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Older Age is Associated With Lower Utilization of Living Donor Kidney Transplant

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Introduction: Older adults (65 years or older) constitute a substantial and increasing proportion of patients with kidney failure, potentially needing kidney replacement therapy. Living donor kidney transplant (LDKT) offers superior outcomes for suitable patients of all ages. However, exploring LDKT and finding a living donor could be challenging for older adults. Here, we assessed the association between age and utilization of LDKT and assessed effect modification of key variables such as ethnicity and language.

Methods: This is a retrospective cohort study of patients with kidney failure referred for kidney transplant (KT) assessment in Toronto between January 2006 and December 2013. The association between age and having a potential living donor identified was assessed using logistic regression and the association between age and the receipt of LDKT was assessed using Cox proportional hazards models.

Results: Of the 1617 participants, 50% were middle-aged (45–64 years old), and 17% were ≥65 years old. In our final multivariable adjusted models, compared to young adults, middle-aged and older adults had lower odds of having a potential living donor identified (odds ratio [OR], 0.47; confidence interval [CI], [0.35–0.63]; OR, 0.30; CI, [0.20–0.43]; $P < 0.001$, for middle-aged and older adults, respectively), and were less likely to receive LDKT (hazard ratio [HR], 0.79; CI, [0.63–0.99]; $P = 0.04$; HR, 0.47; CI, [0.30–0.72]; $P = 0.001$, for middle-aged and older adults, respectively.)

Conclusion: Age is an independent predictor of receiving LDKT. Considering that nearly 90% of patients with kidney failure in Canada are >45 years of age, these results point to important and potentially modifiable age-related barriers to LDKT.

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Older adults constitute a rapidly increasing proportion of patients with kidney failure, potentially needing kidney replacement therapy (KT or dialysis).[1,2] In Canada, more than 50% of the patients who started kidney replacement therapy in 2019 were aged 65 years and older.[3] Older adults are also increasingly waitlisted for KT.[4]

LDKT is associated with fewer perioperative complications, shorter waiting time, and better graft and patient survival, compared to deceased donor kidney transplantation (DDKT), even for older adults.[5–11] Among older KT recipients, the outcomes of LDKT, even from older living donors, are superior when compared to DDKT.[12] Nevertheless, LDKT remains underutilized among older adults. Previous studies found that older age was associated with lower likelihood of approaching and recruiting living donors,[13–15] and receiving LDKT.[14,16,17]

Social isolation,[18] smaller social networks,[19] and concerns about transplant-related risks to donors[20] may impact older adults' ability and motivation to actively identify a potential donor. Compared to young adults, older adults perceive relatively short life expectancy, which may reduce their motivation to approach potential living donors, who are often younger family members. The spouse or siblings of older patients may be perceived as being too old to donate by the patient or health care professionals. They may also be ineligible because of comorbidities, thus precluding donor candidacy. Furthermore, the public and internalized stigma associated with aging may result in feelings of

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shame and guilt for wanting a KT, further discouraging older adults from even considering this treatment option or accepting a living donor offer.

There may be cultural variations in attitudes and behaviors toward older family members,[21] which could potentially influence the likelihood of an older individual finding a potential donor candidate. Additionally, cultural values and beliefs, traditional health perceptions and religious concerns may influence attitudes of older adults toward identifying and approaching potential living donors.[22] For similar reasons, adults from various ethnic backgrounds may be more hesitant to consider donating their kidney, thus limiting the potential living donor pool for older recipients. For example, older African American individuals are less likely to consider living donation due to concerns regarding the perceived impact of living donation on eventual burial and spiritual considerations.[23]

Patients who are referred to a transplant center are routinely asked if they have a potential living donor identified at the first pretransplant assessment visit. A positive response to this question can serve as a surrogate marker of advanced stages of readiness for LDKT, because it implicitly identifies patients who have contemplated LDKT, considered potential donors, or even engaged in discussions with them.[24-26] In contrast, a negative response suggests the potential presence of barriers (external or self-perceived) to LDKT, which may include age-related medical, cultural, religious, or emotional factors.[27,28]

Although the association between older age and lower likelihood of receiving an LDKT has been reported previously,[14,16,17] to our knowledge, no recent studies have systematically assessed this association in the setting of a publicly-funded, universally accessible health care system and an ethnically diverse population. Therefore, we designed this retrospective cohort study to assess whether older age is associated with reduced utilization of LDKT at a large Canadian transplant center and whether this association is modified by the ethnicity of the recipient.

METHODS

Study Design and Population

This was a single center, retrospective cohort study of 1617 adults (≥18 years) referred for KT assessment to the Toronto General Hospital in Toronto, Canada, conducted between January 1, 2006 and December 31, 2013. Multiorgan transplant candidates, patients with missing psychosocial information, and patients with no information about potential living donor at the time of pretransplant assessment were excluded. The KT program at Toronto General Hospital is the largest in Canada, and 1 of the 3 KT programs serving the Greater Toronto Area, which has a population of approximately 5 million. In Toronto, many patients with estimated glomerular filtration rate <20 or kidney failure fisk equation >10% over 2 years are followed in multicare kidney clinics, where modality education and preparation take place. KT education and workup may be started in these clinics, or in dialysis programs. Once KT workup testing is near complete, the patient is referred to the transplant program; a patient can only be referred or waitlisted at one transplant program at any given time.

The Research Ethics Board of the University Health Network (REB # 15-8863 AE) approved this study and waived the requirement for informed consent. The clinical and research activities reported are consistent with the Principles of the Declaration of Istanbul as outlined in the "Declaration of Istanbul on Organ Trafficking and Transplant Tourism."

Data Sources and Management

Information regarding having a potential living donor was abstracted from clinical notes housed within the Organ Transplant Tracking Record (OTTR) software, which is the electronic medical record system used by the Toronto General Hospital Transplant Program for patients who are referred and/or receiving care at our center since the year 2000. We also recorded the relationship of the potential donor to the recipient. This information was then entered into our research database.

The remaining of our data collection procedures have been described elsewhere.[29] Of note, information about ethnicity, language barrier, employment status, and marital status were abstracted from the pretransplant social work assessment notes, found in OTTR.

The data abstracted for this study was audited and merged with our in-center research database, the Comprehensive Renal Transplant Research Information System (CoReTRIS).[30] CoReTRIS contains recipient, donor, transplant, laboratory, pathology, treatment, and follow-up data for all patients who received a KT at our center since the year 2000. These data elements were abstracted from patient charts (electronic and paper), audited for completeness and quality, and entered into the database.

Exposure and Outcome Variables

The primary exposure of interest was age, categorized as young (<45 years of age), middle-aged (45−64 years of age), and older (≥65 years of age) adults. The coprimary outcomes of interest were as follows: (i) likelihood of having at least 1 potential living donor identified at the time of pretransplant assessment and

(ii) time from transplant referral to receipt of LDKT. We also assessed the time from referral for transplant to receipt of any KT (LDKT or DDKT).

Patient Follow-up and Censoring Events

The dates of referral to the transplant center, receipt of KT (LDKT or DDKT), or death were stored in the CoReTRIS.[30] The time of origin for the time-to-event analyses was the date of referral. Patients were followed until transplantation or the end of study (March 31, 2016). For time to receipt of LDKT analysis, censoring events included being deemed ineligible for transplantation, receipt of DDKT, death, lost to follow-up, or transfer to another center.

