

Frailty and Postkidney Transplant Health-Related Quality of Life

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Background. Health-related quality of life (HRQOL) reflects a patient's disease burden, treatment effectiveness, and health status and is summarized by physical, mental, and kidney disease-specific scales among end-stage renal disease patients. Although on average HRQOL improves postkidney transplant (KT), the degree of change depends on the ability of the patient to withstand the stressor of dialysis versus the ability to tolerate the intense physiologic changes of KT. Frail KT recipients may be extra vulnerable to either of these stressors, thus affecting change in HRQOL after KT. **Methods.** We ascertained frailty, as well as physical, mental, and kidney disease-specific HRQOL in a multicenter prospective cohort of 443 KT recipients (May 2014 to May 2017) using Kidney Disease Quality of Life Instrument Short Form. We quantified the short-term (3 months) rate of KT HRQOL change by frailty status using adjusted mixed-effects linear regression models. **Results.** Mean HRQOL scores were 43.3 (SD, 9.6) for physical, 52.8 (SD, 8.9) for mental, and 72.6 (SD, 12.8) for kidney disease-specific HRQOL; frail recipients had worse physical (0.001) and kidney disease-specific HRQOL ($P = 0.001$), but similar mental HRQOL ($P = 0.43$). Frail recipients experienced significantly greater rates of improvement in physical HRQOL (3.35 points/month; 95% confidence interval [CI], 0.65-2.05; nonfrail, 0.34 points/month; 95% CI, -0.17-0.85; $P = 0.02$) and kidney disease-specific HRQOL (frail, 3.75 points/month; 95% CI, 2.89-4.60; nonfrail, 2.41 points/month; 95% CI, 1.78-3.04; $P = 0.01$), but no difference in mental HRQOL (frail, 0.54 points/month; 95% CI, -0.17-1.25; nonfrail, 0.46 points/month; 95% CI, -0.06-0.98; $P = 0.85$) post-KT. **Conclusions.** Despite decreased physiologic reserve, frail recipients experience improvement in post-KT physical and kidney disease-specific HRQOL better than nonfrail recipients.

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Health-related quality of life (HRQOL) is an important indicator of a patient's disease burden, treatment effectiveness, and health status.^{1,2} Poor HRQOL is associated with increased risks of hospitalizations, graft failure, and mortality in both patients with end-stage renal disease (ESRD) and those undergoing kidney transplantation (KT).^{3–6} On average,

HRQOL improves after KT^{7–9}; improvements in HRQOL are particularly important in the months immediately after KT because short-term dynamic changes in HRQOL are associated with subsequent morbidity and mortality.^{3,6} However,

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the degree of change in HRQOL depends on the ability of the patient to withstand the stressor of dialysis versus the ability to tolerate the intense physiologic changes of KT.¹⁰ These stressors likely have a different impact on physical, mental, and kidney disease-specific HRQOL, the constituent components of HRQOL for ESRD patients. KT may have a greater impact on kidney disease-specific HRQOL by improving symptoms, effects, and burden, but the surgical stressor may have an adverse effect on physical and mental HRQOL by reducing energy and physical functioning in the first few months. The phenotype of patients who will have short-term improvements in physical, mental, and kidney disease-specific HRQOL remains poorly understood.

Frailty, a phenotype of decreased physiologic reserve and vulnerability to stressors,¹¹ has been associated with adverse clinical outcomes among dialysis patients including poor cognitive function, falls, hospitalizations, and mortality.¹²⁻¹⁵ Our previous work demonstrated that frail patients with CKD are more than twice as likely to experience a decline in HRQOL while awaiting KT,¹⁶ resulting in lower HRQOL compared with their nonfrail peers at the time of KT and that frailty is associated with post-KT adverse outcomes including delayed graft function (DGF), longer length of stay, early hospital readmission, immunosuppression intolerance, and mortality.¹⁷⁻²⁰ Candidates who are frail before KT may be extra vulnerable to the stressor of dialysis, but may also be extra vulnerable to the stressors of KT and post-KT immune system regulation. As such, it is unclear whether KT recipients who are frail at the time of KT experience improvements in physical, mental, and kidney disease-specific HRQOL immediately after KT at the same rate as nonfrail recipients.

The goals of this study were to (1) compare the pre-KT physical, mental, and kidney disease-specific HRQOL by frailty status at the time of KT; (2) describe the short-term change in physical, mental, and kidney disease-specific HRQOL in the first 3 months post-KT; (3) quantify the association between pre-KT frailty and the rate of change in physical, mental, and kidney disease-specific HRQOL after KT.

