Functional independence, access to kidney transplantation and waitlist mortality

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ABSTRACT

Background. Approximately half of the patients who progress to end-stage kidney disease (ESKD) and undergo dialysis develop difficulties carrying out essential self-care activities, leading to institutionalization and mortality. It is unclear what percentage of kidney transplant (KT) candidates, a group of ESKD patients selected to be healthy enough to withstand transplantation, are functionally independent and whether independence is associated with better access to KT and reduced waitlist mortality.

Methods. We studied a prospective cohort of 3168 ESKD participants (January 2009 to June 2018) who self-reported functional independence in more basic self-care Activities of Daily Living (ADL) (needing help with eating, dressing, walking, grooming, toileting and bathing) and more complex instrumental ADL (IADL) (needing help using a phone, shopping, cooking, housework, washing, using transportation, managing medications and managing money). We estimated adjusted associations between functional independence (separately) and listing (Cox), waitlist mortality (competing risks) and transplant rates (Poisson).

Results. At KT evaluation, 92.4% were independent in ADLs, but only 68.5% were independent in IADLs. Functionally independent participants had a higher chance of listing for KT [ADL: adjusted hazard ratio (aHR) = 1.55, 95% confidence interval (CI) 1.30–1.87; IADL: aHR = 1.39, 95% CI 1.26–1.52]. Among KT candidates, ADL independence was associated with lower waitlist mortality risk [adjusted subdistribution HR (aSHR) = 0.66, 95% CI 0.44–0.98] and higher rate of KT [adjusted incidence rate ratio (aIRR) = 1.58, 95% CI 1.12–2.22]; the same was not observed for IADL independence (aSHR = 0.86, 95% CI 0.65–1.12; aIRR = 1.01, 95% CI 0.97–1.19).

Conclusions. Functional independence in more basic self-care ADL was associated with better KT access and lower waitlist

mortality. Nephrologists, geriatricians and transplant surgeons should screen KT candidates for ADLs, and identify interventions to promote independence and improve waitlist outcomes.

Keywords: functional performance, outcomes, renal

INTRODUCTION

Functional independence reflects a patient's ability to care for themselves [1, 2] and is a health priority for patients with advanced chronic kidney disease [3]. Lack of functional independence leads to poor outcomes including institutionalization in assisted care facilities [4] and mortality [5–7] in end-stage kidney disease (ESKD) patients of all ages. Dialysis initiation is associated with the transition from independence to dependence, regardless of the patient's age [7–9], resulting in 50% of dialysis patients being functionally dependent [10–12]. Nearly one in five patients report needing help with at least one or more basic self-care activities of daily living (ADL) [13], including eating, dressing, walking, grooming, toileting and bathing [12, 14]. Furthermore, ~80% of ESKD patients report needing help with more complex instrumental ADL (IADL) [15], such as using a phone, shopping, cooking, housework, washing, using transportation, managing medications and managing money [7, 9, 10, 12, 14, 16–18]. While it is likely that some kidney transplant (KT) candidates are not functionally independent resulting from their high burden of frailty and years of chronic conditions [19–21], the prevalence of functional independence in this population of ESKD patients is unknown.

While a lack of functional independence is associated with higher mortality risk in dialysis patients of all ages [5, 6, 19], it remains unclear if the same holds true for those listed for KT. The risks associated with not being independent among KT candidates are unclear and cannot be extrapolated from

patients undergoing hemodialysis, because KT candidates are a group of ESKD patients who are selected to be healthy enough to withstand transplant surgery. KT candidates are typically younger and healthier than the general ESKD population [22], and include patients not on dialysis who are pursuing preemptive KT. Among KT candidates, understanding the impact of functional independence and waitlist mortality as well as access to KT is important and novel.

There are clear links between certain domains of independence and adverse outcomes. For example, the inability to manage medications is likely associated with access to KT because treatment and medication nonadherence contribute to adverse ESKD outcomes, and is considered prior to listing [23, 24]. While some domains of independence are directly observable by clinicians during KT evaluation (such as inability to walk), others may not be (such as needing help with housework). Therefore, understanding the role of these individual self-care domains among KT candidates is important for the care of KT candidates.

