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Review

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Minimally invasive surgery approaches in major liver resection for hepatocellular carcinoma

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Abstract

Over the past two decades, minimally invasive liver resection (MILR) has progressively become the standard for minor resection of hepatocellular carcinoma (HCC). In contrast, its implementation in major hepatectomy has been slower due to its higher technical complexity and morbidity. However, studies published in recent years have demonstrated that minimally invasive major hepatectomy (MIMH) is safe and feasible with less blood loss, fewer complications, earlier recovery, decreased hospital stay, and improved cosmetic outcomes compared with open surgery. This review examines the current status of MIMH, focusing on the respective strengths and weaknesses of the laparoscopic and robotic approaches, as well as assessing their cost-effectiveness and possible future directions. The earlier introduction of laparoscopic liver resection has led to its widespread utilization as a safe and accurate alternative to open hepatectomy. Of note is that the robotic approach has also been increasingly utilized, demonstrating better perioperative outcomes and decreased need for conversion to open hepatectomy *vs.* the laparoscopic approach. Advantages associated with the robotic approach include the three-dimensional large visual field and instrumental flexibility, allowing for improved bleeding control. Even though evidence has been slowly accumulating regarding long-term outcomes, most studies report no notable differences between open, robotic, and laparoscopic resection for HCC. Regarding cost-effectiveness, MIMH has been characterized by higher operating room and anesthesia costs, especially for robotic procedures that require highly expensive equipment. The increase in cost is often offset by the lower morbidity and, thus, shorter hospital stays associated with MIMH. Future developments, such as the implementation of artificial intelligence and augmented reality, may potentially maximize the safety and applicability of MIMH and, in time, lead to improved postoperative and oncological outcomes.

Keywords: Hepatocellular carcinoma, laparoscopic surgery, robotic surgery

INTRODUCTION

Primary liver cancer represents the 6th most common malignancy worldwide, and was responsible for approximately 8.2% of total cancer deaths in 2020[1,2]. Hepatocellular carcinoma (HCC) is the most common primary liver cancer, accounting for 75%-85% of liver malignancies. Chronic hepatitis, together with aflatoxins, alcohol abuse, smoking, obesity, and type 2 diabetes, are the main risk factors for HCC, with marked differences in prevalence worldwide[1,3]. The HCC incidence differs significantly based on geographic location, with approximately four out of five worldwide HCC cases reported in Asia and Africa[4]. Globally, chronic HBV and HCV infections are responsible for approximately 50% and 20% of HCC cases, respectively[5]. However, the rising prevalence of obesity and metabolic syndrome among Western populations has led to higher rates of non-alcoholic fatty liver disease (NAFLD)/metabolic associated liver disease (MALD), leading to a progressive increase in the incidence of HCC in these historically lower prevalence areas[6].

The treatment of HCC requires a multidisciplinary approach with surgeons, medical oncologists, radiation oncologists, and interventional radiologists cooperating to establish an optimal therapeutic plan, always considering patient- and tumor-specific factors, such as the extent of liver disease[7]. Curative-intent treatment options, including liver resection, transplantation, and ablation, require patients to meet specific criteria, with resection generally reserved for patients with HCC and adequate liver function[8]. Approximately one-third of patients with HCC meet the requirements for surgical resection based on the quality of the liver parenchyma and the planned extent of resection. In general, patients without cirrhosis are usually candidates for surgical resection. Current guidelines consider tumor size, number of lesions, liver function, the presence of portal hypertension, performance status, and extent of resection as factors that determine whether HCC on a cirrhotic liver would be amenable to hepatectomy[7,9,10].

Laparoscopic surgery was first introduced toward the end of the 1980s, with the first video-assisted laparoscopic cholecystectomy completed in the US in 1988 by McKernan and Saye[11]. Through the years, the laparoscopic approach has been further developed and employed in various general surgery procedures, including appendectomy, hernia repair, and bariatric operations[12]. A trend toward robotic surgery has been growing over the past three decades due to advantages over the laparoscopic approach, including 3D vision, stability and magnification of the image, EndoWrist instruments, filtering of physiologic tremor, and motion scaling[13]. Especially since the introduction of the robotic platform in clinical practice in the late 1990s, surgeons worldwide have utilized the robotic approach in various operations, demonstrating its versatility, feasibility, and safety[14-16]. Although the initial use of the robotic device was cardiac surgery, the most impressive results have been reported in general surgery[17]. However, there are still drawbacks preventing the implementation of robotic surgery as the standard of minimally invasive surgery (MIS), such as higher costs and lack of haptic feedback. In addition, several comparative studies have not been able to demonstrate any superiority of the robotic approach relative to the laparoscopic one in terms of perioperative and postoperative outcomes[13].

Over the last several decades, MIS has quickly become the standard of care for several abdominal procedures. However, its widespread implementation in liver surgery was initially delayed by safety concerns, a demanding learning curve, and a lack of appropriate equipment[18]. Minimally invasive liver resection (MILR) has undergone a substantial evolution in terms of equipment, surgical expertise, and perioperative care since the early 1990s, when the first cases of laparoscopic liver resection (LLR) were reported in the literature[19,20]. The first consensus meeting was held in 2008 in Louisville, Kentucky, where 45 leading experts established the safety and efficiency of LLR when performed by experienced surgeons[21].

The value of LLR was officially acknowledged during the 2nd International Consensus Conference on LLR (ICCLLR) in 2014, which highlighted the improved visibility associated with LLR, as well as improved transection precision and smaller surgical incisions [Figure 1]. LLR was also noted to be associated with lower blood loss, postoperative morbidity, medication use, and length of stay(LOS), while also allowing for quicker recovery of patient functional status[18,22,23]. While the ICCLLR focused on comparisons between open and laparoscopic liver surgery, the goal of the first European Guidelines Meeting on laparoscopic liver surgery (EGMLLS) in 2017 was to present and validate the first clinical practice guidelines for LLR. A total of 67 guidelines were included, combining up-to-date evidence and expert opinion, allowing for the progression and safe dissemination of laparoscopic liver surgery by reducing the variability in clinical practice and ensuring the appropriateness of care[24].

Despite the widespread implementation of two randomized controlled trials confirming advantages for minor hepatectomy, MILR use for major hepatectomy remains controversial[25-27]. The Morioka Consensus recommended that minimally invasive major hepatectomy(MIMH) should only be attempted at tertiary specialist centers by experienced hepatobiliary surgeons with a high volume of laparoscopic cases[25]. In recent years, several studies have retrospectively evaluated the safety and benefits of MIMH performed in experienced settings relative to the open approach[20,28-32]. The aim of the current study was to provide an overview of the current status of MIMH, focusing on the benefits and potential drawbacks that accompany the increasing implementation of laparoscopic major hepatectomy (LMH) and robotic major hepatectomy (RMH) among patients with HCC.

SEARCH STRATEGY

A thorough search of PubMed was conducted to identify relevant publications in March 2024. The following keywords were used: "Minimally invasive", "Laparoscopic", "Robotic", "Hepatocellular Carcinoma", "Hepatectomy", "Major Hepatectomy". Only studies in English were evaluated and similar article suggestions were simultaneously explored. Study inclusion was performed by two researchers separately and results were cross-validated. In total, 37 studies were included that compared minimally invasive and open liver resections(OLR), providing data on HCC and major hepatectomy. Specifically, for MILR *vs.* OLR, 14 studies were included (2016-2024); 10 were focused on HCC and 4 reported on hepatectomy for a broad range of indications[20,33-45]. For LMH *vs.* open major hepatectomy(OMH), the number of studies included was 11 (2009-2024), with 5 focusing solely on HCC and the rest on major hepatectomy for various malignancies, including HCC[31,46-55]. Just 5 studies (2017-2024) were identified that compared RMH and OMH, of which 4 reported data on HCC only[37,39,56-58]. In addition, 9 studies (2013-2023) were included on the topic of LMH *vs.* RMH, with 4 focusing on HCC[59-66].

