Effect of Donor Race-Matching on Overall Survival for African-American Patients Undergoing Liver Transplantation for Hepatocellular Carcinoma

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BACKGROUND: Liver transplantation (LT) is the preferred treatment for early hepatocellular carcinoma (HCC) in select patients. Differences in outcomes after LT have been previously described between recipient races, but the role of donor race is not well defined. This study sought to examine the effect of donor-recipient race-matching on overall survival after liver transplantation for HCC in African-American patients (AA).

STUDY DESIGN: Adult AA patients with HCC undergoing liver transplantation were identified using the Organ Procurement and Transplantation Network database (1994 to 2015). Recipient and donor demographic and clinical characteristics were collected. Patients were separated into unadjusted cohorts based on whether the liver donor was AA (matched) or another race (unmatched). The primary outcome was overall survival, which was analyzed by log-rank test and graphed using the Kaplan-Meier method. Multivariate regression modeling was used to determine adjusted hazard ratios (HR) for overall survival.

RESULTS: Of 1,384 AA patients identified, 325 (23.5%) were race-matched. Matched patients experienced significantly better median overall survival when compared with the unmatched cohort (135 vs 78 months, $p = 0.007$). Multivariate analysis revealed an adjusted hazard ratio of 0.66 for race-matched transplantation (95% CI 0.49 to 0.88; $p = 0.004$). Matched patients also experienced an improved 5-year survival (64.2% vs 56.9%; $p = 0.019$).

CONCLUSIONS: African-American HCC patients undergoing liver transplantation experienced significantly improved overall survival when the donor race matched the recipient race. Donor-recipient race-matching remained an independent predictor of improved survival after adjusting for comorbidities and disease characteristics. Race-matching should be considered in the process of organ allocation because it may affect long-term survival in African-American HCC patients. (J Am Coll Surg 2019;228:245−254. © 2019 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

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Liver cancer is now the second most common cause of cancer death worldwide, and hepatocellular carcinoma (HCC) is the predominant histologic subtype.[1,2] For eligible, early-stage HCC patients, liver transplantation remains the most viable curative treatment option. African-American (AA) HCC patients experience relatively worse overall survival compared with other races, and a smaller percentage undergo liver transplantation.[3-6] African Americans receiving a liver transplant experience worse graft and overall survival compared with recipients of other races.[7,8] This

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Abbreviations and Acronyms

AA = African-American
HCC = hepatocellular carcinoma
HCV = hepatitis C virus
HR = hazard ratio
LT = liver transplantation
MELD = Model for End-Stage Liver Disease
OPTN = Organ Procurement and Transplant Network
TIPS = transjugular intrahepatic portosystemic shunt
UNOS = United Network for Organ Sharing

discrepancy in outcomes has been extensively investigated with regard to recipient characteristics. African-American liver transplant recipients are more likely to have underlying hepatitis C (HCV), and many present with more advanced oncologic disease.[9-13] Some have also cited socioeconomic and geographic factors contributing to transplant accessibility and survival differences.[14-16] Research less commonly focuses on the role that donor characteristics play in postoperative outcomes, but some studies have investigated the influence of donor race on survival.

The relationship between donor and recipient race is associated with differences in outcomes after transplantation of a variety of organs. Donor-recipient race-mismatching has been linked to worse graft and overall survival in kidney, lung, and heart transplant patients.[17-19] Few studies have examined the role of donor and recipient race in liver transplantation, and the results are inconsistent. Some reports describe AA donor race as a risk factor for overall and graft survival after liver transplantation.[19,20] Conversely, 1 study investigating multiple races found no difference in outcomes when considering donor-recipient race-matching.[21] Descriptions of AA donor race as a predictor of poor outcomes often do not account for the heterogeneity of the recipient population, which contributes to the inconsistencies in previous findings. In a well-matched population of AA liver transplant recipients with HCV, race-unmatched transplantation was described as an independent predictor of graft failure.[11] This study focuses on AA transplant recipients with HCC. This population is important to examine because of the relatively worse outcomes seen in both AA HCC patients and AA liver transplant patients when compared with those in other races. Identifying factors that contribute to poor outcomes in these patients may influence survival by improving donor and patient selection. Recipient characteristics have been identified as contributors to this discrepancy, but are often not adjusted for when analyzing donor characteristics.

