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ORIGINAL ARTICLE

Solid organ donor–recipient race-matching: analysis of the United Network for Organ Sharing database

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SUMMARY

Donor ethnicity is a prognosticator in organ transplant. However, the impact of donor/recipient race-matching is unclear. We hypothesized that there would be increased survival in donor–recipient race-matched organ recipients because of genetic and physiologic similarities. The UNOS database from 1999 to 2018 was queried for all solid organ transplantations including heart, lung, liver, kidney, and pancreas transplants. Data were sorted by donor and recipient race into matched and unmatched categories for Caucasian, African American, and Hispanic transplant recipients. After controlling for potential confounders via inverse propensity of treatment weighting, post-transplant patient and graft survival were compared between race-matched and -unmatched donor groups for each organ. Race-matched Caucasian recipients experienced 1–3% improvement in mortality across most time points in lung, liver, and pancreas transplants, while Hispanics did not benefit. Matched African American recipients experienced 4–6% improvement in patient and graft survival in liver transplant but had 7–9% worse survival rates at 5 years in lung and pancreas transplants. Race-matching does not influence patient outcomes enough to factor into organ transplant offers. African American liver transplant recipients benefited the most. Matching was detrimental to African American lung and pancreas transplant recipients indicating there may be other factors influencing the outcomes of these transplants.

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Introduction

Donor–recipient race-matching is thought to be an important prognosticator in organ transplant outcomes, as receiving an organ from someone of similar ethnogeographic origin could provide greater physiologic and genetic similarities between the organ donor and recipient [1]. Although one study reported a strong enough association to warrant the inclusion of race-matching in Donor Risk Index tools developed to improve transplant outcomes [2], there are several studies with conflicting results [3,4]. A complete analysis across all organ types has never been performed and prior studies of donor–recipient race-matching are limited in scope with respect to population and/or organ type [3,5–7]. Most prior studies of the Organ Procurement/United Network for Organ Sharing (OPTN/UNOS) database are now outdated and do not reflect the post-transplant

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care and health equity improvements over the last ten years. The results of these studies are also cloudy at best because of the use of unique population selection criteria among different studies [5–8].

Herein, we performed an updated and uniform investigation of the potential significance of race-matching on both patient and graft survival in solid organ transplants utilizing OPTN/UNOS data. The primary objective of this study was to determine and quantify the impact of race-matching on patient and graft survival on organ transplant at various post-transplant time points. We hypothesized that there would be an increase in patient and graft survival in race-matched organ recipients as opposed to unmatched organ recipients because of genetic and physiologic similarities in matched pairings. To the best of our knowledge, this is the first study describing the potential significance of race-matching on both patient and graft survival across all major solid organ types.

Methods and materials

We obtained data on all heart, lung, liver, kidney, and pancreas transplants from 1999 to 2018 from the OPTN/UNOS registry. These data were divided into individual, single organ transplant categories, except for pancreas for which combined transplants (e.g. kidney–pancreas) were also included. Patients with any previous organ transplant were excluded from analysis. Organ transplant categories were sorted based on donor and recipient race into matched and unmatched categories. Race categories included Caucasian, African American, and Hispanic recipients. "Asian" and "Other" recipient groups were also identified, but statistical analysis was not performed on this group because of the small number of race-matched donor–recipient pairs for these groups.

Patient demographics and clinical characteristics were selected for propensity model covariates including general factors that could impact any transplant, such as donor age, body mass index (BMI), transplantation year, ABO and HLA compatibility, and socioeconomic status, as well as organ specific factors (Table S4). These variables were compared between race-matched and race-mismatched donor groups using unpaired, unmatched t-tests for continuous variables, and chi-square tests for categorical variables (exploratory analysis, results not shown). The propensity for being matched with a same race donor was modeled using logistic regression, and the predicted probabilities were used to calculate inverse probability of treatment (IPT) weights for estimation of the average treatment effect (ATE). All available patient and clinical characteristics were included as predictors in the propensity model. Missing data were imputed prior to propensity modeling by inclusion of a "missing" category for categorical variables and mean imputation for continuous variables. Covariate balance was compared before and after applying inverse probability of treatment weighting (IPTW) using a "Love" plot of the standardized mean differences (results not shown) and a summary of the mean and maximum absolute standardized mean differences (results not shown). A standardized mean difference within 0.2 was used as the criteria for assessing balance.

