RESEARCH LETTER

Imbalance in Heart Transplant to Heart Failure Mortality Ratio by Sex

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Allocation of heart transplants may be inequitable by sex. For over a decade, women have received <25% of heart transplants.1 Women have similar prevalence of heart failure (HF) as men, but higher HF mortality.2 Women also have higher prevalence of HF with preserved ejection fraction, which has limited benefit with heart transplant, than men.3 However, among the highest risk population that has recurrent heart failure hospitalizations, women have similar prevalence of HF with preserved ejection fraction and HF with reduced ejection fraction (HFrEF).3 Adding the intersection of race results in higher prevalence of HFrEF among subgroups such as Black women.3 In comparison, the majority of men with recurrent HF hospitalizations have HFrEF.3 Since HFrEF can be treated with heart transplants, this suggests a heart transplant sex disparity.

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Geographic and center culture may contribute to disparities in heart transplant allocation.4 Given observed sex bias in the allocation of heart transplants,4 we sought to determine whether heart transplant rate to HF mortality rate varied geographically across the United States for women compared with men.

It is important to identify geographic areas with the greatest disparities so that interventions can be appropriately tailored to achieve equity.

Using data from the United Network for Organ Sharing and Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiological Research, we examined heart transplant and HF mortality (underlying cause of death International Classification of Diseases, Tenth Revision [ICD-10: I50 [I50.0, I50.1, I50.9]] ratio by sex from 2016 to 2018 nationally and by state among adults aged 35 to 64 years since this age group receives the majority of heart transplants. All 50 states plus D.C. were included for the national analysis. Among state analyses, states were excluded for missing HF mortality (9 states+D.C.), which was either suppressed or marked unreliable by Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiological Research for <20 HF deaths or risk of identifying individuals. The national cohort included 19 784 HF deaths and 5800 heart transplants; the final state cohort included 19 497 HF deaths and 5641 heart transplants (n=41 states). The University of Arizona Institutional Review Board exempted this study from review. Data are publicly available from United Network for Organ Sharing and Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiological Research.

The primary outcome was heart transplant rate to HF mortality rate ratio. Ratios were calculated for each sex nationally and by state as the number of transplants per 100 000 population per year divided by the age-adjusted HF mortality rate per 100 000 population per year. Heart transplant to HF mortality ratios were compared between women and men, with the ratio for men as the control. Calculations were completed using R version 3.6.3 (Vienna, Austria).

In national analyses, women received 0.789 heart transplants per 100 000 per year, and men received 2.330 heart transplants per 100 000 per year. The heart transplant to HF mortality ratio was 0.263 for women and 0.424 for men, resulting in lower ratio for women versus men at 0.620. In the state analyses, 98% (40 of 41 states)
Table. Ratio of Heart Transplantation to Heart Failure Mortality by Sex 2016 to 2018

