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Liver Transplantation Outcomes Among Caucasians, Asian Americans, and African Americans with Hepatitis B

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Abstract

Several previous studies found that Asians transplanted for hepatitis B virus (HBV) infection had worse post-transplant outcomes than Caucasians. Data on post-transplant outcomes of African Americans and waitlist outcomes of Asian Americans and African Americans with hepatitis B are scant. The aim of this study was to compare waitlist and post-transplant outcomes among Asian Americans, African Americans, and Caucasians who had HBV-related liver disease. Data from a retrospective-prospective study on liver transplantation for HBV infection were analyzed. A total of 274 patients (116 Caucasians, 135 Asians, and 23 African Americans) from 15 centers in the United States were enrolled. African Americans were younger and more Asian Americans had hepatocellular carcinoma (HCC) at the time of liver transplant listing. The probability of undergoing transplantation and the probability of survival on the waitlist were comparable in the 3 racial groups. Of the 170 patients transplanted, 19 died during a median follow-up of 31 months. The probability of post-transplant survival at 5 years was 94% for African Americans, 85% for Asian Americans, and 89% for Caucasians ($P = 0.93$). HCC recurrence was the only predictor of post-transplant survival, and recurrence rates were similar in the 3 racial groups. Caucasians had a higher rate of HBV recurrence: 4-year recurrence was 19% versus 7% and 6% for Asian Americans and African Americans, respectively ($P = 0.043$). In conclusion, we found similar waitlist and post-transplant outcomes among Caucasians, Asian Americans, and African

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Americans with hepatitis B. Our finding of a higher rate of HBV recurrence among Caucasians needs to be validated in other studies.

Conflicting data exist as to whether race affects outcomes after orthotopic liver transplantation (OLT) in the United States. Results from 1 center found no significant difference in patient survival between African Americans and Caucasians after solid organ transplantation, including liver transplantation.[1] In contrast, a retrospective analysis of the United Network of Organ Sharing (UNOS) database of over 14,000 OLT procedures performed between 1988 and 1996 revealed that 2- and 5-year patient survival was significantly lower for both African Americans and Asians compared to white Americans and Hispanics.[2] This study found that the racial difference in post-OLT survival was related to the etiology of liver disease, with lower survival rates among African Americans with hepatitis C or acute liver failure and among Asians with hepatitis B virus (HBV). A second analysis of the UNOS database, which included more than 17,000 OLT procedures performed during the same period (1990-1996), also concluded that post-OLT survival was lower in minority races.[3] However, a recent analysis of 2823 patients transplanted in 4 centers between 1985 and 2000 found no difference in post-OLT patient or graft survival among racial groups.[4] In this study, a significantly increased risk of mortality was observed among patients of other races (not Caucasian or African American) transplanted before 1994, and this was attributed to the poor outcome of patients transplanted for hepatitis B or hepatocellular carcinoma (HCC). These data indicate that racial differences in post-OLT outcome observed in some studies may be related to differences in the predominant cause of liver disease.

Several studies have compared outcomes of Caucasians and Asians transplanted for HBV infection. Three early studies found that Asians who had liver transplants for hepatitis B had higher rates of post-OLT mortality.[5-7] Data from these single-center studies were confirmed by analysis of the large databases cited previously.[2,4] Studies conducted after the introduction of hepatitis B immune globulin (HBIG) and lamivudine were more encouraging. A retrospective study of 70 Asians and 99 whites transplanted in the late 1990s found that post-OLT survival and HBV recurrence were comparable between the 2 groups.[8] Similarly, an analysis of the UNOS database of all adult patients transplanted for HBV between 1997 and 2002 found that post-OLT survival of Asians was similar to that of other races.[9] These data indicate that outcomes of Asians and Caucasians after liver transplantation for HBV infection in the recent era are comparable, but there are very little data on the outcomes of African Americans who had liver transplantation for hepatitis B. To date, most studies have focused on post-OLT outcomes; whether transplantation rates and outcomes on the waiting list are comparable among racial groups is unclear. Furthermore, most studies have not included data on HBV markers and HBV prophylactic regimen, factors that may affect post-OLT HBV recurrence and survival.

The National Institutes of Health (NIH)—sponsored HBV-OLT study is a multicenter retrospective-prospective study on the outcomes of liver transplant patients with HBV infection. The large number of enrolled patients permitted a comparison of post-OLT outcomes as well as outcomes on the waiting list among Caucasians, Asian Americans, and

African Americans in an era in which oral nucleos/tide analogues and HBIG are available. This study also allowed a comparison of the clinical and virological characteristics of the patients in these racial groups.

PATIENTS AND METHODS

Patient Population

The NIH HBV-OLT study is a retrospective-prospective observational study that enrolled hepatitis B surface antigen–positive patients who were 13 years of age or older from 15 centers in the United States.[10] All patients either were on the liver transplant waiting list or were within 12 months post-transplant. Patients were listed between March 12, 1996 and June 10, 2005 and transplanted between March 28, 2001 and September 27, 2007. The study was approved by the institutional review board at each of the participating centers, and written informed consent was obtained from all patients prior to study entry. For patients enrolled at the time of listing, data were collected prospectively. For patients enrolled after placement on the liver transplant waiting list, data after enrollment were collected prospectively, while data prior to enrollment were collected retrospectively up to the time of listing.