Covariates

Demographic and clinical covariates for multivariable analyses were selected based on potential association with exposure and/or outcome variables supported by theoretical considerations, clinical experience, and data from the literature. These covariates included sex, ethnicity, marital status, language barrier (as described by the social worker in the notes), employment status, socioeconomic status, presence of diabetes, presence or history of coronary heart disease or myocardial infarction, history of previous transplant, cause of kidney failure, and blood type. We also included the variable "having a potential living donor identified" in the time to event analyses, where receipt of LDKT or any KT was the outcome.

In order to characterize the socioeconomic status of participants, in addition to individual level self-reported variables, such as employment, we used the Ontario Marginalization Index.[31] The Ontario Marginalization Index is a census-based and geographically-based index of material deprivation. Participants are assigned to a deprivation quintile according to their residential postal code, with quintile 1 representing the least deprived and quintile 5 representing the most deprived group.

Statistical Analysis

Categorical variables were described as frequencies and percentages whereas continuous variables were presented using mean (SD) for normally distributed data and median (interquartile range) for skewed variables. We used parametric and nonparametric tests to identify potential differences in baseline characteristics across the 3 age groups, as appropriate.

To assess the association between age group and having a potential living donor identified, we built multivariable logistic regression models that were successively fitted with expanding sets of covariates. Four models were explored, as follows: (i) unadjusted model; (ii) adjusted for ethnicity, sex, and marital status; (iii) Model 2 plus Ontario Marginalization Index, employment status, and presence of language barrier; and (iv) Model 3 plus blood group, cause of kidney failure, history of diabetes, coronary artery disease or myocardial infarction, and previous transplant.

We graphically assessed the cumulative probabilities of LDKT and any KT using the Kaplan–Meier product limit method and examined differences across survival functions using the log-rank test. We further explored the association between age group and the receipt of LDKT and any KT using Cox proportional hazards models. The multivariable models were successively fitted with expanding sets of covariates. Five models were explored, which were as follows: (i) unadjusted model; (ii) adjusted for having a potential donor identified at the time of pretransplant assessment; (iii) Model 2 plus ethnicity, sex, and marital status; (iv) Model 3 plus Ontario Marginalization Index, employment status, and presence of language barrier; and (v) Model 4 plus blood group, cause of kidney failure, history of diabetes, coronary artery disease or myocardial infarction, and previous transplant.

For the time-to-event analyses, date of referral was considered the time of origin. Patients who were deemed ineligible for transplantation, were lost to follow-up, transferred to another center or died were censored at the time of the event. Patients who were still in the cohort at study end ($n = 355$) were censored at that time. For analyses using LDKT as end point, patients receiving DDKT were censored at the time of the transplant.

The proportional hazards assumptions were tested using scaled Schoenfeld residuals. No important departures from proportionality were detected. Multicollinearity was assessed using a variance-covariance matrix > 0.4 and variance inflation factor > 5.

We also tested the association between age group and receipt of LDKT in predefined subgroups formed by the following variables: sex, ethnicity, diabetes, having a potential living donor identified at pretransplant assessment, and presence of language barrier. Potential interactions were formally tested by including relevant interaction terms to assess effect modification. Because preemptive transplant candidates may represent a group of patients with characteristics that are different from the recipient pool as a whole, we performed a sensitivity analysis in which preemptive candidates ($n = 229$) were excluded. These findings are presented in the Supplementary Materials.

Missingness was <5% for all variables, except for history of coronary artery disease or myocardial infarction variable (11%). We used the method of multiple imputation by chained equations to address missingness.[32] All statistical analyses were performed

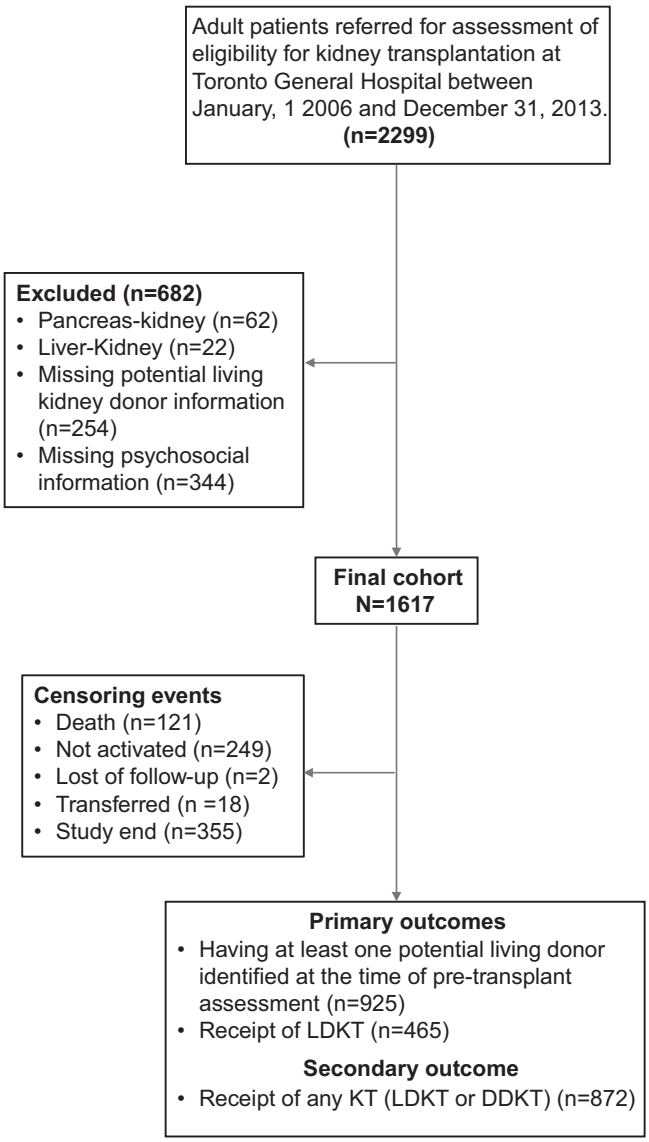

Figure 1. Study flow diagram. DDKT, deceased donor kidney transplant; KT, kidney transplant; LDKT, living donor kidney transplant.

using Stata 15.0 (StataCorp, College Station, TX). A 2-sided P value of <0.05 was considered statistically significant.

RESULTS

Of the 2299 patients referred for assessment of KT eligibility, 1617 patients were included in the final study cohort (Figure 1). Patients who were included in the analysis had similar characteristics (age and sex) to those who were excluded due to missing living donor or psychosocial information. Of the 1617 included patients, 526 (33%) were young (<45 years), 816 (50%) were middle-aged (45−64 years), and 275 (17%) were older adults (≥65 years). The baseline characteristics of the study cohort are shown in Table 1. Diabetes was the most common cause of kidney failure among the middle-aged and older adults, and glomerular disease was the most frequent cause of kidney failure among the young adults.

