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Timing Matters: Longitudinal Changes in Frailty Among Elderly Patients with End-Stage Renal Disease

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ABSTRACT

Background. Frailty is often first assessed near the dialysis decision point, when acute illness, uremia, and metabolic instability may influence Clinical Frailty Scale (CFS) scores. Attrition through death may further alter the frailty profile observed over time, making assessment timing important for interpretation.

Objectives. To describe longitudinal changes and category transitions in CFS scores and to explore their relationship with treatment trajectory, mortality, and follow-up completeness.

Methods. This secondary, exploratory longitudinal analysis used data from a prospective single-center cohort of 64 patients aged 65 years or older with end-stage renal disease (ESRD) at the dialysis decision point, baseline CFS ≥5, and Charlson Comorbidity Index ≥3. Treatment trajectories were stable comprehensive conservative care (CCC; n=19), stable dialysis (n=35), and treatment transition (n=10). CFS was assessed at baseline and during the 3-, 6-, and 12-month intervals. Paired changes from baseline were estimated using available observations without imputation. Baseline CFS and 12-month mortality were examined using univariable logistic regression.

Results. CFS observations were available for 64, 61, 33, and 27 patients at baseline and during the 3-, 6-, and 12-month intervals, respectively; corresponding median scores were 7, 8, 6, and 6. The CCC group showed a modest increase from baseline to the first 3-month interval (+0.44; P=0.028). No baseline-to-6-month within-group change was statistically significant. From baseline to 12 months, CFS decreased in the stable dialysis group (−1.23; P=0.047), while other groups showed no significant change. After the first 3-month interval, most participants with paired observations remained in the same CFS category. Thirty patients (46.9%) died, including 20 within 3 months, and only 27 participants had complete CFS follow-up. Participants alive and under follow-up at 12 months were younger and had lower baseline CFS than those who died. Baseline

Conclusions. CFS values in older, frail patients with ESRD varied according to assessment time, while death and incomplete follow-up changed the composition of the observed cohort. A CFS score obtained at the dialysis decision point should therefore be interpreted in its clinical context. Recording assessment conditions and repeating CFS after stabilization may provide a more complete view of patient trajectory. These exploratory findings require confirmation in larger longitudinal studies that account for death and informative dropout.

Keywords. Chronic kidney disease; Conservative management; Dialysis; Elderly; End-stage renal disease; Frailty; Mortality prediction; Prognostic score.

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BACKGROUND

Frailty is a clinical syndrome characterized by a decline in physiological reserve and increased vulnerability to adverse health outcomes, particularly during acute stressors,[1-4] It is highly prevalent among patients with chronic kidney disease (CKD), affecting approximately 30% to 82% of individuals receiving dialysis.[5,6] Frailty has been consistently identified as an independent predictor of mortality in patients receiving dialysis.[7,8] Moreover, functional status is a key component of the Renal Epidemiology and Information Network (REIN) score, recommended by the European Renal Best Practice (ERBP) guidelines for patients with CKD stages 3b or higher.[9] This score is widely used to support clinical decision-making regarding the initiation of kidney replacement therapy (KRT) versus treatment. with comprehensive conservative care (CCC).[10,11]

Existing evidence suggests that frailty is highly prevalent at the time of dialysis initiation and that functional status often declines after initiation of KRT in older adults.[12,13] However, several important limitations should be considered. First, standardized definitions and validated assessment tools for frailty in CKD populations are lacking.6 Second, despite its clinical importance, frailty is frequently under-assessed

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in routine practice. In many cases, frailty is evaluated for the first time during hospitalization, often in the context of severe uremia or acute clinical deterioration. Under such conditions, frailty scores may be artificially elevated compared with measurements obtained earlier in CKD, when glomerular filtration rate (GFR) is higher and metabolic disturbances are less pronounced.

These considerations raise important concerns regarding the timing and interpretation of frailty assessment in CKD patients. In particular, frailty measured at advanced stages of disease may partly reflect acute, potentially reversible factors, and survival-related selection may change the frailty profile observed over time. Whether this leads to overestimation of the prognostic value of frailty remains a hypothesis.[14]

In Georgia, a substantial proportion of patients initiate dialysis in an unplanned setting ("crash landers"), and systematic frailty assessment remains limited in clinical practice. The objective of this study was to describe changes in CFS scores and frailty-category transitions at baseline and during the 3-, 6-, and 12-month intervals across three treatment trajectories: stable dialysis, stable comprehensive conservative care (CCC), and treatment transition.