MATERIALS AND METHODS

Study Design

This was a prospective, multicenter longitudinal cohort study of 443 KT recipients at Johns Hopkins Hospital (n = 370), Baltimore, Maryland (May 2014 to May 2017) and the University of Michigan (N = 73), Ann Arbor, Michigan (March 2015 to June 2016). Study participants were enrolled at admission for KT, just before transplantation, and frailty and HRQOL (described below) were ascertained now. Recipient and donor factors (age, sex, race, education level, donor type, DGF, and Kidney Donor Profile Index [KDPI]) were abstracted from the medical chart. A Charlson Comorbidity Index adapted for patients with ESRD was calculated based on self-reported comorbidities at the time of KT.²¹ Subsequent post-KT assessments of HRQOL were conducted during routine postoperative clinical follow-up visits. This study was approved by the Johns Hopkins Institutional Review Board (IRB number: NA_00015758).

Frailty

At admission for KT, frailty was measured as defined and validated by Fried and colleagues^{11,22-31} in older adults and

by our group in ESRD and KT populations.^{12-14,17,30,32-34} The phenotype was based on 5 components: **weight loss** (self-report of unintentional weight loss of more than 10 lbs in the past year based on dry weight), **grip strength** (grip strength below an established cutoff based on gender and BMI), **fatigue** (self-report), **physical activity** (kcal/week below an established cutoff), and **walking speed** (walking time of 15 f. below an established cutoff by gender and height).¹¹ Participants received a score of 0 or 1, representing the absence or presence respectively of each of the 5 components. The aggregate frailty score was calculated as the sum of the component scores (range, 0-5); nonfrail was defined as a score of 0 or 1, intermediate frailty was defined as a score of 2, and frailty was defined as a score of 3 or higher.^{12-14,17-20,32-34} In this study, we empirically combined intermediately frail and frail groups because both groups were associated with a similar change in post-KT HRQOL; we refer to this group as frail throughout the rest of this article.

HRQOL Assessment

We assessed HRQOL using the Kidney Disease Quality of Life instrument short form (KDQOL-SF) version 1.3,^{35,36} which has been validated in KT recipients.³⁷ The KDQOL-SF consists of a generic core [Short Form-36 (SF-36)], as well as kidney disease-specific scales. The SF-36 consists of multi-item scales that address domains of physical and mental health: physical functioning, role limitations due to physical health problems, bodily pain, general health, emotional well-being, role limitations due to emotional health problems, social functioning, and energy. We calculated SF-36 domain scores per published guidelines; converting question items to a 100 scale with higher transformed scores reflecting better HRQOL. These SF-36 domain scores were aggregated into a physical component and a mental component with summary scores standardized to the 1998 US adult population for comparison (ie, mean 50, standard deviation 10).^{35,38} The kidney disease-specific domains included: symptoms of ESRD, effects of ESRD on daily life, burden of ESRD, cognitive function, quality of social interactions, sleep, and social support. We linearly converted kidney disease-specific domain scores to a 0 to 100 scale in a similar manner to that used for the SF-36 domain scores. A kidney disease-specific component summary score was generated as an average of these kidney disease-specific scales as has previously been reported.^{39,40}

Frailty and HRQOL

Univariable linear regression models were used to examine the relationship between frailty and physical, mental, and kidney disease-specific HRQOL at KT. We used paired *t* tests to assess the within-individual changes in HRQOL scores among frail and nonfrail recipients and compared to scores at 1 month and 3 months post-KT. Paired *t* tests were also used to compare HRQOL scores between frail and nonfrail recipients at these follow-up intervals. Multilevel mixed effects linear regression models, with random slopes and intercepts, were used to perform a longitudinal analysis of post-KT HRQOL change among frail and nonfrail recipients. Models also included an interaction term for time of follow-up and frailty status at KT to test whether the rates of change in HRQOL in the frail and nonfrail populations were statistically different. Models were adjusted for pre-KT HRQOL as well as potential predictors of post-KT HRQOL including age, sex,

race, education level, donor type, and the presence of comorbidities measured by the Charlson comorbidity index. Using a similar approach, we estimated the rate of change of physical, mental, and kidney-disease specific HRQOL by donor type, DGF, and KDPI.

Statistical Analyses

Statistical significance was defined as *P* less than 0.05 for all analyses. All analyses were performed using Stata version 14.0 (Stata Corp., College Station, TX).

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RESULTS

Study Population

Among 443 KT recipients, the mean age was 52.0 years (SD, 14.1; range, 19.9-86.0), 37.3% were women, 38.2% were African-American, 38.2% had a high school education or less, 34.8% received a live donor KT, and 37.0% were categorized as frail/intermediate frail. The median follow-up post-KT was 7.7 months. Before KT, 73.27% of participants were undergoing hemodialysis, 58.91% were undergoing peritoneal dialysis, 14.36% were preemptive KT recipients. The median time on dialysis for those undergoing dialysis was 3.26 years (interquartile range, 1.56-5.62).