The survival distributions for race-matched and mismatched groups were plotted using IPTW Kaplan–Meier methods and compared using a IPTW log-rank test. The IPTW Kaplan–Meier survival estimates were compared using a Z-test at 1, 3, 5, and 10 years post-transplant. An IPTW Cox proportional hazards regression model was also performed comparing race-matched vs. -mismatched groups. Standard errors and corresponding P-values for all IPTW analyses were calculated using bootstrap procedures (100 replicates) where the propensity model and IPT weights were re-estimated separately in each bootstrap sample. This analysis was repeated independently for each organ and each recipient race subgroup. Survival outcomes included both patient survival and graft survival. Statistical analysis was done using R version 3.5.2 (R Foundation for Statistical Computing, http://www.R-project.org). All P-values were 2-sided, and $P < 0.05$ was considered statistically significant. No corrections were made for multiple testing. Because the OPTN/UNOS database data is deidentified, no IRB approval was needed for this project.

Results

*For full listing of data values and Kaplan–Meier plots, please see the supplemental materials referenced. Statistics indicating the success of our matching and the appropriateness of weighting can be found in a Table S1 of our Supporting Information.

Heart transplant

The OPTN/UNOS followed 38 212 heart transplants from 1999 to 2018, including 26 806 to Caucasian recipients (70.0%), 7131 to African American recipients (18.6%), and 2866 to Hispanic recipients (7.5%; Table S5). There was no statistically significant benefit from donor–recipient race-matching in heart transplant

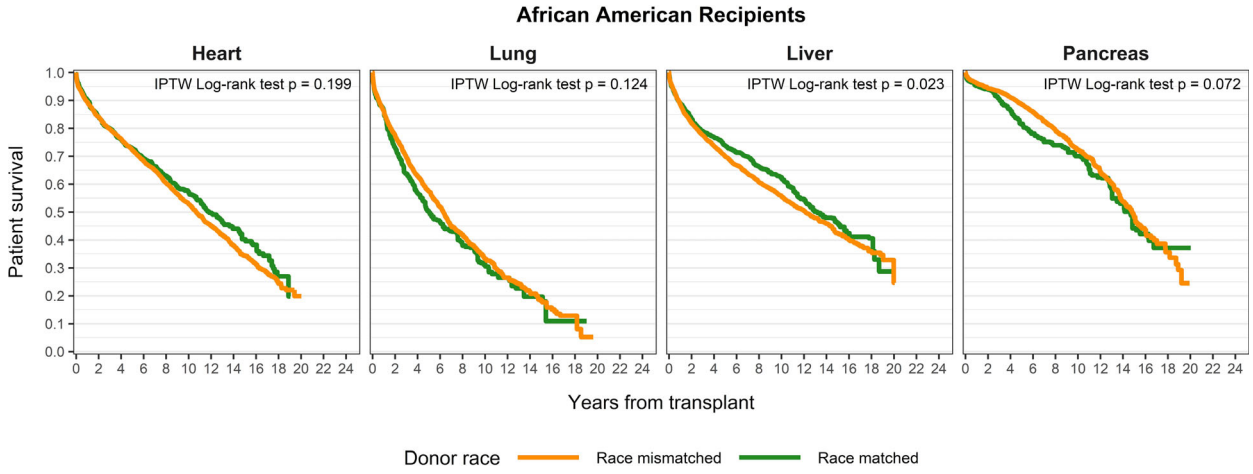

Figure 1 Propensity score weighted Kaplan–Meier curves and log-rank results comparing patient survival in donor–recipient race-matched versus unmatched African American recipients.

for any ethnic group for either patient survival or graft survival at any time point. Kaplan–Meier analysis suggests that matching may improve patient and graft survival in African American patients at time points beyond 10 years (Fig. 1), but the significance of this finding is limited by the small sample size for matched African American heart transplants (1382 matched African American heart transplants compared to 18 776 such matched transplants in Caucasian recipients).