To better understand the impact of functional independence on access to KT and waitlist mortality, we leveraged a prospective cohort study of ESKD participants undergoing evaluation for KT. The objectives of this study were to: (i) estimate the prevalence of functional independence overall and report the domains of independence in this population and (ii) test whether functional independence, overall and by domain, is associated with access to KT (including likelihood of listing and rates of KT) and waitlist mortality. Understanding the role of functional independence in KT candidates may provide quantitative evidence that substantiates patient perspectives of an important health priority.

MATERIALS AND METHODS

Participants

We studied a prospective cohort of 3168 ESKD participants being evaluated for KT at Johns Hopkins University in Baltimore, Maryland (January 2009 to June 2018, $n = 2910$) and the University of Michigan in Ann Arbor, Michigan (January 2015 to April 2016, $n = 258$), as previously described [25–29]. Participants were included in the study if they were English-speaking, ≥ 18 years of age and were measured for functional independence at the time of evaluation, as described below. Other participant characteristics were obtained via self-report at KT evaluation or abstracted from medical records, including age, sex, race, education, body mass index (BMI), diabetes status, depressive symptoms (Center for Epidemiologic Studies Depression Scale score < 16), bodily pain (based on the Kidney Disease Quality of Life), years on dialysis, cause of ESKD and Charlson comorbidity index (CCI) adapted for ESKD [30, 31]. Surveys were verbally administered in English.

Functional independence

Functional independence was derived from the National Long Term Care Survey verbally administered by study staff at the time of evaluation for KT. Participants self-reported whether they needed help with eating, dressing, walking,

grooming, toileting or bathing, which comprised the six basic self-care ADL domains [13]. Participants also self-reported whether they needed help with using a phone, shopping, cooking, housework, washing, using transportation, managing medications or managing money, which comprised the eight more complex self-care IADL domains [15]. An individual was classified as ADL independent if they were not functionally dependent in any of the ADL domains reported; we used a similar approach to define IADL independence. A Venn diagram was generated to depict the proportion of participants classified as both ADL and IADL independent. The physicians at Johns Hopkins Hospital and the University of Michigan were not aware of the functional independence assessment results at the listing meeting in which physicians decide whether or not to list a patient.

Correlates of functional independence

Among ESKD participants who were listed for KT (KT candidates) ($n = 1703$), odds ratios (ORs) for assessing associations with ADL independence and demographic and health characteristics were obtained from adjusted logistic regression models. The same methods were used to identify correlates of IADL independence.

Chance of listing by functional independence

Among ESKD participants being evaluated for KT ($n = 3168$), adjusted Cox proportional hazards regressions were used to estimate the chance of listing by ADL independence. Time to listing was defined as the time from evaluation for KT to the date of active placement on the KT waitlist or administrative censoring at the end of the study period (May 2018). Proportional hazards assumptions were confirmed by visual inspection of the complementary log–log plots and Schoenfeld residuals. All models were adjusting for age, sex, race, education and diabetes. To test whether the association between ADL independence and time to KT listing varied by participant age, sex and race, an interaction between participant age (age < 65 versus age ≥ 65 years), race (black versus non-black) or sex (male versus female) and ADL independence in separate models was explored using Wald tests. The impact of each of the six individual ADL domains on the chance of listing was subsequently explored in a single model; this model quantified the association for each individual ADL domain above and beyond the other domains. The same methods were used to assess the chance of listing by IADL independence, as well as the eight IADL domains.