This study sought to examine overall survival in AA HCC patients who underwent liver transplantation, with the hypothesis that AA patients receiving AA donor livers have improved overall survival, even after adjusting for known comorbidities. This is the first study to directly analyze the role of donor race in outcomes after liver transplantation for a select population of AA HCC patients.

METHODS

Patient selection

The United Network for Organ Sharing (UNOS) Organ Procurement and Transplant Network (OPTN) database Standard Transplant Analysis and Research (STAR) files were used to obtain records for liver transplantations that occurred from 1994 to 2015. Liver recipients with hepatocellular carcinoma were selected using liver diagnosis codes 4400 and 4401. Patients with any other diagnosis code were excluded from the study, including secondary malignancies. Only recipients older than 18 years were selected. Preliminary data analysis was performed on the entire population of HCC patients to confirm results from previous studies. Before the primary statistical analysis, all recipient races other than African American were excluded. The UNOS database stratifies race as one of the following categories: White, Black or African-American, Hispanic, Asian, American Indian/Alaskan Native, Pacific Islander, or Multiracial, not distinguishing from ethnicity. Patients receiving livers from AA donors were labeled "matched," and patients receiving livers from a donor of any other race were labeled "unmatched." Unmatched patients were further stratified by donor race (Caucasian, Hispanic, or Asian). Data were collected for donor and recipient demographic and clinicopathologic information in addition to post-transplantation outcomes. All variables included are shown in Table 1. The primary outcome of interest was median overall survival. Other outcomes examined were length of stay, rejection, and survival rates at 1, 5, and 10 years. Overall survival was defined as the number of months from transplantation until death.

Data analysis

Continuous variables were described by medians with interquartile ranges (IQR), and categorical variables were reported as absolute values and proportions. Rejection and survival rates were reported as percentages with 95% CI. Unadjusted cohorts of unmatched vs matched patients were compared using Fisher's exact test for categorical variables and the Kruskal-Wallis test for continuous variables. Kaplan-Meier curves for OS were performed for each group, and results were compared with log-rank tests for equality of survivor functions (Fig. 1). Recipients lost to follow-up before death were censored. Comparison of

survival rates among the 4 included donor races was performed by multiple proportions chi-square test. Cox regression was used to identify variables associated with overall survival for the entire study population. Factors identified as significant on univariate analysis ($p < 0.1$) were included in the multivariate model. Furthermore, any variables that differed between the unadjusted cohorts ($p < 0.05$) were also included in the final model. Race-matching or donor race was included automatically as the variable of interest. The final model adjusted for the following variables: recipient age, recipient sex, recipient BMI, days on waiting list, distance from donor hospital to transplant center, recipient portal vein thrombosis, recipient diabetes, recipient hepatitis (B or C), cold ischemic time, previous transjugular intrahepatic portosystemic shunt (TIPS), donor age, donor sex, donor cytomegalovirus (CMV), donor cardiac arrest, partial/split liver, transplant region, and year. Stata version 12 IC (StataCorp LP) was used for all statistical analysis. Statistical significance was set at $\alpha = 0.05$; all tests were 2-sided. This study was approved by the institutional review board at the Medical College of Wisconsin.

RESULTS

Population characteristics

Of the 15,141 HCC patients who underwent liver transplantation, 1,384 (9.1%) were African American, and 2,497 (16.5%) received livers from African-American donors. Preliminary unadjusted survival analysis stratified by recipient race revealed that African Americans had the lowest 5-year survival rate (95% CI), at 58.6% (55.2% to 61.9%). Survival rates for Caucasian, Hispanic, and Asian patients at 5 years were 68.1%, 71.4%, and 74.7%, respectively ($p < 0.001$). Before the recipient race exclusion criterion was applied, analysis revealed no difference in overall survival when stratified by donor race ($p = 0.796$). Unadjusted 5-year survival rates for patients receiving livers from Caucasian, AA, Hispanic, and Asian donors were 68.6%, 69.2%, 66.4%, and 67.2%, respectively.

After exclusion of Caucasian, Hispanic, and Asian patients, the main study population consisted of 1,384 African Americans with HCC who underwent liver transplantation. Demographic and clinicopathologic characteristics, in addition to postoperative outcomes, are shown in Table 1.

