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Liver transplantation for hepatocellular carcinoma: analysis of factors predicting outcome in 1074 patients in OPTN Region 5

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Abstract

Previous studies on loco-regional therapy (LRT) and alpha-fetoprotein (AFP) in predicting outcome after liver transplant (LT) for hepatocellular carcinoma (HCC) have shown inconsistent results. We analyzed the OPTN database in Region 5 from January 2004 to January 2009 and performed univariate and multivariate analysis of 11 pre-transplant recipient and donor variables in 1074 patients with HCC meeting Milan criteria to detect association with post-LT tumor recurrence or mortality. Mean waitlist time was 438 d. The 1- and 5-yr post-LT survival was 91.1% and 71.1%, respectively. In multivariate analysis, AFP before LT was the only predictor of HCC recurrence. The association between AFP and HCC recurrence was observed only in the subgroup receiving LRT but not in the subgroup without LRT. Predictors of mortality in multivariate analysis were HCC recurrence, Donor Risk Index, last AFP before LT, and MELD score. AFP before LT was the strongest predictor of post-transplant HCC recurrence or death in multivariate analysis. In conclusion, in Region 5 with prolonged waitlist time, high AFP was the only pre-transplant variable predicting post-transplant tumor recurrence and mortality for HCC meeting Milan criteria. Our results also supported the importance of the effects of LRT on AFP in predicting prognosis.

Keywords

alpha-fetoprotein; hepatocellular carcinoma; liver transplant; loco-regional therapy

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Authors' contributions

BM: participated in research design, writing of the manuscript, and analysis of data. JLS: participated in research design, writing of the manuscript, and analysis of data. AMH: participated in the collection and analysis of data. JPR: participated in research design and writing of the manuscript. FYK: participated in research design, writing of the manuscript, and analysis of data.

In the United States, the incidence of hepatocellular carcinoma (HCC) has continued to rise for the past 2 decades, and approximately 20 000 new cases of HCC are diagnosed each year (1). Liver transplantation (LT) has made a substantial impact on the treatment of HCC for more than a decade, to the point where we no longer question the value of this life-saving therapy but instead grapple with how best to use a scarce resource for the maximum benefit of the rapidly growing population with HCC (2–4). While the Milan criteria (5) based on tumor size and number are considered the benchmark for the selection of candidates for LT (3), recurrence of HCC still occurs in 10–20% of patients within the first 5 yr after LT (2, 5–9).

It has become increasingly evident that additional factors beyond the size and number of HCC are important determinants of post-transplant outcome (2, 10). Microvascular invasion is well established to be an important risk factor for HCC recurrence after LT (6–10), but there are currently no reliable means to identify microvascular invasion prior to LT (11). Identification of tumor and biologic markers that may reliably predict tumor recurrence or microvascular invasion has been an area of intense research interest. The optimal alpha-fetoprotein (AFP) cutoff that correlates with the risk of HCC recurrence has not been well defined (10). Whether pre-transplant loco-regional therapy (LRT), including trans-arterial chemoembolization and radiofrequency ablation, is beneficial remains unclear (3, 10, 12). Interpretation of published data on the impact of these pre-transplant factors is difficult due to small sample size in many single center studies, and the heterogeneous nature of the patient populations being studied, with significant differences in pre-transplant tumor stage, selection criteria for LT, the use of LRT prior to LT, and the length of waitlist time (10).

The primary objective of this study was to evaluate pre-transplant recipient and donor factors that predict post-transplant outcome using a large Organ Procurement and Transplantation Network (OPTN) database in Region 5. We only included patients with pre-transplant HCC stage meeting Milan criteria who received priority status for LT under the model for end-stage liver disease (MELD) system of organ allocation.

Materials and methods

Study design and subject selection

This study was approved by the Institutional Review Board of the University of California San Francisco. We analyzed OPTN data for LT in Region 5 from January 2004 to January 2009 under the MELD system of organ allocation. Region 5 includes California, Arizona, Nevada, New Mexico, and Utah. Subjects were identified through the OPTN database and were included if they had pre-transplant diagnosis of HCC and had been granted OPTN exception points for HCC meeting Milan criteria. Patients were excluded if the liver explant demonstrated malignancy other than HCC, or if their pre-transplant tumor size or number was outside of Milan criteria.

