Is laparoscopic mesohepatectomy superior to the open approach for patients with centrally located hepatocellular carcinoma?

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Laparoscopic liver resection (LLR) has become a standard procedure for hepatocellular carcinoma (HCC) as well as liver metastases and other benign and malignant liver tumors (1-3). Numerous cohort studies and their reviews or meta-analyses comparing LLR with open liver resection (OLR) for HCC frequently have serious selection biases in terms of the differences in the size, number, tumor location, and malignancy degree (4-6).

To our knowledge, no randomized controlled trials (RCTs) have compared LLR and OLR for HCC. In most cohort studies, LLR was selected for easier and newly diagnosed cases; therefore, number of studies has been increasing using propensity score matching (PSM) to minimalize selection biases (7). PSM studies that have used entire patients' cohort have clearly demonstrated that LLR involves less intraoperative blood loss and transfusion rates, lower morbidity, shorter hospital stays, and similar mortality compared as that achieved with OLR (8-13). In addition, the long-term survival was comparable in both the groups. A recent Japanese multi-center study for limited elderly HCC patients (age ≥75 years) confirmed similar results that showed the superiority of short-term outcomes with LLR (14). A recent meta-analysis of PSM studies has showed that LLR can be performed with 50% lower rates of blood transfusion and postoperative complications, can shorten the hospital stay by an average of 4 days, and achieve lower 30-day mortality compared to OLR (5).

Mesohepatectomy is usually applied for centrally located HCC (CL-HCC). Mesohepatectomy has two large cutting live surfaces; therefore, it must be one of complexed liver resections even if being performed with open approach. Further, mesohepatectomy is performed to preserve the liver parenchyma to lower the risk of postoperative liver dysfunction or liver failure (15). In LLR, owing to the technical complexities, wedge resection or left-sided hepatectomy is commonly selected over mesohepatectomy (1,2). With advances in laparoscopic instruments and procedures, pure laparoscopic mesohepatectomy (LM) is being increasingly used (15-18).

We congratulate Dr. Wei Li and colleagues for their recently published article entitled "*Laparoscopic versus open mesohepatectomy for patients with centrally located hepatocellular carcinoma: a propensity score matched analysis*" in *Surgical Endoscopy* (19). In this exceptional paper, the authors have compared LM and open mesohepatectomy (OM) for patients with CL-HCC. The authors stated that the selection of the surgical procedures (LM or OM) was based on the tumor number, tumor size, tumor location, residual liver volume, and underlying liver function. In both the procedures, harmonic scalpel (Ethicon Endo-Surgery, USA), cavitron ultrasonic aspiration (CUSA, ValleyLab, Inc., USA), and/or LigaSure (ValleyLab, Inc., USA) were used for transection of the liver parenchyma. However, information about the number of surgeons and their previous experience of LM or OM was unavailable.

CL-HCC was divided into 4 groups, mainly based on the tumor location (20,21). Total 78.0% of the patients in LM group were classified as type III, and no patient was classified as type IV. In OM group, 24.1% and 18.6% of the patients were classified as Type III and Type IV, respectively. Type III was defined by a tumor located between the segments IVa and VIII and segments V and IVb, not adjacent to the large Glissonean capsules; therefore, liver resection was relatively easier than other types of resection. Type IV was characterized by the presence of the tumor in the most challenging location and was defined as the presence of a tumor that occupied a large proportion of the parenchyma between the first and second Glissonean pedicle. As per the authors' recommendation, type II and type IV patients with direct vascular invasion are contraindicated for LM in the present technical condition. It is important to use LM and OM appropriately.

