Impact of Gender on Access to the Renal Transplant Waiting List for Pediatric and Adult Patients

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Abstract. While the public and policy-makers place a priority on equity in the organ allocation process, several studies suggest that women may be less likely than men to receive a renal transplant. However, the cause of this disparity and whether it exists among children with end-stage renal disease (ESRD) are unknown. To address these issues, two nationally representative cohorts of incident patients were examined: (1) 7594 adults with ESRD onset between 1986 and 1993 for whom detailed data were available from the medical record on health status; and (2) 3217 patients <20 yr old who developed ESRD between 1988 and 1993. Patients were followed from initiation of dialysis for up to 10 yr until first activation on the United Network of Organ Sharing renal transplant waiting list. Access to the list for female and male patients with ESRD was compared using Cox proportional hazards models with adjustment for demographic, socioeconomic, and clinical factors. Crude rates of wait-listing per 100 person-years of ESRD were lower for female patients than male patients in both the pediatric (28.89 versus 34.18) and adult (3.94 versus 6.54) populations. Despite adjustment for numerous confounding factors, this gender-based disparity persisted in multivariate analysis. Among children with ESRD, female patients were 14% less likely to be listed than male patients (relative hazard [RH] 0.86; 95% confidence interval [CI], 0.78 to 0.93), and in the adult group, women were 18% less likely to be activated for transplant than men (RH 0.82; 95% CI, 0.72 to 0.93). These findings suggest that female patients of all ages with ESRD face barriers in being activated for cadaveric renal transplantation. Greater attention to this issue is necessary to improve equity in the organ allocation system and potentially improve the outcomes of female patients with ESRD.

Renal transplantation is preferred over dialysis for the treatment of end-stage renal disease (ESRD) because it has been associated with improved patient survival and quality of life (1–3). However, when no living-related kidney donor is available, many ESRD patients must rely on the limited supply of cadaveric donor organs. Although the public and policy-makers have emphasized the principle of equity in the distribution of this scarce human resource (4,5), several studies have documented that women are less likely to receive a cadaveric transplant than men (6–10).

To elucidate the reasons for this gender-based disparity in transplantation, researchers have examined the sequential steps that lead to transplantation and found that women face barriers in being identified as transplant candidates and being activated on the cadaveric transplant waiting list (6,7,11,12). However, past studies have been limited in at least two respects. First, previous research on access to the waiting list among adult women has not considered the impact of comorbid medical conditions that may confound the relationship between gender and wait-listing. Second, it is unclear whether these gender differences also exist among pediatric patients with ESRD, a population with few comorbid conditions in whom transplantation is clearly the treatment goal. The few studies of access to the waiting list that have included young patients have not examined the pediatric experience separately (7) or enrolled few patients under the age of 19 yr (6).

We report the results of a nationally representative study in which we separately examined pediatric and adult patients with ESRD to identify whether access to the cadaveric renal transplant waiting list differed by gender after adjusting for differences in demographic factors and socioeconomic status. In addition, for the adult population, we were able to account for differences in health status based on detailed chart-abstracted data.
Materials and Methods

Study Design

We conducted a longitudinal cohort study to assess gender-based disparities in access to the United Network of Organ Sharing (UNOS) renal transplant waiting list for adult and pediatric patients with new-onset ESRD. Onset of ESRD was defined as the date of initiation of dialysis. We excluded patients who received live-donor transplants (because those with identifiable living donors may not be activated for cadaveric transplant) and patients whose date of listing could not be reconciled with transplantation data. Finally, as done by previous investigators, we did not include patients with less than 90 d of follow-up or those who were missing data on more than 50% of the clinical variables because of concerns regarding data reliability (8).

