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FRAILITY AND HEALTH-RELATED QUALITY OF LIFE IN END STAGE RENAL DISEASE PATIENTS OF ALL AGES

M.A. MCADAMS-DEMARCO^{1,2}, H. YING², I. OLORUNDARE¹, E.A. KING¹, N. DESAI¹, N. DAGHER¹, B. LONZE¹, R. MONTGOMERY¹, J. WALSTON³, and D.L. SEGEV^{1,2}

¹Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD, USA

²Department of Epidemiology, Johns Hopkins School of Public Health, Baltimore, MD, USA

³Division of Geriatric Medicine and Gerontology, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Abstract

Background: Frailty is associated with worse health-related quality of life (HRQOL) in older adults and worse clinical outcomes in adults of all ages with end stage renal disease (ESRD). It is unclear whether frail adults of all ages with ESRD are more likely to experience worse HRQOL.

Objective: The goal of this study was to identify factors associated with worsening HRQOL in this population.

Design, setting and measurements: We studied 233 adults of all ages with ESRD enrolled (11/2009-11/2013) in a longitudinal cohort study. Frailty status was measured at enrollment and HRQOL was reported (Excellent, Very Good, Good, Fair or Poor) at the initial assessment and follow-up (median follow-up 9.4 months). We studied factors associated with Fair/Poor HRQOL at follow-up using logistic regression and factors associated with HRQOL change using multinomial regression. All models were adjusted for age, sex, race, education, BMI, diabetes status, history of a previous transplant, type of dialysis and time between assessments.

Results: Fair/Poor HRQOL was reported by 28% at initial assessment and 33% at follow-up. 47.2% of participants had stable HRQOL, 22.8% better HRQOL, and 30.0% worse HRQOL at follow-up ($P < 0.001$). In adjusted models, only frailty was associated with Fair/Poor HRQOL at follow-up (OR: 2.79, 95% CI: 1.32-5.90) and worsening HRQOL at follow-up (RR: 2.91, 95% CI: 1.08-7.80).

Conclusions: Frail adults of all ages with ESRD are more likely to experience fair/poor HRQOL and worsening HRQOL over time. Frailty represents a state of decreased physiologic reserve that impacts not only clinical outcomes but also the patient-centered outcome of HRQOL.

Corresponding author: Mara McAdams-DeMarco, Ph.D., Assistant Professor of Epidemiology, 615 N. Wolfe St, W6033; Baltimore, MD 21205, 410-502-1950 (tel) mara@jhu.edu.

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Keywords

End stage renal disease; frailty; Health-related quality of life

Introduction

End stage renal disease (ESRD) greatly impacts health-related quality of life (HRQOL), a subjective measure of the overall impact of health status, disease processes, and treatments. Patients with this chronic condition have worse HRQOL compared to their healthy counterparts. Among adults with ESRD, worse HRQOL is associated with poor outcomes (1, 2); hemodialysis patients with the lowest HRQOL are at 1.93-fold increased risk of mortality and 1.56-fold increased risk of hospitalization (2). Most studies of HRQOL in dialysis patients are cross-sectional, allowing for only a snap-shot of the impact of ESRD on a patient's perceived health. The majority of patients undergo dialysis until transplantation or death and so it is unlikely that HRQOL is static. Yet, little is known about changes in HRQOL for adults of all ages with ESRD.

Furthermore, it is unclear which patients with ESRD are most likely to report poor HRQOL. In one study of patients with ESRD, patient reported symptoms were associated with HRQOL (3). It is likely that there are sub-groups of patients with ESRD who are most vulnerable to poor HRQOL and/or likely to experience worsening HRQOL over time. One group of particular interest is frail adults with ESRD. Frailty, a measure of physiologic reserve or a patient's ability to respond to stressors, was initially described and validated in geriatric populations (4). However, presumably due to the physiological changes associated with kidney disease, this phenotype is emerging as an important risk factor for clinical outcomes in patients of all ages with ESRD, including falls (5), hospitalization (6) and mortality (6). Yet little is known about the association of frailty and this patient-centered outcome. While frailty is associated with worse HRQOL in general populations of older adults (7-12), it is unclear whether frail older adults with ESRD, and even frail younger adults with ESRD, are more likely to experience worse HRQOL and worsening HRQOL over time.

