm that parenchymal sparing resections should continue to be the basis of treatment of CRLM. The guidelines conclude that with appropriate expertise, the laparoscopic approach is a valid alternative to the treatment of CRLM (R1.1 and R1.2; see supplementary Table S1; <http://links.lww.com/SLA/B340> for complete list of recommendations).

*What is the Role of Laparoscopy in the Management of Simultaneous Colonic and Liver Resection for Synchronous Colorectal Metastases?* A laparoscopic approach was associated with a shorter hospital stay than an open approach with no difference in overall survival for patients with synchronous hepatectomy and colectomy.<sup>14</sup> There is, however, insufficient comparative data for combined major liver and colorectal resections. The experts agreed that combined laparoscopic major liver and colonic resections are complex and lengthy procedures with the potential for increased operative risks. However, simultaneous resections for nonrectal primaries with peripheral liver lesions requiring limited hepatectomy or left lateral sectionectomy were considered a good treatment option. Systematic review suggests that the timing of liver resection for synchronous liver metastasis should be decided according to technical and oncological considerations.<sup>15</sup> The guidelines emphasize a need for a multidisciplinary approach to these patients (see R2.2, R2.2, and R2.3).

#### Topic 2: Benign and Rare Noncolorectal Metastases

*What is the Role of LLR in the Management of Benign Disease and Rare Noncolorectal Metastases?* Operative trends for benign disease demonstrate that the proportion of cases performed laparoscopically is increasing.<sup>16</sup> LLR for benign lesions has lower intraoperative blood loss, frequency of complications, postoperative analgesic requirements, time to oral intake, and a shorter hospital stay.<sup>17</sup> With respect to neuroendocrine tumors (NETs), observational studies<sup>18</sup> highlight the feasibility, safety, and oncological efficiency of LLR for NETs and other noncolorectal liver metastasis when clinically indicated (see R3.1 and R3.2).

#### Topic 3: Hepatocellular Carcinoma (HCC)

*Is LLR Indicated for the Management of HCC?* Meta-analysis and large propensity score-matched studies of open versus laparoscopic liver resection for HCC have strongly suggested that LLR for HCC is associated with reduced blood loss, transfusion rate, postoperative ascites, and liver failure and hospital stay with comparable operation time, disease-free margin, and recurrence rates.<sup>19,20</sup> This has been confirmed for major resections in a recent series.<sup>21</sup> For minor resections, a laparoscopic approach was found to be the only independent factor to reduce the complication rate in resections for HCC<sup>22</sup> (see R4.1, R4.2, R4.3, and R4.4).

*What is the Role of LLR in Cirrhotic Patients?* No differences in operative time, blood loss, intraoperative complications, hospital stay, and morbidity were found in LLR for cirrhotics compared with noncirrhotics.<sup>23</sup> A laparoscopic approach appears to reduce the incidence of postoperative ascites, liver failure,<sup>24</sup> and morbidity assessed in terms of "Comprehensive Complication Index," with no difference in overall or disease-free survival at 2 years.<sup>25</sup> The

evidence for both LLR in patients with significant portal hypertension, ascites, and Child-Pugh B cirrhosis is limited to single studies,<sup>26,27</sup> and as such the guidelines recommend caution with these patient cohorts (see R5.1, R5.2, and R5.3).

#### Topic 4: Living Donor

*What is the Role of the Laparoscopic Technique for Living Donor Hepatectomy (LDH)?* The evidence suggests that there is an improved quality of life with LLS for LDH that includes a shorter hospital stay and an earlier return to work.<sup>28</sup> The experts discussed the differences between left lateral graft retrieval for pediatric transplantation and full right or full left hepatectomy for adult transplantation. It was highlighted that the evidence for full right and full left hepatectomy is primarily based on laparoscopic-assisted procedures (hybrid) with only limited studies focusing on pure laparoscopic donor hepatectomy and hence minimally invasive donor major hepatectomy has not yet been standardized and should be restricted to expert centers (see R6.1, R6.2, R6.3, and R6.4).

### Section 2: Patients and Complex Diseases

#### Topic 5: High-risk Patients

*Are There Contraindications for LLR in Elderly and High Body Mass Index (BMI) Patients (Fragile Patients)?* Laparoscopic liver resection for elderly patients has demonstrated lower intraoperative blood loss, hospital stay, and morbidity, with comparable oncological outcomes to OLR.<sup>12,29</sup> There are limited comparative studies regarding LLR in obese patients, but evidence suggests that in selected patients, it is an appropriate treatment strategy<sup>30</sup> (see R7.1, R7.2, and R7.3).