The two primary outcomes of interest are HCC recurrence and patient survival after LT. HCC recurrence was identified using OPTN data derived from both the post-transplant malignancy form and the cause of death on the transplant follow-up form. We evaluated 11 pre-transplant variables to detect association with post-transplant HCC recurrence or death.

They included recipient age, gender, race, blood group, liver disease, AFP at the time MELD exception was granted, latest AFP before LT, calculated MELD score before LT, waitlist time, history of loco-regional therapy, and donor characteristics using the Donor Risk Index (DRI). DRI is used to assess the quality of donor organ based on seven variables: age, cause of death, race, partial vs. whole grafts, height, cold ischemic time, and location of donor relative to the transplant center (13). Race was divided into five categories: white, black, Asian/Pacific Islander, Hispanic, and others. The latest laboratory MELD score prior to LT was used. The diagnosis of liver disease was divided into five categories: hepatitis B, hepatitis C, alcoholic liver disease, HCC only, and others. LRT included chemoembolization, radiofrequency ablation, cryoablation, or chemical ablation.

Statistical analysis

Patient survival was estimated using the Kaplan–Meier method. Univariate analysis was performed to identify correlates of the primary outcome measures. For continuous variables, *t*-tests were used for normally distributed variables, and Mann– Whitney *U*-tests were used for variables lacking normal distribution. Chi-square analysis was used to compare categorical variables. Variables with documented univariable association with HCC recurrence or death were subsequently entered into multivariate logistic regression models, along with variables of expected clinical relevance. Continuous independent variables lacking normal distribution were entered into regression models with natural log transformation.

Results

Survival and HCC recurrence

During the study period from January 2004 to January 2009, a total of 1074 patients underwent LT for HCC meeting Milan criteria who were granted OPTN MELD exception points in Region 5. An additional 14 patients who had diagnosis of tumors other than HCC who received LT during the same period were excluded.

The mean waitlist time to LT was 438 d. LRT was performed before LT in 802 of 1074 (74.7%) patients, including 505 patients who received TACE, 238 with RFA, 52 with chemical ablation, and seven with cryoablation. The mean waiting time to LT was 492 d for the group receiving LRT vs. 410 d for the group not receiving LRT before LT ($p = 0.03$). Those who received LRT had a significantly lower median MELD score than those who did not (11 vs. 13, $p < 0.001$).

The 1- and 5-yr overall patient survival was 91.1% and 71.1%, respectively. HCC recurrence was documented in 68 patients (6%). The mean time to HCC recurrence was 437 d (SD 382.4), and the median time to HCC recurrence was 297 d (range 33–1723 d) from LT among 34 of 68 patients in whom information on the date of HCC recurrence was available.

Predictors of HCC recurrence

Table 1 summarizes the results of the univariate analysis of the pre-transplant variables in predicting HCC recurrence. Whether the patient received LRT or not and the type of LRT were not significant predictors of HCC recurrence. Only initial AFP at the time MELD exception was granted and the last AFP prior to LT was significant predictors of HCC recurrence in univariate analysis. Based on an *a prioiri* hypothesis, we included waitlist time along with AFP at the time of listing and prior to LT, and only the most recent AFP prior to LT proved to be a significant predictor of HCC recurrence (Table 2). We performed additional analyses to determine the interaction of LRT with AFP in predicting tumor recurrence. When we separated the patients into those who had received LRT and those who had not, both initial and latest AFP were predictive of HCC recurrence in only the subgroup with loco-regional therapy (Table 3).

The receiver operating characteristics (ROC) curve generated for the AFP level, and HCC recurrence showed an area under the curve (AUC) of 0.633. We then evaluated ascending centile cutoff values of AFP sequentially and found an AFP value ≥ 300 ng/dL to have the highest odds ratio (OR) (2.52; 95% CI 3.5–4.72) in predicting HCC recurrence.