A better understanding of how HRQOL changes as adults of all ages with ESRD is necessary to assess the overall impact of this chronic condition. Furthermore, it is important to understand whether frail adults with ESRD, regardless of the age, are at risk of experiencing worse HRQOL. The goal of this longitudinal study of 233 adults with ESRD was to assess the change in HRQOL over time and test whether frailty was associated with poor HRQOL and worsening HRQOL.

Methods

Study Design

We studied prospective, longitudinal HRQOL measurements from a cohort of 233 adults with ESRD (enrolled 11/2009-11/2013) who eventually received a kidney transplant (by 5/2014). In this study, we measured HRQOL at two time periods: at the time of initial

waitlisting and then right before transplantation, so we were able to ascertain changes in HRQOL using these measurements. HRQOL was measured at both assessments and frailty was measured at the initial assessment. In addition, ESRD factors (sex, age, race, education, body mass index (BMI), diabetes, previous transplant and type of dialysis) were ascertained from medical records. The Johns Hopkins Institutional Review Board approved the study.

Frailty Measurement

Frailty was measured as defined and validated by Fried et al (4, 13-22) and as we have previously validated in ESRD and transplant populations (5, 6, 23-25). The phenotype was based on 5 components: shrinking (self-report of unintentional weight loss of more than 10 lbs in the past year based on dry weight); weakness (grip-strength below an established cutoff based on gender and BMI); exhaustion (self-report); low activity (Kcals/week below an established cutoff); and slowed walking speed (walking time of 15 feet below an established cutoff by gender and height) (4). Each of the 5 components was scored as 0 or 1 representing the absence or presence of that component. 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 as we previously have published (5, 6, 23-25).

Health-related Quality of Life (HRQOL)

HRQOL was assessed using a single question instrument for global subjective health from the kidney disease quality of life (KDQOL) assessment: "In general, would you say your health is...". Participants reported HRQOL as being "Excellent", "Very Good", "Good", "Fair" or "Poor" at both assessments. We used logistic regression to identify factors associated with reporting fair or poor HRQOL at follow-up; the model was adjusted for age, sex, race, education, BMI, previous transplant, type of dialysis and time between assessments.

Changes in HRQOL

Then we estimated the change in HRQOL score: no change in HRQOL, worse HRQOL, or improved HRQOL. Next, we identified predictors of HRQOL change (no change vs. improved HRQOL; worse HRQOL vs. improved HRQOL) using multinomial regression. This regression model allows for different associations between the predictors of HRQOL change and the different levels of the outcome (improved HRQOL, no change, or worse HRQOL). We adjusted for age, sex, race, education, BMI, previous transplant, type of dialysis, diabetes and time between assessments as potential predictors.

Statistical Analysis

For all analyses, a P value <0.05 was considered significant. All analyses were performed using STATA 12.0 (College Station, Texas).

Results

Study Population

Participants were an average of 53.3 years old (SD=14.0, range 18-82), and 24.9% were 65 and older; 42.1% were female, 31.8% were African American, 60.1% hemodialysis patients, 14.2% were peritoneal dialysis patients, 18.9% had diabetes, and 21.0% had received a previous kidney transplant. 23.6% of participants were frail. The median time between the initial and follow-up assessment was 9.4 months (IQR: 6-16 months).

HRQOL at the Initial Assessment

At the initial assessment, 10.7% reported excellent health, 23.6% very good health, 37.3% good health, 18.9% fair health and 9.4% poor health. Frailty was associated with HRQOL at the initial assessment ($P<0.001$, Table 1). There was an increase in prevalence of frailty with worsening HRQOL among those who reported very good, good, fair or poor HRQOL. Notably, 59.1% of participants who reported poor HRQOL at the initial assessment were frail (Table 1).

HRQOL at Follow-up

By follow-up, HRQOL worsened overall; 10.7% reported excellent health, 18.0% very good health, 28.6%, good health, 24.0% fair health and 8.6% poor health (Table 2). A higher percentage of participants reported fair/poor health at follow-up than at the initial assessment (32.6% vs. 28.3%).