#### Topic 6: Redo Liver Resections

*Are LLRs Feasible in Patients With Previous Liver Resection?* Evidence suggests that LLR for re-do liver surgery is an appropriate option, although repeat resections have greater operative time and blood loss than primary resections.<sup>31,32</sup> The experts suggested that an initial laparoscopic resection may facilitate repeated resections by limiting the amount of adhesions, thereby providing an important advantage (see R8).

#### Topic 7: Technically Complex Settings

*Is There a Role for LLR in Patients Requiring 2-Stage Hepatectomy?* There are limited comparative studies specifically regarding LLR for 2-stage hepatectomies. Observational studies suggests it is feasible and without detrimental effects on long-term outcomes<sup>33,34</sup> (see R9).

*Is LLR Feasible in Patients With Large Lesions and Lesions in Close Proximity to Major Vessels?* Reports from cohorts studies of large (5–10 cm) and giant (>10 cm) tumors suggest that the resection of such lesions can be addressed laparoscopically with no increased morbidity. However, greater operative time and blood loss was observed when compared with LLS for smaller tumors.<sup>35,36</sup> Other reports have shown that in expert hands, lesions located in close proximity to the major vasculature can be addressed laparoscopically without detrimental effects<sup>37</sup> (see R10.1 and R10.2).

### Section 3: Procedures

#### Topic 8: Major Hepatectomies

*What is the Role of the Laparoscopic Technique for Right Hemihepatectomies?* The largest meta-analysis to date has shown that laparoscopic major hepatectomies have less blood loss, morbidity, and length of stay with similar operative times, transfusion rates, and completeness of resection compared with OLR.<sup>38</sup> The expert panel

suggested that the feasibility, reproducibility, and implementation of left and right hepatectomies is sufficiently different that they should be considered separately. In experienced hands, laparoscopic right hemihepatectomies are associated with reduced hospital stay and blood loss. Mortality and completeness of resection are comparable with an open approach<sup>39,40</sup> (see R11.1, R11.2, R11.3, and R11.4).

*What is the Role of the Laparoscopic Technique for Left Hemihepatectomies?* Compared with an open approach, a laparoscopic approach is associated with reduced blood loss, morbidity, and hospital stay with comparable operative times, completeness of resection, and mortality<sup>41,42</sup> (see R12).

#### Topic 9: Minor Resections, Resections on Difficult Segments, Parenchymal Sparing/Anatomical Segmentectomies

*What is the Role of the Laparoscopic Technique for Minor Liver Resections?* A meta-analysis reports lower blood loss, transfusions rates, morbidity, and length of hospital stay for laparoscopic minor resections compared with open resections.<sup>38</sup> Laparoscopic left lateral sectionectomies are consistently associated with shorter hospital stay when compared with the open approach.<sup>43</sup> The evidence for a laparoscopic approach to segments 4b, 5, and en bloc cholecystectomy for gallbladder cancer is limited, but suggests similar perioperative outcomes to the open approach for T1 and T2 gallbladder cancers<sup>44,45</sup> (see R13.1 and R13.2).

*What is the Role of the Laparoscopic Technique for Liver Resections in the “Difficult Segments (1, 4a, 7, and 8)”?* The expert panel acknowledged that resections in these segments, especially when anatomical, are highly complex and require advanced expertise in LLS. Minor LLRs in segment 1, 4a, 7, and 8 are associated with greater operative time and blood loss than equivalent resections in the anterolateral segments. However, mortality and morbidity is not different.<sup>46</sup> Compared with OLR, LLR is associated with reduced blood loss and hospital stay.<sup>47</sup> A transthoracic approach and modifications to the patient’s position may be useful alternatives to the classic approach to the postero-superior segments.<sup>48,49</sup> The perioperative outcomes of robotic and laparoscopic resections of the postero-superior segments appear to be similar in terms of blood loss, hospital stay, morbidity, and completeness of resection<sup>50</sup> (see R14.1, R14.2, and R14.3).

*Is LLR Applicable for Parenchyma-sparing Procedures and Anatomic Segmentectomies?* Laparoscopic and open sectionectomies have been found to have similar perioperative outcomes.<sup>39</sup> Various techniques, including a Glissonian approach, staining and indocyanine green fluorescence imaging have been suggested to facilitate a true anatomical segmentectomy.<sup>51–53</sup> Evidence for parenchyma-sparing LLR for centrally located lesions is limited. However, studies document R0 and recurrence rates that fall within the average published data<sup>54,55</sup> (see R15.1 and R15.2).

### Section 4: Technique

#### Topic 10: Minimally Invasive Approaches, Surgical Devices, Intraoperative Staging, and Planning

*What is the Role of the Hand-assisted Technique and Hybrid Procedures for Liver Resections?* The evidence suggests that no 1 approach (open, hybrid, HALS, or pure laparoscopic) is totally superior in terms of operative or postoperative factors, but it has been suggested that HALS and hybrid techniques may serve as a bridge from open to laparoscopic surgery during the learning curve<sup>56</sup> (see R16).

