Research Article

JOURNAL OF HEPATOLOGY

Laparoscopic versus open liver resection for hepatocellular carcinoma: Case-matched study with propensity score matching

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Background & Aims: Laparoscopic liver resection has gained wide acceptance and is established as a safe alternative to open liver resection. Until now, there is no prospective randomized comparative study between laparoscopic and open liver resection. Previous comparative studies reported minor resections for peripheral tumors, and enrolled small numbers of patients. Moreover, few reported the long term outcomes. The aim of this study is to compare perioperative and long term outcomes of laparoscopic versus open liver resection for hepatocellular carcinoma between two matched groups.

Methods: 389 patients underwent liver resection for hepatocellular carcinoma during the period between 2004 and 2013. To overcome selection bias, we performed 1:1 match using propensity score matching between laparoscopic and open liver resection.

Results: After propensity score matching, 88 patients were included in each group. Laparoscopic group had shorter hospital stay (8 *vs.* 10 days, $p \leqslant 0.001$), and lower postoperative morbidity (12.5% *vs.* 20.4%, $p = 0.042$). The 1-, 3- and 5-year overall survivals were 91.6%, 87.5%, and 76.4%, for laparoscopic group, and were 93.1%, 87.8%, and 73.2%, for open group ($p = 0.944$). The 1-, 3- and 5-year disease free survivals were 69.7%, 52%, and 44.2%, for laparoscopic group, and 74.7%, 49.5%, 41.2%, for open group ($p = 0.944$).

Conclusions: Our study showed comparative perioperative and long term outcomes between both groups, providing evidence regarding the safety and efficacy of laparoscopic liver resection for hepatocellular carcinoma.

Introduction

Since the first description in 1992 [1], laparoscopic liver resection (LLR) has become widely accepted and is established as a safe alternative to open liver resection (OLR) [2]. Nowadays, LLR has become the standard procedure for left lateral sectionectomy [3]. The introduction of new surgical equipment and the increased experience in this procedure allowed major liver resections to be performed more frequently and safely than before [4].

Many studies reported favourable results after LLR for HCC [5–12]. However, most of these studies reported left lateral sectionectomy and minor hepatic resections for peripherally located tumors, and reported small numbers of patients [6–9]. Moreover, few reports have described the long term oncological outcomes of LLR for HCC [11,12].

Up to now, there is no prospective randomized comparative study comparing the outcomes between LLR and OLR. In clinical practice, it is difficult to perform a prospective randomized study to compare the outcomes between different surgical procedures. Propensity score matching (PSM) has been proposed as a method to overcome selection bias and increase the evidence level in observational non-randomized studies [13].

The aim of this study is to compare perioperative and postoperative long term outcomes of LLR and OLR for HCC utilizing PSM.

Patients and methods

Study design

We retrospectively reviewed the data for all patients who underwent either LLR or OLR for HCC at Seoul National University Bundang Hospital during the period between January 2004 and December 2013.

Preoperative evaluation

All patients underwent detailed laboratory evaluation including complete blood count, liver function tests, serum α-feto-protein, blood glucose, and indocyanine green clearance (15 min). The diagnosis and staging of HCC were done by triphasic computed tomography of the abdomen. Some patients were also assessed by contrast-enhanced ultrasound (US) and magnetic resonance imaging to detect additional lesions.

Keywords: Hepatocellular carcinoma; Laparoscopic liver resection; Open liver resection.

Received 14 November 2014; received in revised form 3 April 2015; accepted 7 April 2015; available online 12 April 2015

☆ DOI of original article: http://dx.doi.org/10.1016/j.jhep.2015.06.028.

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Abbreviations: LLR, laparoscopic liver resection; OLR, open liver resection; PSM, propensity score matching; US, ultrasound; OS, overall survival; DFS, disease free survival.

Cancer

All patients were discussed at weekly multidisciplinary conferences including hepato-pancreato-biliary surgeons, hepatologists, interventional radiologists, and medical oncologists. The indications and the type of liver resection were not modified by the use of laparoscopy.

Generally, liver resection was performed in patients with preserved liver function (i.e. sufficient future liver remnant), without signs of severe portal hypertension, or evidence of extrahepatic metastasis, and with American Society of Anesthesiologists grade <III [14].

Surgical procedures

The types of liver resections were defined according to Brisbane 2000 terminology [15]. Anatomical resections were generally more preferred if the future liver remnant was adequate, otherwise non-anatomical resections were used. Liver resections were classified into minor (two or fewer segments) or major (more than two segments) according to Couinaud's classification.

For OLR, the patient was placed in supine position and a right subcostal incision with upward midline extension was made. General abdominal evaluation to exclude metastasis was done, and then liver evaluation was done by manual palpation and intraoperative US to determine tumor's location, proximity to vessels, and to exclude multiplicity of tumors. Parenchymal transection was done using Cavitron ultrasonic surgical aspirator (CUSA; Valleylab, Inc., Boulder, CO, USA), LigaSure (ValleyLab, Inc.) and bipolar forceps. Fibrin glue sealant (Greenplast, Green Cross Corp., Seoul, Korea) was applied to the cut surface of the liver.