Unadjusted comparison

Of the 1,384 AA patients, 325 (23.5%) received livers from AA donors and were labeled "matched," with the remaining 1,059 (76.5%) labeled "unmatched." The unadjusted cohort comparison (Table 1) showed that relative to the unmatched group, race-matched donor livers traveled a shorter distance from the donor hospital to the transplant center, had a shorter cold ischemic time, were more likely to be partial/split, and were more likely to have cytomegalovirus. Some small differences in transplant region existed, and race-matched recipients were more likely to have a history of portal vein thrombosis. Other surrogate markers for disease burden like physiologic Model for End-Stage Liver Disease (MELD) score, ascites, and transjugular intrahepatic portosystemic shunt (TIPS), were similar between groups. Race-matched patients experienced a higher incidence of rejection within 6 months, but higher survival rates at 5 and 10 years, and a median overall survival nearly 2-fold that of the race-unmatched patients (Table 1).

Analysis of outcomes for AA patients stratified by donor race (AA, Caucasian, Hispanic, Asian) revealed significant differences in unadjusted survival rates at 1, 5, and 10 years (Table 2). African-American and Hispanic donor races were associated with the highest 1-year survival ($p = 0.047$). Five-year survival was the highest for patients with AA donors ($p < 0.001$), as was 10-year survival ($p < 0.001$).

Cox regression

Cox regression revealed many variables associated with differences in overall survival on univariate analysis (Table 3). The multivariate model showed recipient age, HCV, donor age, and transplantation year to have significant adjusted hazard ratios (HR) for overall survival. Additionally, race-matched transplantation independently predicted improved overall survival (HR 0.66; 95% CI 0.49 to 0.88; $p = 0.004$). On repeat Cox regression analysis using donor race as the variable of interest, Caucasian donor race was an independent negative predictor of survival, with AA donor race as a reference (HR 1.53; 95% CI 1.14 to 2.06; $p = 0.004$). Hispanic donor race (HR 1.38; 95% CI 0.91 to 2.08; $p = 0.132$) and Asian donor race (HR 1.76; 95% CI 0.90 to 3.44; $p = 0.098$) also demonstrated elevated hazard ratios, but were not significant.

DISCUSSION

These results have confirmed studies showing worse overall survival for African-American HCC patients undergoing liver transplantation, compared with patients of other recipient races. The study also demonstrated the importance of adjusting for the heterogeneity of the recipient population when analyzing donor race. By isolating a select AA cohort and correcting for known comorbidities,

Table 1. Unadjusted Comparison of Race-Recipient Unmatched and Matched African-American Hepatocellular Carcinoma Patients Who Underwent Liver Transplantation. Donor and Recipient Characteristics and Post-Transplant Outcomes Are Compared