Lung transplant

From 1999 to 2018, the OPTN/UNOS registry reported 29 755 lung transplants, including 24 911 to Caucasian recipients (83.7%), 2515 to African American recipients (8.5%), and 1691 into Hispanic recipients (5.7%; Table S5). Donor–recipient race-matching in Caucasian recipients improved patient survival by 2.9% at 1 year, 2.9% at 3 years, 2.5% at 5 years, and 2.2% at 10 years as well as graft survival in this group by 3.1% at 1 year, 3.2% at 3 years, 2.9% at 5 years, and 2.4% at 10 years (Fig. 2, Tables S2 and S3). Patient survival and graft survival in Caucasian recipients had hazard ratios of 0.912 and 0.905, respectively, when comparing race-matched to race-mismatched recipients (CI 0.876–0.950, 0.865–0.947 respectively, P-values < 0.001; Table 1). In contrast, race-matched African American recipients had worse outcomes than their nonmatched counterparts. Matched African Americans experienced a 5.8% and 7.5% worse patient survival at 3 and 5 years, respectively, while graft survival at 5 years decreased by 7.7% (Figs 2, 3, and 4, Tables S2 and S3). Hispanic recipients did not experience statistically significant differences in outcomes from race-matching.

Liver transplant

99 987 liver transplants were reported from 1999 to 2018 including 72 951 to Caucasian recipients (73.0%), 8410 to African American recipients (8.4%), and 13 021 into Hispanic recipients (13.0%). Caucasian recipients experienced a 0.8% improvement in patient survival at 1 year and 1% improvements at 3 and 5 years, while graft survival improved by 1.6%, 1.9%, 1.8%, and 1.8% at 1, 3, 5, and 10 years post-transplants, respectively, with a graft survival hazard ratio of 0.941 (CI 0.909–0.975, P-value < 0.001). African American recipients experienced a 4% benefit in patient survival at 5 years post-transplant and a 6.8% benefit at 10 years. Graft survival was also 4.7% higher in matched recipients at 10 years post-transplant. The patient survival hazard ratio for African American recipients of matched liver transplants was 0.88 (CI 0.785–0.986, P-value 0.027). Hispanic recipients did not experience statistically significant differences in outcomes from race-matching.

Kidney transplant

There were 265 177 kidney transplants recorded from 1999 to 2018 including 134 972 to Caucasian recipients (50.9%), 69 470 to African American recipients (26.2%), and 39 967 into Hispanic recipients (15.1%). There was limited benefit to race-matching in kidney transplant. Caucasian recipients experienced a 1.7% increase in graft survival at 5 years. Hispanic recipients had a significant 3.4% increase in patient survival at 10 years, while graft survival was not impacted. Patient survival in Hispanic kidney transplant recipients had a hazard ratio of 0.897 comparing donor–recipient race-