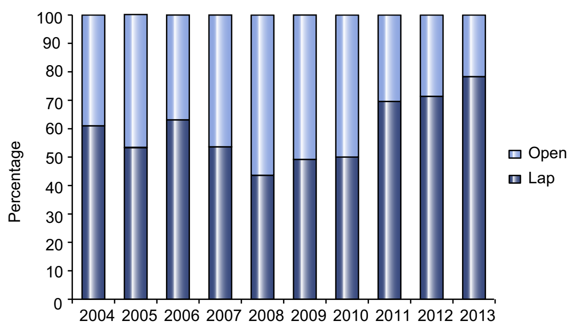

Fig. 1. Yearly adoption rates of laparoscopic liver resection for HCC during the study period.

For LLR, the patient was placed in the supine or French position, and a peri-umbilical port was placed under direct vision. Carbon dioxide pneumo-peritoneum was created with pressure 12 mmHg and three or four additional ports were used. Intraoperative US was routinely used to guide the resection planes. Pringle manoeuver was used in some cases. Parenchymal transection was done by combination of ultrasonic shears (harmonic scalpel; Ethicon Endo-Surgery Inc., Cincinnati, OH, USA), CUSA, and LigaSure. Larger vessels were secured by Hem-o-lock clips (Teleflex Medical, Research Triangle Park, NC, USA). Hepatic veins were divided by vascular staplers. Fibrin glue was applied to the cut surface, and the specimen was placed in a retrieval bag and extracted through an enlarged port site or Pfannenstiel incision.

Postoperative care and follow up

Postoperatively, all patients underwent daily follow up of liver functions and abdominal computed tomography was done routinely on fifth postoperative day.

After discharge, all patients were followed up every three months in the first two years, then every four to six months. Follow up assessments included liver function tests, serum α-feto-protein, and triphasic computed tomography scan of the abdomen.

Clinical outcomes

The primary outcome of our study is to compare the long term oncological outcomes between two matched groups. The secondary outcomes include operative outcomes (operation time, blood loss, and transfusion requirements) and short term outcomes (hospital stay, and postoperative complications).

Postoperative morbidity was defined as events occurring during the first 60 postoperative days and was graded by Clavien–Dindo classification [16]. Postoperative biliary fistula and liver cell failure were defined according to the International Study Group of Liver Surgery [17,18]. Postoperative mortality was defined as death within 90 days after liver resection. Overall survival (OS) was calculated from the day of surgery to the day of death or last follow up. Disease free survival (DFS) was calculated from the day of surgery to the day of tumor recurrence or the day of death or last follow up.

Statistical analysis

To overcome possible selection bias between LLR and OLR patients, we performed one to one match using PSM. The PSM overcomes the different distribution of covariates among individuals allocated to specific interventions in the study.

The propensity score model was generated using all potential covariates that could affect the group allocation; aiming to draw more reliable results. Although

Table 1. Baseline characteristics.

	LLR (n = 88)	OLR (n = 88)	*p* value
Age (years)	60 (26-81)	59.5 (20-85)	0.575
Sex (male:female)	72:16 (81.8:18.2%)	74:14 (84.1:15.9%)	0.841
BMI (kg/m^2)	23.7 (15.9-35.4)	23.6 (15.7-33.8)	0.866
Previous abdominal operations	8 (9.1%)	8 (9.1%)	1
Previous TACE	27 (30.7%)	28 (31.8%)	1
Previous RFA	6 (6.8%)	7 (8%)	1
Child-Pugh class (A:B:C)	79:6:3 (89.8:6.8:3.4%)	77:9:2 (87.5:10.2:2.3%)	0.662
Albumin (g/dl)	4.1 (2.8-5.2)	4.1 (2.7-4.8)	0.911
Bilirubin (mg/dl)	0.7 (0.2-3.8)	0.8 (0.3-2.8)	0.188
INR	1.1 (0.9-1.7)	1.1 (0.9-1.56)	0.973
ALT (IU/L)	33.5 (10-338)	31 (7-260)	0.676
AST (IU/L)	31 (14-291)	33 (12-189)	0.41
Platelets (*1000/µl)	152 (56-400)	159 (28-424)	0.364
Virology (HBV:HCV:Both +ve:Both -ve)	61:6:1:20 (69.3:6.8:1.1:22.7%)	65:4:0:19 (73.9:4.5:0:21.6%)	0.67
ICG 15 min (%)	8.1 (0.1-43.2%)	8.1 (1.2-52.4%)	0.712
AFP (ng/ml)	14.2 (1.2-35,000)	11.45 (1.4-34,100)	0.812

TACE, trans-arterial chemoembolization; RFA, radiofrequency ablation; INR, international normalized ratio; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ICG, indocyanine green clearance; AFP, α-feto-protein; HBV, hepatitis B virus; HCV, hepatitis C virus.