Mini-invasive Surgery

Review

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Minimally-invasive anatomical liver resection for hepatocellular carcinoma: a literature overview with technical and anatomical tips and tricks

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Abstract

Since its introduction in 1985, anatomical liver resection (AR) has been performed to treat early-stage hepatocellular carcinoma. The minimally-invasive AR (MIALR) approach can be safely performed at high-volume tertiary referral centers. The resection techniques can vary among surgeons, depending on the center's experience, patient characteristics, hepatic segment involvement, and tumor characteristics. Profound knowledge of the liver's surgical anatomy and a standardized inflow control approach is fundamental to performing MIALR safely. This article aims to summarize the applications of the MIALR and its outcomes, focusing on the techniques for vascular inflow control and the essential tips and tricks to standardize these techniques for laparoscopic and robotic approaches.

Keywords: Laparoscopic liver resection, robotic liver resection, minimally-invasive liver surgery, tips and tricks, anatomical liver resection, hepatocellular carcinoma

INTRODUCTION

Since the first laparoscopic liver resection (LLR) was reported in 1991, minimally-invasive liver surgery (MILS) has been used extensively to treat liver tumors. However, its widespread adoption has been more challenging than in other surgical fields due to its technical complexity and oncological issues[1,2]. Several LLR reports have shown that MILS is viable for treating primary and secondary hepatic tumors[3].

For hepatocellular carcinoma (HCC), the most recent guidelines approved the use of MILS in early-stage treatment[4-6]. Indeed, several studies showed that LLR reduces the risk of postoperative decompensation of HCC patients with chronic liver disease[7-9]. Advances in preoperative assessment of HCC patients (including the evaluation of the future remnant liver), surgical techniques, and perioperative management have substantially extended the boundaries of MILS[10,11].

The principles of hepatic surgical oncology are based on resectioning the hepatic lesion with negative margins while saving as much parenchyma as possible to prevent post-hepatectomy liver failure[12]. However, HCC management should consider tumor biology and the liver's peculiar anatomy. For these reasons, Makuuchi first proposed the concept of anatomical liver resection (AR) in 1985, which was initially reported to be as fundamental as a tumor-free margin. The underlying principle is that complete resection of an entire anatomic area should improve survival by reducing local recurrence[13,14]. AR includes segmentectomy or wider resection, including bisectionectomy, hemihepatectomy, and trisectionectomy[15]. AR is based on the theory that HCC spreads preferentially into the portal flow branches, leading to microscopic tumor thrombi and then into satellite nodules[16]. Thus, AR plays a critical role in the surgical treatment of early-stage HCC aimed at obtaining optimal local control[17]; nevertheless, there is debate regarding its survival outcomes compared to non-anatomical resection (NAR).

This review aims to introduce the applications of minimally-invasive anatomical liver resection (MIALR) and to suggest the most important technical aspects to standardize this technique.

CURRENT CONTROVERSIES SURROUNDING MIALR

Since the introduction of AR by Makuuchi in 1985, it has been proposed that it could result in better oncological outcomes[15] based on the theory that HCC invades the portal branches, spreading tumor cells into the portal flow and forming satellite nodules[16]. Several comparative survival studies were performed, including large retrospective reports showing an advantage in local recurrence comparing AR and NAR, especially for solitary tumors without microvascular invasion[18,19]. A recent multi-institutional propensity-score matched study involving 250 patients with solitary HCC showed a better five-year disease-free survival (DFS) for AR than NAR (62% *vs.* 35%; $P = 0.005$), although without differences in overall survival (OS). The authors suggest that a similar OS was associated with aggressive management of recurrences, as demonstrated by the higher rate of curative repeat resection or ablation therapy in the NAR group (42% *vs.* 10%, $P = 0.001$)[20]. Similar results came from another multicenter study on 546 patients with a micro-vascular invasion that showed a lower local recurrence rate after AR, even if survival outcomes were similar between the cohorts[21]. Finally, a meta-analysis of propensity score matching studies and randomized studies enrolling 3554 patients found similar five-year survival with a better DFS after AR at one and three years[19].

In liver surgery, unintentional damage to the parenchymal inflow or outflow can result in ischemia of tissue supplied by the damaged vessel (also known as remnant liver ischemia), as in the case of NAR. Remnant liver ischemia was associated with worse surgical and oncological outcomes in a study of 328 patients, showing more complications, more extended hospital stays, and worse OS (OR 6.98; $P < 0.001$) and DFS (OR 5.15; 95%; $P < 0.001$)[22].