The median waitlist time was 215 d (IQR 125–380 d) for those who received LRT and 230 d (IQR 100–595 d) for those who did not, and the mean waitlist time was 410 d and 490 d, respectively ($p = 0.03$). We did not find any significant interaction between waitlist time and LRT in this multivariate analysis.

Predictors of post-transplant mortality

Table 4 summarizes the results of univariate analysis of pre-transplant variables associated with post-transplant mortality. HCC recurrence was the strongest predictor of mortality – 79.7% of those with HCC recurrence had died vs. 20.3% of those without HCC recurrence ($p < 0.001$). Recipient age, calculated MELD score, initial and last AFP before LT, and DRI were statistically significant predictors of mortality after LT. In the multivariate logistical regression model, HCC recurrence, the last AFP before LT, calculated MELD score, and DRI were significant predictors of mortality (Table 5).

Predictors of the combined end points of post-transplant HCC recurrence or mortality

Due to the possibility of underreporting of tumor recurrence as the cause of death after LT, we performed additional analysis for predictors of the combined end point of either HCC recurrence or death. In the multivariate logistic regression (Table 6), the last AFP before LT was the strongest predictor of post-transplant HCC recurrence or mortality. Calculated MELD score and DRI were also significant predictors of the combined end points.

Discussion

It has been suggested that deceased donor LT for HCC should achieve similar post-transplant survival compared to non-malignant indications in the current era of severe organ shortage (3). Although many single center studies have shown excellent post-transplant outcome for HCC using Milan or modestly expanded criteria for patient selection (5, 6, 10,

14), registry data that reflect more global experience with LT have continued to show inferior results with HCC compared to non- HCC indications (15). As clearly shown in the present study, recurrence of HCC after LT is the most important cause of post-transplant mortality. Consequently, there is a need to identify additional factors beyond Milan criteria that may further reduce the likelihood of tumor recurrence and refine the current selection criteria. A plethora of studies have been published to address this issue, but many are limited by the small sample size leading to a lack of statistical power, or the heterogeneity of the study population (10). Many studies included a substantial proportion of patients with tumors beyond Milan criteria.

The present study focused on pre-transplant variables predicting HCC recurrence in a large cohort of patients with pre-transplant HCC meeting Milan criteria in the MELD era. We found AFP prior to LT to be the only pre-transplant variable associated with HCC recurrence, and also one of the independent predictors of post-transplant survival, supporting the growing evidence that high pre-transplant AFP has a negative impact on post-transplant outcome (6, 10, 15–20). In a separate analysis of patients who received LRT, both AFP at listing and the latest AFP before LT were found to be independent predictors of post-transplant tumor recurrence. This finding suggests that persistently elevated AFP despite LRT is an important marker for tumor progression or worse tumor biology, leading to a higher risk for post-transplant tumor recurrence. An AFP level ≥ 300 ng/mL appears to best predict HCC recurrence in our study. However, the association between AFP and tumor recurrence over a wide range of AFP levels has yielded an AUC of only 0.633 for the ROC. Other published studies have reported a pre-transplant AFP level greater than 300 ng/mL (8), 400 ng/mL (16, 18, 19), or 1000 ng/mL (6, 20–22) to be the best cutoff in predicting tumor recurrence. The most appropriate AFP level to serve as an additional exclusion criterion for LT still needs to be further elucidated in future studies.

Loco-regional therapy has been used frequently in clinical practice to control tumor growth, serving as a bridge to LT, but the benefits of LRT in this setting have remained unproven (3, 12). It has been suggested that LRT is cost-effective if the waiting time for LT exceeds 6 months (23). According to Scientific Registry of Transplant Recipient (SRTR) data, the percentage of patients with HCC on the waiting list for LT who have received LRT ranged from 31% to 65% in different regions (24). In the present study, the percentage of patients receiving LRT is considered high at 66% when compared to the national average. This is not surprising given the prolonged mean waiting time of 438 d in our region during the study period. A previous analysis of SRTR data (24) showed a small but statistically significant survival benefit at 3 yr after LT for patients who received LRT when compared to those who did not (79% vs. 75%, respectively). However, the survival analysis was not controlled for recipient and donor factors that might influence survival. The present study failed to demonstrate a benefit of LRT on either tumor recurrence or survival. A meta-analysis of published studies similarly did not demonstrate a clear benefit of LRT on post-transplant tumor recurrence or survival (12). An important factor not evaluated in the present study is the response to LRT based on imaging, which has been suggested to be a key determinant of prognosis after LT (25, 26). This observation has also filtered into the “ablate and wait” concept (27) that may prove to be an important selection tool for LT based on the effects of LRT. These are intriguing issues that require validation in large, multicenter studies.