Frailty and HRQOL at Follow-up

Similar to the initial assessment, frailty was associated with HRQOL at the follow-up assessment ($P=0.01$) (Figure 1 and Table 2). Frailty was more common among participants who reported poor HRQOL: 28.0% of those with excellent health were frail, 11.9% of those with very good health, 17.8% of those with good health, 33.9% of those with fair health and 40.0% of those with poor health. In the adjusted models, frailty was the only factor that was associated with HRQOL (Table 3); participants who were frail at the time of initial assessment were at 2.79-fold (95% CI: 1.32-5.90) increased odds of reporting fair or poor HRQOL at follow-up.

Change in HRQOL

HRQOL remained stable in 47.2% of participants, improved in 22.8%, and worsened in 30.0% (Figure 2) and this general shift towards worse HRQOL was statistically significant ($P<0.001$) (Table 4). Among those who reported excellent HRQOL at the initial assessment, 64.0% reported worsening HRQOL at follow-up (28.0% reported very good health, 28.0% reported good health and 12.0% fair health). In contrast, among those who reported poor health at the initial assessment 27.3% reported fair health, 18.2% reported good health and 13.6% reported very good health at follow-up. The overall pattern of change in HRQOL suggested that most participants had stable HRQOL but when there was a change in HRQOL it was more likely to be worse by one or two categories.

Frailty and Change in HRQOL

Participants who were frail at the initial assessment were 2.91-fold (95% CI: 1.08-7.80) more likely to report worse HRQOL at follow-up (Table 3). Importantly, the association of frailty at initial assessment and change in HRQOL was independent of age, sex, race, education, BMI, diabetes, previous transplant, type of dialysis and time between assessments. No other factors were associated with a change in HRQOL over follow-up.

Discussion

In this single-center prospective study of adults with ESRD, 47.2% reported stable HRQOL, but when there was a change in HRQOL it was most likely to be towards worse HRQOL. Importantly, we identified frail adults of all ages with ESRD as being high risk for worsening HRQOL: frail patients were more than twice as likely to report fair or poor HRQOL and nearly three-times as likely to experience a decline in HRQOL. In fact, frailty status was the only factor that was associated with HRQOL and change in HRQOL in our study. Our findings highlight frail ESRD patients as a highly vulnerable population that is significantly impacted by their health status, regardless of their age.

Findings from a prospective study of adults with CKD suggest that HRQOL declines proportionally to the severity grade of CKD (26). While this study explored factors associated with change in specific domains of HRQOL, they did not include novel risk factors. Our findings extended the previous work on change in HRQOL for adults with ESRD and suggest that a novel marker of physiologic reserve is also an important driver of HRQOL in adults of all ages with ESRD.

We have previously demonstrated that frail patients on dialysis of all ages are at high risk of falls, hospitalization, and mortality (5, 6), this work extends the previous findings to include a patient-centered outcome. It is possible that frailty not only captures a patient's ability to withstand stressors like those associated with ESRD, but frailty also leads to worse and declining HRQOL because frail patients experience more adverse clinical outcomes like falls and hospitalizations.

While HRQOL is often critiqued because it is a subjective measure of the impact of a disease or treatment, this is actually a strength of our study because we capture the overall patient-centered impact of ESRD. We were able to measure changes in 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 (4). One of the main limitations of the study is that we have only a single instrument to measure HRQOL which is not specific to kidney disease.

In this study of adults of all ages with ESRD, those who were frail were most vulnerable to fair or poor HRQOL and worsening HRQOL. We were able to demonstrate that frail ESRD patients are not only at risk of poor clinical outcomes but also a patient-centered outcome, HRQOL. Frail ESRD patients may be targeted for interventions to improve their outlook on their health and cope with ESRD.