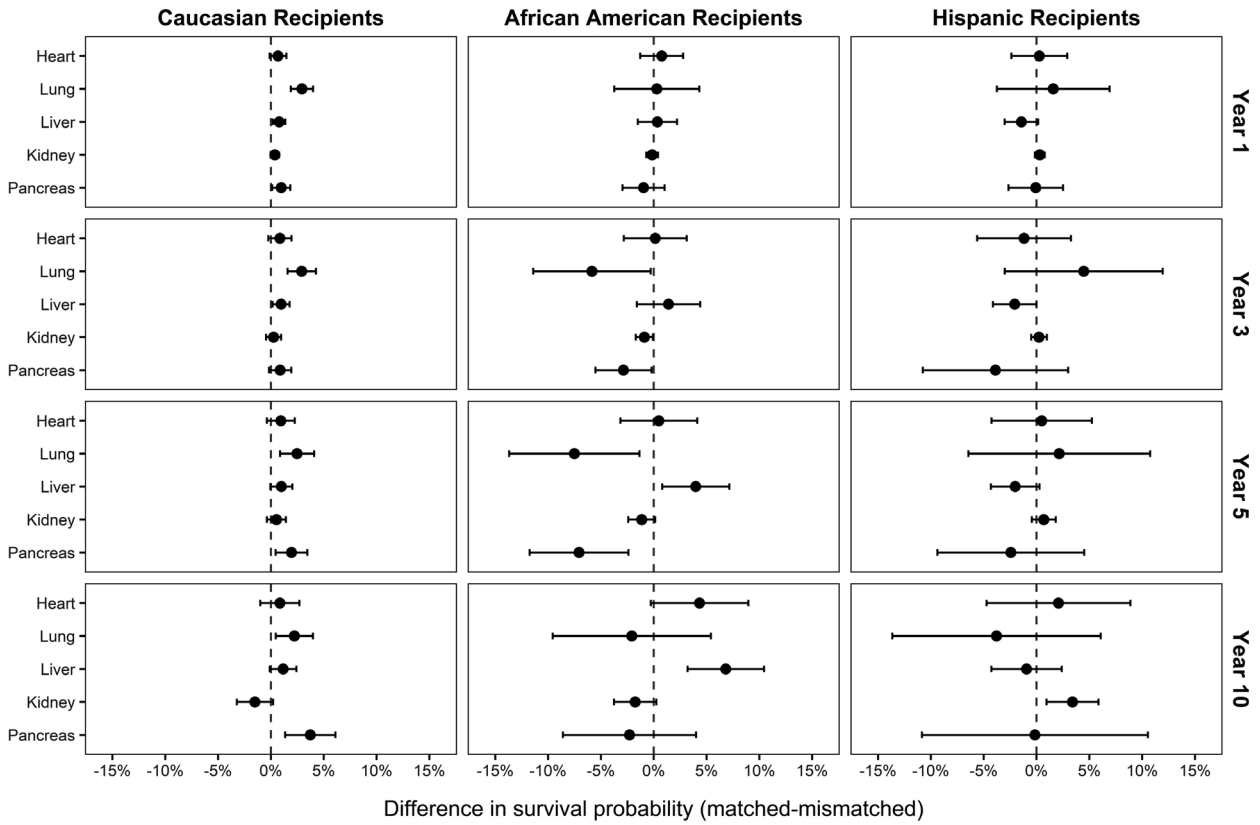

Figure 2 Propensity-weighted survival analysis of donor–recipient race-matching on patient survival at 1, 3, 5, and 10 years post-transplant.

matched to race-mismatched recipients (CI 0.833–0.967, *P*-value: 0.004). Interestingly, in African Americans, race-matching had little impact on patient survival, but afforded a 0.8%, 3.2%, 4%, and 3.2% decrease in graft survival at 1-, 3-, 5-, and ten-year time points respectively. Graft survival in African American recipients had a hazard ratio of 1.18 (CI 1.066–1.172, *P*-value < 0.001).

Pancreas transplant

From 1999 to 2018, 18 242 combined kidney–pancreas or isolated pancreas transplants were reported including 13 015 to Caucasian recipients (71.3%), 2995 to African American recipients (16.4%), and 1755 into Hispanic recipients (9.6%). Caucasian, race-matched recipients had slightly improved patient and graft survival. Patient survival in Caucasian increased by 1% at 1 year, 1.9% at 5 years, and 3.7% at 10 years, while graft survival increased 2.5% at 3 years, 3.6% at 5 years, and 2.7% at 10 years. Patient survival in Caucasian recipients had a hazard ratio of 0.885 (CI 0.821–0.953, *P*-value 0.001), while graft survival in this group had a hazard ratio of 0.897 (CI 0.84–0.96, *P*-value 0.002) when comparing race-matched to race-mismatched recipients. African Americans had worse outcomes with race-matching as patient survival in the matched group was 7.1% worse at 5 years, while graft survival was 6.8% and 9.5% worse at 3 and 5 years, respectively. Graft survival in African American recipients had a hazard ratio of 1.206 (CI 1.05–1.41, *P*-value 0.028). Hispanic recipients did not experience statistically significant differences in outcomes from race-matching.