For this analysis, patients with race/ethnicity other than Caucasian, Asian American, or African American, those coinfected with hepatitis C virus or human immunodeficiency virus, and those listed for retransplantation were excluded. Hispanics were not included as there were only 2 in this study. Demographic, clinical, laboratory [blood counts, creatinine, liver panel, prothrombin time/international normalized ratio, alpha-fetoprotein, hepatitis B serology, and HBV DNA], and radiological (for patients with HCC) data as well as start and stop dates of antiviral therapy and HBIG (for post-transplant patients) were entered into an electronic database. Data were collected at enrollment, transplant listing, and time of transplant and every 6 months on the transplant waiting list, every 3 months during the first year post-transplant, and every 6 months after the first post-transplant year. Race/ethnicity assignment was based on self-reporting by the patients. All laboratory tests except for HBV DNA and antiviral drug-resistant mutations were performed with commercially available assays at the participating centers. An additional 10 mL of blood was collected at each visit, centrifuged, divided into aliquots, and stored at −70°C at the participating centers and shipped in batches to the central laboratory at the University of Michigan, where serum samples were stored at −80°C until testing.

Because the NIH HBV-OLT study was an observational study, no specific treatment was tested, but the protocol did provide guidelines on the use of antiviral therapy pre-transplant and post-transplant and the use of HBIG post-transplant.

HBV DNA assays

Serum HBV DNA levels were quantified with the Cobas Amplicor HBV Monitor assay (Roche Molecular Systems, Inc., Branchburg, NJ) at the central laboratory. The lower limit of detection of this assay is 200 copies/mL. Samples with values > 100,000 copies/mL were diluted 1:1000- to 1:100,000-fold and retested. For patients with missing central laboratory

samples, HBV DNA results at the participating centers were used, and the results were converted into $\log_{10}$ copies/mL with conversion formulae provided by the manufacturers.

HBV Antiviral Resistance Mutation Testing

Samples from patients with virological breakthrough during antiviral therapy prior to transplant were tested for antiviral resistance mutations by direct sequencing of the HBV polymerase gene (rt9-250) as well as a line probe assay (INNO-LiPA DRv2 and DRv3, Innogenetics, Ghent, Belgium).[11,12]

Statistical Analyses

Categorical data were presented as number and percentage and compared with the chi-square test or Fisher's exact test as appropriate. Continuous variables were expressed as mean and standard deviation unless specified otherwise and compared with the *t* test or Mann-Whitney U test. The serum HBV DNA level was expressed as copies/mL and was logarithmically transformed.

An analysis of outcomes on the transplant waiting list, including deaths, dropouts (deaths or delisting due to disease progression), and time to transplant, and an analysis of outcomes post-transplant, including deaths, HBV recurrence, and HCC recurrence, were estimated with Kaplan-Meier analysis. Univariate analyses of factors associated with outcomes on the waiting list and outcomes post-transplant were performed with Kaplan-Meier analysis with the log rank test. Variables included in each analysis are shown in Table 1. Continuous variables were dichotomized, with the median taken as the cutoff value, except for serum HBV DNA, for which the cutoff used was 5 $\log_{10}$ copies/mL. Variables that had a *P* value of <0.2 on univariate analysis were entered into a Cox regression hazards model by forward logistic regression to determine the independent predictors of waitlist and post-OLT outcomes. All statistical analyses were performed with SPSS version 14.0.8 statistical software (SPSS, Inc., Chicago, IL).

RESULTS

Characteristics of Patients at Transplant Listing

A total of 274 patients, including 116 Caucasians, 135 Asian Americans, and 23 African Americans, were included. Characteristics of the patients at transplant listing are summarized in Table 2. The vast majority of the patients were men: 82% of Caucasians, 76% of Asian Americans, and 74% of African Americans. African Americans were younger at the time of listing, but there was no difference in age between Asian Americans and Caucasians, with mean ages in the 3 groups being 45, 53, and 54 years, respectively ($P < 0.001$). Asian Americans were more likely to have HCC at listing than African Americans and Caucasians: 47% versus 17% and 16%, respectively ($P < 0.001$). Among the patients with HCC, a similarly high proportion in the 3 racial groups had tumors within the Milan criteria. Asian Americans were less likely to have acute liver failure as an indication for liver transplant and were less likely to be listed for end-stage cirrhosis than African Americans and Caucasians ($P = 0.016$ and $P = 0.001$). At listing, hepatitis B e antigen (HBeAg) status, HBV DNA levels, liver chemistries, and international normalized ratio

were comparable among the 3 groups; however, Asian Americans had lower creatinine levels ($P = 0.025$), possibly because of the lower proportion of patients listed for acute liver failure or end-stage cirrhosis. Among the patients listed for end-stage cirrhosis, African Americans had higher Model for End-Stage Liver Disease (MELD) scores, but the difference was not significant. Similar percentages (52%-60%) of patients in the 3 groups were receiving antiviral therapy at listing.

