Minimally Invasive Liver Surgery for Primary and Secondary Liver Malignancies

MUNYA H. TALUKDER, MD; JENNA WILSON, DO; ANDREW B. CROCKER, MD; ALI AHMAD, MD, FACS; PONNANDAI SOMASUNDAR, MD, MPH, FACS

ABSTRACT

Minimally invasive (MIS) liver surgery has grown tremendously in the past two decades and today represents a major weapon in the fight against primary and metastatic neoplasms of the liver. This review catered towards the modern evolution of MIS hepatectomy techniques in addition to the role of robotic surgery in this field. The article also addresses the utility of advanced intra-operative techniques in hepatic parenchymal transection ranging from the Glissonian pedicle approach to the use of indocyanine green (ICG) guided near-infrared fluorescence in non-anatomic resections. In addition, we briefly discuss ablation techniques utilized for liver cancer, including microwave ablation and the novel histotripsy ablation.

KEYWORDS: Minimally invasive; laparoscopic; robotic; hepatectomy; ablation

INTRODUCTION

In current times, surgical resection is still considered the gold standard treatment for patients with resectable liver malignancies. Liver surgery has dramatically evolved in recent decades, improving its safety profile with peri-operative mortality rates below 2% for most MIS hepatectomies.[1] Successful oncologic outcomes in liver surgery are reliant on obtaining a R0 resection margin with preservation of healthy liver parenchyma.

Surgery remains the mainstay of treatment in patients with primary hepatic neoplasms such as hepatocellular carcinoma (HCC) and intra-hepatic cholangiocarcinoma (ICC).[2] The use of MIS approach to hepatectomy for HCC has shown promise worldwide, with up to 30% of HCC resections estimated to be minimally invasive.[3] The majority of patients with HCC also harbor chronic liver disease (CLD). The presence of CLD and liver cirrhosis pose substantial challenges such as increased hemorrhagic complications and higher rates of post-hepatectomy liver failure (PHLF). Therefore, locoregional tumor ablative treatments such as microwave ablation (MWA), trans-arterial chemoembolization (TACE) and Yttrium-90 (Y-90) radio-embolization have gained substantial traction. In addition, liver transplant remains a viable option for some patients with HCC who meet the criteria.

Colorectal cancer liver metastasis (CRLM) is the most common indication for MIS hepatectomy in the United States; about a quarter of laparoscopic liver resection (LLR) for malignancy is performed for CRLM.[4] Liver resection (LR) for CRLM in selected patients offers excellent oncologic outcomes, with a five-year overall survival rate of 40–50%.[5]

In the modern era, robotic surgery has allowed for expansion of MIS approach to liver surgery. The technological advantages offered by the robotic platform, such as multi-articulated instruments, increased dexterity along with the 3D visualization, has allowed surgeons to tackle more complex resections via MIS approach.

Parenchymal transection techniques have also evolved with a drive towards parenchyma preservation. The past decade has seen a substantial increase in non-anatomic parenchyma-sparing resections with an expected decrease in the rate of extended hepatectomies. Owing to this paradigm shift in the surgical management of liver metastases, techniques such as ICG-guided resections and Glissonian pedicle guided segmentectomies have emerged as attractive approaches to tackle non-anatomic and anatomic resections.

LAPAROSCOPIC LIVER RESECTION

Similar to minimally invasive surgery in other fields, LLR for hepatic pathology has been increasingly utilized over the last several decades with promising results in the literature. Two international consensus conferences and several retrospective studies supported that LLR is equivalent to open approach for both minor and major hepatic resections in terms of oncological outcomes, but is associated with less blood loss, decreased postoperative morbidity and a shorter hospital stay.[6] A randomized control study, conducted to evaluate Enhanced recovery after surgery (ERAS) in LLR verified these advantages. For example, the median postoperative hospital stay was 6.2 (±2.6) days in the ERAS group, compared to 9.9 (±5.9) days in the control group (p-value<0.01). The morbidity rate was 22.5% (18 of 80 patients) in the ERAS group and 43.9% (47 of 107 patients) in the control group (P = 0.002).[7] While MIS approach has been shown to be safe and effective relative to open surgery, surgeon comfort remains an important factor in the use of LLR.

ROBOTIC HEPATECTOMY

Robotic surgery has the potential to overcome some of the limitations of laparoscopy. The stability of the robotic platform, combined with the 3D, magnified high-definition vision, increased degrees of freedom of the instruments and tremor filtering provide higher dexterity to the surgeon and allow for the same movements of open surgery. Furthermore, the robotic platform allows for easier integration of technologies, such as near-infrared fluorescence for vascular and biliary identification and 3D ultrasound instruments with integrated probes for section margin assessment. In 2014, Tsung et al performed a matched series comparison of surgical and postsurgical outcomes between robotic (n=57), laparoscopic (n=114), and open hepatic resections (n=21). A statistically significant difference was seen when comparing the EBL of robotic versus open surgery, as well as in the hospital length of stay.[8] With continued technological advances and improved access to robotic consoles, the role of robotic hepatectomies should continue to develop over time.

