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ORIGINAL ARTICLE

Laparoscopic liver resection for hepatocellular carcinoma in early and advanced cirrhosis

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Abstract

Background: Laparoscopic liver resection for hepatocellular carcinoma is well described in early cirrhosis. Less is known regarding outcomes with more advanced cirrhosis, and this study aimed to compare these groups.

Methods: A retrospective review of resections at a high-volume hepatobiliary center over a 15-year period was performed. Primary end-points were 30 and 90-day mortality. Secondary end-points included complications and survival.

Results: 80 early (Child's A) were compared to 26 advanced (20 Child's B and 6 Child's C) patients. Baseline patient and tumor characteristics were similar except for parameters indicating degree of cirrhosis. Only early cirrhotic patients underwent anatomic hepatectomies (six cases) and median operative times were longer (151 vs 99 min, p = 0.03). Intraoperative blood loss, conversion, R0 resection, length-of-stay and perioperative complications were comparable. 30 and 90-day mortality were statistically similar (2.5 vs 0%, OR 1.69, 95% CI 0.08–36.19 and 2.5 vs 7.7%, OR 0.31 95% CI 0.04–2.30). There was a trend toward longer survival in the early cirrhotic group but this did not reach significance (50 vs 21 months, p = 0.077).

Conclusions: In carefully selected advanced cirrhotic patients, laparoscopic liver resection may be performed with acceptable outcomes. Though this is not yet well established, further trials may be warranted.

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Introduction

Hepatocellular carcinoma (HCC) remains one of the most common malignancies worldwide and one of the leading causes of cancer related death, with cirrhosis constituting the primary risk factor.[1] Surgical treatment options include liver transplantation for patients that fall within Milan or University of San Francisco (UCSF) criteria, and surgical resection for those who have adequate predicted remnant liver function.[2,3] Other treatment options include local therapies such as radiofrequency ablation (RFA), microwave ablation, transarterial chemoembolization (TACE) and selective internal radiation therapy with 90 Yttrium microspheres (Y90), as well as therapy with the oral multikinase VEGF inhibitor sorafenib.[4] Candidacy for surgical resection is dictated by the severity of a patient's underlying liver dysfunction and the degree of resection that would be mandated by the size and number of tumors. The ideal candidate is a non-cirrhotic or early Child's A cirrhotic patient with a single small lesion. However as surgical resection offers a greater chance for cure and long-term survival than other therapies, there is interest in broadening the eligibility of patients who can undergo such operations. One approach has been the development of minimally invasive laparoscopic approaches that aim to minimize operative stress and enhance patient recovery, with the subsequent application of such techniques in advanced cirrhotic patients.

Laparoscopic liver resection is rapidly expanding to include major hepatectomies for malignancy.[5–8] Laparoscopic liver resection for HCC is well described in the literature for early, or

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Child's A, cirrhotics.[9] (Table 1) Small series have reported on such operations in Child's B and C cirrhotics as well, though the data is more scant and originates primarily from Asian cohorts in Japan, South Korea and Taiwan (Table 2). Several studies have compared outcomes after laparoscopic versus open resection, largely with comparable or favorable outcomes with the laparoscopic approach.[10–19] Other series have compared resections in non-cirrhotic and cirrhotic patients, with acceptable outcomes demonstrated in cirrhotic patients.[20–22] This study aims to compare safety, outcomes and survival between early, Child's A, cirrhotics and advanced, Child's B and C, cirrhotics undergoing laparoscopic liver resection for HCC in a Western patient cohort.

Methods

After institutional review board approval, a retrospective review was performed of a prospectively maintained database containing all laparoscopic liver resections performed between May 2002 and July 2016 at a single high-volume center. Specialized hepatobiliary surgeons performed all operations after presentation at a multidisciplinary tumor board including oncologists, surgeons, hepatologists and radiologists where patients were considered for all possible interventions including transplantation, radiofrequency ablation, transarterial chemoembolization (TACE) and surgical resection. Reasons for selection for resection rather than ablation included lesions that were superficial and easily accessible with minimal loss of functional liver volume, lesions that were in close proximity to major vessels or other organs thereby preventing safe ablation, and lesions that were too large for adequate ablation. In some cases, laparoscopic resection was combined with intraoperative radiofrequency ablation of other lesions, and some patients were treated with TACE to downsize tumors prior to undergoing surgical resection.