Of the 1617 patients, 925 (57%) said they had at least 1 potential living donor identified at time of pretransplant assessment. Of these patients, 368 (40%) were young, 443 (48%) were middle-aged, and 114 (12%) were older adults. In addition, 872 (54%) of the sample underwent a KT during the study period. The median follow-up was 2.58 (interquartile range, 1.30−4.29) years. Of the 872 KTs, 465 (53%) were LDKT. The proportion of LDKT was highest among young adults (42%), followed by middle-aged adults (26%), and older adults (10%) ($P < 0.001$). The number of patients with a potential living donor at the time of presentation who eventually received an LDKT differed considerably between the age cohorts as follows: 58% of young patients with a potential living donor eventually received LDKT, compared to 43% and 20% of middle-aged and older recipients, respectively (Table 2).

The most commonly reported relationship to the identified potential living donor were spouse (32%, 299 patients) and sibling (32%, 294 patients). Among older adults, the most commonly reported relationship were children (52%, 59 patients), followed by spouse (34%, 39 patients); whereas the most commonly reported relationship among the middle-aged were spouse (38%, 167 patients) and sibling (30%, 131 patients); and among young adults were sibling (40%, 149 patients) and parent (32%, 118 patients).

Compared to young adults, middle-aged and older adults were less likely to have a potential living donor identified at the time of pretransplant assessment (unadjusted odds ratio [OR], 0.51; confidence interval [CI], [0.40−0.64]; $P < 0.001$; and OR, 0.30; CI, [0.22−0.41]; $P < 0.001$, respectively) (Table 3). Unadjusted OR estimates did not substantially change after covariates were sequentially added to the models. In the fully adjusted model (Model 4), both middle-aged and older adults were less likely to have a potential donor identified at the time of pretransplant assessment, compared to young adults (OR, 0.47; CI, [0.35−0.63]; $P < 0.001$, and OR, 0.30; CI, [0.20−0.43]; $P < 0.001$, respectively).

Compared to young adults (53% [48−59]), both middle-aged (36% [32−41]), and older adults (13% [9−19]) had lower cumulative probability of receiving LDKT during the follow up period ($P < 0.001$; Figure 2). In a univariable Cox proportional hazards model, middle-aged and older adults were significantly less likely to receive an LDKT (hazard ratio [HR], 0.58; CI, [0.48−0.70]; $P < 0.001$; and HR, 0.23; CI, [0.16−0.35]; $P < 0.001$, respectively), compared to young adults. The point estimates did not substantially change when covariates were sequentially added to the

Table 1. Baseline characteristics by age group

Characteristics	Whole cohort (N = 1617)	Young (<45) (n = 526, 33%)	Middle-aged (45–64) (n = 816, 50%)	Older (≥65) (n = 275, 17%)	P value
Age, mean (SD)	51 (14)	34 (8)	55 (5)	69 (3)	< 0.001
Male n (%)	986 (61)	291(55)	508 (62)	187 (68)	0.001
Ethnicity n (%)					
Caucasian	827(53)	259(51)	413(53)	155(59)	0.08
African-Canadian	198(13)	73(14)	90(11)	35(13)	
Asian (East Asian and South Asian)	392(25)	125 (25)	217(28)	50(19)	
Other	135(9)	49(10)	62(8)	24(9)	
Dialysis vintage n (%)					
Preemptive	229 (16)	105 (23)	104 (14)	20 (7)	< 0.001
0–24 mo	954 (65)	265 (59)	500 (67)	189 (70)	
>24 mo	279 (19)	81 (18)	137 (18)	61 (23)	
Cause of kidney failure n (%)					
GN	506 (31)	240 (46)	208 (25)	58 (21)	< 0.001
DM	486 (30)	73 (14)	295 (36)	118 (43)	
PKD	160 (10)	39 (7)	106 (13)	15 (5)	
HTN	163 (10)	35 (7)	83 (10)	45 (16)	
Other/unknown	302 (19)	139 (26)	124 (15)	39 (14)	
Had previous kidney KT (yes) n (%)	131 (8)	57 (11)	68 (8)	6 (2)	< 0.001
Blood group n (%)					
A	535 (33)	187 (35)	264 (32)	84 (31)	0.86
AB	85 (5)	27 (5)	44 (5)	14 (5)	
B	266 (16)	82 (16)	137 (17)	47 (17)	
O	731 (45)	230 (44)	371 (45)	130 (47)	
Marital status n (%)					
Single, never married	328 (20)	240 (46)	78 (10)	10 (4)	< 0.001
Married, domestic partnership or common law	1012 (63)	239 (46)	570 (70)	203 (74)	
Widowed, divorced or separated	272 (17)	44 (8)	166 (20)	62 (22)	
Language barrier (present) n (%)	138 (9)	23 (4)	85 (10)	30 (11)	< 0.001
Employment n (%)					
Unemployed	700 (44)	230 (44)	438 (54)	32 (12)	< 0.001
Employed Other	535 (33) 365 (23)	243 (46) 50 (10)	271 (33) 102 (13)	21 (8) 213 (80)	
Ontario marginalization index n (%)					
1 (least deprived)	297 (19)	103 (21)	157 (20)	37 (14)	0.48
2	338 (22)	102 (20)	180 (23)	56 (21)	
3	343 (22)	105 (21)	173 (22)	65 (25)	
4	279 (18)	91 (18)	139 (17)	49 (18)	
5 (most deprived)	303 (19)	100 (20)	146 (18)	57 (22)	
Comorbidity n (%)					
DM	609 (39)	96 (19)	364 (46)	149 (58)	< 0.001
CAD/MI	396 (28)	38 (8)	237 (33)	121 (47)	< 0.001
CHF	112 (7)	12 (2)	58 (7)	42 (16)	< 0.001
Stroke/TIA	112 (7)	23 (4)	56 (7)	33 (12)	< 0.001
PVD	157 (10)	21 (4)	78 (10)	58 (22)	< 0.001
Chronic lung disease	108 (7)	26 (5)	66 (8)	16 (6)	0.06
Nonskin cancer	124 (8)	20 (4)	65 (8)	39 (15)	< 0.001

CAD, coronary artery disease; CHF, congestive heart failure; DM, diabetes mellitus; GN, glomerulonephritis; HTN, hypertension; KT, kidney transplant; MI, myocardial infarction; PKD, polycystic kidney disease; PVD, peripheral vascular disease; TIA, transient ischemic attack.

Table 2. The number of patients who had a living donor identified, received an LDKT, or any KT

Outcome variable	Whole cohort (N = 1617)	Young (n = 526)	Middle-aged (n = 816)	Older (n = 275)	P value
Had a living donor at pretransplant assessment (yes), n (%)	925 (57)	368 (70)	443 (54)	114 (41)	< 0.001
Number of patients who said they had a living donor at pretransplant assessment and eventually received an LDKT, n (%)	427 (46)	212 (58)	192 (43)	23 (20)	< 0.001
Received KT (yes), n (%)	872 (54)	326 (62)	430 (53)	116 (42)	< 0.001

KT, kidney transplant; LDKT, living donor kidney transplant.