LEARNING CURVE

A variety of approaches can be used for MILR, including pure laparoscopy, hand-assist procedures, hybrid procedures, and robotic-assisted hepatectomy[67,68]. Pure laparoscopy is performed entirely through trocars, with the specimen extracted through a separate incision. This approach optimizes cosmesis and minimal pain, but is the most technically challenging with potentially more limited options to control bleeding[67]. Hand-assist refers to a laparoscope-visualized procedure with instruments inserted through trocars, in addition to a planned limited incision through which the surgeon's hand reaches into the abdomen. Although there is a larger incision and a higher risk of incisional hernia, this approach allows for increased options for dealing with unexpected operative events. Sometimes, hand-assist may be preferable for larger tumors, posterior resections, and surgeons in training[69,70]. The hybrid approach constitutes an initial laparoscopic approach to mobilize the liver, as well as parenchymal transection via a planned open incision. This method helps ensure safety, although resection of the liver via a small incision is technically

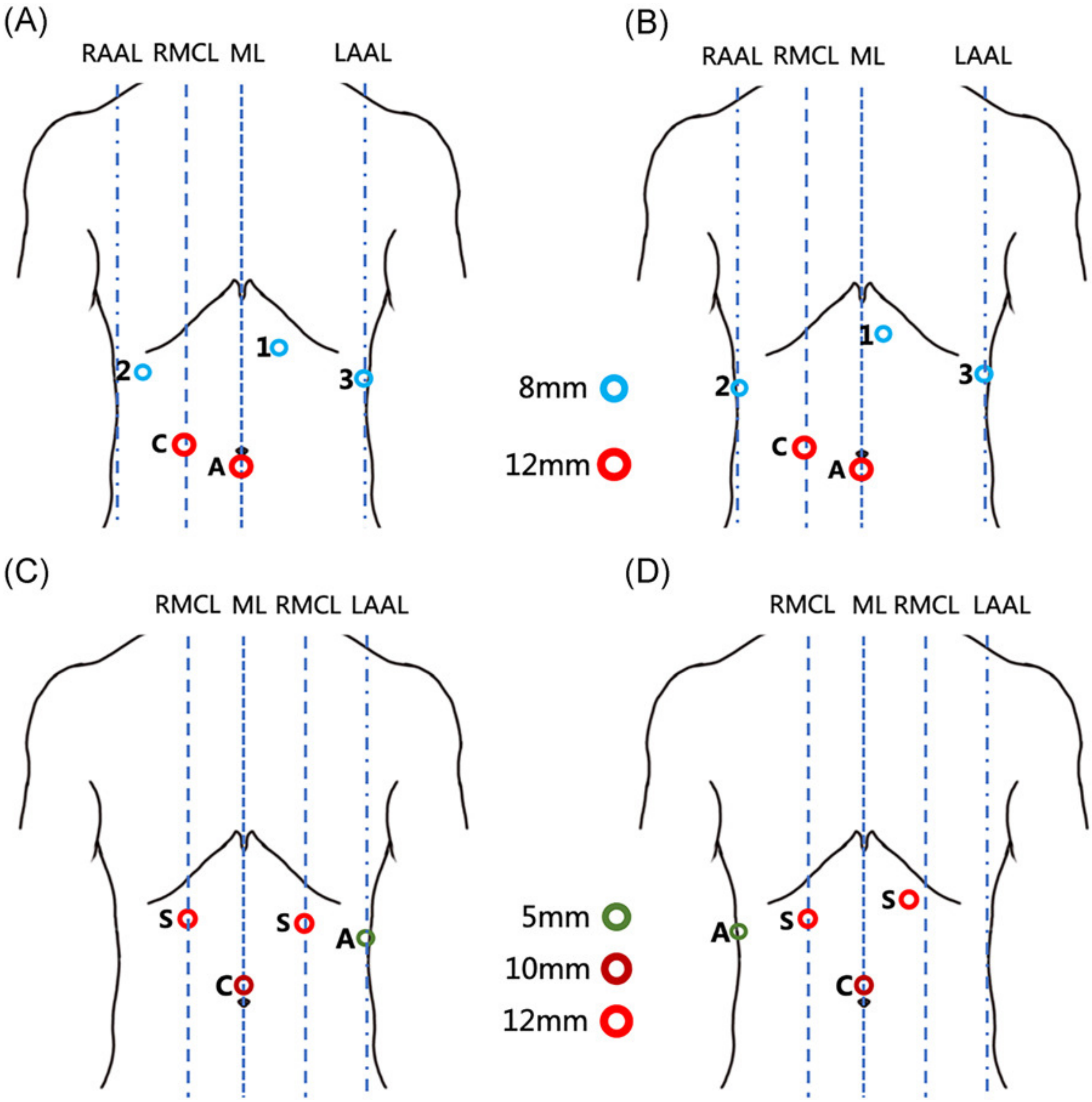

Figure 1. Ports placement of (A) robotic left hepatectomy, (B) robotic right hepatectomy, (C) laparoscopic left hepatectomy, and (D) laparoscopic right hepatectomy. RAAL: Right anterior axillary line; RMCL: right midclavicular line; ML: median line; LAAL: left anterior axillary line.

demanding and may lead to greater incisional pain[71,72]. A hepatectomy is defined as robotic-assisted when the robotic surgical platform is utilized for any or all portions. Even though limited availability and higher equipment costs are inherent limitations of the robotic platform, some experts have theorized the superiority of this approach, as it allows easier access to the most difficult liver segments[66].

In MILR, the learning curve is characterized as an improvement in performance over time in which a surgeon gains the ability to limit failure to a constant acceptable rate when performing a specific task[67,73]. Measures that usually define a surgeon's position on the learning curve include operative duration, blood loss, rate of conversions, transfusion rate, LOS, as well as morbidity and mortality[67]. In fact, studies analyzing the learning curve in minimally invasive liver surgery(MILS) have suffered from variability relative to the definition and measurement of the learning curve. This variability can lead to inconsistencies in research findings, highlighting the need for a more standardized definition of the learning curve in MILS. It is worth noting that an individual surgeon's learning curve depends on the proficiency of the senior surgeons at the center, in addition to the learning curve of the specific field itself. For example, a research study by Nomi *et al.* described how LMH seemed to have three learning phases when performance was measured relative to operative time, with 45 initial cases in the first phase, followed by 30 cases in the middle phase, and 98 final cases to reach the final learning phase[73]. During phase 3, surgeons treated older patients, utilized pedicle clamping less, and reported decreased operative duration, blood loss, conversion rates, and LOS compared with phase 1. Similarly, Dagher *et al.* demonstrated that, relative to the first 90 combined cases from six centers, the latter 120 cases had lower operative duration, estimated blood loss, Pringle maneuver utilization, conversion rate, and a shorter LOS[55]. Notably, morbidity and mortality were comparable between the two groups. Even though this study failed to quantify the learning curve in terms of operative cases, the existence of a learning curve has been further corroborated in the literature[72,74].