Large registry data generally relied on only survival information (15, 16, 18, 19, 24). In the present study, we obtained HCC recurrence data and included both HCC recurrence and survival as the end points in our analysis. A recent study (28) compared the observed HCC recurrence data in the OPTN database to expected rates calculated using a hierarchical model for recurrence adjusted for recipient and tumor characteristics and found that the observed HCC recurrence rate was not significantly lower than the expected rate at any center, suggesting that no systematic underreporting has occurred. The study therefore validated the OPTN HCC recurrence data and supported the potential for further analysis (28).

Several non-tumor factors that are associated with post-transplant mortality in this study merit further discussions. We found that higher recipient calculated MELD score was associated with worse post-transplant survival. A previous study using OPTN data also reported higher post-transplant mortality in HCC patients with a calculated MELD score of ≥ 20 (15). In the non-HCC population, published data evaluating recipient MELD score as a predictor of mortality after LT have shown inconsistent results (29–33). As patients in this study received LT under MELD exception for HCC and had low mean calculated MELD score (Table 4), the observation that calculated MELD score is a predictor of post-transplant mortality is somewhat surprising and its implications are also unclear. Prospective studies are needed to further evaluate the impact of calculated MELD score on both waitlist mortality and post-transplant mortality in patients with HCC. Another finding in the present study is the correlation between higher DRI and worse post-transplant survival. The DRI, originally developed based on analysis of OPTN data (13), has recently been validated independently as an outcome predictor after LT in a large cohort of patients in the Euro-transplant region (34), where the mean DRI was remarkably higher when compared to that in OPTN (1.71 vs. 1.45) as well as our cohort. Weighing the risk of waitlist dropout due to tumor progression against the risk for worse post-transplant outcome using lower quality organs continues to be a challenging task facing the transplant surgeons.

In conclusion, in Region 5 with prolonged waitlist time, patients receiving MELD exception for HCC meeting Milan criteria had a 5-yr post-transplant survival of 71%. High preoperative AFP was the sole predictor of HCC recurrence and also one of the independent predictors of mortality after LT. We did not demonstrate a significant impact of preoperative LRT on post-transplant outcome, but high AFP despite LRT was associated with a worse prognosis after LT. This finding supported the importance of the effects of LRT on AFP in predicting post-transplant outcome. Considerations should be made for incorporating AFP as an additional selection criterion for LT among patients with HCC meeting Milan criteria.

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References

1. El-Serag HB. Hepatocellular carcinoma. N Engl J Med. 2011; 365:1118. [PubMed: 21992124]

2. Pomfret EA, Washburn K, Wald C, et al. Report of a national conference on liver allocation in patients with hepatocellular carcinoma in the United States. Liver Transpl. 2010; 16:262. [PubMed: 20209641]

3. Clavien PA, Lesurtel M, Bossuyt PM, Gores GJ, Langer B, Perrier A. OLT for HCC Consensus Group. Recommendations for liver transplantation for hepatocellular carcinoma: an international consensus conference report. Lancet Oncol. 2012; 13:11.