*What is the Role of the Robotic Approach for Liver Resections?* The robotic approach has a longer operative time and higher costs compared with a laparoscopic approach, but comparable blood

loss, length of stay, resection margins, and morbidity.<sup>57,58</sup> Compared with an open approach, a study found total in-hospital cost to be reduced despite elevated operative cost<sup>59</sup> (see R17).

*What is the Role of Intraoperative Ultrasound for LLR?* The increased sensitivity of intraoperative ultrasound (compared with preoperative imaging and diagnostic laparoscopy) has been strongly suggested by numerous studies.<sup>60,61</sup> Multiple technical papers describe ultrasound as a necessary tool to investigate liver anatomy and tumor location, and to plan transection lines and margins<sup>62,63</sup> (see R18).

*What are the Available Techniques for Parenchymal Transection?* Multiple technical and comparative papers highlight the roles of differing transection devices. However, there is no universal agreement regarding the optimal technique<sup>64–66</sup> (see R19.1, R19.2, and R19.3).

### **Topic 11: Anatomic Major Resection (Formal Right/Left Hemi-hepatectomies)**

*What are the Available Safe Techniques for Inflow Control During Major Anatomical Resections?* The majority of European centers have a preference for the hilar approach, regularly demonstrating its safety and reproducibility.<sup>67</sup> However, several centers outside of Europe report good outcomes with a Glissonian approach<sup>51</sup> (see R20).

*What are the Available Safe Techniques During Right Hemi-hepatectomy?* Although the anterior approach to liver transection, without prior liver mobilization, has been recommended by many a conventional approach with liver mobilization before transection is also possible and recommended by others. The choice between the 2 techniques depends on surgeon's preference, tumor size, and liver fragility. Whereas the hanging maneuver has been used and recommended by some surgeons its reproducibility has not yet been demonstrated<sup>68,69</sup> (see R21.1, R21.2, R21.3, R21.4, and R21.5).

### **Topic 12: Bleeding Control/Conversion**

*What are the Hemostatic Techniques During Laparoscopic Liver Resections?* The use of an intermittent Pringle maneuver has been reported to have no detrimental effects on postoperative liver function.<sup>70</sup> Continuous hemi-hepatic inflow control has been shown to reduce blood loss compared with an intermittent Pringle maneuver with no detriment to postoperative liver function.<sup>71</sup> Several technical papers highlight the importance of a sufficient cuff of tissue when applying clips and endovascular staplers.<sup>72</sup> Lower intraoperative blood loss is reported in patients with a central venous pressure (CVP) lower than 5 cm H<sub>2</sub>O.<sup>73</sup> The efficacy of stroke volume variation as an alternative to CVP monitoring has been demonstrated<sup>74</sup> (see R22.1, R22.2, R22.3, and R22.4).

*When and How Should Conversions to Open Surgery Be Considered?* Conversion during LLR is associated with higher postoperative morbidity; however, in comparison to planned OLR, the outcomes were found to be similar.<sup>75</sup> Risk factors for conversion include an increasing BMI, tumor size, and resection extent, and also resections in the postero-superior segments and cirrhosis.<sup>36,76,77</sup> In the case of conversion for significant vascular injury, temporary control of the bleeding source before conversion is highly recommended (see R23.1, R23.2, and R23.3).

## **Section 5: Implementation**

### **Topic 13: Surgeon/Center/Learning Curves**

*What Training and Preparation Should Surgeons Pursue Before Performing Minor, Major, and Complex Liver Resections?* With experience both operative time and blood loss decreases<sup>78,79</sup> and experience gained during minor resections may shorten the

learning curve for major resections.<sup>80</sup> The learning curve for minor resections is suggested to be 60 cases<sup>78</sup> and that for major resections is 55 (having already developed experience on minor resections)<sup>81</sup> (see R24.1, R24.2, R24.3, and R24.4).

*Which Centers Should Be Performing Laparoscopic Liver Resections?* Laparoscopic liver surgery should not be developed in isolation from an open liver program. Major and complex LLS should be gradually implemented with increasing collective expertise for safe patient selection and management<sup>82</sup> (see R25.1, R25.2, and R25.3).

*Should Laparoscopic Liver Resection Become Adopted in All Liver Surgical Centers?* A meta-analysis has found that the laparoscopic approach offers fewer complications, decreased blood loss, and a shorter hospital stay with comparable oncological outcomes in selected patients.<sup>38</sup> Therefore, the guidelines confirm that all centers should implement a program of LLS and offer it to patients with the appropriate indications according to the local level of proficiency. Ideally, at least 2 surgeons proficient in LLS in each center are recommended (see R26).

