## **ORIGINAL RESEARCH**

# Combined Heart-Lung Transplantation Outcomes in Asian Populations



## **National Database Analysis**

Yasuhiro Shudo, MD, PhD,<sup>a</sup> Matthew Leipzig, BS,<sup>a</sup> Hao He, PhD,<sup>a</sup> Shreya Mukund Ingle, BA,<sup>a,b,c</sup> Rishab Harish Bhatt,<sup>a,c,d</sup> Hye-Sook Shin, BS,<sup>a</sup> Y. Joseph Woo, MD<sup>a</sup>

## **ABSTRACT**

**BACKGROUND** Heart-lung transplantation (HLTx) is a definitive surgical procedure for end-stage cardiopulmonary failure. Studies to understand the relationship between ethnicity and race and outcomes after HLTx are needed to uphold equitable HLTx access to the increasingly diverse U.S. population facing advanced cardiopulmonary failure.

**OBJECTIVES** This study sought to examine the outcomes of HLTx recipients of Asian origin, with emphasis on the ethnic and racial disparities in the outcomes.

METHODS We analyzed data from the United Network for Organ Sharing (UNOS) for patients of ≥18 years of age who underwent HLTx between 1987 and 2021. Propensity-score matching was performed between Asian and non-Hispanic Whites (NHWs), with a 1:3 matching ratio based on the propensity score of each patient estimated by multivariable logistic regression.

**RESULTS** We identified 42 Asian and Asian American heart-lung transplant recipients and 834 NHW recipients. In the pre-matched cohort, the median survival was 1,459 days (IQR: 1,080-2,692 days) in Asian recipients after transplantation, whereas it was 1,521 days (IQR: 1,262-1,841 days) in White recipients. Of the 876 recipients, 156 transplants were successfully matched (Asian, n = 36; NHW, n = 108). Among the post-transplantation outcomes, there were no significant differences in morbidity and mortality between Asian and NHW cohorts.

**CONCLUSIONS** This large-scale analysis in Asian patients will have important implications in Asian countries that have relatively fewer HLTx surgeries. An outcome equivalent to NHW in Asian patients, as demonstrated in our study, could be the driving force for further expansion of HLTx surgeries in Asian countries. (JACC: Asia 2022;2:504-512) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

ombined heart-lung transplantation (HLTx) is a definitive surgical procedure that has been used to treat irreversible lifethreatening cardiopulmonary failure. It was first performed successfully at Stanford Hospital in 1981<sup>1</sup> and

has since been used to treat more than 3,200 patients worldwide. In the last decade, the number of HLTx surgeries each year has significantly decreased;<sup>2</sup> however, together with the improvement of short-term outcomes,<sup>3,4</sup> HLTx remains a viable treatment

From the <sup>a</sup>Department of Cardiothoracic Surgery, Stanford University School of Medicine, Stanford, California, USA; <sup>b</sup>Department of Natural Sciences, Rice University, Houston, Texas, USA; <sup>c</sup>Stanford Center for Asian Health Research and Education, Stanford University School of Medicine, Stanford, California, USA; and the <sup>d</sup>Departments of Neuroscience and Behavioral Biology and Computer Science, Emory University, Atlanta, Georgia, USA.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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option for patients with end-stage cardiopulmonary

Studies to understand the relationship between ethnicity and race and outcomes after HLTx are needed to uphold equitable HLTx access to the increasingly diverse U.S. population facing advanced cardiopulmonary failure. Studies have shown that various recipient risk factors, such as donor age and recipient sex, can affect patient outcomes significantly, but no large multicenter study has analyzed ethnicity and race as risk factors.<sup>4</sup>

We aimed to examine the outcomes of HLTx recipients who were of Asian origin, with special attention to whether ethnic or racial disparities in the outcomes of HLTx with propensity-scored matching.

#### **METHODS**

failure.5

STUDY COHORT. This study was a retrospective review using deidentified data supplied by the United Network for Organ Sharing (UNOS) as the contractor for Organ Procurement and Transplantation Network. The study cohort was selected from the UNOS database, which included patients of ≥18 years of age who underwent HLTx between January 1987 and 2021. Our study was exempted from review by the institutional review board of our institution because no patient identifiers were included in the UNOS database.

PATIENT SELECTION. We primarily examined the survival outcomes of Asian and Asian American heartlung transplant recipients. For comparative purposes, we also included non-Hispanic White (NHW) recipients in the cohort. Patients were excluded if they were <18 years of age at the time of surgery, if they underwent HLTx with other concomitant procedures, if they underwent redo heart or lung transplantation through combined HLTx, or if their ethnicity was not described as NHW or Asian.

