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Dynamic Frailty Before Kidney Transplantation—Time of Measurement Matters

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ABBREVIATIONS

95%CI, 95% confidence interval; **BMI**, body mass index; **CVD**, cardiovascular disease; **DCGL**, death-censored graft loss, **DGF**, delayed graft function; **ESRD**, end-stage renal disease; **HR,** hazard ratio; **IQR**, interquartile range; **KT,** kidney transplant(ation); **LOS**, length of stay; **OPTN**, Organ Procurement and Transplantation Network; **OR**, odds ratio; **PFP**, physical frailty phenotype; **RRR,** relative risk ratio; **SD**, standard deviation

ABSTRACT

Background: Frail kidney transplant (KT) recipients have higher risk of adverse post-KT outcomes. Yet, there is interest in measuring frailty at KT evaluation and then using this information for post-KT risk stratification. Given long wait times for KT, frailty may improve or worsen between evaluation and KT. Patterns, predictors, and post-KT adverse outcomes associated with these changes are unclear.

Methods: 569 adult KT candidates were enrolled in a cohort study of frailty (11/2009-09/2017) at evaluation and followed-up at KT. Patterns of frailty transitions were categorized as: 1) binary state change (frail/nonfrail); 2) 3-category state change (frail/intermediate/nonfrail); and 3) raw score change (-5 to 5). Adjusted Cox proportional hazard and logistic regression models were used to test whether patterns of frailty transitions were associated with adverse post-KT outcomes.

Results: Between evaluation and KT, 22.0% became more frail, while 24.4% became less frail. Black race (RRR=1.98, 95%CI:1.07-3.67) was associated with frail-to-nonfrail transition; diabetes (RRR=2.56, 95%CI:1.22-5.39) was associated with remaining stably frail. Candidates who became more frail between 3-category states (HR=2.27, 95%CI:1.11-4.65) or frailty scores (HR=2.36, 95%CI:1.12-4.99) had increased risk of post-KT mortality and had higher odds of length of stay (LOS) ≥2 weeks (3-category: OR=2.02, 95%CI:1.20-3.40; scores: OR=1.92, 95%CI:1.13-3.25).

Conclusions: Almost half of KT candidates experienced change in frailty between evaluation and KT, and those transitions were associated with mortality and longer LOS. Monitoring changes in frailty from evaluation to admission may improve post-KT risk stratification.

INTRODUCTION

The physical frailty phenotype (PFP), a syndrome of diminished physiologic reserve—or the body's ability to recover from stressors[1]— was initially described among community-dwelling older adults (≥65 years old)[1] and is common among adult patients (≥18 years old) with end-stage renal disease (ESRD).[2-5] Approximately, 18.4% of kidney transplant (KT) candidates on the waitlist are frail at evaluation,[5] and 19.9% of KT recipients are frail at KT.[3] Among adult patients with ESRD, the PFP was strongly associated with cognitive decline, as well as higher risk of mortality, hospitalizations, and falls.[2-5] The PFP has also proved itself a key predictor of adverse post-KT outcomes among patients undergoing KT, including delirium, longer length of stay, delayed graft function (DGF), early hospital readmission, and mortality.[6-11]

Despite subsequent recommendations to measure frailty as part of regular clinical practice at time of KT, a recent survey of US KT centers demonstrated that most transplant centers assess frailty at the time of evaluation rather than at KT.[12] It remains unclear as to whether a measure of frailty at the time of evaluation adequately represents frailty status at KT. Given long waitlist times between evaluation and KT, it is likely that frailty status changes while on the waitlist due to its dynamic process as shown in community-dwelling older adults,[13] hemodialysis patients,[14] and patients post-KT.[15] Additionally, while recommendations were designed with the goal of identifying patients at higher risk of adverse outcomes and to improve the decision-making process for KT-candidacy and post-KT care,[7,9,16] it remains unclear whether updating frailty measurement at KT improves risk stratification for post-KT outcomes.

