

# Advances in minimally invasive liver surgery

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## ABSTRACT

As in many surgical branches, minimally invasive methods are becoming increasingly prominent in hepatobiliary surgery. Nowadays, robotic and laparoscopic methods are among the hot topics in the current literature. Both laparoscopic and robotic surgery have better short-term results than open surgery in terms of the blood loss, need for blood transfusion, length of intensive care unit and hospital stay, and postoperative major complication rate. In addition to cosmetic benefits, minimally invasive methods have similar results to open surgery in terms of oncologic outcomes. Minimally invasive techniques for hepatocellular carcinoma, colorectal cancer liver metastasis and cholangiocarcinoma, which are the most common indications for surgery, also for donor and recipient surgeries in organ transplantation, can be safely applied in high-volume centers and by experienced surgeons. The use of robotic surgery is increasing especially in major hepatectomy operations. The main advantages of robotic surgery over laparoscopic surgery are less bleeding, less conversion rate and a shorter learning curve. However, there is a need for studies investigating the cost-effectiveness of robotic surgery, the production of devices such as robotic ultrasonographic dissectors, and the establishment of structured minimally invasive hepatobiliary surgery training programs. The aim of this review is to evaluate the recent findings and current evidence on minimally invasive hepatobiliary surgery.

*Keywords:* Laparoscopic donor hepatectomy; laparoscopic liver surgery; minimally invasive hepatobiliary surgery; robotic donor hepatectomy; robotic liver surgery; robotic recipient hepatectomy.

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Following the first laparoscopic liver surgery performed in 1992, laparoscopic minor hepatectomies have become common, particularly for benign lesions [1]. With the development of technology and increased experience in laparoscopy, major liver resections are now performed laparoscopically. The first Louisville International Consensus Meeting on Laparoscopic Liver Surgery was held in 2008 to standardize patient selection and operative techniques, to make laparoscopic surgery available in more centers, and to improve surgical outcomes [2]. Subsequently, the Moriaka consensus meeting in 2014 and the Southampton consensus meeting in 2017 were held to set the standards for laparoscopic liver surgery [3, 4]. Many studies have been published reporting less bleeding, shorter hospital stay, fewer postoperative complications, and similar oncologic outcomes in laparoscopic surgery compared to open surgery [5].

The first robotic liver surgery was performed in 2003 [6] and over the years, robotics has become a widely used technique in many abdominal fields such as gynecologic, urologic, and rectal surgery [6, 7]. With the effect of the decisions stated in previous consensus meetings, which stated that liver posterosuperior segment surgeries cannot be the standard for laparoscopic surgery, robotic systems, providing more stable visualization and fine dissection, have been used for difficult hepatectomies. While the first publications in this field were comparisons with open surgery, recently, studies comparing laparoscopy and robotics in the form of propensity score match analysis have been published. [8, 9] Similar to laparoscopy, numerous studies have reported fewer complications and shorter hospital stay compared to open surgery [8], as well as less bleeding and less open conversion rate in robotic surgery compared to laparoscopic surgery [9–11].



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In this review, we review the findings and discussions of recent studies on minimally invasive techniques for liver surgery.

## LAPAROSCOPIC LIVER SURGERY

The emergence of minimally invasive surgery has led to radical changes in the techniques and approaches of all surgical branches in the last 30 years as this technique offers patients less pain, shorter hospital stay, better cosmetic results, and more cost-effectiveness. These changes also affected hepatobiliary surgery and the first laparoscopic liver resection was performed in 1992 [1]. In the following period, case series and reviews were published. The first international laparoscopic liver surgery consensus meeting was held in Louisville in 2008 to standardize patient selection and surgical techniques, to make laparoscopic surgery available in more centers, and to improve surgical outcomes [2]. Subsequently, the Moriaka consensus meeting in 2014 and the Southampton consensus meeting in 2017 brought together experts in laparoscopic liver surgery from around the world, aiming to set the standards of laparoscopic liver surgery [3, 4].