HRQOL at KT

The mean HRQOL scores at the time of KT was 43.3 points (SD, 9.6) for physical HRQOL, 52.8 points (SD, 8.9) for mental HRQOL, and 72.6 points (SD, 12.8) for kidney disease-specific HRQOL. HRQOL at KT did not differ by age, sex, race, educational status, donor type, or pre-KT dialysis; except for slightly better mental HRQOL scores (55.0 vs 51.7, *P* < 0.001) and kidney disease-specific HRQOL (75.6 vs 72.8, *P* = 0.04) among African Americans (Table 1).

Frailty and HRQOL at the Time of KT

At the time of KT, frail KT recipients had significantly worse scores in physical HRQOL (39.3 vs 45.6, *P* < 0.001) and kidney disease-specific HRQOL (70.2 vs 76.1, *P* < 0.001), but not mental HRQOL (52.4 vs 53.1, *P* = 0.43) (Table 2). After adjusting for recipient and donor factors, frailty was associated with significantly worse physical HRQOL (−6.31 points; 95% confidence interval [CI], −8.16 to −4.46, *P* < 0.001), and worse kidney disease-specific HRQOL (−6.53 points; 95% CI, −9.17 to −3.89, *P* < 0.001) but no difference in mental HRQOL (−1.21 points; 95% CI, −2.96 to 0.54, *P* = 0.18) at the time of KT (Table 3); there were no differences in physical, mental, or kidney disease-specific HRQOL at the time of KT by donor type or KDPI.

At the domain level, frail KT recipients had worse scores in physical functioning, role limitations due to physical health problems, bodily pain, general health, social functioning, energy, symptoms of disease, effects of disease on daily living, burden of disease, cognitive functioning, sleep, and social support after adjusting for recipient and donor factors.

Frailty and Change in HRQOL at 1-Month Post-KT

There were statistically significant declines in physical HRQOL for both frail and nonfrail recipients (frail, −5.25 points, *P* < 0.001; nonfrail, −7.26 points, *P* < 0.001) at 1-month post-KT (Table 2); these declines were greater among those who were frail (*P* for interaction = 0.04) (Figure 1). There was no change in mental HRQOL among frail recipients (1.47 points, *P* = 0.145) and improvement in the nonfrail recipients (1.59 points, *P* = 0.025) although there was no evidence of a difference in the changes in mental HRQOL scores by frailty status (*P* for interaction = 0.95). There was significant improvement in kidney disease-specific HRQOL at 1 month for frail (4.15 points, *P* = 0.001) and

TABLE 1.

Physical, mental, and kidney disease-specific HRQOL at kidney transplantation by recipient and donor factors

	Physical HRQOL, mean (SD)	<i>P</i>	Mental HRQOL, mean (SD)	<i>P</i>	Kidney disease-specific HRQOL, mean (SD)	<i>P</i>
Age, y						
< 65	43.11 (9.68)	0.83	52.45 (8.87)	0.02	73.62 (13.84)	0.49
≥ 65	42.86 (9.67)		54.97 (7.54)		74.76 (12.32)	
Sex						
Male	43.44 (9.43)	0.31	52.89 (8.57)	0.80	73.07 (13.61)	0.13
Female	42.42 (10.06)		53.12 (8.83)		75.18 (13.33)	
Race						
Non-AA	42.79 (9.50)	0.47	51.67 (8.74)	<0.001	72.76 (13.50)	0.04
AA	43.50 (9.94)		54.99 (8.15)		75.55 (13.45)	
Education status						
> High school	43.16 (9.84)	0.80	52.71 (8.73)	0.44	73.85 (13.17)	0.99
≤ High school	42.91 (9.42)		53.40 (8.55)		73.86 (14.13)	
Donor type						
DDKT	43.23 (9.65)	0.62	53.52 (8.47)	0.07	73.90 (13.90)	0.91
LDKT	42.72 (9.74)		51.84 (8.96)		73.75 (14.04)	
Dialysis type						
HD	42.73 (9.89)	0.31	53.47 (9.07)	0.23	73.65 (14.02)	0.69
PD	42.41 (9.18)		53.88 (7.01)		74.24 (11.57)	
Preemptive	44.33 (9.47)		51.91 (8.16)		75.02 (13.22)	

All measures of HRQOL made using the KDQOL-SF.³⁵ Higher scores indicate better HRQOL.
AA, African-American; HD, hemodialysis; PD, peritoneal dialysis.

TABLE 2.**Physical, mental, and kidney disease-specific HRQOL pre- and post-KT by frailty status**