Study Population and Data Sources

Adult Patient Population. We identified adult patients with baseline clinical data within three nationally representative cohort studies of incident and prevalent ESRD patients conducted by the U.S. Renal Data System (USRDS). In all three studies, facilities were systematically sampled to ensure that they were representative according to ESRD Network, distance from the Network office, and size. Case-Mix Severity (Severity) was a study of 5255 Medicare-entitled patients throughout the United States who began dialysis in 1986 and 1987. Case-Mix Adequacy (Adequacy) included 7096 patients who were receiving in-center hemodialysis on December 31, 1990. Dialysis Morbidity & Mortality Study-Wave 1 (Wave 1) was a study of 5534 patients who were receiving in-center hemodialysis on December 31, 1993 (13).

Because all three special studies used similar sampling schemes to identify nationally representative cohorts and nearly identical abstraction instruments to catalog comorbid conditions, we combined the data for all patients with incident-ESRD (onset of ESRD in calendar year 1986–1987 for Severity, 1990 for Adequacy, and 1993 for Wave 1) to form our analytic file. Chart abstractors in all three special studies obtained information on comorbid conditions present within the 10 yr up to ESRD onset and other clinical and demographic data not found in routinely collected administrative records.

Pediatric Patient Population. Because insufficient numbers of patients under age 20 were included in the three special studies for our analysis, we identified pediatric patients from the USRDS Standard Analysis File that lists all ESRD patients in the United States (13). We included in the pediatric cohort all patients under age 20 who underwent their first dialysis between January 1, 1988, and December 31, 1993.

Linkage to Additional USRDS Data Sources

We used each patient’s unique identifier to retrieve routinely collected USRDS demographic data as well as each person’s longitudinal history documenting changes in dialysis providers and treatment modalities. Using unique facility identifiers, we linked USRDS data on facility ownership and structure to the patients’ longitudinal treatment files. Additionally, we linked each patient’s record to the median household income for their zip code of residence using 1990 U.S. Census data. Finally, we obtained data from the USRDS for each patient which noted their date of first listing on the UNOS renal transplant waiting list.

Potential Confounding Factors

Data were available to adjust for the impact of several demographic factors on access to the transplant waiting list: year of ESRD onset (1986–1987, 1988–1989, 1990–1991, 1992–1993), age at onset of ESRD (≤4, 5 to 9, 10 to 14, 15 to 19, 20 to 35, 36 to 50, 51 to 65, >65 yr), race (white, black, other), quartile of median household income from zip code (<$21,000, $21,000 to 27,000, $27,000 to 35,000, >$35,000), and geographic region (Northeast: ESRD Networks 1 to 5; Southeast: ESRD Networks 6 to 8, 13, and 14; Midwest: ESRD Networks 9 to 12; West: ESRD Networks 15 to 18). A categorical variable based on Health Care Financing Administration criteria was included to designate the type of dialysis facility providing the majority of care for each patient during their first year of ESRD (free-standing for-profit, freestanding not-for-profit, hospital-based, or transplant/government centers). Additionally, for the adult cohort only, chart-abstracted data were available for three additional demographic variables: high school graduation, marital status (single/divorced, married/separated, widowed), and employment in first year of ESRD (full-time, part-time, other).

We adjusted for the assigned cause of ESRD according to ICD-9-CM diagnosis codes recorded by the USRDS. However, we categorized these conditions differently in the two analyses because common causes of ESRD in adults and children differ and assigned causes may have an unequal impact on the likelihood of wait-listing. For adults, assigned causes of ESRD were classified as diabetes mellitus, glomerulonephritis, hypertension, and other. For pediatric patients, causes of ESRD were categorized as congenital anomalies, focal and segmental glomerulosclerosis (FSGS), lupus nephritis, malignancy, HIV-related illness, and other (which includes non-FSGS glomerulonephritis and hereditary and metabolic causes of renal failure).

On the basis of chart-abstracted data available for the adult cohort only, we evaluated the impact of 15 additional clinical factors that were assessed at ESRD onset. These included active smoking, body mass index, living in a nursing home, serum albumin, and the presence or absence of 11 comorbid conditions (cancer, cardiomegaly by chest x-ray, cerebrovascular disease, congestive heart failure, coronary artery disease, dependence on others for activities of daily living, diabetes mellitus, hypertension, left ventricular hypertrophy by electrocardiogram or echocardiogram, peripheral vascular disease, or pulmonary disease).