METHODS

We conducted a prospective, single-center observational cohort study. The study population comprised patients aged ≥65 years with ESRD at the dialysis decision point. Participants were followed for 12 months from enrollment.

This study is a secondary, exploratory longitudinal analysis of the same prospectively followed single-center cohort previously reported by Metskhvarishvili et al.[15] The earlier report focused on implementing comprehensive conservative care and clinical outcomes across treatment trajectories. In contrast, the present analysis addresses a distinct research question: longitudinal changes in CFS scores, transitions between frailty categories, and their associations with treatment modality and mortality. Baseline cohort characteristics are repeated here to describe the analytic sample and overlap with those reported in the previous publication.

Inclusion criteria were: (i) age ≥65 years, ESRD at the dialysis decision point, (ii) a baseline CFS score ≥5, (iii) a Charlson Comorbidity Index ≥3, and (iv) provision of written informed consent. Patients who declined participation were excluded.

Patients were classified according to their observed treatment trajectory during follow-up rather than baseline modality alone. The stable CCC group remained on comprehensive conservative care, the stable dialysis group remained on hemodialysis or peritoneal dialysis, and the treatment-transition (TT) group changed from CCC to dialysis or vice versa. Hemodialysis and peritoneal dialysis were combined in the stable dialysis group. Participants who transferred to another center remained in the baseline cohort and were censored from subsequent CFS assessments at the time of transfer. Withdrawal from active follow-up was included in the missing/unreachable disposition category.

Frailty was assessed in the nephrology clinic by the study nephrologist using the Clinical Frailty Scale, standard CFS guidance, and clinical experience. Assessments were conducted during clinic encounters and hospitalizations and were recorded at baseline and during the 3-, 6-, and 12-month follow-up intervals. The assessor was aware of the treatment modality, and inter-rater reliability was not evaluated.

For patients who died within the first 90 days, the CFS value recorded for the 3-month interval represented a second assessment performed after baseline and before death, rather than an assessment performed at exactly 3 months. Accordingly, the 3-month interval analysis included the last available pre-death CFS assessment for these patients.

Ethical approval and informed consent

The Tbilisi State Medical University Biomedical Research Ethics Committee approved the study (approval No. 6-2020/83, dated December 14, 2020). Written informed consent was obtained from each participant or caregiver. Patient data were anonymized and maintained confidentially.

