ORIGINAL ARTICLE

Laparoscopic versus open liver resection for hepatocellular carcinoma at a North-American Centre: a 2-to-1 matched pair analysis

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Abstract

Introduction: Oncological implications of laparoscopic resection in primary hepatic malignancy are not well defined. Laparoscopic liver resection (LLR) for hepatocellular carcinoma (HCC) in comparison to an open liver resection (OLR) in peri-operative and long-term oncological outcomes are described from a single North American institution.

Methods: From 2006 to 2013, all forty-three LLR patients for HCC were evaluated. Each patient was matched to two OLR patients for age at operation, maximal tumour size and tumour number.

Results: When compared with OLR, LLR had a lower severity of complication (0% versus 27%, $P = 0.050$) and lower 30-day readmission rate (2.3% versus 18.6%, $P = 0.010$). The length of stay (LOS) was shorter in LLR patients (5 versus 7 days, $P < 0.001$) and the estimated blood loss was also lower in LLR (300 versus 700 ml, $P = 0.004$). Admission to intensive care unit (ICU), emergency room (ER) visits and complication rates were similar. Overall, recurrence-free and intra-hepatic recurrence-free survival were comparable between LLR and OLR.

Discussion: LLR confers the widely-accepted benefits of laparoscopic surgery, namely severity of complication, 30-day readmission rate, LOS and blood loss. Further studies are required to examine intra- and extra-hepatic recurrence after LLR. LLR for HCC should be considered for appropriately selected patients in centres with requisite volume and expertise.

Received 28 April 2014; accepted 13 August 2014

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Introduction

Hepatocellular carcinoma (HCC) is the most common solid tumour in the world and the third leading cause of cancer-related death.[1] In recent years, there has been a clear increase in HCC incidence in North America as a result of a multitude of factors including trends in the prevalence of predisposing conditions including non-alcohol-related fatty liver disease as well as hepatitis B and C infections.[2,3] Curative options for HCC include surgical resection and liver transplantation. In the majority of North American centres, liver transplantation is reserved for patients with advanced cirrhosis and early HCC that meet regional transplantation guidelines.[4] In contrast, hepatic resection may be considered as a primary therapy in patients with HCC and well-preserved liver function. Indeed, a resection may also be performed in patients with cirrhosis with well-persevered hepatic function who have been deemed unsuitable for, or declined, a liver transplantation.[5]

The surgical management of HCC is complicated by the concomitant management of two disease processes, the primary malignancy and the underlying liver disease. To date, an open liver resection (OLR) has been the accepted standard operative approach for resectable HCC. Owing to the presence of underlying liver disease, patients with HCC undergoing OLR are at a high risk of developing significant post-operative complications compared with open liver resections for other indications.[6] A laparoscopic liver resection (LLR) offers a less-invasive alternative to OLR and may therefore be of particular benefit in this patient population. LLR has been slow to gain widespread traction because of the relative technical complexity and dearth of formal

training; however, recent data reveal that an increasing number of centres are implementing LLR for both benign and malignant liver lesions.[7] Emerging data suggest that LLR is safe,[8] however, whereas its role in the treatment of benign and metastatic disease is well described, its application to primary hepatic malignancy is not well defined and the oncological outcomes are not clear. The aim of this study was to compare the outcomes of HCC patients with LLR versus OLR on a 2-to-1 matched-case basis.

Patients and methods

Study design and patient selection

Ethical approval for this study was granted by the institutional research ethics board at the University Health Network. A prospectively maintained database of all hepatic resections was interrogated to identify all patients who underwent a primary liver resection for HCC. Forty-three patients who underwent a liver resection for HCC were identified during the period from 30 May 2007 to 18 October 2013. Previous studies have demonstrated that variables including tumour size, tumour number and age are independent risk factors for survival, based on multivariate analysis.[9–11] Thus, each patient was matched to two patients who received OLR according to the age at operation within 15 years, tumour size within 2.5 cm and tumour number was matched for solitary or multifocal tumours. All resections were performed by a specialist hepato-pancreatobiliary (HPB) surgeon at a university teaching centre.

