



## Original Research

# Transplantation versus hepatectomy for HCC beyond the Milan criteria: A propensity score analysis



Jun-yi shen, Chuan Li, Tian-fu Wen<sup>\*</sup>, Lv-nan Yan, Bo Li, Wen-tao Wang, Jia-yin Yang, Ming-qing Xu, Jun wen

Department of Liver Surgery & Liver Transplantation Center, West China Hospital, Sichuan University, Chengdu, China

## HIGHLIGHTS

- Our propensity-score-matched study provided evidences to support the use of LT in HCC patients beyond Milan criteria.
- Patients with AFP >800 ng/ml or tumor > 8 cm achieved similar survival benefits from both therapy.
- patients with AFP ≤800 ng/ml or tumor ≤ 8 cm, LT had more advantages on prognosis of HCC beyond Milan criteria.

## ARTICLE INFO

*Article history:*

Received 9 February 2017

Received in revised form

1 May 2017

Accepted 15 May 2017

Available online 19 May 2017

*Keywords:*

Surgical resection

Liver transplantation

Prognosis

Hepatocellular carcinoma

Propensity scoring matching

## ABSTRACT

**Background:** Increasing studies have suggested that surgical resection (SR) or liver transplantation (LT) could bring survival benefits for patients with hepaticellular carcinoma (HCC) beyond Milan criteria. This study compared the long-term survival of patients beyond the Milan criteria who received SR or LT.

**Material and methods:** A total of 461 HCC patients were retrospectively collected. Analysis was performed using propensity score matching (PSM), the Kaplan-Meier method and the Cox proportional hazards model.

**Results:** Prognosis was significantly better for the LT group than the SR group before ( $P < 0.001$ ) and after PSM ( $p = 0.003$ ). In subgroup analysis, for patients with lower AFP level, the 1-, 3-, and 5-year OS rates for the two groups were significantly different (86.7, 71.9, and 71.9% for group LT vs. 75.8, 48.1, and 10.7% for group SR,  $P = 0.003$ ). For patients with smaller tumor size, the 1-, 3-, and 5-year OS rates were 78.3, 66.7, and 66.7% for group LT, and 83.8, 42.6, and 18.6% for group SR,  $p = 0.009$ ). Transplantation was a favorable factor associated with prognosis before and after propensity score matching (HR 2.643).

**Conclusion:** Our propensity model suggested that LT provided significantly better long-term survival than SR for HCC beyond Milan criteria before and after PSM.

© 2017 Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd.

## 1. Introduction

Liver cancer, one of the most deadly cancers, is the second-most common cancer in China. Approximately 383,000 people die from liver cancer every year in China, accounting for 51% of the deaths from liver cancer worldwide [1]. Curative treatment for HCC includes resection, transplantation and ablation (if tumor size was smaller than 3 cm). Surgical resection (SR) remains a popular curative treatment for early stage HCC patients with well preserved

liver function [2]. Unfortunately, the majority of HCC were diagnosed at intermediate or advanced tumor stage with variable tumor size and number due to lack of specific symptoms at an early stage. Based on Barcelona Clinic Liver Cancer (BCLC) staging system, transarterial chemoembolization (TACE) should be considered for patients with intermediate HCC who might have large or multiple tumors. With advance in surgical technique and perioperative management, as well as experienced in restrictive selection of patients, many qualified medical centers challenge TACE for HCC beyond Milan criteria recommended by BCLC staging system. They reported SR could result in survival benefits over TACE for HCC patients with well preserved liver function regardless of their BCLC stage [3–6], including one randomized controlled trial (RCT) study reporting 3-year OS rates of 51.5% [5]. These findings suggested that

<sup>\*</sup> Corresponding author. Department of Liver Surgery & Liver Transplantation Center, West China Hospital, Sichuan University, Chengdu, 610041, Sichuan Province, China. Tel. +86 18980601471.

E-mail address: [cdhxwentianfu@163.com](mailto:cdhxwentianfu@163.com) (T.-f. Wen).

SR might be better treatment option for patients with HCC beyond the Milan criteria. Liver transplantation (LT) is widely accepted as the best treatment method because it could eliminate both the tumor and the underlying liver disease. The Milan criteria has been widely accepted as standard selection criteria for LT because it could provide satisfactory long-term survival [7]. Consequently, patients with HCC beyond Milan criteria will not be given priority and few patients thus could undergo LT. Recently, the use of adult-to-adult living donor liver transplantation (LDLT) has increased and some patients with HCC beyond Milan criteria might get the opportunity to receive LT [8]. Moreover, some retrospective studies have revealed that some patients beyond the Milan criteria were suitable for LT [9–12]. Even some study reported patients with intermediate HCC achieved 5-year survival of 70% [11]. Only one study reported liver transplantation resulted in a poorer long-term outcome than the liver resection in patients with HCC beyond Milan criteria [13]. Numerous investigators try to prove that SR or LT could bring more benefits for patients with HCC beyond Milan criteria compared with TACE, however, there was no consensus on best treatments for treatment of HCC beyond Milan criteria [14,15]. Since SR could provide a hope of cure for intermediate stage HCC, whether HCC patients should obtain transplantation opportunity should be determined based on the expected prognosis after LT. However, the conclusions of most investigations were derived from either unbalanced baseline clinicopathological features or relatively small sample size. Given that carrying out a RCT is not feasible, performing propensity score matching analysis is a good option because it could eliminate baseline differences [16].