For donors, we mainly investigated the following factors available from the database: age, sex, body mass index (BMI), left ventricular ejection fraction, blood group, past medical history (diabetes mellitus, hypertension, cocaine use, coronary artery disease, cigarette use, heavy alcohol consumption, renal function, and liver function), and cause of death.

For recipients, we assessed the important demographics and clinical characteristics of HLTx: age, sex, surgery year, BMI, body surface ratio, blood group, waitlist time, past medical history (diabetes mellitus, cigarette use, renal function, and liver function), etiology of cardiopulmonary failure,

previous cardiac and lung surgeries, need for preoperative life support such as an intraaortic balloon pump or extracorporeal membrane oxygenation (ECMO), hospitalization status at the time of transplantation (hospitalized in an intensive care unit, hospitalized but not in intensive care unit, or outpatient), lung allocation score, total waiting time, and allograft ischemic time.

## STATISTICAL ANALYSIS. In this study, pa-

tient characteristics and outcomes were summarized and compared according to race. Continuous variables were expressed as mean  $\pm$  SD or median (IQR), and compared using the Student's t-test or Wilcoxon rank-sum test. Chi-squared test or Fisher's exact test was used to compare categorical variables.

Patient survival was visually presented, based on race using Kaplan-Meier survival estimation, and survival curves were compared using log-rank test. To better understand survival and other outcomes between NHWs and Asians, balance sample sizes of the 2 races and eliminate potential confounding factors, propensity-score matching analysis was performed. The important demographic or clinical characteristics of recipients and donors, which were unbalanced based on a standardized mean difference (SMD) of > 0.1, showed sound diversity between the 2 races and had no-or very few-missing values in the cohort, were selected to estimate propensity scores of patients through multivariable logistic regression. As the Asian cohort had no patients with diabetes, we performed exact matching as per diabetes status and subset in our cohort on patients without diabetes first, to balance the populations. We then performed propensity-score matching on the remaining confounding factors. These factors included recipient factors of age, sex, BMI, pre-operative ECMO status, donor sex, body surface ratio, allograft ischemic time, and surgery year based on the estimated propensity score of each patient; Asian and NHW patients were matched with a ratio of 1:3, using the algorithm of optimal matching without replacement by the MatchIt package in R.6 An absolute standardized mean difference of <0.1 was considered to represent relative balance. Only patients who were successfully matched were assessed in the after-match assessment of ethnicity and race impact on post-transplantation outcomes. For all statistical analyses, a 2-sided alpha (α)-level of 0.05 was considered statistically significant. All analyses were performed using the R software version 4.0.5.7