Statistical Analyses

Data on year of ESRD onset, age, race, gender, and assigned cause of ESRD were available for all patients. However, some patients were missing data on income (10% of pediatric patients, 2% of adults) and region (8% of pediatric patients; 2% of adults). Because they received transplants soon after the onset of ESRD, 735 (23%) pediatric patients lacked an identifiable majority dialysis provider. In addition, the magnitude of the abstraction used to obtain the 18 medical chart-based variables (education, employment, marital status, and the 15 clinical variables) resulted in some additional missing data among the adult patients. A total of 72% of adult patients were missing data for zero to two and 17% were missing data for three or four of these 18 variables. These patterns of missing data did not differ by gender. To avoid excluding patients who lacked information for a few data elements, a category for “missing” was constructed for each covariate and included in the multivariate model.

Comparisons of proportions and means were performed using $\chi^2$ statistics and t test, respectively. The impact of gender on access to the waiting list was tested in separate models for adult and pediatric patients using the Cox proportional hazards method (14). All patients were followed from the date of ESRD onset for a minimum of 3 and a maximum of 10 yr until the date of first placement on the UNOS cadaveric renal transplant waiting list. If the date of a patient’s first activation on the transplant waiting list preceded the date of his/her
first dialysis, the date of wait-listing was reset to 1 d after the initiation of dialysis for statistical purposes. Patients not listed were censored at the time of death, loss to follow-up, May 31, 1996 (adult population), or October 31, 1996 (pediatric population). Conditions that were not predictive in bivariate analysis or not independently associated with the probability of wait-listing in multivariate analysis were not included so as to create the most parsimonious models. We tested for significant interactions between gender and all of the other demographic variables. Because of the facility-level sampling of patients used to assemble the adult cohort, we calculated robust variances using the Huber–White method to adjust for clustering by facility (15). However, because these did not significantly alter the results, standard variances are reported. For all models, the proportionality of hazards assumption was verified graphically. All analyses were performed using SAS Statistical Software (SAS Institute, Cary, NC) and STATA 5.0 (Stata Corp., College Station, TX).

**Results**

**Patient Populations**

There were 8816 incident adult patients eligible for the study. We excluded 191 (2%) patients who received live-donor transplants, 279 (3%) patients whose date of listing was missing or irreconcilable with transplant information, 329 (4%) with less than 90 d of follow-up, and 423 (5%) patients because of extensive missing data. As a result, 7594 patients, who were treated in 1184 unique facilities, were included in the study cohort. The 1222 excluded patients were more likely to be white (69% versus 61%; P < 0.001), younger at onset of ESRD (median age of 58 yr versus 64 yr; P < 0.001), more affluent (median household income of $29,500 versus $26,800; P < 0.001), and less likely to have ESRD caused by diabetes mellitus or hypertension than other causes (P < 0.001) than those who were included.

There were 5448 patients under age 20 who had their first dialysis for ESRD between January 1, 1988 and December 31, 1993 who were eligible for the study. Of these patients, 1899 who received kidney transplants from living donors during the follow-up period were excluded from analysis. Additionally, 299 patients were excluded because of irreconcilable wait-listing dates, and 43 were excluded for <90 d of follow-up. As a result, 3217 patients less than 20 yr old were eligible for the study. Excluded patients in the pediatric population were also more likely to be white (79% versus 66%; P < 0.001), younger at first dialysis for ESRD (42% versus 56% in the 15 to 19 yr age group; P < 0.001), and more affluent (30% versus 22% in the highest quartile of income; P < 0.001) than included patients.

**Patient Characteristics**

Table 1 shows the demographic characteristics of the 3217 pediatric patients and 7594 adult patients in the study. In both study populations, male patients tended to be younger when they presented with ESRD. Among adults, a greater proportion of women than men were black and in the lower quartiles of income. There were also minor differences between men and women with regard to the facility type and region in which they were treated. Adult female patients had less education, were more often widowed, and were less likely to be employed than male patients at the onset of ESRD.