Discussion

The results from this study shed light onto the slight impact donor–recipient race-matching have on solid organ transplant outcomes. While there is a statistically significant benefit or detriment from matching in some organs, donor–recipient race-matching does not universally influence patient outcomes enough to warrant inclusion as an independent factor in all organ transplant allocation based on propensity-matched analysis. Our findings indicate that Caucasians have slightly improved outcomes when receiving race-matched organs, while African Americans benefitted from receiving matched livers but had significantly worse survival

Table 1. Propensity score weighted cox proportional hazard regression for patient and graft survival.

Propensity score weighted cox proportional hazards regression- same vs. different race donor			
Recipient	HR	CI	*P* value
Patient survival			
Heart			
Caucasian	0.975	[0.927, 1.024]	0.31
African American	0.919	[0.806, 1.047]	0.204
Hispanic	0.966	[0.788, 1.184]	0.74
Lung			
Caucasian	0.912	[0.876, 0.950]	<0.001
African American	1.116	[0.972, 1.281]	0.12
Hispanic	0.99	[0.794, 1.234]	0.927
Liver			
Caucasian	0.967	[0.929, 1.006]	0.099
African American	0.88	[0.785, 0.986]	0.027
Hispanic	1.063	[0.968, 1.167]	0.201
Kidney			
Caucasian	1.024	[0.973, 1.078]	0.368
African American	1.056	[0.999, 1.116]	0.056
Hispanic	0.897	[0.833, 0.967]	0.004
Pancreas			
Caucasian	0.885	[0.821, 0.953]	0.001
African American	1.203	[0.995, 1.455]	0.056
Hispanic	1.034	[0.609, 1.756]	0.902
Graft survival			
Heart			
Caucasian	0.983	[0.933, 1.035]	0.514
African American	0.92	[0.820, 1.033]	0.16
Hispanic	0.952	[0.776, 1.168]	0.639
Lung			
Caucasian	0.905	[0.865, 0.947]	<0.001
African American	1.117	[0.970, 1.286]	0.125
Hispanic	0.961	[0.791, 1.168]	0.691
Liver			
Caucasian	0.941	[0.909, 0.975]	<0.001
African American	0.937	[0.850, 1.033]	0.191
Hispanic	1.048	[0.943, 1.165]	0.382
Kidney			
Caucasian	0.958	[0.913, 1.006]	0.084
African American	1.118	[1.066, 1.172]	<0.001
Hispanic	0.97	[0.908, 1.036]	0.365
Pancreas			
Caucasian	0.897	[0.84, 0.96]	0.002
African American	1.206	[1.05, 1.41]	0.028
Hispanic	1.068	[0.74, 1.43]	0.755

outcomes from receiving matched lungs and pancreases. As such, it may still be clinically beneficial to consider donor and recipient ethnicity matching among the complex milieu of factors considered in organ transplant decision making.

In our study, African American liver transplant recipients were the only population group to experience significant and substantial benefit from matching, a finding consistent with existing literature. Silva *et al.* [8] previously found that race-matching improved five-year survival by 7.3% in African American recipients of liver transplant for hepatocellular carcinoma with an adjusted hazard ratio of 0.66 (95% CI 0.49–0.88; *P*- 0.004). The results of our study demonstrate that race-matching benefits all African American liver transplant recipients, independent of transplant indication.

In contrast, matching was very detrimental to African American lung and pancreas transplant recipients at certain time points indicating the presence of systemic or physiologic factors influencing the outcomes of these transplants that warrant further investigation. When Allen *et al.* [5] preformed a similar analysis of lung transplants from the OPTN/UNOS database using data from 1997 to 2002, they found that race-matching decreased mortality after lung transplant at the 30-, 90-day, 1-, 2- and 5-year intervals, but that when deaths in the first year were censored, race-matching did not have an impact on survival. While our study did find improvements in recipient survival in Caucasian race-matched lung transplants similar to the 3.3% improvement for all races noted in the Allen *et al.* study, most values for African American and Hispanic transplants were not significant.