To better understand whether frailty status should be remeasured among KT candidates who are admitted for KT, we sought to: 1) understand the dynamic nature of frailty between evaluation and KT by identifying frailty transition patterns, 2) identify the risk factors of change in frailty

status during this time, and 3) quantify the associations of these frailty transition patterns with post-KT outcomes.

METHODS

Study Design

We leveraged a cohort study of 569 English-speaking KT recipients (≥18 years old) at Johns Hopkins Hospital, Baltimore, Maryland (November 2009 - September 2017), for whom frailty was measured both at time of evaluation and admission for KT as described below. Recipient, donor, and transplant factors—such as age, sex, race, body mass index (BMI), history of diabetes mellitus, history of cardiovascular disease (CVD), time on dialysis, dialysis modality, cause of ESRD, DGF, and number of hospitalizations— were also assessed at these times or abstracted from the medical record.

All clinical and research activities being reported are consistent with the Declaration of Helsinki and the Declaration of Istanbul. The Institutional Review Board of Johns Hopkins Hospital approved this study (approval: CR00011133 and protocol: NA_00015758), and all enrolled participants provided written informed consent.

Frailty Measurement

Frailty, measured using the PFP as defined and validated in older adults[1,17-19] and by our group in ESRD and KT populations,[2,6-8,20,21] is based on five criteria: shrinking (self-reported unintentional weight loss >10 lbs in the past year); weakness (grip-strength below an established cutoff based on gender and BMI); exhaustion (self-report of moderate or higher frequency of effort and low motivation); low activity (kcals/week below an established cutoff); and slowed walking speed (walking time for 15 feet below an established cutoff by gender and height).[1] Participants were scored as 0 or 1 indicating the absence or presence of each criterion

respectively, which were then summed to create an aggregate frailty score (0-5). Consistent with prior studies, nonfrail was defined as a score of 0 or 1, intermediately frail was defined as a score of 2, and frail was defined as a score of 3 or higher.[2-4,8,9]

Change in Frailty Between Evaluation and KT

Change in frailty between time of evaluation and KT was identified using three approaches, including change between: 1) binary states (frail vs. nonfrail) 2) 3-category states (frail vs. intermediately frail vs. nonfrail, and 3) raw frailty score. For binary state transitions between time of evaluation and KT, participants were classified as being stably nonfrail (score of 0-2 at both visits), frail-to-nonfrail (drop in score ≥ 3 to 0-2), nonfrail-to-frail (increase in score of 0-2 to ≥3) or stably frail (score ≥ 3 at both visits). For 3-category state transitions between time of evaluation and KT, participants were classified as being stable category (same category at both visits), more frail (nonfrail to intermediately frail/frail or intermediately frail to frail) or less frail (frail to intermediately frail/nonfrail or intermediately frail to nonfrail). For change in frailty score between time of evaluation and KT, participants were classified as being stable score (same score at both visits), more frail (increased score), or less frail (decreased score).

Statistical Analysis

Differences in participant characteristics by classifications of binary-state frailty transitions were tested using: 1) ANOVA to compare means for normally distributed continuous variables; 2) a non-parametric Kruskal-Wallis H rank-based test for non-normally distributed continuous variables; 3) and a chi-squared test to compare proportions for categorical variables.

Predictors of binary state transitions of frailty between time of evaluation and KT were identified using a multinomial logistic regression to estimate relative risk ratios (RRR), comparing each correlate with the four classification of frailty transitions in a single model, controlling for

recipient and donor factors including age, sex, race, BMI, history of diabetes, history of CVD, time on dialysis, and dialysis modality.[22]

Associations between frailty transitions and mortality were explored using Cox proportional hazards models, adjusting for recipient and donor factors; proportional hazards assumptions were tested and confirmed using Schoenfeld's residuals. Additionally, logistic regression was used to evaluate the association between frailty transitions and longer length of stay (≥ 2 weeks),[10,11] adjusting for recipient and donor factors, in addition to a transplant factor—DGF. For models involving 3-category frailty state transitions and changes in frailty score, baseline frailty category and score were additionally accounted for in each model, respectively. Additionally, we conducted a sensitivity analysis assessing whether associations between frailty transitions and longer length of stay remained robust without adjusting for transplant factors (DGF).