Donor/recipient characteristic	Total n = 1,384	Unmatched n = 1,059 (76.5)	Matched n = 325 (23.5)	p Value
Recipient age, y, median (IQR)	58 (54–62)	58 (54–62)	58 (54–62)	0.634
Recipient sex, n (%)				0.419
Female	372 (26.9)	279 (26.4)	93 (28.6)	
Male	1,012 (73.1)	780 (73.6)	232 (71.4)	
Recipient BMI, kg/m^2, median (IQR)	27.8 (24.4–31.2)	27.7 (24.4–31.2)	27.8 (24.4–31.2)	0.895
Days on waiting list, median (IQR)	118 (38–289)	123 (42–297)	102.5 (33–264)	0.172
Miles from donor hospital to transplant center, median (IQR)	41 (6–139)	49 (7–148)	14 (3–100)	<0.001*
Working for income, n (%)	373 (32.2)	279 (32.0)	94 (33.1)	0.721
Insurance type				0.354
Private	744 (53.8)	562 (53.1)	182 (56.0)	
Public	640 (46.2)	497 (46.9)	143 (44.0)	
Portal vein thrombosis, n (%)	78 (5.8)	50 (4.9)	28 (9.0)	0.007*
Diabetes (any type), n (%)	402 (29.1)	304 (28.7)	98 (30.3)	0.074
Hepatitis B, n (%)	124 (9.5)	91 (9.1)	33 (10.9)	0.364
Hepatitis C, n (%)	1,057 (80.5)	809 (80.1)	248 (81.9)	0.500
MELD Score, median (IQR)	13 (9–20)	13 (9–20)	13 (9–19)	0.945
Cold ischemic time, min, median (IQR)	361 (285–480)	367 (294–480)	353 (255–480)	0.025*
Ascites, n (%)	749 (54.1)	570 (53.8)	179 (55.1)	0.679
Previous TIPS, n (%)	26 (1.9)	15 (1.4)	11 (3.4)	0.053
Previous upper abdominal surgery, n (%)	555 (41.0)	432 (41.7)	123 (38.7)	0.332
Creatinine, mg/dL, median (IQR)	1.0 (0.8–1.3)	1.0 (0.8–1.3)	1.0 (0.8–1.3)	0.940
Donor age, y, median (IQR)	43 (28–54)	43 (28–54)	44 (27–54)	0.864
Donor sex, n (%)				0.090
Female	570 (41.2)	423 (39.9)	147 (45.2)	
Male	814 (58.8)	636 (60.1)	178 (54.8)	
Donor race, n (%)				
White	874 (63.2)	874 (82.5)	0 (0)	
African American	325 (23.5)	0 (0)	325 (100)	
Hispanic	154 (11.1)	1545 (14.5)	0 (0)	
Asian	31 (2.2)	31 (2.9)	0 (0)	
Donor BMI, kg/m^2, median (IQR)	26.2 (23.1–30.6)	26.1 (23.0–30.1)	26.2 (23.4–31.7)	0.121
Donor HCV, n (%)	122 (9.0)	90 (8.5)	32 (10.4)	0.304
Donor CMV, n (%)	895 (65.8)	647 (61.4)	248 (80.5)	<0.001*
Donor cardiac arrest, n (%)	99 (7.5)	79 (7.8)	20 (6.7)	0.542
Donor liver type, n (%)				<0.001*
Whole organ	1,350 (97.5)	1,045 (98.7)	305 (93.9)	
Partial/split	34 (2.5)	14 (1.3)	20 (6.2)	
Donor microsteatosis >10% (75th percentile), n (%)	95 (22.3)	68 (21.5)	27 (24.6)	0.501
Donor macrosteatosis >10% (75th percentile), n (%)	86 (19.0)	70 (20.8)	16 (13.7)	0.089
ABO mismatch, n (%)	71 (5.2)	52 (4.9)	20 (6.2)	0.377
HLA mismatch, n (%)				0.280
5–6 mismatches	401 (68.8)	322 (69.8)	79 (64.7)	
0–4 mismatches	182 (31.2)	139 (30.2)	43 (35.3)	

(Continued)

Table 1. Continued

Donor/recipient characteristic	Total n = 1,384	Unmatched n = 1,059 (76.5)	Matched n = 325 (23.5)	p Value
Height mismatch >15 cm, n (%)	389 (28.1)	303 (28.6)	86 (26.5)	0.451
OPTN transplant region, n (%)				0.007*
1 (CT, RI, MA, NH, ME)	40 (2.9)	38 (3.6)	2 (0.6)	
2 (WV, DC, MD, DE, NJ, PA)	296 (21.4)	225 (21.3)	71 (21.9)	
3 (AR, LA, MS, AL, GA, FL, Puerto Rico)	197 (14.2)	141 (13.3)	56 (17.2)	
4 (TX, OK)	128 (9.3)	102 (9.6)	26 (8.0)	
5 (AZ, NM, UT, NV, CA)	96 (6.9)	81 (7.7)	15 (4.6)	
6 (AK, HI, WA, OR, ID, MT)	14 (1.0)	13 (1.2)	1 (0.3)	
7 (ND, SD, MN, WI, IL)	122 (8.8)	91 (8.6)	31 (9.5)	
8 (WY, CO, NE, KS, IA, MO)	80 (5.8)	67 (6.3)	13 (4.0)	
9 (NY, VT)	153 (11.1)	110 (10.4)	43 (13.2)	
10 (MI, IN, OH)	137 (9.9)	107 (10.1)	30 (9.2)	
11 (TN, KY, VA, NC, SC)	121 (8.7)	84 (7.9)	37 (11.4)	
Transplantation year, n (%)				0.671
2011−2015	666 (48.1)	508 (48.0)	158 (48.6)	
2006−2010	505 (36.5)	389 (36.7)	116 (35.7)	
2001−2005	171 (12.4)	133 (12.6)	38 (11.7)	
1994−2000	42 (3.0)	29 (2.7)	13 (4.0)	
Outcome				
Length of stay after transplantation, d, median (IQR)	9 (7−14)	9 (6−14)	9 (7−14)	0.411
Rejection at 6 mo, n (%)	111 (11.4)	77 (10.3)	34 (15.0)	0.049*
Median overall survival, mo, median (IQR)	90.9 (25.0−171.3)	77.9 (22.1−170.1)	135.0 (34.6−N/A)	0.007*
1-y survival rate (95% CI)	86.8 (84.2−88.6)	85.9 (83.5−87.9)	90.0 (85.9−92.9)	0.056
5-y survival rate (95% CI)	58.6 (55.2−61.9)	56.9 (52.9−60.7)	64.2 (57.0−70.5)	0.019*
10-y survival rate (95% CI)	42.8 (37.2−48.2)	38.7 (32.0−45.4)	54.4 (44.1−63.6)	<0.001*