Outcomes on the Transplant Waiting List

Probability of Transplantation—During a mean follow-up of 22.9 ± 28.7 [median 8 (range 0-127)] months from listing, 170 (62%) patients had been transplanted, including 74% of African Americans, 61% of Asian Americans, and 59% of Caucasians (Table 3). African Americans had the highest probability of undergoing transplantation, but the difference among the 3 groups was not statistically significant ($P = 0.487$; Fig. 1A). The probability of transplantation 1, 3, and 5 years after listing was 53%, 75%, and 88% for African Americans, 48%, 58%, and 66% for Asian Americans, and 48%, 57%, and 63% for Caucasians. As expected, the interval between listing and transplantation was shortest for patients with acute liver failure, and they were followed by those with HCC and those with end-stage cirrhosis (Fig. 1B). All patients with acute liver failure were transplanted within 8 days, while the probability of transplantation 1, 3, and 5 years after listing was 68%, 79%, and 83% for those listed for HCC and 34%, 46%, and 55% for those listed for end-stage cirrhosis ($P < 0.001$). Cox regression analysis showed that transplant indication ($P < 0.001$) and MELD score for end-stage cirrhosis patients ($P = 0.001$) were the only predictors of transplantation; race was not.

Waitlist Mortality—A total of 24 patients died while on the transplant waiting list, including 6 (4%) Asian Americans, 15 (13%) Caucasians, and 3 (13%) African Americans (Table 3). The probability of waitlist mortality at 1, 3, and 5 years was 3%, 3%, and 12% for Asian Americans, 10%, 18%, and 23% for Caucasians, and 6%, 31%, and 31% for African Americans ($P = 0.15$; Fig. 2). Cox regression analysis found that race, transplant indication, MELD score at listing among patients with end-stage cirrhosis, and tumor stage among patients with HCC did not predict waitlist mortality. Pairwise comparisons showed that Asian Americans had significantly lower waitlist mortality than Caucasians when all deaths were included, even after adjustments for transplant indication and listing MELD ($P = 0.05$). However, this difference was not significant when only liver-related deaths were analyzed ($P = 0.14$).

Dropout—Only 3 patients (1 Caucasian and 2 Asians) were removed from the waiting list because of disease progression (Table 3). Therefore, the probability of dropout (death or removal from the waiting list due to disease progression) in the 3 groups was similar to the probability of waitlist mortality.

New HCC Diagnosis While on the Waiting List—Of the 169 patients who had end-stage cirrhosis and no HCC at listing, 23 (14%) had a new HCC diagnosis while on the waiting list, including 14 (16%) Caucasians, 8 (12%) Asian Americans, and 1 (7%) African

American (Table 3). The probability of a new HCC diagnosis while on the waiting list was similar in the 3 racial groups (data not shown).

Characteristics of the Transplanted Patients

Characteristics of the 170 patients who underwent liver transplantation are listed in Table 4. The 3 racial groups were comparable, except for a younger age among African Americans and a higher proportion listed for HCC among Asian Americans. The 3 groups were also similar with respect to the proportion of patients receiving antiviral therapy, experiencing virological breakthrough or confirmed genotypic resistance pre-transplant, or having serum HBV DNA levels > 5 $\log_{10}$ copies/mL at the time of transplant. All except 5 patients (97%) received a combination of antiviral therapy and HBIG post-transplant. There was no difference in HBIG regimens among the 3 racial groups.

Post-Transplant Outcomes

Post-Transplant Survival—During a median follow-up of 31 months (range 0-67), 19 patients died, including 1 (6%) African American, 11 (13%) Asian Americans, and 7 (10%) Caucasians (Table 5). The probability of post-transplant survival at 1, 3, and 5 years was 94%, 94%, and 94% for African Americans, 90%, 85%, and 85% for Asian Americans, and 94%, 89%, and 89% for Caucasians ($P = 0.93$; Fig. 3). Cox regression analysis found that HCC recurrence was the only predictor of post-transplant mortality, while race, indication for transplant, and HBV recurrence were not.

HBV Recurrence—A total of 13 (8%) patients had HBV recurrence, including 1 (1%) Asian American, 1 (6%) African American, and 11 (16%) Caucasians (Table 5). Univariate analysis showed that the probability of HBV recurrence was significantly higher among Caucasians ($P = 0.043$). The probability of HBV recurrence at 1, 2, and 4 years post-transplant was 0%, 2%, and 7% for Asian Americans, 6%, 6%, and 6% for African Americans, and 8%, 13%, and 19% for Caucasians (Fig. 4). Cox regression analysis found that HBeAg status at listing ($P = 0.003$) was the only factor significantly associated with HBV recurrence post-transplant, while race showed a trend ($P = 0.057$; Table 6).

HCC Recurrence—A total of 89 patients had HCC: 68 at listing, 13 while on the waiting list, and 8 on explant liver. Of these, 7 (8%) had HCC recurrence, including 3 (10%) Caucasians and 4 (7%) Asian Americans. The probability of HCC recurrence at 1, 2, and 4 years was 4%, 4%, and 4% for Caucasians, 1%, 5%, and 7% for Asian Americans, and 0%, 0%, and 0% for African Americans ($P = 0.50$).