All statistical analyses were performed using Stata 15.1 (College Station, Texas), and a p-value of <0.05 was considered significant.

RESULTS

Study Population

Of the 569 KT recipients participating in the study, the mean age was 51.7 years (standard deviation [SD]=14, range=18-85), 60.8% were male, and 39.0% self-identified as Black. The median time between evaluation and KT was 1.1 years (interquartile range [IQR]=0.6-1.9); 46.0% of recipients were transplanted within 1 year of being evaluated.

Change in Frailty

In terms of transition between binary frailty states, 7.0% of recipients remained stably frail, 9.5% transitioned from frail to nonfrail, 9.0% transitioned from nonfrail to frail, and 74.5% remained stably nonfrail between time of evaluation to KT (Table 1).

For the 3-category state transitions between time of evaluation to KT, 22.0% of individuals became more frail, while 24.4% became less frail. Frailty status was static for 53.6% of KT candidates between time of evaluation to KT; specifically, 36.4% remained nonfrail, 10.2% remained intermediately frail, and 7.0% remained frail (Table 2).

For changes in frailty score, 29.0% of participants became more frail, 34.6% of participants became less frail, and 36.4% of participants were stably frail between time of evaluation and KT.

Factors Associated with a Change in Frailty

Recipient factors that were associated with changes in frailty status were age (mean=50.8 in stable nonfrail vs 54.9 in nonfrail-to-frail, 54.5 in frail-to-nonfrail and 54.5 in stable-frail; p=0.04), diabetes (25.5% in stable nonfrail vs 41.2% in nonfrail-to-frail, 42.6% in frail-to-nonfrail and 52.5% in stable frail; p<0.001) and cause of ESRD (in the order of glomerular, diabetes, hypertension, cystic and other respectively: 25.0%, 13.7%, 30.4%, 11.8%, 19.1% in stable nonfrail vs 31.4%, 11.8%, 33.3%, 5.9%, 17.6% in nonfrail-to-frail, 24.1%, 29.6%, 37.0%, 3.7%, 5.6% in frail-to-nonfrail and 22.5%, 30.0%, 27.5%, 5.0%, 15.0% in stable frail; p=0.01) (Table 1).

There were no factors associated solely with change from nonfrail-to-frail status. Compared to candidates who remained stably nonfrail, candidates of Black race (RRR=1.98, 95% CI: 1.07, 3.67) were more likely to transition from frail-to-non-frail between time of evaluation and KT. Conversely, with each year on dialysis, candidates were less likely to transition from frail-to-nonfrail (RRR=0.88, 95% CI: 0.78, 1.00) between time of evaluation and KT. Additionally, individuals with diabetes (RRR=2.56, 95%CI: 1.22, 5.39) had a higher risk of remaining stably frail (Table 3).

Change in Frailty Status and Mortality

For 3-category frailty transitions, those candidates who became more frail at KT had a 2.27-fold (95%CI: 1.11, 4.65) higher risk of post-KT mortality than individuals who remained stable after adjusting for recipient and donor factors. Additionally, among individuals who became more frail based on their frailty score, the risk of mortality was 2.36-fold (95%CI: 1.12, 4.99) higher than those who remained stable, adjusting for recipient and donor factors. All other frailty transitions were not associated with post-KT mortality (Table 4).

Change in Frailty Status and Length of Stay

The odds of ≥2 weeks length of stay was 2.02-fold (95%CI: 1.20, 3.40) higher among candidates who became more frail by KT based on the 3-category frailty transition than those who remained stable after adjusting recipient, donor, and transplant factors. The odds of ≥2 weeks length of stay was also 1.92-fold (95%CI: 1.13, 3.25) higher for candidates who became more frail based on their frailty score than those who maintained a stable score, after adjusting for recipient, donor, and transplant factors (Table 4).