4. Volk ML, Vijan S, Marrero JA. A novel model measuring the harm of transplanting hepatocellular carcinoma exceeding Milan criteria. Am J Transplant. 2008; 8:839. [PubMed: 18318783]

5. Mazzaferro V, Regalia E, Doci R, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. N Engl J Med. 1996; 334:693. [PubMed: 8594428]

6. Yao FY, Xiao L, Bass NM, Kerlan R, Ascher NL, Roberts JP. Liver transplantation for hepatocellular carcinoma: validation of the UCSF-expanded criteria based on preoperative imaging. Am J Transplant. 2007; 7:2587. [PubMed: 17868066]

7. Jonas S, Bechstein WO, Steinmuller T, et al. Vascular invasion and histopathologic grading determine outcome after liver transplantation for hepatocellular carcinoma in cirrhosis. Hepatology. 2001; 33:1080. [PubMed: 11343235]

8. Figueras J, Ibanez L, Ramos E, et al. Selection criteria for liver transplantation in early-stage hepatocellular carcinoma with cirrhosis: results of a multicenter study. Liver Transpl. 2001; 10:877. [PubMed: 11679986]

9. Parfitt JR, Marotta P, Alghamdi M, et al. Recurrent hepatocellular carcinoma after transplantation: use of a pathological score on explanted livers to predict recurrence. Liver Transpl. 2007; 13:543. [PubMed: 17394152]

10. Prasad KR, Young RS, Burra P, et al. Summary of candidate selection and expanded criteria for liver transplantation for hepatocellular carcinoma. A review and consensus statement. Liver Transpl. 2011; 17:S81. [PubMed: 21748847]

11. Gouw AS, Balabaud C, Kusano H, Todo S, Ichida T, Kojiro M. Markers for microvascular invasion in hepatocellular carcinoma; where do we stand? Liver Transpl. 2011; 17(Suppl 2):S72. [PubMed: 21714066]

12. Lesurtel M, Mullhaupt B, Pestalozzi BC, Pfammatter T, Clavien PA. Transarterial chemoembolization as a bridge to liver transplantation for hepatocellular carcinoma: an evidence-based analysis. Am J Transplant. 2006; 6:2644. [PubMed: 16939518]

13. Feng S, Goodrich NP, Bragg-Gresham JL, et al. Characteristics associated with liver graft failure; the concept of a donor risk index. Am J Transpantl. 2006; 6:783.

14. Duffy JP, Vardanian A, Benjamin E, et al. Liver transplantation criteria for hepatocellular carcinoma should be expanded: a 22-year experience with 467 patients at UCLA. Ann Surg. 2007; 246:502. [PubMed: 17717454]

15. Ioannou GN, Perkins JD, Carithers RL. Liver transplantation for hepatocellular carcinoma: the impact of the MELD allocation system and predictors of survival. Gastroenterology. 2008; 134:1342. [PubMed: 18471511]

16. Toso C, Asthana S, Bigam DL, Shapiro J, Kneteman NM. Reassessing selection criteria prior to liver transplantation for hepatocellular carcinoma utilizing the Scientific Registry of Transplant Recipient Database. Hepatology. 2009; 49:832. [PubMed: 19152426]

17. Hakeem AR, Young RS, Marangoni G, Lodge JP, Prasad KR. Systematic review: the prognostic role of alpha-fetoprotein following liver transplant for hepatocellular carcinoma. Aliment Pharmacol Ther. 2012; 35:987. [PubMed: 22429190]

18. Merani S, Majno P, Kneteman NM, et al. The impact of waiting list alpha-fetoprotein changes on the outcome of liver transplant for hepatocellular carcinoma. J Hepatol. 2011; 55:814. [PubMed: 21334400]

19. Mailey B, Artinyan A, Khalili J, et al. Evaluation of absolute serum a-fetoprotein levels in liver transplant for hepatocellular cancer. Arch Surg. 2011; 146:26. [PubMed: 21242442]

20. Sotiropoulos GC, Lang H, Nadalin S, et al. Liver transplantation for hepatocellular carcinoma: University Hospital Essen experience and metaanalysis of prognostic factors. J Am Coll Surg. 2007; 205:661. [PubMed: 17964442]