*Significant.
CMV, cytomegalovirus; HCV, hepatitis C virus; HLA, human leukocyte antigen; IQR, interquartile range; MELD, Model for End-Stage Liver Disease; OPTN, Organ Procurement and Transplant Network; TIPS, transjugular intrahepatic portosystemic shunt.

the results of this study demonstrate a potential impact of race-matched liver transplantation on overall survival.

The survival disparity for African Americans with HCC and African Americans undergoing liver transplantation is well established.[3,7] Despite improvements in post-transplant outcomes for AA patients, survival relative to that in other races is consistently worse. Five-year survival for AA liver recipients from 1988 to 1996 UNOS data was 48%, compared with 58% in Caucasians, and AA race carried a hazard ratio of 1.36 compared to that of Caucasians (95% CI 1.16 to 1.60; $p < 0.001$).[22] Current UNOS data (1994 to 2015) showed a significant improvement in 5-year survival for both AA (58.6%) and Caucasian patients (68.1%), but the survival difference continues to exist. This study was not aimed to identify causes of worse survival in AA patients, but the results of the Cox regression complement findings reported in previous research. African-American patients selected for liver transplantation have been shown to demonstrate a higher incidence of HCV than other races,[10] and HCV was independently associated with a 2-fold mortality risk in this analysis (hazard ratio [HR] 2.03; 95% CI 1.38 to 2.98; $p < 0.001$). Other explanations for the racial survival disparity after liver transplantation include socioeconomic status and/or tumor characteristics at presentation for AA patients. These factors are not sufficiently captured in the UNOS database.[9,23]

Studies investigating the influence of donor characteristics are less prevalent, but some have examined the relationship between donor race and survival outcomes after organ transplantations. Locke and colleagues[24] studied kidney transplant patients and found that among AA recipients, receiving a kidney from an AA donor was associated with a 59% reduction in risk for death compared with a Caucasian donor (HR 0.41; 95% CI 0.20 to 0.87; $p = 0.02$). In a cohort of pediatric heart transplant patients, donor-recipient race mismatch was

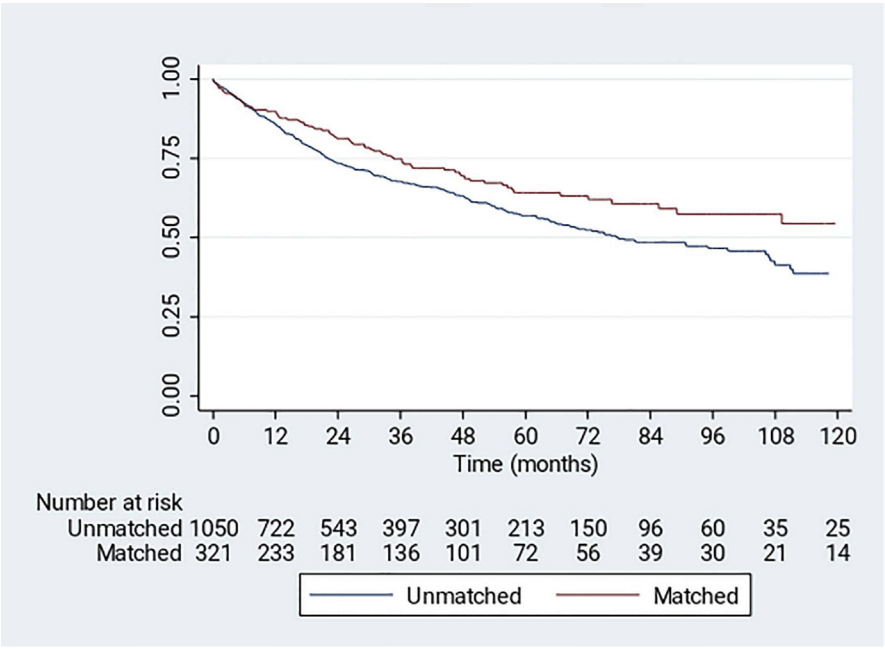

Figure 1. Kaplan-Meier plot of overall survival for African-American hepatocellular carcinoma patients who underwent liver transplantation. Race-recipient matched and unmatched groups are compared, with a maximum 10-year follow-up period.