A learning curve is also evident in the robotic-assisted approach, demonstrated mostly in terms of the overall learning curve in the field itself, as cases in the later stages of robotic-assisted liver resection (RLR) adoption have been associated with lower blood loss, as well as shorter operative time and hospital LOS[66,67]. In general, a robotic approach in surgery may be beneficial in more complex tasks, as it has been associated with less frustration among both novice and experienced surgeons. Less experienced surgeons may improve more rapidly in specific tasks, including suturing when using the robotic compared with the laparoscopic platform[75,76]. In an attempt to define the learning curve for RMH, Chen *et al.* retrospectively evaluated 92 cases evaluating operative time as a proxy for surgical proficiency. The median operative time was 434 minutes (IQR 142-805), and the median blood loss was 195 mL (IQR 50-2,000). The suggested training program consisted of 15 initial cases, followed by a 25-case intermediate phase and a 52-case mature phase. Completion of phase 1 was associated with a shorter operative duration and LOS, while lower blood loss was observed following phase 2[77].

DIFFICULTY SCORING SYSTEMS

MILR is regarded as a technically demanding surgical procedure, which underlines the importance of difficulty scoring systems (DSSs) for the assignment of appropriate cases to surgeons based on their respective skills and experience[67]. Table 1 summarizes the main scoring systems for MILS. Among a variety of DSSs, there are five that have been externally validated and proven to be predictive, although none has been universally adopted[18]. Among these five DSSs, the first was proposed by Ban *et al.*[78]. and was subsequently revised based on expert consensus to create the IWATE criteria[25]. In quick succession, three additional DSSs were developed, namely the Hasegawa[79], the institut mutaliste montsouris (IMM) [80], and the Southampton[81] scoring systems. It is worth noting that these DSSs have been validated mostly in LLR and less extensively in RLR.

The Ban DSS is a 10-point system assessing tumor location and size, extent of resection, liver function, and major vessel proximity as contributors to the difficulty level of MILR. Following reports of LLR-related clustered deaths in Japan, the ICCLLR in Morioka noted that, although LLR presented theoretical advantages of better magnification and decreased bleeding compared with open hepatic resection, safety concerns should be addressed by a difficulty classification system that effectively stratified LLRs according to each surgeon's position on the learning curve. Thus, the proposed IWATE criteria proceeded to advance the existing Ban DSS, by implementing a weighted 12-point system that took into account hand-assisted laparoscopic surgery (HALS) and hybrid surgery – part of LLR performed via a small open incision that

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Table 1. Comparison of the main difficulty scoring systems for MILS

Difficulty Scoring System	Indicators	Difficulty Surrogate	Developed Based on	LLR Discriminators	RLR Discriminators	Difficulty Classification	Characteristics
Ban[78]	1) Tumor location 2) Tumor size 3) Extent of resection 4) Liver function 5) Major vessel proximity		63% Hepatocellular carcinomas 31% Metastatic neoplasms 6% Benign neoplasms	1) Operative time 2) Blood loss 3) Transfusion requirement 4) Pringle's maneuver requirement 5) Time required for Pringle's maneuver 6) Conversion rate 7) Postoperative Complication rate 8) Length of stay	1) Operative time 2) Blood loss 3) Complication rate 4) Length of stay	1-3: Low (surgeons with < 10 LLR cases) 4-6: Medium (surgeons with ≥ 10 and < 50 LLR cases) 7-10: High (surgeons with ≥ 50 LLR cases)	Easiest to use Small sample size Lin *et al.*[93]: Prediction of conversion to open (*vs.* Hasegawa, IMM, Southampton) Yang *et al.*[86]: Correlated with conversion to open and length of stay (*vs.* IMM)
IWATE[25]	1) Tumor location 2) Tumor size 3) Extent of resection 4) Liver function 5) Major vessel proximity 6) Hand-assisted laparoscopic surgery 7) Hybrid surgery		Ban criteria and expert consensus	1) Operative time 2) Blood loss 3) Transfusion requirement 4) Pringle's maneuver requirement maneuver 5) Conversion rate 6)Intraoperative complication rate 7) Postoperative Complication rate 8) Length of stay 9) Mortality	1) Operative time 2) Blood loss 3) Length of stay	≤ 3: Low 4-6: Intermediate 7-9: Advanced ≥ 10: Expert (-1 point: Hand-assisted laparoscopic surgery and Hybrid surgery)	Superior in terms of selecting cases for beginner surgeons
Hasegawa[79]	1) Tumor location 2) Extent of resection 3) Obesity 4) Platelet count	Operative time	49.2% Hepatocellular carcinomas 40.6% Malignant neoplasms 10.2% Benign neoplasms	1) Operative time 2) Blood loss 3) Transfusion requirement 4) Pringle's maneuver requirement 5) Time required for Pringle's maneuver 6) Postoperative Complication rate 7) Length of stay	-	≤ 1: Low 2-3: Medium ≥ 4: High	Optimal procedure selectio*n* Single-institution Least validated
Institut Mutualiste Montsouris[80]	1) Intraoperative time 2) Blood loss 3) Conversion to open hepatectomy	Major complications and overall morbidity	54.8% Colorectal Liver Metastases 9.5% Hepatocellular carcinomas 5.8% Intrahepatic cholangiocarcinomas 16.2% Other malignant	1) Operative time 2) Blood loss 3) Transfusion requirement 4) Pringle's maneuver requirement 5) Time required for	-	0: Low(surgeons with < 10 LLR cases) 2: Intermediate 3: High	Stratifies the difficulty among major LLRs (*vs.* Ban) Based on intraoperative objective parameters

			neoplasms	Pringle's maneuver 6) Conversion rate 7) Postoperative Complication rate 8) Length of stay 9) Liver failure 10) Mortality			
Southampton[81]	1) Prior open hepatectomy 2) Neoadjuvant chemotherapy 3) Lesion type 4) Lesion size	Intraoperative complications	75.3% Malignant neoplasms 24.7 Benign neoplasms	1) Operative time 2) Blood loss 3) Transfusion requirement 4) Pringle's maneuver requirement 5) Time required for Pringle's maneuver 6) Conversion rate 7) Postoperative Complication rate 8) Length of stay 9) Intraoperative complications	-	0-2: Low (< 10% risk) 3-5: Moderate (10%-20% risk) 6-9: High (20%-50% risk) Extremely ≥ 10: High (> 50% risk)	More robust for scientific analysis Russolillo *et al.*[101]: Correlated less with Pringle maneuver, Pringle time, Blood loss, and Operative time (*vs.* Hasegawa and IMM) Tripke *et al.*[91]: Better performance in morbidity and mortality prediction (*vs.* IWATE) Goh *et al.*[100]: Poorest calibration (*vs.* IWATE, Hasegawa, IMM, Southampton)

LLR: Laparoscopic liver resection; RLR: robotic liver resection; IMM: Institut Mutaliste Montsouris

eases certain challenges[18]. Hasegawa *et al*. used operative time as a proxy for LLR difficulty and developed a weighted numerical scale that evaluates the previously utilized extent of resection and tumor location, in addition to obesity and platelet count[79]. For the development of the IMM DSS, difficulty was evaluated based on the effect that intraoperative time, blood loss, and conversion to open hepatectomy had on major complications and overall morbidity. As a result, the type and extent of surgery categorized procedures into three separate difficulty groups. In addition, Halls *et al*. proposed the Southampton DSS, which noted that prior open hepatectomy, neoadjuvant chemotherapy, lesion type and size, and classification of resection were associated with a higher likelihood of intraoperative complications as a surrogate for LLR difficulty[81].