Waitlist mortality

Among KT candidates ($n = 1703$), Fine and Gray competing risk models [32] were used to estimate the risk [subdistribution hazard ratios (SHR)] of waitlist mortality by ADL independence, accounting for KT as a competing risk. The time of origin was the date of active listing, and KT candidates were followed to date of death; candidates were censored at the end of the study period (May 2018) if it preceded mortality or KT. All models were adjusted for age, sex, race, education and diabetes. To test whether the association between ADL

independence and mortality varied by participant age, sex and race, an interaction between participant age (age <65 versus age ≥65 years), race (black versus non-black) or sex (female versus male) and ADL independence in separate models was explored using Wald tests. The impact of each of the six individual ADL domains on waitlist mortality was subsequently explored in a single model; this model quantified the association for each individual ADL domain above and beyond the other domains. The same methods were used to assess the chance of listing by IADL independence, as well as the eight IADL domains.

Transplant rate

Among KT candidates ($n = 1703$), Poisson regression was used to estimate adjusted incidence rate ratio (aIRR) by ADL independence, accounting for age, sex, race, education and diabetes. Person-years were calculated from the date of KT listing to the date of KT, mortality or censoring at the end of the study period (May 2018). To test whether the association between ADL independence and transplant rate varied by participant age, sex and race, an interaction between participant age (age <65 versus age ≥65 years), race (black versus non-black) or sex (female versus male) and ADL independence in separate models was explored using Wald tests. The impact of each of the six individual ADL domains on transplant rate was subsequently explored in a single model; this model quantified the association for each individual ADL domain above and beyond the other domains. The same methods were used to assess the chance of listing by IADL independence, as well as the eight IADL domains.

Sensitivity analysis

We conducted a sensitivity analysis additionally adjusting for CCI, diagnosis of dementia and the Modified Mini-Mental State (3MS) score for global cognitive function to determine if the impact of ADL and IADL independence on waitlist outcomes remained robust to the presence of comorbidities and cognitive function. We additionally conducted sensitivity analyses adjusting for depressive symptoms and bodily pain to assess whether inferences could be explained by these often under-treated symptoms.

Statistical analysis

All analyses were performed using Stata version 14.0/MP for Linux (Stata Corp, College Station, TX, USA).

RESULTS

Study population

Among the 3168 ESKD participants at time of KT evaluation (Table 1 and Figure 1), the median [interquartile range (IQR)] age was 56.0 years (45.3–64.8), with ages ranging from 18 to 89 years; 24.7% were over the age of 65 years, 58.9% were male, 45.9% were black and 44.9% had no more than a high school education. Additionally, 41.9% had diabetes as comorbidity, and 21.4% had diabetes as the cause of ESKD. ESKD participants had been on dialysis for a median (IQR) of 1.4 years (0.6–

3.3) at the time of KT evaluation, and 52.3% were undergoing hemodialysis.

Functional independence at time of evaluation

At the time of evaluation, 92.5% were independent in basic self-care ADLs, and 68.5% were independent in more complex IADLs (Table 1). Older ESKD participants had similar levels of ADL independence (94.8% versus 95.6%) but were less likely to have IADL independence (65.8% versus 69.4%) compared with their younger counterparts. The prevalence of ADL independence by domain ranged from 95.2% (walking) to 99.4% (eating). By comparison, the prevalence of IADL independence by domain ranged from 76.3% (shopping) to 84.4% (house-keeping). Among the ESKD participants, 66.4% were classified as having both ADL and IADL independence (Figure 2).

Those with ADL or IADL independence were generally younger (ADL: median age = 55.7 versus 58.7 years; IADL: median age = 55.5 versus 57.0 years), and more likely to be male (ADL: 59.7% versus 50.2%; IADL: 60.0% versus 57.0%), white (ADL: 49.0% versus 46.0%; IADL: 49.0% versus 48.0%) and have higher educational attainment (ADL: 58.3% versus 52.3%; IADL: 59.6% versus 53.8%). Additionally, those with ADL or IADL independence were less likely to have diabetes as a comorbidity (ADL: 40.7% versus 56.5%; IADL: 39.3% versus 47.5%) and diabetes as a cause of ESKD (ADL: 20.6% versus 33.0%; IADL: 19.8% versus 25.0%).

