

# Living donor liver transplantation in hepatocellular carcinoma: A single-center experiences

## Hepatosellüler karsinomda canlı vericili karaciğer nakli: Tek merkez deneyimi

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### Abstract

**Aim:** Hepatocellular carcinoma (HCC) is the most common primary solid tumor of the liver. Hepatitis B virus (HBV) infections, Hepatitis C virus (HCV) infections and at alcoholism can be seen. The aim of this study was to evaluate living donor liver transplantation in hepatocellular carcinoma.

**Methods:** This is a retrospective cohort study. Between April 2014 and December 2017 at Medipol University Medical Faculty Hospital Organ Transplantation Department, 38 patients in living donor liver transplantation for HCC were evaluated.

**Results:** The mean patient age was 58.0 (9.9) (20–74) years; 31 (81.6%) of the 38 were male. The mean MELD score was 14.2 (8–32). Outside Milan criteria ( $P=0.003$ ), poorly differentiated and cholangiocarcinoma tumor component ( $P=0.003$ ) appears to be worse in living donor liver transplantation in hepatocellular carcinoma.

**Conclusions:** In this study, outside Milan criteria, poorly differentiated and cholangiocarcinoma tumor component appears to be worse in living donor liver transplantation in hepatocellular carcinoma.

**Keywords:** Hepatocellular carcinoma, Living donor liver transplantation

### Öz

**Amaç:** Hepatosellüler karsinom (HCC) karaciğerin en sık görülen primer solid tümördür. Hepatit B virus (HBV) enfeksiyonları, hepatit C virus (HCV) enfeksiyonları veya alkolizm zemininde de görülebilir. Bu çalışmanın amacı, HCC nedeniyle canlı vericili karaciğer nakli yapılan hastaların değerlendirilmesidir.

**Yöntemler:** Retrospektif kohort çalışma planlandı. Nisan 2014 – Aralık 2017 tarihleri arasında Medipol Üniversitesi Tıp Fakültesi, Organ Nakli Merkezi'nde HCC nedeniyle canlı vericili karaciğer nakli yapılan 38 hasta değerlendirildi.

**Bulgular:** Ortalama yaş 58,0 (9,9) (20-74) yılı; 38 kişiden 31'i (%81,6) erkekti. Ortalama MELD skoru 14,2 (8–32) idi. Milan kriterleri dışında ( $P=0,003$ ), kötü farklılaşmış ve kolanjiokarsinom tümör bileşeni ( $P=0,003$ ), olan hepatosellüler karsinomda canlı vericili karaciğer naklinde daha kötü görünmektedir.

**Sonuçlar:** Bu çalışmada Milan dışı, az differansiye ve kolanjiokarsinom komponenti olan tümörlerin daha kötü olduğu görünmektedir.

**Anahtar kelimeler:** Hepatosellüler karsinom, Canlı vericili karaciğer nakli

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Ethics Committee Approval: Ethics committee approval was not received because of the retrospective design of the study.

Etik Kurul Onayı: Etik kurul onayı çalışmanın retrospektif doğasından dolayı alınmamıştır.

Conflict of Interest: No conflict of interest was declared by the authors.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.

Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Published: 4/25/2019  
Yayın Tarihi: 25.04.2019

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## Introduction

Hepatocellular carcinoma (HCC) is the most common malignant solid tumor of the liver, and the seventh most fatal cancer worldwide [1]. HCC is threefold more common in males than females [2]. The etiology usually involves hepatitis B infection hepatitis C infection and liver cirrhosis caused by alcoholism [3, 4].

Percutaneous alcohol injection (PAI), transarterial chemoembolization (TACE), radiofrequency ablation (RF), and microwave coagulation are local ablative treatments. Surgical resection in patients with adequate liver size without cirrhosis, and liver transplantation (LT) for those with extensive cirrhosis, are curative [5, 6]. The aim of this study was to evaluate living donor liver transplantation in hepatocellular carcinoma.

## Materials and methods

Between April 2014 and December 2017 at Medipol University Medical Faculty Hospital Organ Transplantation Department, Istanbul, Turkey, 38 patients in living donor liver transplantation for HCC were studied retrospectively.

Thirty eight patients with living donor liver transplantation were evaluated demographic features, recurrence rates and mortality rates.

### Post-transplant follow-up

In our center, Immunosuppression regimens were based on calcineurin inhibitor (tacrolimus or cyclosporine), mycophenolate mofetil and corticosteroids in pediatric recipients. Patients received control once a week for the first month after discharge, and every 15 days for the second month and monthly after that period. Every 3 months abdominal magnetic resonance imaging and thorax computed tomography was performed in these patients.

### Statistical analysis

SPSS 22.0 (SPSS for Windows, 2007, Chicago) was used for statistical analysis. Continuous variables which have normal distribution were presented as mean (standard deviation). Statistical analysis for the parametric variables was performed by the Student's T-test. The qualitative variables were given as percent and the correlation between categorical variables was investigated by the chi-square test and Fisher's exact test. Statistical significance level was defined as  $p < 0.05$ .