21. Todo C, Furukawa H, Tada M. Japanese Liver Transplantation Study Group. Extending indication: role of living donor liver transplantation for hepatocellular carcinoma. Liver Transpl. 2007; 13(Suppl 2):S48. [PubMed: 17969069]
22. Duvoux C, Roudot-Thoraval F, Decaens T, et al. Liver transplantation for hepatocellular carcinoma: a model including a-fetoprotein improves the performance of Milan criteria. Gastroenterology. 2012; 143:986. [PubMed: 22750200]
23. Llovet JM, Mas X, Aponte JJ, et al. Cost effectiveness of adjuvant therapy for hepatocellular carcinoma during the waiting list for liver transplantation. Gut. 2002; 50:123. [PubMed: 11772979]
24. Freeman RB Jr, Steffick DE, Guidinger MK, Farmer DG, Berg CL, Merion RM. Liver and intestinal transplantation in the United States, 1997–2006. Am J Transpl. 2008; 8:958.
25. Otto G, Herber S, Heise M, et al. Response to transarterial chemoembolization as a biological selection criterion for liver transplantation in hepatocellular carcinoma. Liver Transpl. 2006; 12:1260. [PubMed: 16826556]
26. Millonig G, Graziadei IW, Freund MC, et al. Response to preoperative chemoembolization correlates with outcome after liver transplantation in patients with hepatocellular carcinoma. Liver Transpl. 2007; 13:272. [PubMed: 17256758]
27. Roberts JP, Venook A, Kerlan R, Yao F. Hepatocellular carcinoma: ablate and wait versus rapid transplantation. Liver Transpl. 2010; 16:925. [PubMed: 20658555]
28. Samoylova ML, Dodge JL, Vittinghoff E, Yao FY, Roberts JP. Validating posttransplant hepatocellular carcinoma recurrence data in the United Network for Organ Sharing database. Liver Transpl. 2013; 19:1318. [PubMed: 24039140]
29. Brown RS Jr, Kumar KS, Russo MW, et al. Model for end-stage liver disease and Child-Turcotte-Pugh score as predictors of pretransplantation disease severity, post-transplantation outcome, and resource utilization in United Network for Organ Sharing status 2A patients. Liver Transpl. 2002; 8:278. [PubMed: 11910574]
30. Narayanan Menon KV, Nyberg SL, Harmsen WS, et al. MELD and other factors associated with survival after liver transplantation. Am J Transplant. 2004; 4:819. [PubMed: 15084180]
31. Desai NM, Mange KC, Crawford MD, et al. Predicting outcome after liver transplantation: utility of the model of end-stage liver disease and a newly derived discrimination function. Transplantation. 2004; 77:99. [PubMed: 14724442]
32. Weismuller T, Fikatas P, Schmidt J, et al. Multicenter evaluation of model for end-stage liver disease-based allocation and survival after liver transplantation in Germany – limitations of the ‘sickest first’ concept. Transpl Int. 2011; 24:91. [PubMed: 20819196]
33. Dutkowski P, Oberkofler CE, Slankamenac K, et al. Are there better guidelines for allocation in liver transplantation? A novel score targeting justice and utility in the model of end-stage liver disease era. Ann Surg. 2011; 254:745. [PubMed: 22042468]
34. Blok JJ, Braat AE, Adam R, et al. Validation of the donor risk index in orthotopic liver transplantation within the Eurotransplant region. Liver Transpl. 2012; 18:113.

Table 1

Population characteristics by HCC recurrence

	No Recurrence N = 1010	Recurrence N = 64	p-value
Male, N (%)	760 (75.3)	48 (75.0)	0.97
Age (yr), mean (SD)	56.7 (7.5)	58.5 (7.4)	0.07
Race, N (%)			
White	469 (46.4)	34 (51.3)	0.37
Black	46 (4.6)	4 (6.3)	
Asian/Pacific Islander	230 (22.8)	16 (25.0)	
Hispanic	175 (17.3)	7 (10.9)	
Other	90 (8.9)	3 (4.7)	
Underlying liver disease, number (%)			
Hepatitis C	577 (57.1)	30 (46.9)	0.16
Hepatitis B	108 (10.7)	8 (12.5)	
Alcoholic liver disease	76 (7.5)	6 (9.4)	
HCC alone	110 (10.9)	13 (20.3)	
Other	139 (13.8)	7 (10.9)	
MELD score, mean (SD)	14.0 (7.7)	15.6 (9.3)	0.11
History of loco-regional therapy, number (%)	659 (65.3)	47 (73.4)	0.18
Radiofrequency ablation	225 (22.3)	13 (20.3)	0.71
Chemoembolization	469 (46.4)	36 (56.3)	0.13
Cryoablation	7 (0.7)	0 (0.0)	0.50
Chemical ablation	47 (4.7)	5 (7.8)	0.25
More than one method of ablation	88 (8.7)	7 (10.9)	0.54
Waitlist time (days), median (IQR)	219 (118–434)	194 (111–374)	0.62
Donor Risk Index, mean (SD)	1.41 (0.36)	1.46 (0.34)	0.30
Initial AFP (ng/dL), median (IQR)	12 (5–42)	25 (7.5–108.5)	0.029
Final AFP (ng/dL), median (IQR)	12 (5–52)	27 (11–187.5)	<0.001