Assigned causes of ESRD differed by gender in both cohorts, as well. In the pediatric group, male patients were more likely to have congenital urologic disease (22% versus 14% of female patients), whereas female patients were more likely to have ESRD due to systemic lupus erythematosus (12% versus 3% of male patients). In the adult group, however, women more often had ESRD attributed to diabetes mellitus (40% versus 30% of men) and less frequently due to hypertension (27% versus 33% of men) or glomerulonephritis (10% versus 15% of men) (data not shown).

Clinical differences between men and women in the adult cohort are shown in Table 2. Men were more likely to smoke and were leaner than women. Women more frequently had cardiomegaly and congestive heart failure but less frequently had chronic obstructive pulmonary disease and left ventricular hypertrophy than men. Women were more likely to live in a nursing home and require assistance with activities of daily living than men.

**Impact of Gender on Activation on the Waiting List**

Table 3 shows crude incidence rates and unadjusted and adjusted relative hazards for placement on the waiting list among pediatric and adult patients with ESRD. Female patients were less likely than male patients to be activated on the kidney transplant waiting list regardless of whether they developed ESRD before adulthood (unadjusted rate per 100 person-years of ESRD: 28.89 versus 34.18 for female patients versus male patients, respectively) or after age 20 (unadjusted rate per 100 person-years of ESRD: 3.94 versus 6.54 for female patients versus male patients, respectively). Wait-listing rates for the pediatric population were approximately fivefold greater than those of the adult group. We identified several potential confounding factors associated both with gender and transplant activation in both populations; these included age, race, income, assigned cause of ESRD, and year of ESRD onset. However, even after adjustment for these characteristics, in the pediatric group female patients with ESRD were 14% less likely to be listed for cadaveric transplant than their male counterparts (adjusted relative hazard [RH] 0.86; 95% confidence interval [CI], 0.78 to 0.93). In addition to the aforementioned covariates, several additional sociodemographic (education, marital status, employment, facility ownership type) and clinical (coronary artery disease, congestive heart failure, peripheral vascular disease, chronic obstructive pulmonary disease, diabetes mellitus, dependence for activities of daily living, cancer, cardiomegaly, residence in a nursing home) factors were found to significantly affect rates of wait-listing in the adult population. Despite adjustment for these confounders, adult women were 18% less likely to be activated for transplant than men (adjusted RH 0.82; 95% CI, 0.72 to 0.93). There were no statistically significant interactions between gender and the other demographic factors, including age, in either patient population. Nevertheless, we observed that the gender-based gap in pediatric wait-listing was most prominent among the 15- to 19-yr-old patients and somewhat narrower among younger patients (data not shown).
Discussion

In this nationally representative, longitudinal study, we found that women were less likely than men to be activated on the renal transplant waiting list. In particular, we identified a consistent, negative association between female gender and wait-listing in both adult and pediatric ESRD patients. This
effect persisted despite adjustment for numerous demographic characteristics in both age populations and comorbid medical conditions in the older study cohort that could confound the relationship between gender and wait-listing. Thus, our findings suggest that the gender-based disparities documented in the appropriate use of other medical services, such as cancer-screening tests (16), cardiovascular procedures (17), and medications for those with HIV (18), also exist in activation for renal transplantation.

This is one of the first studies to document that among children and adolescents with ESRD, female patients are less likely to be listed for transplant than male patients. Although a recent regional study that included 380 patients up to 25 yr of age failed to find a gender disparity among young patients (6), several differences in study design may explain the discrepancy in our findings. Our study included a national pediatric population. Also, in evaluating access to the cadaveric waiting list, we excluded patients who received living-related transplants, rather than censoring them at the time of transplantation. Given the large proportion of young patients who receive live-donor transplants (19), including these patients in the analysis would bias the results toward the null. In addition, we adjusted for common causes of ESRD in childhood that may affect the likelihood of transplantation instead of using categories applicable to adult populations. Finally, we accounted for differences in patient socioeconomic status that have an impact on wait-listing, as well.

