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RAPID COMMUNICATION

Orthotopic liver transplantation as a rescue operation for recurrent hepatocellular carcinoma after partial hepatectomy

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Abstract

AIM: To compare post-orthotopic liver transplantation (OLT) survival between patients with recurrent hepatocellular carcinoma (HCC) after partial hepatectomy and those who received *de novo* OLT for HCC and to assess the risk factors associated with post-OLT mortality.

METHODS: From July 2003 to August 2005, 77 consecutive HCC patients underwent OLT, including 15 patients with recurrent HCC after partial hepatectomy for tumor resection (the rescue OLT group) and 62 patients with *de novo* OLT for HCC (the *de novo* OLT group). Thirty-three demographic, clinical, histological, laboratory, intra-operative and post-operative variables were analyzed. Survival was calculated by the Kaplan-Meier method. Univariable and multivariable analyses were also performed.

RESULTS: The median age of the patients was 49.0 years. The median follow-up was 20 mo. Three patients (20.0%) in the rescue OLT group and 15 patients (24.2%) in the *de novo* OLT group died during the follow-up period (P = 0.73). The 30-day mortality of OLT was 6.7% for the rescue OLT group *vs* 1.6% for the *de novo* OLT group (P = 0.27). Cox proportional hazards model showed that pre-OLT hyperbilirubinemia, the requirement of post-OLT transfusion, the size of the tumor, and family history of HCC were significantly associated with a higher hazard for mortality.

CONCLUSION: There are no significant differences in survival/mortality rates between OLT as *de novo* therapy and OLT as a rescue therapy for patients with hcc. Pre-OLT hyperbilirubinemia, post-OLT requirement of transfusion, large tumor size and family history of HCC are associated with a poor survival outcome.

Key words: Orthotopic liver transplantation; Liver cancer; Resection; Recurrence; Survival

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INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide. An estimated number of 372000 new cases of HCC are diagnosed each year, constituting 4.6% of all new cancers (6.3% in men, 2.7% in women)[1,2]. Endemic areas include the Far East and Africa. The number of patients with HCC in China comprises approximately 40%-50% of all HCC patients of the world and HCC is the 2nd leading cause of death among cancer mortalities in the country[3]. While the etiology and pathogenesis of HCC are not entirely clear, the major contributing factors for the high prevalence of HCC in the country include chronic hepatitis B infection and dietary contamination of aflatoxin[4].

Partial hepatectomy with tumor resection and orthotopic liver transplantation (OLT) are the two commonly used surgical modalities for HCC treatment. Partial hepatectomy with tumor resection may be performed as a definitive or bridging therapy. Post-operative recurrence of HCC is common in patients undergoing hepatectomy, affecting long-term outcome. For patients with recurrent HCC after partial hepatectomy, rescue treatment options include percutaneous ethanol injection (PEI), trans-catheter

arterial chemoembolization (TACE), and surgical resection of recurrent tumor[5,6]. In addition, OLT appears to be a valid rescue option for these patients[7]. Poon *et al*[7] reported that OLT as a salvage operation is feasible and effective in patients with transplantable small HCC (solitary ≤ 5 cm, or 2 or 3 tumors ≤ 3 cm) who initially had primary resection and had preserved liver function. However, OLT has not been routinely performed in patients with recurrent advanced HCC[8]. In our clinical practice, we found that these patients with recurrent HCC, even at an advanced stage, might still benefit from OLT as a rescue operation. We hypothesized that OLT as a rescue operation for patients with recurrent HCC after initial resection surgery may have a similar outcome to these patients with HCC who had *de novo* OLT. The aims of the study were to compare post-OLT survival rates between patients who have recurrent HCC and those who have no history of resection surgery, and to evaluate the risk factors associated with postoperative mortalities.