Correlates of functional independence at time of evaluation

Among KT candidates ($n = 1703$), males had a 1.65 times [95% confidence interval (CI) 1.09–2.52; $P = 0.02$] greater odds of having ADL independence, and for every 1-U increase in the comorbidity index, KT candidates had a lower odds [adjusted OR (aOR) = 0.91, 95% CI 0.83–0.99] of having ADL independence (Table 2). Similarly, for every 1-U increase in the comorbidity index, KT candidates had lower odds (aOR = 0.88, 95% CI 0.83–0.93) of IADL independence. Additionally, for every 10-kg/m² increase in BMI, KT candidates had 1.36 times (95% CI 1.11–1.65; $P < 0.001$) increased odds of having IADL independence.

Chance of listing and functional independence

ESKD participants ($n = 3168$) were followed for a median (IQR) of 0.4 years (0.1–1.2) and a total of 2832 person-years, during which 1703 (53.8%) were listed for KT. ADL independence was associated with 1.55 times (95% CI 1.30–1.87; $P < 0.001$) higher chance of listing (Table 3). The association between ADL independence and a chance of listing did not differ by age ($P = 0.29$), sex ($P = 0.86$) or race ($P = 0.39$). Independence in each ADL domains, including dressing, walking, grooming, using a toilet and bathing, was associated with a higher chance of listing after adjusting for the other respective domains; independence in eating was the only domain that was not associated with a higher chance of listing after adjusting for the other respective domains [adjusted HR (aHR) = 1.69, 95% CI 0.91–3.15; $P = 0.10$] (Figure 3).

Table 1. Characteristics of ESKD participants at time of evaluation for kidney transplantation (*n* = 3168)^a

Characteristic	ADL		IADL	
	Independence (<i>n</i> = 2929)	Dependence (<i>n</i> = 239)	Independence (<i>n</i> = 2171)	Dependence (<i>n</i> = 997)
Age [median (IQR)], years	55.7 (44.9–64.6)	58.7 (50.2–65.9)	55.5 (44.7–64.4)	57.0 (46.4–65.5)
Male (%)	59.7	50.2	60.0	57.0
Race (%)				
White	49.0	46.0	49.0	48.0
Black	43.9	49.0	44.2	44.4
Other	7.1	5.0	6.8	7.6
High school or less (%)	41.7	47.7	40.4	46.2
BMI [median (IQR)], kg/m ²	28.2 (24.0–32.7)	30.0 (24.5–35.5)	28.2 (24.1–32.7)	28.6 (24–33.7)
3MS score, median (IQR)	94 (9–97)	93 (87–97)	95 (90–98)	94 (88–97)
Depressive symptoms (%)	79.5	64.0	82.5	69.0
CCI, median (IQR)	2 (0–3)	3 (1–4)	2 (0–3)	2 (0–4)
Comorbidity (%)				
Myocardial infarction	9.3	11.8	8.0	12.7
Peripheral vascular disease	6.3	7.5	5.2	8.9
Cerebral vascular disease	5.3	12.6	4.6	8.6
Dementia	0.3	1.7	0.2	0.8
Chronic lung disease	6.1	6.3	6.6	5.2
Rheumatological disease	6.3	11.4	6.1	8.0
Peptic ulcer disease	3.4	3.8	3.1	4.1
Diabetes	40.7	56.5	39.3	47.5
Diabetes complication	24.8	44.8	23.7	32.0
Moderate/severe liver disease	3.2	6.7	3.2	4.0
Metastatic cancer	1.1	1.3	0.9	1.5
Leukemia	0.3	0.4	0.3	0.3
Lymphoma	1.0	0.4	1.0	1.0
HIV	3.1	3.3	2.9	3.7
Congestive heart failure	13.7	21.2	11.7	21.3
Cause of ESKD (%)				
Hypertension	29.3	33.7	30.0	28.8
Diabetic	20.6	33.0	19.8	25.0
Glomerular disease	21.7	15.3	21.7	20.2
Other	28.4	18.0	28.5	26.0
Years on dialysis [median (IQR)], years	0.1 (0.0–1.5)	0.2 (0.0–1.2)	1.2 (0.0–1.6)	0.1 (0.0–1.1)

