



Comparison of laparoscopic versus open liver resection for hepatocellular carcinoma using propensity score matching

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Abstract: Laparoscopic liver resection (LLR) has become one of standard treatments for hepatocellular carcinoma (HCC). Numerous reports have demonstrated that LLR might be less invasive and provide better short-term results and identical oncological outcome compared to conventional open liver resection (OLR); however almost reports in the past were not conclusive. Propensity score matching (PSM) is a quite useful tool to match different background factors in the two groups; therefore, we reviewed papers assessing laparoscopic and OLR using PSM. We have already published the largest study of LLR for HCC from the “Project Committee of the Endoscopic Surgery” of the Japanese Society of Hepato-Biliary-Pancreatic Surgery. We summarized 10 documents including this paper. After PSM, maximum 387 patients undergoing laparoscopic and OLR were investigated. Less intraoperative blood loss or low rate of blood transfusion, and shorter hospital stay are solid advantageous results of LLR. Long-term outcome was quite equivalent in the two groups and special recurrence pattern in the LLR was rarely observed. These PSM studies clearly demonstrated that LLR can provide excellent perioperative benefits without oncologic disadvantages; therefore, we can strongly recommend LLR as a standard practice for properly selected patients with HCC.

Keywords: Laparoscopic liver resection (LLR); open liver resection (OLR); hepatocellular carcinoma (HCC); propensity score matching analysis (PSM analysis)

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Introduction

Laparoscopic liver resection (LLR) become a gold standard for not only benign liver tumors but also malignant tumors, including hepatocellular carcinoma (HCC) and colorectal liver metastases (CRLM) (1-3). Many papers have demonstrated that LLR is less invasive and can provide better short-term results and identical oncological outcome compared to conventional open liver resection (OLR) (4-8). However, these reports in the early period

were based on the examinations of retrospective case-matched studies or meta-analysis of non-randomized studies. In clinical situation, numerous selection biases can exist with regard to selecting LLR; therefore, the previous results are not definitive. Unfortunately, there has been no conclusive randomized control trial in this field (3,9). More recently, ORANGE II study was closed due to slow patients' collection (10). This randomized control trial was conducted to compare open versus laparoscopic left lateral sectionectomy in terms of an enhanced recovery after

Table 1 Perioperative findings and outcomes in HCC patients undergoing LLR and OLR using PSM

First author year	Patients' number, LLR/OLR	Operation time	Blood loss	Morbidity	Mortality	Hospital stay	RFS, DFS	OS
Kim, 2014 (16)	29/29	Equal	LLR [#] less	LLR M-less, P=0.065	Equal	LLR shorter	Equal	Equal
Takahara, 2015 (13)	387/387	LLR longer	LLR less	LLR less	Equal	LLR shorter	Equal	Equal
Beppu, 2015 (17)	52/52	Equal	LLR less	Equal	Equal	LLR shorter	Equal	Equal
Meguro, 2015 (18)	35/35	Equal	LLR less	Equal	Equal	NA	Equal	Equal
Han, 2015 (19)	88/88	LLR M-longer, P=0.07	LLR M-less, P=0.08	LLR less	Equal	LLR shorter	Equal	Equal
Yoon ^{#2} , 2015 (20)	58/174	LLR shorter	LLR less	LLR less	NA	LLR shorter	Equal	Equal
Sposito, 2016 (21)	43/43	Equal	Equal	LLR less	Equal	LLR shorter	Equal	Equal
Han ^{#3} , 2016 (22)	99/198	LLR M-longer, P=0.085	LLR less	LLR less	Equal	LLR shorter	Equal	Equal
Cheung ^{#4} , 2016 (23)	110/330	LLR shorter	LLR less	Equal	Equal	LLR shorter	Equal	LLR better
Yoon ^{#5} , 2016 (24)	33/33	LLR longer	Equal	Equal	NA	LLR shorter	Equal	Equal

[#], blood transfusion rate; ^{#2}, limited to HCC smaller than 5 cm; ^{#3}, robot operation; ^{#4}, limited to patients with liver cirrhosis; ^{#5}, limited to right hepatectomy. HCC, hepatocellular carcinoma; PSM, propensity score matching; LLR, laparoscopic liver resection; OLR, open liver resection; RFS, recurrence-free survival; DFS, disease-free survival; OS, overall survival; NA, not available; M-, marginally.

surgery program.

