Frailty, Length of Stay, and Mortality in Kidney Transplant Recipients

A National Registry and Prospective Cohort Study

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Objective: To test whether frailty, a novel measure of physiologic reserve, is associated with longer kidney transplant (KT) length of stay (LOS), and modifies the association between LOS and mortality.

Background: Better understanding of LOS is necessary for informed consent and discharge planning. Mortality resulting from longer LOS has important regulatory implications for hospital and transplant programs. Which recipients are at risk of prolonged LOS and its effect on mortality are unclear. Frailty is a novel preoperative predictor of poor KT outcomes including delayed graft function, early hospital readmission, immunosuppression intolerance, and mortality.

Methods: We used registry-augmented hybrid methods, a novel approach to risk adjustment, to adjust for LOS risk factors from the Scientific Registry of Transplant Recipients (n = 74,859) and tested whether (1) frailty, measured immediately before KT in a novel cohort (n = 589), was associated with LOS (LOS: negative binomial regression; LOS ≥2 weeks: logistic regression) and (2) whether frailty modified the association between LOS and mortality (interaction term analysis).

Results: Frailty was independently associated with longer LOS [relative risk = 1.15, 95% confidence interval (CI): 1.03–1.29; $P = 0.01$] and LOS ≥2 weeks (odds ratio = 1.57, 95% CI: 1.06–2.33; $P = 0.03$) after accounting for registry-based risk factors, including delayed graft function. Frailty also attenuated the association between LOS and mortality (nonfrail hazard rate = 1.55 95% CI: 1.30–1.86; $P < 0.001$; frail hazard rate = 0.97, 95% CI: 0.79–1.19, $P = 0.80$; P for interaction = 0.001).

Conclusions: Frail KT recipients are more likely to experience a longer LOS. Longer LOS among nonfrail recipients may be a marker of increased mortality risk. Frailty is a measure of physiologic reserve that may be an important clinical marker of longer surgical LOS.

Keywords: frailty, kidney transplantation, length of stay, mortality

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Better understanding of hospital length of stay (LOS) after a kidney transplant (KT) is necessary for informed consent, patient and caregiver counseling, and discharge planning. The sequelae of longer LOS may also have important implications for hospital reimbursements[1] and regulatory flagging.[2] Although there has been a reduction in LOS over time,[3] there remains a subset of KT recipients who experience a prolonged stay. Longer LOS is often attributed to greater disease burden in the recipient[4–6] or organ issues including delayed graft function (DGF).[7] The full picture of which preoperative recipient, donor, and transplant factors are associated with LOS is, however, unclear, as is the independent role of DGF on LOS.

In addition to traditional national registry-based predictors of KT LOS, novel factors such as frailty may also be associated with longer LOS. Frailty, a phenotype of decreased physiologic reserve and inability to overcome physiologic stressors,[8] is distinct from comorbidity and represents a novel preoperative predictor of poor KT outcomes including DGF, early hospital readmission, immunosuppression intolerance, and mortality.[9–12] KT represents a large physiologic stressor and, thus, it is possible that recipients who are frail are at risk of a prolonged LOS, perhaps independent of other known predictors of LOS. Also, given the increased mortality risk associated with both frailty[10] and LOS[13] among KT recipients, it is possible that the association between LOS and mortality differs by frailty status.

The goals of this study were to (1) better understand the trends, risk factors, and subsequent mortality associated with LOS using national registry data on 74,859 KT recipients and (2) test whether frailty is associated with LOS and is an effect modifier of the association between LOS and mortality in a prospective novel cohort of 589 KT recipients.

METHODS

National Registry Data

We used national registry data from the Scientific Registry of Transplant Recipients (SRTR) to better understand LOS as detailed below. The SRTR data system includes data on all donors, wait-listed candidates, and transplant recipients in the United States, submitted by the members of the Organ Procurement and Transplantation Network. The Health Resources and Services Administration, US Department of Health and Human Services provides oversight to the

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activities of the Organ Procurement and Transplantation Network, and SRTR contractors. The benefits of including the entire registry are that we can examine trends in LOS for more than 20 years, and identify recipient, transplant, and donor factors that predict LOS on the national level with a large sample size and generalizability.