^aParticipants were evaluated at the Johns Hopkins Hospital (*n* = 2910) and University of Michigan (*n* = 258). The same patient population is presented on the left (ADL) and right (IADL) hand sides of the Table. Depressive symptoms are characterized by a Center for Epidemiologic Studies Depression score of <16. The description of years on dialysis excludes those who were preemptively listed.

Similarly, IADL independence was associated with a higher chance of listing (aHR = 1.39, 95% CI 1.30–1.52; *P* < 0.001) (Table 3). The association between IADL independence and a chance of listing did not differ by age (*P* = 0.85), sex (*P* = 0.91) or race (*P* = 0.37). Independence in each of the IADL domains, including using a phone, shopping, cooking, washing, using transportation, managing medications and managing money, was associated with a higher chance of listing after adjusting for the other respective domains; independence in housekeeping was the only domain that was not associated with a higher chance of listing after adjusting for the other respective domains (aHR = 1.10, 95% CI 0.98–1.24; *P* = 0.11) (Figure 3).

Waitlist mortality and functional independence

There were 1703 KT candidates who were listed for transplantation as active and they were followed for a median (IQR) of 1.2 years (0.5–2.5 years) and a total of 3103 person-years, during which 244 died before receiving KT. ADL independence was associated with a 34% (SHR = 0.66, 95% CI 0.44–0.98; *P* = 0.04) lower risk of waitlist mortality (Table 3). The association between ADL independence and waitlist mortality did not

FIGURE 1: Proportion of those who died and underwent KT among ESKD participants (*n* = 3168, average follow-up time: 10.7 months) and KT candidates (*n* = 1703, average follow-up time: 2.4 years).

differ by age (*P* = 0.54) or sex (*P* = 0.09). However, the association between ADL independence and waitlist mortality differed by race (*P* = 0.02), such that among blacks, ADL independence was not associated with waitlist mortality (SHR = 1.31, 95% CI 0.50–3.20), while among non-blacks, ADL independence was associated with a 58% (SHR = 0.42, 95% CI 0.26–0.68) lower

FIGURE 2: Proportion of ADL and IADL functional independence in ESKD participants being evaluated for kidney transplantation ($n = 3168$). Circles represent the proportion of participants evaluated for a kidney who are independent in ADLs and/or IADLs.

FIGURE 3: Chance of listing by domains of ADL and IADL functional independence among ESKD participants evaluated for kidney transplantation ($n = 3168$). Dots represent aHRs comparing the functionally independent with the functionally dependent in the specified daily activity; the bars represent the 95% CI of the HR. All models adjusted for age, sex, race, education and diabetes status. The y-axis is on a log scale.

risk of waitlist mortality. Independence in eating (SHR = 0.32, 95% CI 0.15–0.70; $P = 0.01$) and dressing (SHR = 0.42, 95% CI 0.19–0.97; $P = 0.04$) were the only ADL domains associated with lower waitlist mortality after adjusting for the other respective domains (Figure 4).

IADL independence was not associated with waitlist mortality (SHR = 0.86, 95% CI 0.65–1.12; $P = 0.28$) (Table 3), nor were any of its individual domains (Figure 4). Additionally, the association between IADL independence and waitlist mortality did not differ by age ($P = 0.54$), sex ($P = 0.05$) or race ($P = 0.33$).

Transplant rate by functional independence

Of the 1703 KT candidates, the median (IQR) follow-up time was 0.8 years (0.3–2.0 years) with a total of 2317 person-years, during which 967 received KT. ADL independence was associated with a higher transplant rate (IRR = 1.58, 95% CI 1.12–2.22; $P = 0.01$) (Table 3). The association between ADL

FIGURE 4: Risk of waitlist mortality by domains of functional independence (ADL/IADL) among KT candidates ($n = 1703$). Dots represent the aSHRs comparing those who were functionally independent with those who were functionally dependent in the specified daily activity; bars represent the 95% CI of the SHR. All models adjusted for age, sex, race, education and diabetes status. The y-axis is on a log scale.