Despite the significant prolongation of survival in gastrointestinal cancers thanks to newly developed drugs in the field of oncology, surgical resections still constitute the potential curative treatment for colorectal cancer metastatic to the liver (CRCLM) [5]. Likewise, although the number of curable patients has increased significantly with the development of medical and local ablative methods in the treatment of hepatocellular carcinoma (HCC), surgical resection is still considered the main treatment that prolongs survival. In a meta-analysis of approximately 9000 liver resections, out of 6190 patients who underwent laparoscopic surgery, 3072 were for HCC and 1582 were for CRCLM [12]. In addition to the success of surgery, complications can be life-threatening. Therefore, laparoscopic methods have been increasingly used for primary and secondary liver tumors to minimize morbidity and surgical mortality. From the early days when feasibility was discussed, the debate has shifted to determining which patients cannot be minimally invasive. According to the study by Ratti et al. [5] 70% of CRCLM patients are considered suitable for laparoscopic surgery in high volume centers. A recently published multicenter study examining the effect of tumor size on laparoscopic surgery showed that as tumor size increased, open conversion rate, operative time, bleeding and transfusion requirement increased,

### Highlight key points

- Compared to open surgery, minimally invasive methods have less bleeding, shorter hospital stay, and similar oncological outcomes.
- With minimally invasive methods, patients have a higher and faster access to adjuvant treatment.
- Robotic liver surgery has less blood loss, shorter hospital stays, lower open conversion rates, and lower R1 resection rate compared to laparoscopy.
- There is doubt about the cost-effectiveness of robotic surgery and instruments such as robotic CUSA need to be developed.
- Pure robotic transplantations have begun to be performed in both recipient and donor hepatectomies.

but overall morbidity did not change. It has been recommended to evaluate tumor size with cutoff values of 5 and 10 cm [13].

### Short-Term Results

Delay of postoperative adjuvant treatment for more than four weeks also negatively affects survival. According to the study by Tohme et al. [14], the median time to start adjuvant treatment was 42 days in the minimally invasive surgery arm and 63 days in the open surgery arm ( $p < 0.001$ ). In the same study, postoperative chemotherapy delay of more than 60 days was associated with poor disease-free survival. Various studies comparing laparoscopic surgery with open surgery have shown less intraoperative bleeding in the laparoscopy arm. According to Luo et al.'s [15] meta-analysis of CRCLM patients, there were less bleeding and shorter hospital stay in the laparoscopy arm. In the presence of synchronous colon tumor liver metastases, a multidisciplinary decision regarding the location of the tumor and the extent of liver resection is recommended. Laparoscopic simultaneous resections resulted in a shorter hospital stay and no difference in the overall survival rate compared to open surgery. Performing major hepatectomies in addition to surgery for tumors located in the rectum and left colon has also been a subject of debate for open surgery. In their review, Lupinacci et al. [16] suggested that laparoscopic major hepatectomies can be safely performed with synchronous colorectal tumors, but patient-based selection should be made due to the lack of data in the literature. According to a recent meta-analysis, patients who underwent major hepatectomy for HCC were analyzed, and the laparoscopy group had shorter hospitalization, less bleeding, less morbidity, and fewer major complications [17].

### Long-Term and Oncological Results

Another important concern about minimally invasive surgery is surgical margin safety and oncologic outcomes. In the Oslo-Comet study by Fretland et al. [18], the first randomized controlled study in this field, there was no difference between the open and laparoscopic groups in terms of R0 resection. In a recent meta-analysis of recurrent liver tumors, the group that underwent laparoscopic resection had higher R0 resection (92% vs. 81.2%,  $p=0.0002$ , laparoscopic vs. open, respectively), better overall survival, and similar disease-free survival compared to open surgery group [19]. According to the randomized controlled trial by Robles-Campos et al. [20], comparing laparoscopic surgery with open surgery in patients with CRCLM, 1-, 3-, 5-, and 7-year survival rates were 92.5%, 71.5%, 49.3%, 35.6% for laparoscopy and 93.6%, 69.7%, 47.4%, 35.5% for open surgery, respectively. In the same study, they concluded that laparoscopic liver surgery could be safely performed in major hepatectomy, simultaneous hepatectomy, parenchyma-sparing surgery, posterosuperior segment surgery, two-stage surgery, and repeat surgery with oncologically similar results to open surgery. A meta-analysis examining the oncologic outcomes of minimally invasive surgery in HCC patients reported no difference between laparoscopy and open surgery in 3- and 5-year survival (83.72 vs. 80.82% and 68.97 vs. 68.12%, respectively) and disease-free survival (46.57% vs. 44.84%, respectively) [21].