	Pre-KT		Post-KT			
			1-month change		3-month change	
	Nonfrail, mean (SD)	Frail, mean (SD)	Nonfrail, mean (SD)	Frail, mean (SD)	Nonfrail, mean (SD)	Frail, mean (SD)
Physical HRQOL	45.55 (8.66)	39.31 (9.88)	−7.26 (9.29) ^a	−5.25 (10.03) ^a	0.97 (9.48)	4.06 (8.78) ^a
Mental HRQOL	53.06 (8.47)	52.36 (9.60)	1.59 (9.77) ^a	1.47 (9.98)	1.61 (9.20) ^a	1.60 (10.10)
Domains						
Physical functioning	77.02 (20.22)	61.61 (25.59)	−12.46 (22.77) ^a	−11.94 (28.12) ^a	2.35 (19.56)	7.29 (24.19) ^a
Role limitations due to physical health problems	55.88 (38.02)	41.93 (38.41)	−28.66 (45.58) ^a	−22.36 (46.90) ^a	3.28 (48.99)	13.97 (45.31) ^a
Bodily pain	79.90 (23.13)	46.00 (23.11)	−19.57 (30.69) ^a	−14.60 (30.23) ^a	0.19 (26.47)	4.00 (27.60)
General health	56.67 (20.45)	43.60 (23.12)	8.49 (17.71) ^a	11.12 (18.98) ^a	6.98 (19.22) ^a	10.07 (20.11) ^a
Emotional well being	83.21 (14.44)	80.79 (15.74)	2.46 (16.30) ^a	3.29 (16.97)	3.01 (14.45)	3.56 (15.22)
Role limitations due to emotional problems	84.50 (29.50)	79.54 (33.17)	0.00 (37.89)	−3.14 (37.02)	1.30 (39.77)	3.33 (37.71)
Social functioning	82.10 (23.43)	76.83 (24.83)	−15.56 (29.66) ^a	−12.75 (31.27) ^a	2.68 (24.59)	1.43 (29.14)
Energy	55.92 (22.85)	45.37 (25.00)	−2.97 (24.60) ^a	0.72 (28.57)	5.81 (24.58) ^a	11.36 (26.35) ^a
Kidney disease-specific HRQOL	76.05 (12.53)	70.23 (14.41)	3.94 (10.64) ^a	4.15 (11.92) ^a	7.90 (10.87) ^a	11.07 (12.31) ^a
Domains						
Symptoms	83.24 (12.45)	77.83 (14.89)	1.94 (11.62) ^a	3.31 (13.96) ^a	5.74 (11.30) ^a	8.05 (13.28) ^a
Effects	74.88 (17.91)	68.02 (22.57)	7.55 (19.80) ^a	8.26 (21.61) ^a	12.06 (17.59) ^a	18.54 (21.08) ^a
Burden	54.65 (28.41)	45.91 (29.37)	11.76 (26.39) ^a	13.95 (25.70) ^a	19.99 (27.61) ^a	22.31 (30.37) ^a
Cognitive function	86.26 (15.57)	80.77 (19.88)	2.35 (14.57)	2.69 (17.43)	5.10 (14.03) ^a	6.81 (13.68) ^a
Social interaction	83.92 (15.47)	79.83 (16.78)	−2.85 (16.56) ^a	−0.44 (15.41)	0.44 (14.48)	3.29 (18.84)
Sleep	64.58 (20.23)	59.46 (22.80)	1.76 (24.55)	−0.13 (22.38)	6.64 (20.44) ^a	11.34 (21.53) ^a
Social support	84.69 (20.15)	79.71 (22.03)	4.47 (23.17) ^a	0.68 (23.92)	5.29 (22.17) ^a	6.72 (22.10)

^a Statistical significant changes in scores compared with KT.Unadjusted mean HRQOL scores were measured pre-KT and compared to scores at 1 month and 3 months post-KT. All measures of HRQOL were made using the KDQOL-SF.³⁵**TABLE 3.****Association between physical, mental, and kidney disease-specific HRQOL with frailty status at kidney transplantation**

	Frail vs nonfrail	DDKK vs LDKT	High vs Low KDPI
	Points (95% CI)	Points (95% CI)	Points (95% CI)
Physical HRQOL	−6.31 (−8.16 to −4.46)	0.51 (−1.75 to 2.77)	−0.03 (−4.73 to 4.66)
Mental HRQOL	−1.21 (−2.96 to 0.22)	0.08 (−1.90 to 2.07)	0.19 (−3.84 to 4.23)
Domains			
Physical functioning	−14.17 (−18.58 to −9.76)	−2.03 (−7.42 to 3.36)	2.24 (−9.43 to 13.90)
Role limitations due to physical health problems	−15.37 (−22.96 to −7.78)	2.66 (−6.27 to 11.59)	−2.89 (−21.00 to 15.22)
Bodily pain	−9.45 (−14.33 to −4.57)	−2.18 (−7.97 to 3.60)	−1.24 (−13.57 to 11.09)
General health	−11.76 (−15.94 to −7.59)	2.85 (−2.10 to 7.79)	−3.18 (−13.23 to 6.89)
Emotional well being	−3.05 (−6.01 to −0.09)	−1.75 (−5.09 to 1.60)	−1.09 (−8.02 to 5.83)
Role limitations due to emotional problems	−5.28 (−11.46 to 0.90)	−2.31 (−9.39 to 4.77)	−0.96 (−15.82 to 13.90)
Social functioning	−6.19 (−10.98 to −1.41)	3.84 (−1.73 to 9.42)	3.83 (−7.48 to 15.13)
Energy	−11.66 (−16.30 to −7.03)	2.67 (−2.78 to 8.12)	2.49 (−8.86 to 13.85)
Kidney disease-specific HRQOL	−6.53 (−9.17 to −3.89)	−2.08 (−5.06 to 0.90)	1.38 (−5.09 to 7.86)
Domains			
Symptoms	−5.50 (−8.20 to −2.79)	−1.30 (−4.50 to 1.89)	0.22 (−6.43 to 6.87)
Effects	−7.69 (−11.66 to −3.72)	−0.81 (−5.45 to 3.82)	1.51 (−8.39 to 11.41)
Burden	−10.19 (−15.94 to −4.44)	−1.79 (−8.52 to 4.95)	−5.94 (−19.43 to 7.55)
Cognitive function	−5.51 (−9.00 to −2.02)	−1.18 (5.19–2.83)	−1.49 (−9.90 to 6.91)
Social interaction	−4.70 (−7.85 to −1.56)	−3.02 (−6.63 to 0.59)	6.01 (−1.55 to 13.57)
Sleep	−6.29 (−10.56 to −2.02)	1.14 (−3.88 to 6.16)	5.23 (−5.32 to 15.79)
Social support	−5.69 (−9.92 to −1.47)	−2.77 (−7.63 to 2.08)	3.69 (−6.63 to 14.01)