MATERIALS AND METHODS

Patients

This is an historical cohort study involving 77 consecutive patients who underwent OLT for HCC from July 2003 to August 2005 in Eastern Hepatobiliary Surgery Hospital, Shanghai, China, a tertiary referral center specializing in surgical treatment of HCC and a variety of other liver disorders. The data were extracted from a prospectively maintained database for OLT which was approved by the Institutional Ethics Committee. The 77 eligible patients were divided into two groups: the study group with OLT performed as a rescue operation for recurrent HCC after initial partial hepatectomy for tumor resection (the rescue OLT group, $n = 15$) and the control group with OLT performed as the 1st line *de novo* therapy for HCC (the *de novo* OLT group, $n = 62$).

Inclusion and exclusion criteria

The inclusion criteria were patients aged > 18 years and those with HCC who underwent OLT. The exclusion criteria were patients who had OLT for etiologies other than HCC and patients who had OLT combined with transplantation of other organ(s).

Criteria for diagnosis and selection

The diagnosis of HCC was based on a combined assessment of clinical presentations, history of HBV infection and liver cirrhosis, imaging data (ultrasound, CT scan, and/or MRI), preoperative laboratory evaluation (alpha-fetoprotein), and pre- and/or postoperative histopathology. Patients considered to be candidates for OLT met the following criteria: (1) primary or recurrent HCC met Shanghai Criteria for OLT[9], i.e., tumor size ≤ 9 cm, number of tumors ≤ 3, the absence of macrovascular tumor embolism, and the absence of extrahepatic metastasis; (2) the ability to take anti-rejection medications after OLT; and (3) the absence of significant comorbidities. Written informed consent was obtained from all patients before the surgery.

Demographic and clinical variables

A panel of demographic and clinical variables were evaluated, including age, sex, excessive alcohol use, tobacco use, family history of HCC, HBV and/or hepatitis C infection, liver cirrhosis, diabetes, cardiopulmonary diseases, renal insufficiency, the time from the tumor detection to OLT, donor source, preoperative blood biochemistry, pre-OLT Child-Pugh scores[10], post-OLT pTNM tumor staging (UICC, International Union Against Cancer, 1953), intraoperative variables, postoperative histopathology and postoperative course.

Clinical outcomes

The primary outcomes were estimated based on the 30-d postoperative mortality, overall survival, and tumor-free survival, and the secondary outcomes were risk factors associated with the mortality.

Statistical analysis

Descriptive statistics were computed for all factors. These include medians and percentiles for continuous factors and frequencies for categorical factors. Time of follow-up is defined as either months from OLT to death, or months from OLT to last follow-up visit. A Kaplan-Meier plot was used for graphical representation of survival probabilities by recurrence of the liver cancer. Univariable and multivariable Cox proportional hazards models were used to estimate the hazard rates for several factors of interest. A stepwise selection method was used to choose the final multivariable model using a 0.50 and 0.25 significance criterions for entering and remaining in the model, respectively. A significance level of 0.05 was considered for all analyses. SAS version 9.1 software (SAS Institute, Cary, NC) and R 2.0.1 software (The R Foundation for Statistical Computing) were used to perform all analyses.

RESULTS

Procedure

In a median waiting period of 2 mo (ranging from 4 d to 3 mo), all 77 patients underwent cadaver OLT. Two patients (13.3%) in the rescue OLT group and 11 patients (17.7%) in the *de novo* OLT group underwent TACE or PEI therapy before OLT operation. As a part of our routine clinical protocol, end-to-end anastomoses of the inferior vena cava, portal veins, hepatic arteries, and bile ducts of the donors and recipients were performed. At anhepatic phase, 4000 units of hepatitis B immunoglobulin (HBIG) were injected intramuscularly. At the completion of the operation, methylprednisolone 500 mg was infused intravenously. As a part of the post-OLT protocol, 74 patients (96.1%) received one to three 6-d courses of intravenous 5-fluorouracil 500 mg on post-operative day 1 and day 4, mitomycin 2 mg