### **Topic 14: Training/Registries**

*Who Should Be Undertaking Training and Mentoring Roles in LLR?* With regards to trainers/mentors and registries/learned societies, no evidence-based studies are available. However, the learning curve for minor resections can significantly be reduced by surgeons assisting one another.<sup>83</sup> The recommendation of the experts is that mentors and trainers must be experienced surgeons with a current and up-to-date knowledge of the literature, whereas registries are necessary for evaluation of LLR and individual surgeons/centers alike (this relates to R27, R28, and R29).

## **DISCUSSION**

The European Guidelines Meeting for Laparoscopic Liver Surgery was devised to produce specific guideline statements to ensure the safe progression and dissemination of laparoscopic liver surgery. The guidelines produced further the work of the previous consensus meetings by providing specific guidance to both expert and training laparoscopic liver surgeons. The 67 guidelines combine the most up-to-date evidence with expert opinion to guide the dissemination of laparoscopic liver surgery. Each guideline reached at least a 95% consensus amongst the expert committee before its acceptance into the meeting. During the meeting, each statement was opened to a vote by all those in attendance (228 surgeons including the faculty). The median agreement was 88% (with at least 160 surgeons responding to each vote), demonstrating the support of these guidelines by those with a special interest in laparoscopic liver surgery. All statements were approved and endorsed by the independent validation committee.

The EGMLLS explored new areas in the application of laparoscopy in an ever-increasing cohort of patients, and provided guidance to the appropriateness of LLR for specific diseases. Indications have been refined taking into account-specific subcategories of high-risk patients and technically complex disease. Moreover, the guidelines re-define the classification of resections adding “technically major” resections, such as those in the postero-superior segments, to the established anatomical minor and major resections. Specific scenarios that require more experience were highlighted with the guidelines advocating caution dependent on the surgeon's expertise and available technical equipment.

The Southampton Guidelines state that when performed by expert surgeons, LLR offers significant advantages in terms of a reduced risk of postoperative ascites and liver decompensation in patients with cirrhosis. For patients with CRLM, LLR was deemed an appropriate option that offers significant benefits in terms of a shorter

hospital stay and lower complication rate. However, the need to adhere to a parenchymal sparing approach was stressed. The use of LLR for living donor hepatectomy is limited to a few highly specialized centers worldwide, but may now be regarded as standard practice for left lateral sectionectomy in adult-to-pediatric donation.

The Southampton Guidelines advocate that the laparoscopic approach should be considered standard practice for lesions in the left lateral and the anterior segments. The guidelines state that in expert hands, LLR for lesions in the postero-superior segments may maintain the advantages seen in the anterolateral segments. Sub-categories of “high-risk” patients, such as the elderly and patients with high BMI, were no longer considered as contra-indications to LLR. Technically challenging resections such as repeat resections or 2-stage hepatectomies, resections for large lesions, and lesions in close proximity to the hilum are now considered possible by surgeons with extensive experiences in LLS.

The Southampton Guidelines highlight the difference in difficulty and outcomes between laparoscopic left and right hemihepatectomies. Hence, it was advised that their uptake occur at different points in the learning curve. Regarding inflow control and parenchymal transection, the guidelines state that the choice of technique is dependent on the characteristics of the disease and the surgeon’s preference. Pringle maneuver and the management of intravascular volume to provide a low CVP are both essential to reduce blood loss during transection. And, as in open liver surgery, the need for intraoperative ultrasound was considered essential.

The guidelines regarding the implementation of LLS are of paramount importance in the EGMLLS. A background in open liver surgery and advanced laparoscopic skills before starting LLR are considered essential. The guidelines recommend fellowships, courses, and proctored programs to facilitate the training and development of laparoscopic liver surgeons. These fellowships should be conducted in established, high-volume centers that routinely perform minor, major, and complex major resections. Those providing supervision, as mentors and proctors, should themselves have already reached competency and are thus able to provide safe guidance during the training of less experienced surgeons. Importantly, it was recommended that each specialist center should offer a laparoscopic approach as part of its multidisciplinary management of liver disease and should ideally have a minimum of 2 surgeons competent in LLS to support, assist, and critique each other to aid development.

It is important to note that the majority of the evidence used in the production of these guidelines report data from specialist liver centers, which may represent a publication bias. However, this factor is of critical importance, as these guidelines should not be misconstrued as an invitation to begin performing laparoscopic liver surgery in the absence of experience and support. The authors must once again stress that laparoscopic liver surgery is complex and requires advanced laparoscopic skills, comprehensive experience of open liver surgery, and the support of an experienced team. Finally, the terms “experienced surgeons” and “selected patients” are not simple, rigid definitions, but represent a malleable spectrum where multiple confounding factors, which will evolve with time and vary between centers, must be considered. Although previous manuscripts have suggested that between 20 to 60 minor resections and 30 to 60 major resections (having already reached competency with minor resections) are required to overcome the learning curve,<sup>78–81</sup> the expert panel was in agreement that no specific number can be given to the number of resections performed for a surgeon to reach “competency,” and patient factors must be weighed with respect to the experience of the surgeon and their team.