Separate linear models of HRQOL at KT by frailty status adjusted for age, sex, race, educational status, donor type. All measures of HRQOL made using the KDQOL-SF.³⁵ Negative coefficients indicate worse HRQOL for frail KT recipients.

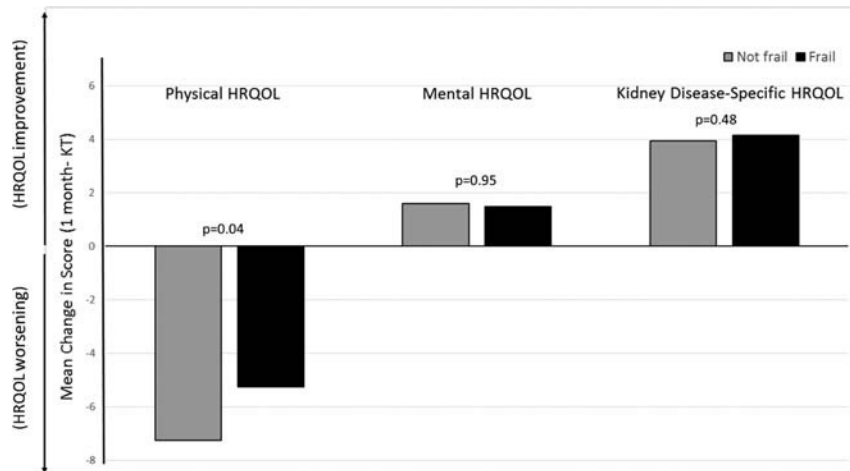


FIGURE 1. Mean change in HRQOL from kidney transplantation to 1 month post-KT by frailty status. Mean 1-month changes in physical, mental, and kidney disease-specific HRQOL were calculated and compared by frailty status at KT. All measures of HRQOL were from the KDQOL-SF.³⁵

nonfrail recipients (3.94 points, $P < 0.001$); these improvements were similar by frailty status (adjusted P for interaction = 0.48).

Frailty and Change in HRQOL at 3 Months Post-KT

There were statistically significant improvements in physical HRQOL among frail (4.06 points, $P < 0.001$) but not nonfrail recipients (0.97 points, $P = 0.21$) at 3 months post-KT (Table 2) and this 3-month improvement was significantly greater among frail recipients (P for interaction = 0.01) (Figure 2). There were significant changes in 3-month mental HRQOL among frail and no change in nonfrail recipients (frail, 1.60 points, $P = 0.03$; nonfrail, 1.61 points, $P = 0.19$; P for interaction = 0.85). There were statistically significant 3-month improvements in kidney disease-specific HRQOL for both frail and nonfrail recipients (frail, 11.07 points, $P < 0.001$; nonfrail, 7.90 points, $P < 0.001$) at 3 months post-KT, and these improvements were greater among those who were frail (P for interaction = 0.02). Among frail KT recipients, those who were younger than 65 years had a greater improvement in physical ($P = 0.02$) and kidney disease-specific HRQOL

($P = 0.04$) (Table 4); live donor kidney transplantation (LDKT) recipients had a greater improvement in physical HRQOL ($P = 0.009$).