In this study, we aimed to retrospectively (a) investigate the long-term survival of patients with HCC beyond Milan criteria who received SR or LT by using PSM to adjust confounding factors; (b) survival analysis stratified by tumor number, tumor size and AFP level after PSM.

## 2. Materials and methods

### 2.1. Patients

This study was approved by the ethical committee of West China Hospital. All study subjects were informed of the benefits and risks of surgery in detail. Written informed was obtained from all patients for their information to be stored in the hospital database and used for research purpose. This study was conducted in accordance with the Declaration of Helsinki. Adult patients with HCC beyond Milan criteria who underwent liver transplantation or liver resection were included in this study. The inclusion period for LT was between 2002 and 2014 and for SR was between 2009 and 2014. HCC of all patients were confirmed by pathologists in west china hospital. Inclusion criteria were as follows: (1) solitary tumor >5 cm in diameter or ≤3 nodules that were >3 cm in diameter or more than 3 nodules in any size; (2) without extrahepatic metastasis or macrovascular invasion; (3) Child–Pugh grade A/B; (4) not be recurrent HCC. Available patients were divided into 2 groups: group LT consisted of 80 patients who received liver transplantation, and group SR consisted of 381 patients who underwent liver resection. Demographic data, treatment method, tumor size, tumor differentiation, presence of microvascular invasion (MVI), satellite lesions, alanine transaminase (ALT), aspartate transaminase (AST), total bilirubin (TBIL), albumin (ALB), hepatitis B virus Antigen (HBsAg), platelets (PLT), alpha-fetoprotein (AFP), and Creatinine (Cre) were assessed 2 days before surgery. All laboratory tests were measured by a uniform method for both groups.

### 2.2. Follow up

The mean follow-up time was  $32.51 \pm 25.48$  months ranging from 1 to 174 mo. Antiviral drugs like nucleoside acid analogues were administered to patients with positive HBV-DNA before and after operation. After operation, patients were routinely monitored by serum AFP examination, liver ultrasonography, or computed tomography (CT) or magnetic resonance imaging (MRI) and chest radiography every 3 months. Recurrence was defined as positive imaging findings and newly rising tumor marker (AFP) values or confirmation by biopsy or resection. Overall survival (OS) time was described as the interval between the operation and death or the last follow up. Disease-free survival (DFS) time was defined as the time interval between the operation and the first incidence of detectable recurrence. A cutoff value of tumor size was 8 cm in survival analysis in subgroups [17].

### 2.3. Statistical analysis

In order to reduce the effect of selection bias and potential confounders, we evaluated the propensity score by means of logistic regression and performed 1:1 patient matching based on each patient's propensity score using a 0.2 caliper width [16]. Variables included in the propensity score model were age (>60y), sex, HBsAg, liver cirrhosis, tumor size, tumor differentiation, tumor number, MVI, satellite lesions, serum AFP (>800 ng/ml), ALT, AST, ALB, PLT, TBIL and Cre. Continuous variables are expressed as mean  $\pm$  Standard Deviation (SD) and categorical variables were reported as number (percent). Continuous variables were analyzed by means of the paired *t*-test or two-sample *t*-test and categorical variables were compared using the Chi-square test or Fisher's exact test. Survival analysis was determined using the Kaplan–Meier method and compared by the log-rank test. Multivariate analysis to identify independent prognostic factors was carried out using the Cox proportional hazard model. Significant factors in the univariate analysis were included in the multivariate analysis [18]. All analyses were performed using SPSS 20.0. A *P* value of less than 0.05 was defined as being statistically significant.

## 3. Results

### 3.1. Characteristics of all study patients

Of 461 patients, 381 patients received liver resection (group SR), whereas 80 patients underwent liver transplantation (group LT). This study included 402 males and 59 females. The mean age was  $49.97 \pm 12.43$  years. As presented in Table 1, there were no significant difference in sex, tumor differentiation, satellite lesions and MVI, preoperative AFP, ALT and proportion of HBsAg positive between the two groups (all *P* > 0.05). Patients in the LT group were significantly younger (*P* = 0.004) and had higher rate of severe cirrhosis (*P* = 0.002), more tumors (*P* < 0.001), lower serum albumin level (*P* = 0.009), lower PLT level (*p* = 0.037) and higher serum AST level (*p* < 0.001). Patients in this group also had significantly higher TBIL level and Cre level (*P* < 0.001 and *P* = 0.001, respectively). Patients in the SR group had larger tumor size (*p* = 0.004) and more aged patients (*p* = 0.004). The incidence of 90-days mortality in the LT group of the current study is higher (11.2% vs 1.5%). According to our data, all the cases suffering 90-days mortality underwent LT before 2008.

Download English Version:

<https://daneshyari.com/en/article/5731658>

Download Persian Version:

<https://daneshyari.com/article/5731658>

[Daneshyari.com](https://daneshyari.com)