In total, including the five validated DSSs, twelve scores of difficulty stratification have been proposed, emphasizing the importance of the learning curve associated with MILR and the need for surgeons to perform procedures that correspond to their skill level to ensure safety. Except for the IMM DSS that focused on the extent of resection, the other four most validated DSSs considered variables relative to tumor, procedure, and parenchyma characteristics. The IWATE, Hasegawa, and IMM scoring systems consider MIMH itself a highly difficult MILR[23,25,79]. Of note, core differences in DSSs were reflective of the different characteristics among patients undergoing MILR in Eastern and Western institutions. As a result, the Ban, IWATE, and Hasegawa DSSs incorporated surrogates for difficulty related to cirrhosis and portal hypertension, due to cirrhosis-related hepatocellular carcinoma being a major indicator for MILR in Asian populations, whereas the Southampton DSS included neoadjuvant chemotherapy, since MILR is highly indicated for colorectal liver metastases treatment in the West[18].

In recent years, multiple studies have evaluated the effectiveness of available DSSs in predicting the difficulty level of MILR cases. In total, 10[78,82-90], 12[91-99], 4[79,93,100,101], 10[23,80,82,86,93,100-104], and 6[81,91,93,100,101,105] studies have assessed the Ban, IWATE, Hasegawa, IMM, and Southampton scoring systems, respectively. Various factors, such as tumor size and location, extent of resection, previous hepatectomy, obesity, and liver parenchymal status, have been utilized as proxy measures of MILR complexity, constituting the basis of DSSs[18,106].

For LLR, all five DSSs were noted to be effective discriminators for operative time and blood loss, requirement for transfusion and Pringle's maneuver, as well as postoperative complication rate[18]. Four out of five criteria were successful in predicting conversion rates (Ban, IWATE, IMM, Southampton), the time required for Pringle's maneuver, and LOS (Ban, Hasegawa, IMM, Southampton). Only two scoring systems managed to assess LLR difficulty by successfully predicting intraoperative complications (IWATE, Southampton) and mortality (IWATE, IMM), while IMM was the sole DSS to discriminate liver failure effectively[18]. Fewer studies have validated DSSs for RLR, demonstrating that both the Ban and IWATE criteria are effective predictors of operative time, blood loss, and LOS, while the Ban DSS has the added benefit of discriminating for complication rate. Previous studies that set out to validate externally and compare DSSs failed to establish the superiority of any particular scoring system, while confirming that all DSSs were, to various degrees, successful in effectively stratifying cases based on expected difficulty[86,91,93,100,101]. Of note, scoring systems allow for standardized auditing of outcomes, as well as drawing comparisons between institutions, countries, and different approaches (i.e., LLR *vs.* RLR) [18,106].

MINIMALLY INVASIVE SURGERY AND OUTCOMES

Advantages of LLR

The first cases of LLR were reported in 1991, when two female patients initially undergoing gynecologic surgery had benign lesions of the liver edge laparoscopically removed[107]. To date, the safety and efficacy of laparoscopic minor hepatectomy have been demonstrated compared with open minor hepatectomy. In fact, improvements in devices and techniques have established laparoscopic minor hepatectomy as the standard surgical procedure for tumors located in the anterolateral liver segments, in line with the recommendations of the 2nd ICCLLR[25]. However, open liver resection (OLR) has, for the most part, remained the standard of care for lesions that are large, multifocal, or that have a high chance of invading the portal vein branches, due to the potential risk of bleeding and the need for biliary reconstruction[108-110].

Among patients undergoing major hepatectomy, the laparoscopic approach has been associated with lower blood loss, morbidity and length of stay compared with open resection, while surgical times, transfusion requirements, and R0 margin have been similar. The feasibility, reproducibility, and utilization of laparoscopy in left and right liver surgery are different, however. In contrast to left major liver resection, right major hepatectomy via laparoscopy should be conducted by experienced surgeons as this can be a more challenging case[24]. In turn, given the difference in difficulty level between left and right hemi-hepatectomy, surgeons should use the minimally invasive right hepatectomy later along the learning curve[24].

Recently, a systematic review of 14 studies and 1,596 patients comparing laparoscopic and open hepatectomies for HCC among elderly patients demonstrated that, compared with OLR, LLR had fewer postoperative complications and a shorter hospital stay[33]. In a meta-analysis of five non-randomized retrospective studies including 888 patients, Goh *et al.* reported that LLR was associated with improved 1-, 3-, and 5-year OS [1-year OS: Hazard Ratio (HR) 0.41, 95% confidence interval (CI) 0.25-0.68; 3-year OS: HR 0.63, 95%CI 0.46-0.87; 5-year OS: HR 0.60, 95%CI 0.45-0.80] compared with OLR[34]. In addition, LLR was associated with a lower likelihood of tumor recurrence [Odds Ratio (OR): 0.65, 95%CI: 0.48-0.89] [34]. In a separate study, Kabir *et al*. noted a 16%-26% lower likelihood of death among patients undergoing LLR *vs.* OLR, with 8 of the 11 pooled studies reporting the extent of hepatic resection[35]. Of note, a large meta-analysis of 44 studies and 5,203 patients, published in 2017, consolidated the existing knowledge of LLR and OLR for HCC, demonstrating that the laparoscopic approach (i.e., pure laparoscopy, hand-assisted laparoscopy, and laparoscopic-assisted hepatectomy) was associated with lower blood loss and need for transfusion, improved achievement of negative resection margins, shorter hospital LOS, decreased morbidity and 30-day mortality rates[36].

Advantages of RLR

The first robotic-assisted abdominal procedure was performed in 1997 by a Belgian surgeon, Jaques Himpens[111]. Only a decade later, the rapid development of robot-assisted surgery has advanced to the point of being utilized even in highly complex procedures, such as liver surgery. To this end, Chen *et al*. reported similar utilization of RLR and OLR among patients with liver cirrhosis (45.7% *vs.* 46.9%)[37]. The robotic-assisted group had longer operative duration (343 *vs.* 220 min; $P < 0.001$), shorter LOS (7.5 *vs.* 10.1 days; $P = 0.001$), and lower dosages of postoperative patient-controlled analgesia (350 *vs.* 554 ng/kg; $P < 0.001$) compared with individuals who underwent open liver resection(OLR). No difference was noted in the 3-year disease free survival(DFS) and OS between the two groups[37]. On a similar note, Zhu *et al*. observed comparable 5-year DFS and OS among patients who underwent RLR, LLR, and ORL. Additionally, MILR was associated with increased operative time and duration of the Pringle maneuver, but shorter LOS compared with OLR. No other differences were noted among the three groups across other intraoperative variables and postoperative complications[38]. RLR, although associated with longer postoperative time, was advantageous *vs.* OLR in terms of safety and postoperative outcomes, including less blood loss and need for transfusion, lower rates of morbidity and 90-day mortality, as well as shorter hospital LOS, while long-term prognosis was usually comparable between the two approaches[39-42].

The continuous improvement of minimally invasive techniques and the development of available instruments has led to MILR having advantageous perioperative and comparable long-term outcomes compared with OLR[42-44,112]. Ultimately, MILR provides a constantly developing, safe and feasible option for patients of all ages with HCC, certainly worthy of consideration during the initiation of a therapeutic plan[20,44].

Comparison of open and laparoscopic major liver resection

MIMH represents a challenging task even for the most experienced surgeons. The laparoscopic approach is inherently limited by the difficulty associated with suturing the bleeding liver parenchyma, the requirement of complex hilar dissection for inflow control, the instability of the laparoscopic platform due to the frequent exchange of instruments, and the possibility of an unstable camera view[113]. As surgeon experience in LLR increased, major hepatobiliary centers worldwide started to perform LMHs, achieving similar clinical and economic outcomes compared with OMHs[46,47]. Therefore, in the last few years, many studies have sought to compare open *vs.* laparoscopic major liver resections.