Table 1 Demographic and clinical data

Factors	Rescue OLT group (n = 15)	De novo OLT group (n = 62)
Age (yr)[1]	50.0 (46.0-55.0)	49.0 (44.0-55.0)
Male, No. (%)	14 (93.3)	51 (82.3)
Excessive alcohol use, No. (%)	5 (33.3)	13 (21.0)
Tobacco use, No. (%)	7 (46.7)	52 (83.9)
Family history of liver cancer, No. (%)	3 (20.0)	8 (12.9)
Hepatitis B infection, No. (%)	15 (100.0)	57 (91.9)
Diabetes, No. (%)	2 (13.3)	7 (11.3)
Liver cirrhosis, No. (%)	15 (100.0)	60 (96.8)
Months from tumor detection to OLT[1]	1.0 (1.0, 3.0)	2.0 (1.0, 3.0)
Child-Pugh Score, No. (%)		
A	7 (46.7)	39 (62.9)
B	6 (40.0)	23 (37.1)
C	2 (13.3)	0 (0.0)
UICC pTNM tumor staging[1]	3.0 (3.0, 3.0)	3.0 (3.0, 3.0)
Total bilirubin (μmol/L)[1]	22.8 (15.0, 54.6)	32.1 (23.0, 55.4)
Direct bilirubin (μmol/L)[1]	10.4 (5.8, 35.3)	14.4 (9.8, 29.5)
Albumin (g/L)[1]	35.3 (32.1, 42.1)	34.5 (32.0, 37.6)
Prealbumin (g/L)[1]	12.7 (9.3, 15.3)	10.3 (6.9, 14.5)
Alanine aminotransferase (U/L)[1]	90.1 (37.7, 183.9)	48.9 (37.8, 91.7)
Asparate aminotransferase (U/L)[1]	85.4 (36.5, 150.0)	65.5 (47.1, 99.4)
Prothrombin time (s)[1]	14.5 (13.3, 17.9)	15.2 (13.4, 17.8)
Activated partial thromboplastin time (s)[1]	34.7 (31.8, 38.0)	34.8 (30.7, 41.3)
OLT operating room time (h)[1]	8.0 (7.2, 8.1)	6.8 (5.7, 7.7)
OLT anhepatic time (min)[1]	65.0 (60.0, 81.0)	62.0 (56.0, 74.0)
OLT intra-op bleeding (L)[1]	2.0 (1.5, 2.3)	1.5 (1.2, 2.0)
OLT intra-op transfusion (L)[1]	1.6 (1.0, 2.0)	0.8 (0.4, 1.4)
OLT post-op transfusion (L)[1]	1.2 (0.8, 2.0)	0.4 (0.0, 1.4)
Pre-OLT α-fetoprotein (U/L)[1]	7.5 (4.9, 27.1)	362.6 (20.4, 3480.0)
Post-OLT α-fetoprotein (U/L)[1]	5.3 (4.1, 10.9)	15.7 (5.4, 120.4)
Change in α-fetoprotein after OLT[1]	4.2 (0.8, 21.8)	337.9 (13.3, 3023.5)
Postoperative histopathology[1]		
Size of largest tumor in diameter (cm)[1]	3.0 (1.5, 6.0)	3.6 (2.5, 6.0)
Number of tumor[1]	1.0 (1.0, 4.0)	1.0 (1.0, 2.0)
Histology differentiation of tumor, No. (%)		
Moderate	8 (53.3)	9 (14.5)
Poor	7 (46.7)	53 (85.5)
Tumor vascular invasion, No. (%)		
None	5 (33.3)	26 (41.9)
Microvascular	8 (53.3)	33 (53.2)
Macrovascular	2 (13.3)	3 (4.8)
Tumor in right lobe, No. (%)	13 (86.7)	53 (85.5)
Post-OLT treatment, No. (%)		
None	1 (6.7)	2 (3.2)
Chemotherapy	14 (93.3)	60 (96.8)
Time of follow-up (mo)[1]	18.0 (12.0, 24.0)	21.0 (14.0, 32.0)

[1]Statistics presented are medians (Q25, Q75).

on post-operative day 2 and day 5, and carboplatin 100 mg on postoperative day 3 and day 6. Post-operative anti-rejection regimens included tacrolimus, methylprednisolone, and mycophenolate mofetil. The blood levels of tacrolimus were maintained at 10-15 ng/mL for 3 mo after OLT and 5-10 ng/mL thereafter. Intravenous methylprednisolone was started on postoperative day 1, at 50 mg per 6 h, and tapered to 20 mg per day. On discharge from the hospital, intravenous methylprednisolone was switched to oral prednisone 15 mg per day with tapering. Prednisone was discontinued at 3 mo post-operatively.