Because advanced surgical techniques and improvements in imaging technologies have facilitated surgical approaches involving AR of individual hepatic segments, the widespread adoption of minimally-invasive anatomic liver resections (MIALR) could lead to better outcomes in HCC patients as proposed by the study group of Precision Anatomy for Minimally-Invasive Hepato-Biliary-Pancreatic (PAM-HBP) surgery[23]; nevertheless, further prospective studies are needed.

CRITICAL POINTS OF SURGICAL ANATOMY

The surgical anatomy of the liver is the basis of MIALR. Because AR is resectioning a part of the liver, including its vascular inflow, the liver surgeon should master the techniques for inflow control. Couinaud described three techniques for inflow control at the hepatic hilus: the intra-fascial approach, the extra-fascial approach, and the extra-fascial transfissural approach, with the latter two now considered the Glissonean approach[24]. The Glissonean pedicle approach provides an excellent guide for the surgical anatomy of the liver during a procedure, especially for AR.

Conventional dissection for isolating the vascular and biliary structures in the hepatoduodenal ligament (the so-called intrafascial approach) is the "classical control method" named by Bismuth[25]. This method has been used for LLR, usually in major or hemihepatectomies. However, in the case of anatomical variations, there is a possibility of injuring the bile ducts or the hepatic vessels[26].

Inflow control: the Glissonean approach

Takasaki first used the term Glissonean approach in 1986 for the extrafascial technique, although this procedure had been initially reported by Tien-Yu Lin in 1960, followed by Ton That Tung in 1963, and then by Bismuth[25,27,28]. In our experience, this procedure is optimal for a standardized MIALR. The Glissonean pedicle of each segment/section (first-, second-, and third-order branches) can be isolated from the surrounding parenchyma and encircled on a tape. The dissection further peripheral to third-order Glissonean branches is also possible, leading to the concept of the "cone unit," i.e., the liver portion supplied by the terminal portal branches[27]. Each hepatic segment contains 6-8 cone units. Every portal branch can be isolated selectively via an extrafascial or interfascial approach. Thanks to the anatomical separation of the Walaeus sheath and the liver Laennec's capsule around the portal triads, the Glissonean pedicles can be approached extrahepatically as described by Sugioka *et al.*[29,30].

Various anatomical landmarks have been proposed to standardize the technique for MIALR. The hilar plate is a classic landmark for liver surgery: it connects the Arantian plate with the cystic and umbilical plates. The Glissonean pedicles can be separated by detaching the connective tissue of the hilar plate from the hepatic parenchyma. Laparoscopy provides some advantages, such as three-dimensional (3D) vision, which facilitates the Glissonean approach.

Recently, the PAM-HBP group agreed on the safety of MIALR, stressing several advantages of the Glissonean approach compared to the conventional hilar approach[31,32].

This approach has no absolute contraindications, even if severe cirrhosis or lesions close to the pedicle make this technique more challenging[33]. Furthermore, we suggest carefully checking the anatomic variations of the portal pedicles[34]. From the oncological point of view, the absolute contraindications to surgical resection are the same as those of the open approach.

TECHNICAL ASPECTS

It remains debatable whether the Glissonean approach provides objective technical advantages over hilar dissection because the concept of the cone unit is not universally recognized. In our experience, the Glissonean approach is the best way to perform MIALR. Accordingly, we will focus on resecting technically challenging positions and major anatomic resections. Situations such as tumors attached to Glissonean pedicles might require changing the approach from an extrafascial to an intrafascial or even a transfissural approach. Thus, the liver surgeon must know these approaches.

General considerations

Patient positioning can vary among surgeons, with the supine position being the most common for any LLR, with an elevation of the right side of about 30 degrees in case of resection of segments 6-7[35]. Other authors suggested using a left lateral decubitus or prone position to change the approach from caudo-cranial to anteromedial for segment 7 resection[36]. Regarding the surgeon's position, some operators prefer to stay between divaricated legs, while others prefer to stay on the right side with closed legs. Neither is superior, and the position should be chosen according to operation type and surgeon's preference. Considering the specific risk of liver surgery, the operator should always be ready to deal with bleeding from the major hepatic vessels and convert to open surgery if needed.