## ABBREVIATIONS AND ACRONYMS

BMI = body mass index

ECMO = extracorporeal membrane oxygenation

HLTx = heart-lung transplantation

NHW = non-Hispanic White

UNOS = United Network for Organ Sharing

|   |    | Asian             |     | White            | P Value | SMD   |
|---|----|-------------------|-----|------------------|---------|-------|
| Recipient baseline characteristics      |    |                   |     |                  |         |       |
| Age (y)                                 | 42 | 36 (29-42)        | 834 | 39 (30-48)       | 0.06    | 0.315 |
| Male                                    | 42 | 13 (31)           | 834 | 366 (44)         | 0.099   | 0.27  |
| Body mass index, kg/m <sup>2</sup>      | 42 | $21.4\pm4.9$      | 812 | $22.9\pm4.3$     | 0.002   | 0.329 |
| Body surface area                       | 40 | 0.93 (0.14)       | 652 | 0.98 (0.13)      | 0.012   | 0.37  |
| Surgery year                            | 42 | 2008 (1997- 2016) | 834 | 1997 (1992-2007) | < 0.001 | 0.82  |
| Past medical history                    |    |                   |     |                  |         |       |
| Diabetes mellitus                       | 38 | 0 (0)             | 505 | 43 (8.5)         | 0.062   | 0.43  |
| Cigarette use                           | 26 | 2 (7.7)           | 235 | 81 (34)          | 0.004   | 0.69  |
| Etiology of cardiopulmonary failure     | 35 |                   | 788 |                  | 0.075   | 0.76  |
| Pulmonary hypertension (idiopathic)     |    | 19 (54)           |     | 237 (30)         |         |       |
| Eisenmenger syndrome                    |    | 10 (29)           |     | 261 (33)         |         |       |
| Cardiomyopathy                          |    | 2 (5.7)           |     | 52 (6.6)         |         |       |
| Congenital heart disease                |    | 1 (2.9)           |     | 94 (12)          |         |       |
| Interstitial pneumonitis                |    | 2 (5.7)           |     | 30 (3.8)         |         |       |
| Cystic fibrosis                         |    | 0 (0)             |     | 47 (6.0)         |         |       |
| COPD                                    |    | 0 (0)             |     | 46 (5.8)         |         |       |
| Valvular heart disease                  |    | 0 (0)             |     | 3 (0.4)          |         |       |
| Others                                  |    | 1 (2.9)           |     | 18 (2.3)         |         |       |
| Lung allocation score                   | 27 | $40\pm16$         | 233 | $46\pm20$        | 0.287   | 0.34  |
| Total waitlist time (days)              | 42 | 108 (44-283)      | 834 | 189 (56-480)     | 0.091   | 0.17  |
| Previous cardiac surgery                | 26 | 2 (7.7)           | 234 | 97 (41)          | < 0.001 | 0.85  |
| Previous lung surgery                   | 30 | 0 (0)             | 262 | 12 (4.6)         | 0.62    | 0.3   |
| Medical condition at time of transplant | 42 |                   | 828 |                  | 0.685   | 0.11  |
| Hospitalized in ICU                     |    | 8 (19)            |     | 178 (21)         |         |       |
| Hospitalized not in ICU                 |    | 6 (14)            |     | 88 (11)          |         |       |
| Outpatient                              |    | 28 (67)           |     | 562 (68)         |         |       |
| Preoperative life support               |    |                   |     |                  |         |       |
| IABP                                    | 42 | 0 (0)             | 834 | 13 (1.6)         | >0.999  | 0.17  |
| ECMO                                    | 42 | 4 (9.5)           | 834 | 37 (4.4)         | 0.127   | 0.20  |
| Blood type                              | 42 |                   | 834 |                  | < 0.001 | 0.74  |
| A                                       |    | 16 (38)           |     | 376 (45)         |         |       |
| AB                                      |    | 6 (14)            |     | 38 (4.6)         |         |       |
| В                                       |    | 13 (31)           |     | 92 (11)          |         |       |
| 0                                       |    | 7 (17)            |     | 328 (39)         |         |       |
| Preoperative data                       |    |                   |     |                  |         |       |
| Creatinine (mg/dL)                      | 41 | $0.82 \pm 0.23$   | 574 | $1.07 \pm 0.54$  | < 0.001 | 0.58  |
| Total bilirubin (mg/dL)                 | 40 | 1.37 ± 1.15       | 547 | 1.25 ± 2.67      | 0.05    | 0.05  |

Values are N, n (%), mean  $\pm$  SD, or median (Q1-Q3)], where Q1 is the first quartile and Q3 is the third quartile. COPD = chronic obstructive pulmonary disease; ECMO = extracorporeal membrane oxygenation; IABP = intra-aortic balloon pump; ICU = intensive care unit.

## **RESULTS**

We identified 42 Asian and Asian American heartlung transplant recipients as well as 834 NHW recipients between 1987 and 2021 who met the studyinclusion criteria.

The baseline characteristics of the pre-matched donors and recipients are shown in **Tables 1 and 2**. Asian recipients were approximately 3 years younger (median age, 36 years) and had smaller body sizes, which were reflected in smaller BMI,  $21.4 \pm 4.9 \text{ kg/m}^2$ ,

than NHW recipients (22.9  $\pm$  4.3 kg/m²) (**Table 1**). Of the other listed variables, the incidence of cigarette use was lower in Asians (7.7% vs 34%; P=0.004); waitlist time was shorter in Asians (median, 108 days vs 189 days); history of previous cardiac surgery was less frequent in Asians (7.7% vs 41%; P<0.001); preoperative creatinine was lower in Asians (0.82  $\pm$  0.23 mg/dL vs 1.07  $\pm$  0.54 mg/dL; P<0.001); no other major differences were noted in other parameters, including the recipient's status at the time of transplantation. The clinical variables of donors were also