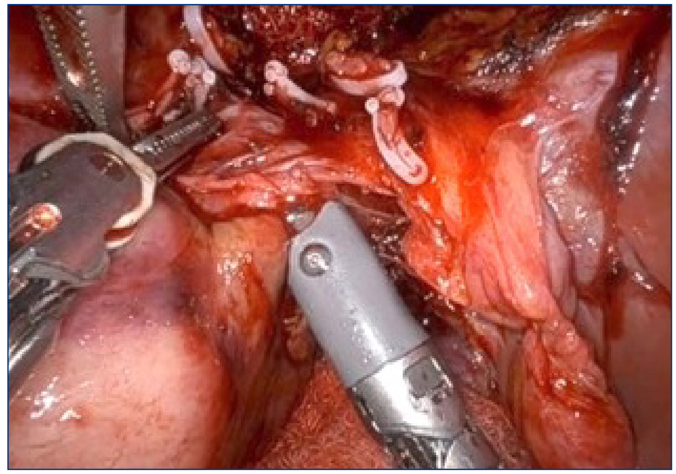
GLISSONIAN PEDICLED APPROACHES

In recent years, parenchymal-sparing liver resections have become the cornerstone approach to preserve residual liver volume, decrease postoperative liver failure, and enhance the possibility of repeated liver resection rates.[9] Small anatomical resections using ICG and Glissonian approaches are techniques employed to achieve a successful parenchymal-sparing liver resection.

The Glisson's capsule wraps the hepatic artery, the portal vein and the bile duct in the liver and forms bundles at the hepatic hilus and in the liver as the Glissonian pedicle tree **(Figure 1)**. The capsule does not connect to the proper membrane of the liver. Therefore, the Glissonian pedicles can be detached from the liver parenchyma without liver dissection. When the Glissonian pedicles are ligated before liver transection, various types of anatomical hepatectomy can be carried out.[10]

Intraoperative bleeding is a predictor of postoperative outcomes following liver surgery; therefore, it is crucial to have vascular control during liver resection. In addition, preservation of future liver remnant is critical in preventing post-hepatectomy liver failure as one of the main causes of postoperative morbidity and mortality. The Glissonian approach to liver resection offers an effective method for vascular inflow control while protecting future liver remnant from ischemia-reperfusion injury. With increasing popularity of minimally invasive surgery, laparoscopic liver resection via Glissonian approach has been shown to be superior to standard laparoscopic hepatectomy.[11] In the intrahepatic Glissonian approach small incisions on well-defined anatomical landmarks are performed to approach the pedicles of both right and left liver, making dissection of the hilar plate unnecessary. Intrahepatic access to Glissonian pedicles complements laparoscopy, since it avoids unnecessary extensive dissection along the hepatic hilum during laparoscopic procedures, which are technically complex and potentially time-consuming with high morbidity.[12]

Figure 1. Glissonian Pedicle



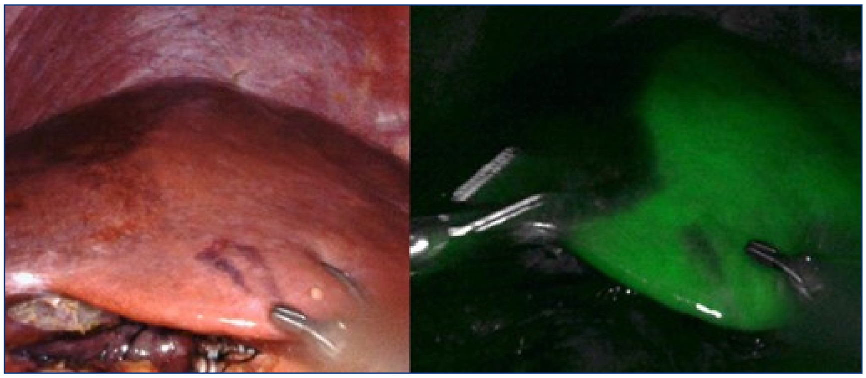
MINIMALLY INVASIVE MAJOR HEPATECTOMY

Major hepatectomy is a complex procedure that requires advanced surgical knowledge and skills. Although minimally invasive resections of the liver have been performed more frequently in recent years, major resections are still a minority of those cases. Current data on these numbers is somewhat sparse, but one report described that out of 149 robotic liver cases studied, 47% of them counted as major resections.[13] The largest series of robotic hepatectomy was reported by Giulianotti et al in 2011 with a total of 70 hepatic resections, of which 27 were major hepatectomies.[14] Spampinato et al performed a retrospective study comparing the perioperative outcomes of robot-assisted major hepatectomy and laparoscopic major hepatectomy in four Italian centers. A total of 50 major hepatectomies were considered, including 25 robotic and 25 laparoscopic resections. The mean robotic operative time was 430 minutes with a median EBL of 250 mL, comparable to laparoscopy.[15]

INDOCYANINE GREEN (ICG) AND INTRA-OPERATIVE ULTRASOUND (IOUS)