### Previous Abdominal Surgery and Recurrent Disease

It is difficult to compare the complexities of surgery due to patient heterogeneity. In this sense, various scoring systems have been developed, but none of them include adhesions due to previous surgeries. A recent study of patients with previous non-liver abdominal surgery showed that there was no difference in operative time, amount of bleeding, length of hospital stay, overall morbidity, open conversion rate, and 30- and 90-day mortality between the groups with and without a history of abdominal surgery [22]. Reoperations for HCCs are also widely discussed in the literature. Goh et al. [23] compared the results of laparoscopic and open surgery in patients with recurrent HCC using propensity score matching method and reported that the laparoscopic group had a longer operation time, a shorter hospital stay, and longer disease-free survival.

### Chronic Liver Disease

Performing liver surgery in the setting of chronic liver disease carries many risks. Even minor resection of the cirrhotic liver can cause refractory ascites, which can be fatal. In these patients, minimally invasive surgery aims to reduce morbidity and mortality by reducing surgical stress. According to a meta-analysis, laparoscopic surgery in cirrhotic liver caused less refractory ascites and liver failure compared to open surgery [24]. According to another meta-analysis that compared open and laparoscopic methods in cirrhotic patients, the laparoscopic group had less bleeding, length of hospital stay, postoperative ascites and liver failure, and fewer surgical site infections [25].

## ROBOTIC LIVER SURGERY

Despite the benefits of laparoscopy in liver surgery, its use in major hepatectomy and particularly in posterosuperior segmental lesions is still a matter of debate due to problems in depth perception and image quality, technical difficulties in terms of bleeding control or reconstruction, and operator dependence of the camera image. The use of robots is increasing due to clear, stable and magnified images, flexible and ergonomic structure, and tremor filter in robotic system [26, 27]. In addition, high cost, lack of tactile sensation, and the absence of some instruments are crucial disadvantages of robotic surgery [26]. After the first robotic liver surgery was performed in 2003 [6], the use of robots has increased in hepatobiliary surgery. Annual robot utilization is increasing by 45% and hepatobiliary surgery accounts for 10% of all robotic surgeries [26]. While minor hepatectomies or wedge resections were performed in the early days, more and more complex robotic surgeries have been performed. According to a 2022 meta-analysis by Ciria et al. [28], out of 2728 operations, 1939 were minor and 765 major hepatectomies. Of the reports, 82.29% were for malignant causes, with 53.4% attributed to HCC and 28.8% attributed to CRCLM.

### Short and Long-Term Results

International consensus report on robotic hepatic surgery study was published in 2018 and accordingly, the robotic group had longer operation time, less bleeding, shorter hospitalization time, and less complication rate. In addition, oncologic results and overall survival rates similar to open surgery were obtained. Robotic surgery can be

safely performed for major hepatectomies in terms of short and long-term results [26]. According to the most recent guideline of the same team in 2023, surgeries for large tumors and tumors adjacent to major vascular structures should be performed in high-volume centers and by experienced surgeons. Furthermore, robotic surgery for HCCs can be performed safely, but there is insufficient evidence to recommend routine robotic surgery for intrahepatic CCC. Robotic surgery can be performed safely for CRCLMs. Although there is insufficient evidence regarding oncologic outcomes, the results are similar to those of laparoscopy and open surgery. In terms of major hepatectomies, robotic surgery was reported to be as safe as laparoscopic and open surgery, with less bleeding, shorter hospital stay, and longer operation time in the robotic group. Although insufficient data were obtained in the cost analysis, robotic surgery was more expensive than laparoscopy, but had a total cost similar to that of open surgery [29]. A study comparing robotic hepatectomy with open surgery showed less bleeding, shorter hospital stay, smaller lesion size, and lower 90-day mortality in the robotic group [30]. In the study by Chen et al. [31], comparing the oncologic outcomes of robotic and open liver resection in HCC patients for the first time, there was no difference between open surgery and robotic groups in 3-year disease-free survival and 3-year overall survival, suggesting that robotic surgery can be performed safely in HCC operations. Di Benedetto et al. [8] compared the results of robotic and open surgery in HCC patients and showed that the robotic group had longer operation time, shorter hospital stay, less need for intensive care unit admission, less posthepatectomy liver failure, similar R1 resection rate, and similar 90-day mortality rates. Sucandy et al. [32] compared robotic and open liver surgery, reporting that major complications and bleeding were lower in robotic surgery. Intensive care unit and hospital stay were shorter than open surgery. Overall survival in CCC and CRCLM patients was similar in all methods, but survival was higher in the robotic group in HCC patients.