LOS for 173,868 first-time, kidney only, adult KT recipients between 1995 and 2014 was ascertained from SRTR. Recipients with LOS of more than 365 days were excluded from all analyses (n = 59) as previously done.[13] We considered recipient factors (age, sex, race/ethnicity, body mass index (BMI), peak panel reactive antibody (PRA), diabetes, and time on dialysis), transplant factors (number of human leukocyte mismatches, cold ischemia time (CIT), and DGF), and donor factors (donor type, age, and race/ethnicity) as potential risk factors for longer LOS. We excluded KT recipients with missing data on any of the key variables. As is standard with SRTR data, mortality was augmented through linkage with the Social Security Death Master File and data from the Centers for Medicare and Medicaid Services.

Novel Cohort Study Data

In addition, we studied frailty, which is not collected in the national registry data, among 589 KT recipients who participated in a prospective, longitudinal cohort study at Johns Hopkins Hospital, Baltimore, Maryland, between December 2008 and May 2014. All participants provided written informed consent and the present study was approved by the Johns Hopkins Institutional Review Board; all procedures were conducted in accordance with the ethical standards of the Committee on Human Experimentation and in accord with the ethical standards of the Helsinki Declaration of 1975. We linked SRTR data (KT LOS, recipient, transplant, and donor factors) to frailty measurements from this prospective cohort study. Frailty was measured on all participants using the physical frailty phenotype as described below. The benefit of studying LOS in the novel cohort study data is that we can ascertain granular measures of risk, like frailty.

Frailty in the Novel Cohort Data

At admission for KT (immediately before KT), frailty was measured by trained research assistants as defined and validated by Fried in older adults[8,14–23] and by our group in end-stage renal disease and KT populations.[9–11,24–26] Frailty 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 sex and BMI); exhaustion (self-report); low activity (kcal/week below an established cutoff); and slowed walking speed (walking time of 15 feet below an established cutoff by sex and height).[8] 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, intermediately frail was defined as a score of 2, and frail was defined as a score of 3 or higher, as we have previously reported.[10–12,24–26] In the present study, we empirically combined the intermediately frail and frail groups (because both groups were associated with a similar risk of prolonged LOS) as we have previously done[12] and refer to this group as frail throughout the manuscript.

Distribution and Trends in Kidney Transplant Length of Stay Between 1995 and 2014 in National Registry Data

We estimated the trends in median and interquartile range (IQR) of LOS and prevalence of LOS exceeding 2 weeks by year of KT (between 1995 and 2014). We also plotted the distribution of LOS overall and by year (between 1995 and 2014). These analyses in trends in LOS were conducted among 173,868 KT recipients using national registry data.

Risk Factors for Longer Length of Stay in National Registry Data

We identified which recipient, transplant, and donor factors were associated with LOS using data from all KT recipients between 2002 and 2014 (n = 133,214). We estimated these associations using negative binomial regression [relative risk (RR)] when LOS was the outcome and logistic regression [odds ratio (OR)] when LOS exceeding 2 weeks was the outcome. In addition to the models limited to factors known at the time of KT, we also explored models that include DGF, given the potential association between DGF and LOS; we considered DGF (a post-KT risk factor) as a mediator of pre-KT factors.

Length of Stay and Mortality in National Registry Data

Cox proportional hazards models were used to calculate adjusted hazard rate ratio (HR) of mortality by LOS exceeding 2 weeks. We adjusted for all recipient, transplant, and donor factors that were associated with LOS.