Primary end-points were 30 and 90-day mortality and secondary end-points included postoperative complications and overall survival. Data regarding patient characteristics and postoperative course were determined on review of the patient chart. To determine the postoperative change in the total bilirubin and prothrombin time levels the most recent preoperative value was compared to the peak value in the first two postoperative weeks. Complications were categorized according to the Clavien-Dindo system, with grade 1 and 2 complications classified as minor and those grades 3 or higher classified as serious.[23] American Society of Anesthesiologists (ASA) class, estimated blood loss (EBL) and transfusion of intraoperative packed red blood cells (PRBC) were determined from anesthesia records. Tumor characteristics, including size and number of lesions, and the severity of cirrhosis, were determined by surgical pathology reports.

Data was analyzed by SAS 9.4 and SPSS 23.0 (IBM Corp). Descriptive analysis was performed to obtain mean, median, distribution and central tendency. For continuous variables, normality was checked before performing the t-test. If the data was not normally distributed, non-parametric Mann–Whitney U test was used. Fisher's exact test was used if one or more cells have the expected number less than 5 for categorical variables. Where "0" caused a problem when computing the mortality odds ratio, "0.5" was added to all cells. Kaplan–Meier estimate was used to measure the fraction of subjects survived or saved after surgery over a period. Log rank test was performed to test the

Table 1 Series reporting laparoscopic liver resection for HCC in early (Child's A) cirrhosis (≥17 patients)

Study	Center	Patients (n)	Reference
Soubrane *et al.* (2014)	Paris, France	275	32
Shehta *et al.* (2016)	Seoul, South Korea	125	20,22
Dagher *et al.* (2010)	Clamart, France	111	27
Cheung *et al.* (2016)	Hong Kong, China	110	11
Chen *et al.* (2008)	Kaohsiung, Taiwan	98	26
Ettorre *et al.* (2015)	Rome, Italy	85	33
Belli *et al.* (2009)	Naples, Italy	49	12
Kobayashi *et al.* (2013)	Osaka, Japan	48	28
Cannon *et al.* (2014)	Louisville, Kentucky	47	34
Memeo *et al.* (2014)	Creteil, France	44	13
Worhunsky *et al.* (2016)	Stanford, California	41	21
Yoon *et al.* (2017)	Seoul, South Korea	37	15
Truant *et al.* (2011)	Lille, France	36	14
Lee *et al.* (2011)	Hong Kong, China	33	16
Herman *et al.* (2014)	Sao Paulo, Brazil	30	35
Kaneko *et al.* (2009)	Tokyo, Japan	30	25
Hu *et al.* (2011)	Yangzhou, China	29	17
Kim *et al.* (2014)	Seoul, South Korea	28	19
Lai *et al.* (2009)	Hong Kong, China	23	18
Cherqui *et al.* (2006)	Creteil, France	20	24
Kanazawa *et al.* (2013)	Osaka, Japan	20	10
Casaccia *et al.* (2011)	Genoa, Italy	17	36
Santambrogio *et al.* (2009)	Milan, Italy	17	37

Table 2 Series reporting laparoscopic liver resection for HCC in advanced (Child's B and/or C) cirrhosis (≥7 patients)

Study	Center	Patients (n)	Reference
Chen *et al.* (2008)	Kaohsiung, Taiwan	18	26
Shehta *et al.* (2016) and Brytska *et al.* (2015)	Seoul, South Korea	16	20,22
Dagher *et al.* (2010)	Clamart, France	9	27
Kaneko *et al.* (2009)	Tokyo, Japan	9	25
Kanazawa *et al.* (2013)	Osaka, Japan	8	10
Kobayashi *et al.* (2013)	Osaka, Japan	8	28
Worhunsky *et al.* (2016)	Stanford, California	7	21

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