### Major Hepatectomy and Challenging Cases

An advantage of the robotic system is its ability to reach the posterior segments and its high suturing capacity. Minor hepatectomies are defined as resection of two or less Couinaud's segments, whereas major hepatectomies are defined as resection of 3 or more Couinaud's segments or surgery for difficult-to-locate lesions such as right posterior sectionectomy (S6-7) and right anterior sectionec-

tomy (S5-8) [33]. Chiow et al. [9] compared laparoscopic and robotic patients who underwent right posterior sectionectomy in a multicenter study and reported less intraoperative bleeding (200 ml vs. 40 ml), less need for blood transfusion (10.2% vs. 23.9%), and less conversion (2.3% vs. 11.4%) in the robotic group after propensity score matching. A study conducted by Masetti et al. [34] in Italy compared laparoscopic and robotic techniques in CRCLM patients. While there was no difference between the groups in terms of postoperative outcomes, the R1 resection rate was higher in the laparoscopic group (19.9% vs. 28.8%). The surgical margin was wider in the robotic group (8 mm vs. 3 mm). Analysis of the R1 resection rate and surgical margin distances showed that the effect of the robotic method on the surgical margin emerged particularly in posterosuperior segment operations. Chong et al. [10] compared right and extended right hepatectomy patients with robotic and laparoscopic techniques, showing that the robotic group had fewer open conversion rates and shorter hospital stays.

### Multivisceral Resections

With the increasing use of robotic surgery, other organ surgeries are now performed simultaneously with hepatectomy. A recent review by Sullivan and Fong [35], has revealed that robotic simultaneous resection can be performed safely with the correct patient selection particularly in colorectal cancer surgeries. In addition, there are approximately 50 case reports published in the literature in this field and other organ surgeries such as pancreas, prostate and lung surgery can also be performed in the same session.

### Scoring Systems

The IWATE scoring system, created by Ban et al. [36] and finalized at the 2014 Morioka meeting, was developed to assess the degree of difficulty of minimally invasive liver surgeries [3]. This system was based on the Japanese cohort and defined as six factors (extent of liver resection, location, size, proximity to major vessel, hand assisted or not, and liver function) and four difficulty levels (low, intermediate, advance, and expert). Studies have shown that the degrees of difficulty defined by these criteria correlate with open conversion rate, operative time, amount of bleeding, and postoperative complications. These criteria have been used quite frequently in the selection of patients who are candidates for robotic and laparoscopic liver resection. Furthermore, these criteria are considered in robotic surgery trainings.

### Learning curve

Another advantage of robotic surgery over laparoscopic surgery is the shorter learning curve compared to laparoscopy. In a study, an average of 43 operative experience was required for laparoscopic hepatectomy and 20 for robotic hepatectomies. This was interpreted as robotic surgery requiring 47.1% less caseload than laparoscopic surgery [37].

### Special Issues

#### Indocyanine Green

Indocyanine green (ICG) can be used to evaluate parenchymal blood supply and biliary tract in both robotic and laparoscopic methods. The absorption spectrum of ICG is in the near-infrared light and gives green light at 840 nm wavelength. After intravenous injection, ICG is taken up into the liver, metabolized, and excreted in the bile. After this feature was discovered, it served to evaluate the functional capacity of the liver. In the following period, it was used for in liver surgery to identify the segments of the liver, and then used to identify the tumor. It can also be used to detect occult metastases. After ICG injection, HCC lesions appear as a rim with a hypo and hyperfluorescent rim. It is usually administered intravenously at doses of 1.25–5 mg. It is not affected by the presence of cirrhosis in the liver. In a recent systematic review, the detection rate of liver tumor with ICG was 87.4% and false positivity was 10.5% [38].