Sensitivity Analyses

After conducting sensitivity analyses to determine if results remained robust with and without adjusting for DGF, inferences remained consistent. Specifically, candidates who became more frail (3-categories or frailty score) still had significantly greater risk of having ≥2 weeks length of stay compared to candidates who were stable.

DISCUSSION

In this prospective cohort study of 569 candidates who are undergoing KT, frailty was dynamic between time of evaluation and KT; based on 3-category states, 22.0% of became more frail and 24.4% became less frail. Age, history of diabetes, and cause of ESRD were associated with

changes in frailty status. Worsening frailty category and score were independently associated with about a 2-fold increased risk of mortality and length of stay ≥ 2 weeks.

These findings are consistent with prior research among older adults, patients undergoing hemodialysis, and KT recipients that document the dynamic nature of frailty as a process of multi-system dysregulation,[13,14] including a study by our group that has demonstrated improvements in frailty status post-KT with successful restoration of kidney function.[15] This study expands these findings, demonstrating that frailty is also subject to change while KT candidates are on the waitlist for a kidney. Our findings were very similar to those reported in adult ESRD patients undergoing hemodialysis, where 35% of patients maintained the same frailty score for 12 months, while equal proportions of individuals improved and worsened in frailty scores;[14] in this study, 36.4% of KT candidates maintained the same frailty score between time of evaluation and KT, 29.0% demonstrated worsened frailty scores and 34.6% demonstrated improvements. Our findings further corroborated that similar proportions of KT candidates became more and less frail between evaluation and KT regardless of the frailty metric used, including transitions between 3-category states (9.0% vs. 9.5%, respectively) and scores (22.0% vs. 24.4%).

Additionally, our study builds upon previous findings in community-dwelling older adults and adult hemodialysis patients of all ages, where diabetes was a common predictor of transition to frailty.[13,14] In this study of ESRD patients, diabetes was associated with being stably frail, which suggests diabetes may be a robust indicator of unfavorable frailty transitions across different definitions of frailty change.[14] Of note, frailty transitions were defined differently across studies, which may explain the inconsistencies found in prior research related to predictors associated with frailty change. Furthermore, some predictors that were used in our model were KT-

candidate specific and may not apply to community-dwelling older adults and patients undergoing hemodialysis.

Our results further demonstrate that the use of frailty measurements at time of evaluation does not adequately represent frailty status at KT, as 1) equal proportions of individuals improve in frailty compared to worsening and 2) our results show that the change in frailty between evaluation and KT is associated with post-KT outcomes. In prior studies, frailty prevalence was shown to increase with older age[23] and progressive decline in kidney function,[24] which suggests that frailty severity should worsen as candidates remain on the waitlist for KT; this is likely why current practice mostly uses single time-point frailty measures at the time of evaluation in order to predict post-KT outcome risk and inform the decision-making process on KT-candidacy.[12] However, our findings indicate that measuring frailty at two time points may improve risk stratification, and emphasizes the need to update measures of frailty at the time of KT in clinical practice.

The main limitations of the study are those inherent to a single-centered design, where generalizability of findings are not certain; demographics of our study design should be taken into account. Furthermore, these findings are only generalizable to KT candidates who survive until transplantation, given that frail candidates are more likely to die while on the waitlist.[5] Finally, we cannot discount that changes in dialysis modality and/or dialysis initiation after evaluation may have had an affect on frailty transitions prior to KT as well given the period of adjustment, however this data was lacking in this study. Notwithstanding these limitations, this study provided the unique opportunity to assess the prospective measurement of a validated frailty instrument in a large sample of KT candidates who subsequently received KT.