In the overall cohort, the LM group had a smaller tumor size and earlier tumor stage compared to the OM group; however, background factors were well balanced in the two groups after 1 to 3 PSM. It is unclear why intraoperative and postoperative parameters were not investigated in the PSM cohort rather than in the overall cohort. In the overall cohort, despite early tumor stage, vascular occlusion time was significantly longer in the LM group; however, the postoperative peak level of liver transaminase in the LM group was lower than that in the OM group. Intraoperative blood loss was relatively small in both the groups (395.8±361.9 mL for OM and 328.2±328.0 mL for LM). It was reported that the average intraoperative blood loss during OM ranged from 380–2,450 mL (22). We think that the operative procedure in this study was stable. The postoperative complications were discussed in detail; however, no specific complications associated with the LM procedure were observed. The survival data were assessed using a PSM cohort. The median follow-up period of 20 months was too short to evaluate the long-term survival. The 3-year survival was 68.4% and 90.5% in the LM and OM groups, respectively. Only 2 patients (9.4%) in the LM group and 30 patients (31.3%) in the OM group were actually alive at 30 months. Based on these results, survival equivalence was unclear in this study. The authors reported in the previous paper that mesohepatectomy can provide better overall survival for CL-HCC than open extended hepatectomy based on a PSM cohort (23). Mesohepatectomy may have a survival benefit because of preservation of liver parenchyma.

Several recent studies have compared the benefits of LLR and OLR for HCC patients undergoing limited difficult procedures (24-27). A systematic review and meta-analysis for major hepatectomy was conducted using individual patient data of those who underwent LLR (n=427) and OLR (n=490) (25). This study included liver tumors other than HCC. The total morbidity was lower, and the hospital stay was significantly shorter in the LLR group. The incidence of major complications was not significantly different. The operative time was longer in the LLR group; however, intraoperative blood loss and blood transfusion were similar in the two groups. The overall survival in the HCC patients of the two groups was not significantly different. With respect to mesohepatectomy, in the recent PSM study that compared LM (n=18) and OM (n=36), the operation time was longer in the LM group; however, blood loss was lower, diet was resumed faster, and hospital stay was shorter for the LM group (26). All the patients were classified as Child's class A cirrhosis. The long-term prognosis was comparable in the two groups.

Some scoring systems have been developed to assess the complexity of LLR. Ban's difficulty scale (28) considers the following 5 factors: extent of liver resection, tumor location, tumor size, liver, function, and tumor proximity to major vessels. For centrally located tumors, 5 points for S8-located tumor is larger than 3 points for S4, S5-located tumor. Segmentectomy and sectionectomy or larger assigned 3 points and for 4 points, respectively. Hasegawa's difficulty prediction model (29) was created to predict the surgical duration and considers the extent of resection (scored 0, 2, or 3), tumor location (scored 0, 1, or 2), presence of obesity (scored 0 or 1), and platelet count (scored 0 or 1). Anatomical segmentectomy had 2 points; however, central bisectionectomy was performed for only two patients. However, in the above two studies, those who underwent CM were not allocated to a separate group. As per Kawaguchi's difficulty classification (30), those who underwent LM were allocated to Group III (most difficult group) that included posterosuperior segmentectomy, right posterior sectionectomy, right hepatectomy, and extended left/right hepatectomy. Even in this recent study, LM was actually performed for only 11 (2.4%) patients.

LM can become safer and easier with the use of an intrahepatic Glissonean approach, and anatomical resection is essential (17). Fluorescence imaging using indocyanine green (ICG) is now being used to identify the boundaries of hepatic segments for complete anatomical resection of the liver (31). In the present scenario, positive and negative staining techniques are used via portal injection of ICG solution and intravenous injection of ICG after closure or division of the target portal pedicle, respectively. This method is believed to be important for mesohepatectomy, and the latter is convenient to use in LM patients.

Finally, LM for CL-HCC is a technically challenging procedure with a steeper learning curve. The learning curve of major hepatectomy including central hepatectomy included the following three phases: phase 1 (45 initial patients), phase 2 (30 intermediate patients), and phase 3 (the subsequent 98 patients) (32). We believe that LM for CL-HCC should be performed by limited skilled LLR team who has sufficient experience of OM. It is important to note that the future of complicated LLR, including LM strongly depends on education initiatives that need to be carefully planned and regularly implemented (33).

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Footnote

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