DISCUSSION

This large study included 274 patients listed for liver transplantation for HBV infection in 15 centers distributed across the United States, providing a good representation of HBV patients in this country. We found that Asians constituted half (49.2%) of the study population. This is not surprising because hepatitis B is endemic in Asian countries and many studies have reported a high prevalence (10%-15%) of chronic HBV infection among Asian Americans.[13-15] The National Health and Nutrition Examination Survey found that

the prevalence of HBV infection is 4-fold higher among African Americans versus whites.[16] It is surprising to see that a low percentage of patients listed for liver transplantation for HBV infection were African Americans. This discrepancy may be related to differences in access to transplantation.[17] We found that African Americans listed for end-stage cirrhosis had similar MELD scores and those listed for HCC had similar tumor staging at listing in comparison with Caucasians and Asian Americans. However, this does not preclude the possibility that fewer African Americans are referred to liver transplant centers or the possibility that more African Americans are referred too late and are not eligible for listing. Interestingly, African Americans were significantly younger at listing. This is surprising because African Americans likely acquired HBV infection during childhood or adult life, while Asian Americans likely acquired HBV infection perinatally or during early childhood. These data suggest that African Americans with chronic HBV infection may have a more rapidly progressive course.

Asian Americans were 3 times as likely to be listed for HCC as Caucasians or African Americans. The higher propensity for HCC may be related to a longer duration of HBV infection among Asian Americans, in whom infection likely occurred at a younger age, or to other factors such as HBV genotype, host genetics, or environmental factors (eg, aflatoxin). Many studies have shown that HBV genotype C, which is common in Asian countries and among Asian Americans, is associated with a higher risk of HCC than HBV genotype B.[18-21] A previous analysis of a subset of patients in the NIH HBV-OLT study for whom HBV genotype data were available showed that patients with genotype C infection were significantly more likely to have HCC at listing than those with genotype non-C (A, B, or D).[22] Once listed, the rate of new HCC diagnosis was similar in all 3 racial groups, underscoring the importance of HCC surveillance for all patients with HBV-related cirrhosis, regardless of race.

Despite differences in age at infection and therefore duration of infection, the prevalence of HBeAg, the percentage of patients with detectable serum HBV DNA, and the mean serum HBV DNA levels at listing were similar in the 3 racial groups. Persistence of HBeAg and high serum HBV DNA levels after a longer duration of infection may have contributed to the high rate of HCC among Asian Americans.[23,24] Similar percentages of patients in all 3 groups were receiving antiviral therapy at listing and at the time of transplant, and this indicated that there was no racial barrier to access to antiviral therapy.

Previous studies found that African Americans were less likely to be transplanted[17,25,26]; however, in this study, we found that African Americans were more likely to be transplanted, but the number of African Americans included was small. Moreover, the anomalous finding may be related to the fact that more African Americans were listed with acute liver failure, and those with end-stage cirrhosis had slightly higher MELD scores at listing. Multivariate Cox regression analysis showed that transplant indication was a significant predictor of time to transplant, but race was not. This finding confirms that the current system of organ allocation (sickest first) is fair across racial groups. Our study also showed that outcomes on the waiting list (waitlist mortality as well as dropout rate) were comparable among Caucasians, Asian Americans, and African Americans.

In accordance with the results of Lee et al.'s study,[4] racial disparity in post-transplant survival was not observed among patients who underwent OLT in an era when nucleos/tide analogues and HBIG prophylaxis are routinely used and the Milan criteria are applied to patients with HCC.[27] In fact, our study found a very high rate of post-transplant survival among African Americans: a 5-year probability of 94% versus 85% for Asian Americans and 89% for Caucasians. The only independent risk factor for mortality after liver transplant was recurrence of HCC. Although the rate of HCC recurrence was similar among the 3 racial groups, a higher proportion of patients transplanted for HCC may explain the slightly lower rate of post-transplant survival among Asian Americans. The disparity in the proportion of patients transplanted for HCC might have contributed to a higher rate of post-OLT mortality among Asian Americans in the era prior to the application of the Milan criteria.

A surprising finding was a higher HBV recurrence rate among Caucasians. Three studies performed in the 1990s reported similar or higher HBV recurrence rates among Asian Americans. One study of 15 Asians and 29 non-Asians reported a significantly higher rate of HBV recurrence among Asians: 72% versus 32% ($P < 0.05$).[6] Another study of 15 Asians and 20 non-Asians did not observe any difference in HBV recurrence rates between the 2 groups.[7] A third study of 70 Asians and 99 whites reported similar rates of HBV recurrence: 11% versus 12%.[8] In the current study, the probability of HBV recurrence 4 years post-transplant was 19% among Caucasians, 7% among Asian Americans, and 6% among African Americans ($P = 0.043$) despite similar HBeAg and HBV DNA status (at listing and at transplant), use of antiviral therapy pre-transplant, occurrence of virological breakthrough/confirmed genotypic resistance to antiviral therapy pre-transplant, and use of antiviral and HBIG prophylaxis post-transplant.