For instance, a multicentric study with 3 European, 2 American, and 1 Australian participating institutions evaluated 210 major liver resections for both benign and malignant disease, of which 36 were for HCC. Among LMH cases, operative time was 250 minutes (range: 90–655 minutes), intraoperative blood loss was 300 mL (range: 20–2500 mL), and conversion to open surgery was required in 12.4% ($n = 26$) of patients. Median LOS was 6 days (range: 1–34 days) and 29 patients (13.8%) experienced postoperative complications[55]. Conversion to open surgery was required in 12.4% of cases, more often due to unsatisfactory progress, intraoperative bleeding, unclear tumor margin, posterior location of the lesion, and injury of the portal vein or the inferior vena cava. An analysis of the National Clinical Database in Japan evaluated 929 LMH and 14,262 OMH cases, further corroborating that the laparoscopic approach was associated with improved immediate postoperative outcomes. The majority of included cases were major resections for HCC, which were more frequently performed laparoscopically (n = 488, 52.5%), rather than via the open approach (n = 6,627, 46.5%)[31].

Among studies focusing on LMH and HCC, a meta-analysis by Ciria *et al*. compared LLR and OLR for HCC, with a sub-analysis of the major hepatectomies (n = 1,984) [49]. No differences in resection margins were noted between the two approaches, a finding that was reproduced in a meta-analysis of 8 non-randomized comparative studies and 780 HCC patients[50]. In yet another retrospective study, Yoon *et al*. assessed 2,335 patients who underwent liver resection for HCC. Notably, a sub-analysis comparing LMH with OMH among patients with HCC and cirrhosis demonstrated that LMH was associated with lower blood loss (277.8 *vs*. 317.6 mL; P = 0.046) and less blood transfusion requirements, as well as shorter LOS (9.4 *vs*. 15.5 days; $P \leq 0.001$) and decreased morbidity (8.6% *vs*. 14.7%; P = 0.045). However, patients undergoing LMH had longer operative time than patients undergoing OMH, whereas no differences were noted regarding the severity of complications, OS, and DFS between the two groups[48,51]. Comparable long-term prognosis (5-year OS: LMH 44.3% *vs*. OMH 44.7%; 5-year DFS; LMH: 29.9% *vs*. OMH 33.2%) was also reported in a single-center study of 115 patients undergoing major hepatectomy[52]. Again, lower blood loss and shorter LOS were associated with LMH, while there was no difference regarding complications. In contrast, a meta-analysis of 3 studies and 164 major resections demonstrated a lower complication rate in the LMH group, in addition to a longer operative time than OMH[53].

The ORANGE II PLUS was the first multicenter, randomized controlled trial comparing LMH with OMH among patients from 16 European institutions that recruited between 2013 and 2018[54]. The primary outcome was median time to functional recovery, which was significantly shorter for the laparoscopic compared with the open approach (LMH: IQR 3-5; range 1-30 *vs*. OMH: IQR 4-6; range 1-33; P < 0.001). Furthermore, global health status and body image were improved among patients undergoing LMH. Although there was a shorter interval between surgery and adjuvant therapy among patients with malignant disease undergoing LMH, oncologic outcomes (i.e., R0 resection margin) were similar with the two approaches (LMH: n = 106, 77.9% *vs*. OMH: n = 122, 84.1%)[54]. This clinical randomized trial demonstrated the benefits of the laparoscopic approach in terms of functional recovery and quality of life.

Ultimately, LLR has all the advantages that have been described for the laparoscopic approach in other surgical specialties, such as less blood loss, fewer complications, earlier recovery, decreased hospital LOS, and improved cosmetic outcomes[28,68]. Evidence regarding prognosis remains scarce, as few studies have assessed long-term outcomes, usually demonstrating no notable differences between the laparoscopic and the open approach[29]. Especially among patients with cirrhosis, preservation of the abdominal wall, better mobility of the diaphragm, and superior collateral venous drainage, as well as decreased ascites rates, have improved the immediate postoperative course among patients undergoing LLR[114].

Comparison of open and robotic major liver resection

The robotic-assisted approach overcomes inherent limitations of laparoscopy in highly complex procedures, allowing for accurate dissection proximal to vascular structures, in addition to easier suturing and knot-tying even in challenging circumstances[56]. Parenchymal transection still constitutes a major challenge for RMH due to the inherent limitations of currently available instrumentation. Thus, inadvertent injury to major hepatic veins is often a cause of massive bleeding. The "rubber band traction" method provides a safe alternative by utilizing all three robotic arms during parenchymal transection, which enables the third arm to control bleeding via compression and suture ligation[43,115]. Existing literature has demonstrated that RMH offers potential benefits, especially in the perioperative setting, including less blood loss and pain, shorter recovery times with earlier ambulation, and shorter hospitalizations[37].

Previous studies have reported that RMH remains less utilized than the open approach, as was the case in a meta-analysis incorporating data from eight series (RMH: 44.7% *vs.* OMH: 58.7%) (OR 0.60, 95%CI 0.39–0.91; $P = 0.02$) [39]. Importantly, these results should be interpreted with consideration of the study period, since studies performed in the early period of robotic surgery adoption might account for the disparities in its use for major liver resection. In fact, a recently published study by Shapera *et al*. evaluating patients who underwent RLR or OLR between 2016 and 2021 demonstrated no significant differences between the number of patients operated with the robotic-assisted and the open approach (60.3% *vs.* 63.2%; $P = 0.57$). In a sub-analysis of major liver resections, the RMH group had lower blood loss [200 mL (250 ± 244.3) *vs.* 300 mL (481 ± 540.6); $P < 0.001$], shorter LOS [4 (5 ± 2.7) *vs.* 6 (7 ± 5.2) days; $P < 0.001$], and 90-day mortality (0.6% *vs.* 10.6%; $P = 0.001$), while no significant differences were noted relative to total costs[57]. In another recent study, Tsilimigras *et al*. analyzed the results of 31 series comprising a total of 1,148 patients who underwent robotic liver resection for both benign and malignant disease, one-third of which were characterized as major hepatectomies[116]. RMH cases had higher operative time (403.4 ± 107.5 min), blood loss (543.4 ± 371 mL), conversion rate (8.6%), and LOS (10.5 ± 4.8 days) [116].

