Dispelling the myth of Asian homogeneity: Improved outcomes of Chinese Americans after kidney transplantation

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Abstract

Objectives: Asians represent the fastest-growing ethnic group in the United States. Despite significant diversity within the group, many transplant studies treat Asians as a homogeneous entity. We compared patient and graft survival among major Asian ethnicities to determine whether any subgroup has superior outcomes.

Methods: We conducted a retrospective analysis of kidney transplants on Asian and White patients between 2001 and 2012. Covariates included gender, age, comorbidities, and donor category. Primary outcomes included one-year patient and graft survival. Secondary outcomes included delayed graft function (DGF) and rejection as a cause of graft loss and death.

Results: Ninety-one Asian patients were identified. Due to the large proportion of Chinese patients (n=37), we grouped other Asians into one entity (n=54) for statistical comparison among Chinese, other Asians, and Whites (n=346). Chinese subjects had significantly lower body mass index (BMI) (p=0.001) and the lowest proportion of living donors (p<0.001). Patient survival ranked highest in our Chinese cohort (p<0.001), while graft survival did not differ.

Discussion: Our study confirms outcome differences among Asian subgroups in kidney transplantation. Chinese subjects demonstrate better patient survival at one year than Whites and non-Chinese Asians despite fewer live donors. Lower BMI scores may partly explain this. Larger, long-term studies would elucidate outcome disparities among Asian subgroups.

Keywords: Chinese, kidney, transplant, Asians, outcome

1. Introduction

Asians represent the fastest-growing ethnic group in the United States. Between 2006 and 2010, the population of Asian Americans grew by 46%, according to the Census Bureau, which constituted the most sizable increase of any major racial group during that period.

In 2010, 17,320,856 Asian Americans formed part of the United States census. This represented 5.6 percent of the total American population. "Asian" is a diverse ethnic group.

According to the census, the largest populations amongst this group were Chinese (3.79 million), Filipino (3.41 million), Indian (3.18 million), Vietnamese (1.73 million), Korean (1.7 million), and Japanese (1.3 million). Other sizable ethnic groups include Pakistani, Cambodian, Thai, Bangladeshi, and Burmese.

Despite significant diversity within the group, many transplant studies treat Asians as a homogeneous entity.

Ethnic subgroup	Frequency	Percent	Cumulative percent
Bangladeshi	2	0.5	0.5
Cambodian	2	0.5	0.9
Chinese	37	8.5	9.4
Indian	10	2.3	11.7
Japanese	1	0.2	11.9
Korean	10	2.3	14.2
Pakistani	6	1.4	15.6
Filipino	13	3.0	18.5
Taiwanese	1	0.2	18.8
Vietnamese	9	2.1	20.8
White	346	79.2	100
Total	437	100	

Table 1: Ethnic breakdown of Asians and Whites.

	Chinese (n=37)	Other Asians (n=54)	Whites (n=346)	Total (n=437)	p-value
$BMI^*(kg/m^2)$, mean $\pm(SD)$	22.4 (4.15)	24.5 (3.5)	27.5 (5.34)	26.6 (5.2)	0.001
Age (years), mean±(SD)	54.6 (13.6)	56.7 (10.8)	56 (12.3)	56 (12.2)	0.734
Recipient gender, n (%)					0.001
Female	16 (43.2)	30 (55.6)	105 (30.3)	151 (34.6)	
Male	21 (56.8)	24 (44.4)	241 (69.7)	286 (65.4)	
Recipient Diabetes Mellitus, n (%)	11 (29.7)	28 (51.9)	143 (41.3)	182 (41.6)	0.07
Recipient Hypertension, n (%)	29 (78.4)	44 (81.5)	239 (69.1)	312 (71.4)	0.174
Recipient HCV ^{**} , n (%)	1 (2.7)	2 (3.7)	40 (11.6)	43 (9.8)	0.066
Wait (days), mean±(SD)	411 (376)	500.5 (480.7)	442 (436.2)	446.9 (436.8)	0.577
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* Body Mass Index

* Hepatitis C Virus

Table 2: Demographic characteristics.

The UNOS database does not differentiate among Asians, and studies on subgroup outcomes are lacking. Yet, the Asian category represents a heterogeneous population in terms of genetic background, culture, and duration of US residence.