With the exponential growth of laparoscopic liver surgery, it will no doubt be necessary to review the current guidance with the passage of time to ensure that they continue to represent the most

contemporary and highest level of evidence available to provide safe guidance in the dissemination of laparoscopic liver surgery.

## CONCLUSIONS

The European Guidelines Meeting for Laparoscopic Liver Surgery has produced a set of clinical practice guidelines that have been independently validated for the safe development and progression of laparoscopic liver surgery. Using a robust methodology the Southampton Guidelines have amalgamated the available evidence and a wealth of experts’ knowledge taking in consideration the relevant stakeholders’ opinions and complying with the international methodology standards. These guidelines are not an endorsement for a novice to perform LLS without the appropriate training, and ideally LLS should be performed within the confines of an institution with an established support network and experience in liver surgery.

## REFERENCES

- Buell JF, Cherqui D, Geller DA, et al. The International Position on Laparoscopic Liver Surgery: The Louisville Statement, 2008. *Ann Surg.* 2009;250:825–830.
- Wakabayashi G, Cherqui D, Geller DA, et al. Recommendations for laparoscopic liver resection: a report from the second International Consensus Conference held in Morioka. *Ann Surg.* 2015;261:619–629.
- Cherqui D. Evolution of laparoscopic liver resection. *Br J Surg.* 2016;103:1405–1407.
- Abu Hilal M. Why do we need guidelines in laparoscopic liver surgery? *HPB (Oxford).* 2017;19:287–288.
- SIGN 50: A guideline developer’s handbook. Scottish Intercollegiate Guidelines Network (SIGN). Available at: [www.sign.ac.uk/guidelines/fulltext/50/index.html](http://www.sign.ac.uk/guidelines/fulltext/50/index.html).
- Dalkey NC, Helmer O. An experimental application of the Delphi method to the use of experts. *Manage Sci.* 1963;9:458–467.
- AGREE II-GRS Instrument. Approval of Guidelines Research and Evaluation (AGREE). Available at: <http://www.agreetrust.org/resource-centre/agree-ii-grs-instrument/>.
- Brouwers MC, Kho ME, Browman GP, et al. The Global Rating Scale complements the AGREE II in advancing the quality of practice guidelines. *J Clin Epidemiol.* 2012;65:526–534.
- Luo LX, Yu ZY, Bai YN. Laparoscopic hepatectomy for liver metastases from colorectal cancer: a meta-analysis. *J Laparoendosc Adv Surg Techn.* 2014;24:213–222.
- Clinicaltrials.gov. Trial Registry. U.S. National Institutes of Health. Available at: <https://clinicaltrials.gov>.
- Cipriani F, Rawashdeh M, Stanton L, et al. Propensity score-based analysis of outcomes of laparoscopic versus open liver resection for colorectal metastases. *Br J Surg.* 2016;103:1504–1512.
- Martínez-Cecilia F, Cipriani F, Vishal F, et al. Laparoscopic versus open liver resection for colorectal metastases in elderly and octogenarian patients. *Ann Surg.* 2017;265:1192–1200.
- Montalti R, Tomassini F, Laurent S, et al. Impact of surgical margins on overall and recurrence-free survival in parenchymal-sparing laparoscopic liver resections of colorectal metastases. *Surg Endosc.* 2015;29:2736–2747.
- Wei M, He Y, Wang J, et al. Impact of surgical margins on overall and recurrence-free survival in parenchymal-sparing laparoscopic liver resections of colorectal metastases. *PLoS One.* 2014;9:e87461.
- Lupinacci RM, Andraus W, De Paiva Haddad LB, et al. Simultaneous laparoscopic resection of primary colorectal cancer and associated liver metastases: a systematic review. *Tech Coloproctol.* 2014;18:129–135.
- Kim Y, Amini N, He J, et al. National trends in the use of surgery for benign hepatic tumours in the United States. *Surgery.* 2015;157:1055–1064.
- Croome KP, Yamashita MH. Laparoscopic vs open hepatic resection for benign and malignant tumours: an updated meta-analysis. *Arch Surg.* 2010;145:1109–1118.
- Kandil E, Noureldine SI, Koffron A, et al. Outcomes of laparoscopic and open resection for neuroendocrine liver metastases. *Surgery.* 2012;152:1225–1231.
- Xiong JJ, Altaf K, Javed MA, et al. Meta-analysis of laparoscopic vs open liver resection for hepatocellular carcinoma. *World J Gastroenterol.* 2012;18:6657–6668.
- Takahara T, Wakabayashi G, Beppu T, et al. Long-term and perioperative outcomes of laparoscopic versus open liver resection for hepatocellular carcinoma with propensity score matching: a multi-institutional Japanese study. *J Hepatobiliary Pancreat Sci.* 2015;22:721–727.