In summary, we found that nearly half of KT candidates experienced a transition in frailty status between time of evaluation and KT, and that similar proportions of candidates improved and worsened in frailty severity by the time of KT. Importantly, this study identified patterns of frailty change that are independently associated with different risk factors and adverse post-KT outcomes, indicating that dynamic frailty may be considered as a tool for risk stratification. Current practice using frailty as a measure of assessment at time of evaluation is appropriate; however, it should not be used as a tool to exclude patients from KT. Instead, our findings suggest that using frailty measures at both time points would help to inform clinical-decision making.

REFERENCES

1. 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-M157.

2. McAdams-DeMarco MA, Law A, Salter ML, et al. Frailty as a novel predictor of mortality and hospitalization in individuals of all ages undergoing hemodialysis. *J Am Geriatr Soc.* 2013;61:896-901.

3. McAdams-DeMarco MA, Suresh S, Law A, et al. Frailty and falls among adult patients undergoing chronic hemodialysis: a prospective cohort study. *BMC Nephrol.* 2013;14:224.

4. McAdams-DeMarco MA, Tan J, Salter ML, et al. Frailty and Cognitive Function in Incident Hemodialysis Patients. *Clin J Am Soc Nephrol.* 2015;10:2181-2189.

5. McAdams-DeMarco MA, Ying H, Thomas AG, et al. Frailty, Inflammatory Markers, and Waitlist Mortality Among Patients with End-Stage Renal Disease in a Prospective Cohort Study. *Transplantation.* 2018;102:1740-1746.

6. Garonzik-Wang JM, Govindan P, Grinnan JW, et al. Frailty and delayed graft function in kidney transplant recipients. *Arch Surg.* 2012;147:190-193.

7. McAdams-DeMarco MA, Law A, Salter ML, et al. Frailty and early hospital readmission after kidney transplantation. *Am J Transplant.* 2013;13:2091-2095.

8. McAdams-DeMarco MA, Law A, Tan J, et al. Frailty, mycophenolate reduction, and graft loss in kidney transplant recipients. *Transplantation.* 2015;99:805-810.

9. McAdams-DeMarco MA, Law A, King E, et al. Frailty and Mortality in Kidney Transplant Recipients. *Am J Transplant.* 2015;15:149-154.

10. McAdams-DeMarco MA, King EA, Luo X, et al. Frailty, Length of Stay, and Mortality in Kidney Transplant Recipients: A National Registry and Prospective Cohort Study. *Ann Surg.* 2017;266:1084-1090.

11. Haugen CE, Mountford A, Warsame F, et al. Incidence, Risk Factors, and Sequelae of Post-kidney Transplant Delirium. *J Am Soc Nephrol.* 2018;29:1752-1759.

12. Kobashigawa J, Khush K, Colvin M, et al. Report From the American Society of Transplantation Conference on Donor Heart Selection in Adult Cardiac Transplantation in the United States. *Am J Transplant.* 2017;17:2559-2566.

13. Gill TM, Gahbauer EA, Allore HG, Han L. Transitions between frailty states among community-living older persons. *Arch Intern Med.* 2006;166:418-423.

14. Johansen KL, Dalrymple LS, Delgado C, et al. Factors Associated with Frailty and Its Trajectory among Patients on Hemodialysis. *Clin J Am Soc Nephrol.* 2017;12:1100-1108.

15. McAdams-DeMarco MA, Isaacs K, Darko L, et al. Changes in Frailty After Kidney Transplantation. *J Am Geriatr Soc.* 2015;63:2152-2157.

16. Garonzik-Wang JM, Govindan P, Grinnan JW, et al. Frailty and delayed graft function in kidney transplant recipients. *Arch Surg.* 2012;147:190-193.

17. Bandeen-Roche K, Xue QL, Ferrucci L, et al. Phenotype of frailty: characterization in the women's health and aging studies. *J Gerontol A Biol Sci Med Sci.* 2006;61:262-266.

18. Xue QL, Bandeen-Roche K, Varadhan R, Zhou J, Fried LP. Initial manifestations of frailty criteria and the development of frailty phenotype in the Women's Health and Aging Study II. *J Gerontol A Biol Sci Med Sci.* 2008;63:984-990.