Early reports indicated that outcomes proved better in the Asian population than in Whites and African Americans (1-3). It was postulated that small body mass, lack of diabetes as a cause of renal failure, improved socioeconomic status, and a low sensitization rate played a role in these significant results (4). In one study of Chinese recipients in Hong Kong, the recipient body mass index cutoff of 25 kg/m2 corresponded with excellent survival rates (5).

However, not all Asians fare well after transplantation. Several reports indicate that South Asians (patients from the Indian Subcontinent, namely India, Pakistan, Bangladesh, Nepal, and Sri Lanka) experience poorer outcomes after transplantation (6), including a higher rate of end-stage renal failure (7) and cardiovascular morbidity (8). Other studies negate a diminution in survival among South Asians. Loucaidou et al. reported an equivalent three-year survival between South Asians and their White counterparts, although their five-year survival curves diverge (9). Given the equivocal data on post-transplant outcomes among Asian subgroups, we sought to compare patient and graft survival among major Asian ethnicities to determine whether any subgroup has superior outcomes. We hypothesized no difference among subgroups.

2. Methods

2.1 Study Design

We conducted an institutional review board-approved retrospective analysis of all Asian kidney transplants between June 2000 and November 2011. We received the list from UNOS and used our databases to ungroup the Asians. United States Census categories classified patients as originating from the Far East, Southeast Asia, or the Indian subcontinent. Ninety-one Asian patients were identified: 88 from deceased donors and three from live donors. Thirtyseven patients came from the ethnic Chinese group, 34 from the Southeast Asian group, and 18 from the Indian

subcontinent (South Asian) group. Due to the small numbers in each group and the large proportion of Chinese subjects

	Chinese (n=37)	Other Asians (n=54)	Whites (n=346)	Total (n=437)	p-value
BMI*(kg/m ²), mean±(SD)	27.6 (7.9)	26.6 (5.8)	26.6 (6.7)	26.7 (6.7)	0.734
Donor gender, n (%)					0.332
Female	19 (51.4)	27 (50)	145 (41.9)	191 (43.7)	
Male	18 (48.6)	27 (50)	201 (58.1)	246 (56.3)	
Donor type, n (%)					< 0.001
CD**	4 (10.8)	9 (16.7)	25 (7.2)	38 (8.7)	
DCD**	4 (10.8)	9 (16.7)	25 (7.2)	38 (8.7)	
SCD***	27 (73)	28 (51.9)	222 (64.2)	277 (63.4)	
ECD****	5 (13.5)	12 (22.2)	26 (7.5)	43 (9.8)	
ECD/DCD	1 (2.7)	0	3 (0.9)	4 (0.9)	
Living	0	5 (9.3)	70 (20.2)	75 (18.5)	
Machine prefused	11 (29.7)	13 (24.1)	57 (16.5)	81 (18.5)	0.001
allografts, n (%)					
* BMI, Body Mass Index					

* BMI, Body Mass Index

** HCV, Hepatitis C Virus

*** Standard Criteria Donor

*** Expanded Criteria Donor Table 3: Donor information.

(41%) in the Far East category in our cohort, we combined the Southeast Asian and Indian subcontinent groups (n=54). Our statistical analysis is thus reflective of the comparison between 37 ethnic Chinese patients and 54 "other Asian" patients. We retrospectively reviewed transplants of White patients (n=346) during the same period for comparison to each of the Asian groups.

2.1.1 Statistical Analysis. We compared comorbidities, demographics, and transplant data between groups to determine any differences (Tables II-III, respectively). We tested the data for normality and used ANOVA and chisquared tests for comparisons. Primary outcomes included one-year patient survival and graft survival. Secondary outcomes included delayed graft function (DGF), defined as the need for dialysis within the first week after transplant, rate of rejection, and cause of death (Table IV). The log-rank test was used for patient and graft survival analysis. Data analysis occurred with Statistical Package for the Social Sciences (SPSS) SPSS, version 20 (IBM, Armonk, New York).

In terms of donor characteristics, more donations after cardiac death (DCD) and expanded criteria donors (ECD) appeared in the other Asian group than in the other two categories. The Chinese group was transplanted from deceased donors (p<0.001). Additionally, the rate of machine perfusion proved significantly higher in the Chinese group (Table 3).