Table 1 summarizes descriptive statistics for all 77 patients in the rescue OLT (n = 15) and *de novo* OLT (n = 62) groups.

Clinical data on the rescue OLT group

Table 2 presents detailed information about the tumor, at the time of tumor resection in the study group. All patients in the rescue OLT group underwent radical tumor resection because of the lack of a donor liver, even though the patients met Shanghai Criteria for OLT. The patients had partial hepatectomy with a tumor-free margin of $\geqslant$ 1.5 cm which was confirmed by postoperative histopathologic evaluation. The majority of patients underwent postoperative adjunctive therapy, including TACE in 12 (80.0%) patients and PEI in 2 (13.3%) patients.

Survival data

Within a median follow-up of 20 mo (interquartile

Table 2 Initial clinical data of HCC at time of tumor resection in the study group (n = 15)

Factors	*n*
Years since tumor detection[1]	4.0 (3.0, 5.0)
Mean diameter of tumor (cm)[1]	4.5 (3.0, 8.0)
Tumor-free interval after resection (mo)[1]	26.0 (6.0, 38.0)
Microsatellite lesions (%)	
0	11 (73.3)
1	4 (26.7)
Number of post-resection trans-catheter Arterial chemoembolization	
0	3 (20)
1	4 (26.7)
2	5 (33.3)
3	2 (13.3)
6	1 (6.7)
Number of post-resection percutaneous ethanol injection	
0	13 (86.7)
3	1 (6.7)
16	1 (6.7)
Tumor in the left lobe (%)	12 (80)
Unifocal tumor (%)	15 (100)
Vascular invasion (%)	
None	10 (66.7)
Microvascular	3 (20)
Macrovascular	2 (13.3)
Non-encapsulated tumor (%)	9 (60)

[1]Statistics presented are median (Q25, Q75).

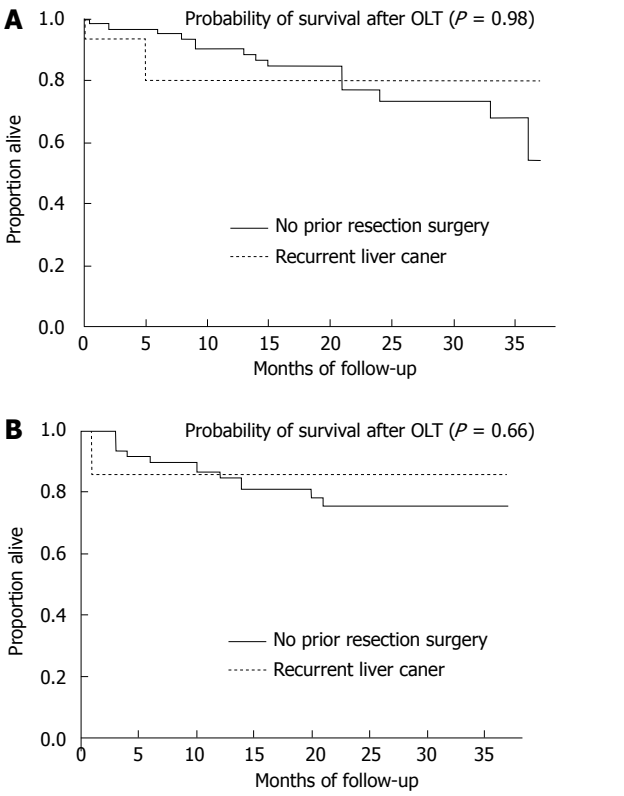

Figure 1 Probability of overall survival and tumor-free survival after ortotopic liver transplantation- Kaplan-Meier curves. **A**: Interaction between time and groups was verified as the two curves cross each other suggest non-proportionality of the hazards but this is not found statistically significant (P = 0.98); **B**: Interaction between time and groups was verified as the two curves cross each other suggest non-proportionality of the hazards, but not statistically significant (P = 0.66).

