

# Gender Disparities in Access to Kidney Transplant: Inequities in the Inequity



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Compared with men, women are less likely to be referred for kidney transplant, less likely to be activated on the waitlist once referred, and less likely to undergo transplant once activated. This may relate to conscious or unconscious provider biases, differential comorbidity burden/frailty distribution, or possible differences in candidate self-selection. In this issue of *KI Reports*, Smothers *et al.*<sup>1</sup> evaluate the modifying effects of patient age, race/ethnicity, and obesity status on gender disparities in transplant referral in a large population in the South-eastern United States. In keeping with earlier literature, women were 14% less likely to be referred for kidney transplant; this was particularly prominent among older and non-Hispanic White women. It is interesting to note the divergence in referral rates by gender was only evident in older adults, with comparable rates of referral in the younger cohorts.

This is not the first study to show this. In a Canadian study from 2010 to 2013, women were 12% less likely to be referred for kidney transplant except in a sub-cohort restricted to those <60 years of age where there were no significant differences by gender.<sup>2</sup> Likewise, Segev *et al.*<sup>3</sup> demonstrated that although young men and women 18 to 45 years of age had equivalent access to transplant (ATT), women >75 years had 59% less ATT compared with older men, despite equivalent or better survival from transplant in women versus men of all ages.

The reason for differential referral rates by gender requires consideration and ultimately distills down to sex- and/or gender-based differences in (i) true transplant eligibility, (ii) provider perception of eligibility, (iii) patient self-perception of eligibility and/or interest in transplant, or (iv) a combination of the above.

It is likely that differential patient or provider perception of frailty by gender contributes to the discrepant transplant referral rates demonstrated between older men and women. Frailty is variably defined as an age-related state of increased vulnerability to

adverse health outcomes<sup>4</sup> and is more common in women than men of the same age. Although a formal frailty assessment is not currently required in the evaluation of transplant candidate eligibility, informal and subjective bedside physician assessments may influence decisions around referral practices. Women have poorer self-rated health than men and are often more willing to identify and report minor or major health issues.<sup>4</sup> This reporting bias may result in more frequent interactions with health care providers, the accrual of more possible diagnoses, and thereby an inflated impression of disease prevalence and frailty in women compared with men.<sup>4</sup> Indeed, nonfrail women on hemodialysis are more likely to be misclassified by their health care providers as subjectively frail compared with nonfrail men.<sup>5</sup> This impression of increased frailty in women may equate to a perception of reduced survival benefit with transplant, and therefore, non referral. However, the implications of frailty differ by gender; frail men have a mortality rate 2.6-fold higher than frail women.<sup>6</sup> In addition, despite being more frail, women of all ages have greater life expectancy than age-matched men; the so-called male-female health survival paradox.<sup>7</sup> This likely relates to a combination of biological, behavioral, and social factors and suggests that the effects of frailty on post-transplant outcomes may similarly vary by gender. Importantly, frailty is not static and has been shown to improve post-kidney transplant.<sup>8</sup> Given that pretransplant frailty is often subjectively determined (and differentially so by gender), is to some extent reversible with transplant, and the relationship

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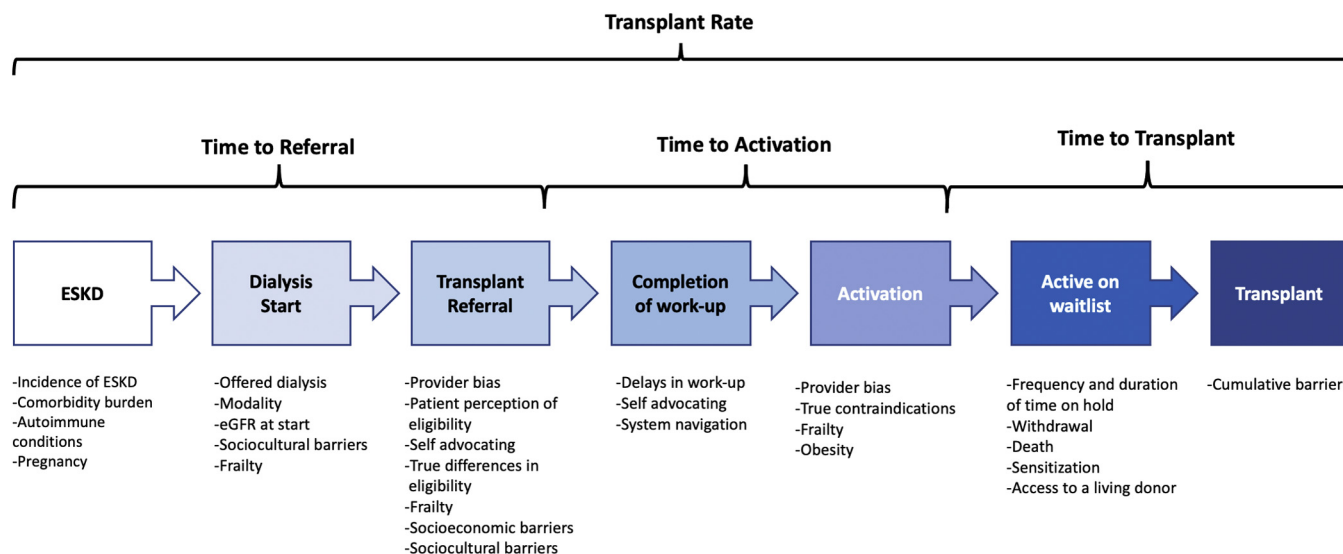
between frailty and survival is modified by gender, limiting ATT for women perceived to be frail on the basis of poor anticipated transplant outcomes is likely short sighted and discriminatory.