Few studies have assessed the use of robotic hepatectomy relative to the open approach among patients with HCC. In a study by Chen *et al*, MRH was performed in 42% of 183 total patients with HCC. The robotic approach was associated with lower blood loss (182 *vs.* 322 mL; $P = 0.026$), shorter LOS (8.9 *vs.* 12.3 days; $P = 0.017$), and decreased requirement for postoperative analgesia. None of the patients undergoing RMH required a blood transfusion *vs.* 9% ($n = 3$) use of transfusion among patients in the OMH group; the incidence of minor complications was comparable between the two groups[37]. In a recent series, Yang *et al.* compared 70 RMHs with 252 OMHs. Among all liver malignancies, patients undergoing RMH had less blood loss, a lower complication rate, and a shorter median hospital stay, although operative time was longer (472 *vs.* 349 min, $P < 0.001$). When dividing the robotic cases into initial and recent cases, the gap in operative time between the robotic and open groups decreased in the recent cases. In total, more than one-half of patients had HCC (RMH: $n = 40$, 57.1%; OMH: $n = 170$, 67.5%), and the RMH group had longer operative times and shorter LOS in both matched and unmatched sub-analyses. Regarding long-term prognosis, no differences were noted in both OS and recurrence-free survival(RFS). OS at 1, 3, and 5 years was 97%, 90%, and 90% in the robotic cohort *vs.* 94%, 84%, and 76% in the open cohort, while RFS was 97%, 90%, and 90% *vs.* 88%, 82%, and 82%, respectively[56]. Interestingly, several studies have even reported improved long-term outcomes associated with RMH compared with the open approach. In 2022, Sucandy *et al.* assessed 183 patients with malignant liver tumors undergoing major hepatectomy (RMH: $n = 125$ *vs.* OMH: $n = 58$)[58]. After propensity score matching(PSM), the open approach was associated with higher estimated blood loss, ICU, and overall LOS *vs.* RMH. The two cohorts were comparable in terms of 30-day readmission, 90-day mortality, and postoperative complications. Achievement of radical resection was similar between the two approaches (OMH: 93% *vs.* RMH: 85%; $P = 0.43$). Interestingly, a sub-analysis of patients with HCC demonstrated that RMH was associated with longer OS than OMH ($P < 0.05$)[58].

A drawback of the robotic approach in liver resection is the more technically challenging right RMH due to the difficult and hazardous mobilization of the right liver. Right RMH may be associated with an increased possibility of injury to the hepatic parenchyma, the tumor, or the inferior vena cava during the procedure, especially for large tumors. Additionally, retaining a three-dimensional orientation of the bulkier right part of the liver can be more challenging; thus, the use of ultrasound is warranted for confirming that the plane of division will ensure a negative resection margin[114]. The frequently observed longer operative duration associated with RMH is not surprising, due to the requirement of docking the robot, changing the appropriate instrumentation, and attempting to dissect with precision in the magnified field.[37] Since the open approach currently serves as the standard treatment for major resections of HCC, the evaluation of oncological outcomes between the different procedures is essential for assessing the benefit[37]. Comparable OS and DFS between RMH and OMH serve as a point of interest regarding treatment strategies for HCC moving forward.

Comparison of laparoscopic and robotic major liver resection

Even though MIMH has seen a progressive increase in its implementation, it is still performed in a minority of cases. In 2017, the minimally invasive approach was used for only 15% of all major hepatic resections, while an analysis of the ACS-NSQIP database for hepatic resection performed between 2014 and 2017 reported that only 33.1% of MILR were major resections[59]. RLR has been considered comparable in terms of clinical outcomes to LLR according to the Consensus of the European Association of Endoscopic Surgeons in 2015[113].

Currently, the instrumentation used for parenchymal resection during MILR is varied. Devices most commonly used in laparoscopic liver transection include ultrasonic scalpel, cavitron ultrasonic surgical aspirator or cautery-based vessel sealer, water-jet dissection and staplers. Other options include crushing clamp, bipolar, diathermy, monopolar sealer, radiofrequency pre-coagulator, and microwave pre-coagulator. The choice of approach should be surgeon-specific and be what the surgeon is most comfortable with. For deeper dissection, cavitron ultrasonic surgical aspirator, crushing clamp, and water-jet dissection with monopolar or bipolar devices are often used. Stapler hepatectomy is mostly utilized for vascular pedicles. Blind transection with a stapler or energy devices should be avoided due to the risk of bleeding and bile duct injury/biloma[117]. Many of the devices utilized in the laparoscopic approach could not be initially integrated into the robotic platform, due to incompatibility with the articulating wrist function[118]. Cly robotic liver resections include Harmonic Ace+7, Vessel Sealer Extend, robotic bipolar graspers, and more recently, the SynchroSeal, which is an articulating radiofrequency seal-and-transection device[118]. In a robotic total right hepatic lobectomy, Sucandy *et al.* reported the use of the robotic cautery hook for the superficial dissection, followed by the robotic vessel sealer for deeper parenchymal dissection[119]. Larger vessels can be handled using robotic clips or laparoscopic linear vascular staplers. Cauterization of bleeding points can be accomplished using the robotic fenestrated bipolar energy device, clips, or sutures[119]. The selection of instruments largely depends on instrument availability, as well as the surgeon's and institution's experience with various devices[117].

The main series comparing major RLR and LLR are summarized in Table 2. In a comparison of the robotic and laparoscopic approaches, after PSM, patients undergoing a LLR had a higher rate of conversion to open hepatectomy (23% *vs.* 7.4%, $P < 0.01$), but a shorter operative time (159 *vs.* 204 min, $P < 0.01$). No difference in morbidity (18% *vs.* 16%, $P = 0.47$) or mortality (1.3% *vs.* 0.8%, $P = 1.00$) was noted comparing the two approaches[59]. The study by Fruscione *et al.* demonstrated that RMH was associated with less fewer postoperative ICU admissions (43.9% *vs.* 61.2%; $P = 0.043$) and 90-day readmissions (7.0% *vs.* 28.5%; $P = 0.001$) than LMH. No differences were identified in terms of complications, blood loss, operative times, and LOS[60]. Similarly, a single-center study by Wang *et al.* assessed the perioperative outcomes between 48 LMH and 92 RMH procedures, with 13 and 39 HCC cases, respectively. Operative time, postoperative LOS, morbidity, and mortality were comparable between the two groups, while RMH was associated with a lower conversion rate (1.09% *vs.* 10.42%, $P = 0.034$) and blood loss than the laparoscopic approach[120]. Comparable performance between the laparoscopic and the robotic approach was demonstrated by Spampinato *et al.*, who reported no differences in operative time, estimated blood loss, allogenic blood transfusion

Table 2. Main series comparing robotic and laparoscopic major hepatectomy

Author and year	Cases	Type of procedure	HPB malignancy	Mean operative time (min)	EBL (mL)	Conversion to open (%)	Morbidity rate (%)	Mortality rate (%)	Mean LOS (days)
Fagenson *et al.*, 2021[59]	Robotic (*n* = 240)	Major 13% Minor 87%	27%	204	-	7.4%	16%	0.8%	3.0
	Laparoscopic (*n* = 240)	Major 14% Minor 86%	27%	159	-	23%	18%	1.3%	3.0
Fruscione *et al.*, 2019[60]	Robotic (*n* = 57)	LH 35% RH 35% Minor 30%	HCC 7% CCC 15%	194	250	-	28%	0%	4.0
	Laparoscopic (*n* = 116)	LH 19% RH 40% Minor 41%	HCC 14% CCC 6%	204	400	-	35%	0%	5.0
Wang *et al.*, 2019[120]	Robotic (*n* = 92)	LH 52% RH 48%	HCC 42% CCC 15%	196	243	1.1%	13%	0%	7.4
	Laparoscopic (*n* = 48)	LH 60% RH 40%	HCC 27% CCC 19%	199	346	10%	10%	0%	7.1
Spampinato *et al.*, 2014[61]	Robotic (*n* = 25)	RH 68% LH 28%	HCC 8% ICC 8%	430	250	4%	16%	0%	8.0
	Laparoscopic (*n* = 25)	RH 60% LH 32%	HCC 4% ICC 12%	360	400	4%	36%	4%	7.0
Lai *et al.*, 2016[62]	Robotic (*n* = 100)	Major 27% Minor 75%	HCC 98%	207	134	4%	14%	0%	7.3
	Laparoscopic (*n* = 35)	Major 97% Minor 3%	HCC 91%	335	336	5.7%	20%	0%	7.1
Liu *et al.*, 2023[64]	Robotic (*n* = 841)	Only major	HCC/ICC 59%	292	200	5.1%	24%	1.8%	6.1
	Laparoscopic (*n* = 841)	Only major	HCC/ICC 63%	300	300	11.9%	25%	2.3%	7.0

LMH: Laparoscopic major hepatectomy; HPB: hepatobiliary; EBL: estimated blood loss; LOS: length of stay; min, minutes; mL: milliliter; LH: left hepatectomy; RH: right hepatectomy; HCC: hepatocellular carcinoma; ICC: intrahepatic cholangiocarcinoma; CCC: cholangiocarcinoma.

requirement, postoperative ICU stay, and LOS among patients undergoing LMH and RMH. However, LMH was associated with faster recovery of bowel activity, evaluated as shorter time to first flatus (1 *vs.* 3 days; $P = 0.023$) and earlier introduction to oral liquid diet (1 *vs.* 2 days; $P = 0.001$). Postoperative outcomes, including complication rate, 90-day mortality, and readmission rate, were comparable between the laparoscopic and robotic approaches[61].