21. Yoon YI, Kim KH, Kang SH, et al. Pure laparoscopic versus open right hepatectomy for hepatocellular carcinoma in patients with cirrhosis: a propensity score matched analysis. *Ann Surg.* 2016;265:856–863.
22. Sposito C, Battiston C, Facciorusso A, et al. Propensity score analysis of outcomes following laparoscopic or open liver resection for hepatocellular carcinoma. *Br J Surg.* 2016;103:871–880.
23. Shehta A, Han HS, Yoon YS, et al. Laparoscopic liver resection for hepatocellular carcinoma in cirrhotic patients: 10-year single-center experience. *Surg Endosc.* 2016;30:638–648.
24. Zhang Y, Huang J, Chen XM, et al. A comparison of laparoscopic versus open left hemihepatectomy for hepatocellular carcinoma. *Surg Laparosc Endosc Percutan Tech.* 2016;26:146–149.
25. Morise Z, Ciria R, Cherqui D, et al. Can we expand the indications for laparoscopic liver resection? A systematic review and meta-analysis of laparoscopic liver resection for patients with hepatocellular carcinoma and chronic liver disease. *J Hepatobiliary Pancreat Sci.* 2015;22:342–352.
26. Harada N, Maeda T, Yoshizumi T, et al. Laparoscopic liver resection is a feasible treatment for patients with hepatocellular carcinoma and portal hypertension. *Anticancer Res.* 2016;36:3489–3497.
27. Cai X, Liang X, Tunan T, et al. Liver cirrhosis grading Child-Pugh B: a Goliath to challenge in laparoscopic liver resection? Prior experience and matched comparisons. *Hepatobiliary Surg Nutr.* 2015;4:391–397.
28. Samstein B, Griesemer A, Cherqui D, et al. Fully laparoscopic left-sided donor hepatectomy is safe and associated with shorter hospital stay and earlier return to work: A comparative study. *Liver Transpl.* 2015;21:768–773.
29. Cauchy F, Fuks D, Nomi T, et al. Benefits of laparoscopy in elderly patients requiring major liver resection. *J Am Coll Surg.* 2016;222:174–184.
30. Uchida H, Iwashita Y, Saga K, et al. Benefit of laparoscopic liver resection in high body mass index patients. *World J Surg.* 2016;22:3015–3022.
31. Cioffi L, Belli A, Fantini C, et al. Repeat liver surgery by laparoscopy for a malignant recurrence after previous open or laparoscopic resection. *Hepatoma Res.* 2015;1.
32. Shelat VG, Serin K, Samim M, et al. Outcomes of repeat laparoscopic liver resection compared to the primary resection. *World J Surg.* 2014;38:3175–3180.
33. Fuks D, Nomi T, Ogiso S, et al. Laparoscopic two-stage hepatectomy for bilobar colorectal liver metastases. *Br J Surg.* 2015;102:1684–1690.
34. Di Fabio F, Whistance R, Rahman S, et al. Exploring the role of laparoscopic surgery in two-stage hepatectomy for bilobar colorectal liver metastases. *J Laparosc Endosc Adv Tech A.* 2012;22:647–650.
35. Jun-hua Ai, Jian-wei Li, Chen J, et al. Feasibility and safety of laparoscopic liver resection for hepatocellular carcinoma with a tumor size of 5–10 cm. *PLoS One.* 2013;8:723–728.
36. Shelat VG, Cipriani F, Basseres T, et al. Pure laparoscopic liver resection for large malignant tumors: does size matter? *Ann Surg Oncol.* 2014;22:1288–1293.
37. Yoon YS, Han HS, Cho JY, et al. Laparoscopic liver resection for centrally located tumors close to the hilum, major hepatic veins, or inferior vena cava. *Surg.* 2013;153:502–509.
38. Ciria R, Cherqui D, Geller A, et al. Comparative short-term benefits of laparoscopic liver resection: 9000 cases and climbing. *Ann Surg.* 2016;263:761–777.
39. Takahara T, Wakabayashi G, Konno H, et al. Comparison of laparoscopic major hepatectomy with propensity score matched open cases from the National Clinical Database in Japan. *J Hepatobiliary Pancreat Sci.* 2016;23:721–734.
40. Abu Hilal M, Di Fabio F, Teng MJ, et al. Single-centre comparative study of laparoscopic versus open right hepatectomy. *J Gastrointest Surg.* 2011;15:818–823.
41. Ye X, Ni K, Zhou X, et al. Laparoscopic versus open left hemihepatectomy for hepatolithiasis. *J Surg Res.* 2015;199:402–406.
42. Namgoong JM, Kim KH, Park GC, et al. Comparison of laparoscopic versus open left hemihepatectomy for left-sided hepatolithiasis. *Int J Med Sci.* 2014;11:127–133.
43. Ding G, Cai W, Qin M. Pure laparoscopic versus open liver resection in treatment of hepatolithiasis within the left lobes: a randomized trial study. *Surg Laparosc Endosc Percutan Tech.* 2015;25:392–394.
44. Agarwal AK, Javed A, Kalayarsan R, et al. Minimally invasive versus the conventional open surgical approach of a radical cholecystectomy for gallbladder cancer: a retrospective comparative study. *HPB (Oxford).* 2015;17:536–541.
45. Itano O, Oshima G, Minagawa T, et al. Novel strategy for laparoscopic treatment of pT2 gallbladder carcinoma. *Surg Endosc.* 2015;29:3600–3607.
46. Lee W, Han HS, Yoon YS, et al. Comparison of laparoscopic liver resection for hepatocellular carcinoma located in the posterosuperior segments or anterolateral segments: a case-matched analysis. *Surgery.* 2016;160:1219–1226.
