Liver surgery—less is more

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The laparoscopic approach to liver surgery has been increasingly utilized since it was first described in 1992 (1). As of 2016, nearly 10,000 cases were reported in the literature establishing laparoscopy as a safe and effective approach to resection of benign and malignant liver tumors (2). Initially reserved for smaller wedge resections in the anterior segments, advances in technology, development of new approaches and improvement in surgeon skill enabled complex laparoscopic approaches for major hepatectomies including challenging posterior segments. In fact, it is estimated that between 30–60% of liver resections are performed laparoscopically at specialty centers (3). International consensus recommends the laparoscopic approach as standard of care for minor resections while major resections are still considered investigational. This substantial progress exemplifies the importance of short and long-term data reporting, international collaboration and consensus publication (3-5).

There is a large body of literature establishing the laparoscopic approach for curative management of benign and malignant liver tumors. Not only has it been proven to be safe in skilled hands, the current evidence finds the laparoscopic approach to be advantageous for patients compared to open surgery in the short term while achieving comparable long-term oncologic outcomes (6-15). Laparoscopy affords unique intraoperative benefits including improved visualization of certain segments from a caudal compared to a ventral approach and lower blood loss from the venous tamponade effect by pneumoperitoneum and reverse Trendelenburg positioning. The article from Dr. Andreou and colleagues published in 2018 in *Surgical Oncology* complements this body of literature with a large propensity-matched comparison of minimally invasive hepatectomy (MIH), which included pure laparoscopic surgery, single-incision laparoscopic surgery (SILS), and the hybrid technique (HYB), versus open hepatectomy (OH) for hepatocellular carcinoma (HCC) (16).

Their cohort included 407 consecutive patients who underwent OH or MIH for HCC between 2005 and 2016 at two centers, with 56 (14%) of them undergoing MIH. The MIH cohort incorporated range of resections, consisting mostly of segmentectomies or wedge resections (n=31), but also several lobectomies (n=8) and bi-segmentectomies (n=16). After propensity score matching based on patient demographics, resection extent, underlying liver characteristics, and tumor number and size, 112 patients were compared between the MIH and OH cohorts. Their analysis demonstrated a statistically significant reduction in length of hospital stay, major and minor complications at 90 days, liver failure rate, and 90-day mortality in the MIH cohort. Aside from longer operative time, MIH did not result in any negative oncologic or perioperative outcomes such as increased percentage of positive surgical margins, prolonged ICU stay, or higher red blood cell transfusions. The authors compared oncologic outcomes after a median follow-up time of 51 months demonstrating MIH to have a comparable 5-year overall survival (54% *vs.* 41% for OH, P=0.151) and 5-year disease free survival rate (50% *vs.* 38% for OH, P=0.956). There are a few limitations of this matched retrospective series to acknowledge. First, the majority of MIH was performed during the last 2 years of the 11-year study period and advances in perioperative care and implementation of Early Recovery After Surgery (ERAS) protocols likely directly influenced perioperative outcomes such as length of stay. There was no mention of incidence of conversion to OH or if the MIH outcomes were recorded for an intention-to-treat assessment. Finally, limited information was provided on complexity of the case

Table 1 Ongoing randomized clinical trials in liver surgery*

Title	Interventions	Location	NCT Number
Short and Long Outcomes Between Laparoscopic and Open Hepatectomy	Open, laparoscopic hepatectomy	China	NCT03672357
Robotic-Assisted Laparoscopic Versus Open Surgery for Complicated Hepatolithiasis	Open, robotic-assisted laparoscopic hepatectomy	China	NCT03297099
ORANGE SEGMENTS: Open Versus Laparoscopic Parenchymal Preserving Postero-Superior Liver Segment Resection	Open, laparoscopic hepatectomy	Belgium; Germany; Italy; Netherlands; Norway; United Kingdom	NCT03270917
Open Versus Laparoscopic Left-sided Hepatectomy Trial	Open, laparoscopic hepatectomy	South Korea	NCT03010085
Open *vs.* Laparoscopic Liver Surgery for Colorectal Liver Metastases	Open, laparoscopic hepatectomy	Spain	NCT02727179
Laparoscopic Versus Open Liver Resection for Hepatocellular Carcinoma	Open, laparoscopic hepatectomy	China	NCT02526043
Laparoscopic Hepatectomy Versus Open Hepatectomy for primary hepatic carcinoma	Open, laparoscopic hepatectomy	China	NCT02014025
Surgical Stress After Laparoscopic Compared to Open Liver Resection	Laparoscopic hepatectomy	China	NCT01819688
Laparoscopic Versus Open Liver Resection in the Treatment of Hepatocellular Carcinoma	Open, laparoscopic hepatectomy	China	NCT01768741
Oslo Randomized Laparoscopic Versus Open Liver Resection for Colorectal Metastases Study	Open, laparoscopic hepatectomy	Norway	NCT01516710
Prospective Randomized Trial of Laparoscopic Versus Open Liver Resection for HCC	Open, laparoscopic hepatectomy	Korea	NCT00606385

*, data abstracted from www.clinicaltrials.gov, as of 3/29/19.

type as all segments are not created equal. Recognizing these limitations, their findings do mirror the current evidence and further establish the short and long-term efficacy of MIH while controlling for selection bias in a large, matched cohort.