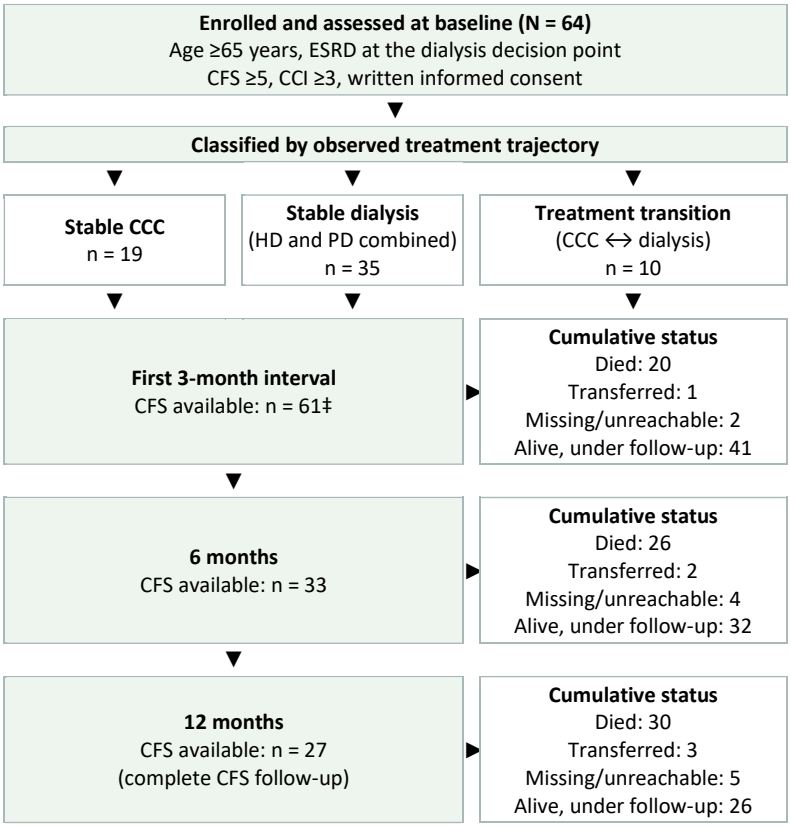
Statistical analysis

Continuous variables were summarized as mean (SD) and median (IQR), and categorical variables as n (%). We evaluated Clinical Frailty Scale scores at baseline and at 3-, 6-, and 12-month intervals in the stable CCC, stable dialysis, and TT groups. Within-participant changes were calculated as the follow-up score minus the baseline score at each assessment interval (baseline to 3, 6, and 12 months). Mean paired changes were estimated using paired t-tests and are reported with 95% CIs and two-sided P values. Positive values indicate increasing frailty and negative values indicate decreasing frailty. Analyses were restricted to participants with observations available at both time

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points; no missing values were imputed. Results were interpreted cautiously and were not intended to establish causal treatment effects or population-level longitudinal trajectories. Statistical significance was assessed at P<0.05. CFS scores were summarized using all available observations at each assessment interval and, for comparison, as mean scores in the complete-case cohort restricted to the 27 participants with CFS values recorded at baseline and during all three follow-up intervals. Transitions between CFS scores at consecutive assessments were summarized as the numbers of participants moving to a lower, the same, or a higher score. Participant flow, deaths, transfers, and missing observations are shown in **Figure 1**.

FIGURE 1. Participant flow and follow-up disposition



Explanations: Numbers of deaths, transfers to another center, and missing/unreachable participants are cumulative from enrollment. Patients who transferred were censored from subsequent CFS assessments at the time of transfer. ‡For the 20 patients who died within 90 days, the 3-month-interval value is the last pre-death CFS assessment obtained after baseline.
Abbreviations: CCC, comprehensive conservative care; CCI, Charlson Comorbidity Index; CFS, Clinical Frailty Scale; ESRD, end-stage renal disease; HD, hemodialysis; PD, peritoneal dialysis.

We examined the association between baseline CFS score and 12-month mortality using univariable logistic regression. We entered 12-month mortality status as the binary outcome and baseline CFS score as a continuous predictor. We reported odds ratios (ORs) with 95% confidence intervals (CIs) for each one-point increase in baseline CFS. We analyzed the overall cohort and, separately, each treatment trajectory. Given the limited cohort and subgroup sizes, we did not perform multivariable adjustment or formally assess model calibration and discrimination. Treatment-specific analyses were considered exploratory.

RESULTS

General description of the cohort

A total of 64 patients were included: 19 (29.7%) in the stable CCC group, 35 (54.7%) in the stable dialysis group, and 10 (15.6%) in the treatment-transition group. The mean age was 79.1 years (SD 6.9), the median age was 79.5 years (IQR 74-84), and the range was 65-92 years. Forty participants (62.5%) were male, and 24 (37.5%) were female. CFS observations during the first 3-month interval were available for 61 participants (95.3%), including 94.7% of the CCC group, 94.3% of the stable dialysis group, and all participants in the treatment-transition group. At 6 and 12 months, observations were available for 33 (51.6%) and 27 (42.2%) participants, respectively (**Fig.1** and **Tab.1**).

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Baseline characteristics by 12-month status and completeness of CFS follow-up are shown in **Table 2**.