19. Heuberger RA. The Frailty Syndrome: A Comprehensive Review. *J Nutr Gerontol Geriatr.* 2011;30:315-368.

20. McAdams-DeMarco MA, Olorundare IO, Ying H, et al. Frailty and Postkidney Transplant Health-Related Quality of Life. *Transplantation.* 2017;102:291-299.

21. Nastasi AJ, McAdams-DeMarco MA, Schrack J, et al. Pre-Kidney Transplant Lower Extremity Impairment and Post-Kidney Transplant Mortality. *Am J Transplant.* 2018;18:189-196.

22. Hamilton LC, Seyfrit CL. Interpreting multinomial logistic regression. *Stata Technical Bulletin.* 1993;13:24-28.

23. McAdams-DeMarco MA, Ying H, Olorundare I, et al. Individual Frailty Components and Mortality In Kidney Transplant Recipients. *Transplantation.* 2017;101:2126-2132.

24. Dalrymple LS, Katz R, Rifkin DE, et al. Kidney Function and Prevalent and Incident Frailty. *Clin J Am Soc Nephrol.* 2013;8:2091-2099.

25. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol.* 1994;47:1245-1251.

26. Hemmelgarn BR, Manns BJ, Quan H, Ghali WA. Adapting the Charlson Comorbidity Index for use in patients with ESRD. *Am J Kidney Dis.* 2003;42:125-132.

TABLES

Table 1: Characteristics of adult KT candidates by classification of binary state frailty transitions (n=569).[a]

Factor	Stable Nonfrail (n=424)	Nonfrail to Frail (n=51)	Frail to Nonfrail (n=54)	Stable Frail (n=40)	p-value
Age, mean (SD)	50.8 (14.0)	54.9 (12.4)	54.5 (14.5)	54.5 (14.0)	**0.04**
BMI, mean (SD)	28.2 (5.4)	27.8 (5.7)	29.9 (5.8)	29.4 (7.1)	0.08
Male	60.4	54.9	74.1	55.0	0.15
Race					0.53
White/Caucasian	58.5	45.1	46.3	47.5	
Black/African American	35.1	51.0	48.1	52.5	
Other	6.4	3.9	5.6	0.0	
Charlson Comorbidity Index, median (IQR)[b]	1.0 (0.0, 2.0)	1.0 (0.0, 3.0)	2.5 (0.0, 4.0)	2.0 (1.0, 4.0)	**<0.001**
Diabetes	25.5	41.2	42.6	52.5	**<0.001**
Cancer	1.7	0.0	0.0	5.0	0.19
Lung Disease	6.1	3.9	13.0	10.0	0.19
CVD	17.3	19.6	22.2	30.0	0.22
HIV	2.1	3.9	3.7	0.0	0.56
Rheumatological disease	7.0	15.2	5.7	8.6	0.23
Cause of ESRD					**0.01**
Glomerular	25.0	31.4	24.1	22.5	
Diabetes	13.7	11.8	29.6	30.0	
Hypertension	30.4	33.3	37.0	27.5	
Cystic	11.8	5.9	3.7	5.0	
Other	19.1	17.6	5.6	15.0	
Years on dialysis, median (IQR)	2.0 (0.0, 4.4)	2.4 (0.0, 5.2)	1.3 (0.4, 2.6)	2.5 (1.0, 4.2)	0.36
Type of dialysis					0.06
Hemodialysis	55.6	56.0	66.7	77.5	
Peritoneal Dialysis	15.2	10.0	16.7	7.5	
Not on dialysis	29.2	34.0	16.7	15.0	
Years between evaluation & KT, median (IQR)	1.1 (0.5, 1.9)	1.1 (0.7, 2.2)	1.1 (0.6, 1.7)	0.9 (0.5, 2.0)	0.81

[a]Percentages are presented unless otherwise stated.
[b]Charlson Comorbidity Index adapted for patients with ESRD.[25,26]

Table 2: Change in 3-category frailty between time of evaluation and admission for KT (n=569).[a]