Frailty and Rate of Change in Post-KT HRQOL Adjusted for Recipient and Donor Factors

After adjusting for recipient and donor factors, there was a significantly greater rate of improvement over 3 months in post-KT physical HRQOL among frail recipients (frail, 1.35 points/month, 95% CI, 0.65-2.05; nonfrail, 0.34 points/month; 95% CI, -0.17-0.85; P for interaction = 0.02) (Table 5). There were no changes in post-KT mental HRQOL regardless of recipient's frailty status (frail, 0.54 points/month; 95% CI, -0.17-1.25; nonfrail, 0.46 points/month; 95% CI, -0.06-0.98; P for interaction = 0.85). Frail and nonfrail KT recipients reported similar rates of improvement in kidney disease-specific HRQOL (frail, 3.75 points/month; 95% CI, 2.89-4.60; nonfrail, 2.41 points/month; 95% CI, 2.89-4.60; P for interaction = 0.01).

Furthermore, frail recipients reported significantly greater rates of improvement in the constituent domain of general

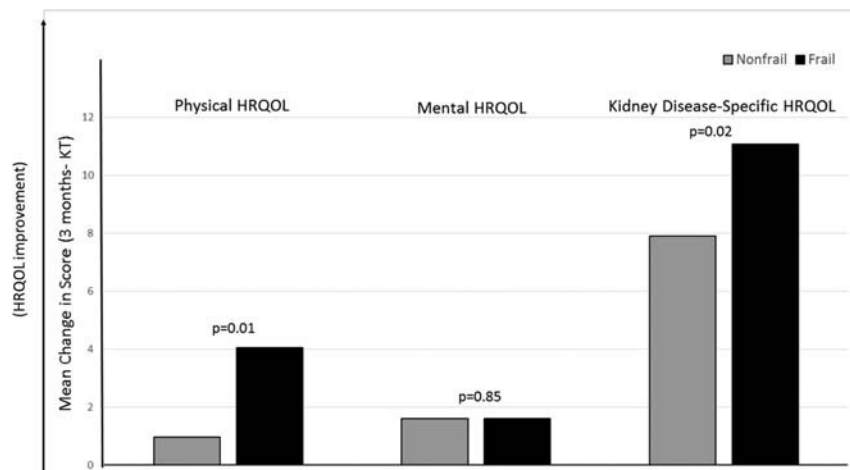


FIGURE 2. Mean change in HRQOL from kidney transplantation to 3 months post-KT by frailty status. Mean 3-month changes in physical, mental, and kidney disease-specific HRQOL were calculated and compared by frailty status at KT. All measures of HRQOL were from the KDQOL-SF.³⁵

TABLE 4.**3-Month change in physical, mental, and kidney disease-specific HRQOL among frail KT recipients by recipient and donor factors**

	Physical HRQOL, mean (SD)	P	Mental HRQOL, mean (SD)	P	Kidney disease-specific HRQOL mean (SD)	P
Age, y						
< 65	5.33 (8.80) ^a	0.02	2.26 (9.82)	0.31	12.55 (9.51) ^a	0.04
≥ 65	−0.50 (7.26)		−0.78 (11.08)		5.17 (14.60)	
Sex						
Male	4.87 (8.10) ^a	0.37	1.95 (9.89)	0.74	12.44 (11.81)	0.27
Female	2.94 (9.68)		1.13 (10.55)		9.13 (12.94)	
Race						
Non-AA	5.36 (8.27) ^a	0.06	2.45 (10.23)	0.29	12.92 (11.42) ^a	0.06
AA	1.09 (9.38)		−0.34 (9.77)		7.04 (13.46) ^a	
Education status						
> High school	5.64 (8.03) ^a	0.07	2.27 (8.85)	0.51	12.58 (11.68) ^a	0.22
≤ High school	1.75 (9.45)		0.62 (11.81)		8.93 (13.05) ^a	
Donor type						
DDKT	1.84 (8.43)	0.009	1.29 (8.27)	0.74	9.61 (12.65) ^a	0.18
LDKT	7.97 (8.14) ^a		2.15 (12.90)		13.71 (11.44) ^a	
Dialysis type						
HD	3.73 (7.94)	0.002	2.90 (11.33)	0.23	10.17 (13.26)	0.47
PD	−4.33 (10.43)		3.51 (5.93)		16.37 (14.24) ^a	
Preemptive	8.58 (6.39) ^a		−1.91 (7.83)		10.43 (9.02) ^a	

^a Statistical significant changes in scores compared to KT. Higher scores indicate greater change HRQOL.All measures of HRQOL made using the KDQOL-SF.³⁵

health (frail, 4.93 points/month; 95% CI, 3.51-6.35; nonfrail, 2.87 points/month; 95% CI, 1.82-3.92; *P* for interaction = 0.02), the effects of ESRD on daily living (frail, 7.10 points/month; 95% CI, 5.68-8.51; nonfrail, 4.01 points/month; 95% CI,

2.99-5.03; *P* for interaction = 0.001), and cognitive function (frail, 2.88 points/month; 95% CI, 1.80-3.96; nonfrail, 1.28 points/month; 95% CI, 0.50-2.07; *P* for interaction = 0.02).