47. Scuderi V, Barkhatov L, Montalti R, et al. Outcome after laparoscopic and open resections of posterosuperior segments of the liver. *Br J Surg.* 2017;104:751–759.
48. Chiow AK, Lewin J, Manoharan B, et al. Intercostal and transthoracic trocars enable easier laparoscopic resection of dome liver lesions. *HPB (Oxford).* 2015;17:299–303.
49. Ogiso S, Conrad C, Araki K, et al. Laparoscopic transabdominal with trans-diaphragmatic access improves resection of difficult posterosuperior liver lesions. *Ann Surg.* 2015;262:358–365.
50. Montalti R, Scuderi V, Patriti A, et al. Robotic versus laparoscopic resections of posterosuperior segments of the liver: a propensity score-matched comparison. *Surg Endosc.* 2016;30:1004–1013.
51. Machado MA, Surjan RC, Basseres T, et al. The laparoscopic Glissonian approach is safe and efficient when compared with standard laparoscopic liver resection: results of an observational study over 7 years. *Surgery.* 2016;160:643–651.
52. Sakoda M, Ueno S, Iino S, et al. Anatomical laparoscopic hepatectomy for hepatocellular carcinoma using indocyanine green fluorescence imaging. *J Laparosc Endosc Adv Surg Tech A.* 2014;24:878–882.
53. Ishizawa T, Zuker NB, Kokudo N, et al. Positive and negative staining of hepatic segments by use of fluorescent imaging techniques during laparoscopic hepatectomy. *Arch Surg.* 2012;147:393–394.
54. Cipriani F, Shelat VG, Rawashdeh M, et al. Laparoscopic parenchymal-sparing resections for nonperipheral liver lesions, the diamond technique: technical aspects, clinical outcomes, and oncologic efficiency. *J Am Coll Surg.* 2015;221:265–272.
55. Conrad C, Ogiso S, Inoue Y, et al. Laparoscopic parenchymal-sparing liver resection of lesions in the central segments: feasible, safe, and effective. *Surg Endosc.* 2015;29:2410–2417.
56. Hasegawa Y, Koffron AJ, Buell JF, et al. Approaches to laparoscopic liver resection: a meta-analysis of the role of hand-assisted laparoscopic surgery and the hybrid technique. *J Hepatobiliary Pancreat Sci.* 2015;22:335–341.
57. Qiu J, Chen S, Chengyou D. A systematic review of robotic-assisted liver resection and meta-analysis of robotic versus laparoscopic hepatectomy for hepatic neoplasms. *Surg Endosc.* 2016;30:862–875.
58. Troisi RI, Patriti A, Montalti R, et al. Robot assistance in liver surgery: a real advantage over a fully laparoscopic approach? Results of a comparative bi-institutional analysis. *Int J Med Robot.* 2013;9:160–166.
59. Sham JG, Richards MK, Seo YD, et al. Efficacy and cost of robotic hepatectomy: is the robot cost-prohibitive? *J Robot Surg.* 2016;10:307–313.
60. Viganò L, Ferrero A, Amisano M, et al. Comparison of laparoscopic and open intraoperative ultrasonography for staging liver tumours. *Br J Surg.* 2013;100:535–542.
61. Milsom JW, Jerby BL, Kessler H, et al. Prospective, blinded comparison of laparoscopic ultrasonography vs. contrast-enhanced computerized tomography for liver assessment in patients undergoing colorectal carcinoma surgery. *Dis Colon Rectum.* 2000;43:44–49.
62. Aldright L, Belli G, Boni L, et al. Italian experience in minimally invasive liver surgery: a national survey. *Updates Surg.* 2015;67:129–140.
63. Cherqui D, Figueroa R, Gelli M. Tips of totally laparoscopic left hepatectomy. *J Hepatobiliary Pancreat Sci.* 2016;23:E1–E4.
64. Berber E, Akyuz M, Aucejo F, et al. Initial experience with a new articulating energy device for laparoscopic liver resection. *Surg Endosc.* 2014;28:974–978.
65. Buell JF, Gayet B, Han HS, et al. Evaluation of stapler hepatectomy during a laparoscopic liver resection. *HPB (Oxford).* 2013;15:845–850.
66. Dural C, Akyuz M, Yazici P, et al. Safety and efficacy of a new bipolar energy device for parenchymal dissection in laparoscopic liver resection. *Surg Laparosc Endosc Percutan Tech.* 2016;26:21–24.
67. Tzani D, Shivathirthan N, Laurent A, et al. European experience of laparoscopic major hepatectomy. *J Hepatobiliary Pancreat Sci.* 2013;20:120–124.
68. Soubrane O, Schwarz L, Cauchy F, et al. A conceptual technique for laparoscopic right hepatectomy based on facts and oncologic principles: the caudal approach. *Ann Surg.* 2015;261:1226–1231.
69. Dokmak S, Ben Safta Y, Ftériche FS, et al. Pure laparoscopic right hepatectomy with the hanging maneuver for multiple hepatocellular adenomas. *Ann Surg Oncol.* 2014;21:3800–3801.
70. Dua MM, Worhunsy DJ, Hwa K, et al. Extra-corporeal Pringle for laparoscopic liver resection. *Surg Endosc.* 2015;29:1348–1355.
71. Zhang Y, Yang H, Deng X, et al. Intermittent Pringle's manoeuvre versus continuous hemihepatic vascular inflow occlusion using extra-glissonian approach in laparoscopic liver resection. *Surg Endosc.* 2016;30:961–970.