2.1.2 Immunosuppressive and infection prophylaxis protocols. All patients received antibody induction therapy with rabbit anti-thymocyte globulin (rATG), started intraoperatively and followed by two to four subsequent daily doses to target a cumulative dosage of 5 to 6 mg/kg ideal body weight. In patients with a weight greater than 130% of their ideal body weight, adjusted body weight helped calculate the dosage. A calcineurin inhibitor was initiated once induction therapy was complete and/or after the resolution of DGF. Target tacrolimus trough levels for the first three months post-transplant were 7 to 10 ng/mL and 4 to 7 ng/mL thereafter. Target cyclosporine trough levels for the first three months post-transplant were 150 to 250 ng/mL and 75 to 150 ng/mL thereafter. On the first postoperative day, 1000 mg of mycophenolate mofetil twice daily was initiated. To avoid discontinuation or dosage reduction of mycophenolate mofetil because of intolerable gastrointestinal adverse effects, mycophenolate mofetil may have been replaced by enteric-coated mycophenolate sodium at therapeutically equivalent MPA doses.

Five to 10 mg/kg of methylprednisolone was administered intraoperatively, and corticosteroids were tapered down to 20 mg of prednisone daily by postoperative day seven, with further dose reduction to 5 mg daily by the third month posttransplant. Perioperative wound infection prophylaxis

	Chinese (n=37)	Other Asians (n=54)	Whites (n=346)	Total (n=437)	p-value
Cold Ischemic Time (hr), mean	13.9 (6)	15.1 (6.9)	14 (7.4)	14.1 (7.2)	0.640
Warm Ischemic Time (min), mean	37.5 (36.2)	31.8 (19.3)	37.3 (19.6)	36.6 (21.5)	0.235
Creatinine at 1 yr (mg/dl), mean	1.5 (1)	1.9 (1.9)	1.7 (0.9)	1.7 (1.2)	0.299
Panel Reactive Antibody (mg/dl),	10.9 (26.3)	11.9 (29.7)	14.7 (30.2)	14 (29.7)	0.655
Terminal Creatinine (mg/dl), mean	1 (0.4)	1.1 (0.5)	1.1 (1.1)	1.1 (1)	0.935
Rejection as a cause of graft failure, n (%)	4 (10.8)	3 (5.6)	15 (4.3)	22 (5)	0.227
Cause of graft failure (other than					0.095
rejection), n (%)					
Graft thrombosis	0	1 (1.9)	1 (0.3)	2 (0.5)	
Infection	0	1 (1.9)	2 (0.6)	3 (0.7)	
Recurrent disease	0	0	2 (0.6)	2 (0.5)	
Other	0	0	9 (2.6)	9 (2.6)	
Renal vein thrombosis	0	0	1 (0.3)	1 (0.2)	
Primary non-function	2 (5.4)	1 (1.9)	5 (1.4)	8 (1.8)	
Unknown	0	0	7 (2)	7 (1.6)	
HUS	0	1 (1.9)	0	0	
Cause of death, n (%)					0.451
Cardiovascular	0	1 (1.9)	11 (3.1)	12 (2.7)	
Cerebrovascular	0	0	2 (0.6)	2 (0.5)	
Infection	0	3 (5.6)	11 (3.2)	14 (3.2)	
Malignancy	0	0	2 (0.6)	2 (0.5)	
Multiple system organ failure	0	0	2 (0.6)	2 (0.5)	
Respiratory failure	0	1 (1.9)	1 (0.3)	2 (0.5)	
Other	1 (2.7)	0	1 (0.3)	1 (0.2)	
Unknown	0	4 (7.4)	54 (15.6)	59 (13.5)	
Delayed graft failure	7 (18.9)	17 (31.5)	113 (32.7)	137 (31.4)	0.231

Table 4: Intraoperative and postoperative variables

consisted of cefazolin. Cefazolin-allergic patients received vancomycin. Cytomegalovirus prophylaxis with renal doseadjusted valganciclovir (maximum 450 mg daily) was given for six months universally. Other infection prophylaxis included Pneumocystis pneumonia prophylaxis with sulfamethoxazole-trimethoprim for six months and fungal prophylaxis with clotrimazole for four weeks post-transplant. Our protocol involves treating borderline and Banff grade I rejections with pulse corticosteroids and Banff grade IIA and higher with rATG (10).