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|  |    | Asian         |     | White         | P Value | SMD   |
|--|----|---------------|-----|---------------|---------|-------|
| Donor characteristics                  |    |               |     |               |         | 35    |
| Age (y)                                | 42 | 24 (17- 37)   | 834 | 26 (18- 38)   | 0.8190  | 0.018 |
| Male                                   | 42 | 17 (40)       | 834 | 443 (53)      | 0.8190  | 0.018 |
| Body mass index, kg/m <sup>2</sup>     | 40 | 23.6 ± 4.6    | 652 | 23.7 ± 4.8    | 0.109   | 0.233 |
| , ,                                    |    |               |     |               |         |       |
| Left ventricular ejection fraction (%) | 30 | 64 ± 6        | 352 | 62 ± 8        | 0.242   | 0.207 |
| Allograft ischemic time (h)            | 41 | 3.99 ± 0.87   | 790 | 3.58 ± 1.19   | 0.012   | 0.392 |
| Cause of death                         | 42 |               | 832 |               | 0.053   | 0.487 |
| Anoxia                                 |    | 6 (14)        |     | 91 (11)       |         |       |
| Cerebrovascular accident               |    | 17 (40)       |     | 235 (28)      |         |       |
| Head trauma                            |    | 18 (43)       |     | 388 (47)      |         |       |
| Other                                  |    | 1 (2.4)       |     | 118 (14)      |         |       |
| Past medical history                   |    |               |     |               |         |       |
| Diabetes mellitus                      | 40 | 0 (0)         | 556 | 21 (3.8)      | 0.387   | 0.28  |
| Hypertension                           | 40 | 4 (10)        | 553 | 65 (12)       | >0.999  | 0.056 |
| Cocaine use                            | 30 | 3 (10)        | 357 | 43 (12)       | >0.999  | 0.06  |
| Coronary artery disease                | 23 | 0 (0)         | 209 | 2 (1.0)       | >0.999  | 0.139 |
| Cigarette use                          | 38 | 9 (24)        | 551 | 121 (22)      | 0.804   | 0.04  |
| Heavy alcohol use                      | 29 | 2 (6.9)       | 255 | 22 (8.6)      | >0.999  | 0.06  |
| Preoperative data                      |    |               |     |               |         |       |
| Creatinine (mg/dL)                     | 40 | $1.18\pm1.13$ | 556 | $1.21\pm1.67$ | 0.725   | 0.02  |
| Total bilirubin (mg/dL)                | 39 | $1.57\pm3.56$ | 553 | $1.33\pm4.13$ | 0.695   | 0.064 |
| Blood type                             | 42 |               | 834 |               | < 0.001 | 0.742 |
| A                                      |    | 18 (43)       |     | 326 (39)      |         |       |
| AB                                     |    | 0 (0)         |     | 19 (2.3)      |         |       |
| В                                      |    | 13 (31)       |     | 65 (7.8)      |         |       |
| 0                                      |    | 11 (26)       |     | 424 (51)      |         |       |

Values are N, n (%), mean  $\pm$  SD, or median (Q1-Q3), in which Q1 is the first quartile and Q3 is the third quartile. SMD = standardized mean difference.

largely comparable (**Table 2**). Allograft ischemic time was significantly longer in Asian recipients (3.99  $\pm$  0.87 hours vs 3.58  $\pm$  1.19 hours; P = 0.012). The percentages of blood type O recipients (Asian vs NHW; 17% vs 39%) and donors (Asian vs NHW; 26% vs 51%) were lower among Asians. A higher incidence of blood type O recipients in the cohort of NHW recipients (39%) was likely to be translated into a significant difference in the total waitlist time between the cohorts. The use of ECMO before transplantation was lower in Asian recipients, with 9.5% of patients requiring ECMO compared with 4.4% of NHW recipients.

In the pre-matched cohort, the median survival was 1,459 days (IQR: 1,080-2,692 days) in Asian recipients and 1,521 days (IQR: 1,262-1,841 days) in White recipients. Asian patients showed a better 1-year survival rate than NHW recipients (Table 3). However, there was no significant difference in any other listed episodes of post-transplantation morbidity. The Kaplan-Meier time-to-event survival

estimation curve revealed that the survival probability of Asian recipients was significantly higher than that of NHW recipients at 1 year (Figure 1) (P = 0.0093). The P values of other survival comparisons of 2 pre-matched groups were 0.077, 0.51, and 0.80 for 30-day mortality, 5-year mortality, and overall survival, respectively.