FIGURE 5: Rate of kidney transplantation by domains of functional independence (ADL/IADL) among KT candidates ($n = 1703$). Dots represent aIRRs comparing those who were functionally independent to those who were functionally dependent in the specified daily activity; bars represent the 95% CI of the IRRs. All models adjusted for age, sex, race, education and diabetes status. The y-axis is on a log scale.

independence and transplant rate did not differ by sex ($P = 0.89$) or race ($P = 0.64$). However, the association between ADL independence and transplant rate differed by age ($P = 0.04$), such that among older ages, ADL independence was associated with 3.05 times (95% CI 1.30–7.15) higher KT rate, while among younger ages, there was no association between ADL independence and KT rate (IRR = 1.16, 95% CI 0.80–1.70). Of the ADL domains, only independence in walking was associated with a higher transplant rate after adjusting for the other respective domains (IRR = 1.79, 95% CI 1.19–2.69; $P = 0.005$). Independence in eating, dressing, grooming, using a

Table 2. Correlates of functional independence (ADL/IADL) among KT candidates (*n* = 1703)^a

Correlate	ADL independence		IADL independence	
	aOR (95% CI)	P-value	aOR (95% CI)	P-value
Age, years				
18–64	Reference		Reference	
≥65	0.91 (0.56–1.48)	0.71	0.94 (0.72–1.22)	0.63
Male	1.65 (1.09–2.52)	0.02	1.22 (0.97–1.52)	0.08
Black race	0.81 (0.53–1.25)	0.34	1.12 (0.89–1.42)	0.31
High school education or less	0.83 (0.54–1.25)	0.38	0.88 (0.70–1.11)	0.29
BMI, per 10-kg/m ² increase	0.96 (0.67–1.37)	0.83	1.36 (1.11–1.65)	<0.001
Diabetes	0.72 (0.43–1.19)	0.20	0.92 (0.68–1.23)	0.56
CCI, per unit increase	0.91 (0.83–0.99)	0.04	0.88 (0.83–0.93)	<0.001
Years on dialysis, per 10-year increase	1.80 (0.65–5.07)	0.26	1.49 (0.91–2.44)	0.11

^aaORs for each characteristic were obtained from adjusted logistic regression models assessing associations with ADL independence simultaneously. In a separate model, the same approach was used to assess associations with IADL independence.

Table 3. Chance of listing, risk of waitlist mortality and KT rate ratios, by functional independence (ADL/IADL)^a

Outcome	Measure of association	P-value
Chance of listing (<i>n</i> = 3168)	aHR (95% CI)	
ADL independence	1.55 (1.30–1.87)	<0.001
IADL independence	1.39 (1.26–1.52)	<0.001
Risk of waitlist mortality (<i>n</i> = 1703)	aSHR (95% CI)	
ADL independence	0.66 (0.44–0.98)	0.04
IADL independence	0.86 (0.65–1.12)	0.28
Transplant rate (<i>n</i> = 1703)	aIRR (95% CI)	
ADL independence	1.58 (1.12–2.22)	0.01
IADL independence	1.01 (0.87–1.19)	0.81

^aEstimates were generated for ADL and IADL independence in separate models. All analyses were adjusted for age, sex, race, education and diabetes status.

toilet and bathing was not associated with the transplant rate (Figure 5).