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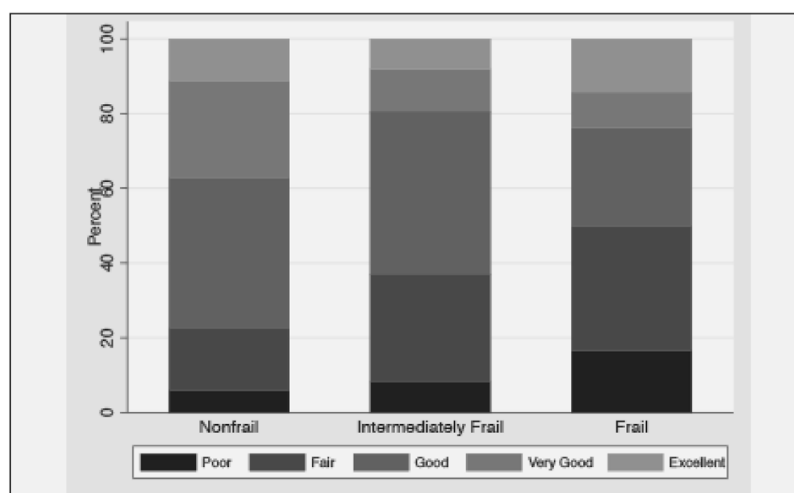


Figure 1. HRQOL Among Adults with ESRD by Frailty Status. Frail adults with ESRD of all ages were more likely to report fair or poor HRQOL at follow-up

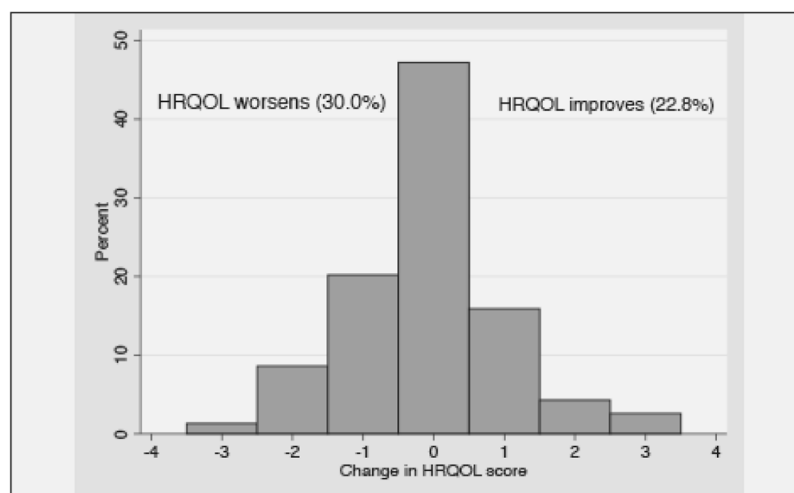


Figure 2.
Change in Health-related Quality of Life (HRQOL)

Characteristics of Adults with ESRD at Initial Assessment, by Health-related Quality of Life (HRQOL) (n=233)

Table 1

	HRQOL at Initial Assessment				
	Excellent n=25	Very Good n=55	Good n=87	Fair n=44	Poor n=22
Age, Mean (SD)	53.1 (14)	55.4(14)	53.8 (15)	51.6(13)	49.8(11)
Male Sex, %	72.0	54.6	54.0	59.1	63.6
African-American Race, %	48.0	21.8	28.7	45.5	22.7
HS Education or Higher, %	96.0	98.2	93.1	84.1	95.5
Diabetes, %	25.0	15.4	20.3	25.0	15.0
Body Mass Index (kg/m ²), Mean (SD)	28.5 (4.2)	26.6 (4.4)	29.2 (5.5)	29.0 (6.3)	29.6 (6.6)
Previous Transplant, %	24.0	21.8	19.9	22.7	36.4
Dialysis Type, %					
Hemodialysis	68.0	58.2	59.8	54.6	68.2
Peritoneal Dialysis	12.0	14.6	16.1	11.4	13.6
Frailty Status, %					
Nonfrail	56.0	72.7	44.8	40.9	22.7
Intermediately frail	20.0	21.8	32.2	29.5	18.2
Frail	24.0	5.5	23.0	29.6	59.1

HS=High School; All factors are measured at the initial assessment.