Propensity-score matching was used to balance factors that could confound the survival probability of Asians compared with Whites. Of the 876 recipients, 144 transplants were successfully matched (Asian, n=36; NHW, n=108) using the optimal matching algorithm. After matching, a good balance was obtained between the matched NHWs and Asians (Central Illustration, Figure 2). The matched NHWs were similar to Asian recipients on most recipient and donor characteristics except for blood group, preoperative creatine, and history of previous cardiac surgery (Tables 4 and 5). Among the post-transplantation outcomes, there was no significant difference in morbidity and mortality between the Asian and NHW

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|                                     |    | Asian   |     | White    | P Value |
|-------------------------------------|----|---------|-----|----------|---------|
| Morbidity                           |    |         |     |          |         |
| Acute rejection (y)                 | 42 | 4 (9.5) | 834 | 40 (4.8) | 0.154   |
| Primary graft failure               | 42 | 27 (64) | 832 | 610 (73) | 0.199   |
| Cerebrovascular accident            | 40 | 1 (2.5) | 547 | 22 (4.0) | >0.999  |
| Hemodialysis                        | 40 | 7 (18)  | 550 | 112 (20) | 0.663   |
| Reintubation                        | 29 | 6 (21)  | 254 | 71 (28)  | 0.512   |
| Permanent pacemaker                 | 40 | 0 (0)   | 545 | 5 (0.9)  | >0.99   |
| Extracorporeal membrane oxygenation | 13 | 0 (0)   | 86  | 12 (14)  | 0.357   |
| Mortality                           |    |         |     |          |         |
| Death at 30 d post-HLTx             | 42 | 3 (7.1) | 832 | 149 (18) | 0.073   |
| Death at 1 y post-HLTx              | 39 | 5 (13)  | 807 | 265 (33) | 0.009   |
| Death at 3 y post-HLTx              | 34 | 12 (35) | 777 | 355 (46) | 0.233   |
| Death at 5 y post-HLTx              | 30 | 16 (53) | 753 | 411 (55) | 0.893   |
| Death                               | 42 | 28 (67) | 832 | 627 (75) | 0.205   |

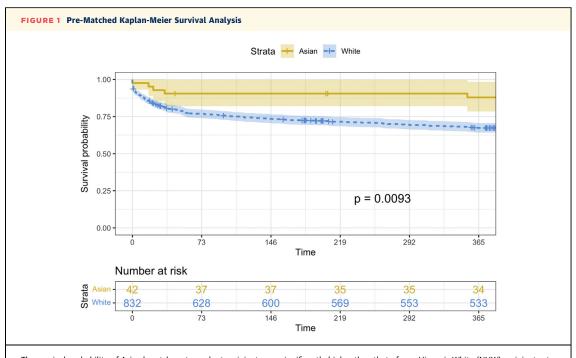
cohorts (**Table 6**). The 1-year survivals for Asian and matched NHW cohorts were 0.89 (95% CI: 0.79-0.99) and 0.79 (95% CI: 0.71-0.87), respectively. The *P* values of the log-rank tests on the Kaplan-Meier survival estimations of the 2 matched groups were 0.40, 0.21, 0.27, and 0.09 for 30-day survival, 1-year survival, 5-year survival, and overall survival, respectively (**Central Illustration**), which did not show

statistically significant differences for 2 matched groups.

## **DISCUSSION**

The most important finding of this study is that Asian ethnicity and race showed a relatively lower risk of short-term and noninferior long-term mortality than Whites in the pre-matched and matched cohorts. Studies have shown that various recipient risk factors, such as donor age and recipient sex, can affect patient outcomes significantly, but no large multicenter study has analyzed ethnicity and race as risk factors.<sup>4</sup> Therefore, our study focused on the impact of ethnicity and race on outcomes following HLTx.

On the other hand, in Asian countries, special attention has been paid to the indications of HLTx because of the nature of conservative posture as well as multiple barriers to HLTx, the scarcity of available donors, and the more technically demanding surgical procedures required. Given the extremely low number of HLTx surgeries performed in Asian countries, it is difficult to examine the outcome with special consideration of each country's circumstances; however, our results that show a favorable equivalent outcome in Asian populations in the United States can possibly encourage HLTx for



The survival probability of Asian heart-lung transplant recipients was significantly higher than that of non-Hispanic White (NHW) recipients at 1 year (P = 0.0093, log-rank test). **Shaded area** = 95% CI. + = censored.

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## **CENTRAL ILLUSTRATION** Matched Kaplan-Meier Survival Analysis

## **Key Question**

Studies to understand the relationship between ethnicity/race and outcomes after heart-lung transplantation (HLTx) are needed to uphold equitable HLTx access to the increasingly diverse U.S. population facing advanced cardiopulmonary failure.

## 1

#### Kev Finding

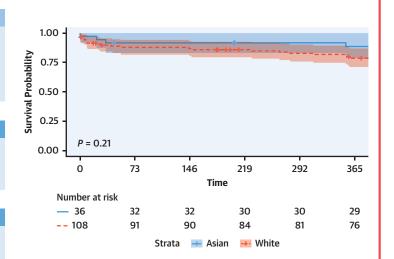
We identified 42 Asian HLTx recipients and 834 non-Hispanic Whites (NHW) recipients. There was no significant differences in morbidity and mortality between the Asian and NHW cohorts.