In summary, in this large retrospective-prospective study involving 274 patients with HBV listed for liver transplantation in the United States, we found similar waitlist and post-transplant outcomes among Caucasians, Asian Americans, and African Americans. There were some differences among these 3 racial groups. Asian Americans were significantly more likely to be listed for HCC, but HCC recurrence rates were similar to those of Caucasians and African Americans. African Americans were significantly younger and had a higher rate of transplantation, which is likely related to the higher proportion with acute liver failure. A surprising finding was a higher rate of HBV recurrence among Caucasians. This finding is inexplicable and needs to be validated. We acknowledge that the number of African Americans included in this study is small (23 in total and 17 transplanted), and patients who are approved for listing for liver transplantation may not represent the patient population at large. Nevertheless, our data indicate that Caucasians, Asian Americans, and African Americans with hepatitis B can be managed similarly in the transplant setting and can expect to have similar outcomes on the waiting list and after transplantation.

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Abbreviations

ALT	alanine aminotransferase
AST	aspartate aminotransferase
CI	confidence interval
HBeAg	hepatitis B e antigen
HBIG	hepatitis B immune globulin
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
INR	international normalized ratio
MELD	Model for End-Stage Liver Disease
NIH	National Institutes of Health
NS	not significant
OLT	orthotopic liver transplantation
SD	standard deviation
UNOS	United Network of Organ Sharing

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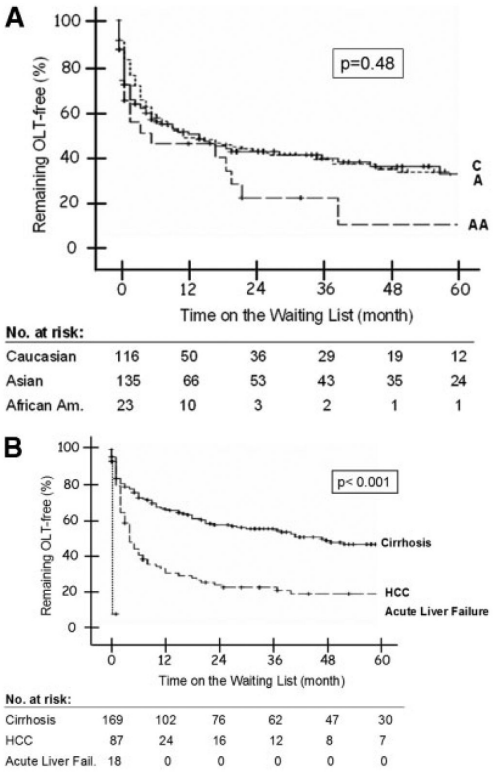
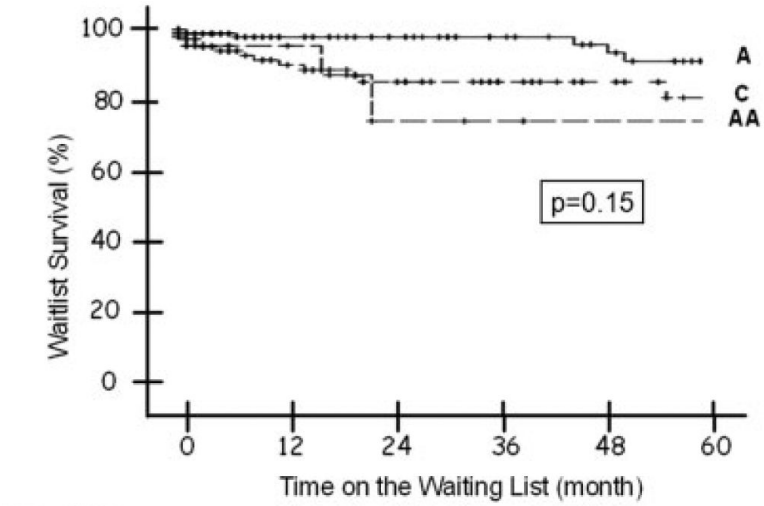


Figure 1.

Probability of undergoing OLT (A) by race and (B) according to transplant indication. Log rank *P* value for race: 0.48; log rank *P* value for transplant indication: <0.001.

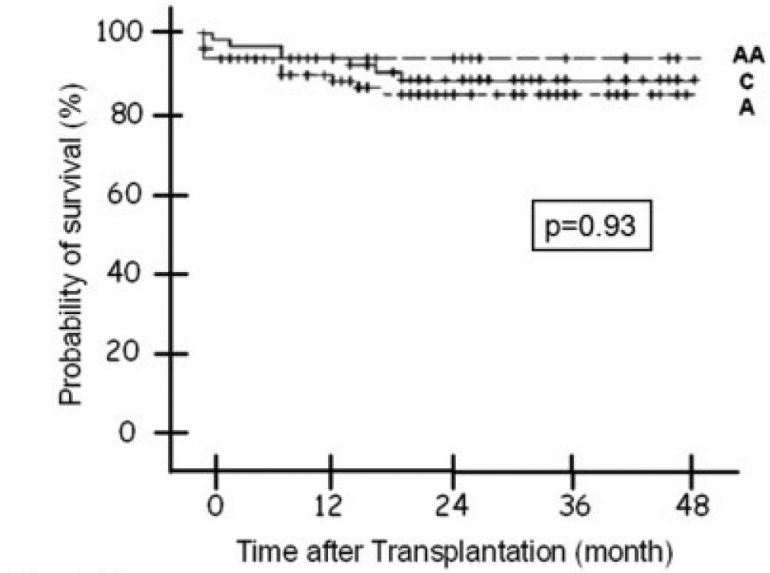
Abbreviations: A, Asian Americans; AA, African Americans; C, Caucasians; HCC, hepatocellular carcinoma; OLT, orthotopic liver transplantation.