Our study corroborates the findings of several studies of

Table 2. Baseline clinical characteristics of the adult study cohort

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Males n = 3916</th>
<th>Females n = 3678</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active smoker (%)</td>
<td>24</td>
<td>14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index (kg/m²), mean (SD)</td>
<td>23.7 (4.5)</td>
<td>24.6 (5.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cancer (%)</td>
<td>11</td>
<td>10</td>
<td>0.480</td>
</tr>
<tr>
<td>Cardiomegaly (%)</td>
<td>45</td>
<td>50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cerebrovascular disease (%)</td>
<td>16</td>
<td>17</td>
<td>0.553</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease (%)</td>
<td>16</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Congestive heart failure (%)</td>
<td>44</td>
<td>51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coronary artery disease (%)</td>
<td>50</td>
<td>49</td>
<td>0.566</td>
</tr>
<tr>
<td>Dependent for activities of daily living (%)</td>
<td>11</td>
<td>17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus (not cause of ESRD) (%)</td>
<td>12</td>
<td>13</td>
<td>0.187</td>
</tr>
<tr>
<td>Hypertension (not cause of ESRD) (%)</td>
<td>41</td>
<td>48</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Left ventricular hypertrophy (%)</td>
<td>42</td>
<td>40</td>
<td>0.046</td>
</tr>
<tr>
<td>Lives in nursing home (%)</td>
<td>4</td>
<td>7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peripheral vascular disease (%)</td>
<td>27</td>
<td>26</td>
<td>0.183</td>
</tr>
<tr>
<td>Serum albumin (g/dl), mean (SD)</td>
<td>3.53 (0.50)</td>
<td>3.46 (0.50)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Percentages and means were derived from the following proportion of patients (similar in males and females) with available data for each of the variables: active smoker, 77%; body mass index, 73%; cancer, 95%; cardiomegaly, 80%; cerebrovascular disease, 96%; chronic obstructive pulmonary disease, 96%; congestive heart failure, 95%; coronary artery disease, 98%; dependent for activities of daily living, 98%; diabetes mellitus, 99%; hypertension, 93%; left ventricular hypertrophy, 78%; lives in nursing home, 97%; peripheral vascular disease, 97%; and serum albumin, 90%.

Table 3. Placement on the renal transplant waiting list according to gender

<table>
<thead>
<tr>
<th>Population/Gender</th>
<th>Follow-Up (person-years)</th>
<th>Crude Wait-Listing Rate b</th>
<th>Unadjusted RH (95% CI)</th>
<th>Adjusted RH (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>males</td>
<td>3604</td>
<td>34.18</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
</tr>
<tr>
<td>females</td>
<td>3309</td>
<td>28.89</td>
<td>0.85 (0.78 to 0.92)</td>
<td>0.86 (0.78 to 0.93)c</td>
</tr>
<tr>
<td>Adult patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>males</td>
<td>10910</td>
<td>6.54</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
</tr>
<tr>
<td>females</td>
<td>11250</td>
<td>3.94</td>
<td>0.62 (0.55 to 0.70)</td>
<td>0.82 (0.72 to 0.93)d</td>
</tr>
</tbody>
</table>