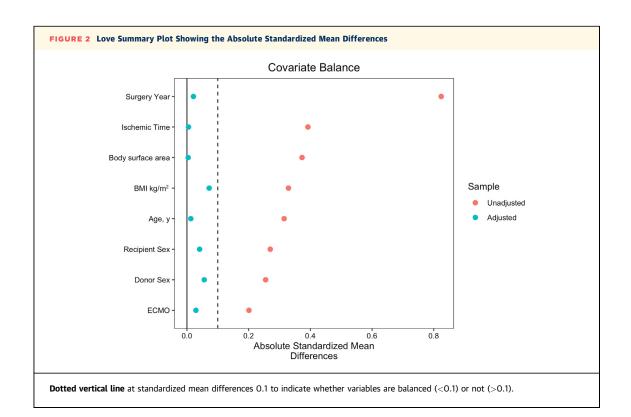
## **Take-Home Message**

An outcome equivalent to NHW in Asian patients could support further expansion of HLTx surgeries in Asian countries.





The survival probability of Asian heart-lung transplant recipients was similar to that of non-Hispanic White (NHW) recipients at 1 year (P = 0.18, log-rank test). **Shaded area** = 95% CI. + = censored.



|   |    | Asian             |     | White                             | P Value | SMD   |
|---|----|-------------------|-----|-----------------------------------|---------|-------|
| Recipient baseline characteristics      |    |                   |     |                                   |         |       |
| Age (y)                                 | 36 | 36 (29, 41)       | 108 | 35 (28, 44)                       | 0.982   | .012  |
| Male                                    | 36 | 11 (31)           | 108 | 31 (29)                           | .832    | .041  |
| Body mass index, kg/m <sup>2</sup>      | 36 | $21.7\pm5.1$      | 108 | $22.0\pm4.2$                      | 0.224   | 0.072 |
| Body surface area ratio                 | 36 | $0.94\pm0.14$     | 108 | $0.94\pm0.12$                     | 0.787   | 0.004 |
| Surgery year                            | 36 | 2010 (2005- 2016) | 108 | 2010 (2004- 2017)                 | 0.939   | 0.021 |
| Past medical history                    |    |                   |     |                                   |         |       |
| Diabetes mellitus                       | 36 | 0 (0)             | 108 | 0 (0)                             |         | NA    |
| Cigarette use                           | 25 | 2 (8.0)           | 72  | 16 (22)                           | 0.144   | 0.405 |
| Etiology of cardiopulmonary failure     | 29 |                   | 99  |                                   |         | 0.709 |
| Pulmonary hypertension (idiopathic)     |    | 15 (52)           |     | 33 (33)                           |         |       |
| Eisenmenger syndrome                    |    | 8 (28)            |     | 30 (30)                           |         |       |
| Cardiomyopathy                          |    | 2 (6.9)           |     | 9 (9.1)                           |         |       |
| Congenital heart disease                |    | 1 (3.4)           |     | 20 (20)                           |         |       |
| Interstitial pneumonitis                |    | 2 (6.9)           |     | 2 (2.0)                           |         |       |
| Cystic fibrosis                         |    | 0 (0)             |     | 1 (1.0)                           |         |       |
| COPD                                    |    | 0 (0)             |     | 1 (1.0)                           |         |       |
| Valvular heart disease                  |    | 0 (0)             |     | 1 (1.0)                           |         |       |
| Others                                  |    | 1 (3.4)           |     | 2 (2.0)                           |         |       |
| Lung allocation score                   | 26 | $40\pm16$         | 74  | $43\pm21$                         | 0.850   | 0.18  |
| Total waitlist time (days)              | 36 | 108 (32- 246)     | 108 | 133 (34- 312)                     | 0.702   | 0.134 |
| Previous cardiac surgery                | 25 | 2 (8.0)           | 71  | 30 (42)                           | 0.002   | 0.86  |
| Previous lung surgery                   | 29 | 0 (0)             | 80  | 3 (3.8)                           | 0.563   | 0.279 |
| Medical condition at time of transplant | 36 |                   | 108 |                                   | 0.319   | 0.299 |
| Hospitalized in ICU                     |    | 8 (22)            |     | 37 (34)                           |         |       |
| Hospitalized not in ICU                 |    | 5 (14)            |     | 17 (16)                           |         |       |
| Outpatient                              |    | 23 (64)           |     | 54 (50)                           |         |       |
| Preoperative life support               |    |                   |     |                                   |         |       |
| IABP                                    | 36 | 0 (0)             | 108 | 0 ( 0)                            | NA      | NA    |
| ECMO                                    | 36 | 4 (11)            | 108 | 13 (12)                           | >0.999  | 0.029 |
| Blood type                              | 36 |                   | 108 |                                   | 0.015   | 0.626 |
| A                                       |    | 14 (39)           |     | 47 (44)                           |         |       |
| AB                                      |    | 4 (11)            |     | 6 (5.6)                           |         |       |
| В                                       |    | 12 (33)           |     | 15 (14)                           |         |       |
| 0                                       |    | 6 (17)            |     | 40 (37)                           |         |       |
| Preoperative data                       |    |                   |     |                                   |         |       |
| Creatinine (mg/dL)                      | 36 | $0.81\pm0.24$     | 108 | $1.03\pm0.68$                     | 0.024   | 0.42  |
| Total bilirubin (mg/dL)                 | 35 | $1.28\pm1.15$     | 107 | $\textbf{0.88} \pm \textbf{0.70}$ | 0.025   | 0.415 |