Frailty, Length of Stay, and Mortality in the Novel Cohort Data

The independent association between frailty and KT LOS was estimated using a hybrid registry-augmented regression model as we have previously described.[10] Briefly, using our SRTR negative binomial model for LOS (n = 74,859 KT recipients between 2008 and 2014). We precisely estimated the coefficients of recipient, transplant, and donor factors and introduced these coefficients back into the single-center model (using forced values). We only included recipients who received KT between 2008 and 2014 to coincide with the years of the primary cohort which included measured frailty. The coefficients of the confounders were constrained to be the coefficients observed in the SRTR model through the use of a model offset. The only coefficient estimated using our single-center data was frailty (frail/intermediately frail vs nonfrail). Robust standard errors (Huber-White sandwich estimator) were used. Similar adjusted models with and without DGF were estimated using LOS. In addition, hybrid registry-augmented logistic regression models, with LOS exceeding 2 weeks as the outcome, were estimated with and without DGF to test for: mediation of the association between frailty and LOS by DGF (a post-KT risk factor).

Effect Modification of Length of Stay and Mortality by Frailty Status in the Novel Cohort Data

We also tested for effect modification on the multiplicative scale for the association between LOS and mortality by frailty using a hybrid registry-augmented Cox proportional hazards model using a similar approach to what is described above. The only coefficients estimated using our single-center data were for the main effects of LOS and frailty and the interaction of LOS with frailty.

Statistical Analysis

All analyses were performed using STATA 13.0. The Johns Hopkins Institutional Review Board approved the cohort study and the use of SRTR data.

RESULTS

Distribution and Trends in Kidney Transplant-Length of Stay in National Registry Data

Of 173,868 KT recipients between 1995 and 2014, the median LOS was 5 days (IQR: 4–8) (Fig. 1). The median LOS decreased over time (Fig. 2A). In 1995, the median LOS was 8 days (IQR: 6–12); in

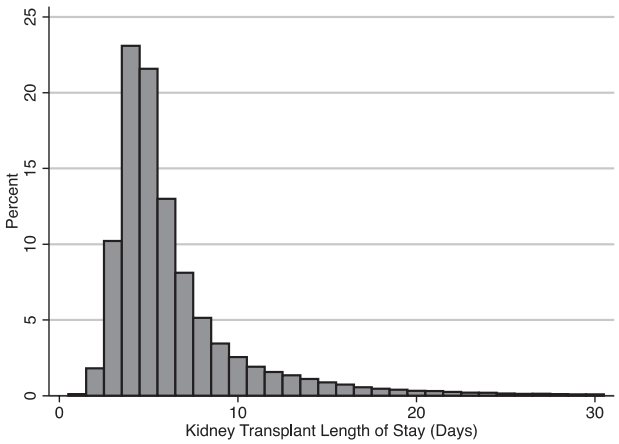

FIGURE 1. Distribution of kidney transplant (KT) length of stay (LOS) using SRTR data between 1995 and 2014 (n = 173,868). The figure shows the distribution of KT LOS within 30 days. 1% had LOS between 30 and 365 days. Those with an LOS of greater than 365 days (n = 59) were excluded from all analyses.

the subsequent years it dropped steadily from 8 days to 7, 6, and then 5 days in 2005. The median LOS then remained at 5 days (IQR: 4–6) through 2014.

The prevalence of LOS exceeding 2 weeks also decreased over time (Fig. 2B). In 1995, 21.4% of recipients were hospitalized for 2 weeks or longer; this decreased each year until 2000, when only 9.6% were hospitalized for 2 weeks or longer. By 2014, only 5.4% were hospitalized for 2 weeks or longer (Table 1).

Risk Factors for Longer Length of Stay in National Registry Data and Novel Cohort Data