Table 3. Multivariable adjusted odds of having a potential living kidney donor at the time of pretransplant assessment (reference = Young)

Logistic regression model	Middle-aged odds ratio (95% CI)	*P* value	Older odds ratio (95% CI)	*P* value
Model 1[a]	0.51 (0.40, 0.64)	< 0.001	0.30 (0.22, 0.41)	< 0.001
Model 2[b]	0.41 (0.31, 0.53)	< 0.001	0.22 (0.16, 0.31)	< 0.001
Model 3[c]	0.44 (0.33, 0.58)	< 0.001	0.27 (0.19, 0.39)	< 0.001
Model 4[d]	0.47 (0.35, 0.63)	< 0.001	0.30 (0.20, 0.43)	< 0.001

CI, confidence interval; OMI, Ontario Marginalization Index.
[a]Univariable.
[b]Model 1 + ethnicity, sex, and marital status.
[c]Model 2 + OMI, employment status, and presence of language barrier.
[d]Model 3 + blood group, cause of kidney failure, history of: diabetes, coronary artery disease/myocardial infarction, and previous transplant.

model and in the fully adjusted model (Model 5), middle-aged and older adults remained significantly less likely to receive an LDKT (HR, 0.79; CI, [0.63−0.99]; $P = 0.04$; and HR, 0.47; CI, [0.30−0.72]; $P = 0.001$, respectively) (Table 4). In a sensitivity analysis, we found overall similar results after excluding preemptive candidates ($n = 229$) (Supplementary Table S1).

Compared to young adults (73% [68−78]), both middle-aged (65% [61−70]), and older adults (61% [53−69]) had lower cumulative probability of receiving KT during the follow-up period ($P = 0.001$; Figure 3). In a univariable Cox proportional hazards model, middle-aged and older adults were significantly less likely to receive KT (HR, 0.82; CI, [0.71−0.94]; $P = 0.006$ and HR, 0.70; CI, [0.56−0.86]; $P = 0.001$, respectively), compared to young adults. The relationship between age and KT remained significant in Model 2 and Model 3. However, in Model 4 and Model 5 (the fully adjusted model), this association was not significant (Table 5).

Table 4. Multivariable adjusted likelihood of receiving LDKT (Cox proportional hazards model; reference = Young)

Cox proportional hazards model	Middle-aged hazard ratio (95% CI)	*P* value	Older hazard ratio (95% CI)	*P* value
Model 1[a]	0.58 (0.48, 0.70)	< 0.001	0.23 (0.16, 0.35)	< 0.001
Model 2[b]	0.70 (0.58, 0.84)	< 0.001	0.33 (0.22, 0.49)	< 0.001
Model 3[c]	0.64 (0.52, 0.80)	< 0.001	0.29 (0.19, 0.44)	< 0.001
Model 4[d]	0.70 (0.57, 0.87)	0.001	0.39 (0.25, 0.59)	< 0.001
Model 5[e]	0.79 (0.63, 0.99)	0.04	0.47 (0.30, 0.72)	0.001

CI, confidence interval; LDKT, living donor kidney transplant; OMI, Ontario Marginalization Index.
[a]Univariable.
[b]Model 1 + having a potential donor identified.
[c]Model 2 + ethnicity, sex, and marital status.
[d]Model 3 + OMI, employment status, and presence of language barrier.
[e]Model 4 + blood group, cause of kidney failure, and history of: diabetes, coronary artery disease/myocardial infarction, previous transplant.

In subgroup analysis, we explored the association between age groups and the likelihood of receiving LDKT. Using the young adults as the reference group, we assessed interaction terms between age group and various characteristics, including sex, ethnicity, presence of diabetes mellitus, availability of a living donor, and presence of language barrier (Figure 4). None of these interactions were significant (Figure 4).

DISCUSSION

We report here that recipient age is an independent predictor of receipt of LDKT in an ethnically diverse Canadian cohort. When compared to adults aged 44 years or younger, both middle-aged (45−64 years of age) and older adults (≥65 years of age) were less likely to have a potential living donor identified at the time of pretransplant assessment. Importantly, both middle-aged and older adults were also less likely to receive an LDKT. Considering that nearly

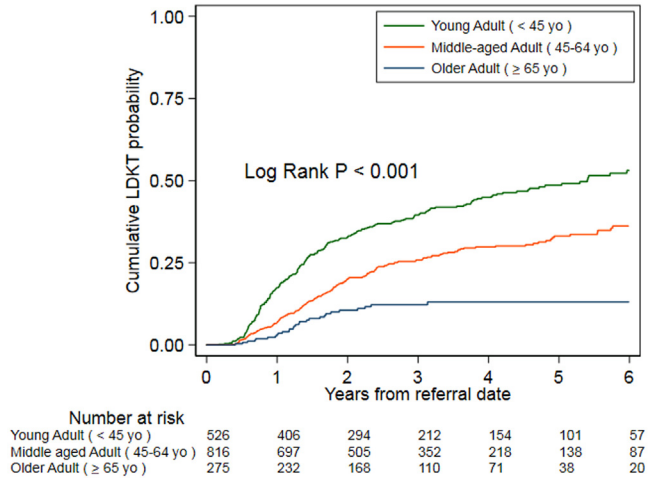

Figure 2. Cumulative probability of receiving LDKT by age group. Censoring events included being deemed ineligible for transplantation, receipt of DDKT, death, lost to follow-up or transfer to another center. DDKT, deceased donor kidney transplant; LDKT, living donor kidney transplant.

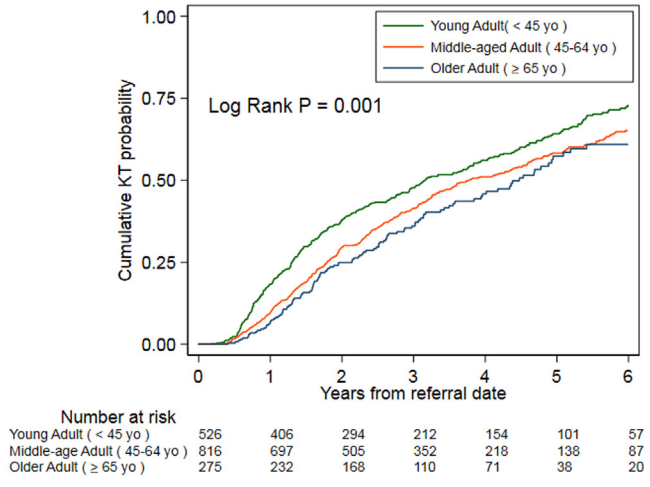

Figure 3. Cumulative probability of receiving KT by age group. Censoring events included being deemed ineligible for transplantation, death, lost to follow-up or transfer to another center. KT, kidney transplant.

Table 5. Multivariable adjusted likelihood of receiving any KT (Cox proportional hazards model; reference = Young)

Cox proportional hazards model	Middle-aged hazard ratio (95% CI)	*P* value	Older hazard ratio (95% CI)	*P* value
Model 1[a]	0.82 (0.71, 0.94)	0.006	0.70 (0.56, 0.86)	0.001
Model 2[b]	0.88 (0.76, 1.01)	0.09	0.80 (0.64, 0.99)	0.04
Model 3[c]	0.84 (0.72, 0.99)	0.03	0.76 (0.58, 0.92)	0.008
Model 4[d]	0.89 (0.75, 1.04)	0.14	0.86 (0.67, 1.09)	0.22
Model 5[e]	0.96 (0.81, 1.13)	0.61	0.96 (0.74, 1.23)	0.74

CI, confidence interval; KT, kidney transplant; OMI, Ontario Marginalization Index.
[a]Univariable.
[b]Model 1 + having a potential donor identified.
[c]Model 2 + ethnicity, sex, and marital status.
[d]Model 3 + OMI, employment status, and presence of language barrier.
[e]Model 4 + blood group, cause of kidney failure, and history of: diabetes, coronary artery disease/myocardial infarction, previous transplant.

