The Race to Liver Transplantation: A Comparison of Patients With and Without Hepatocellular Carcinoma from Listing to Post-Transplantation

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BACKGROUND: There are geographic and disease-specific inequities in liver allograft distribution. We examined differences between hepatocellular carcinoma (HCC) and non-HCC liver transplantation (LT) candidates from listing through LT in a region with prolonged wait times.

STUDY DESIGN: We performed a single-center retrospective study, from 2005 to 2013, of adult, primary, nonstatus 1 candidates who were listed and subsequently underwent LT (n = 270), or were removed because of death or clinical deterioration (n = 277).

RESULTS: Of the HCC candidates removed from the waitlist (n = 184), 5.5% died waiting, 25.5% deteriorated clinically, and 69% had LT. Of the non-HCC candidates (n = 363), 38.8% died waiting, 21.8% clinically deteriorated, and 39.4% had LT. Of the LT recipients, 127 (47%) had HCC. When compared with non-HCC transplant recipients, HCC recipients spent more time on the waitlist (435 ± 475 vs 301 ± 604 days, p = 0.045) and from listing until LT had higher total pre-transplant hospital admissions per patient (1.1 ± 1.2 vs 0.8 ± 1.8, p < 0.001). These admissions were more often planned (0.65 ± 0.88 vs 0.17 ± 0.52 planned admissions per patient, p < 0.001) and of shorter duration (2.7 ± 2.8 vs 5.2 ± 4.6 days, p < 0.001). The HCC and non-HCC recipients demonstrated similar overall post-transplant survival (5 year 80% vs. 83%, respectively; p = 0.84).

CONCLUSIONS: Despite a shorter wait to have LT, non-HCC candidates at our center have inferior waitlist outcomes. National reprioritization of liver allocation to improve access for non-HCC candidates may lead to increased wait time and resource use for the HCC population; however, a mortality benefit may exist for the non-HCC candidate lacking the benefit of time. (J Am Coll Surg 2015;220:1001−1007. © 2015 by the American College of Surgeons)

Since 2002, allocation of livers for transplantation has been based on the Model for End-Stage Liver Disease (MELD) score, which is used to predict 90-day waitlist mortality from the time of listing. The MELD score does not accurately capture 90-day mortality for particular subsets of transplant candidates, including most notably, patients with hepatocellular carcinoma (HCC). This group has a low risk of death from liver failure alone, so patients whose tumors meet Milan criteria are granted exception points that accrue over time in order to allow for timely access to liver transplants. However, the initial exception point allocation system for HCC resulted in giving HCC candidates an advantage over non-HCC candidates.[1] Given this, there were 2 subsequent downward adjustments in exception point allocation for HCC patients in April 2003 and again in January 2004.[2] Despite these corrections, multiple studies have shown that non-HCC transplant candidates continue to have significantly

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Abbreviations and Acronyms
HCC = hepatocellular carcinoma
LT = liver transplantation
MELD = Model for End-Stage Liver Disease
UNOS = United Network for Organ Sharing

higher waitlist drop-off rates than HCC patients due to mortality or clinical deterioration.[3-7]

Although MELD scores aim for allocation based on severity of illness, a geographic disparity persists in liver allograft distribution, as demonstrated by the inequity across donation service areas (DSAs) with regard to the availability of livers, death rates, transplantation rates, and mean transplantation MELD scores.[8] Our group previously demonstrated that there is considerable geographic inequity in the demand-to-supply ratio in United Network for Organ Sharing (UNOS) Region 1 as compared with other regions, leading to prolonged waitlist times for both HCC and non-HCC transplant candidates.[9,10]

Given the listing prioritization of HCC patients, and the increased waitlist drop-off rate of non-HCC candidates, further assessment of the current system of liver allocation is warranted. We sought to compare patient characteristics, pre-transplantation hospital resource use, and post-transplantation outcomes of HCC vs non-HCC transplant candidates at a single center in a region with prolonged waitlist times.

METHODS

A single center retrospective study was conducted from January 2005 to January 2013 at a tertiary care center within UNOS Region 1. All adult, primary, non-status 1 recipients who were listed and subsequently underwent liver transplantation (LT) or were removed because of death or clinical deterioration were included in the study. Patients were divided into 2 groups depending on the presence or absence of HCC. Patients with final pathology demonstrating cholangiocarcinoma or mixed HCC-cholangiocarcinoma were excluded from the analysis. Vital status, date of recurrence, and date of death were determined by review of medical records and verified by the Social Security Death Master File. In addition, all adult, primary transplant candidates who were removed from the waitlist for reasons coded as either deterioration in their condition or death were noted and analyzed.

Primary end points were LT candidate pre-transplantation resource use, as demonstrated by hospital admissions, and overall survival from the time of LT for recipients. Differences in patient wait time, sex, age at transplantation, MELD score (at listing, at transplantation, and match MELD), cause of liver failure, use of MELD exception points, patient insurance, and race were compared between HCC and non-HCC groups. Immunosuppression was similar for the HCC and non-HCC cohorts, and consisted of high dose steroids at the time of transplantation, as well as an antiproliferative agent and a calcineurin inhibitor. Per institutional protocol, patients with hepatitis C virus underwent rapid steroid withdrawal. MELD exception points for HCC in UNOS Region 1 were granted for those candidates with HCC within Milan criteria; MELD exception points were not, however, granted for patients within University of California, San Francisco criteria or beyond. Causes of liver failure were categorized into hepatitis C virus, hepatitis B virus, alcohol, cholestatic (inclusive of autoimmune hepatitis, primary biliary cirrhosis, and primary sclerosing cholangitis), nonalcoholic steatohepatitis, and other (inclusive of Alagille syndrome, acetaminophen overdose, hemachromatosis, cryptogenic cirrhosis, alpha 1 antitrypsin, amyloidosis, biliary atresia, Caroli disease, granulomatous hepatitis, Wilson disease, and Budd-Chiari). A primary cause was identified in patients who had multiple causes of liver failure by retrospective chart review performed by 2 independent reviewers. Pre-transplantation admissions were categorized as either planned or unplanned. Planned admissions included those during which a patient received a pre-transplantation treatment for HCC (eg, chemoembolization, radiofrequency ablation, etc) or admissions for cancelled transplants or elective procedures.

Continuous variables were compared using unpaired 2-sample t-tests, and categorical variables were compared using 2-group proportion tests. Differences in admissions between the 2 groups were compared using Wilcoxon rank-sum tests. Stratified Kaplan-Meier analyses using right-censored datasets were used to evaluate disease-free as well as overall survival. Disease-free survival was defined as the lack of both mortality and disease recurrence in the HCC group, compared with the lack of mortality in the non-HCC group. Differences in disease-free and overall survival between the non-HCC and HCC groups were assessed using log-rank tests. For all statistical tests, a pre-specified 2-sided p value < 0.05 was considered significant. Statistical analyses were primarily conducted using STATA/MP 11 (StataCorp). This study was approved by the Massachusetts General Hospital Institutional Review Board (Protocol 2014P000230).

RESULTS

Over the 8-year study period, 547 LT candidates met inclusion criteria (Fig. 1). Of these patients, 184 had HCC