TABLE 1. Baseline characteristics of the study cohort by treatment trajectory

Variable	Overall, N=64	Stable CCC, n=19	Stable dialysis, n=35	Treatment transition, n=10
Age, years				
Mean (SD)	79.1 (6.9)	78.9 (6.5)	79.9 (7.3)	77.1 (6.2)
Median (IQR)	79.5 (74.0–84.0)	79.0 (74.0–83.5)	81.0 (75.0–85.5)	79.5 (74.0–80.0)
Minimum–maximum	65.0–92.0	67.0–89.0	65.0–92.0	67.0–84.0
Sex, n (%)				
Female	24 (37.5%)	8 (42.1%)	12 (34.3%)	4 (40.0%)
Male	40 (62.5%)	11 (57.9%)	23 (65.7%)	6 (60.0%)
ESRD etiology, n (%)				
Diabetes mellitus	33 (51.6%)	8 (42.1%)	20 (57.1%)	5 (50.0%)
Hypertension	22 (34.4%)	8 (42.1%)	12 (34.3%)	2 (20.0%)
ADPKD	2 (3.1%)	2 (10.5%)	0 (0.0%)	0 (0.0%)
Unknown	3 (4.7%)	1 (5.3%)	1 (2.9%)	1 (10.0%)
Other	4 (6.3%)	0 (0.0%)	2 (5.7%)	2 (20.0%)
Major comorbidities, n (%)				
Diabetes	33 (51.6%)	8 (42.1%)	20 (57.1%)	5 (50.0%)
Heart failure	41 (64.1%)	10 (52.6%)	24 (68.6%)	7 (70.0%)
Ischemic heart disease	18 (28.1%)	3 (15.8%)	9 (25.7%)	6 (60.0%)
Cerebrovascular disease	11 (17.2%)	5 (26.3%)	4 (11.4%)	2 (20.0%)
Malignancy	10 (15.6%)	4 (21.1%)	6 (17.1%)	0 (0.0%)
Charlson Comorbidity Index				
CCI, mean (SD)	4.7 (1.5)	4.8 (1.4)	4.9 (1.6)	4.2 (1.3)
CCI, median (IQR)	5.0 (4.0–5.3)	5.0 (4.0–5.0)	5.0 (4.0–6.0)	4.0 (3.0–5.0)
CCI, minimum–maximum	3.0–11.0	3.0–8.0	3.0–11.0	3.0–6.0
Age-adjusted CCI, mean (SD)	8.1 (1.4)	8.2 (1.4)	8.3 (1.5)	7.5 (1.4)
Age-adjusted CCI, median (IQR)	8.0 (7.0–9.0)	8.0 (7.0–9.0)	8.0 (7.0–9.0)	7.5 (7.0–8.8)
Kidney function and albumin levels				
eGFR, mL/min/1.73 m², mean (SD)	11.03 (3.87)	13.21 (2.46)	9.77 (3.97)	11.30 (4.08)
eGFR, mL/min/1.73 m², median (IQR)	12.00 (7.75–15.00)	15.00 (11.50–15.00)	10.00 (5.00–13.50)	12.50 (8.25–14.75)
Albumin >35 g/L, n (%)	27 (42.2%)	8 (42.1%)	15 (42.9%)	4 (40.0%)
Albumin 30–35 g/L, n (%)	16 (25.0%)	4 (21.1%)	7 (20.0%)	5 (50.0%)
Albumin 25–<30 g/L, n (%)	16 (25.0%)	5 (26.3%)	10 (28.6%)	1 (10.0%)
Albumin <25 g/L, n (%)	5 (7.8%)	2 (10.5%)	3 (8.6%)	0 (0.0%)
Clinical Frailty Scale				
Mean (SD)	6.94 (1.23)	6.84 (1.26)	7.06 (1.21)	6.70 (1.34)
Median (IQR)	7.0 (6.0–8.0)	7.0 (6.0–8.0)	7.0 (6.0–8.0)	6.5 (6.0–7.8)
Minimum–maximum	5.0–9.0	5.0–9.0	5.0–9.0	5.0–9.0

Explanations: Values are n (%) unless otherwise indicated. No between-group P values are presented. The baseline characteristics describe the same cohort reported previously by Metskhvarishvili et al.[15]

Abbreviations: CCI, Charlson Comorbidity Index; CFS, Clinical Frailty Scale; CCC, comprehensive conservative care; ESRD, end-stage renal disease; eGFR, estimated glomerular filtration rate; IQR, interquartile range; SD, standard deviation.

TABLE 2. Baseline characteristics according to 12-Month status and completeness of clinical frailty scale follow-up