Contrary to most earlier studies where Black and minority patients have reduced ATT (despite fewer medical barriers),<sup>9</sup> in the current study, non-Hispanic White patients had a lower likelihood of referral for transplant than all other racial/ethnic groups. The reason for this is unclear but may reflect a greater awareness of racial inequities in ATT and a corresponding attention to referral practices given the large Black population in the Southeastern United States; 53.3% of the study participants were non-Hispanic Black. Although sample sizes were too small to draw any meaningful conclusions for Hispanic and “other” race groupings, the greatest gender disparity in ATT was for White women versus men, particularly at older ages (15% and 36% lower odds of referral for White women vs. men aged 45–64 and 65–80 years, respectively; 2% and 8% lower odds of referral for Black women vs. men of the same age groupings). The authors do not provide a breakdown of baseline characteristics by race and gender; whether older White women were more likely to be excessively frail (objectively or subjectively) or multimorbid and therefore considered transplant ineligible relative to older White men remains to be seen. Importantly, higher referral rates do not uniformly translate into higher activation or subsequent transplant rates. For example, an earlier study in the same Southeastern US population demonstrated that although non-Hispanic Black patients had a higher rate of transplant referral, they were significantly less likely

than White patients to subsequently initiate transplant work-up.<sup>51</sup> In this same study, women were 14% less likely than men to be referred for transplant, but only 6% less likely to begin transplant work-up. Similarly, contrary to earlier literature, Smothers *et al.*<sup>1</sup> also demonstrate increased referral rates in overweight and class I/II obese versus normal-weight individuals. Although earlier studies have shown that obese (body mass index >35–39 kg/m<sup>2</sup>) women, but not men, have a lower likelihood of activation on the transplant waitlist and subsequent transplantation,<sup>52</sup> the study by Smothers *et al.*<sup>1</sup> suggests that obesity does not modify the association between gender and referral for transplant (acknowledging the interaction term was borderline significant [ $P = 0.063$ ]). The current study does not evaluate subsequent steps in the continuum from referral to transplant however, and although obesity may not limit referral for women, whether subsequent activation and transplantation rates for obese individuals differ by gender in this unique population remains to be seen.

Although ATT for men and women may be partially driven by biology and differential comorbidity distribution, statistical models evaluating the association of candidate sex with transplantation rates indicate significant unexplained variability,<sup>53</sup> which suggests other unmeasured factors are also contributing, including potential social or behavioral differences. An important factor for consideration is the candidate’s perception of their own eligibility for transplant and self-advocacy for referral. Women are generally more risk averse under stress<sup>54</sup> and are less likely to be self-promoting than men in business, academia, and health care.<sup>55,56</sup> Older adults

and women have reported less interest in kidney transplant compared with younger adults and men.<sup>57</sup> This may contribute to the greater disparity in transplant referral rates among older men and women who overall have reduced referral rates compared with younger cohorts. In younger, healthier cohorts, referral is relatively ubiquitous, yet among older, more medically complex populations where referral is more selective, self-advocacy and patient interest may play a greater role in prompting referral. This requires investigation. Among Black dialysis patients, women were more positive than men about the dialysis experience and often reluctant to pursue kidney transplant.<sup>57</sup> A 2014 study of incident dialysis patients in Baltimore demonstrated that women reported more health-related and psychosocial concerns regarding future kidney transplant than men<sup>58</sup> and, correspondingly, men have been shown to be more likely than women to “want” a kidney transplant.<sup>58,59</sup> Compared with men, women on dialysis are up to 45% less likely to discuss kidney transplant with their health care provider<sup>510</sup> and more likely to “completely trust” their nephrologist,<sup>59</sup> which may lead to women being less likely to challenge non-referral for transplant. Women were more likely to report experiencing gender-based discrimination in the transplant referral process, and 56% of surveyed White women accepted their experience with gender discrimination in ATT as “just a fact of life.” Those who accepted discrimination as a fact of life were less likely to be listed for transplant than patients who attempted to change such situations.<sup>511</sup> Patients’ attitudes may thus influence treatment decisions and form an



**Figure 1.** Access to transplant is a continuum consisting of a series of sequential steps with potential gender-based barriers throughout. eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease.

unintentional, unconscious barrier to accessing transplantation that may explain, in part, the observed gender disparities in transplantation rates.<sup>S12</sup>

Smothers *et al.*<sup>1</sup> evaluate kidney transplant referral rates by gender in the first year after dialysis initiation. Earlier studies have shown that the disparate referral rates by race (in the setting of lower referral rates among Black compared with White patients) are abolished if a longer time horizon is used (e.g., referral within 4–5 years).<sup>9</sup> This may provide clues to the barriers faced, as eventual referral indicates those bypassed for referral in the first year lack absolute contraindications to transplant. A study evaluating later referral rates by gender may likewise identify reversible or modifiable barriers for under-referred women. In addition, no study to date has thoroughly reviewed transplant eligibility in a systematic manner among the non-referred to ascertain whether true disparate contraindications exist by gender. Men have been shown to have greater comorbidity burden and shorter life expectancy than age-matched females, and

therefore eliminating ineligible patients from the transplant denominator would likely only exacerbate the discrepant referral rates between men and women; however, this requires future study.

Access to kidney transplant involves a series of sequential steps related to medical suitability, candidate identification and referral, pretransplant work-up, activation on the waitlist, and progression through the waiting list to eventual transplantation<sup>S13</sup> (Figure 1). Gender disparities have been identified throughout, but a comprehensive overview of modifiable barriers for women and those who identify as female along the transplant journey is lacking. Although ATT is a continuum, non-referral is a critical roadblock that halts the entire process; an un-referred female patient will *not* be transplanted. Equal ATT is a cornerstone of organ allocation policy. The first step is demanding gender equity in transplant referral.

## DISCLOSURE

The author declared no competing interests.

## SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary References.

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