No. at risk:						
Caucasian	116	50	36	29	19	12
Asian	135	66	53	43	35	24
African Am.	23	10	3	2	1	1

Figure 2.

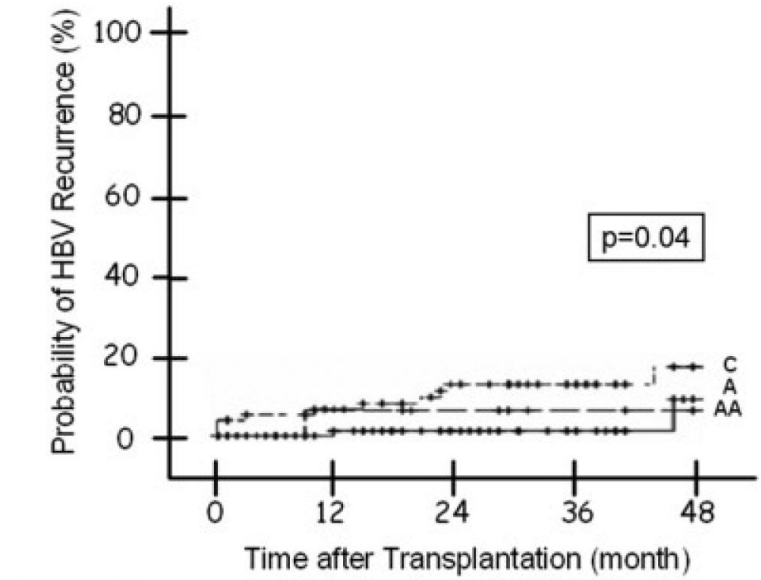
Probability of death on the waiting list by race. Log rank *P* value: 0.15. Abbreviations: A, Asian Americans; AA, African Americans; C, Caucasians.



No. at risk:					
Caucasian	68	62	50	37	21
Asian	85	68	47	29	8
African Am.	17	14	12	8	7

Figure 3.

Probability of post-transplant survival by race. Log rank *P* value: 0.93. Abbreviations: A, Asian Americans; AA, African Americans; C, Caucasians.



No. at risk:					
Caucasian	68	57	45	32	15
Asian	85	68	46	28	8
African Am.	17	13	11	8	7

Figure 4.

Figure 4. Probability of post-transplant HBV recurrence by race. Log rank *P* value: 0.04. Abbreviations: A, Asian Americans; AA, African Americans; C, Caucasians; HBV, hepatitis B virus.

TABLE 1

Variables Included in the Analyses of Outcomes

	Probability of Transplantation	Waitlist Mortality	Post-OLT Survival	HBV Recurrence	HCC Recurrence
Demographics	X	X	X	X	X
HBeAg status at listing	X	X	X	X	X
HBV DNA at listing	X	X	X	X	X
OLT indication at listing	X	X	X	X	X
Computed MELD score at listing	X	X			
HCC staging at listing	X	X			
New diagnoses of HCC on waiting list	X	X			X
OLT indication at transplant			X	X	
HBeAg status at transplant			X	X	
HBV DNA at transplant			X	X	
Tumor stage at transplant			X		X
Use of antiviral therapy prior to OLT			X	X	
Duration of antiviral therapy prior to OLT			X	X	
Antiviral breakthrough prior to OLT			X	X	
HBV recurrence post-OLT			X		
HCC recurrence post-OLT			X		
HBV prophylaxis post-OLT			X	X	
Treatment for rejection			X	X	
Duration of steroid use post-OLT			X	X	
Transplant center	X	X	X	X	X

Abbreviations: HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; MELD, Model for End-Stage Liver Disease; OLT, orthotopic liver transplantation.