Characteristic	12-month status		CFS follow-up	
	Alive and under follow-up n=26	Deceased n=30	Complete CFS follow-up n=27	Incomplete CFS follow-up n=37
Age, years, mean (SD)	77.2 (6.8)	81.9 (6.1)	76.7 (6.5)	81.0 (6.7)
Female sex	9 (34.6%)	12 (40.0%)	9 (33.3%)	15 (40.5%)
Baseline CFS, median (IQR)	7.0 (6.0-8.0)	8.0 (6.0-8.0)	7.0 (6.0-8.0)	8.0 (6.0-8.0)
CCI, median (IQR)	5.0 (4.0-6.0)	4.0 (4.0-5.0)	5.0 (4.0-6.0)	4.0 (4.0-5.0)
Age-adjusted CCI, median (IQR)	8.0 (7.0-9.0)	8.0 (7.0-9.0)	8.0 (7.0-9.0)	8.0 (7.0-9.0)
eGFR, mL/min/1.73 m², mean (SD)	12.2 (3.1)	9.7 (4.1)	12.6 (2.8)	9.9 (4.2)
ESRD etiology, n (%)				
Diabetes mellitus	17 (65.4%)	12 (40.0%)	18 (66.7%)	15 (40.5%)
Hypertension	5 (19.2%)	15 (50.0%)	4 (14.8%)	18 (48.6%)
ADPKD	2 (7.7%)	0 (0.0%)	2 (7.4%)	0 (0.0%)
Unknown	0 (0.0%)	2 (6.7%)	1 (3.7%)	2 (5.4%)
Other	2 (7.7%)	1 (3.3%)	2 (7.4%)	2 (5.4%)
Major comorbidities, n (%)				
Diabetes	17 (65.4%)	12 (40.0%)	18 (66.7%)	15 (40.5%)
Heart failure	17 (65.4%)	19 (63.3%)	16 (59.3%)	25 (67.6%)
Ischemic heart disease	8 (30.8%)	9 (30.0%)	8 (29.6%)	10 (27.0%)
Cerebrovascular disease	4 (15.4%)	6 (20.0%)	5 (18.5%)	6 (16.2%)
Malignancy	4 (15.4%)	6 (20.0%)	4 (14.8%)	6 (16.2%)
Albumin category, n (%)				
>35 g/L	13 (50.0%)	10 (33.3%)	13 (48.1%)	14 (37.8%)
30-35 g/L	5 (19.2%)	8 (26.7%)	6 (22.2%)	10 (27.0%)
25-<30 g/L	6 (23.1%)	9 (30.0%)	6 (22.2%)	10 (27.0%)
<25 g/L	2 (7.7%)	3 (10.0%)	2 (7.4%)	3 (8.1%)
Treatment trajectory, n (%)				
Stable comprehensive conservative care	9 (34.6%)	7 (23.3%)	9 (33.3%)	10 (27.0%)
Stable dialysis	13 (50.0%)	19 (63.3%)	13 (48.1%)	22 (59.5%)
Treatment transition	4 (15.4%)	4 (13.3%)	5 (18.5%)	5 (13.5%)

Explanations: The 12-month status comparison excludes eight patients whose 12-month status was not directly observed because they transferred to another center or were lost to follow-up. Complete CFS follow-up was defined as recorded CFS values at baseline and during the 3-, 6-, and 12-month assessment intervals.

The malignancy category follows the clinically verified CCI coding used in Table 1.

Abbreviations: CCC, comprehensive conservative care; CCI, Charlson Comorbidity Index; CFS, Clinical Frailty Scale; eGFR, estimated glomerular filtration rate; IQR, interquartile range; SD, standard deviation.

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Clinical frailty scale Scores by treatment trajectory

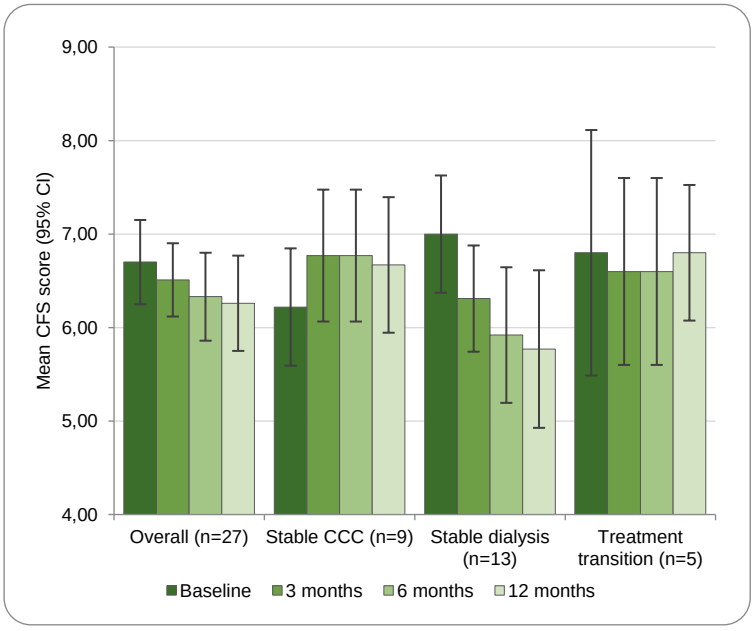
CFS scores are summarized primarily as medians and interquartile ranges because the scale is ordinal. In the overall cohort, the median CFS was 7 (Q1–Q3, 6–8) at baseline, 8 (6–8) during the first 3-month interval, 6 (6–8) at 6 months, and 6 (6–8) at 12 months. The corresponding numbers of observed participants were 64, 61, 33, and 27. In the stable dialysis group, the median CFS declined from 8 (6–9) during the first 3-month interval to 6 (5–7) at 6 months and 6 (4–6) at 12 months. The CCC group had median scores of 7 (6–8), 8 (6–8), 7 (6–8), and 6 (6–8), respectively, whereas the treatment-transition group had median scores of 6 (6–8), 7 (6–8), 7 (7–8), and 7 (6–7), respectively (**Tab.3**). Fig. 2 shows mean CFS scores with 95% CIs in the complete-case cohort of 27 participants assessed at all four time points. For patients who died within 90 days, the value assigned to the 3-month interval was the second post-baseline CFS assessment obtained before death.