IADL independence was not associated with the transplant rate (IRR = 1.01, 95% CI 0.87–1.19; *P* = 0.81) (Table 3). The association between IADL independence and transplant rate did not differ by age (*P* = 0.83), sex (*P* = 0.30) or race (*P* = 0.97). However, several domains of IADL independence were associated with lower transplant rates after adjusting for the other respective domains, including independence in use of a phone (IRR = 0.77, 95% CI 0.64–0.94; *P* = 0.009), cooking (IRR = 0.82, 95% CI 0.87–0.98; *P* = 0.03), washing (IRR = 0.83, 95% CI 0.69–0.99; *P* = 0.04), and managing money (IRR = 0.80, 95% CI 0.66–0.97; *P* = 0.02). Independence in shopping, using transportation, managing medications, managing money and housekeeping were not associated with transplant rate after adjusting for the other respective domains (Figure 5).

Sensitivity analysis

Across all sensitivity analyses, inferences remained robust. Specifically, after further adjusting all models for CCI, diagnosis of dementia and 3MS score, both ADL (aHR = 1.54) and IADL (aHR = 1.12), independence were associated with a greater chance of listing. Additionally, ADL independence was associated with a lower risk of waitlist mortality (aSHR = 0.79) and an increased rate of transplant (aIRR = 1.38). Results also

remained robust after adjusting for depressive symptoms and bodily pain. For models controlling for depressive symptoms, both ADL (aHR = 1.47) and IADL (aHR = 1.12), independence were associated with a greater chance of listing, and ADL independence was associated with a lower risk of waitlist mortality (aSHR = 0.79) and increased rate of transplant (aIRR = 1.38). After adjusting for bodily pain, both ADL (aHR = 1.66) and IADL (aHR = 1.12) independence were also associated with a greater chance of listing, and ADL independence was associated with a lower risk of waitlist mortality (aSHR = 0.46) and increased rate of transplant (aIRR = 2.24).

DISCUSSION

In this prospective cohort study of 3168 ESKD participants, 92.4% were independent in basic self-care ADLs, but only 68.5% were independent in more complex self-care IADLs at the time of evaluation for KT. ESKD participants with ADL or IADL independence at time of evaluation for KT had a higher chance of listing for KT (ADL: aHR = 1.55, 95% CI 1.30–1.87; IADL: aHR = 1.39, 95% CI 1.26–1.52), and these associations did not differ by age, sex or race. Unlike KT candidates with IADL independence at the time of listing, KT candidates with ADL independence had a lower waitlist mortality risk (SHR = 0.66, 95% CI 0.44–0.98) overall and particularly among non-black candidates (SHR = 0.42, 95% CI 0.26–0.68). Additionally, ADL independence was associated with a higher rate of KT overall (IRR = 1.58, 95% CI 1.12–2.22), and particularly among older adults aged ≥65 years (IRR = 3.05, 95% CI 1.30–7.15).

This study extends these findings among dialysis patients to a novel population of ESKD patients of all ages who are being evaluated for KT, in which 92.4% were functionally independent based on ADLs and 68.5% were functionally independent based on IADLs. Even among this subgroup of ESKD patients selected to be healthy enough to withstand transplantation, these findings support prior research conducted among dialysis patients. Specifically, prior studies have found that impairments in basic self-care ADLs, including eating, dressing, walking, grooming, toileting and bathing, are less common than impairments in more complex self-care IADLs, such as using a phone,

shopping, cooking, housework, washing, using transportation, managing medications and managing money [11].

Additionally, to our knowledge, this is the first study to investigate whether functional independence is associated with better outcomes in ESKD participants being evaluated for KT and candidates listed for KT. Prior research has mainly focused on the role of dependence on poor adverse outcomes among patients on dialysis generally [4–7, 16], findings from which cannot be generalized to KT candidates selected to be healthy enough to withstand transplant surgery. Our findings highlight that while ADL independence is more common in KT candidates than IADL independence, only ADL independence is associated with all three waitlist outcomes. Specifically, unlike IADL independence, ADL independence was associated with lower waitlist mortality and higher rate of KT, mirroring prior research on functional dependence that identified significant reductions in survival among ESKD patients with ADL impairments, but not in ESKD patients with IADL impairments [6]. ADLs represent more basic self-care activities [13], compared with the more complex self-care IADL, which require higher levels of functional ability [15]. It follows, therefore, that overall independence in conducting the most basic, day-to-day self-care activities has a greater impact on KT waitlist outcomes compared with those activities that require higher levels of functional abilities, particularly among older adults, where ADL independence more than doubled rate of KT. Therefore, clinicians and transplant centers may consider including ADL screening among KT candidates, but not necessarily IADL screening.