Characteristics of Adults with ESRD, by Health-related Quality of Life (HRQOL) at Follow-up (n=233)

Table 2

	HRQOL at Follow-up				
	Excellent n=25	Very Good n=42	Good n=90	Fair n=56	Poor n=20
Age, Mean (SD)	52.4 (15)	55.3 (15)	55.5 (14)	53.7 (14)	51.0 (12)
Male Sex, %	68.0	61.9	55.6	51.8%	65.0%
African-American Race, %	32.0	33.3	32.2	39.3%	5.0%
HS Education or Higher, %	100.0	97.6	91.1	91.1%	90.0%
Diabetes, %	22.7	30.0	9.3	27.8	23.5
Body Mass Index (kg/m ²), Mean (SD)	26.6 (5.0)	26.9 (4.4)	29.0 (6.9)	28.5 (6.0)	29.9 (6.0)
Previous Transplant, %	28.0	16.7	16.7	25.0	30.0
Dialysis Type, %					
Hemodialysis	64.0	69.1	54.4	58.9	65.0
Peritoneal Dialysis	16.0	9.5	13.3	17.9	15.0
Frailty Status, %					
Nonfrail	52.0	71.4	52.2	34.0	35.0
Intermediately frail	20.0	16.7	30.0	32.1	25.0
Frail	28.0	11.9	17.8	33.9	40.0
Years Between Assessments, Mean (SD)	1.1 (0.6)	1.1 (0.8)	1.0 (0.75)	1.0 (0.8)	0.78 (0.7)

Note: Age and BMI were ascertained at follow-up; HS=High School

Factors Associated with Health-related Quality of Life (HRQOL) at Follow-up and Change in HRQOL for Adults with ESRD (n=219)

Table 3

	FAIR/Poor HRQOL at Follow-up		Change in HRQOL - Compared to Better HRQOL at KT	
	OR (95% CI)	RR (95% CI) of No Change in HRQOL	RR (95% CI) of Worse HRQOL	
Frailty Status at Initial Assessment				
Non-/ Intermediately frail	Reference	Reference	Reference	
Frail	2.79 (1.32, 5.90)	1.15 (0.46, 2.87)	2.91 (1.08, 7.80)	
Age (5 year increase)	0.90 (0.80, 1.02)	0.96 (0.85, 1.09)	0.94 (0.81, 1.10)	
Male Sex	0.78 (0.42, 1.44)	0.92 (0.48, 1.77)	1.30 (0.60, 2.85)	
African-American Race	0.72 (0.35, 1.45)	1.56 (0.72, 3.37)	1.89 (0.78, 4.61)	
HS Education or Higher	0.54 (0.17, 1.69)	0.56 (0.14, 2.29)	1.25 (0.22, 7.16)	
BMI (5 kg/m ²)	1.03 (0.81, 1.32)	1.10 (0.84, 1.44)	0.82 (0.58, 1.16)	
Diabetes	2.03 (0.89, 4.66)	1.08 (0.43, 2.70)	0.78 (0.26, 2.40)	
Previous Transplant	1.41 (0.66, 3.05)	0.62 (0.26, 1.46)	1.20 (0.47, 3.10)	
Dialysis Type				
No Dialysis	Reference	Reference	Reference	
Hemodialysis	1.04 (0.49, 2.21)	0.69 (0.31, 1.53)	0.79 (0.30, 2.08)	
Peritoneal Dialysis	1.25 (0.46, 3.41)	0.68 (0.23, 1.97)	0.40 (0.10, 1.61)	
Years Between Assessments	0.86 (0.58, 1.27)	1.38 (0.90, 2.12)	1.12 (0.67, 1.86)	

Table 4

Change in Health-related Quality of Life (HRQOL) for Adults with ESRD (P <0.001) (n=233)

Initial Assessment	Follow-up				
	Excellent	Very Good	Good	Fair	Poor
Excellent	32.0%	28.0%	28.0%	12.0%	0
Very Good	20.0%	32.7%	34.6%	12.7%	0
Good	3.5%	12.6%	58.6%	18.4%	6.9%
Fair	6.8%	6.8%	20.4%	54.6%	11.4%
Poor	0	13.6%	18.2%	27.3%	40.9%

The percentage of participants who reported excellent, very good, good, fair and poor HRQOL at the follow-up by their HRQOL status at the initial assessment (row percentages are provided).