Propensity score matching (PSM) is a quite useful tool to compare the usefulness in the two groups with different backgrounds. The treatment effects assessed by well-designed PSM study were similar to those obtained by randomized control trial (11). We have previously reported the results of PSM study for CRLM patients undergoing LLR and OLR in the recent issue of "Annals of Laparoscopic and Endoscopic Surgery" (12).

In this paper, we reviewed the surgical results of LLR compared to OLR for HCC patients.

LLR versus OLR for HCC using PSM

We have published the two largest study of LLR for HCC and CRLM from the "Project Committee of the Endoscopic Surgery" of the Japanese Society of Hepato-Biliary-Pancreatic Surgery (13,14). In a HCC study, we retrospectively analyzed 3,405 patients undergoing initial liver resection for HCC from 31 specialized centers all over Japan between 2000 and 2010. Among them, after PSM, 774 (387 LLR and 387 OLR) patients were selected. The receiver operating characteristic area under the curve of

the propensity score for undergoing LLR was excellent; 0.786. LLR for patients with HCC showed similar long-term outcomes, associated with less blood loss, fewer postoperative complications, and shorter hospital stay compared with OLR. In PSM, it is quite important what is selected as a matching item. In that study, we examined difficult location or not; posterosuperior segments or anterolateral segments (15). In 3 papers in *Table 1*, difficult tumor location was currently assessed and used for PSM analysis. Tumor location (superficial or deeper position) and proximity to the large vessels were also important points. We investigated all these subjects for PSM in Kumamoto University study (17).

From 2014 ten PSM studies have published comparing LLR and OLR limited to HCC patients (*Table 1*) (13,16-24). One to one, one to two and one to three PSM was performed. After PSM, 29-387 LLR patients and 29-387 OLR patients were investigated. One study included only robot operation (22). In terms of perioperative parameters, the operation time for LLR was similar in 6 studies, longer in two, and shorter in two compared with OLR and the blood loss amount or blood transfusion rate was less in 7 of 10 studies.

Morbidity was equal in 5 studies and less in 5 for LLR compared to OLR and mortality was comparable in all studies. HCC patients with live cirrhosis could have specific advantages, including postoperative fluid collection (16). LLR and can be completed through a minimal wound and can avoid massive liver mobilization and can preserve collateral vessels (25,26). General morbidity, not surgical one was less in LLR (23) and low severity of morbidity was observed in LLR (24). In HCC patients requiring repeated treatments, reduced post-operative adhesion may allow successful laparoscopic radio-frequency ablation or LLR for the future recurrence (27). The hospital stay was shorter in all papers that were mentioned. Regarding to long-term outcome, disease-free or recurrence-free survival and overall survival were comparable in almost all studies. In one paper, overall survival was better in LLR compared to OLR and the better long-term survival was explained by significantly less blood loss and high frequency of non-touch anterior approach in LLR (23).

Less intraoperative blood loss or low rate of blood transfusion, and shorter hospital stay are solid beneficial advantages of LLR. Additionally, postoperative complication rates were significantly lower in a half of the patients compared to those in OLR. These less invasive futures of LLR can decrease the recurrence rates and can allow adequate treatment for the recurrence because of preserved liver function (28-32). Long-term outcome was quite equivalent in the two groups and special recurrence pattern in the LLR was rarely observed; therefore, LLR might have no obvious oncological disadvantages compared to OLR (13,16-24). Nevertheless, the utility of laparoscopic systematic resection or laparoscopic major resection was not fully understood.

These PSM studies clearly demonstrated that LLR can provide excellent perioperative benefits without oncologic disadvantages; therefore, LLR is strongly recommended as a standard practice for properly selected patients with HCC. In the future, advantages of LLR should be assessed minutely in consideration of the tumor location assessment (difficult location or not) or difficulty scoring system (15,17,33).

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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