Surgeons and anesthesiologists should establish a standardized perioperative protocol to manage risks associated with dissecting hepatic and portal veins and from the parenchymal transection. Higher postoperative morbidity and mortality have been reported in cases of massive intraoperative blood loss needing perioperative blood transfusions[37]. A propensity-matched study involving 209 patients demonstrated the effectiveness of the Pringle maneuver when performing major resections[38]. Similarly, a randomized trial showed that a low central venous pressure could lower intraoperative bleeding and the need for transfusions, highlighting the role of the anesthesiologist[39].

Based on the Takasaki approach, intraoperative fluorescence can be used to obtain positive enhancement of the segments to be resected by injecting indocyanine green (ICG) into the secondary/tertiary order portal branch under intraoperative ultrasound (US) guidance or directly after surgical dissection[40]. Similarly, a negative enhancement (counterstaining) can guide MIALR by injecting ICG intravenously after selective isolation and clamping of the pedicle[41,42]. According to our experience, the negative counterstaining procedure is easier to perform.

Hemihepatectomy

The patient is placed in the supine position with spread legs. Five trocars are usually needed for laparoscopic major hemihepatectomy, with the operator standing between the legs [Figure 1]. The flexible scope is introduced through the umbilical trocar, with the other four trocars surrounding the lobe to be resected.

Laparoscopic US is performed to confirm preoperative imaging and to examine the vascular structures and their relationships with the lesions.

First, the falciform ligament is divided to expose the confluence of the middle and right hepatic veins into the inferior vena cava. Then, the ipsilateral triangular ligament is divided.

After the liver mobilization, the postero-inferior surface is exposed by lifting the involved lobe using liver retractors with a small gauze interposed to protect the liver (to avoid damaging the cirrhotic liver surface

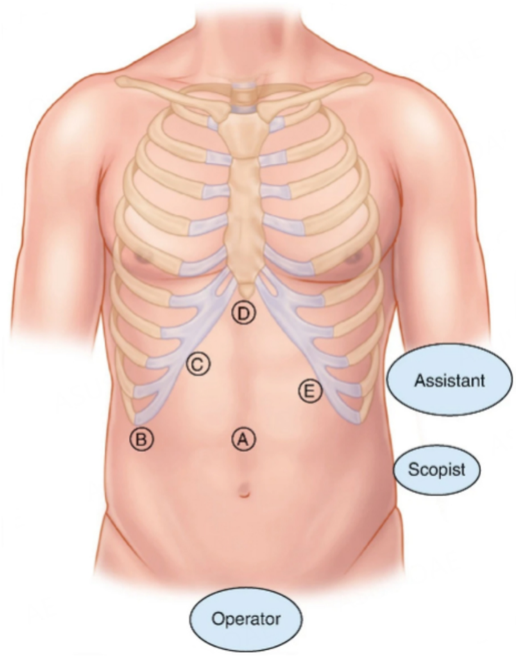

Figure 1. Trocar positioning.

and the tumoral capsule). For right hepatectomy, the gallbladder is resected to obtain better access to the Rouviere's sulcus and right portal pedicles.

The major vascular structures at the hepatic hilum are encircled with tape around the hepatoduodenal ligament to prepare for an eventual Pringle maneuver. For the Glissonean approach, a gentle and blunt pedicle dissection is performed using a dissector or suction tips to identify the right-left bifurcation of the vascular elements. En bloc pedicle division at the level of the right main pedicle carries a risk of injury to the contralateral vasculature; the division at the anterior and posterior levels is safe because it does not risk injury to the left vasculature. Individual control of the hepatic artery and portal vein is also frequently used in hemihepatectomy [Figure 2]. The arterial structures are approached first in the pedicle, followed by portal branch exposure. Vessels are encircled with vessel loops or clamped with bulldog forceps to highlight the transection line, facilitated by the ischemic demarcation. Then parenchymal transection is performed using a Cavitron Ultrasonic Surgical Aspirator (CUSA). The intraparenchymal course of the middle hepatic vein can be reconfirmed using ultrasounds during this phase. The ipsilateral bile duct is dissected but usually divided later during parenchymal transection at the hilar plate dissection. This hilar plate is reached, avoiding direct contact with energy devices to avoid biliary injury. A liver hanging maneuver can be performed in cirrhotic patients, even if it can be challenging in laparoscopy, mainly hanging around the paracaval portion of the caudate lobe[43]. The hepatic veins should be meticulously dissected, and the room should be created to permit space sufficient to place the stapler transversely. The specimen can be retrieved using a Pfannenstiel incision.