	At Admission for KT		
At Evaluation	Nonfrail[b]	Intermediately Frail[c]	Frail[d]
Nonfrail	207 (36.4)	74 (13.0)	21 (3.7)
Intermediately Frail	85 (14.9)	58 (10.2)	30 (5.3)
Frail	26 (4.6)	28 (4.9)	40 (7.0)

[a]The table displays numbers (percentages) of patients who were nonfrail, intermediately frail, and frail at time of admission for KT according to frailty status at time of evaluation for KT. [b]Nonfrail was defined as a score of 0 or 1. [c]Intermediately frail was defined as a score of 2. [d]Frail was defined as a score of 3-5.

Table 3: Predictors of transitions between binary states between time of evaluation and admission for KT among KT candidates (n=569).[a]

	Nonfrail to Frail	Frail to Nonfrail	Stable Frail
Factor	**Relative Risk Ratios (95% Confidence Interval)**		
Male	1.38 (0.75, 2.53)	0.56 (0.29, 1.09)	1.46 (0.74, 2.88)
Age (per 5-years)	1.11 (0.99, 1.25)	1.05 (0.94, 1.18)	1.06 (0.92, 1.21)
Black Race	1.80 (0.98, 3.32)	**1.98 (1.07, 3.67)**	1.62 (0.81, 3.22)
BMI	0.96 (0.90, 1.02)	1.04 (0.99, 1.10)	1.01 (0.95, 1.08)
CVD	0.92 (0.43, 1.98)	1.20 (0.58, 2.48)	1.61 (0.75, 3.43)
Diabetes	1.91 (0.97, 3.79)	1.39 (0.73, 2.64)	**2.56 (1.22, 5.39)**
Peritoneal Dialysis	0.74 (0.28, 1.99)	1.41 (0.63, 3.14)	0.52 (0.15, 1.78)
Time on Dialysis (years)	1.00 (0.93, 1.08)	**0.88 (0.78, 1.00)**	1.01 (0.93, 1.10)
Hospitalizations	1.27 (0.94, 1.70)	0.88 (0.53, 1.49)	1.27 (0.94, 1.71)

[a]All relative risk ratios (RRR) were adjusted for recipient and donor factors including sex, age, black race, BMI, CVD, diabetes, dialysis modality, time on dialysis, and number of hospitalizations. Using a multinomial logit model, all RRRs were compared to a reference group of stable nonfrail candidates.

Table 4: Mortality and length of stay by change in frailty between evaluation and admission for KT (n=569).

	Mortality Hazard Ratio (95% CI)	Length of Stay (≥ 2 weeks) Odds Ratio (95% CI)
One-state frailty transition frail/nonfrail		
Stable Nonfrail (ref)	1.00	1.00
Nonfrail to Frail	1.60 (0.72, 3.56)	1.43 (0.71, 2.89)
Frail to Nonfrail	1.24 (0.54, 2.88)	0.71 (0.32, 1.57)
Stable Frail	1.58 (0.65, 3.81)	1.68 (0.79, 3.55)
Change in 3 categories nonfrail/ intermediate frail/ frail		
Less Frail	1.12 (0.54, 2.31)	0.81 (0.44, 1.48)
Stable category (ref)	1.00	1.00
More Frail	**2.27 (1.11, 4.65)**	**2.02 (1.20, 3.40)**
Change in frailty score		
Less Frail	1.16 (0.55, 2.44)	0.70 (0.40, 1.21)
Stable Score (ref)	1.00	1.00
More Frail	**2.36 (1.12, 4.99)**	**1.92 (1.13, 3.25)**

All hazard ratios and ORs are adjusted for demographic factors (age, sex, black race, BMI), diabetes, years on dialysis, cause of ESRD, donor type (live/deceased). Length of stay additionally was adjusted for delayed graft failure for all exposures. Change within the 3 frailty categories was additionally adjusted for baseline frailty category and change in frailty score was additionally adjusted for baseline frailty score.