associated with a significantly lower 5-year graft survival compared with 5-year survival of matched patients (48.9% vs 72.3%; p = 0.003).[25] The authors also concluded that the relatively worse unadjusted graft survival in AA recipients (compared with Caucasians) was partially attributed to lower race-matching rates. Allen and associates[18] used the UNOS database to investigate lung transplantation outcomes stratified by donor-recipient race-matching. They determined that race-matching independently predicted improved overall survival for all patients (HR 0.88; 95% CI 0.80 to 0.96; p = 0.006). The authors also found no survival differences between recipient races, but worse survival for patients with an AA lung donor.[18] Several studies have also investigated the role of donor race for liver transplantation, with inconsistent results.

Studies identifying AA donor race as a contributor to overall survival after liver transplantation often do not adequately adjust for recipient characteristics or allow sufficient follow-up time. Asrani and coworkers[26] proposed that donor race may not predict graft survival after liver transplantation, but the authors did not control for recipient race, and follow-up was limited to 3 years. Conversely, this study evaluated patients of a single race up to 10 years after surgery and demonstrated significant differences in long-term survival depending on donor race. A race-adjusted analysis beyond 3 years is preferred for evaluating liver transplantation outcomes. Preliminary data analysis of all recipient races in this study showed no difference in unadjusted survival based on donor race. After isolating the study population to only AA recipients, the effect of donor race could be evaluated without potential confounding from recipient race. African-American recipients with Caucasian donor race demonstrated a significant adjusted hazard ratio (1.53) for overall survival compared with AA recipients of AA donor race.

The factors influencing survival in race-matched liver transplantation for African Americans with HCC are

Table 2. Unadjusted Comparison of Survival Rates for African-American Hepatocellular Carcinoma Patients Who Underwent Liver Transplantation, Stratified by Donor Race

	Donor race				
Survival rate, % (95% CI)	**African American (n = 325)**	**Caucasian (n = 874)**	**Hispanic (n = 154)**	**Asian (n = 31)**	**p Value**
1 y	90.0 (85.9–92.9)	85.1 (82.3–87.4)	90.9 (84.8–94.6)	82.3 (62.6–92.3)	0.047*
5 y	64.2 (57.0–70.5)	57.8 (53.5–61.9)	54.1 (43.5–63.6)	50.3 (26.0–70.4)	<0.001*
10 y	54.4 (44.1–63.6)	37.2 (29.7–44.8)	47.3 (35.6–58.2)	50.3 (26.0–70.4)	<0.001*

*Significant.

Table 3. Univariate and Multivariate Cox Regression Analysis Showing Unadjusted and Adjusted Hazard Ratios for Overall Survival in African-American Hepatocellular Carcinoma Patients Who Underwent Liver Transplantation