In the national registry data, older recipients (age ≥65 years) had an LOS that was 1.10-fold longer [95% confidence interval (CI): 1.09–1.12] than that of younger recipients (Table 2). Female recipients had an LOS that was 1.02-fold longer (95% CI: 1.01–1.03) and African American recipients had an LOS that was 1.05-fold longer (95% CI: 1.04–1.07). Recipients with a BMI 35 kg/m^2 or higher had an LOS of 1.03-fold longer (95% CI: 1.01–1.05) than those who had a BMI between 18.5 and 24 kg/m^2. In addition, peak PRA >80 (RR = 1.08, 95% CI: 1.05–1.11) and diabetes (RR = 1.09, 95% CI: 1.08–1.11) were associated with a longer LOS. Compared to preemptive KT, longer time on dialysis was associated with a longer LOS: 0 to 1 year (RR = 1.06, 95% CI: 1.03–1.08), 1 to 2 year (RR = 1.14, 95% CI: 1.11–1.16), 2 to 3 year (RR = 1.19, 95% CI: 1.16–1.22), and more than 3 years (RR = 1.28, 95% CI: 1.25–1.30). In addition, longer CIT was associated with a longer LOS: 12 to 23 hours (RR = 1.06, 95% CI: 1.04–1.08), 24 to 36 hours (RR = 1.10, 95% CI: 1.08–1.12), and more than 36 hours (RR = 1.06, 95% CI: 1.05–1.08). Compared with live donor recipients, deceased standard criteria donor recipients had an LOS that was 1.08-fold longer (95% CI: 1.06–1.10), donation after cardiac death (DCD) donor recipients had an LOS that was 1.18-fold longer (95% CI: 1.15–1.21), and expanded criteria donor (ECD) recipients had an LOS that was 1.17-fold longer (95% CI: 1.14–1.20). Recipients with DGF had an LOS that was 1.66-fold longer (95% CI: 1.63–1.69), independent of all of the factors known at the time of KT.

Similar risk factors for LOS exceeding 2 weeks were observed (Table 2). Notably, longer time on dialysis was associated with an increased odds of LOS exceeding 2 weeks; 0 to 1 year (OR = 1.42, 95% CI: 1.28–1.57), 1 to 2 years (OR = 1.80, 95% CI: 1.63–1.98), 2 to 3 year (OR = 2.09, 95% CI: 1.89–2.31), and more than 3 year (OR = 2.60, 95% CI: 2.38–2.85). DGF was associated with a 5.66-fold (95% CI: 5.63–5.94) increased odds of LOS exceeding 2 weeks, independent of all of the factors known at the time of KT.

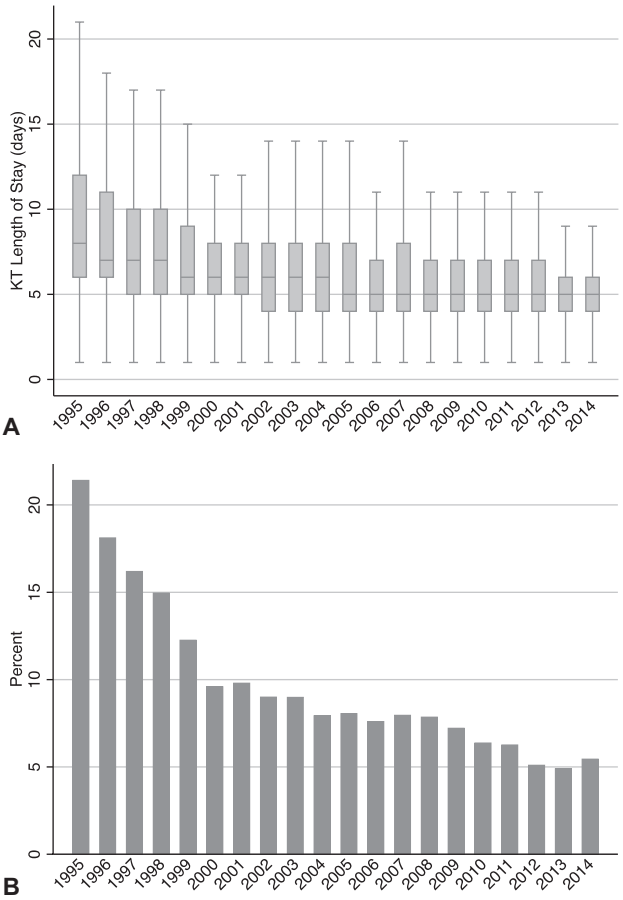

FIGURE 2. A, Distribution of kidney transplant (KT) length of stay (LOS) by year of KT using SRTR data between 1995 and 2014 (n = 173,868). Note: outliers (data points that fall outside the lower quartile – 1.5 × IQR, upper quartile + 1.5 × IQR) were excluded from the figure. B, The prevalence of length of stay exceeding 2 weeks, by year of KT using SRTR data between 1995 and 2014 (n = 173,868).