TABLE 3. Clinical frailty scale scores and changes from baseline according to treatment trajectory

Assessment	n	Median (Q1–Q3)	Mean (SD)	Change from baseline, mean (95% CI); P*
Overall cohort				
Baseline	64	7 (6–8)	6.9 (1.2)	—
Up to 3 months†	61	8 (6–8)	7.3 (1.3)	—
6 months	33	6 (6–8)	6.5 (1.4)	—
12 months	27	6 (6–8)	6.3 (1.3)	—
Stable CCC				
Baseline	19	7 (6–8)	6.8 (1.3)	—
Up to 3 months†	18	8 (6–8)	7.3 (1.1)	+0.44 (0.05 to 0.83); P=0.028
6 months	9	7 (6–8)	6.8 (1.1)	+0.56 (−0.12 to 1.23); P=0.096
12 months	9	6 (6–8)	6.7 (1.1)	+0.44 (−0.33 to 1.22); P=0.225
Stable dialysis				
Baseline	35	7 (6–8)	7.1 (1.2)	—
Up to 3 months†	33	8 (6–9)	7.3 (1.5)	+0.21 (−0.25 to 0.68); P=0.362
6 months	17	6 (5–7)	6.2 (1.5)	−0.65 (−1.52 to 0.22); P=0.135
12 months	13	6 (4–6)	5.8 (1.5)	−1.23 (−2.44 to −0.02); P=0.047
Treatment transition				
Baseline	10	6 (6–8)	6.7 (1.3)	—
Up to 3 months†	10	7 (6–8)	7.1 (1.2)	+0.40 (−0.62 to 1.42); P=0.399
6 months	7	7 (7–8)	7.1 (1.3)	+0.29 (−1.29 to 1.86); P=0.673
12 months	5	7 (6–7)	6.8 (0.8)	0.00 (−1.96 to 1.96); P=1.000

Explanations: *n, median (Q1–Q3), and mean (SD) are based on all available observations at each interval. *Mean paired change (follow-up minus baseline score) with 95% CI and two-sided P value from paired t-tests among participants with observations at both time points; positive values indicate increasing frailty and negative values decreasing frailty. Paired changes were not estimated for the overall cohort. †For deaths within 90 days, the 3-month-interval value is the second post-baseline CFS assessment obtained before death.*
Abbreviations: CCC, comprehensive conservative care; CFS, Clinical Frailty Scale; CI, confidence interval; SD, standard deviation.

FIGURE 2. Mean Clinical Frailty Scale scores over time in the complete-case cohort (n=27), overall and by treatment trajectory.



Explanations: Error bars indicate 95% confidence intervals. The complete-case cohort includes participants with CFS values recorded at baseline and at the 3-, 6-, and 12-month assessment intervals (stable CCC, n=9; stable dialysis, n=13; treatment transition, n=5); therefore, estimates differ from
Table 3, which summarizes all available observations.
Abbreviations: CCC, comprehensive conservative care; CFS, Clinical Frailty Scale