In recent years, various studies have confirmed that the use of the robotic platform in laparoscopic major hepatectomy could potentially raise the surgeon's confidence and ultimately increase the rate of RMH[66,114]. Benefits of the robotic approach entail improved visualization and dexterity that allow for precise hilar dissection during inflow control, in addition to better exposure during hepatocaval dissection by retraction of the third robotic arm[113,121]. The biggest comparative series has been published by Tsung *et al.*, who demonstrated comparable risk of total complications, mortality, negative margins, and conversion, although at the expense of increased operative duration for RLR. Among major hepatectomies, utilization of the robotic approach allowed for a higher percentage of cases performed in a purely minimally invasive manner[66,113]. A similar trend was reported by Lai *et al.*, who evaluated 129 patients undergoing MILR (LLR: $n = 35$, RLR: $n = 95$) and demonstrated that the robotic approach was performed in a higher proportion of major hepatectomies (RMH: 27% *vs.* LMH: 2.9%). Even though RMH was associated with longer mean operation duration (207.4 ± 77.1 *vs.* 134.2 ± 41.7 min; $P = 0.001$), RMH and LMH had comparable intraoperative blood loss, perioperative transfusion rate, LOS, overall morbidity, and operative mortality. Existing literature on the oncological and long-term outcomes of patients undergoing RMH for HCC has been limited. One study reported no difference in 5-year OS (65% *vs.* 48%; $P = 0.28$) and 5-year DFS (42% *vs.* 38%; $P = 0.65$)[62]. Another single-center study of 41 patients and 10 RMH procedures reported a 93% R0 resection rate, and 2-year OS and DFS of 94% and 74%, respectively; however, the significance of these findings remains uncertain[63].

The superior perioperative outcomes observed in most studies comparing RMH and LMH may be attributed to the technical advantages that characterize the robotic approach, such as a three-dimensional large visual field, which allows for the precise identification of anatomical structures, and the flexibility of the "Endowrist", which helps to perform a more meticulous dissection and easier suturing, therefore improving hemostasis. In fact, being able to control intraoperative bleeding is vital in MIMH, as massive bleeding adversel IQR y impacts the safety and prognosis of patients, with reported conversion rates in the literature being substantially lower for RMH than LMH, due to these above-mentioned technical advantages[120]. Fittingly, differences were noted in a multicentric cohort of patients undergoing RMH (n = 237) or LMH (n = 3,930), in which RMH was associated with decreased blood loss (200mL, IQR 100-450 *vs.* 300ml, IQR 150-500; $P = 0.012$), lower rates of Pringle maneuver (47.1% *vs.* 63.0%; $P < 0.001$), and decreased need for conversion to OMH (5.1% *vs.* 11.9%; $P < 0.001$) relative to LMH. Specifically, among patients with cirrhosis, individuals undergoing RMH demonstrated lower postoperative morbidity (19.5% *vs.* 29.9%; $P = 0.02$) and shorter postoperative stay (6.9 days, IQR 5.0-9.0 *vs.* 8.0, IQR 6.0-11.3; $P < 0.001$)[64].

Ultimately, RMH has demonstrated comparable safety to LMH with significant advantages in perioperative outcomes and no notable differences in oncological prognosis. The utilization of the robotic approach for major hepatectomy has been increasing in recent years, as many studies have confirmed its safety and feasibility, allowing for the performance of major hepatectomy in a purely minimally invasive manner, reaping the benefit of minimal trauma and quicker recovery[65,120].

COST COMPARISON

Deciding on the most appropriate approach for major liver surgery depends on various factors, including patient characteristics and surgeon expertise. Nonetheless, cost-effectiveness remains an important parameter in the implementation of every new technology, especially when comparing approaches with generally similar outcomes. Notably, both the laparoscopic and robotic approaches can be cost-effective alternatives to open surgery for major liver resection. In fact, while laparoscopic surgery tends to have higher operative costs, these are usually offset by lower hospitalization expenses. The benefit of robotic surgery is related to decreased morbidity and shorter hospital stays, minimizing postoperative costs. However, the costs of RMH need to be further assessed to justify the systematic implementation of this approach[122]. Notably, cost analyses should always be interpreted in terms of the specific healthcare system, patient population, and surgeon's expertise[123,124].

In assessing median overall total costs among case-matched studies, LLR has 17.4% lower costs *vs.* OLR. The 3% higher operation-related costs for LLR were negated by 32.9% lower hospital ward-related costs relative to OLR[125]. This difference in costs can be mainly attributed to the lower LOS associated with the laparoscopic approach. However, the difference in costs is less pronounced when assessing MIMH alone, which has demonstrated comparable costs to OMH, with higher operating room costs being offset by lower hospital costs and shorter LOS[125]. In a recent study by Cipriani *et al.*, the higher intraoperative expenses of LMH (+ 32.1%, $P < 0.001$) were offset by the postoperative savings (– 27.2%, $P = 0.030$) *vs.* OMH, resulting in cost-neutrality between the two approaches (– 7.2%, $P = 0.807$) in the intention-to-treat analysis. Of note, the per-protocol analysis reported less severe complications, interventional procedures, and readmission rates for patients who underwent LMH, resulting in a 29.9% ($P = 0.02$) cost advantage compared with

OMH; however, in this analysis, the additional expenses associated with conversion were significant[126].

Even though robotic–assisted surgery represents a good alternative to laparoscopy and open techniques, the costs of this approach have been an important barrier to widespread adoption among many hospitals[39,123,127]. In fact, robotic-assisted liver resection is often perceived as more expensive than open liver resection. When evaluating costs, it is important to assess both the surgery-related and the hospitalization costs. The occurrence of comorbidities, leading to extended hospital stays, potential ICU admissions, as well as readmissions, can increase total costs. Thus, different studies have demonstrated that the average total cost of the robotic approach may actually be comparable or lower than OLR[39,128,129]. For instance, Shapera *et al*. noted no significant differences among RLR and OLR in total hospital charges, total cost, variable cost, fixed direct cost, or fixed indirect cost in a series of 370 patients. Furthermore, reimbursements [$29,297 (58,105 ± 61,202.32) *vs.* $19,646 (42,851 ± 43,347.89); P = 0.030] and profits [$– 4420 (20,753 ± 62,297.45) *vs.* -$8735 (6,405 ± 45,405.81); P = 0.05] were greater after OLR compared with RLR.[57] In another study of 68 and 55 patients undergoing RLR and OLR, respectively, the percentage of patients undergoing major liver resection was comparable (RMH: 42.7% *vs.* OMH: 43.6%; P > 0.05). The average total cost of liver resection, including readmissions, was $37,518 for RLR and $41,948 for OLR. Furthermore, RLR was associated with lower overall morbidity, ICU, and LOS. These findings suggest that despite higher operative and equipment-related costs, the overall costs of RMH can be lower than OMH due to fewer complications and postoperative expenses[130]. Similarly, a study comparing RLR with OLR for benign and malignant tumors demonstrated that RLR was indeed associated with higher operating room and anesthesia costs but lower postoperative expenses. The adjusted direct costs of the robotic approach were lower ($14,754 *vs.* $18,998; P = 0.001) *vs*. OLR; however, no secondary analysis was conducted for major resection[131].