| State       | Region | Transplant Rate Women | HF Mortality Rate Women | Transplant Rate Men | HF Mortality Rate Men | Transplant to Mortality Ratio Women | Transplant to Mortality Ratio Men | Ratio Women to Men |
|-------------|--------|-----------------------|------------------------|---------------------|----------------------|------------------------------------|-----------------------------------|-------------------|
| All         |        | 0.789                 | 3.00                   | 2.330               | 5.50                 | 0.263                              | 0.424                             | 0.620             |
| West Virginia | South  | 0.367                 | 4.08                   | 2.518               | 5.39                 | 0.090                              | 0.467                             | 0.193             |
| New Jersey  | Northeast | 0.413               | 2.13                   | 2.410               | 3.65                 | 0.194                              | 0.660                             | 0.294             |
| Tennessee   | South   | 0.947                 | 4.34                   | 4.008               | 7.11                 | 0.218                              | 0.564                             | 0.387             |
| Alabama     | South   | 0.306                 | 7.91                   | 1.508               | 15.97                | 0.039                              | 0.094                             | 0.413             |
| Delaware    | South   | 0.866                 | 2.70                   | 2.646               | 3.46                 | 0.321                              | 0.765                             | 0.419             |
| Kentucky    | South   | 0.832                 | 6.41                   | 2.895               | 9.49                 | 0.130                              | 0.305                             | 0.426             |
| Idaho       | West    | 0.320                 | 1.98                   | 1.286               | 3.67                 | 0.162                              | 0.350                             | 0.461             |
| Wisconsin   | Midwest | 0.618                 | 1.54                   | 2.232               | 2.57                 | 0.401                              | 0.869                             | 0.462             |
| Arkansas    | South   | 0.583                 | 4.93                   | 2.303               | 9.50                 | 0.118                              | 0.242                             | 0.488             |
| New Mexico  | West    | 0.256                 | 2.16                   | 0.977               | 4.06                 | 0.118                              | 0.241                             | 0.492             |
| Nevada      | West    | 0.461                 | 2.11                   | 1.660               | 3.81                 | 0.219                              | 0.436                             | 0.502             |
| Georgia     | South   | 0.445                 | 6.42                   | 1.609               | 11.66                | 0.069                              | 0.138                             | 0.502             |
| New York    | Northeast | 0.742             | 1.32                   | 2.709               | 2.50                 | 0.562                              | 1.084                             | 0.519             |
| Mississippi | South   | 0.800                 | 11.13                  | 2.533               | 18.29                | 0.072                              | 0.138                             | 0.519             |
| Ohio        | Midwest | 0.784                 | 3.53                   | 2.331               | 5.49                 | 0.222                              | 0.425                             | 0.523             |
| Minnesota   | Midwest | 0.622                 | 1.23                   | 2.162               | 2.33                 | 0.505                              | 0.928                             | 0.545             |
| Massachusetts | Northeast | 0.982         | 2.06                   | 2.667               | 3.05                 | 0.477                              | 0.874                             | 0.545             |
| Florida     | South   | 0.804                 | 2.10                   | 2.500               | 3.63                 | 0.383                              | 0.689                             | 0.556             |
| Utah        | West    | 0.711                 | 2.47                   | 2.048               | 4.02                 | 0.288                              | 0.509                             | 0.565             |
| Oklahoma    | South   | 0.503                 | 3.94                   | 1.447               | 6.43                 | 0.128                              | 0.225                             | 0.567             |
| Hawaii      | West    | 0.372                 | 1.89                   | 1.494               | 4.36                 | 0.197                              | 0.343                             | 0.575             |
| North Carolina | South   | 0.984             | 4.25                   | 2.762               | 7.03                 | 0.232                              | 0.393                             | 0.589             |
| California  | West    | 0.626                 | 2.03                   | 2.110               | 4.33                 | 0.309                              | 0.487                             | 0.633             |
| Oregon      | West    | 0.575                 | 3.04                   | 1.339               | 4.51                 | 0.189                              | 0.297                             | 0.638             |
| Missouri    | Midwest | 0.730                 | 4.49                   | 1.893               | 7.46                 | 0.163                              | 0.254                             | 0.641             |
| Illinois    | Midwest | 0.963                 | 3.40                   | 2.851               | 6.50                 | 0.283                              | 0.439                             | 0.645             |
| Michigan    | Midwest | 0.642                 | 3.26                   | 1.731               | 5.68                 | 0.197                              | 0.305                             | 0.647             |
| Iowa        | Midwest | 0.914                 | 1.93                   | 1.986               | 2.88                 | 0.473                              | 0.690                             | 0.686             |
| South Carolina | South   | 0.632             | 5.52                   | 1.665               | 10.04                | 0.115                              | 0.166                             | 0.691             |
| Virginia    | South   | 0.999                 | 3.95                   | 2.797               | 7.82                 | 0.253                              | 0.358                             | 0.707             |
| Kansas      | Midwest | 1.303                 | 2.51                   | 3.314               | 4.56                 | 0.519                              | 0.727                             | 0.714             |

(Continued)
had lower ratios for women compared with men (Table). Ratios were higher for women compared with men only in Connecticut. The lowest median heart transplant to HF mortality ratio was observed in the Southern region at 0.537 (interquartile range, 0.424–0.695) followed by Northeast at 0.545 (interquartile range, 0.519–0.716), West at 0.604 (interquartile range, 0.517–0.719), and Midwest at 0.646 (interquartile range, 0.569–0.707).

Multiple factors contribute to low allocation of heart transplant to women. This study was not able to adjust for clinical factors, patients’ preferences, social determinants of health, or sex bias. Rather a general overview of transplant disparities is provided at a geographic level. Given known sex inequities in pharmacological and non-pharmacological management of heart failure, this study provides fuel to explore cultural decision-making contributing to low transplant rates among women.

As crude analyses, we were unable to stratify results by phenotype contributing to HF mortality and are at risk for unmeasured confounding variables as with any observational study. However, among the highest risk group with recurrent HF hospitalizations, HF with preserved ejection fraction was a greater cause of annual mortality than HFrEF among White men in 1 national study. Conversely HFrEF was a greater cause of annual mortality than HF with preserved ejection fraction among women. This suggests that sex disparities in transplant to mortality ratio may be underestimated. In addition, taking ratios of ratios may amplify small differences. For this reason, we included a table of individual rates and ratios by sex to surmise sex differences among and across states.

Among the United States, women had lower heart transplant to HF mortality rate ratios than men. Disparities were widespread but were the worst in the US South. Implementation of strategies to achieve sex equity in allocation of heart transplants should be investigated across the United States.

### ARTICLE INFORMATION

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