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Relative to baseline, at 3 months the frailty score increased by 0.44 points in the CCC group (95% CI, 0.05–0.83; P=0.028), while the changes in the dialysis group (+0.21; 95% CI, −0.25–0.68; P=0.362) and transition treatment group (+0.40; 95% CI, −0.62–1.42; P=0.399) were not statistically significant. At 6 months, the CCC group increased by 0.56 points (95% CI, −0.12–1.23; P=0.096), whereas the dialysis group decreased by 0.65 points (95% CI, −1.52–0.22; P=0.135). The change at the same time point in the transition treatment group was +0.29 points (95% CI, −1.29–1.86; P=0.673). At 12 months, the CCC group increased by 0.44 points (95% CI, –0.33 to 1.22; P=0.225), while the dialysis group decreased by 1.23 points (95% CI, −2.44 to −0.02; P=0.047). No change was observed in the transition treatment group at 12 months (0.00; 95% CI, –1.96 to 1.96; P=1.000) (**Tab.3**). Transitions between CFS scores at consecutive assessments were heterogeneous early in follow-up. From baseline to the first 3-month interval (n=61), 9 participants (14.8%) moved to a lower CFS score, 30 (49.2%) remained unchanged, and 22 (36.1%) moved to a higher score. Between 3 and 6 months (n=33), the corresponding numbers were 5 (15.2%), 25 (75.8%), and 3 (9.1%), and between 6 and 12 months (n=27) they were 4 (14.8%), 21 (77.8%), and 2 (7.4%). Most changes after the first 3-month interval involved a single CFS category.

Follow-up disposition and mortality

At the 3-month assessment, 41 patients (64.1%) were alive and remained under follow-up, 20 (31.3%) had died, 1 (1.6%) had transferred to another center, and 2 (3.1%) were missing or otherwise no longer observed. At 6 months, the corresponding numbers were 32 (50.0%), 26 (40.6%), 2 (3.1%), and 4 (6.3%). At 12 months, 26 patients (40.6%) remained alive and under follow-up, 30 (46.9%) had died, 3 (4.7%) had transferred, and 5 (7.8%) were missing or otherwise no longer observed (Fig. 1). During follow-up, 20 patients (31.3% of the baseline cohort) died within the first 3 months. Among the 44 patients who survived beyond 3 months, 6 additional deaths occurred between 3 and 6 months (13.6%). Among the 38 patients who survived beyond 6 months, 4 additional deaths occurred between 6 and 12 months (10.5%). Overall, 30 of 64 participants (46.9%) died during the 12-month follow-up. Twelve-month mortality was 36.8% (7/19) in the stable CCC group, 54.3% (19/35) in the stable dialysis group, and 40.0% (4/10) in the treatment-transition group. By baseline CFS score (5, 6, 7, 8, or 9), mortality was 40.0% (4/10), 37.5% (6/16), 30.0% (3/10), 58.3% (14/24), and 75.0% (3/4), respectively.

In the overall cohort, baseline CFS was not significantly associated with 12-month mortality (OR 1.40 per one-point increase, 95% CI 0.92–2.13; P=0.111). In treatment-specific exploratory analyses, higher baseline CFS was associated with mortality in the comprehensive conservative care group (OR 4.74, 95% CI 1.24–18.18; P=0.023), whereas no statistically significant association was observed in the stable dialysis group (OR 1.27, 95% CI 0.72–2.23; P=0.411) or the treatment-transition group (OR 0.41, 95% CI 0.11–1.56; P=0.192). These subgroup estimates should be interpreted cautiously because of the small sample sizes and wide confidence intervals. All logistic models were unadjusted; the eight participants who transferred or were lost to follow-up without a recorded death were classified as not having died.

DISCUSSION

In this prospective cohort of older, frail, and comorbid patients with ESRD at the dialysis decision point, CFS scores varied over time, and individual patients moved between frailty categories. The overall median CFS increased from 7 at baseline to 8 during the first 3-month interval and was 6 at both 6 and 12 months among those with available observations. These findings indicate that frailty measured at a single late-stage assessment is not necessarily stable. However, because the number and composition of observed participants changed substantially over follow-up, the later scores cannot be interpreted as the trajectory of the original cohort as a whole.

Changes from baseline did not show a uniform pattern across treatment trajectories. The CCC group had a modest increase in CFS from baseline to the first 3-month interval (+0.44; P=0.028), whereas the corresponding changes in the stable dialysis and treatment-transition groups were not statistically significant. No within-group change from baseline to 6 months was statistically significant. From baseline to 12 months, the stable dialysis group showed a decrease in CFS (−1.23; P=0.047), while no statistically significant change was observed in the other groups. Category transitions were heterogeneous between baseline and the first 3-month interval, whereas most participants with paired observations remained in the same CFS category between 3 and 6 months (75.8%) and between 6 and 12 months (77.8%). Given the small paired samples and multiple comparisons, these findings should be regarded as descriptive and exploratory rather than evidence of a treatment effect.