90% of those living with kidney failure in Canada are older than 45 years of age,[3] these results represent an important and potentially modifiable gap in the utilization of LDKT among patients with kidney failure.

In our study, both older and middle-aged adults had lower odds of having a potential living donor identified at the time of pretransplant assessment, compared to young adults. Previous studies have shown that individuals who had a potential living donor were subsequently more likely to receive LDKT.[33] Although both middle-aged and older adults were less likely to have a potential living donor identified, the lower likelihood of receiving LDKT was not entirely explained by this, as demonstrated by the multivariable analysis. Moreover, in our study, among older patients with a living donor identified, only 20% went on to eventually receiving an LDKT, in contrast to 43% and 58% of middle-aged and younger patients,

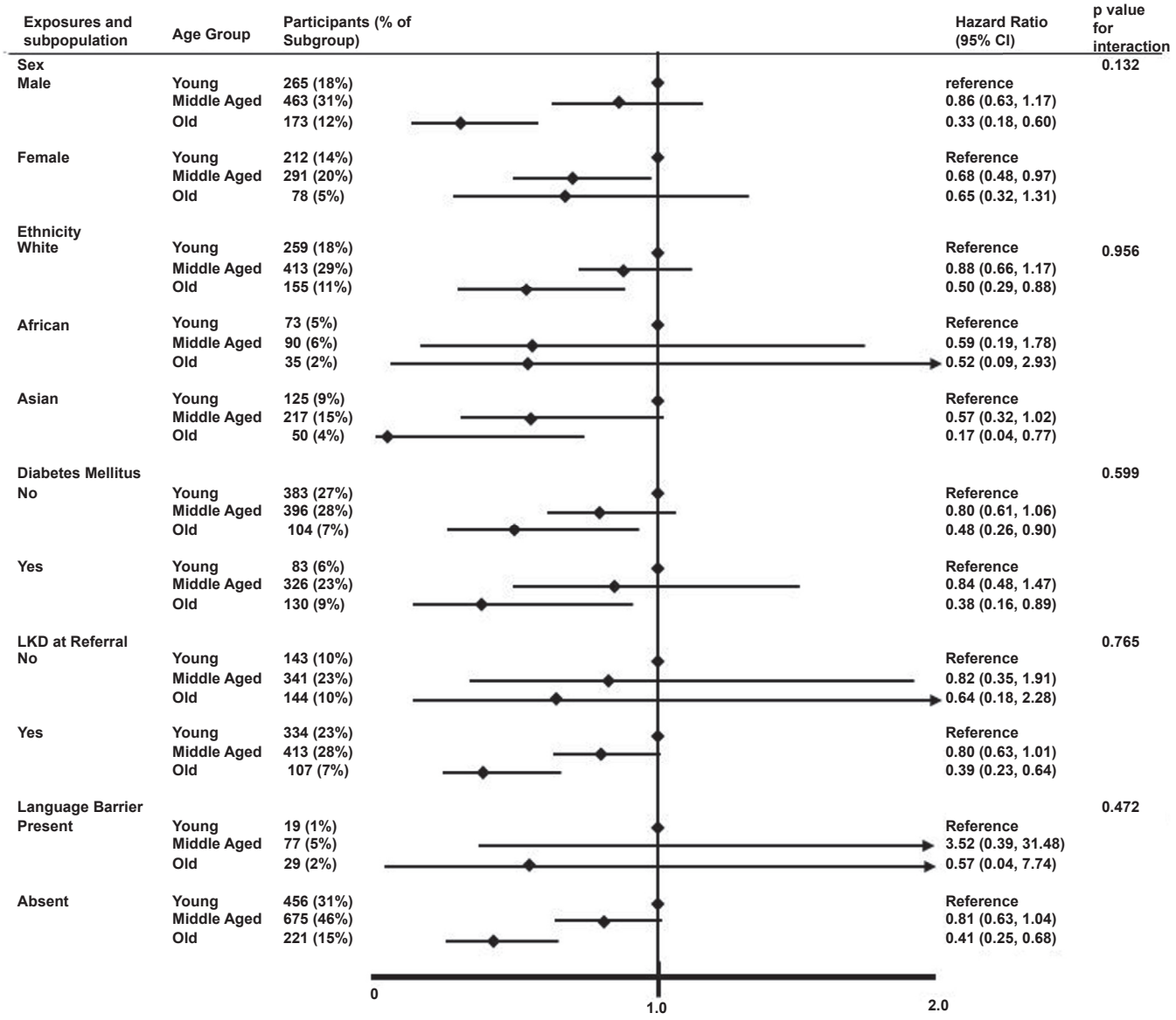

Figure 4. The association between age group and the receipt of LDKT in subgroups of participants. Multivariable adjusted hazard ratios from the fully adjusted models are shown with corresponding confidence intervals. Adjusted for: sex, ethnicity, presence of diabetes, having a living donor identified, and presence of language barrier. CI, confidence interval; LDKT, living donor kidney transplant; LKD, living kidney donor.

respectively. The differences in the proportion of patients with identified donors who eventually received LDKT might have been in part due to the fact that older recipients may have had older donor candidates who were not cleared as donors.

Our findings are consistent with previous reports from the United States[14,17] and the United Kingdom.[16] There may be medical and motivational reasons underlying the lower likelihood of receiving LDKT by older adults. Comorbidities, including chronic lung and heart diseases, cognitive decline, and frailty are more prevalent among older adults.[34-36] These comorbidities may have an impact on self-perceived life expectancy and may limit the motivation to explore LDKT and to ask potential eligible donors, who are often younger and healthier individuals, for a kidney. These comorbidities can also make active search for a living donor difficult. Although communicating the need for a donor through internet and social media may be quite effective, older adults are less likely to use these media.[37,38]

Ageism, both at individual (directed toward self or others) and at structural levels may contribute to the presented disparities. Older adults who hold negative attitudes toward aging (self-directed ageism) are less likely to engage in physical activities[39] and preventive health behaviors.[40] Self-directed ageism can prevent older patients from approaching potential living donors. In addition, people have negative perceptions about those who are older and more disabled than themselves.[41] Therefore, older healthy adults may also be reluctant to offer living donation to older friends with kidney failure.

Structural ageism, "explicit or implicit policies, practices, or procedures of societal institutions that discriminate against older persons," may potentially influence attitudes or actions of health care professionals.[42] A systematic review on ageism and health found that 84.6% of over 400 studies identified age as an important determinant of receiving certain procedures or treatments, making "age dependent access to health services and treatment" the most commonly cited form of structural ageism.[42] A study of 216 nephrologists from the United States reported that age above 65 years was one of the top three reasons for not considering a KT referral.[43] Although age is not a contraindication to KT, physicians may approach patients differently depending on their age. This may result in older patients receiving limited information regarding LDKT.

