

Outcome of Liver Transplantation in Hepatocellular Carcinoma Patients at Siriraj Hospital

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ABSTRACT

Background. Liver transplantation (LT) is one of the standard treatments for hepatocellular carcinoma (HCC), and the outcomes have become better after introduction of strict patient selection, such as the Milan criteria. However, several expanded criteria, such as the University of California San Francisco (UCSF) criteria, have demonstrated similar survival outcomes. The aim of this study was to verify survival outcomes of LT for HCC at Siriraj Hospital.

Methods. Sixty-three patients diagnosed with HCC who underwent cadaveric LT at Siriraj Hospital from 2002 to 2011 were included. All patients' characteristics, blood chemistries, size and number of tumors, bridging therapy, and survival and recurrence data were retrospectively reviewed and analyzed.

Results. Nearly all (62 patients, 98.4%) fulfilled the Milan criteria based on preoperative imaging. Explant pathology revealed that 40 patients (63.5%) were within Milan criteria and 50 patients (83%) within UCSF criteria. Demographic data, clinical laboratory, and bridging therapy were similar in patients within and outside both Milan and UCSF criteria. The 1-, 3-, and 5-year survival rates of patients within Milan were 85%, 75%, and 67.5%, and of those outside Milan were 69.6%, 52.2%, 52.2%, respectively ($P = .25$). Interestingly, with the use of the UCSF criteria, the 1-, 3-, and 5-year survival rates of patients within UCSF were significantly better than of those outside UCSF (84%, 76%, and 70% vs 61.5%, 30.8%, and 30.8%, respectively; $P = .01$).

Conclusions. Outcome of LT in HCC patients within Milan criteria demonstrated good long-term survival. However, providing the opportunity for HCC patients by expanding from Milan to UCSF criteria revealed similar outcomes.

HEPATOCELLULAR carcinoma (HCC) is one of the most common malignancies worldwide and the 3rd most common cause of death from cancer. The incidence of HCC is relatively higher in east and southeast Asia [1], where there is high incidence of chronic hepatitis B and C infection. Because of the poor prognosis of HCC, overall survival of untreated HCC patients is only 8.7 weeks to 6 months and 1-year survival is only 23% [2,3].

Liver transplantation (LT) is one of the standard treatments for HCC. Outcome after LT has become better in terms of both survival and tumor recurrence after the introduction of strict patient selection criteria [4]. In 1996,

following the Milan criteria, single HCC sized ≤ 5 cm or multiple HCC of ≤ 3 tumors with each tumor ≤ 3 cm and without major vascular invasion can achieve 4-year survival of 85%. However, several expanded criteria, such as the

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University of California San Francisco (UCSF), demonstrated similar patient survival outcomes, with 5-year survival of 75.2% [5].

The aim of the present study was to evaluate the outcome of LT for HCC patients at Siriraj Hospital, which is a tertiary hospital and one of the biggest liver transplant centers in Thailand.

METHODS

A retrospective review of adult patients with HCC who underwent LT from January 2002 to December 2011 at Siriraj Hospital, Bangkok, Thailand, was performed. Patient demographic data, clinical factors, preoperative imaging, perioperative data, and postoperative outcomes were reviewed. A single pathologist reviewed all explanted liver histology evaluating pathologic Milan criteria status, UCSF criteria status, and vascular invasion.

Treatment Protocol

All patients underwent cadaveric caval-replacement LT. Almost all of the patients who underwent LT before January 2004 received either cyclosporine (CsA) or tacrolimus (Tac) together with tapered prednisolone, and those underwent LT from 2004 received additional mycophenolate mofetil (MMF) as maintenance immunosuppression. Steroids were weaned and withdrawn within 3 months after the operation. Trough level of Tac and CsA level 2 hours after dose were used for monitoring graft function. The goal of immunosuppressive agent level was determined by clinician based on patients' clinical and blood chemistry data.