While patient survival in kidney transplant was not affected by race-matching, African Americans experienced worse graft survival at all time points, most notably a 4% decrease in graft survival at 5 years post-transplant (CI −2.3 to 5.6%, *P*-value < 0.001) with a graft survival hazard ratio of 1.118 (*P*-value < 0.001). This contrasts the 70% reduction in risk of graft loss in African American recipients of race-matched kidneys from donation-after-cardiac-death donors (DCD) suggested by Locke *et al.* [9] in their 1993–2006 review of UNOS data. However, the limited scope of DCD donors, dramatic improvements in the care and allocation of DCD organs in the succeeding 14 years since this study, and small sample size (142 transplants) limits the applicability of this study.

The significant decrease in patient and graft survival in African American recipients of race-matched pancreas transplants is particularly notable, as the 7.1% decrease in patient survival at 5 years (CI −2.4 to −11.7%, *P*-value 0.003) and 9.5% decrease in graft survival at 5 years (CI −3.4 to −15.6%, *P*-value < 0.001) were the greatest differences noted in any race category or organ system. Few prior studies have looked at the impact of racial factors on pancreas transplant outcomes [10], but as with most organ systems, organ

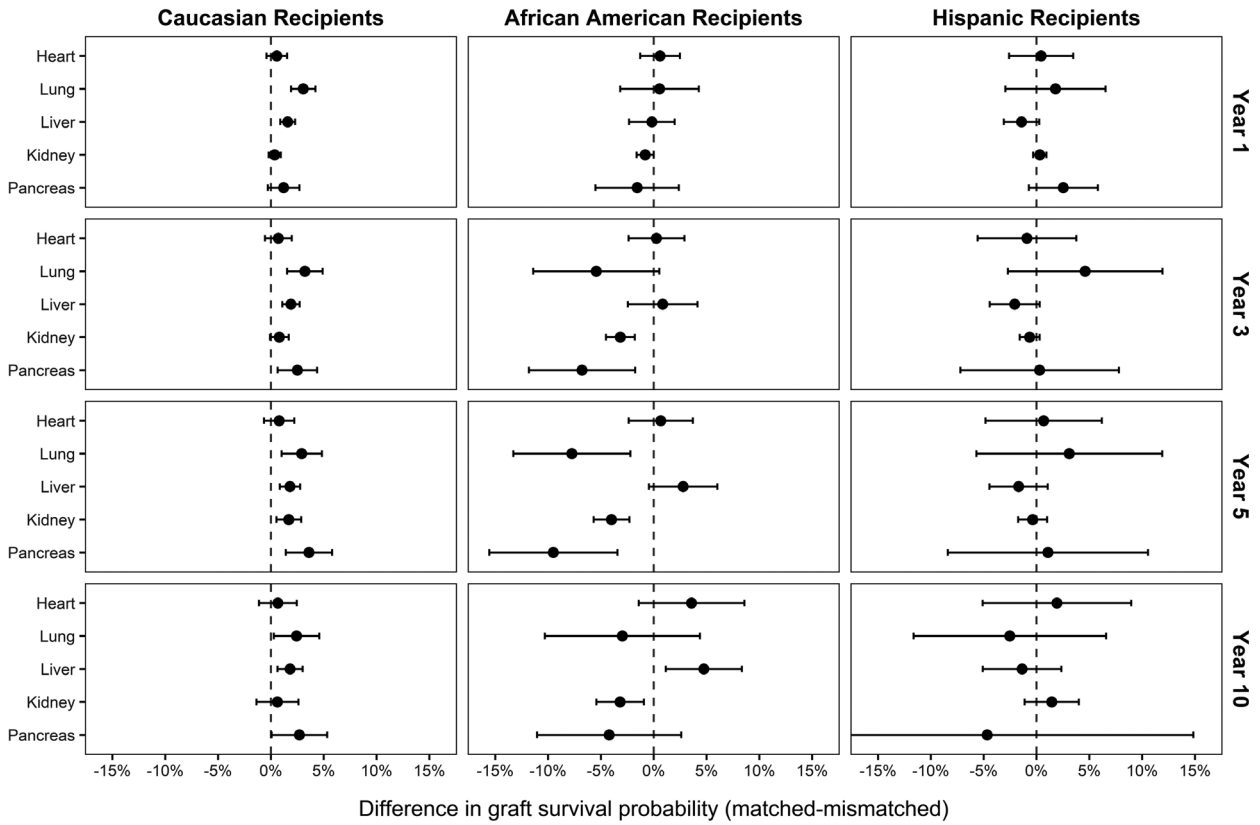

Figure 3 Propensity-weighted survival analysis of donor–recipient race-matching on graft survival at 1, 3, 5, and 10 years post-transplant.