In general, dialysis is associated with poor quality of life and loss of independence. Older adults on dialysis will not be able to contribute to their family (emotionally and materially) and they will need more support from family members. This can result in a substantial physical and mental burden on the family caregivers.[44] In addition, many older adults want to enjoy the freedom to travel during their retirement years; however, this could be greatly limited because dialysis limits mobility and freedom to travel. KT can lessen older adults' dependence on family members, and enable them to travel, and contribute to supervision of children or grandchildren.

In our study, lower utilization of LDKT was not limited to older adults. Middle-aged adults (45−64 years) were 42% less likely to receive LDKT, as opposed to DDKT, compared to younger adults. Although we defined middle age as 45 years to 64 years, 50% of these patients were below 55 years. This is particularly important because nearly 40% of the individuals who work full time or part time in Canada are between 45 and 65 years of age. Currently, the average wait time to receive KT in Ontario is between 1 and 8 years.[45] Wait time is usually longer for younger patients, meaning that they will have to spend at least 2 to 4 years on dialysis before they could return to work. Patients on dialysis face many challenges to stay employed.[46,47] The ability to work is not only integral for financial security, but also for maintaining one's identity, independence, and mental health.[48,49] Importantly, loss of productivity due to unemployment and/or premature death of individuals with kidney failure also has economic consequences for the society.[48,50]

The finding that LDKT is underutilized among middle-aged and older adults has important societal implications. Dialysis is more expensive than KT. It has been reported that caring for patients on dialysis costs more than twice that for patients with a functioning transplant.[51] If older patients remain on dialysis instead of opting for KT and LDKT, this results in increasing strain on health care systems. If more older patients are waiting for DDKT, the waiting time for both younger and older patients will become longer. Allocating older, more marginal deceased donor kidneys for older adults may address this to some extent; however, the outcomes of those transplants are inferior compared to receiving a KT from live donors.[9]

Preemptive transplant and LDKT might be a more cost-effective treatment compared to DDKT,[52] even for this age group,[53,54] because long waiting times can significantly diminish the clinical and economic benefits of transplantation. An LDKT, even from older donors, offers better outcomes for older recipients compared to DDKT,[12] because it eliminates waiting time and allows time to plan surgery. Moreover, because the surgical mortality and longterm survival for older live donors are not significantly different than for the age-matched non-donor population,[55] LDKT from older donors remains a suitable choice for eligible older recipients. Although the advantages of KT, and LDKT in particular, in older adults are well-

documented, a thorough evaluation of comorbidities, particularly cardiovascular disease, cancer, cognitive impairment, depression, and other factors such as frailty and physical functioning is strongly needed.[56,57]

In this study, we have confirmed and extended previous findings in a large, ethnically diverse Canadian cohort. Previous studies have reported diverse culturally influenced considerations about caring for older family members. African-Americans[58,59] reported stronger feelings of responsibility to provide care for older family members compared to White Americans. In a meta-analysis of more than 100 studies, minority caregivers had stronger "filial obligation" beliefs and provided more hours of care to their older adults, compared to White caregivers.[21] In our study, the association between age and LDKT was not moderated by ethnicity. Further qualitative research is needed to understand if attitudes to LDKT differ between ethnocultural groups.

The strengths of this study include a relatively large and ethnically diverse sample size, long follow-up, and availability of detailed clinical and sociodemographic information. However, we do recognize that our study has several limitations. First, this study is a single center study, which could limit the generalizability of the findings. Second, compared to the number of young adults and middle-aged adults, the number of older adults was relatively small. Third, although we adjusted for a number of key clinical variables, we were not able to account for frailty, which is also associated with poor KT outcomes.[60] Fourth, we did not systematically assess health literacy or transplant knowledge, which may vary significantly with age. Fifth, lower rates of LDKT among older adults might be, in part, related to incompatibility due to sensitization, which could potentially be alleviated through paired exchange programs. However, we did not have data to assess this point. This can be investigated in future studies. Finally, we did not have data to assess potential underlying reasons for the observed disparities, which would require qualitative research methods. Although we speculate that education focused on outlining the benefits of LDKT, the negative impact of spending years on dialysis while waiting for a DDKT, clarifying the suitability of older donors and the safety of live kidney donation may improve LDKT rates both for older and middle-aged patients with kidney failure, we did not have data to confirm this hypothesis.

Although age itself is not modifiable, some of the contributing factors to the observed age-related disparities in accessing LDKT might be modifiable and could be investigated through qualitative research. There are several potential strategies to promote LDKT among older patients. Creating easily accessible, age-specific, educational materials to inform both patients and the general public (potential donor candidates) about the benefits and safety of LDKT for older patients might encourage potential donor candidates to come forward and also motivate recipient candidates to accept those potential offers. Social isolation may also contribute to our findings. A recent systematic review on social isolation[61] showed that group interventions may improve mental and physical health, alleviate social isolation, and result in increased social activation among older adults. Such interventions may also help patients with kidney failure to find potential donors by fostering meaningful relationships. The reluctance of older individuals to accept a kidney from their children may also be amenable to culturally appropriate educational interventions, because the well-being of parents and older adults are key concepts among many cultures. Communicating through patient stories, and connecting older recipient and donor candidates to volunteers with lived experience (either as kidney recipients or donors) could further improve awareness and acceptability of LDKT for older recipients. Furthermore, strategies to promote LDKT among the nephrology community should be considered. Informing community nephrologists, family physicians, nurses, and allied health professionals in dialysis centers and in outpatient clinics about the safety of KT and living donation for older patients could help reduce these age-related disparities. Finally, accepting older live donors, even with minor comorbidities (e.g., mild, well-controlled hypertension) could increase the potential pool for older recipient candidates.

In this Canadian cohort, older age independently predicted a lower likelihood of receiving LDKT. Compared to young adults, both middle-aged and older adults were less likely to have a potential living donor identified at the time of pretransplant assessment, and were less likely to receive an LDKT. Although age itself is not modifiable, some of the factors behind these disparities may be modifiable. Qualitative research is needed to help better understand these factors and to design appropriate educational interventions to potentially mitigate these disparities.

DISCLOSURE

All the authors declared no competing interests.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request, conditional on IRB approval.

AUTHOR CONTRIBUTIONS

Conception and study design: AR and IM; Data acquisition: AB, OE, OF, SB, and NE; Data analysis/interpretation: AR, AB, OE, OF, SB, NE, SJK, and IM; Manuscript drafting: AR; All authors edited and finalized the manuscript; Supervision or mentorship: IM and SJK. Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual's own contributions and to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated and resolved, including with documentation in the literature if appropriate.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Multivariable adjusted likelihood of receiving LDKT (Cox proportional hazards model; reference = Young) after excluding preemptive candidates ($n = 229$).

STROBE Statement.