In the novel cohort data, frail KT recipients had an LOS that was 1.14-fold longer (95% CI: 1.02–1.28; $P = 0.02$) than nonfrail recipients, even after accounting for all other donor, recipient, and transplant factors known at the time of KT (Table 3). After additionally adjusting for DGF, frailty was still an independent risk factor for longer LOS (RR = 1.15, 95% CI: 1.03–1.29; $P = 0.01$). In addition, frail KT recipients had a 1.6-fold (OR = 1.63, 95% CI: 1.13–2.37; $P = 0.01$) greater odds of LOS exceeding 2 weeks, even after adjusting for factors known at the time of KT. This risk remained significant (OR = 1.57, 95% CI: 1.06–2.33; $P = 0.03$) even after additionally accounting for DGF.

Length of Stay and Mortality in National Registry Data and Novel Cohort Data

The unadjusted risk of mortality was greater in KT recipients with an LOS exceeding 2 weeks ($P < 0.001$) (Fig. 3) and remained

TABLE 1. Recipient, Transplant, and Donor Factors by Kidney Transplant (KT) Length of Stay (LOS) Exceeding 2 Weeks Using National Registry Data Between 2002 and 2014 and Novel Cohort Data

	National Registry Data (n = 133,214)		Novel Cohort Study (n = 589)	
	LOS Exceeding 2 Weeks		LOS Exceeding 2 Weeks	
	No	Yes	No	Yes
Recipient factors				
Age ≥65	16.8	22.5	22.8	17.4
Female	39.0	40.6	36.0	50.0
African American race/ethnicity	25.0	34.6	36.7	45.4
BMI (kg/m^2)				
<18.5	2.0	2.1	3.4	3.5
18.5–24	30.6	27.8	34.3	33.1
25–29	34.2	32.7	34.1	25.6
30–34	22.4	24.1	20.1	25.0
≥35	10.8	13.2	8.2	12.8
Peak PRA >80	6.2	9.0	14.2	36.6
Diabetes	33.9	43.3	15.8	22.1
Years on dialysis				
0 (Preemptive KT)	16.8	6.9	0.2	0.6
0–1	16.4	9.8	12.5	7.6
1–2	16.0	13.8	10.8	6.4
2–3	13.2	14.6	9.4	7.0
>3	37.6	54.9	67.2	78.5
KT factors				
0 HLA mismatches	9.6	6.8	6.0	1.7
CIT (h)				
≤12	47.1	35.3	54.7	50.0
12–23	31.3	40.3	17.8	18.6
24–36	9.6	14.2	21.6	22.1
>36	12.0	10.2	6.0	9.3
DGF	14.3	52.2	11.8	29.7
Donor factors				
Deceased standard criteria	42.0	47.5	41.5	35.5
Donation after cardiac death	6.9	12.3	6.5	13.4
Expanded criteria	10.9	17.5	5.5	7.6
Age ≥65	3.1	4.4	4.3	3.5
African American race/ethnicity	13.3	14.6	18.9	19.8

Percentages are presented.
HLA indicates human leukocyte.

significant even after accounting for all the factors that were associated with LOS, including DGF (HR = 2.38, 95% CI: 2.20–2.58). For every 1 week increase in LOS there was a 1.08-fold (95% CI: 1.07–1.09, $P < 0.001$) increased risk of mortality after accounting for all the factors that were associated with LOS, including DGF.

In the novel cohort data, the risk of mortality associated with LOS differed for frail and nonfrail recipients (P for interaction = 0.001) after accounting for factors known at the time of KT. Among those who were nonfrail, for every 1 week increase in LOS there was a 1.55-fold (95% CI: 1.30–1.86; $P < 0.001$) increased risk of mortality. Among recipients who were frail, longer LOS was not associated with any increased risk of mortality (HR = 0.97, 95% CI: 0.79–1.19; $P = 0.80$).