Segment 1

Caudate lobe resection is technically demanding and possibly dangerous, even for experienced surgeons. Recently, a retrospective study involving 21 patients undergoing S1 resections showed similar results for LLR and open liver resection (OLR) regarding intraoperative bleeding, operation time, postoperative complications, and length of hospital stay[44].

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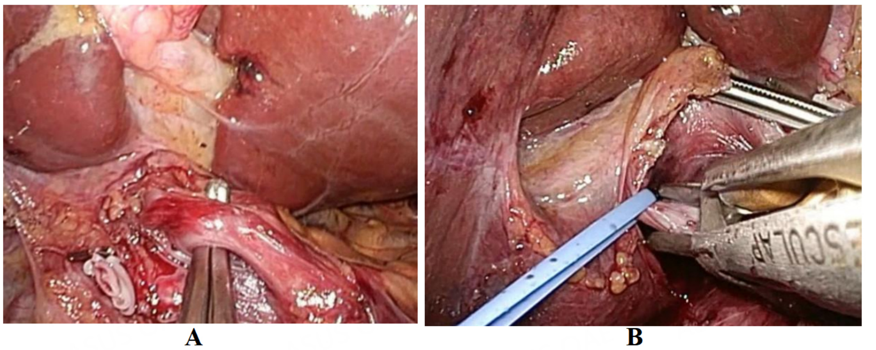

A B

Figure 2. Isolation of the right hepatic artery (A) and right portal vein (B).

The patient is placed in the supine position. The operator stands on the right side for liver mobilization and between the patient's legs during the resection. The working ports are placed in the right subcostal area, and the assistant's trocars are in the epigastrium and left subcostal area.

A five-port laparoscopy is usually performed as well. The subsequent steps are similar to the open approach. Intraoperative ultrasounds confirm the lesion and highlight its margins and the relationships with the vascular structures. The left liver is fully mobilized, and the hepato-gastric ligament is divided to access the caudate lobe. All attachments between segment 1 and the inferior vena cava are carefully sectioned. The right or right posterior Glissonian pedicle is selectively isolated and clamped [Figure 3] to obtain an ischemic counter-demarcation of the caudate process. Thus, this transection line is followed, and laparoscopic CUSA performs the consequent parenchymal transection. The posterior surface of the caudate lobe is then carefully separated from the inferior vena cava, and the short hepatic veins or the terminal portal branches are secured by endoclips, continuing then with the dissection of the paracaval portion. During parenchymal dissection, several Glissonean structures to the caudate lobe can be encountered: they can be clipped or sealed with vessel sealing devices. During the transection, the peripheral branch of the right hepatic vein and the middle hepatic vein can be encountered. Transection should be meticulous to avoid injuring these vessels. Parenchymal transection then continues along the resection plane. The short hepatic veins to the caudate lobe are carefully secured from the left to the right side, and the resection is completed. The specimen can also be extracted by enlarging the umbilical incision.

Segments 2-3

Anatomical resections of segments 2 or 3 are less commonly performed; however, they can be helpful in the case of small right liver or to avoid too much parenchymal sacrifice.

The patient is placed in the lithotomy position, with the operator standing on the right side or between the legs. The working ports are placed in the right subcostal area, and the assistant's trocars are in the epigastrium and left subcostal area.

The liver is mobilized by dividing the falciform and left triangular ligaments. Laparoscopic US confirms the lesion and its relationship to vascular and biliary structures.

The dissection of G2 and G3 can be performed at the umbilical plate following the round ligament's insertion (the technique is shown in the supplementary material). CUSA is helpful, as is the assistant's retraction of the left liver. Liver transection is initiated from the medial to lateral direction using the

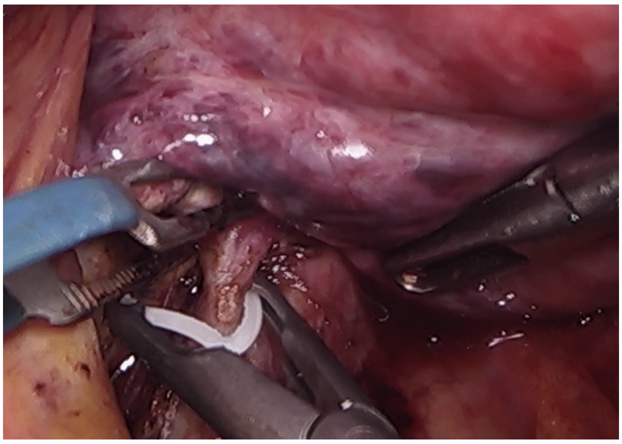

Figure 3. Securing a Spigelian vessel during laparoscopic caudatectomy.

