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

Farah Karipineni [a], Afshin Parsikia [a], Po-nan Chang [a], John Pang [a], Stalin Campos [a], Kamran Khanmoradi [a], Radi Zaki [a], Jorge Ortiz [a b 1]

[a]Albert Einstein Medical Center, Philadelphia, PA 19141, and [b]University of Toledo Health Science Campus, Toledo, OH 43614

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 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 had the lowest proportion of living donors (p<0.001). Patient survival was 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 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 are needed to elucidate outcome disparities among Asian subgroups.**

kidney | transplant | Asians | Chinese | outcomes

Asians represent the fastest growing ethnic group in the United States. The total population of Asian Americans grew by 46% from 2000 to 2010 according to the Census Bureau, which constituted the largest increase of any major racial group during that period.

In 2010, there were a total of 17,320,856 Asian Americans in the United States census. This represented 5.6 percent of the total American population. “Asian" is a diverse ethnic group. The largest amongst this group according to the census 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. The UNOS database does not differentiate among Asians, and studies on subgroup outcomes are lacking. Yet, the Asian category represents a heterogenous population in terms of genetic background, culture and duration of US residence.

Early reports indicated that outcomes were better in the Asian population than 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 rate of sensitization played a role in these excellent results (4). In one study of Chinese recipients in Hong Kong, recipient body mass index cutoff of 25 kg/m^2 was associated with excellent survivals (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. While Loucaidou et al. report equivalent 3-year survival between South Asians and their white counterparts, their 5-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 in outcomes among subgroups.

Methods

Study Design. We conducted an institutional review board-approved retrospective analysis of all Asian kidney transplants performed between June 2000 and November 2011. We received the list from UNOS and then used our databases to ungroup the Asians. United States Census categories were used to classify patients as originating from the Far East, Southeast Asia, or the Indian subcontinent South Asians. Ninety-one Asian patients were identified. Eighty-eight were from deceased donors, and three were from live donors. Thirty-seven patients were in the ethnic Chinese group, 34 in the Southeast Asian group, and 18 in the Indian subcontinent (South Asian) group. Due to the small numbers in each group, and the large proportion of Chinese subjects (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 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.

Statistical Analysis. We compared comorbidities, demographics and transplant data between groups to determine any differences (Tables

[1]To whom correspondence should be sent: Jorge.Ortiz@utoledo.edu

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, JO takes responsibility for the paper as a whole.

The authors declare no conflict of interest

Freely available online through the UTJMS open access option

II-III, respectively). We tested the data for normality and used ANOVA and chi squared tests for comparisons. Primary outcomes included one-year patient survival and graft survival. Secondary outcomes included delayed graft function (DGF), defined as need of 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 was done with Statistical Package for the Social Sciences (SPSS) SPSS, version 20 (IBM, Armonk, New York).

Immunosuppressive and infection prophylaxis protocols. All patients received antibody induction therapy with rabbit anti-thymocyte globulin (rATG), started intraoperatively and followed by 2 to 4 subsequent daily doses to target a cumulative dosage of 5 to 6 mg/kg ideal body weight. In patients whose actual weight was greater than 130% of their ideal body weight, an adjusted body weight was used to calculate the dosage. A calcineurin inhibitor was initiated once induction therapy was complete and/or after resolution of DGF. Target tacrolimus trough levels for the first 3 months post-transplant were 7 to 10 ng/mL and 4 to 7 ng/mL thereafter. Target cyclosporine trough levels for the first 3 months post-transplant were 150 to 250 ng/mL and 75 to 150 ng/mL thereafter. Mycophenolate mofetil 1000 mg twice daily was initiated on postoperative day 1. 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. Methylprednisolone 5 to 10 mg/kg was administered intraoperatively, and corticosteroids were tapered down to prednisone 20 mg daily by postoperative day 7, with further dose reduction to 5 mg daily by 3 months post-transplant.

Perioperative wound infection prophylaxis consisted of cefazolin. Cefazolin-allergic patients were administered vancomycin. Cytomegalovirus prophylaxis with renal dose-adjusted valganciclovir (maximum 450 mg daily) for 6 months was given universally. Other infection prophylaxis included Pneumocystis pneumonia prophylaxis with sulfamethoxazole-trimethoprim for 6 months, and fungal prophylaxis with clotrimazole for 4 weeks after transplant. It is our protocol to treat borderline and Banff grade I rejections with pulse corticosteroids, and Banff grade IIA and higher with rATG (10).

Results

In our cohort the Chinese ethnicity was the most frequent ethnicity after Whites (n=37, 8.5%). A full breakdown of all the included ethnic subgroups included is displayed in Table 1. There were significantly more males than females 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). There was no statistical difference in recipient age, incidence of diabetes, hypertension, hepatitis C, and duration of wait (Table 2).