range: 14-29 mo), 18 (23.4%) patients died: 3 (20%) in the rescue OLT group and 15 (24.2%) in the *de novo* OLT group. One patient from each group died in 30 d of OLT (6.7% *vs* 1.6%) because of disseminated intravascular coagulation and pneumonia, respectively. One patient in the control group died of graft-versus-host disease 2 mo after OLT. The main cause of the death was recurrent tumor and metastasis, and 15 patients died more than 30 d after OLT.

Risk factors associated with survival outcome

Table 3 presents univariable hazard rates for the association between several factors of interest and overall survival rate. Younger age, pre-operative hyperbilirubinemia, large tumor size, family history of liver cancer, and tumor microembolism were found to significantly influence the hazard for post-OLT mortality. Figure 1 presents the Kaplan-Meier curves of overall survival and tumor-free survival by the two groups, respectively. Interaction between time and the study groups was verified as the two curves cross each other suggested non-proportionality of the hazards; but this was not found statistically significant.

Table 4 shows the results of the multivariable Cox proportional hazards model. Total bilirubin, the requirement for post-operative transfusion, the size of the largest tumor, family history of HCC, and microembolisms remained in the final model. Recurrence of HCC was kept in the final model because of clinical importance, even though it was not found significantly associated with survival rate. The hazard of dying after OLT increases by 1% for every 1 unit increase in total bilirubin. Also, for every 1 L increase in the amount of post-OLT blood transfusion, the hazard of dying increases by 40%. In addition, the hazard of dying increases by 30% for every 1 cm increase in the size of the largest tumor. Finally, subjects with a family history of HCC have 7.7 times of the hazards of dying that of those without a family history of HCC.

DISCUSSION

Partial hepatectomy and OLT are effective treatment modalities for HCC patients with underlying cirrhosis[11-13]. The surgical outcome of the two approaches appeared to be comparable, with each of the treatment modalities having its advantages and disadvantages. For example, operative mortality was lower for partial hepatectomy which may be preferably applied to HCC patients with a well compensated cirrhotic liver, while OLT can be performed selectively in patients with tumor recurrence and/or decompensated liver. Although the decision of choice on partial hepatectomy and OLT can be difficult to make[14-16], it appears that the latter treatment modality may have a survival advantage[17,18]. The main barrier for the routine application of OLT in the patient population has been the availability of a donor organ. On the other hand, partial hepatectomy can be offered as a sole surgical treatment or as a bridging procedure for OLT. However,

Table 3 Univariable Cox proportional hazards models

	Factor	Hazard ratio (95% CI)	*P*
Demographic	Age	0.92 (0.88-0.97)	< 0.001
	Gender (male *vs* female)	1.6 (0.36-6.9)	0.54
	Tobacco (yes *vs* no)	1.7 (0.48-5.8)	0.42
	Excess alcohol use (no *vs* yes)	1.1 (0.37-3.4)	0.83
	Family history liver cancer (yes *vs* no)	4.4 (1.6-11.9)	0.004
	Diabetes (yes *vs* no)	1.4 (0.42-5.0)	0.57
	Interval from tumor detection to OLT in mo	0.99 (0.91-1.07)	0.74
Disease groups	Recurrent liver cancer (yes *vs* no)	1.02 (0.29-3.5)	0.98
Preoperative laboratory tests	Total bilirubin	1.01 (1.004-1.01)	< 0.001
	Direct bilirubin	1.01 (1.01-1.01)	< 0.001
	Albumin	0.99 (0.90-1.10)	0.91
	Pre-albumin	0.91 (0.82-1.02)	0.11
	Alanine aminotransferase	1.00 (1.00-1.01)	0.57
	Asparate aminotransferase	1.00 (1.00-1.01)	0.15
	Prothrombin time	1.04 (0.92-1.2)	0.51
	Activated partial thromboplastin time	1.01 (0.96-1.08)	0.62
Tumor histopathology	Size of largest tumor (cm)	1.1 (1.03-1.2)	0.009
	Tumor staging	1.6 (0.43-6.2)	0.47
	Tumor range	1.3 (0.90-1.9)	0.16
	Tumor location (left *vs* right)	1.2 (0.33-4.0)	0.82
	Microembolism (micro *vs* none)	2.1 (0.67-6.7)	0.2
	Microembolism (macro *vs* none)	10.5 (2.3-48.3)	0.003
Preoperative staging	Child-Pugh Score	1.5 (0.67-3.4)	0.31
Intraoperative factors	OLT operative room time (h)	1.1 (0.80-1.6)	0.48
	OLT anhepatic time (min)	0.97 (0.92-1.01)	0.11
	OLT intra-op bleeding (L)	0.47 (0.20-1.1)	0.097
	OLT intra-op transfusion (L)	0.73 (0.43-1.2)	0.24
	OLT post-op transfusion (L)	1.1 (0.90-1.4)	0.33

