CLINICAL STUDY

Role of Locoregional Therapy and Predictors for Dropout in Patients with Hepatocellular Carcinoma Listed for Liver Transplantation

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ABSTRACT

Purpose: To identify factors associated with removal from the liver transplantation waitlist because of death, deterioration of condition, or exceeding Milan criteria in patients with hepatocellular carcinoma (HCC), with emphasis on the role of locoregional therapy (LRT), defined as percutaneous thermal ablation and drug-eluting embolic chemoembolization, as bridge therapy.

Materials and Methods: All patients listed for liver transplant at a single institution with exception points for HCC during 2004–2012 were evaluated. The most common cause of cirrhosis was hepatitis C (68%; 121/177). Seventy-one percent (125/177) of patients underwent liver transplantation, and 83% (147/177) underwent at least 1 LRT procedure. Of the 52 patients who did not undergo liver transplantation, 31 (60%) of livers were removed because of progression of HCC.

Results: The likelihood of transplant was higher for patients who received LRT (odds ratio [OR], 2.9; confidence interval [CI], 2.2–7.2) and lower for patients with multifocal tumors (OR, 0.25; CI, 0.12–0.52) and with larger tumors (OR, 0.94; CI, 0.90–0.98). Time on the waitlist (OR, 0.99; CI, 0.99–1.0) was not found to correlate with removal. LRT increased the likelihood of liver transplantation, specifically for patients with prolonged wait times. Patients who demonstrated complete response (CR) to LRT on the first follow-up imaging study were more likely to undergo liver transplantation.

Conclusions: LRT increased the likelihood of a patient with HCC achieving liver transplant, particularly in patients facing prolonged waiting times. CR after LRT significantly increased the likelihood of liver transplantation.

ABBREVIATIONS

AFP = α-fetoprotein, CI = confidence interval, CR = complete response, HCC = hepatocellular carcinoma, LRT = locoregional therapy, OR = odds ratio

Orthotopic liver transplantation is the best curative therapy for patients with unresectable hepatocellular carcinoma (HCC). However, scarcity of organ donors can result in prolonged wait times for transplantation. Dropout rates from the liver transplant waiting list are high—approximately 15%–30% at 1 year (1). Moreover, geographic variations in organ availability and rates of transplant candidate listings result in marked inequities in waitlist durations and mortality (2).

Locoregional therapy (LRT) is the cornerstone in maintaining patients with HCC within transplant criteria while awaiting a suitable organ. LRT includes percutaneous and intraarterial techniques such as thermal ablation and conventional and drug-eluting embolic transarterial chemoembolization. These techniques can be used to eradicate tumors locally within the liver and can be repeated while the patient is on the waitlist to contain tumor progression. Although no randomized

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controlled trials have been performed to demonstrate its efficacy, LRT is accepted as the standard of care for patients expected to stay on the liver transplantation waitlist for longer than 6 months (3,4).

Organ scarcity creates the need for effective bridging therapy as well as evidence-based stratification of liver transplant candidates. Identifying patients who are at high risk for dropout from the waitlist is critically important for numerous reasons. Potentially modifiable risk factors can be addressed to increase the patient's likelihood of undergoing transplantation. Furthermore, patients at high risk for tumor progression can be counseled to establish realistic expectations. Risk factors can be integrated into organ allocation algorithms such that high-risk patients are appropriately prioritized.

Previously identified risk factors for dropout from the transplantation list include demographic, imaging, and serologic factors such as elevated Model for End Stage Liver Disease score, advanced tumor stage, elevated α-fetoprotein (AFP), and larger tumor size (5–8). Conversely, LRT is believed to reduce the risk of dropout: Patients who undergo LRT and demonstrate complete response (CR) based on enhancement-based objective imaging response criteria may have lower dropout rates (6,8). In this study, a single institutional experience with patients listed for liver transplantation with exception points for HCC in a region with prolonged waitlist times was analyzed. Specifically, variables that were associated with liver transplantation, removal from the transplant waitlist, deterioration of condition, and tumor progression were evaluated. The impact of LRT on clinical outcomes was also assessed.

MATERIALS AND METHODS

Patients

This retrospective study was compliant with the Health Insurance Portability and Accountability Act and approved by the institutional review board. The study evaluated all patients with HCC listed for liver transplantation during the period 2004–2012 in a single tertiary medical center. Only patients who underwent deceased donor transplantation were included; patients who were recipients of a liver from a living donor were excluded. The diagnosis of HCC was made by meeting Organ Procurement and Transplantation Network/United Network for Organ Sharing imaging criteria for HCC from computed tomography or magnetic resonance imaging studies or by biopsy. The image-based diagnosis of HCC was confirmed by a radiologist (R.A.S.) with fellowship training in abdominal imaging. LRT was defined in this analysis as percutaneous thermal ablation (specifically, radiofrequency and microwave ablation) and drug-eluting embolic chemoembolization. Two patients who received external proton beam radiation therapy in a clinical trial setting were also included.

Data Collection

Electronic medical records and imaging data were reviewed, and demographic and serologic data were collected. Imaging data including largest tumor size (largest long-axis dimension) and solitary or multifocal HCC at the time of transplantation listing and total number of LRT procedures were obtained. Patients who successfully underwent liver transplantation were followed until March 31, 2014, to assess for tumor recurrence. Response to the initial LRT procedure based on modified Response Evaluation Criteria In Solid Tumors criteria was determined for all patients who underwent at least one LRT procedure.

Patient Demographics

Between 2004 and 2012, 177 patients were listed for liver transplantation with Model for End Stage Liver Disease exception points for HCC (Table 1). The most common cause of cirrhosis was hepatitis C (68%; 121 of 177), followed by alcohol consumption (14%; 24 of 177). Most patients (86%; 152 of 177) were men. Liver transplantation was performed in 71% of patients (125 of 177). One hundred forty-seven patients (83%; 147 of 177) underwent at least one LRT procedure; 217 LRT procedures in total were performed. Thermal ablation was more commonly performed (69%; 149 of 217) than drug-eluting embolic chemoembolization (30%; 66 of 217). Of the 52 patients who did not undergo liver transplantation, 31 (60%) were removed from the waiting list because of progression of HCC exceeding Milan criteria; 14 (27%) died while on the waiting list, including four patients whose deaths were related to LRT procedures; and seven patients (13%) were removed because of deterioration of their condition precluding liver transplantation.

Data and Statistical Analysis

Statistically significant correlations between demographic and imaging variables with removal from the liver

Table 1. Baseline Characteristics of Study Cohort

Variables	Transplant	Nontransplant	*P*
No. (% total)	125 (71%)	52 (29%)	
Age (y), median (range)	58.4 (40.5–71.5)	57.5 (49–70)	.38
Sex (M/F)	106/19	46/6	.64
ABO type			.6
A	32%	39%	
B	17%	9%	
AB	8%	7%	
O	43%	43%	
Cause of cirrhosis			.35
HCV	64%	78.8%	
EtOH	15.2%	9.6%	
HBV	7.2%	3.8%	
Other	13.6%	7.7%	

EtOH = ethyl alcohol; F = female; HBV = hepatitis B virus; HCV = hepatitis C virus; M = male.