## Results

The mean patient age was 58.0 (9.9) (range 20–74) years; 31 (81.6%) of the 38 were male. The mean Model for End-Stage Liver Disease (MELD) score was 14.2 (8–32). In terms of etiological factors, 14 patients (36.8%) had HBV infections, 12 (31.6%) had cryptogenic, 8 (21.1%) had HCV infections, and 4 (10.5%) had alcohol-induced liver cirrhosis.

Figure 1 shows patient survival by the Milan criteria. Survival was significantly higher in patients whose tumors met the criteria than in those whose tumors did not (43 vs. 18 months,  $P = 0.003$ ).

Figure 2 shows patient survival by tumor grade; survival was significantly higher in patients with well-to-moderately differentiated than poorly differentiated carcinomas or tumors with cholangiocarcinoma components (45, 18, and 20 months, respectively,  $P = 0.003$ ).

The mean follow-up time was 18.5 months (7–44 months). Recurrence developed in 16 patients (42.1%) and 15 (39.4%) died by 44 months. The overall survival rate was 86.9% for the first year and 60.6% for the first 4 years.

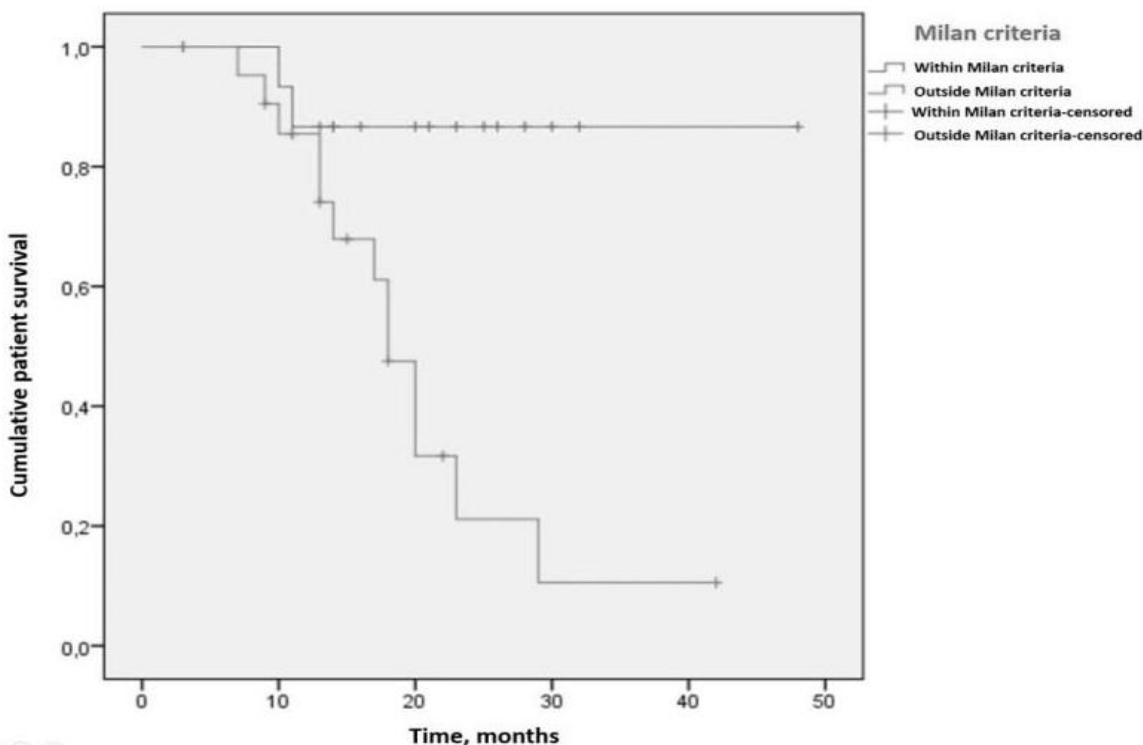


Figure 1: Patient survival by the Milan criteria

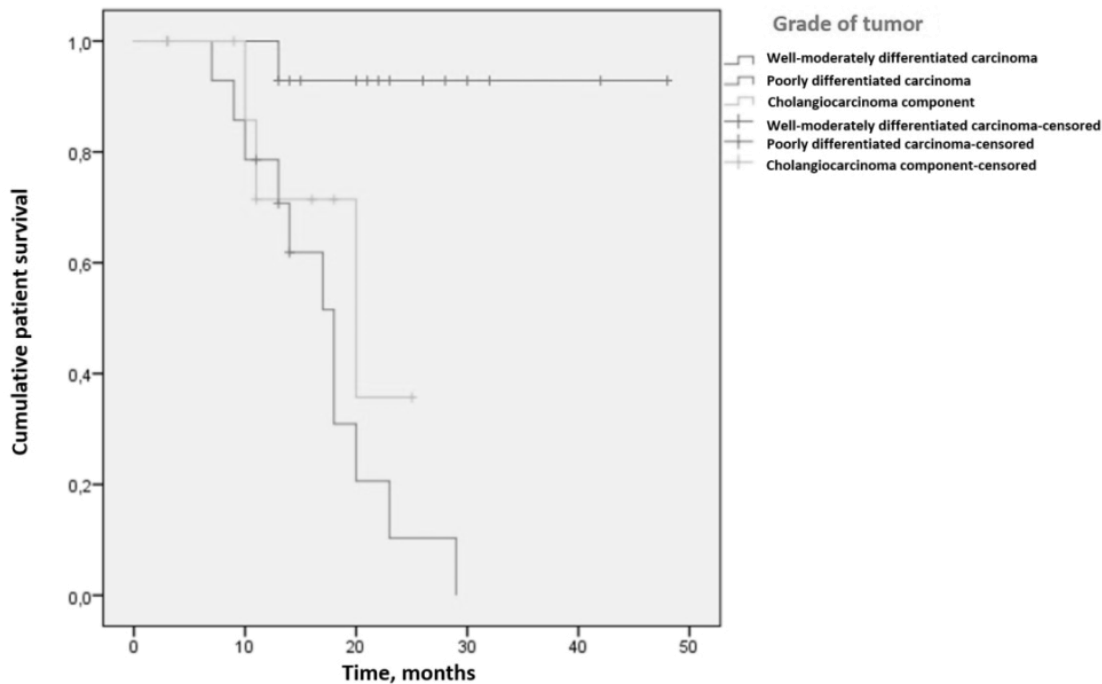


Figure 2: Patient survival by tumor grade

## Discussion

Hepatocellular carcinoma is the most common malignant solid tumor of the liver, and the seventh most fatal cancer worldwide [1]. Males constitute 75% of all patients [2]. More than 80% of hepatocellular carcinomas develop on the surface of a cirrhotic liver; the annual incidence in cirrhotic patients is 1–6% [7,8]. In non-Western countries, HCC is associated with HBV infection [9-12] and, in Western countries, with alcohol-induced cirrhosis and HCV infection [13]. In our study, 14 patients (36.8%) had HBV infections, 12 (31.6%) had cryptogenic, 8 (21.1%) had HCV infections, and 4 (10.5%) had ethanol-induced liver cirrhosis. Hematogenous spread is more common than lymphatic spread [14,15].

It is very important to evaluate both primary HCC and recurrence. Pre-transplant sensitivity of CT is about 70%. Gadolinium enhancement increases MRI sensitivity. In highly suspicious cases, Positron Emission Tomography combined with a Computed Tomography (PET/CT) and whole-body bone scintigraphy are valuable [2]. In our clinic, every 3 months, abdominal magnetic resonance imaging and thorax computed tomography was performed in these patients.