Upon diagnosis of HCC, all patients were staged with multiphasic computed tomography (CT) of the chest and abdomen. If necessary, contrast-enhanced ultrasound (CEUS) and or magnetic resonance (MR) imaging were employed to confirm the diagnosis of HCC as per the American Association for the Study of Liver Diseases (AASLD) guidelines.[4] All HCC patients were discussed at weekly multidisciplinary conferences consisting of HPB surgical oncologists, hepatologists, medical and radiation oncologists and interventional radiologists. In general, a liver resection was recommended for solitary lesions greater than 2 cm with well-preserved liver function as defined by Child–Pugh Class (A/B) and evidence of limited portal hypertension (platelet count > 100 000/μl, or hepatic venous pressure gradient <10 mmHg). Ablation was recommended as a definitive treatment for small, solitary HCC ≤2 cm. Liver transplantation was recommended for patients with multifocal HCC or decompensated cirrhosis. Patients with resectable multifocal lesions who were ineligible for, or declined transplantation, were offered a surgical resection.

Surgical technique

The technique employed for LLR has been described previously.[12] In general, the approach to both OLR and LLR was similar. A major anatomical resection was reserved for larger tumours or where major vascular relations mandated a formal anatomical resection. For the purpose of parenchymal sparing, a non-anatomical and segmental resection was performed when an adequate margin could confidently be predicted. Inflow occlusion was obtained in all LLR and OLR lobectomies before parenchymal transection. Standard vascular stapling devices were used in both OLR and LLR when required. Water-jet dissection was used for parenchymal transection in all OLR and major (> 3 segments) LLR patients (Helix Hydrojet, ERBE and AMT Electrosurgery). Ultrasonic shears were used for parenchymal transection in all laparoscopic patients.[13]

Clinical outcomes

Patient demographics, including gender, age at resection and Child–Pugh classification, were recorded. Peri-operative outcomes included complication rate, severity of complications based on Clavien–Dindo classification,[14] type of hepatic resection, estimated blood loss, admission to the intensive care unit (ICU), 30-day readmission rate, emergency room (ER) visits within 3 months, resection margin, length of stay (LOS), incision to closure time and conversion rate. Histological analysis of resected HCC specimens was also assessed, including underlying liver disease, WHO histological grade, microvascular invasion, liver fibrosis based on Laennec classification,[15] tumour number and maximal tumour diameter.

Follow-up, survival and recurrence

After resection, patients were followed every 3 months in the first two post-operative years and then at 4-month intervals for post-operative years 3–5 with contrast-enhanced CT imaging of the abdomen and chest and or ultrasound (US). Suspected recurrence was further investigated with contrast enhanced CT, CEUS or MRI to confirm the diagnosis of HCC per AASLD criteria. After 5 years, patients returned to normal screening with US performed at 6-monthly intervals as per AASLD guidelines.[4]

The overall survival (OS) was calculated from the day of surgery until the day of death or last contact. The recurrence-free survival of patients who recurred was defined as the time from the day of surgery to the day of imaging study that confirmed tumour recurrence. For patients who did not develop recurrent disease, the day of surgery to the day of death or last contact was used.

Statistical analysis

Descriptive statistics were reported as median and range for continuous variables and as a number and percentage for discrete variables. The chi-square test or Fisher's exact test, where appropriate, was conducted to compare discrete variables between groups. The Mann–Whitney *U*-test was conducted for continuous variables, such as tumour margin and tumour diameter. Overall survival and recurrence-free survival were calculated by the Kaplan–Meier method and differences were compared by the log-rank test. The Cox-regression test was used for univariate and multivariate analysis using a confidence interval of 95%. Statistical significance was defined as $P < 0.05$. Statistical analysis was carried out using SPSS software (version 20; SPSS, Chicago, IL, USA).