	Univariate		Multivariate	
Donor/recipient characteristic	**HR (95% CI)**	**p Value**	**HR (95% CI)**	**p Value**
Recipient age (continuous)	1.01 (1.00−1.03)	0.026*	1.02 (1.00−1.04)	0.026*
Recipient sex				
Female	Ref		Ref	
Male	1.05 (0.85−1.29)	0.667	0.96 (0.74−1.24)	0.763
Recipient BMI (continuous)	0.98 (0.96−1.00)	0.036*	0.99 (0.97−1.01)	0.225
Days on waiting list (continuous)	1.00 (1.00−1.00)	0.862	1.00 (1.00−1.00)	0.404
Miles from donor hospital to transplant center (continuous)	1.00 (1.00−1.00)	0.522	1.00 (1.00−1.00)	0.621
Working for income	0.87 (0.69−1.11)	0.269		
Insurance type				
Private	Ref			
Public	1.12 (0.93−1.35)	0.216		
Portal vein thrombosis	0.81 (0.49−1.33)	0.399	1.02 (0.59−1.78)	0.939
Diabetes (any type)	1.21 (1.01−1.46)	0.040*	1.17 (0.93−1.46)	0.177
Hepatitis B	0.59 (0.41−0.85)	0.005*	0.86 (0.52−1.42)	0.551
Hepatitis C	1.91 (1.45−2.53)	<0.001*	2.03 (1.38−2.98)	<0.001*
MELD Score (continuous)	1.00 (0.99−1.01)	0.539		
Cold ischemic time, minutes (continuous)	1.00 (1.00−1.00)	0.264	1.00 (1.00−1.00)	0.512
Ascites	1.14 (0.97−1.34)	0.118		
Previous TIPS	1.30 (1.09−1.55)	0.004*	1.23 (0.80−1.89)	0.339
Previous upper abdominal surgery	1.14 (0.95−1.38)	0.167		
Creatinine (continuous)	1.03 (0.99−1.08)	0.147		
Donor age (continuous)	1.01 (1.01−1.02)	<0.001*	1.01 (1.00−1.02)	0.003*
Donor Sex				
Female	Ref		Ref	
Male	0.92 (0.77−1.12)	0.413	0.93 (0.74−1.17)	0.547
Donor Race				
White	Ref			
African American	0.71 (0.56−0.91)	0.006*		
Hispanic	0.89 (0.67−1.20)	0.453		
Asian	0.95 (0.52−1.74)	0.878		
Donor BMI (continuous)	1.00 (0.98−1.01)	0.681		
Donor HCV	0.82 (0.57−1.20)	0.315		
Donor CMV	1.18 (0.96−1.45)	0.108	1.16 (0.91−1.48)	0.231
Donor cardiac arrest	0.69 (0.46−1.05)	0.082	0.73 (0.46−1.15)	0.172
Donor liver type				
Whole organ	Ref		Ref	
Partial/split	1.23 (0.71−2.14)	0.458	1.44 (0.52−4.01)	0.488
Donor microsteatosis >10% (75th percentile)	1.12 (0.72−1.75)	0.607		
Donor macrosteatosis >10% (75th percentile)	1.01 (0.64−1.59)	0.975		
ABO mismatch	0.95 (0.64−1.40)	0.776		
HLA mismatch				
5−6 mismatches	Ref			
0−4 mismatches	1.07 (0.80−1.42)	0.665		
Height mismatch >15cm	0.97 (0.79−1.20)	0.800		
OPTN transplant region				
1 (CT, RI, MA, NH, ME)	0.76 (0.42−1.39)	0.377	1.02 (0.55−1.89)	0.957

(Continued)

Table 3. Continued

Donor/recipient characteristic	Univariate		Multivariate	
	HR (95% CI)	p Value	HR (95% CI)	p Value
2 (WV, DC, MD, DE, NJ, PA)	Ref		Ref	
3 (AR, LA, MS, AL, GA, FL, Puerto Rico)	0.83 (0.61−1.14)	0.253	1.02 (0.71−0.47)	0.904
4 (TX, OK)	0.77 (0.54−1.09)	0.146	0.98 (0.63−1.52)	0.931
5 (AZ, NM, UT, NV, CA)	0.68 (0.44−1.03)	0.072	0.74 (0.46−1.20)	0.222
6 (AK, HI, WA, OR, ID, MT)	0.74 (0.30−1.81)	0.504	0.66 (0.24−1.85)	0.431
7 (ND, SD, MN, WI, IL)	0.77 (0.53−1.13)	0.188	0.78 (0.48−1.29)	0.338
8 (WY, CO, NE, KS, IA, MO)	0.77 (0.50−1.19)	0.240	0.79 (0.49−1.27)	0.327
9 (NY, VT)	0.78 (0.56−1.08)	0.132	0.82 (0.55−1.23)	0.346
10 (MI, IN, OH)	0.68 (0.48−0.96)	0.028*	0.64 (0.42−0.97)	0.036*
11 (TN, KY, VA, NC, SC)	0.49 (0.32−0.77)	0.002*	0.64 (0.38−1.08)	0.092
Transplant year				
2011−2015	Ref		Ref	
2006−2010	1.08 (0.85−1.36)	0.552	1.17 (0.89−1.52)	0.263
2001−2005	1.56 (1.17−2.07)	0.002*	2.02 (1.41−2.89)	<0.001*
1994−2000	2.26 (1.49−3.41)	<0.001*	0.98 (0.13−7.26)	0.986
Donor/recipient race−match	0.73 (0.58−0.92)	0.007*	0.66 (0.49−0.88)	0.004*

*Significant.