#### Central Venous Pressure

Studies have shown that keeping the central venous pressure (CVP) value low during liver surgery is associated with less bleeding. It has been showed that an average of 800 ml of blood was lost between when preserving the CVP below 5 cmH<sub>2</sub>O and above 5 cmH<sub>2</sub>O (200 ml vs. 1000 ml) and less blood transfusion was required in the low CVP group (5% vs. 48%). According to a recent meta-analysis, there was less bleeding and less need for blood transfusion in the low CVP group [39]. In their randomized controlled trial investigating the effect of CVP in laparoscopic hepatectomy, Pan et al. [40] showed that the amount of intraperative bleeding was lower in the group with a CVP value below 5 cmH<sub>2</sub>O (188 vs. 346 ml).

#### Geriatric population

In a study by Martinez-Cecilia et al. [41] on the outcomes of laparoscopic and open liver surgery in CRCLM pa-

tients over 70 years of age, the laproscopic group had less bleeding and morbidity, shorter hospital stay, similar R0 resection rate, similar recurrence free survival, and overall survival rates. The main benefit of minimally invasive surgery was demonstrated in the 70–74 age subgroup. In a study of HCC patients over 65 years of age, the length of hospital stay and overall morbidity were lower in the laparoscopic group and there was no difference between the groups in terms of overall and disease-free survival [42]. Similar results have been reported in other recent studies.

### MINIMALLY INVASIVE LIVER TRANSPLANTATION

As the use of minimally invasive surgery has become widespread in liver surgery, minimally invasive methods have become frequently used in liver transplantation. Both donor hepatectomies and recipient hepatectomies, as well as donor liver implantation with both laparoscopic and robotic techniques have been performed in some centers. In a recent meta-analysis by Ziogas et al. [43], pure laparoscopic donor hepatectomies were associated with less bleeding, fewer overall complications, shorter hospital stay, and longer operative time than laparoscopically assisted and open donor hepatectomies. Due to the insufficient data to evaluate robotic donor hepatectomy at the meta-analysis level, a clear evaluation could not be made. However, it has slightly better results than the laparoscopic group in terms of bleeding amount and hospitalization time and further studies are needed in terms of cost analysis. In 2020, the expert consensus report published by Cherqui et al. [44] on laparoscopic donor hepatectomy provided guidelines on patient selection, as well as patient and graft safety. Although left lateral sectionectomy has become a standard procedure in laparoscopic donor hepatectomies, more major donor hepatectomies are recommended in experienced centers [45]. With the widespread use of robotic surgery, robotic donor hepatectomies are now performed [46]. With experience, completely minimally invasive donor and recipient surgeries have been performed and become one of the hot topic areas in the field of transplantation [47].

One study reported that the technique could be standardized after reaching an annual number of 60 operations in pure laparoscopic donor right hepatectomy [48]. Similarly, another study examining pure laparoscopic donor right hepatectomies, reported the learning curve as 65–70 cases [49].

## Limitations

According to a survey study conducted in European centers performing 100 or more hepatobiliary surgeries annually, 58% of the participating surgeons stated that robotic surgery was superior to laparoscopy in extended left hepatectomy + hepaticojejunostomy, 60% in extended right hepatectomy + hepaticojejunostomy, 60% in right posterosuperior segment resections and 52% in central hepatectomy. Of those who performed robotic surgery, 70% expressed dissatisfaction with the lack of a robotic CUSA device and 88% of surgeons stated that they believed robotic surgery would become significantly superior to open surgery in the future [50]. For this reason, some centers perform robotic surgeries using the two-surgeon technique. In this technique, one surgeon operates the robotic console and the other stands next to the patient to use the laparoscopic CUSA device. Another limitation is that no cost-effectiveness studies have been conducted yet and there is a technological accessibility problem, especially in poor countries.

## Conclusion

Minimally invasive techniques stand out with similar oncologic outcomes and better short-term results compared to open surgery. The main advantages of robotic surgery over laparoscopy are less bleeding, less conversion rate to open surgery and a shorter learning curve. The use of robotic surgery is increasing especially in major hepatectomy, posterosuperior segment surgery and surgeries requiring reconstruction. However, there is a need for studies investigating the cost-effectiveness of robotic surgery, development of devices such as robotic CUSA, and structured minimally invasive hepatobiliary surgery training program.

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