ultrasonic dissector, with a deeper dissection in the case of segment 2. Hemolocks secure the portal pedicles. The left hepatic vein must be preserved while securing its tributaries with endoclips. The specimen is relatively small and can be retrieved by extending the umbilical incision.

Segments 6-7

Resection of segment 7 and right posterior sectionectomy are treated together because of the similar approach. LLR of posterosuperior segments is recognized as a technically major procedure because of the significantly higher estimated blood loss, open conversion rate, longer operative time, and length of hospital stay than anterolateral resections[45,46]. Nonetheless, recent studies showed improved outcomes after posterosuperior resections for HCC, with reduced blood loss, fewer complications, and shorter postoperative hospital stay than with OLR, thanks to newer technologies and devices[47]. An international multicenter randomized trial comparing OLR and LLR in postero-superior (PS) segments is ongoing[48].

The procedure is usually performed with the patient in a semilateral supine position, but a prone position has been described by other authors[49]. The surgeon stands between the legs. A flexible laparoscope is inserted in the paraumbilical, and four additional ports are placed around the correspondent part of the liver to remove, with the possibility to insert a trans-costal trocar if needed, especially for a pure segment 7 segmentectomy[50].

Laparoscopic US is performed to localize the tumor and locate its relationship with the major hepatic veins. Initially, a cholecystectomy is performed. After the liver is lifted anteriorly by a retractor on a gauze, the right triangular ligament and other ligamentous structures are divided using an energy device from below. After mobilization of the right liver, the major Glissonian pedicle of the right posterior section is dissected at de Ruviere sulcus and then encircled with vessel loops or umbilical tape. Transection of the branch of interest is carried out on secure clips [Figure 4]. The liver transection is performed with the aid of the CUSA, following the ischemic line. The smaller branches of the hepatic vessels can be controlled with a sealing device or endoclips, while the main branch of the right hepatic vein can be secured with an EndoGIA[51]. The specimen can be extracted through a Pfannenstiel incision.

Segments 5-8

For segment 8 resection, the patient lies supine, and the operator stands between the patient's legs. The minimally-invasive technique is always based on a flexible tip scope and the other four trocars in the upper

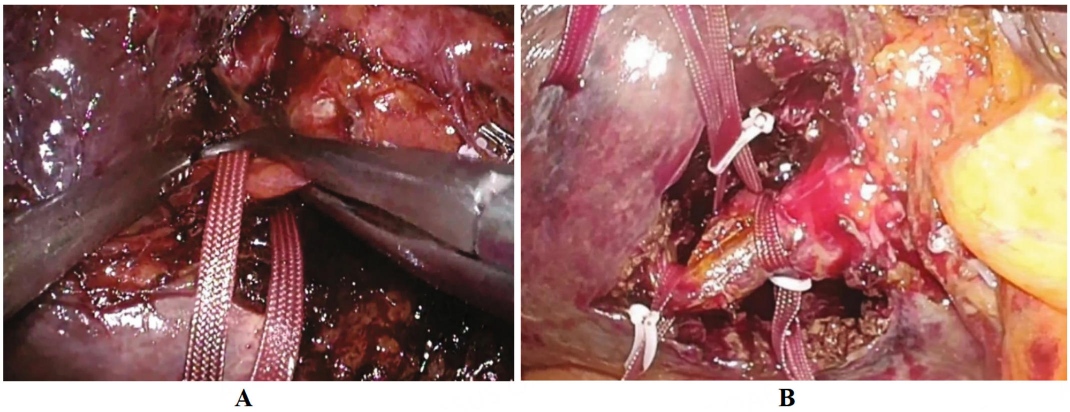

Figure 4. Isolation of segments 6 (A) and 7; (B) Glissonean pedicles from the right posterior pedicle.

right quadrant. Additional intercostal trocars can be used because of the distance of these tumors for the liver margins. To achieve this aim, the Southampton group described the "reversed-L" configuration around the medial and inferior parts of the tumor, obtaining four planes for the parenchymal transection[45].