Values are N, n (%), mean  $\pm$  SD, or median (Q1-Q3)], in which Q1 is the first quartile and Q3 is the third quartile.

 ${\sf COPD} = {\sf chronic obstructive pulmonary disease; ECMO} = {\sf extracorporeal membrane oxygenation; IABP} = {\sf intra-aortic balloon pump; ICU} = {\sf intensive care unit; SMD} = {\sf standardized mean difference.}$ 

patients with end-stage cardiopulmonary failure in Asian countries. One plausible explanation for the favorable outcomes seen among Asians is better adherence to immunosuppressive medications, monitoring of immunosuppressive medication levels, and rejection surveillance.<sup>10</sup>

Therefore, HLTx in carefully selected candidates with advanced cardiopulmonary failure remains the treatment of choice globally, and large-scale analysis in patients of Asian origin will have important

implications in these countries that, until now, have performed relatively fewer HLTx surgeries. A slightly better—or at least equivalent—survival in Asian to White patients, as demonstrated in our study, could be the driving force for further expansion of HLTx surgeries in Asia.

**STUDY LIMITATIONS.** This study has some limitations that are consistent with the performance of a retrospective analysis, rather than a randomized controlled clinical trial, and the use of a national

|  |    | Asian           |     | White           | P Value | SMD  |
|--|----|-----------------|-----|-----------------|---------|------|
| Donor characteristics                  |    |                 |     |                 |         |      |
| Age (y)                                | 36 | 26 (18- 37)     | 108 | 26 (19- 39)     | 0.993   | 0.01 |
| Male                                   | 36 | 15 (42)         | 108 | 48 (44)         | 0.771   | 0.05 |
| Body mass index, kg/m <sup>2</sup>     | 36 | $23.8\pm4.5$    | 108 | $24.3\pm5.1$    | 0.610   | 0.10 |
| Left ventricular ejection fraction (%) | 29 | $64\pm 6$       | 97  | $63\pm7$        | 0.679   | 0.06 |
| Allograft ischemic time (hours)        | 36 | $3.98 \pm 0.89$ | 108 | $3.98 \pm 1.16$ | 0.947   | 0.00 |
| Cause of death                         | 36 |                 | 108 |                 | 0.165   | 0.46 |
| Anoxia                                 |    | 6 (17)          |     | 22 (20)         |         |      |
| Cerebrovascular accident               |    | 16 (44)         |     | 27 (25)         |         |      |
| Head trauma                            |    | 14 (39)         |     | 56 (52)         |         |      |
| Other                                  |    | 0 (0)           |     | 3 (2.8)         |         |      |
| Past medical history                   |    |                 |     |                 |         |      |
| Diabetes mellitus                      | 36 | 0 (0)           | 106 | 4 (3.8)         | 0.572   | 0.2  |
| Hypertension                           | 36 | 3 (8.3)         | 105 | 14 (13)         | 0.560   | 0.1  |
| Cocaine use                            | 29 | 3 (10)          | 94  | 12 (13)         | >0.999  | 0.0  |
| Coronary artery disease                | 23 | 0 (0)           | 67  | 2 (3.0)         | >0.999  | 0.2  |
| Cigarette use                          | 34 | 6 (18)          | 104 | 18 (17)         | 0.964   | 0.0  |
| Heavy alcohol use                      | 28 | 1 (3.6)         | 78  | 9 (12)          | 0.285   | 0.3  |
| Preoperative data                      |    |                 |     |                 |         |      |
| Creatinine (mg/dL)                     | 36 | $1.20 \pm 1.19$ | 108 | $1.30 \pm 1.26$ | 0.525   | 0.0  |
| Total bilirubin (mg/dL)                | 35 | $1.70 \pm 3.74$ | 108 | $1.05\pm3.20$   | 0.117   | 0.18 |
| Blood type                             | 36 |                 | 108 |                 | 0.021   | 0.5  |
| A                                      |    | 15 (42)         |     | 42 (39)         |         |      |
| AB                                     |    | 0 (0)           |     | 2 (1.9)         |         |      |
| В                                      |    | 11 (31)         |     | 12 (11)         |         |      |
| 0                                      |    | 10 (28)         |     | 52 (48)         |         |      |