Table 4 Multivariable Cox proportional hazards model

Factors	Hazard ratio (95% CI)	*P*
Recurrent liver cancer (yes *vs* no)	1.7 (0.38-7.2)	0.5
Total bilirubin	1.01 (1.006-1.02)	< 0.0001
OLT post-op transfusion (L)	1.4 (1.1-1.8)	0.008
Size of largest tumor (cm)	1.3 (1.1-1.4)	0.0004
Family history liver cancer (yes *vs* no)	7.7 (2.2-26.9)	0.001
Microembolism (yes *vs* no)	3.4 (0.85-13.5)	0.08

partial hepatectomy can be associated with a short-term risk for postoperative hepatic failure with a 5%-10% mortality and a 30%-50% morbidity[19,20] and with a long-term risk for tumor recurrence, affecting 80% of the patients at 5 years[21-24]. Since the recurrence of the tumor after partial hepatectomy is common, rescue medical, radiographic, and surgical therapies are often needed.

There are scanty data on the clinical outcome of OLT as a rescue operation for patients with recurrent HCC after the initial tumor resection. We evaluated 77 consecutive patients with OLT, of whom 15 patients had rescue OLT for recurrent HCC. All the 15 patients had concomitant liver cirrhosis. These patients all had postoperative single or multiple sessions of TACE and/or PEI. We found no difference in the overall and tumor-free survivals between the rescue OLT and *de novo* OLT groups, suggesting that OLT may be a valid option for patients with recurrent HCC after the tumor resection.

In addition to its application in advanced stage HCC, OLT can also be a valid treatment option for patients with early stage tumors if partial hepatectomy is not amenable[25], even though the survival advantage of OLT over partial hepatectomy in these patients has not been confirmed[26,27]. When compared with partial hepatectomy, OLT for resectable HCC may offer a survival benefit in a subset of patients as long as the donor organ is available within 6-10 mo[16].

OLT has increasingly been performed for HCC where reported 1- and 2-year cumulative survival rates were 90.0% and 65.6%, and the disease-free survival rates were 77.5% and 62.5%, respectively[28]. The 3-year survival reached 77%-80%[29,30]. Poon *et al*[7] reported that a 5-year overall survival and tumor-free survival of OLT for patients with recurrent small HCC (diameter $\leqslant$ 3 cm) after initial tumor resection were 48% and 0%, respectively. The 5-year survival rate of 422 HCC patients with OLT was 44.4%, and histologic grade of HCC and tumor size (> 5 cm) were found associated with tumor-free survival[31]. Multiple factors may have contributed to the improvement in survival in HCC patients after OLT, including appropriate selection of candidate patients, the application of surgical techniques minimizing the risk for intraoperative tumor spread, and postoperative adjunct medical therapy.