REFERENCES

1. Mallappallil M, Friedman EA, Delano BG, McFarlane SI, Salifu MO. Chronic kidney disease in the elderly: evaluation and management. *Clin Pract (Lond)*. 2014;11:525–535. https://doi.org/10.2217/cpr.14.46
2. Stevens LA, Viswanathan G, Weiner DE. Chronic kidney disease and end-stage renal disease in the elderly population: current prevalence, future projections, and clinical significance. *Adv Chronic Kidney Dis*. 2010;17:293–301. https://doi.org/10.1053/j.ackd.2010.03.010
3. Canadian Institute for Health Information. Treatment of End-Stage Organ Failure in Canada, Canadian Organ Replacement Register, 2011 to 2020: End-Stage Kidney Disease and Kidney Transplants — *Data Tables*. Ottawa, ON: CIHI; 2021.
4. Laging M, Kal-van Gestel JA, Weimar W, Roodnat JI. Living donor kidney transplantation should be promoted among "elderly" patients. *Transplant Direct*. 2019;5:e496. https://doi.org/10.1097/TXD.0000000000000940
5. Okumi M, Unagami K, Kakuta Y, et al. Elderly living donor kidney transplantation allows worthwhile outcomes: the Japan Academic Consortium of Kidney Transplantation study. *Int J Urol*. 2017;24:833–840. https://doi.org/10.1111/iju.13443
6. Cooper M, Forland CL. The elderly as recipients of living donor kidneys, how old is too old? *Curr Opin Organ Transplant*. 2011;16:250–255. https://doi.org/10.1097/MOT.0b013e328344bfd6
7. Macrae J, Friedman AL, Friedman EA, Eggers P. Live and deceased donor kidney transplantation in patients aged 75 years and older in the United States. *Int Urol Nephrol*. 2005;37:641–648. https://doi.org/10.1007/s11255-004-0010-6
8. Cecka M. Clinical outcome of renal transplantation. Factors influencing patient and graft survival. *Surg Clin North Am*. 1998;78:133–148. https://doi.org/10.1016/s0039-6109(05)70639-3
9. Gill J, Bunnapradist S, Danovitch GM, Gjertson D, Gill JS, Cecka M. Outcomes of kidney transplantation from older living donors to older recipients. *Am J Kidney Dis*. 2008;52:541–552. https://doi.org/10.1053/j.ajkd.2008.05.017
10. Molnar MZ, Streja E, Kovesdy CP, et al. Age and the associations of living donor and expanded criteria donor kidneys with kidney transplant outcomes. *Am J Kidney Dis*. 2012;59:841–848. https://doi.org/10.1053/j.ajkd.2011.12.014
11. Sener A, Schweitzer EJ, Munivenkatappa R, et al. Deceased-donor renal transplantation in the geriatric population demonstrates equal graft survival compared with younger recipients. *Transplantation*. 2009;87:1549–1554. https://doi.org/10.1097/TP.0b013e3181a4b67d
12. Knoll GA. Kidney transplantation in the older adult. *Am J Kidney Dis*. 2013;61:790–797. https://doi.org/10.1053/j.ajkd.2012.08.049
13. Reese PP, Shea JA, Berns JS, et al. Recruitment of live donors by candidates for kidney transplantation. *Clin J Am Soc Nephrol*. 2008;3:1152–1159. https://doi.org/10.2215/CJN.03660807
14. Weng FL, Reese PP, Mulgaonkar S, Patel AM. Barriers to living donor kidney transplantation among black or older transplant candidates. *Clin J Am Soc Nephrol*. 2010;5:2338–2347. https://doi.org/10.2215/CJN.03040410
15. Reese PP, Shea JA, Bloom RD, et al. Predictors of having a potential live donor: a prospective cohort study of kidney transplant candidates. *Am J Transplant*. 2009;9:2792–2799. https://doi.org/10.1111/j.1600-6143.2009.02848.x
16. Wu DA, Robb ML, Watson CJE, et al. Barriers to living donor kidney transplantation in the United Kingdom: a national observational study. *Nephrol Dial Transplant*. 2017;32:890–900. https://doi.org/10.1093/ndt/gfx036
17. Gore JL, Danovitch GM, Litwin MS, et al. Disparities in the utilization of live donor renal transplantation. *Am J Transplant*. 2009;9:1124–1133. https://doi.org/10.1111/j.1600-6143.2009.02620.x
18. Fassett RG. Current and emerging treatment options for the elderly patient with chronic kidney disease. *Clin Interv Aging*. 2014;9:191–199. https://doi.org/10.2147/CIA.S39763
19. Bruine de Bruin W, Parker AM, Strough J. Age differences in reported social networks and well-being. *Psychol Aging*. 2020;35:159–168. https://doi.org/10.1037/pag0000415
20. Hanson CS, Chadban SJ, Chapman JR, et al. The expectations and attitudes of patients with chronic kidney disease toward living kidney donor transplantation: a thematic synthesis of qualitative studies. *Transplantation*. 2015;99:540–554. https://doi.org/10.1097/TP.0000000000000433
21. Pinquart M, Sorensen S. Ethnic differences in stressors, resources, and psychological outcomes of family caregiving: a meta-analysis. *Gerontologist*. 2005;45:90–106. https://doi.org/10.1093/geront/45.1.90
22. Purnell TS, Hall YN, Boulware LE. Understanding and overcoming barriers to living kidney donation among racial and ethnic minorities in the United States. *Adv Chronic Kidney*