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

Table 1: Ethnic breakdown of Asians and Whites

Ethnic subgroup	Frequency	Percent	Cummulative 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
Philippino	13	3.0	18.5
Tiwanese	1	0.2	18.8
Vietnamese	9	2.1	20.8
White	346	79.2	100
Total	437	100	

In terms of intra-operative and post-transplant variables, there was no difference in proportion of grafts with DGF. The incidence of rejection, or other causes of graft failure were also not statistically significant. Additionally, there was no difference in cause of death, cold ischemic time (CIT), warm ischemic time (WIT), Panel Reactive Antibody (PRA), terminal creatinine, or cause of death (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 was significantly higher among all Asians compared to Whites (94% vs. 88%; p<0.001). One-year graft survival did not differ significantly among groups.

Discussion

American studies of Asians tend to focus on East Asians, indicating improved survivals (1-2). In contrast, Canadian and British studies tend to focus on Indo-Asians and generally report worse survivals (11). Interestingly, comparative outcomes among Asian subgroups have not specifically been examined in the United States.

Others have demonstrated a higher incidence of comorbidities among specific Asian subgroups. Prasad et al. found that South Asian ethnicity was associated with higher rates of diabetes and prior cardiac disease among kidney transplant recipients (8). Filippinos are also at increased risk for heart disease when compared to their Chinese and Japanese counterparts. Despite these disparate analyses in

Table 2: Demographic characteristics

	Chinese (n=37)	Other Asians (n=54)	Whites (n=346)	Total (n=437)	p-value
BMI[a](kg/m^2), mean±(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

[a] BMI, Body Mass Index
[b] HCV, Hepatitis C Virus

Table 3: Donor Information

	Chinese (n=37)	Other Asians (n=54)	Whites (n=346)	Total (n=437)	p-value
BMI[a](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
DCD[b]	4 (10.8)	9 (16.7)	25 (7.2)	38 (8.7)	
SCD[c]	27 (73)	28 (51.9)	222 (64.2)	277 (63.4)	
ECD[d]	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 allografts, n (%)	11 (29.7)	13 (24.1)	57 (16.5)	81 (18.5)	0.001

[a] Body Mass Index
[b] Donation after Cardiac Death
[c] Standard Criteria Donor
[d] Expanded Criteria Donor

the literature, we did not detect a statistical difference in the incidence of hypertension and diabetes among our subgroups. This may be due to the grouping of “other Asians" which in itself 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/m^2 has been cited as 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, it is noteworthy that our Chinese cohort had the lowest BMI scores. This correlated with their overall superior post-transplant 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 suggests that obesity is an independent predictor of outcomes.

Lower panel reactive antibody (PRA) scores have also been cited as a factor for improved survival among Asians undergoing transplantation. PRA is considered one of 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 high risk of DGF, acute rejection, and even kidney loss. Ethnic disparities in peak PRA levels among organ recipients has been well-established in the lit-

Table 4: Intraoperative and postoperative variables

	Chinese (n=37)	Other Asians (n=54)	Whites (n=346)	Total (n=437)	p-value
Cold Ischemic Time (hr), mean (SD)	13.9 (6)	15.1 (6.9)	14 (7.4)	14.1 (7.2)	0.640
Warm Ischemic Time (min), mean (SD)	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 (SD)	1.5 (1)	1.9 (1.9)	1.7 (0.9)	1.7 (1.2)	0.299
Panel Reactive Antibody (mg/dl), mean (SD)	10.9 (26.3)	11.9 (29.7)	14.7 (30.2)	14 (29.7)	0.655
Terminal Creatinine (mg/dl), mean (SD)	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 rejection), n (%)					0.095
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

erature. 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-up are required to 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 is consistent with Go's report comparing patient survival among Chinese, Malaysian and Indian subgroups (12). While this was performed in Malaysia, Go similarly found Chinese race to be associated with improved survival. This is also consistent with publications that show superior outcomes for Asians compared to Whites (13). Although the rate of machine perfusion was 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). While our patients experienced similar overall comorbidity profiles, lower BMI scores among our Chinese cohort may in part explain their superior survival. These findings are consistent 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 be more apparent in our population among Whites than among Asians. According to a recent publication, life expectancy at birth by race/ethnicity in Pennsylvania was 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 is unclear whether increased life expectancy actually 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). Indeed, our living donor recipients were overwhelmingly White, with no Chinese recipients and very few Asian recipients overall. Superior survival among Asians despite a lower number of living donors in our study is an unexpected finding that merits further study of the relationship between donor type and recipient survival among Asians and Whites.

The underutilization of living donors among Asians is well-documented, yet poorly understood. The shortage of organs for transplantation among Asians is so chronic in the United Kingdom that public initiatives have been designed to promote awareness and willingness to donate (20). Deceased donation among Asians is also relatively uncommon. One British study found that relatives of 78.7% of Asian British potential non-heart-beating donors refused consent in a 3-year study period compared to relatives of 31.8% of White potential donors (21). The authors identified factors attributing reluctance to donate to religious beliefs, lack of awareness of need for transplantation, distrust of the medical community, worries that the organ may be used for medical research, concerns that the donor's wellbeing would not be prioritized, and concerns about leaving the body intact after death (21). Culturally tailored transplant education approaches must be made available at appropriate literacy levels and in various languages, with the use of 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 is sparse and requires attention.