Local ablative treatments are used to treat HCCs in patients not suited to resection or transplantation. The treatments include PAI, TACE, RF, and microwave coagulation. If liver reserve is lacking because of cirrhosis, or if multiple lesions are present, surgical resection is usually not feasible. LT is highly effective and curative in those with both cirrhosis and HCC [5,6]. In this study, six patients who did not meet the Milan criteria exhibited significant tumor regression after TACE, and then underwent living donor LT.

Literatures have identified the male gender, multiple tumors, multiple lobe involvement, tumor size, metastasis, and lymphovascular invasion as poor prognostic factors [16-19]. Ernesto et al. [20] found that poorly differentiated tumors >5 cm in diameter featuring lymphovascular invasion were poorly prognostic. Mohamed et al. [21] found that many relapsed tumors were poorly differentiated and exhibited lymphovascular invasion. Tumor cells may exhibit a wide range of differentiation [22,23]. Those with intrahepatic cholangiocarcinomas are contraindicated for liver transplantation because of early recurrence and poor prognosis [24,25]. The rarest malignant liver tumor is combined hepatocellular carcinoma and cholangiocarcinoma (1% of all liver cancers). The 5-year survival rate of such patients (determined via pathological examination after transplantation) ranges from 8–85% [26]. If HCC is not treated, the 5-year survival rate is <5% [27]. Mazzaferro et al. [28] defined the Milan criteria in 1996. The Milan criteria are cirrhosis associated with a single small tumor ≤5 cm in diameter or up to three tumors <3 cm in diameter, with no vascular invasion or extra-liver metastasis. Such patients exhibited very good results after LT [28]. In most studies, the 5-year survival rates were >70% and the recurrence rates <15% [29,30].

Here, recurrence developed in 16 patients (42.1%) over the 44-month follow-up time. Two underwent resection. Fifteen patients (39.4%) died. The overall survival rate was 86.9% for the first year and 60.6% for the first four years.

Our study has several limitations. First, this study was retrospective. Second, the number of cases was small.

## Conclusion

Despite the limitations described, outside Milan criteria, poorly differentiated and cholangiocarcinoma tumor component appears to be worse in living donor liver transplantation in hepatocellular carcinoma.

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The National Library of Medicine (NLM) citation style guide is used in this paper. Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: <http://www.nlm.nih.gov/citingmedicine>