Dis. 2012;19:244–251. https://doi.org/10.1053/j.ackd.2012.01.008

23. Purnell TS, Powe NR, Troll MU, et al. Measuring and explaining racial and ethnic differences in willingness to donate live kidneys in the United States. *Clin Transplant*. 2013;27:673–683;
24. Waterman AD, Robbins ML, Paiva AL, et al. Measuring kidney patients' motivation to pursue living donor kidney transplant: development of stage of change, decisional balance and self-efficacy measures. *J Health Psychol*. 2015;20:210–221. https://doi.org/10.1177/1359105313501707
25. Prochaska JO. Decision making in the transtheoretical model of behavior change. *Med Decis Mak*. 2008;28:845–849. https://doi.org/10.1177/0272989X08327068
26. Waterman AD, Robbins ML, Peipert JD. Educating prospective kidney transplant recipients and living donors about living donation: practical and theoretical recommendations for increasing living donation rates. *Curr Transplant Rep*. 2016;3:1–9. https://doi.org/10.1007/s40472-016-0090-0
27. Vamos EP, Novak M, Mucsi I. Non-medical factors influencing access to renal transplantation. *Int Urol Nephrol*. 2009;41:607–616. https://doi.org/10.1007/s11255-009-9553-x
28. Vamos EP, Csepanyi G, Zambo M, et al. Sociodemographic factors and patient perceptions are associated with attitudes to kidney transplantation among haemodialysis patients. *Nephrol Dial Transplant*. 2009;24:653–660. https://doi.org/10.1093/ndt/gfn660
29. Mucsi I, Bansal A, Jeannette M, et al. Mental health and behavioral barriers in access to kidney transplantation: a Canadian cohort study. *Transplantation*. 2017;101:1182–1190. https://doi.org/10.1097/TP.0000000000001362
30. Famure O, Phan NA, Kim SJ. Health information management for research and quality assurance: the comprehensive renal transplant research information system. *Healthc Manag Forum*. 2014;27:30–36. https://doi.org/10.1016/j.hcmf.2013.11.002
31. Matheson FI, Dunn JR, Smith KL, Moineddin R, Glazier RH. Development of the Canadian Marginalization Index: a new tool for the study of inequality. *Can J Public Health*. 2012;103(8 suppl 2):S12–S16. https://doi.org/10.1007/BF03403823
32. White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med*. 2011;30:377–399. https://doi.org/10.1002/sim.4067
33. Vedadi A, Bansal A, Yung P, et al. Ethnic background is associated with no live kidney donor identified at the time of first transplant assessment-an opportunity missed? A single-center retrospective cohort study. *Transpl Int*. 2019;32:1030–1043. https://doi.org/10.1111/tri.13476
34. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet*. 2013;381:752–762. https://doi.org/10.1016/S0140-6736(12)62167-9
35. Greco A, Paroni G, Seripa D, Addante F, Dagostino MP, Aucella F. Frailty, disability and physical exercise in the aging process and in chronic kidney disease. *Kidney Blood Press Res*. 2014;39:164–168. https://doi.org/10.1159/000355792
36. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56:M146–M156. https://doi.org/10.1093/gerona/56.3.m146
37. Kazley AS, Hamidi B, Balliet W, Baliga P. Social media use among living kidney donors and recipients: survey on current practice and potential. *J Med Internet Res*. 2016;18:e328. https://doi.org/10.2196/jmir.6176
38. Ali-Hassan H, Sekharan V, Kim T. Internet non-use among the Canadian older adult population: General Social Survey (GSS). *J Community Inform*. 2019;15:61–77. https://doi.org/10.15353/joci.v15i.3428
39. Wurm S, Tomasik MJ, Tesch-Romer C. On the importance of a positive view on ageing for physical exercise among middle-aged and older adults: cross-sectional and longitudinal findings. *Psychol Health*. 2010;25:25–42. https://doi.org/10.1080/08870440802311314
40. Levy BR, Myers LM. Preventive health behaviors influenced by self-perceptions of aging. *Prev Med*. 2004;39:625–629. https://doi.org/10.1016/j.ypmed.2004.02.029
41. Ayalon L, Tesch-Romer C. Taking a closer look at ageism: self- and other-directed ageist attitudes and discrimination. *Eur J Ageing*. 2017;14:1–4. https://doi.org/10.1007/s10433-016-0409-9
42. Chang ES, Kannoth S, Levy S, Wang SY, Lee JE, Levy BR. Global reach of ageism on older persons' health: a systematic review. *PLoS One*. 2020;15:e0220857. https://doi.org/10.1371/journal.pone.0220857
43. Bartolomeo K, Tandon Gandhir A, Lipinski M, Romeu J, Ghahramani N. Factors considered by nephrologists in excluding patients from kidney transplant referral. *Int J Organ Transplant Med*. 2019;10:101–107.
44. Belasco A, Barbosa D, Bettencourt AR, Diccini S, Sesso R. Quality of life of family caregivers of elderly patients on hemodialysis and peritoneal dialysis. *Am J Kidney Dis*. 2006;48:955–963. https://doi.org/10.1053/j.ajkd.2006.08.017
45. Trillium Gift of Life Network. Factors Impacting Wait Times for a Deceased Donor Kidney Transplant Toronto, Ontario: Ontario Health (Trillium Gift of Life Network). Accessed November 27, 2022. https://www.giftoflife.on.ca/resources/pdf/transplant/4_Estimating_Kidney_Transplant_Wait_Times.pdf
46. Hallab A, Wish JB. Employment among patients on dialysis: an unfulfilled promise. *Clin J Am Soc Nephrol*. 2018;13:203–204. https://doi.org/10.2215/CJN.13491217
47. Erickson KF, Zhao B, Ho V, Winkelmayer WC. Employment among patients starting dialysis in the United States. *Clin J Am Soc Nephrol*. 2018;13:265–273. https://doi.org/10.2215/CJN.06470617
48. Himmelfarb J, Vanholder R, Mehrotra R, Tonelli M. The current and future landscape of dialysis. *Nat Rev Nephrol*. 2020;16:573–585. https://doi.org/10.1038/s41581-020-0315-4
49. Rajkumar R, Baumgart A, Martin A, et al. Perspectives on ability to work from patients' receiving dialysis and caregivers: analysis of data from the global SONG initiative. *J Nephrol*. 2021;35:255–266. https://doi.org/10.1007/s40620-021-01105-y
50. Wang V, Vilme H, Maciejewski ML, Boulware LE. The economic burden of chronic kidney disease and end-stage renal disease. *Semin Nephrol*. 2016;36:319–330. https://doi.org/10.1016/j.semnephrol.2016.05.008

51. Zelmer JL. The economic burden of end-stage renal disease in Canada. *Kidney Int*. 2007;72:1122–1129. https://doi.org/10.1038/sj.ki.5002459

52. Smith CR, Woodward RS, Cohen DS, et al. Cadaveric versus living donor kidney transplantation: a medicare payment analysis. *Transplantation*. 2000;69:311–314. https://doi.org/10.1097/00007890-200001270-00020

53. Fu R, Sekercioglu N, Berta W, Coyte PC. Cost-effectiveness of deceased-donor renal transplant versus dialysis to treat end-stage renal disease: a systematic review. *Transplant Direct*. 2020;6:e522. https://doi.org/10.1097/TXD.0000000000000974

54. Jassal SV, Krahn MD, Naglie G, et al. Kidney transplantation in the elderly: a decision analysis. *J Am Soc Nephrol*. 2003;14:187–196. https://doi.org/10.1097/01.asn.0000042166.70351.57

55. Segev DL, Muzaale AD, Caffo BS, et al. Perioperative mortality and long-term survival following live kidney donation. *JAMA*. 2010;303:959–966. https://doi.org/10.1001/jama.2010.237

56. Segall L, Nistor I, Pascual J, et al. Criteria for and appropriateness of renal transplantation in elderly patients with end-stage renal disease: a literature review and position statement on behalf of the European renal association-European Dialysis and Transplant Association descartes working group and European renal best practice. *Transplantation*. 2016;100:e55–e65. https://doi.org/10.1097/TP.0000000000001367

57. Basu A. Role of physical performance assessments and need for a standardized protocol for selection of older kidney transplant candidates. *Kidney Int Rep*. 2019;4:1666–1676. https://doi.org/10.1016/j.ekir.2019.09.014

58. Dilworth-Anderson P, Brummett BH, Goodwin P, et al. Effect of race on cultural justifications for caregiving. *J Gerontol B Psychol Sci Soc Sci*. 2005;60:S257–S262. https://doi.org/10.1093/geronb/60.5.s257

59. Fabius CD, Wolff JL, Kasper JD. Race differences in characteristics and experiences of black and white caregivers of older Americans. *Gerontologist*. 2020;60:1244–1253. https://doi.org/10.1093/geront/gnaa042

60. Chowdhury R, Peel NM, Krosch M, Hubbard RE. Frailty and chronic kidney disease: a systematic review. *Arch Gerontol Geriatr*. 2017;68:135–142. https://doi.org/10.1016/j.archger.2016.10.007

61. Manjunath J, Manoj N, Alchalabi T. Interventions against social isolation of older adults: a systematic review of existing literature and interventions. *Geriatrics (Basel)*. 2021;6:82. https://doi.org/10.3390/geriatrics6030082