CMV, cytomegalovirus; HCV, hepatitis C virus; HLA, human leukocyte antigen; IQR, interquartile range; MELD, Model for End-Stage Liver Disease; OPTN, Organ Procurement and Transplant Network; Ref, reference; TIPS, transjugular intrahepatic portosystemic shunt.

undefined. Recipient and donor age, HCV, and transplantation year were all identified as independent predictors of overall survival. However, none of these variables were different among race-matched vs unmatched patients. The groups compared were similar with the exception of a few variables (Table 1) that demonstrated no association with overall survival on Cox regression analysis (Table 3). The difference in survival is not apparent until 1 year after surgery. Rejection rate within the first 6 months is actually higher in the race-matched group. Similar findings were reported by Allen and colleagues[18] in their evaluation of lung transplantations. These findings point to the effect of long-term variables that may not be captured in the database, such as surveillance protocol compliance, recurrence, or secondary disease development. Recurrence after surgery is associated with a poor prognosis, and the recipient population could be susceptible to a return of HCV or HCC after transplantation. The UNOS database provides variables describing reasons for graft failure, but poor data capture coupled with the low incidence of graft failure prevented meaningful evaluation. Post-hoc analysis revealed that race-unmatched patients had a higher incidence of hepatitis recurrence, but sample size was limited and the difference was not significant.

Improvements in surgical technique, immunosuppression therapy, and donor selection have led to better survival after liver transplantation. Increased rates of liver donation by African Americans may have also contributed to improved outcomes in AA recipients.[19,23] Race is not considered during compatibility screening in the current allocation system based on Model for End-Stage Liver Disease (MELD) score.[27] However, geographic proximity is important for allocation, and it likely explains the nonrandom distribution of same-race liver transplantations. From 1988 to 1996, 11% of liver transplantations recorded in the UNOS database involved AA donors, but 17% of AA patients had an AA donor.[28] The most recent data from 2011 to 2015 showed that 18% of liver donors are African American, and 25% of AA patients received an AA donor liver. The survival advantage shown in this analysis provides evidence that the observed increase in race-matched transplantations over time may contribute to improved long-term survival for the AA population.

Additional stratification of the race-unmatched group revealed that Caucasian donor race was the primary contributor to the significant hazard ratio for overall survival compared with that in race-matched patients. Caucasian donor race comprised 83% of the race-unmatched group and was the only race revealed as an independent predictor of survival. Hazard ratios were elevated for the other donor races, but did not reach significance.

This study is subject to some inherent limitations. As with any retrospective database review, the results are subject to a degree of selection bias, with no insight into the individual process of choosing donors and recipients. More specifically, many of the important tumor characteristics relevant for HCC patients were not available in the database, such as tumor stage, size, number, and

location. The UNOS database also did not provide a potential suspected mechanism driving these results and whether the increased survival is the result of specific unknown genetic similarity, biochemical process, or from a more loosely defined socioeconomic or cultural phenomenon. Despite the limited specific characterization of HCC, disease burden was defined by surrogate variables including portal vein thrombosis, MELD score, ascites, and TIPS. Long-term surveillance and recurrence variables that affect overall survival were also unable to be evaluated. Variables included in the database to describe the cause of primary graft failure were often uncaptured. Also, the inherent low rate of graft failure in the follow-up period precluded meaningful analysis. However, of the patients with documented graft failure causes, disease recurrence was not significantly different among race-matched and unmatched patients. The timing, treatment, and eradication of secondary diagnoses like HCV was not able to be determined, although donor and recipient HCV serology was similar between groups. Survival rates for AA patients with Hispanic and Asian donors were lower than those for race-matched patients on unadjusted comparison, but small donor numbers may have limited the findings on Cox regression analysis for those races. This study is meant to analyze African-American HCC patients only, and the effect of race-matching may not apply to liver transplant recipients of other races.

CONCLUSIONS

In conclusion, African-American HCC patients demonstrated improved overall survival beyond 1 year after liver transplantation if their donor was also AA. Furthermore, after adjusting for known comorbidities, donor-recipient race-matching was an independent predictor of improved overall survival for this group of patients. Despite previous studies linking AA donor race to worse outcomes, this finding does not apply to AA recipients. For African Americans with HCC eligible for liver transplantation, donor race-matching may aid in future organ allocation because it is associated with improved long-term survival.

Author Contributions

Study conception and design: Silva, Gamblin
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Analysis and interpretation of data: Silva, Maurina, Tsai, Christians, Clarke, Mogal, Saeian, Gamblin
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