TABLE 5.**Rates of change in posttransplant HRQOL within 3 months by frailty status at kidney transplantation**

		Nonfrail	Frail	Interaction, <i>P</i>
		Points/month (95% CI)	Points/month (95% CI)	
50	Physical HRQOL	0.34 (−0.17 to 0.85)	1.35 (0.65-2.05) ^a	0.02
	Mental HRQOL	0.46 (−0.06 to 0.98)	0.54 (−0.17 to 1.25)	0.85
rick Yihong Wu	Domains			
	Physical functioning	0.72 (−0.46 to 1.89)	2.62 (1.02, 4.22) ^a	0.06
	Role limitations due to physical health problems	−1.33 (−3.84 to 1.17)	1.55 (−1.86, 4.75)	0.18
	Bodily pain	0.92 (−0.56 to 2.39)	1.67 (−0.37, 3.70)	
51	General health	2.87 (1.82-3.92) ^a	4.93 (3.51, 6.35) ^a	0.51
	Emotional well being	0.98 (0.15-1.81) ^a	1.45 (0.32-2.58) ^a	
rick Yihong Wu	Role limitations due to emotional problems	−0.09 (−2.08 to 1.90)	0.49 (−2.22 to 3.21)	0.93
	Social functioning	0.49 (−1.09-2.07)	−0.07 (−2.24 to 2.10)	0.68
	Energy	1.91 (0.57-3.25) ^a	3.98 (2.15-5.81) ^a	
52	Kidney disease-specific HRQOL	2.41 (1.78-3.04) ^a	3.75 (2.89-4.60) ^a	
rick Yihong Wu	Domains			
	Symptoms	2.21 (1.55-2.86) ^a	3.27 (2.38-4.17) ^a	
53-54	Effects	4.01 (2.99-5.03) ^a	7.10 (5.68-8.51) ^a	0.01
2 notes:	Burden	6.38 (4.88-7.88) ^a	7.94 (5.90-9.98) ^a	
	Cognitive function	1.28 (0.50-2.07) ^a	2.88 (1.80-3.96) ^a	
55	Social interaction	−0.57 (−1.47 to 0.33)	1.18 (−0.06 to 2.43)	0.23
	Sleep	2.02 (0.81-3.22) ^a	3.28 (1.62-4.95) ^a	
rick Yihong Wu	Social support	1.73 (0.55-2.91) ^a	2.53 (0.90-4.18) ^a	0.43

^a Statistical significant difference in rates of change of HRQOL.

Separate longitudinal models of change in HRQOL by frailty status adjusted for age, sex, race, educational status, donor type and HRQOL at transplant. Interaction *P* value indicates whether rates of change in frail and nonfrail KT recipients are significantly different. All measures of HRQOL made using the KDQOL-SF.³⁵ Negative rates indicate worsening HRQOL.

TABLE 6.**Rates of change in posttransplant HRQOL within 3 months by transplant factors**

	DDKT	LDKT	Interaction, <i>P</i>
	Points/month (95% CI)	Points/month (95% CI)	
Physical HRQOL	0.18 (−0.25 to 0.62)	1.57 (0.98-2.17) ^a	<0.001
Mental HRQOL	0.38 (−0.11 to 0.87)	0.72 (0.12-1.33) ^a	0.39
Kidney disease-specific HRQOL	2.48 (1.84-3.13) ^a	3.67 (3.03-4.32) ^a	0.01

	DGF	No DGF	Interaction, <i>P</i>
	Points/month (95% CI)	Points/month (95% CI)	
Physical HRQOL	0.28 (−0.39 to 0.96)	0.85 (0.42-1.28) ^a	0.17
Mental HRQOL	−0.13 (−0.78 to 0.52)	0.69 (0.23-1.16) ^a	0.04
Kidney disease-specific HRQOL	2.23 (1.16-3.31) ^a	3.18 (2.64-3.82) ^a	0.12

	High KDPI	Low KDPI	Interaction, <i>P</i>
	Points/month (95% CI)	Points/month (95% CI)	
Physical HRQOL	0.15 (−1.72, 2.02)	0.31 (−0.13 to 0.75)	0.87
Mental HRQOL	−0.69 (−2.29 to 0.92)	0.47 (−0.03 to 0.98)	0.18
Kidney disease-specific HRQOL	0.33 (−1.73 to 2.39)	2.65 (1.96-3.33) ^a	0.04

^a Statistical significant difference in rates of change of HRQOL.Separate longitudinal models of change in HRQOL by transplant factors adjusted for age, sex, race, educational status, donor type and HRQOL at transplant. Interaction *P* value indicates whether rates of change in living vs deceased donor KT recipients (as well as DGF and KDPI) are significantly different. All measures of HRQOL made using the KDQOL-SF.³⁵ Negative rates indicate worsening HRQOL.**Transplant Factors and Rate of Change in Post-KT HRQOL Adjusted for Recipient and Donor Factors**

Among LDKT recipients, there was a significantly greater rate of improvement over 3 months in post-KT physical HRQOL (LDKT, 1.57 points/month; 95% CI, 0.98-2.17; deceased donor kidney transplantation [DDKT], 0.18 points/month; 95% CI, −0.25-0.62; *P* for interaction < 0.001) and kidney disease-specific HRQOL (LDKT, 3.67 points/month; 95% CI, 3.03-4.32; DDKT, 2.48 points/month; 95% CI, 1.84-3.13; *P* for interaction = 0.01) (Table 6).