3. Results

In our cohort, the Chinese ethnicity comprised the most frequent ethnicity after Whites (n=37, 8.5%). A full breakdown of all the included ethnic subgroups appears in Table 1. Significantly more males than females appeared in the Chinese and White groups (p=0.001). The Chinese cohort had the lowest BMI (22.4 compared to 24.5 in other Asians and 27.5 in Whites, p=001). No statistical difference

appeared in terms of recipient age, incidence of diabetes, hypertension, hepatitis C, and duration of wait (Table 2).

In terms of intra-operative and post-transplant variables, no difference revealed itself in the proportion of grafts with DGF. The incidence of rejection, or other causes of graft failure, did not prove statistically significant. Additionally, no difference became apparent in the cause of death, cold ischemic time (CIT), warm ischemic time (WIT), Panel Reactive Antibody (PRA), or terminal creatinine (Table 4).

The Chinese cohort demonstrated superior one-year patient survival than both Whites (97% vs. 88%; p <0.001) and other Asians (97% vs. 92%; p=0.049). One-year patient survival proved significantly higher among all Asians than Whites (94% vs. 88%; p<0.001). One-year graft survival did not differ significantly among groups.

4. Discussion

American studies of Asians tend to focus on East Asians, indicating improved survival (1-2). In contrast, Canadian and

British studies tend to focus on Indo-Asians and generally report worse survival (11). Comparative outcomes among Asian subgroups have not undergone examination in the United States.

Others have demonstrated a higher incidence of comorbidities among specific Asian subgroups. Prasad et al. found that South Asian ethnicity correlated with higher rates of diabetes and prior cardiac disease among kidney transplant recipients (8). Filipinos also face an increased risk of heart disease compared to their Chinese and Japanese counterparts. Despite these disparate analyses in the literature, we did not detect a statistical difference in the incidence of hypertension and diabetes among our subgroups. This development may have occurred due to the grouping of "other Asians," which includes a heterogeneous Asian population with disparate comorbidity profiles.

The relationship between lower recipient BMI scores and better outcomes has been well-established. Recipient BMI above 25 kg/m2 represents a significant independent risk factor for graft failure (5). Asians have historically had lower BMI scores than their White counterparts. Therefore, it was not surprising that Whites in our study had the highest BMI scores. However, our Chinese cohort had the lowest BMI scores. This situation correlated with their superior posttransplant survival. While many studies tend to group obesity, diabetes, and hypertension into one clinical entity (metabolic syndrome), our findings of isolated differences in BMI scores among our subgroups suggest obesity constitutes an independent predictor of outcomes.

Lower panel reactive antibody (PRA) also represents a factor for improved survival among Asians undergoing transplantation. PRA ranks among the most sensitive immunologic parameters to provide clinically useful information on the status of a deceased donor kidney recipient. Recipients with high PRA levels have a higher risk of DGF, acute rejection, and kidney loss. Ethnic disparities in peak PRA levels among organ recipients have been wellestablished in the literature. Our study found no difference in PRA levels among Chinese, other Asians, and Whites, indicating that immunologic variation may not explain survival differences among ethnic subtypes. However, our cohort was small, and larger investigations with longer follow-ups would elucidate the relationship between PRA levels and ethnic survival differences.

Our study found superior one-year patient survival among Chinese compared to other Asians and Whites. This development corresponds with Go's report comparing patient survival among Chinese, Malaysian, and Indian subgroups (12). While this occurred in Malaysia, Go similarly found the Chinese race to be associated with improved survival, which aligns with publications that show superior outcomes for Asians compared to Whites (13). Although the rate of machine perfusion proved significantly higher in Chinese recipients, the rate of DGF did not reach statistical significance. Some studies cite fewer comorbidities, higher

education, and better compliance as explanations for improved survival (14). Meanwhile, our patients experiencing similar overall comorbidity profiles and lower BMI scores among the Chinese cohort may help explain their superior survival. These findings align with the literature (15). Whites also had a more than three-fold higher incidence of hepatitis C. Furthermore, our urban community hospital consistently sees patients of low socioeconomic status, which may contribute to lower survival rates across ethnicities. While our study did not control for socioeconomic status, social status discrepancies may become more apparent in our population among Whites than among Asians. According to a recent publication, life expectancy at birth by race/ethnicity in Pennsylvania amounted to 78.9 years for Whites, 73.4 years for African-Americans, 85.3 years for Latinos, and 89.0 years for Asian-Americans (18). Therefore, regardless of transplantation, in Pennsylvania, Asian people are expected to live longer. It remains unclear whether increased life expectancy played a role in one-year survival.