DISCUSSION

In this national study of KT recipients, we identified a decreasing trend in LOS from 8 days in 1995 to 5 days in 2014. A substantial number of KT recipients, however, still remain hospitalized for longer than 2 weeks. Recipients who were older, female, African American, obese, diabetic, those who received a deceased donor organ experienced longer LOS; also, longer time on dialysis and longer CIT and DGF were associated with longer LOS. As expected, DGF was associated with more than a 5-fold increased risk of LOS exceeding 2 weeks. Applying these findings to our prospective cohort, we found that recipients who were frail were 1.6-fold more likely to have an LOS exceeding 2 weeks. Although frail recipients have a greater risk of post-KT mortality on average,[10] nonfrail recipients with a longer LOS are also at elevated mortality risk; there was effect modification of the association to LOS and mortality by frailty. Our study is consistent with previous findings of decreasing KT LOS through 2008,[3] but we found that this decrease has plateaued (median of 5 days from 2005 to 2014). It is possible that the current LOS is the limit of what can be done with respect to shortening the LOS after KT.

There have been few studies of the risk factors for longer KT LOS.[4–6,27] Although some studies have found that recipient comorbidities such as obesity and diabetes were associated with longer KT LOS,[4–6,27] DGF has been identified as the strongest predictor of KT LOS.[5] Our study confirmed these risk factors and also identified other recipient, transplant, and donor factors from the national registry data such as older age, longer time on dialysis, longer CIT, higher peak PRA, DCD, and ECD.

Most importantly, our study is the first to show that physiologic reserve, as measured by frailty, is a novel risk factor for longer LOS. We have previously shown that frailty is associated with DGF

TABLE 2. Correlates of Kidney Transplantation (KT) Length of Stay (LOS), Using National Registry Data (n = 133,214) Between 2002 and 2014

	Ratio (95% CI) of LOS (Days)		OR (95% CI) of LOS Exceeding 2 Weeks	
Recipient Factors	**Without DGF**	**With DGF**	**Without DGF**	**With DGF**
Age (≥65 vs <65)	1.10 (1.09–1.12)	1.10 (1.08–1.12)	1.32 (1.26–1.40)	1.34 (1.27–1.41)
Female	1.02 (1.01–1.03)	1.04 (1.03–1.05)	1.06 (1.02–1.11)	1.20 (1.14–1.25)
African American race/ethnicity	1.05 (1.04–1.07)	1.03 (1.02–1.04)	1.25 (1.19–1.31)	1.15 (1.09–1.21)
BMI (kg/m^2)				
<18.5	1.08 (1.03–1.13)	1.08 (1.04–1.13)	1.24 (1.07–1.44)	1.27 (1.09–1.49)
18.5–24	Reference	Reference	Reference	Reference
25–29	1.00 (0.98–1.01)	0.99 (0.97–1.00)	0.98 (0.92–1.03)	0.93 (0.88–0.98)
30–34	1.00 (0.98–1.01)	0.97 (0.96–0.99)	1.05 (0.99–1.12)	0.94 (0.88–1.00)
≥35	1.03 (1.01–1.05)	0.98 (0.97–1.00)	1.15 (1.07–1.24)	0.94 (0.87–1.02)
Peak PRA >80	1.08 (1.05–1.11)	1.08 (1.05–1.11)	1.33 (1.23–1.44)	1.32 (1.21–1.43)
Diabetes	1.09 (1.08–1.11)	1.07 (1.06–1.09)	1.32 (1.26–1.38)	1.22 (1.17–1.28)
Years on dialysis				
0 (Preemptive KT)	Reference	Reference	Reference	Reference
0–1	1.06 (1.03–1.08)	1.03 (1.01–1.05)	1.42 (1.28–1.57)	1.23 (1.11–1.36)
1–2	1.14 (1.11–1.16)	1.09 (1.07–1.12)	1.80 (1.63–1.98)	1.46 (1.32–1.62)
2–3	1.19 (1.16–1.22)	1.12 (1.10–1.15)	2.09 (1.89–2.31)	1.59 (1.44–1.76)
>3	1.28 (1.25–1.30)	1.16 (1.13–1.19)	2.60 (2.38–2.85)	1.75 (1.59–1.92)
KT factors				
0 HLA mismatches	0.96 (0.94–0.98)	0.97 (0.95–0.99)	0.77 (0.71–0.84)	0.81 (0.74–0.88)
CIT (h)				
≤12	Reference	Reference	Reference	Reference
12–23	1.06 (1.04–1.08)	1.03 (1.01–1.05)	1.17 (1.10–1.24)	1.04 (0.98–1.10)
24–36	1.10 (1.08–1.12)	1.03 (1.00–1.05)	1.38 (1.28–1.48)	1.07 (0.99–1.15)
>36	1.06 (1.05–1.08)	1.04 (1.02–1.06)	1.31 (1.22–1.42)	1.18 (1.09–1.27)
DGF	–	1.66 (1.63–1.69)	–	5.66 (5.39–5.94)
Donor factors				
Live donor KT	Reference	Reference	Reference	Reference
Deceased standard criteria	1.08 (1.06–1.10)	1.04 (1.02–1.06)	1.17 (1.09–1.25)	0.91 (0.85–0.98)
Donation after cardiac death	1.18 (1.15–1.21)	1.04 (1.02–1.07)	1.68 (1.55–1.83)	0.96 (0.88–1.05)
Expanded criteria	1.17 (1.14–1.20)	1.09 (1.06–1.11)	1.45 (1.33–1.57)	0.99 (0.91–1.08)
Age (≥65 vs <65)	1.02 (0.98–1.05)	1.01 (0.98–1.05)	1.03 (0.92–1.16)	1.02 (0.91–1.15)
African American race/ethnicity	0.98 (0.96–0.99)	0.99 (0.97–1.00)	0.97 (0.91–1.03)	1.01 (0.95–1.08)