COMPUTING FEATURES AND FUTURE DEVELOPMENTS

Innovative technologies have already been implemented in clinical practice, such as indocyanine green (ICG) fluorescence or ultrasound-guided resections. The ultrasonic dissector currently has restricted freedom of motion relative to other instruments. Furthermore, the development of an ultrasonic aspirator for the robotic arm may prove very useful for parenchymal transections[113]. ICG fluorescence has been utilized for the determination of ischemic demarcation lines, which allow for the transection of an exact anatomical plane during parenchymal transection[115]. ICG fluorescence represents an advantage of the robotic compared with the laparoscopic approach. In pure laparoscopy, the ICG platform is independent, requiring the time-consuming exchange of special instrumentation. In contrast, the robotic platform integrates ICG fluorescence, providing direct and real-time visualization of vascular structures and bile ducts[132,133].

Emerging technologies, such as augmented reality (AR) and artificial intelligence (AI), are expected to play a significant role in improving the performance of MILR; however, these methodological approaches are still evolving [Table 3]. AR technology may help the surgeon with preoperative planning and three-dimensional reconstruction of liver imaging, thus aiding visualization before and during surgery. This technology could prove particularly useful in the robotic approach, improving intraoperative detection of malignant liver lesions and the characterization of the liver pathology in terms of understanding the surrounding biliary and vascular structures, allowing for a more precise anatomical dissection[113,134]. AR-based tracking systems and visual reconstructions could provide precise mapping of resection planes and assist in identifying vascular structures during transection. Furthermore, the use of AI could assist surgeons in delicate operations, such as major liver resection, through the virtual identification of anatomical structures, estimation of liver volumes, and instrument use during surgery. Even though the clinical application of AI is still theorized far in the future, AI seems promising in helping balance the absence of

Table 3. Summary of the main emerging technologies and their applications in MILR

Technology	Description	Advantages	Limitations
ICG Fluorescence	Real-time visualization of vascular structures and bile ducts using a fluorescent substance visible in near-infrared light.	- Enhanced determination of ischemic demarcation lines - Improved anatomical plane transections - Integration with robotic platforms	- Time-consuming - Special instrumentation needed
3D reconstruction of liver imaging	Three-dimensional reconstruction of the liver parenchyma and malignant liver lesions and their spatial relationship to vascular and biliary structures.	- Improved characterization of malignant lesions - Better understanding of the spatial relationship between malignant lesions and surrounding vascular and biliary structures - Allows for a more precise dissection	- Not yet standardized for clinical use - Special instrumentation needed
AR-based tracking systems	Live mapping of resection planes and tracking of the surgical resection	- Assist in identifying vascular and biliary structures during transection - Allows for a more precise dissection	- Not yet standardized for clinical use - Special instrumentation needed
AI-assisted resection	Virtual identification of anatomical structures, estimation of liver volumes, and guidance in instrument use during surgery through the application of AI	- Assist in identifying vascular and biliary structures during transection - Promising for overcoming the lack of tactile feedback of the robotic platform	Clinical application is still theoretical
AR-based Training	Tools for training based on augmented reality implementation for skills such as suturing	- May reduce learning curve for complex procedures - Allows faster and safer skill acquisition in younger surgeons	Requires integration into training programs and development of effective methodologies
Tele-Mentoring	Training tools by senior surgeons based on digital communication	- May reduce learning curve for complex procedures - Available as both real-time or asynchronous interactions	- Requires integration into training programs and development of effective methodologies - Heavy technical limitations - Possible data security concerns

MILR: Minimally invasive liver resection; ICG: indocyanine green; AR: augmented reality; AI: artificial intelligence

tactile feedback, and helping recognize intrahepatic biliary or vascular structures during parenchymal transection[134].

The absence of tactile feedback is undoubtedly one of the main issues in MILR. In fact, tactile sensation not only helps perform common surgical tasks, but also helps locate some intrahepatic landmarks. For example, if during an OLR, vascular and biliary structures often present as a thickened fibrotic sheath and can therefore be felt, the lack of feeling of the robotic platform can disorient surgeons during the dissection, leading to possible vascular injuries[134]. Moreover, these lesions are often located in critical areas such as the hepatic confluence. In this framework, preoperative 3D planning and AR-based imaging superimposition and tracking systems may be used to map resection planes and show vascular structures during liver transection[134].

New technologies could also potentially help surgeons in improving their technical skills. In fact, AR-based training and tele-mentoring may speed up simple skill acquisition, such as suturing, thereby reducing the learning curve for complex procedures[135]. In this context, computing features could be a useful tool to support young surgeons in developing basic robotic skills before performing liver resections. Advancements in computing features could pave the way for MIS to become even more precise and effective in major liver resection for HCC, maximizing the ability to provide the best possible care for patients[136]. Technical innovations are particularly interesting in the setting of RLR, as this platform allows for the implementation of AR, image-guided surgery, and 3D ultrasound instruments. These features, together with comparable oncologic outcomes, better postoperative outcomes, and enhanced recovery, will possibly translate into superior results as surgeons become more familiar with the robotic platform[136].

CONCLUSION

In conclusion, MIMH represents a safe and feasible procedure, with improved perioperative and comparable long-term oncologic outcomes compared to OMH in patients with HCC. MIMH has been associated with decreased intraoperative blood loss and improved immediate postoperative outcomes, but at the cost of longer operative duration. LOS has been consistently lower than in the open approach, both for the laparoscopic and the robotic approaches. Notably, the improved perioperative outcomes and shorter hospital stays of MIMH can often offset the higher operating room and anesthesia costs linked to the minimally invasive approaches. Interestingly, total MIMH costs may be lower than OMH, even though further studies are required to justify the systematic implementation of the minimally invasive approach. In addition, previously published studies have suggested a less steep learning curve for RLR compared to LLR, which could allow for a quicker, more widespread implementation of the robotic platform. All possible future developments of MILS, such as AR, AI, and 3D reconstruction, have the potential to elevate both the safety and the efficiency of MIMH, contributing to the possible future adoption of the minimally invasive approach as a standard in major hepatectomy for HCC.

In the last few decades, MILS has progressively become the standard of treatment. As surgeon's experience increases and minimally invasive technologies advance, more complex surgeries such as major hepatectomy will be routinely performed purely in a minimally invasive fashion. In conclusion, MIMH for HCC is feasible and safe compared to open surgery, with better immediate postoperative and at least comparable oncological outcomes. Nevertheless, most existing evidence is based on retrospective analyses, thus being susceptible to significant biases. Therefore, there is a need for randomized studies to further investigate the topic and draw definitive conclusions.

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Authors' contributions

Made substantial contributions to conception, literature review, and manuscript drafting and revising: Chatzipanagiotou OP, Catalano G, Kawashima J, Pawlik TM

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