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Advanced age is not a contraindication for liver resection in cases of large hepatocellular carcinoma

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Abstract

Background: The role of surgery in the management of large hepatocellular carcinomas (HCCs) is controversial. Advanced age and comorbidities are taken into account when major surgery is considered.

Purpose: To compare the outcomes of liver resection (LR) and transarterial chemoembolization (TACE) for resectable HCC in patients aged 70 years or older.

Patients and materials: This study included 70 patients aged 70 years or older treated for large HCCs (≥5 cm) between January 2007 and December 2012: 37 underwent LR and 33 underwent TACE. The outcomes of these patients were retrospectively analyzed. Univariate and multivariate Cox proportional hazard models were established. Kaplan–Meier survival curves were generated, and survival data were compared using the log-rank test.

Results: Hospital stay was significantly longer in the LR group than in the TACE group (10 days vs 8.5 days; $P = 0.003$). Treatment-related complications were more frequent in the TACE group, but this difference was not statistically significant. LR was associated with a better disease-free survival rate, median survival rate and cumulative overall survival rate.

Conclusion: Our results showed that LR could be a safe and effective treatment option for HCC tumors ≥5 cm in patiets aged 70 years or older.

Keywords: Hepatocellular carcinoma; Liver resection; Transarterial chemoembolization; Charlson comorbidity index

Introduction

Hepatocellular carcinoma (HCC) is the fifth most common malignancy in men and the sixth most common in women worldwide.[1] The Barcelona Clinic Liver Cancer (BCLC) staging system is used as a treatment algorithm for HCC.[2] Liver resection (LR) is recommended for patients with a single small tumor and good liver function.[3,4] The BCLC staging system recommends transarterial chemoembolization (TACE) for single large HCCs in patients with Child-Pugh class A or B liver function, classified as intermediate-stage HCC.[2] TACE has been reported to result in a survival improvement by 20 months.[5,6] Surgical treatment options for large HCCs or multifocal HCC are limited,[7] and only a few studies have reported the use of LR for the treatment of large HCCs.[8,9] Accordingly, the role of surgery in the management of large HCCs is controversial.

The BCLC staging of HCC accounts for the Child-Pugh classification, performance status, and tumor stage, but not patient age. However, in practice, patient age, the presence of comorbidities, and tumor size are accounted for when considering liver surgery for HCC. The purpose of this study was to compare the outcomes of LR and TACE for resectable large HCC in patients aged 70 years or older.

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Patients and materials

Patients

Between January 2007 and December 2012, 284 patients aged 70 years or older underwent LR or TACE for HCC at our hospital and received follow-up care. The records of these patients were retrospectively reviewed. The inclusion criterion for this study was HCC of ≥5 cm. Patients with recurrent HCC, distant metastases or lymph node involvement identified before treatment, or Child-Pugh class C liver cirrhosis were excluded from the analysis. Patient characteristics of age, gender, diagnosis, and Child-Pugh classification and HCC characteristics of tumor size, tumor number, and rupture were recorded. The severity of comorbidities was scored according to the Charlson comorbidity index.[10]

LR and TACE criteria

The treatment plans of patients with HCC were kept under surveillance of a multi-disciplinary conference for liver cancer at Tri-Service General hospital. Patient selection for LR was based on the absence of prohibitive medical conditions, favorable Child-Pugh class (A and selected B), and the ability to resect all tumors while leaving an adequate volume of liver parenchyma. The remnant liver volume was estimated from a preoperative volumetric computed tomography (CT) scan and should be greater than 30 % of total liver volume excluding tumor mass. The LR criteria for large HCC was the absence of ascites, total bilirubin level less than 2.0 mg/dL, combined with an indocyanine green retention rate at 15 min of less than 20% or serum platelet count more than 100,000/uL.[11,12] LR had priority over other loco-regional therapies for those whose were eligible for surgery. Patients who had declined surgery after discussing with the treatment team could be provided with TACE therapy according to their own will. Liver function criteria for enrolment in TACE therapy included bilirubin <3 mg/dL and liver enzymes (aspartate aminotransferase and alanine aminotransferase) <270 IU/L. The exclusion criteria for treatment with TACE were patients with: extrahepatic metastasis, biliary obstruction, encephalopathy, main portal vein thrombosis, portosystemic shunts, recent gastrointestinal bleeding, and Child-Pugh class C cirrhosis.

TACE procedure

At the commencement of the angiography, a 5 French introducer sheath was inserted into the common femoral artery under local anesthesia. All patient underwent initial evaluation of the vascular supply to the HCCs with superior mesenteric, celiac and common hepatic arteriography using a 4.1 French catheter (Cook Incorporated, Bloomington, IN). The tumor feeding arteries and surrounding vascular anatomy were identified. The venous phase was then carefully examined to evaluate the portal flow. A 2.7 French microcatheter (Progreat, Terumo Corporation, Japan) was inserted coaxially into the 4.1 French catheter and placed in the segmental or subsegmental hepatic arteries supplying the tumors. An emulsion of 5–20 mL iodized oil (Lipiodol; Laboratoire Guerbet, Aulnay-sous-Bois, France) and doxorubicin hydrochloride (10–50 mg) was injected into the feeding arteries, followed by embolization with gelatine sponge particles (Gelfoam; Pfizer, Tokyo, Japan).

Follow-up after treatment

Postsurgical follow-up evaluations included alpha-fetoprotein (AFP) level monitoring every 1–2 months and abdominal sonography every 3 months. In cases of an increased AFP level, abdominal ultrasonography or computed tomography was performed. The time and site of tumor recurrence and patient death were established through follow-up studies. Hospital stay and surgical complications were retrospectively recorded by reviewing patient medical charts. Treatment-related complications were

Table 1
Patient characteristics.

	Liver resection (n = 37)	Transarterial chemoembolization (n = 33)	P value
Age (y)[a]	76 (10.5)	77 (10.7)	0.571
Gender[b]			0.306
Male	28 (75.6%)	21 (63.6%)	
Female	9 (24.4%)	12 (36.4%)	
Diagnosis[b]			
HBV	14 (37.8%)	12 (36.4%)	0.420
HCV	7 (18.9%)	11 (33.3%)	
HBV + HCV	1 (2.7%)	0	
NBNC	15 (40.5%)	10 (30.3%)	
Child-Pugh classification[b]			0.233
A	33 (89.1%)	26 (78.8%)	
B	4 (10.9%)	7 (21.2%)	
Tumor pattern			
Size (cm)[a]	7.5 (5)	7.4 (4.9)	0.795
Single[b]	26 (70.2%)	23 (69.6%)	1.000
Rupture[b]	6 (16.2%)	3 (9.1%)	0.485
Charlson score[a]	5 (2)	5 (2.75)	0.599
Outcome			
Hospital stay (day)[a]	10 (4.5)	8.5 (9.5)	0.03[c]
Treatment-related complications[b]	6 (16.2%)	12 (36.4%)	0.062
Grade II	5	8	
Grade III	1	1	
Grade IV	0	3	

The median (interquartile range) is presented for continuous variables and number (percentage) is presented for categorical variables.
HBV = hepatitis B virus; HCV = hepatitis C virus; HBV + HCV = co-infection of hepatitis B and hepatitis C virus; NBNC = patients who have negative serological markers for hepatitis B and C.
P values were derived from:
[a] the Mann–Whitney U test and
[b] the chi-square test.
[c] $P < 0.05$.