Of note, our study found that these associations differed by race and age, such that there was no observed association between ADL independence and waitlist mortality among blacks and no observed association between ADL independence and KT rate among younger ages. It is possible other protective factors among these subgroups not captured by this study lead to better waitlist outcomes such that the added benefit of being ADL independent is mitigated. The null associations may also be due to the lack of power or unmeasured confounding. Future studies are needed to better understand these causal interactions.

Our study additionally expands on prior findings that demonstrated associations between overall dependence and adverse outcomes in dialysis populations by examining the specific domains of basic and more complex functional independence. We found that independence in eating (SHR = 0.32, 95% CI 0.15–0.70; $P = 0.01$) and dressing (SHR = 0.42, 95% CI 0.19–0.97; $P = 0.04$) were the ADL domains driving the association with lower waitlist mortality, and independence in walking was driving the association with higher transplant rate (IRR = 1.79, 95% CI 1.19–2.69; $P = 0.005$). Further investigation into why these domains drive the associations with waitlist outcomes among KT candidates is needed.

There were notable limitations to this study. First, ADLs and IADLs were self-reported, which could have led to potential misclassification. However, self-report is typically how these data are collected in gerontologic studies [13, 15]. Second, important variables, such as social support, were not collected in

this study but may mitigate the impact of ADL and IADL independence on waitlist outcomes. Third, patients were enrolled at the time of evaluation for KT rather than at the time they were referred for dialysis. It is possible that those with the greatest burden of ADL or IADL dependence do not get referred to a transplant center; however, this question is beyond the scope of this research. It is also possible that some patients who were listed were subsequently ineligible for KT due to poor functional status. While this study did not have access to reasons why patients were de-listed, it is unlikely to bias results substantially given that neither ADL independence ($P = 0.504$) nor IADL independence ($P = 0.554$) were associated with de-listing. Additionally, the number of centers incorporated limits inferences to those contexts, and may not be generalizable to the entire US ESKD population being evaluated or listed for KT. However, to our knowledge, this is the largest study to date of ADL and IADL independence, listing practices and outcomes on the KT waitlist. This study has several notable strengths, including its large sample size, its prospective study design, as well as its carefully collected measurements of health characteristics and functional status. Additionally, this study leverages a novel population of ESKD patients who were selected to be healthy enough to withstand transplant surgery.

In conclusion, our results suggest that independence in basic self-care ADL was associated with better KT access and lower waitlist mortality, underscoring the importance of maintaining functional independence with basic self-care activities. Despite being more common, independence in basic self-care ADLs has a greater impact on KT waitlist outcomes compared with independence in more complex self-care IADLs. Nephrologists, geriatricians and transplant surgeons should consider screening for and identifying the source of dependence in this basic self-care ADL [19, 33], particularly in eating, dressing and walking, but do not need to screen for the more complex self-care IADL. Geriatric syndromes such as frailty are known risk factors of ADL dependence, and may be identified via comprehensive geriatric assessments [19]. Implementing comprehensive geriatric assessments may help reduce the burden and severity of functional dependence by identifying its etiologies and targeting treatment strategies accordingly [19]. Additionally, novel interventions, such as encouraging the use of patient navigators for referrals to prehabilitation to target the identified underlying etiologies of ADL dependence, can then be explored to promote ADL independence and improve KT waitlist outcomes.

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AUTHORS' CONTRIBUTIONS

N.M.C. participated in data analysis, interpretation, drafting, critical revision and approval of the article. S.S. participated in

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CONFLICT OF INTEREST STATEMENT

None declared.

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