* RH, relative hazard; CI, confidence interval.
* Adjusted for age, race, income, assigned cause of ESRD, and year of ESRD onset.
* Adjusted for age, race, income, education, marital status, employment status, assigned cause of ESRD, year of ESRD onset, coronary artery disease, congestive heart failure, peripheral vascular disease, chronic obstructive pulmonary disease, diabetes mellitus, dependence for activities of daily living, cancer, cardiomegaly, residence in a nursing home, and facility ownership type.
adults with ESRD that have found that women are less likely to be placed on the waiting list than men (6,7,12). However, because previous studies have lacked the necessary data, some have hypothesized that differences in health status and socioeconomic status may be responsible for at least a portion of this difference (6,12,20). Although adjustment for detailed indicators of health and social class did reduce the magnitude of the observed disparity, we are able to document that these factors do not fully explain lower rates of wait-listing among adult female patients. Of note, a previous study reported that women with new-onset ESRD were approximately 30% less likely than men to receive a kidney transplant, even after accounting for comorbid medical conditions (8). The gender disparity that we found may be smaller because we focused on the period from first dialysis for ESRD to wait-listing, thereby excluding the additional barriers that women may face in getting a transplant once they are activated on the waiting list (6,7,12). The specific cause of longer waiting times for transplant-activated women compared to men is unknown; however, some have speculated that this may be the result of gender-based differences in antibody status (6).

Although some potential explanations for the lower rates of wait-listing among women were not addressed by our analysis, several are unlikely given the results of previous studies. Female patients may appear to have reduced access to the cadaveric transplant waiting list if they are preferentially getting live-donor transplants; however, recent data suggest that women are less likely than men to receive a living-related transplant (21). Because men and women are referred to nephrologists at similar stages of renal failure (22,23), reduced wait-listing rates for women cannot be explained by delays in presentation that preclude early discussion of modality choices. In fact, a recent study of renal transplant waiting list registrants demonstrated that although men outnumbered women by nearly 50%, the wait-listed women were slightly more likely than corresponding men to have been activated before initiating dialysis (24). While reduced access to transplantation may be appropriate if women are being excluded for noncompliance, mental illness, or substance abuse, data also suggest that these barriers are not more prevalent among women than men with ESRD (25–27). Additionally, provider concerns about patient outcomes after transplantation are not likely to be explanatory, because studies have shown comparable patient and graft survival for men and women after transplantation (3,28). Nevertheless, there are several plausible reasons for this gap that will require further investigation. Little is known about gender-based differences in patient or family preferences for transplant. Although studies have not shown that women are less likely to want a transplant than men (29,30), these studies included few patients and were not national in scope. Furthermore, parents’ modality preferences for their children with ESRD have not been examined. Our data suggest that these access differences may be less prominent among the youngest pediatric patients, for whom the parents are likely to have the strongest influence on transplantation decisions; however, the small number of patients in several age strata limits our ability to draw definitive conclusions about age-defined subgroups. Lower rates of wait-listing also may result if women are less aggressive about negotiating the multiple steps necessary for activation on the waiting list (12). Finally, the possibility of a gender bias by providers, as shown in the use of cardiovascular procedures (31), also must be explored, given the results of a previous study showing that women may be less likely to be identified as potential transplant candidates by dialysis facility staff (11).

Our data allowed us to separately examine the experience of nationally representative samples of children and adults with ESRD who were followed prospectively for up to 10 yr to document differences in access to the renal transplant waiting list. However, several limitations remain. First, we lacked data on comorbid medical conditions among the pediatric population. However, young patients, who frequently have primary renal causes of ESRD, are unlikely to have developed significant comorbid conditions that would be contraindications to transplant. Furthermore, the assigned cause categories we used were specifically chosen to include diseases that might influence a pediatric patient’s eligibility for transplantation. Second, we were unable to adjust for differences in insurance coverage. Recent data suggest that Medicare ESRD patients who lack private supplementary insurance may face financial barriers that limit their access to the waiting list (32). Nevertheless, despite the inclusion of insurance information, women were less likely than men to be wait-listed in that study, as well.

In summary, our findings indicate that female patients with ESRD have reduced access to the transplant waiting list as children and as adults. Furthermore, this disparity is not due to differences in social class or health status. Although a specific cause has not been identified, the results of our study and previous evaluations suggest that this gender gap is more likely due to attitudinal and interpersonal factors, such as patient preferences, provider biases, and patient-provider interactions, than to biologic or clinical differences between male and female patients with ESRD. As a result, the equity of the kidney allocation process and the health of women of all ages with ESRD may be improved if greater emphasis is placed on evaluating and improving patient-physician communication about renal transplantation.

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