The most commonly used criteria for transplantation for HCC patients are the Milan criteria: solitary tumor $\leqslant$ 5 cm in diameter or 2 or 3 tumor nodules with the largest diameter $\leqslant$ 3 cm and the absence of macroscopic vascular invasion or extrahepatic metastasis[11]. In the current study, we used the Shanghai Criteria[9], i.e., tumor size $\leqslant$ 9 cm, number of tumors $\leqslant$ 3, the absence of macrovascular tumor embolism(s), and the absence of

extrahepatic metastasis. The main difference between the Milan Criteria and Shanghai Criteria was the tumor size with cut-off 5 cm *vs* 9 cm.

A variety of factors were reported to be associated with a poor surgical outcome after OLT, including large tumor size[13,28,31,32], the presence of vascular invasion[13], the presence of portal vein thrombosis[28], and poor histologic differentiation[31]. In the current study, the risk factor associated with a poor survival were pre-OLT hyperbilirubinemia, the requirement of post-OLT blood transfusion, large tumor size, family history of liver cancer, and the presence of tumor microembolism. The recurrence of HCC after the tumor resection as an indication of OLT was not found associated with a poor survival outcome after OLT. Therefore, OLT appears to be a valid option as rescue operation for recurrent HCC after tumor resection.

Post-operative corticosteroid use may be associated with a high risk for tumor recurrence in patients with OLT. Mazzaferro *et al*[11,33] reported that discontinuation of corticosteroid use for 3-6 mo in HCC patients with OLT had a lower risk for tumor recurrence and post-operative long-term corticosteroid use had a 4-fold increase in tumor recurrence after OLT. In addition, post-operative corticosteroid use appears to pose a higher risk for post-operative infection and metabolic side effects. It appears that post-operative immunosuppression with omission of cortisteroid use may be safe[34]. In our study protocol, all patients had corticosteroid tapering and discontinued the agent at one month after OLT.

There are some limitations to the study. First, this is not a randomized trial with a small sample size in the rescue OLT group (n =15), which would have been subjected to a type Ⅱ error. Second, longer follow-up would be needed. Finally, the study was conducted in a tertiary care center specializing in surgical treatment of HCC and other liver disorders and there might have been a selection bias.

In conclusion, there are no significant differences in survival/mortality rates between OLT as a *de novo* therapy and OLT as a rescue therapy for patients with HCC. Pre-OLT hyperbilirubinemia, post-OLT requirement of transfusion, large tumor size, and family history of HCC are associated with a poor survival outcome.

COMMENTS

Background

Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide. Liver transplantation (LT) appears to be a valid rescue option for these patients. However, LT has not been routinely performed in patients with recurrent advanced HCC. Meanwhile, the risk factors of orthotopic liver transplantation (OLT) for HCC patients are unclear. So we hypothesized that OLT as a rescue operation for patients with recurrent HCC after initial resection surgery may have a similar outcome to these patients with HCC who had *de novo* OLT. The aims of the study were to compare post-OLT survival rates between patients who have recurrent HCC and those who have no history of resection surgery; and to evaluate risk factors associated with postoperative mortalities.

Research frontiers

Liver transplantation is one of the hotspots in researches on liver tumors. But few studies have tried to find the risk factors of OLT for HCC using the statistical method.

Innovations and breakthroughs

No significant differences were found in survival/mortality rates between OLT as a *de novo* therapy and OLT as a rescue therapy for patients with HCC in this study. And Pre-OLT hyperbilirubinemia, post-OLT requirement of transfusion, large tumor size, and family history of HCC were found associated with a poor survival outcome.

Applications

This study shows that there were no significant differences in survival/mortality rates between OLT as a *de novo* therapy and OLT as a rescue therapy for patients with HCC. And pre-OLT hyperbilirubinemia, post-OLT requirement of transfusion, large tumor size, and family history of HCC were associated with a poor survival outcome. The main limit in this research are the biology and genetics of tumors.

Peer review

The authors described excellent results of the OLT for HCC patients using statistical methods. This article identified that recurrent HCC was not a risk factor of OLT. Meanwhile, pre-OLT hyperbilirubinemia, post-OLT requirement of transfusion, large tumor size, and family history of HCC play important roles in the prognosis of OLT. The findings are potentially important for planning of further studies.

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