TABLE 2

Characteristics of Patients at Listing

	Characteristics of Patients at Listing				*P* Values		
	C	As	AA	All	C Versus As Versus AA	C Versus As	C Versus AA
No. of patients	116 (42.3)	135 (49.2)	23 (8.3)	274 (100)			
Gender, male	95 (81.9)	103 (76.3)	17 (73.9)	215 (78.5)	NS	NS	NS
Age, years (mean ± SD)	53.73 ± 8.92	52.76 ± 9.75	45.26 ± 14.20	52.54 ± 10.08	0.001	NS	0.001
OLT indication					<0.001	0.001	NS
End-stage cirrhosis	87 (75.0)	67 (49.6)	15 (65.2)	169 (61.7)	0.001	<0.001	NS
HCC	19 (16.4)	64 (47.4)	4 (17.4)	87 (31.8)	<0.001	<0.001	NS
Acute liver failure	10 (8.6)	4 (3.0)	4 (17.4)	18 (6.5)	0.016	0.03	NS
Labs at listing							
HBeAg (+)	39/105 (33.6)	35/118 (25.9)	6/18 (26.1)	80/241 (29.2)	NS	NS	NS
HBV DNA detectable	62/107 (57.9)	70/117 (59.8)	10/21 (47.6)	142/245 (57.9)	NS	NS	NS
HBV DNA, $\log_{10}$ copies/mL (mean ± SD)	4.1 ± 2.5	4.1 ± 2.2	3.9 ± 2.3	4.1 ± 2.4	NS	NS	NS
HBV DNA > 5 log10 copies/mL	38/107 (35.5)	47/117 (40.2)	6/21 (28.6)	91/245 (37.1)	NS	NS	NS
ALT, U/L	59 (6–2387)	53 (3–8985)	59 (22–1940)	55 (3–8985)	NS	NS	NS
AST, U/L	77 (15–1132)	62 (8–7234)	78.5 (18–1251)	66 (8–7234)	NS	NS	NS
Bilirubin, mg/dL	1.9 (0.4–41.5)	1.5 (0.3–51.4)	2.6 (0.4–28.7)	1.8 (0.3–51.4)	NS	NS	NS
INR	1.3 (0.9–7.3)	1.3 (0.9–6.7)	1.4 (1–3)	1.3 (0.9–7.3)	NS	NS	NS
Creatinine, mg/dL	1.0 (0.5–7.1)	0.8 (0.4–6.4)	1.0 (0.6–5.8)	0.9 (0.4–7.1)	0.02	0.04	0.028
End-stage cirrhosis: MELD	13.0 (6–40)	14.0 (6–40)	15.5 (8–26)	13.0 (6–40)	NS	NS	NS
HCC: within Milan criteria*	13/19 (68.4)	46/64 (71.8)	4/4 (100)	63/87 (72.4)	NS	NS	NS
Antiviral treatment at listing	70 (60.3)	78 (58.2)	12 (52.2)	160 (58.3)	NS	NS	NS

NOTE: The results are expressed as number (%) or median (range) unless specified otherwise.

Abbreviations: ALT, alanine aminotransferase; AA, African Americans; As, Asian Americans; AST, aspartate aminotransferase; C, Caucasians; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; INR, international normalized ratio; MELD, Model for End-Stage Liver Disease; NS, not significant; OLT, orthotopic liver transplantation; SD, standard deviation.

*See Mazzaferro et al. 27

TABLE 3

Pretransplant Outcomes

	Pretransplant Outcomes			
	Caucasians	**Asian Americans**	**African Americans**	**All**
No. of patients at listing	116	135	23	274
No. transplanted	68/116 (58.7)	85/135 (61.4)	17/23 (73.9)	170/274 (62.0)
No. that died on waiting list	15/116 (12.9)	6/135 (4.4)	3/23 (13.0)	24/274 (8.7)
End-stage cirrhosis	12/87(13.7)	3/67 (4.4)	3/15 (20.0)	18/169 (10.7)
HCC	3/19 (15.7)	3/64 (4.6)	0/4 (0)	6/87 (6.8)
Acute liver failure	0/10 (0)	0/4 (0)	0/4 (0)	0/18(0)
Cause of death				
HCC	2	2	0	4/24 (16.7)
Other liver causes	7	4	3	14/24 (58.3)
Non-liver	6	0	0	6/24 (25.0)
No. of dropouts from waiting list	16/116 (13.7)	8/135 (5.9)	3/23 (13.0)	27/274 (9.8)
Cirrhosis	13/87 (14.9)	3/67 (4.4)	3/15 (20.0)	19/169 (11.2)
HCC	3/19 (15.7)	5/64 (7.8)	0/4 (0)	8/87 (9.1)
Acute liver failure	0/10 (0)	0/4 (0)	0/4 (0)	0/18 (0)
No. with new HCC diagnosis	14/87 (16.0)	8/67 (11.9)	1/15 (6.6)	23/169 (13.6)
Diagnosed on the waiting list	8	7	0	15
Diagnosed on explant liver	6	1	1	8

NOTE: The results are expressed as number (%).

Abbreviation: HCC, hepatocellular carcinoma.