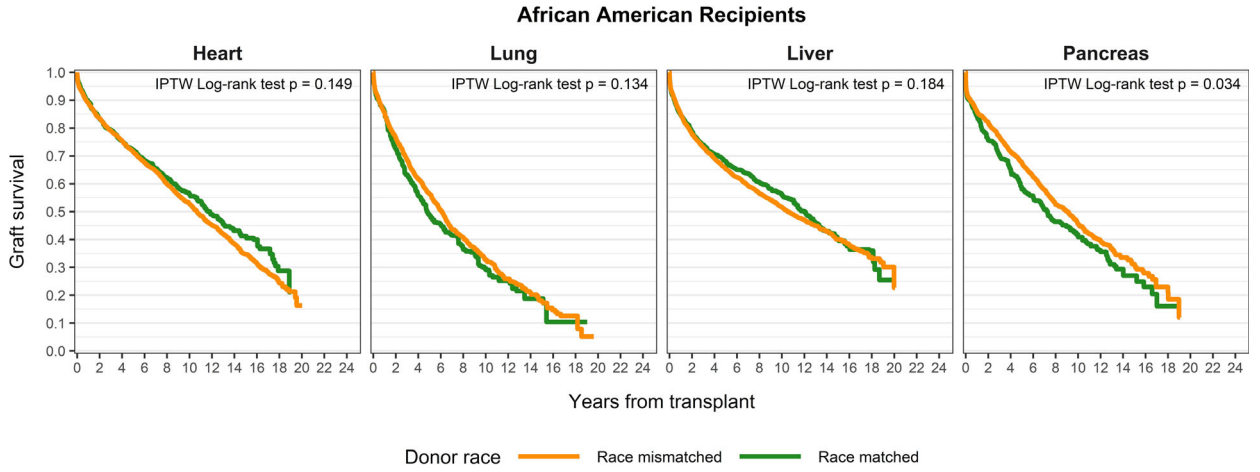

Figure 4 Propensity score weighted Kaplan–Meier curves and log-rank results comparing graft survival in donor–recipient race-matched versus unmatched African American recipient.

scarcity, and annual transplant volume limit the utility of this finding to warrant consideration of race-matching in allocation of pancreas grafts.

While the worsening of outcomes in race-matched African American recipients is surprising, it is not unprecedented. Callender *et al.* preformed a similar analysis of heart, kidney, and liver transplant outcomes of various donor–recipient race pairings using OPTN/UNOS data from 1994 to 2000. They found that when African Americans received race-matched organs, the risk of graft loss was 50.9% higher for kidneys and 36.6% higher for liver compared to Caucasian race-matched transplants [7]. Recipient mortality was also 50.9% higher in African American-to-African American

heart transplant when compared to their Caucasian-to-Caucasian counterparts [7].

Racial disparities may be a possible explanation for these findings. Racial disparities in organ transplant outcomes were first recognized in 1977 with poor rates of recipient and graft survival in African American kidney transplant recipients [11]. Despite the numerous advances in transplant medicine over the last 50 years such as surgical technique and immunosuppressant therapy, ethnic disparities persist. Several studies describe worse outcomes in both in African American organ recipients [4,12] and recipients of organs from African American donors [5,7]. The literature describes several factors contributing to poor organ transplant outcomes in different ethnic groups.

Poorer access to health care and subspecialists among minorities is one such factor [13]. However, Chakkera *et al.* [14] demonstrated that healthcare system access does not account for all racial disparities by showing a 10% higher risk of death and a 30% higher risk of graft failure in African American kidney transplant recipients within the Veterans Affairs system, a healthcare system with equivalent access to care. It is possible that the effects of race-matching noted herein may contribute to the racial disparities not yet accounted for.