Statistical Analysis

Overall survival (OS) and disease-free survival (DFS) rates of patients were calculated by means of Kaplan-Meier method. OS and DFS between those within and outside Milan criteria and between those within and outside UCSF criteria were compared by means of the log-rank test. Furthermore, a subgroup analysis was performed comparing survival rates in 3 subgroups of patients: group 1:

Table 1. Patient Characteristics and Underlying Liver Disease (n = 63)

Variable	n (%)
Patient characteristics	
Age, y, median (range)	55 (32–72)
Male	46 (73)
Female	17 (27)
Underlying liver disease	
Chronic hepatitis B	32 (50.8)
Chronic hepatitis C	18 (28.6)
Alcoholic steatohepatitis	5 (7.9)
Cryptogenic cirrhosis	5 (7.9)
Nonalcoholic steatohepatitis	1 (1.6)
Primary biliary cirrhosis	1 (1.6)
Coinfection (hepatitis B and C)	1 (1.6)
Child-Pugh classification	
A	13 (20.6)
B	27 (42.8)
C	23 (36.5)
Pre-transplantation bridging therapy	
Transarterial chemoembolization	37 (58.7)
Radiofrequency ablation	4 (6.3)

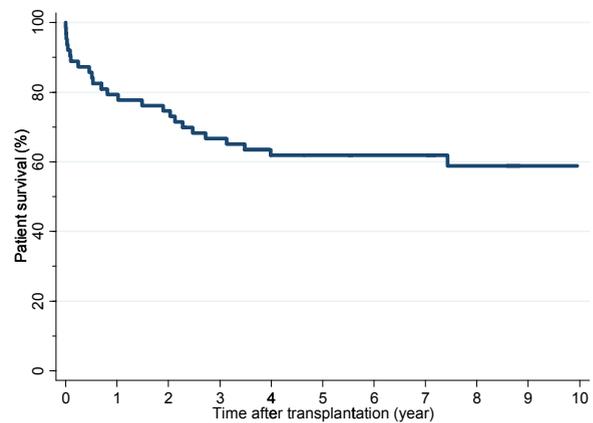


Fig 1. Overall survival of hepatocellular carcinoma patients after liver transplantation.

patients with tumors within Milan criteria; group 2: patients with tumors outside Milan criteria but within UCSF criteria; and group 3: patients with tumors outside UCSF criteria. Stata version 11 (Statacorp, College Station, Texas) was used for all statistical analyses.

RESULTS

Patient Characteristics

From January 2002 to December 2011, 137 adult patients underwent LT at Siriraj Hospital. Sixty-three patients were diagnosed with HCC and included in the analysis. The characteristics of these patients are summarized in Table 1. There were 46 men and 27 women, with an overall median age of 55 (range, 32–72) years. Hepatitis B virus was positive in 32 patients (50.8%), and hepatitis C virus was positive in 18 patients (28.6%). The mean Model of End-Stage Liver Disease score at the time of transplantation was 17, ranging from 6 to 39. Sixty-nine percent of patients received locoregional therapy for HCC before undergoing LT, comprising 37 (58.7%) transarterial chemoembolization and 4 (6.3%) radiofrequency ablation.

Among these HCC patients, 62 of 63 (98.4%) were within the Milan criteria based on preoperative imaging and clinical data. Explanted liver pathologic examination revealed that only 40 patients (63.5%) and 50 patients (83%) were within the Milan and the UCSF criteria, respectively. The most common reason why HCC patients were outside Milan criteria was exceeded size of the tumor (87%).

Patient Survival

OS of the whole cohort at 1 and 5 years was 79.4% and 61.9%, respectively (Fig 1), with the death of 24 patients during the entire follow-up period. The causes of death were mainly from recurrence of disease (41.7%) and sepsis (20.8%), as presented in Table 2. DFS of the whole cohort at 1 and 5 years was 94.5% and 79.1%, respectively. Twelve patients (19%) had recurrence of HCC, but only 2 of them (16.6%) were intrahepatic recurrence. The sites of

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