Values are N, n (%), mean  $\pm$  SD, or median (Q1-Q3), in which Q1 is the first quartile and Q3 is the third quartile. SMD = standardized mean difference.

multicenter database. Although we used the data of the national UNOS database, the sample size for Asian recipients (N = 42) was still extremely small compared with NHW recipients (N = 834). Furthermore, the potential for misclassification of ethnicity, diagnosis, and reason for waitlist removal exists because these were registry-reported data fields that are dependent on the data collected and reported by the transplant centers. The UNOS data are not disaggregated by Asian subgroups; therefore, it is unclear whether donors and recipients are Asian Indians, Filipinos, Chinese, or Korean. This may lead to some discrepancies, as there is much literature on the heterogeneity in Asian subgroups with regard to other cardiovascular diseases. The UNOS database was also not free of missing data, which limited the matching variables' selection and resulted in reducing sample sizes in statistical analyses, which could increase the chance of Type 2 error. Further, the UNOS database is based on U.S. organ allocation and HLTx practice, and the external validity of our results outside of the United States needs to be assessed carefully in individual countries in Asia.

## CONCLUSIONS

This large-scale analysis in Asian patients will have important implications in Asian countries that

|                                     |    | Asian   | 1   | Vhite   | P Valu |
|-------------------------------------|----|---------|-----|---------|--------|
| Morbidity                           |    |         |     |         |        |
| Acute rejection (y)                 | 36 | 3 (8.3) | 108 | 15 (14) | 0.562  |
| Primary graft failure               | 36 | 23 (64) | 108 | 54 (50) | 0.148  |
| Cerebrovascular accident            | 36 | 1 (2.8) | 107 | 6 (5.6) | 0.680  |
| Hemodialysis                        | 36 | 6 (17)  | 107 | 20 (19) | 0.785  |
| Reintubation                        | 29 | 6 (21)  | 78  | 25 (32) | 0.249  |
| Permanent pacemaker                 | 36 | 0 (0)   | 105 | 2 (1.9) | >0.99  |
| Extracorporeal membrane oxygenation | 13 | 0 (0)   | 32  | 4 (12)  | 0.308  |
| Mortality                           |    |         |     |         |        |
| Death at 30 d post-HLTx             | 36 | 2 (5.6) | 108 | 11 (10) | 0.518  |
| Death at 1 y post-HLTx              | 33 | 4 (12)  | 100 | 21 (21) | 0.258  |
| Death at 3 y post-HLTx              | 28 | 11 (39) | 87  | 32 (37) | 0.812  |
| Death at 5 y post-HLTx              | 24 | 14 (58) | 77  | 35 (45) | 0.270  |
| Death                               | 36 | 23 (64) | 108 | 52 (48) | 0.102  |

perform relatively fewer HLTx surgeries. A slightly better—or at least equivalent—survival to NHW in Asian patients, as demonstrated in our study, could support further expansion of HLTx surgeries in Asian countries.

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ADDRESS FOR CORRESPONDENCE: Dr Yasuhiro Shudo, Falk Cardiovascular Research Center, 870 Quarry Road, Stanford, California 94305-2200, USA. E-mail: yshudo@stanford.edu.

## **PERSPECTIVES**

competency in patient care: Asian ethnicity and race undergoing combined heart-lung transplantation showed a relatively lower risk of short-term and noninferior long-term mortality than Whites in the pre-matched and matched cohorts, which could be the driving force for further expansion of heart-lung transplant surgeries in Asian countries that, until now, have performed relatively fewer heart-lung transplants.

**TRANSLATIONAL OUTLOOK:** Large-scale prospective clinical trials will be necessary to provide important implications in Asian countries while efforts continue to expand and improve the options of combined heart-lung transplantation.

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