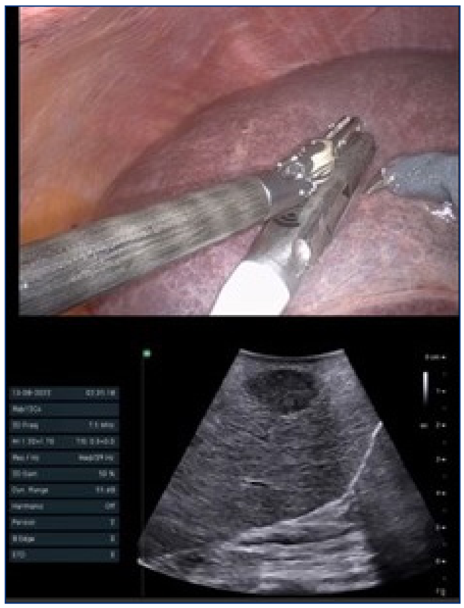
Due to the intricate anatomy and 3D contouring of the liver segments, non-anatomic parenchymal sparing resections can be technically challenging. Use of adjuncts such as intra-operative ultrasound (IOUS) and ICG fluorescence can help with adequate mapping of tumors in relation to vasculo-biliary pedicles. The use of intraoperative ICG fluorescence has been proven to be a high potential navigation tool during liver surgery. The variability of ICG accumulation within tumors as opposed to the background hepatic parenchyma

Figure 2. Indocyanine Green (ICG)



allows for precise anatomic delineation of lesions for safe liver resection [**Figure 2**]. Studies have reported higher detection rates of primary lesions and additional metastases after intravenous administration of ICG.[16] Handgraaf et al reported better survival after ICG-oriented liver resections due to the resection of additional nodules, which had been missed by conventional imaging.[17] Marino et al compared robot-assisted liver resections with and without additional ICG application and reported significantly higher R0 resection rates after ICG application.[18] However, since the plasma clearance of ICG is primarily dependent on hepatocyte function, the sensitivity of ICG-guided tumor detection is somewhat limited in patients suffering from advanced liver cirrhosis. Although early data is promising, further studies are needed to determine the true benefit and potential pitfalls of ICG guided hepatectomies including its use among patients with cirrhosis.

Figure 3. Intra-operative Ultrasound



Intra-operative liver ultrasound can also provide an additionally useful adjunct in mapping of tumors in relation to inflow pedicles and outflow veins. Assessment of such anatomy can prove critical in surgical planning especially in the context of non-anatomic resections. With the newer robotic platforms, IOUS can be used with a flexible cord allowing it to be used with high accuracy even in difficult to visualize portions such as the posterior and superior segments of the liver. **Figure 3** shows an intra-operative picture of IOUS being used during a hepatectomy procedure.

MICROWAVE/THERMAL ABLATION

Resection is the standard of care for patients with resectable primary and secondary liver cancers. However, large number of patients who are diagnosed with primary and secondary liver cancers are not eligible for resection or transplantation due to inadequate functional liver function, and multifocal or advanced disease. As a result, microwave (MVA) and radiofrequency thermal ablations (RFA) are increasingly utilized. Both RFA/MWA induce tumor cell death through frictional heating resulting in protein denaturation and coagulation necrosis. MWA generates heat at a faster rate, creates larger ablation zones, and have reduced heat-sink effect compared to RFA leading to more utilization when tumors are nearby vascular structures.[19]

HISTOTRIPSY ABLATION

Histotripsy is a novel non-invasive technique recently FDA-approved to treat liver cancers. It utilizes focused ultrasound to ablate targeted regions of tissues into acellular debris. The first human clinical trial of histotripsy for liver cancers, named the THERESA Study (NCT03741088), resulted in the establishment of histotripsy's efficacy in destroying targeted tissue without harmful device-related effects.[20] Studies further suggests that local tumor ablation by histotripsy induces systemic immunomodulation, contributing to enhanced anti-tumor responses that can synergistically work with immunotherapy. Considering that this combinatorial approach with histotripsy potentially leads to better prognosis for cancer patients, it will be pivotal to translate these findings into clinical use to effectively optimize the potency of immunotherapy.[21]

CONCLUSION

Liver resection continues to be the gold standard treatment for patients with liver malignancies. such as hepatocellular carcinoma (primary liver cancers) and colorectal liver metastasis (secondary liver cancers). Minimally invasive liver surgery is increasingly used over open approach with data showing reduced postoperative morbidity/complications and length of stay. Current technological advances such as robotic platform have facilitated this trend by making liver MIS safer and more precise. By understanding available treatment options and cultivating a patient centered approach to treatment planning, we can continue to improve the treatment of patients with primary and secondary liver malignancies.

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Authors

Munya H. Talukder, MD, St. Elizabeth Medical Center, Brighton, MA.

Jenna Wilson, DO, St. Elizabeth Medical Center, Brighton, MA.

Andrew B. Crocker, MD, St. Elizabeth Medical Center, Brighton, MA.

Ali Ahmad, MD, FACS, University of Kansas School of Medicine, Wichita, KS.

Ponnandai Somasundar, MD, MPH, FACS, Boston University; Roger Williams Medical Center, Providence, RI.

Disclosures

None

Correspondence

Ponnandai Somasundar, MD
psomasun@bu.edu