72. Abu Hilal M, Underwood T, Taylor MG, et al. Bleeding and haemostasis in laparoscopic liver surgery. *Surg Endosc*. 2009;24:572–277.
73. Jones RM, Moulton CE, Hardy KJ. Central venous pressure and its effect on blood loss during liver resection. *Br J Surg*. 1998;85:1058–1060.
74. Ratti F, Cipriani F, Reineke R, et al. Intraoperative monitoring of stroke volume variation versus central venous pressure in laparoscopic liver surgery: a randomized prospective comparative trial. *HPB*. 2016;18:136–144.
75. Cauchy F, Fuks D, Nomi T, et al. Risk factors and consequences of conversion in laparoscopic major liver resection. *Br J Surg*. 2015;102:785–795.
76. Ratti F, D'alessandro V, Cipriani F, et al. Influence of body habitus on feasibility and outcome of laparoscopic liver resections: a prospective study. *J Hepatobiliary Pancreat Sci*. 2016;23:373–381.
77. Troisi RI, Montalti R, Van Limmen JG, et al. Risk factors and management of conversions to an open approach in laparoscopic liver resection: analysis of 265 consecutive cases. *HPB*. 2014;16:75–82.
78. Vigano L, Laurent A, Tayar C, et al. The learning curve in laparoscopic liver resection: improved feasibility and reproducibility. *Ann Surg*. 2009;250:772–782.
79. Dagher I, Gayet B, Tzanis D, et al. International experience for laparoscopic major liver resection. *J Hepatobiliary Pancreat Sci*. 2014;21:732–736.
80. Hasegawa Y, Nitta H, Takahara T. Safely extending the indications of laparoscopic liver resection: when should we start laparoscopic major hepatectomy? *Surg Endosc*. 2017;31:309–316.
81. Van der Poel MJ, Besselink MG, Cipriani F, et al. Outcome and learning curve in 159 consecutive patients undergoing total laparoscopic hemihepatectomy. *JAMA Surg*. 2016;151:923–928.
82. Kluger MD, Vigano L, Barroso R, et al. The learning curve in laparoscopic major liver resection. *J Hepatobiliary Pancreat Sci*. 2013;20:131–136.
83. Goh BK, Chan CY, Wong JS, et al. Factors associated with and the outcomes of open conversion after laparoscopic minor hepatectomy: Initial experience at a single institution. *Surg Endosc*. 2015;29:2636–2642.