Table 2

Multivariate analysis of factors associated with recurrence of HCC

Variable	Odds ratio	95% confidence interval	p-value
Initial AFP (natural log)	0.86	0.67–1.09	0.21
Final AFP (natural log)	1.40	1.11–1.76	0.004
Wait list time (days)	0.99991	0.9995–1.0004	0.72

Table 3

Association between AFP and HCC recurrence in patients with and without loco-regional therapy

	No Recurrence	Recurrence	p-value
Any history of loco-regional therapy (number)	659	47	
Initial AFP, median (IQR)	11 (5–36)	22 (7–86)	0.047
Final AFP, median (IQR)	11 (5–41)	37 (10–305)	0.001
No history of loco-regional therapy (number)	346	17	
Initial AFP, median (IQR)	14 (5–63)	25 (9–139)	0.42
Final AFP, median (IQR)	15 (5–73)	25 (14–139)	0.21

Table 4

Population characteristics by mortality after liver transplant

	Alive at last follow-up N = 907	Dead at last follow-up N = 167	p-value
Male, n (%)	683 (75.3)	125 (74.9)	0.90
Age (yr), mean (SD)	56.6 (7.6)	58.1 (7.1)	0.02
Race, n (%)			
White	417 (46.0)	86 (51.5)	0.55
Black	40 (4.4)	10 (6.0)	
Asian/Pacific Islander	217 (23.9)	29 (17.4)	
Hispanic	155 (17.1)	27 (16.2)	
Other	78 (8.6)	15 (9.0)	
Underlying liver disease, number (%)			
Hepatitis C	504 (55.6)	103 (61.7)	0.35
Hepatitis B	104 (11.5)	12 (7.2)	
Alcoholic liver disease	69 (7.6)	13 (7.8)	
HCC alone	104 (11.5)	19 (11.4)	
Other	126 (13.9)	20 (12.0)	
MELD score, mean (SD)	13.8 (7.5)	15.7 (14.3)	0.004
History of loco-regional therapy, number (%)	600 (66.2)	106 (63.5)	0.50
Waitlist time (days), median (IQR)	209 (118–415)	248 (118–620)	0.05
Donor Risk Index, mean (SD)	1.41 (0.36)	1.48 (0.38)	0.01
Initial AFP (ng/dL), median (IQR)	11 (5–41)	17 (7–90)	0.005
Final AFP (ng/dL), median (IQR)	12 (5–49)	23 (7–141)	0.002
HCC recurrence, number (%)	13 (1.4)	51 (30.5)	<0.001

Table 5

Multivariate regression of factors associated with death after liver transplant

Variable	Odds ratio	95% confidence interval	p-value
HCC recurrence	28.0	14.6–53.7	<0.001
MELD	1.03	1.01–1.05	0.007
Final AFP (natural log)	0.11	1.01–1.23	0.031
Donor Risk Index	1.74	1.05–2.89	0.031
Age (yr)	1.03	0.9995–1.05	0.55

Table 6

Multivariate regression of factors associated with HCC recurrence or death after liver transplant

Variable	Odds ratio	95% confidence interval	p-value
MELD	1.03	1.01–1.05	0.005
Final AFP (natural log)	1.17	1.08–1.29	<0.001
Donor Risk Index	1.60	1.03–2.49	0.038
Age (yr)	1.04	1.01–1.06	0.054