Mortality-related attrition is central to interpreting these patterns. Thirty participants (46.9%) died during 12 months, including 20 deaths within the first 3 months, and complete CFS follow-up was available for only 27 of 64 participants. Patients who were alive and still under follow-up at 12 months were younger at

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baseline than those who died (mean age, 77.2 vs 81.9 years), had a lower median baseline CFS (7 vs 8), and had a higher mean eGFR (12.2 vs 9.7 mL/min/1.73 m²) (**Tab.2**). Similar differences were observed between participants with complete and incomplete CFS follow-up. In addition, the complete-case mean CFS during the first 3-month interval (6.51) was lower than the mean of all available observations at that interval (7.3), indicating that participants who subsequently died or left follow-up had higher frailty scores (**Tab.3** and **Fig.2**). Thus, later assessments increasingly represented a younger and clinically different subset of the original cohort. This pattern is compatible with informative attrition and survivor-related selection, although it does not quantify the extent to which either process influenced the observed CFS changes.[14]

Baseline CFS was not significantly associated with 12-month mortality in the overall cohort (OR 1.40 per one-point increase, 95% CI 0.92-2.13; P=0.111). The association observed in the CCC subgroup (OR 4.74, 95% CI 1.24-18.18; P=0.023) was not reproduced in the stable dialysis or treatment-transition groups. Because the subgroup samples were small, the confidence interval for the CCC estimate was wide, and the models were unadjusted, the treatment-specific findings should be viewed as hypothesis-generating. They do not establish that the prognostic performance of CFS differs by treatment trajectory.

Several mechanisms may contribute to lower observed CFS scores at later time points. Correction of uremia, fluid overload, metabolic acidosis, inflammation, or other reversible illness after treatment stabilization could result in genuine functional improvement. Conversely, selective death or loss of participants with greater frailty could lower the average score among those remaining under observation. Regression to the mean, differences in the clinical context of assessment, and non-random treatment selection may also contribute. Although repeated frailty assessment is therefore clinically informative, the present data cannot distinguish the relative contribution of these mechanisms or support a causal comparison between treatment strategies.[12,13,15,16] Previous longitudinal studies have likewise shown that frailty in patients receiving hemodialysis can improve or worsen over time,[17] that CFS scores vary over the first year of dialysis and that worsening scores are associated with mortality,[18] and that transitions between frailty states are common among older adults.[19]

These results have implications for using frailty in dialysis decision-making. CFS can contribute clinically relevant information, but a score obtained when a patient is acutely unwell or approaching kidney replacement therapy may partly reflect a transient state. Earlier assessment, documentation of the clinical context, and reassessment after stabilization may provide a more complete picture than reliance on a single measurement. At the same time, the present study does not directly demonstrate that a late-stage CFS assessment overestimates prognostic risk; rather, it supports this as a plausible hypothesis that requires validation through models comparing the predictive performance of CFS measured at different time points.[18]

This study has several strengths, including prospective follow-up, repeated CFS assessment, presentation of medians and interquartile ranges for the ordinal CFS, individual CFS transitions between consecutive assessments, and detailed reporting of deaths, transfers, missing observations, and baseline characteristics according to survival and follow-up completeness. Important limitations remain. The study was conducted at a single center and included only 64 patients, all aged 65 years or older, with baseline CFS scores of at least 5 and CCI scores of at least 3. The findings therefore apply specifically to an older, frail, comorbid ESRD population at the dialysis decision point and should not be generalized to all patients with advanced CKD or ESRD. Treatment allocation was not randomized, repeated-measures analyses were limited to available paired observations, missing values were not imputed, and death represents an outcome that cannot be treated as ordinary missingness.[20] Overall, the findings show that observed frailty scores and frailty categories changed during follow-up in this selected ESRD cohort. The apparent reduction in CFS among later survivors, particularly in the stable dialysis group, may reflect a combination of clinical stabilization and survival-related selection. These results support cautious interpretation of single late-stage frailty measurements and favor repeated assessment, while emphasizing the need for larger studies using longitudinal methods that can address informative dropout and death.

CONCLUSIONS

In older, frail patients with ESRD, the Clinical Frailty Scale should be interpreted in relation to when and under what clinical conditions it is assessed. CFS values obtained at the dialysis decision point were not fixed during subsequent follow-up, indicating that assessment timing may materially influence the clinical picture. Recording the assessment context and repeating CFS after stabilization may strengthen its usefulness for prognosis and shared decision-making. These exploratory findings require confirmation in larger longitudinal studies that account for death and informative dropout.

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