As such, others have proposed genetic causes for this discrepancy like HLA mismatching or heightened immune response in African Americans [15,16]. African Americans have higher frequencies of *CYP* alleles involved in the metabolism of certain immunosuppressive drugs such as calcineurin inhibitors, leading to faster metabolism of these drugs and an undermining of their immune suppressive effects [17]. This population also has higher frequencies of high risk *APOL1* genes, which significantly increase an individual's risk of cardiovascular disease and hypertension associated kidney failure which could negatively affect long term graft survival [18]. Schweizer *et al.* [19] reported in their retrospective review that medication and treatment noncompliance rates are higher in African American and Hispanic populations, but the overall lower socioeconomic status among minorities likely plays a role in this finding. While such factors may contribute to the outcomes seen, the matching strategy used in this study incorporates HLA mismatch and socioeconomic status to help control for the impact of these factors. As such, the poor health status of African Americans may be contributing to these outcomes. African Americans have higher rates of many systemic diseases like heart disease and diabetes [20] which when accompanied by worse access to quality healthcare [13] places African American organ recipients at risk for worse outcomes before their organ transplant ever occurs.

This study has several notable limitations. The patient population for race-matched recipients was much larger for Caucasian recipients compared to African American and Hispanic populations across all solid organ groups. This contributed to wider variability and confidence intervals for minority groups. For example, in heart transplants, there were 18 776 Caucasian recipients of matched organs compared to only 1382 in African Americans and 887 Hispanics. As a retrospective database review, this study is limited by the constraints of the OPTN/UNOS database and results are subjected to confounding factors that we are unable to control for. Finally, the current analysis encompasses a large time period over which there have multiple dramatic improvements in transplantation care, particularly immunosuppression, organ preservation and perfusion, and perioperative care. While effort was made to consider all potential confounders as covariates in a propensity-weighted analysis, certain factors are outside the scope of the OPTN/UNOS dataset and thus could not be considered in propensity analysis. Further study regarding the impact of transplantation advances on race-matched donor–recipient solid organ transplantations is warranted and a topic for future study.

Conclusions

Race-matching does not seem to be a solitary influential prognosticator of organ transplant outcomes. However, such matching should still be considered among the many variables accounted for in clinical decision making, as some organs and ethnicities were found to disproportionately benefit or detriment from race-matched. In particular, African American recipients benefitted from race-matching in liver transplant, but experienced worse outcomes from matching in lung and pancreas transplant. The reasons for these outcomes may be related to the well-known healthcare disparities among ethnic minorities as well as systemic and/or physiologic factors which remain topics for future investigation.

Authorship

JML: preformed literature review, experimental design, created figures, and wrote the manuscript. SC and NS: contributed to intellectual discussions and manuscript editing. LR: preformed statistical analysis, created figures, and contributed to intellectual discussions. MK:

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performed literature review and contributed to intellectual discussions. TK, LDJ and DLJ: contributed to intellectual discussions. MS: writing and editing. All analysis was performed at Medical College of Wisconsin, Milwaukee, Wisconsin, USA.

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Conflicts of interest

The authors have declared no conflicts of interest.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Standard mean differences before and after Inverse Probability of Treatment Weighting (IPTW).

Table S2. Propensity score weighted Kaplan Meier survival estimate differences in patient survival at 1, 3, 5, and 10 years post-transplant.

Table S3. Propensity score weighted Kaplan Meier survival estimate differences in graft survival at 1, 3, 5, and 10 years post-transplant.

Table S4. Donor and recipient characteristics used as predictors in propensity score modeling.

Table S5. Frequency of recipient–donor race pairings.

Figure S1. Propensity score weighted Kaplan-Meier curves and log rank results comparing patient survival in donor-recipient race-matched versus unmatched recipients.

Figure S2. Propensity score weighted Kaplan-Meier curves and log rank results comparing graft survival in donor-recipient race-matched versus unmatched recipients.

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