The liver surgeon today is afforded with numerous technical approaches to tumor resection including conventional laparotomy, laparoscopic and robot-assisted laparoscopic techniques. Several randomized control trials are being conducted to better control for patient selection and compare these different modalities (*Table 1*). Published laparoscopic techniques include pure laparoscopic liver surgery (PLAP), SILS, hand-assisted laparoscopic surgery (HALS) and a HYB (17), which utilizes PLAP for liver mobilization and a mini-laparotomy for parenchymal transection and hilar dissection. Numerous factors influence selection of surgical approach including tumor location, size, extent of resection, parenchymal characteristics, and surgeon or regional preference. PLAP was originally reserved for peripherally accessible lesions while a hybrid or hand-assisted technique for lobectomies and larger formal resections, however as surgeon skill improves the application of these techniques has significantly broadened (18,19). The recent publication of the Southampton Consensus has provided important guidelines for liver surgeons in choosing an approaching a variety of indications, complex diseases, and operations (3).

In addition to traditional laparoscopy, robot surgical systems are increasingly being used for liver surgery since the system was approved by the US Food and Drug Administration (FDA) in 2000. An international consensus statement on robotic hepatectomy was published in 2018 to promote development of standardization of robotic hepatectomy and improve patient safety (20). In this statement, seven recommendations establishing safety and feasibility were based on low to very low levels of evidence (grade 2C and 2D), highlighting the need for higher quality investigations examining robot liver surgery in comparison to conventional techniques. The importance of prospective studies is further reinforced by the recent FDA warning regarding the safety and effectiveness of robot-assisted surgeries for early cervical and breast cancers (21). One randomized control trial is ongoing comparing robotic-assisted versus open surgery for complicated hepatolithiasis, and the hepatobiliary community looks forward to the results of this and other analyses.

Data examining the short and long-term differences in minimally invasive surgical approaches are limited and many are hampered by selection bias in retrospective series. No single approach has been identified as superior, although the hybrid approach has been encouraged as a technical bridge to pure laparoscopy. Fiorentini and colleagues recently reported the first propensity-matched analysis of pure laparoscopic versus hand-assisted/hybrid major hepatectomies at two centers (22). Comparing PLAP to HALS and HYB after 1:1 propensity matching, the two cohorts had comparable rate of open conversion, length of ICU stay, red blood cell transfusion, and postoperative morbidity or mortality. Operative time for PLAP and HALS were comparable while HYB approach reduced operative time by 100 minutes. Tsung *et al.* conducted a matched comparison of robotic and laparoscopic hepatectomy, demonstrating comparable safety and feasibility in 57 robotic to 114 laparoscopic hepatic resections (23). Several systematic reviews and meta-analyses comparing approaches demonstrate no proven advantage of any minimally invasive technique (24,25). Based on current evidence, multiple forms of MIH appear to achieve the same goals for our patients and we would predict that utilization of these techniques will be dependent upon surgeon skills, preference and institutional resources.

New and exciting technologies accompanying minimally invasive liver surgery are continuously being developed to improve pre-operative planning and intra-operative decision making (26). Although still mostly in exploratory phase, image-guided liver surgery, surgical resection maps, indocyanine green fluorescence with near-infrared fluorescent imaging and 3D modeling were developed to assist the surgeon and surgical trainee. Recent advances in virtual and augmented reality have been applied to liver surgery, with systems developed to help with surgical navigation. A recent report from our group has demonstrated the feasibility of rendering pre-operative axial imaging in three-dimensions on the robotic surgical console to guide liver resection in a porcine model (27). With technological advances and innovation in minimally invasive liver surgery, we hope to see continued improvement in surgical outcomes.

Faced with many choices, it can be challenging for liver surgeons to determine the optimal surgical approach for a given patient. With important contributions by Dr. Andreou *et al.* and others, there is mounting evidence that in skilled hands and in select patients, a minimally invasive approach is advantageous in liver surgery and should be offered.

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