Usually, the reverse Trendelenburg position and the contralateral retraction of the falciform ligament are sufficient to perform an S8 segmentectomy for a full mobilization of the right lobe. Ultrasonography is performed to locate the lesion and the main vascular structures. The courses of the right and median hepatic veins must be exposed. Segments 8 (and 7) can be fed by one to three portal vessels. Segment 8 branches can be dissected and isolated extrahepatically through the space between the Glissonean pedicle and the liver at the hepatic hilum, allowing dissection of the third-order Glissonean pedicle, moving from the right anterior main second-order branch [Figure 5][52]. Once the correct delimitation of these segments has been verified by identifying the ischemic line, transection is performed. To improve the operative view, it is fundamental to obtain the aid of a second surgeon for trocar positioning and camera use. CUSA helps preserve the middle and right hepatic veins. The specimen can be extracted by enlarging the umbilical incision or through a supra-umbilical incision.

ROBOTIC ANATOMICAL LIVER RESECTION

Robotic liver resection (RLR) has been reported to be above the primary limitation of LLR, thanks to a stable camera system with three-dimensional high-definition magnification, tremor-filtrated robotic arms, 360° of freedom of the robotic endo-wrists[53]. Furthermore, the robotic platform has integrated the possibility to visualize preoperative 3D reconstructions and renderings (the *tile-pro system*), allowing continuous checking and comparisons of the vascular and tumoral anatomy of the 3D model. The same system also integrates the US images. Similarly, the *firefly* system on the Da Vinci platform allows an integrated high-definition ICG-fluorescence during RLR that can be helpful for visualization of the tumor and the ischemic demarcation line during MIALR[54,55]. The learning curve of RLR was shorter than that of LLR; for pure laparoscopic donors, the necessary number of hemihepatectomies was between 45 to 60[56,57]. For robotic donors, the number of hemihepatectomies was 15 without the need for prior knowledge of laparoscopic surgery when initiating robot donor hepatectomy program in an experienced open transplant center[58-60]. In our opinion, simplifying surgical maneuvers could lead to greater adoption of the minimally-invasive approach for anatomical resections with outcomes improvements[61,62]. Thanks to many series and retrospective comparative studies, evidence supporting the safety and effectiveness of RLR generated the publication of the first international consensus statement on RLR in 2018[63,64]. A recent meta-analysis including 487 RLR demonstrated a lower rate of perioperative bleeding after RLR than LLR with similar

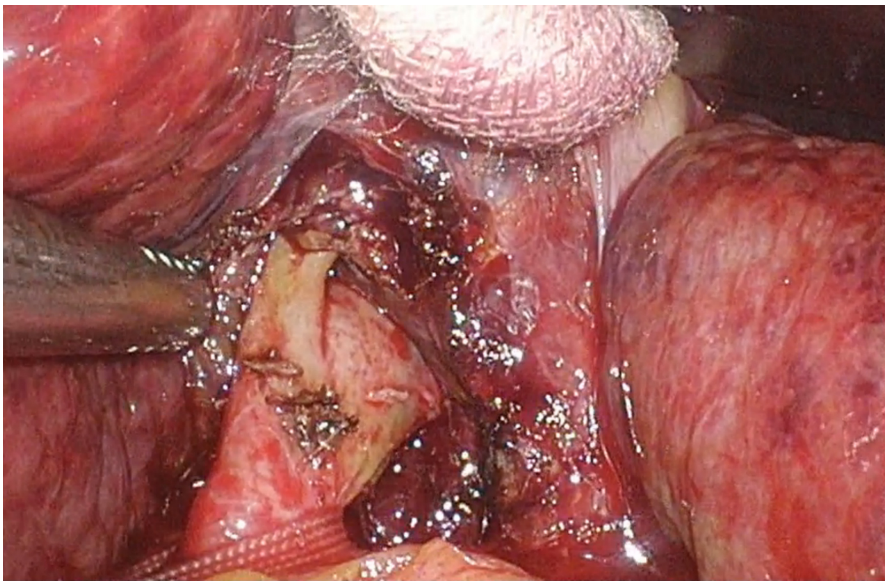

Figure 5. Isolation of a segment 8 Glissonean pedicle, arising from the right-anterior pedicle.

long-term outcomes at the cost of a more prolonged operation time[62]. The primary limitation of RLR is the high costs, the logistical and organizational aspects, and the lack of randomized trials. Nevertheless, the advent of a new robotic platform will likely create commercial competition that could lower prices and resolve logistical problems.