In contrast to patient survival, graft survival was not significantly different among subgroups. Our findings are consistent with Tonelli's report of comparable death-censored graft loss among Indo-Asian, East Asian and Caucasian descent (17).ă It is possible that compliance with medication and follow-up as well as lower BMI counterbalance the deleterious effects of increased utilization of deceased donor transplants among Chinese recipients. Our findings are in contrast to Medcalf's United Kingdom study of 2,650 patients reporting worse graft survival in South Asian patients compared to Whites (19). Their group could not explain the discrepancies between ethnic groups, but it may be attributable to a higher prevalence of diabetes (11) and coronary artery disease (8) among this subgroup. Further studies with larger numbers of subgroups are required to make meaningful comparisons between demographic variables and outcomes after renal transplantation.

Strengths and Weaknesses

This study examines an area of kidney transplantation that has not previously been addressed. This 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 simply 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 important distinctions between groups. Furthermore, we were not able to 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.

Conclusions

In conclusion, our study confirmsăoutcome 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 this. However, better outcomes could not be correlated with diabetes or other comorbidities. Our findings may have significant ramifications for outcomes expectations and reimbursement. Larger, longer term studies are needed to further elucidate the relationship between comorbidity profiles, donor type and transplant outcomes among Asian subgroups.

1. **Katznelson S, Gjertson DW, Cecka JM (1995) The effect of race and ethnicity on kidney allograft outcome. *Clin Transplant* 379-94.**
2. **Cecka JM, Gjertson D, Terasaki PI (1992) Superior allograft survival among Asian recipients. *Transplant Proc* 24(4):1431-432.**
3. **Cho YW, Terasaki PI (1996) Comparison of kidney graft survival in Asian and Caucasian patients transplanted in the United States. *Transplant Proc* 28(3):1571-1573.**
4. **Goh A (2009) Graft survival trends in kidney transplants: An analysis of the UNOS database. *Clin Transplant* 41-54.**
5. **Chow KM, Szeto CC, Leung CB, Lui SF, et al. (2006) Body mass index as a predictive factor for long-term renal transplant outcomes in Asians. *Clin Transplant* 20(5):582-589.**
6. **Jeffrey RF et al. (2002) Indo-Asian experience of renal transplantation in Yorkshire: Results of a 10-year survey. *Transplantation* 73(10):1652-1657.**
7. **Roderick PJ, Jones I, Raleigh VS, McGeown M, Mallick N (1994) Population need for renal replacement therapy in Thames regions: Ethnic dimension. *Br Med J* 29(309):1111-1114.**
8. **Prasad GV, Vangala SK, Silver SA, Wong SC, Huang M (2011). South Asian ethnicity as a risk factor for major adverse cardiovascular events after renal transplantation. *Clin J Am Soc Nephrol* 6(1):204-211.**
9. **Loucaidou M, et al. (2004) Outcome of renal transplantation in South Asian recipients is similar to that of non-Asians. *Transplantation* 78(7):1021-1024.**
10. **Racusen LC, et al. (1999) The Banff 97 working classification of renal allograft pathology. *Kidney Int* 55(2):713-723.**

11. Dooldeniya MD, et al. (2006) Renal Transplantation in Indo-Asian patients in the UK. *Am J Transplant* 6(4):761-769.
12. Go KW, Teo SM (2004) Comparison of patient survival between various subgroups among renal transplant patients: a single center experience. *Transplant Proc* 36(7):2046-2047.
13. Fan PY, et al. (2010). Access and outcomes among minority transplant patients, 1999-2008, with a focus on determinants of kidney graft survival. *Am J Transplant* 10(4):1090-1107.
14. Gordon EJ, Ladner DP, Caicedo JC, Franklin J (2010) Disparities in kidney transplant outcomes: a review. *Semin Nephrol* 30(1):81-89.
15. Gill JS, et al. (2013) The survival benefit of kidney transplantation in obese patients. *Am J Transplant* 13(8):2083-2090.
16. Prasad GV (2007) Renal transplantation for ethnic minorities in Canada: inequity in access and outcomes. *Kidney Int* 72(4):390-392.
17. Tonelli M, et al. (2007) Patient and allograft survival of Indo Asian and East Asian dialysis patients treated in Canada. *Kidney Int* 72(4):499-504.
18. Life Expectancy at Birth (in years) by Race/Ethnicity. Available at kkf.org. Accessed September 26, 2015.
19. Medcalf JF, et al.(2011) Poorer graft survival in ethnic minorities: results from a multi-centre UK study of kidney transplant outcomes. *Clin Nephrol* 75(4):294-301.
20. Baines, LS. Joseph, JT. Jindal, RM (2002) A public forum to promote organ donation amongst Asians: the Scottish initiative. *Transplant Int* 15(2-3):124-131.
21. Perera, S and Mamode, N (2011) South Asian patients awaiting organ transplantation in the UK. *Nephrol Dial Transplant* 26(4):1380-1384.