DISCUSSION

In this longitudinal study of 443 KT recipients, we found that frail KT recipients had worse physical and kidney disease-specific HRQOL before KT, but they had a greater rate of improvement in the first 3 months post-KT compared with their nonfrail counterparts. Importantly, they also had substantial gains in general health (4.93 points per month) and the effects of ESRD on daily living (7.10 points per month) in the first 3 months post-KT. Finally, there were no differences in mental HRQOL at KT or changes in mental HRQOL by frailty status.

Previous studies suggest that KT recipients have better HRQOL and life participation than ESRD patients undergoing dialysis,^{41,42} and that overall HRQOL improves for most recipients after KT.⁴³ However, the impact of KT on mental HRQOL is small.^{8,9} We have extended these findings on physical, mental, and kidney disease-specific HRQOL after KT and found that by 3 months post-KT frail KT recipients have a 4-point increase in physical HRQOL, and a 10-point increase in kidney disease specific HRQOL. These changes

are substantial and meaningful given that a 2- to 3-point difference in SF-36 scores is clinically relevant for patients.^{44,46} Interestingly, the 3-month improvement in HRQOL occurs at the same time that frailty improves, on average, after KT.³²

We also found that the impact of KT on mental HRQOL

was minimal for both frail and nonfrail KT recipients; this is likely the case because the measure of mental HRQOL (MCS) emphasizes how a patient feels and reflect their emotional well-being which may require more than 3 months to improve.

Few studies have identified phenotypes of patients who do and do not experience an HRQOL benefit from KT. Sarcopenia and muscle weakness are associated with worse physical HRQOL after KT.⁴³ Additionally, KT recipients with diabetes were found to have worse post-KT HRQOL.⁴⁷ We have previously demonstrated that frail KT recipients are at high risk of adverse KT outcomes including DGF, longer length of stay, early hospital readmission, immunosuppression intolerance, and mortality.^{17-20,34} This work extends these previous findings on frailty among KT recipients to include a patient-centered outcome and demonstrates that frail recipients benefit from KT with respect to physical HRQOL. It is possible that although frail KT recipients experience the greatest decline in HRQOL while undergoing the stressor of dialysis¹⁶ particularly those undergoing hemodialysis,⁴⁸ the restoration of kidney function through KT greatly improves their HRQOL even if they experience proximal adverse outcomes like early hospital readmission or DGF.⁴⁹⁻⁵¹

This study has several strengths and limitations. Although HRQOL is often critiqued because it is a subjective measure of the impact of a disease or treatment, this is a strength of our study because we captured the overall patient-centered impact of ESRD on physical, mental, and kidney-disease specific HRQOL. We could measure changes in HRQOL after KT while accounting for pre-KT HRQOL which has not been previously characterized in frail adults; the longitudinal nature of our study is a clear strength. Additionally, we have ascertained a prospective measurement of a validated, objective frailty instrument to capture decreased physiologic reserve.¹¹ One of the main limitations of the study is that we have only a single validated instrument to measure HRQOL; however, the KDQOL is the most commonly used measure of

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2 note

HRQOL in this population and one of the only instruments that is specific to ESRD patients. Additionally, this study focused on HRQOL immediately after KT because this is a critical time of recovery and did not have long-term measures of HRQOL. However, this is a particularly important postoperative period with dynamic changes in HRQOL which are associated with subsequent morbidity and mortality.^{3,6} Finally, we did not collect information on formal physical rehabilitation after KT discharge.

In this study of KT recipients of all ages, recipients who were frail before KT experienced a greater change in physical HRQOL and kidney-disease specific HRQOL than their nonfrail counterparts even though frail KT recipients had worse HRQOL before KT. Frail recipients who undergo KT experience better improvement in physical and kidney disease-specific HRQOL despite their increased vulnerability to stressors and impaired HRQOL pre-KT. Our findings highlight that even a high risk group like frail KT recipients experience the benefit of improved HRQOL with KT. These findings have important implications for KT candidates, especially those who are frail and unable to tolerate the stressor of dialysis; KT may improve physical and kidney-disease specific HRQOL.

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Frailty and Postkidney Transplant Health-Related Quality of Life

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	The icHD (in-center hemodialysis) and PD (peritoneal dialysis) patients benefited the most from KT (kidney transplant) and HHD (home hemodialysis) the least.	
	Low pill burden and employment were linked to a better HRQoL.	
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