Technical considerations for RLR

The surgical team consists of the operating surgeon at the robotic console and the assistant surgeon at the operating table positioned between the patient's spread legs. The patient is usually supine, with legs apart and tilted approximately 30 degrees in the reverse Trendelenburg. Pneumoperitoneum is created using the same technique as the laparoscopic approach. The first 12-mm trocar is positioned in the umbilical site and is used by the assistant for aspiration/irrigation, traction, insertion and withdrawal of any instruments or gauze, or operative purposes during parenchymal transection. It should be remembered that currently, there is no dedicated robotic CUSA; therefore, if it is preferred to proceed with the transection of the liver parenchyma with this device, the assistant surgeon should perform this phase of the operation assisted by the first operator in the console (the "robo-lap" approach)[65]. The optics are then introduced through the umbilical trocar to proceed with the insertion under the vision of the trocars for the robotic arms, which are 8 mm in diameter in the case of the Da Vinci Xi robot. It is best practice to accurately explore the abdominal cavity to search for any visceral or peritoneal metastases or other lesions that might contraindicate the scheduled procedure. This exploration must be carried out before opening the disposable robotic tools because the higher costs of using the robot are attributable to these tools. As a chamber port, the first robotic trocar is inserted on the right midclavicular line (approximately 10 cm diagonally from the umbilical trocar to avoid impingement). The subsequent trocars are then similarly inserted on a transversal line parallel to the hepatic border, positioning the port for the first robotic arm on the anterior axillary line, that of the third arm on the left midclavicular, and the fourth arm on the left anterior axillary line. This arrangement can be adapted according to the patient's habitus, with any necessary adjustments to avoid collisions between the robotic arms and the assistant. The robotic cart is brought into the surgical field from the patient's left side.

The surgical times of robotic anatomical resections are the same as those of laparoscopy. In our experience, the camera is placed on the robotic arm 2, on the right hemi-clavicular line, with an energy device on arm 3 (harmonic scalpel or vessel sealer), while arm 4 is responsible for lifting or retracting the liver using a grasper.

For the inflow control using the Glissonean approach (conducted according to the same principles described for the LLR), instead of using an aspirator for blunt dissection, one can proceed with the bipolar Maryland, which facilitates the dissection thanks to the thinner tip and the simplified maneuvers from the 360° of wrist mobility.

For parenchymal transection, two approaches are reproducible. First, the surgeon can use the energy device generally on the surface and then with movements perpendicular to the section line when in parenchymal depth, as with the CUSA. Second, the assistant surgeon can use the CUSA at the table while the first operator guides him from the console. Using intracorporeal and extracorporeal Pringle's maneuvers can also be helpful in robotic surgery, especially when the risk of bleeding or the operator is in the learning phase. The Pringle maneuver preparation is the same as in LLR, and the assistant must clamp the pedicle if the extracorporeal approach is chosen[66,67].

CONCLUSIONS

MIALR is a safe procedure when performed in hepato-pancreato-biliary (HPB) centers with high expertise, and it can be carried out in cirrhotic patients with associated HCC. The surgical anatomy of the liver is not a static concept and must be mastered by the minimally-invasive HPB surgeon because it represents the actual basis for performing AR. Various techniques have been described, and there is debate about the procedure of choice, even if MILS experts suggest the advantages of the Glissonean approach. However, accurate knowledge of the liver's surgical anatomy and the various approaches to inflow control (intrafascial, extrafascial, and extrafascial transfissural) are fundamental to performing laparoscopic anatomical resections safely.

Because anatomic resections require training and precision, we broadcast our experience of complex anatomic resections to encourage the dissemination of these techniques and assist the critical standardization process to perform minimally-invasive anatomic liver resection safely.

DECLARATIONS

Authors' contributions

Contributed substantially to the paper's conception and design: Han HS, Cassese G, Troisi RI
Wrote the manuscript: Cassese G, Lee B
Participated in the coordination of the work and final revision: Han HS, Cho JY, Lee HW, Troisi RI
All authors approved the final manuscript.

Availability of data and materials

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Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate
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Consent for publication
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