Another possible explanation for superior outcomes in Asians is that fewer overall Asian patients are transplanted compared to Whites, thereby distorting statistical analysis. Prasad attributes this access disparity in part to the lower rates of living donor transplants among East Asian and Indo-Asian subgroups (16). Our living donor recipients were overwhelmingly White, with no Chinese and very few Asian recipients. Superior survival among Asians despite a lower number of living donors in our study is an unexpected finding that merits further assessment of the relationship between donor type and recipient survival among Asians and Whites.

The underutilization of living donors among Asians remains well-documented yet poorly understood. The shortage of organs for transplantation among Asians proves so chronic in the United Kingdom that public initiatives seek to promote awareness and willingness to donate (20). Deceased donation among Asians also remains relatively uncommon. One British study found that relatives of 78.7% of Asian British potential non-heart-beating donors refused consent in a three-year study period compared to relatives of 31.8% of White potential donors (21). The authors identified the reluctance to donate to religious beliefs, lack of awareness of the need for transplantation, distrust of the medical community, worries that the organ may form part of medical research, concerns that the donor's wellbeing would not be prioritized, and fears about leaving the body intact after death (21). Culturally tailored transplant education approaches must be made available at appropriate literacy levels in various languages, with live interpreters, when appropriate, to address these barriers. While Canada and the United Kingdom have made efforts to tackle these issues, literature on efforts in the United States to overcome the Asian donor shortage remains sparse and requires attention.

In contrast to patient survival, graft survival did not prove significantly different among subgroups. Our findings align with Tonelli's report of comparable death-censored graft loss among those of Indo-Asian, East Asian, and Caucasian descent (17). It remains possible that compliance with medication, follow-up, and lower BMI counterbalance the deleterious effects of deceased donor transplants among Chinese recipients. Our findings contrast Medcalf's United Kingdom study of 2,650 patients reporting worse graft survival in South Asian patients than in Whites (19). Their group could not explain the discrepancies between ethnic groups, but it may result from a higher prevalence of diabetes (11) and coronary artery disease (8) among this subgroup. Further studies with more subgroups would engender meaningful comparisons between demographic variables and outcomes after renal transplantation.

5. Strengths and Weaknesses

This study examines an area of kidney transplantation not previously addressed, which also represents one of the largest experiences of ethnic Chinese immigrants in kidney transplant literature. Weaknesses include its retrospective nature and the grouping of non-Chinese Asians into one statistical entity. While our study sought to avoid homogenizing Asian ethnicities, our sample size of individual subgroups was not large enough to treat any ethnic group other than Chinese as a separate entity. The use of creatinine or calculated glomerular filtration rate (GFR) based on creatinine measurements with small sample sizes may not enable us to detect clinically critical distinctions between groups. Furthermore, we could not distinguish South Asians from patients from the Indian subcontinent due to insufficient sample sizes, leading to an incomplete stratification of Asian subgroups. We also did not study socioeconomic factors that may contribute to disparities in access to renal transplants among Asians and specific Asian subgroups.

6. Conclusion

Our study confirms outcome differences among Asian subgroups in kidney transplantation. Chinese Americans demonstrate better patient survival at one year than Whites and non-Chinese Asians. This finding was true despite the lack of live donors among the Chinese. A lower BMI may partly explain such a development. However, better outcomes could not align with diabetes or other comorbidities. Our findings may have significant ramifications for outcomes, expectations, and reimbursement. Larger, longer-term studies would further elucidate the relationship between comorbidity profiles, donor type, and transplant outcomes among Asian subgroups.

Author contributions

JO and KK designed the research protocol; SC and RZ performed the study; AP collected the data; PC and AP conducted the analysis; FK and JP drafted the manuscript; and JO takes responsibility for the paper as a whole.

Competing interests

The authors declare no conflicts of interest.

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