The ratio (95% CI) of days hospitalized was estimated using negative binomial regression and odds risk (OR) (95% CI) of 2-week length of stay was estimated using logistic regression. DGF was ascertained post-KT and thus, including DGF in the model tests for mediation by this post-KT risk factor.

DGF indicates delayed graft function; HLA, human leukocyte.

in KT recipients.[9] We now extend these findings to show that frailty is associated with longer LOS, independent of DGF. This suggests that, although frailty increases the risk of DGF, the association between frailty and LOS is not fully mediated through DGF. This independent association is plausible given that frailty is a measure of physiologic reserve that captures a patient's ability to respond to stressors. Transplantation, like most surgeries, represents a major stressor, and those who are frail are most likely to require more physical recovery time in the hospital, regardless of whether or not they experience DGF.

Previous studies have identified frailty as an important predictor of postsurgical outcomes in general surgery,[28] gastrointestinal surgery,[29] cardiac surgery[30,31] and mortality among patients on the liver and lung transplant waitlist.[32,33] While this is the first study to show that frailty is associated with longer KT LOS, it is likely that this measure of physiologic reserve is also associated with longer LOS, in other surgical settings.

One study identified an increased risk of post-KT mortality for those recipients with a longer LOS.[13] Our findings confirm these findings in general, but show that they are modified by frailty. For nonfrail patients, LOS was indeed associated with higher risk of post-KT mortality. For frail patients, the mortality risk that accompanied this decrease in physiologic reserve was no different regardless of LOS. Although this may seem counterintuitive, it is likely that frailty

TABLE 3. Frailty and Kidney Transplant Length of Stay (LOS) Using Novel Cohort Data (n = 589)

	Ratio (95% CI) of LOS (Days)		OR (95% CI) of LOS Exceeding 2 Weeks	
	Without DGF	**With DGF**	**Without DGF**	**With DGF**
Frailty	1.14 (1.02–1.28)	1.15 (1.03–1.29)	1.63 (1.13–2.37)	1.57 (1.06–2.33)
P value	0.02	0.01	0.01	0.03

The ratio (95% CI) of days hospitalized was estimated using negative binomial regression and odds risk (OR) (95% CI) of 2 week length of stay was estimated using logistic regression. DGF was ascertained post-KT and thus, including DGF in the model tests for mediation by this post-KT risk factor.