TABLE 4

Characteristics of the Transplanted Patients

	Characteristics of the Transplanted Patients				*P* Values		
	C	As	AA	All	C Versus As Versus AA	C Versus As	C Versus AA
No. of patients	68 (40.0)	85 (50.0)	17 (10.0)	170 (100)			
Gender, male	53 (78.0)	63 (74.1)	13 (76.5)	129 (75.9)	NS	NS	NS
Age, years (mean ± SD)	53.1 ± 8.6	53.0 ± 10.5	43.0 ± 14.9	51.9 ± 10.7	0.001	NS	<0.001
OLT indication					0.008	0.014	NS
End-stage cirrhosis	30 (44.2)	26 (30.5)	8 (47.0)	64 (37.6)	NS	NS	NS
HCC	29 (42.6)	55 (64.7)	5 (29.4)	89 (52.4)	0.003	0.006	NS
Acute liver failure	9 (13.2)	4 (4.8)	4 (23.6)	17 (10.0)	0.032	0.06	NS
Labs at transplantation							
HBeAg (+)	15/56 (26.8)	18/69 (21.2)	4/13 (23.5)	37/138 (26.8)	NS	NS	NS
HBV DNA detectable	43/64 (67.2)	46/71 (54.1)	9/16 (52.9)	98/151 (64.9)	NS	NS	NS
Log_{10} copies/mL (mean ± SD)	4.2 ± 2.4	4.2 ± 0.2	3.7 ± 0.5	4.1 ± 2.2	NS	NS	NS
HBV DNA > 5 log_{10} copies/mL	25/43 (58.1)	29/46 (63.0)	4/9 (44.4)	58/98 (59.1)	NS	NS	NS
ALT, U/L	58 (13–2796)	49 (20–3543)	76 (13–1649)	53 (13–3543)	NS	NS	NS
AST, U/L	80 (16–6270)	66 (24–3907	71 (30–1946)	71 (16–6270)	NS	NS	NS
Bilirubin, mg/dL	2.8 (0.5–39)	2.1 (0.4–59.4)	5.4 (0.3–24.9)	2.6 (0.3–59.4)	NS	NS	NS
INR	1.5 (1–7.3)	1.4 (0.8–4.8)	1.8 (1.1–4.4)	1.5 (0.8–7.3)	NS	NS	NS
Creatinine, mg/dL	1.1 (0.1–7.8)	1.0 (0.5–6)	1.0 (0.5–9)	1.5 (0.1–9.0)	NS	NS	NS
End-stage cirrhosis: lab MELD	20 (9–38)	21 (8–40)	23 (11–40)	21 (8–40)	NS	NS	NS
HCC: within Milan criteria*	11/24 (45.3)	27/52 (52.0)	3/4 (75.0)	41/80 (51.2)	NS	NS	NS
Antiviral treatment pre-OLT†	49 (72.0)	66 (77.6)	10 (58.8)	125 (73.5)	NS	NS	NS
Breakthrough pre-OLT	9/49 (18.3)	10/66 (15.1)	3/10 (30)	22/125 (17.6)	NS	NS	NS
Confirmed genotypic resistance pre-OLT‡	4/5 (80.0)	5/6 (83.3)	2/3 (66.6)	11/14 (78.5)	NS	NS	NS
HBV prophylactic regimen post-OLT							
HBIG + antiviral	67 (98.5)	82 (96.4)	16 (94.1)	165 (97.0)	NS	NS	NS
HBIG only	0 (0)	1 (1.1)	0 (0)	1 (0.5)			
Antiviral only	1 (1.5)	2 (2.3)	1 (5.9)	4 (2.3)			
No. of patients treated for rejection	7 (10.2)	14 (16.4)	2 (11.7)	23 (13.5)	NS	NS	NS
Duration of steroid use, months	5 (0–27)	7 (0–17)	7 (3–13)	6 (0–27)	NS	NS	NS

NOTE: The results are expressed as number (%) or median (range) unless specified otherwise.

Abbreviations: ALT, alanine aminotransferase; AA, African Americans; As, Asian Americans; AST, aspartate aminotransferase; C, Caucasians; HBeAg, hepatitis B e antigen; HBIG, hepatitis B immune globulin; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; INR, international normalized ratio; MELD, Model for End-Stage Liver Disease; NS, not significant; OLT, orthotopic liver transplantation; SD, standard deviation.

*See Mazzaferro et al.[27]

†Ninety-eight of 123 (76.4%) patients transplanted after September 2002 when adefovir was approved were on antiviral therapy at the time of transplant versus 27 of 47 (57.1%) patients transplanted before September 2002.

[‡]Fourteen of 22 patients with virological breakthrough pre-transplant with blood samples collected prior to the initiation of rescue therapy were tested for antiviral resistance

TABLE 5

Post-Transplant Outcomes

	Post-Transplant Outcomes			
	Caucasians	**Asian Americans**	**African Americans**	**All**
No. of transplanted patients	68/116 (58.7)	85/135 (61.4)	17/23 (73.9)	170/274 (62.0)
No. that died	7/68 (10.2)	11/85 (12.9)	1/17 (5.8)	19/170 (11.1)
Cause of death				
Recurrent HCC	3	2	0	5
Other liver causes	2	3	0	5
Peritransplant complications	0	3	1	4
Other non-liver causes	2	3	0	5
No. with HBV recurrence	10/68 (14.7)	2/85 (2.3)	1/17 (5.8)	13/170 (7.6)
No. with HCC recurrence	3/29 (10.0)	4/55 (7.2)	0/5 (0)	7/89 (7.7)

NOTE: The results are expressed as number (%).

Abbreviations: HBV, hepatitis B virus; HCC, hepatocellular carcinoma.

TABLE 6

Multivariate Analysis of Factors Associated with HBV Recurrence

	Factors Associated with HBV Recurrence		
	***P* Value**	**Hazard Ratio**	**95% CI**
Listing HBeAg	0.003	12.903	2.368–70.321
Race	0.057	0.512	0.168–1.162
HBV DNA at transplant > 5 $\log_{10}$ copies/mL	0.624	0.536	0.272–8.769
Transplant date after 09/2002*	0.655	0.712	0.161–3.150
Center	0.936	0.962	0.966–1.124

Abbreviations: CI, confidence interval; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus.

*Date when adefovir was approved.