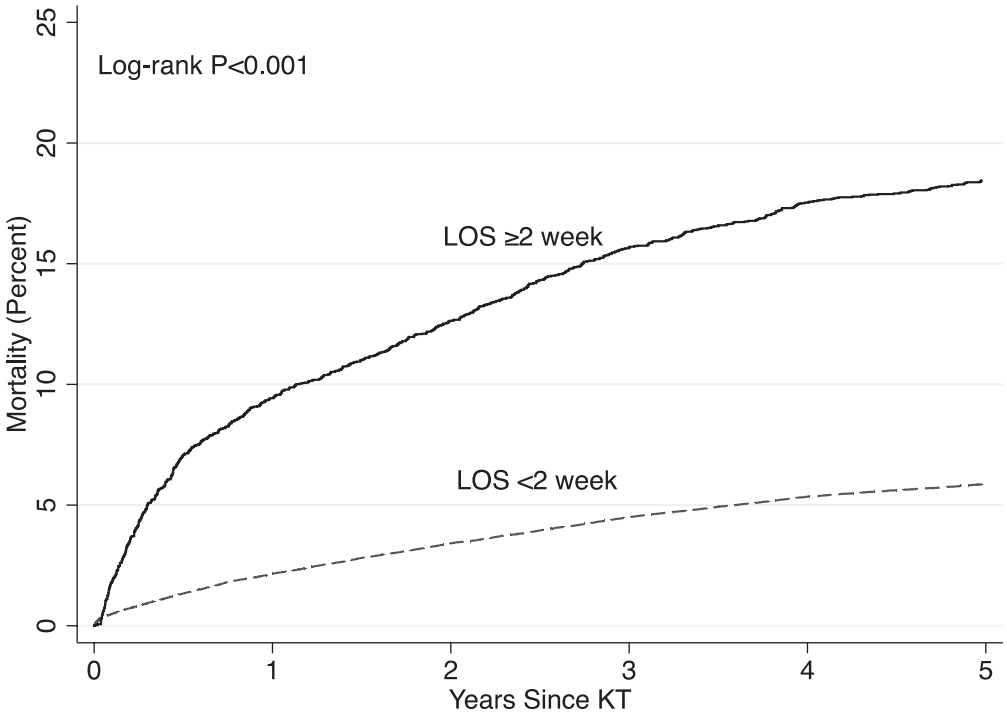

FIGURE 3. Mortality by kidney transplant (KT) length of stay (LOS) using national registry data between 2008 and 2014 (n = 74,859). A KT LOS exceeding 2 weeks was associated with an increased risk of mortality (Log-rank *P* value <0.001).

captures a unique domain of risk. Therefore, if a recipient is frail they are already at an increased risk of mortality,[10] and their prolonged LOS is not a driver of mortality beyond this baseline physiologic risk.

One notable limitation of the present study was that frailty was only measured in our single-center cohort. We were, however, able to estimate with great precision and generalizability the associations between other characteristics and LOS, and these formed a strong framework for estimating this effect accurately for frailty. Strengths of the present study were also the prospective measurement of a validated frailty instrument, and reliable ascertainment of the recipient, transplant, and donor factors. In addition, our novel analytical method helped us properly yet efficiently adjust for many confounders without overfitting the model.

In conclusion, a number of recipient, transplant, and donor factors are associated with LOS, including frailty, a novel measure of physiologic reserve adapted from gerontology. Frail recipients and nonfrail recipients with a long LOS both have a greater risk of post-KT mortality. These results may have important implications for informed consent, patient and caregiver counseling, and discharge planning by aiding in identifying which KT recipients are at increased risk of longer LOS and potentially, subsequent mortality. It is possible that in other surgical settings, frailty increases the risk of longer LOS and these patients could be targeted for special counseling and management planning.

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