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Changes in Symptom Burden and Physical Performance with Initiation of Dialysis in Patients with Chronic Kidney Disease

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To the Editor

The optimal timing of initiation of maintenance dialysis in patients with end stage renal disease (ESRD) is not currently known.¹ Recent clinical trial results have challenged the established paradigm of using estimates of glomerular filtration as the primary guide for initiation of maintenance dialysis.² Even though clinical practice guidelines recommend using symptom burden to guide the decision to start dialysis, no published study has reported on the longitudinal changes in symptom burden and physical performance of community-dwelling adults with chronic kidney disease (CKD) through the transition to ESRD.^{3–5} Such data are critical to adequately inform clinical decision making as it is presently not known which symptoms or physical performance measures might consistently improve with initiation of dialysis. In this study, we investigated changes in symptom burden and measures of physical performance before and after the initiation of chronic dialysis.

Participants were identified from the Seattle Kidney Study (SKS), a clinic-based prospective cohort study of CKD based in Seattle, WA.⁶ Annually during follow-up, study participants were administered the Kidney Disease Quality of Life (KDQOL) questionnaire, a self-report measure of health status that includes a generic core (SF-36) combined with number of multi-item scales targeted at areas of concern for patients with kidney disease.⁷ Physical performance data including the Short Physical Performance Battery (SPPB), timed-get-up-and-go, 6 minute walk distance, and lung spirometry were also collected annually. Of the 682

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participants enrolled in SKS, we identified 53 participants who initiated hemodialysis or peritoneal dialysis during the study and had at least one completed KDQOL assessment pre-dialysis. Of these, 32 completed a follow-up assessment post-dialysis (Figure S1).

The primary outcome was change in the KDQOL symptom/problem score, which is calculated from responses to 12 items that query respondents about kidney-disease specific symptoms, and has been shown to have robust psychometric properties.⁸ Secondary outcomes were changes in other KDQOL/SF-36 scores, in specific symptoms, and in physical performance measures. Change scores were calculated as the difference in measurements obtained from the last visit with complete data prior to dialysis initiation and the first visit with complete data post-initiation. Mean scores pre- and post-initiation for each outcome were compared using a two-sided paired t test. P-values of <0.05 were considered significant. Our sample size of 32 participants provided 80% power to detect a 10 point change in the primary outcome KDQOL symptom/problem score.

The mean time from the baseline study visit to dialysis initiation was 171 days (IQR 138, 315), and from dialysis initiation to the follow-up visit was 198 days (IQR 84, 302). Hemodialysis was the initial dialysis modality for 30 of the 32 participants, with the remaining 2 individuals initiating peritoneal dialysis. Characteristics of the study cohort at the baseline study visit prior to dialysis initiation are shown in Table 1. Overall, there was no significant change in the primary outcome, the KDQOL symptom/problem score, from baseline to post-dialysis initiation follow-up (P=0.60) (Table 2). Of the secondary outcome KDQOL scales, only the physical functioning score showed a significant change between the baseline and follow-up visit, improving by 10.9 points (P=0.03). Most specific symptoms examined did not show significant change over the study period. There was, however, a significant improvement in self-reported shortness of breath (P=0.01). There was a clinically meaningful decrease in SPPB score; however, this also did not reach statistical significance (P=0.08). No other objective measure of physical function, including measures of lung function, demonstrated a clinically meaningful or statistically significant change from baseline.

Our study has some limitations. First, approximately 40% of the subjects who initiated dialysis with a completed baseline KDQOL did not return for follow-up assessment, which may have introduced bias. Second, the number of eligible study participants was small and follow-up time variable between assessments, increasing the chance of null results. In particular, our study was underpowered to detect small but clinically significant differences in the KDQOL subscores, determined in prior studies to be 3-5 points.⁸ Non-significant P values for comparisons of mean scores pre- and post-initiation should thus be interpreted with caution. Finally, the KDQOL was developed in patients undergoing maintenance dialysis, and may not accurately capture symptom burden in the non-dialysis dependent CKD population. Newer instruments are needed that are specifically developed to measure symptoms present in patients with advanced CKD.

Notwithstanding these limitations, our findings represent the first examination of changes in symptom burden and physical performance in a cohort of community-dwelling adults who initiate chronic renal replacement therapy. We found that a composite measure of symptom

burden did not change with dialysis initiation, an observation that is consistent with prior cross-sectional studies that have demonstrated that the range, severity, and prevalence of symptoms are similar in advanced CKD and ESRD.^{9,10} However, our results suggest that there may be individual symptoms that do consistently improve. Additionally, we found that though patients' self-reported physical functioning may improve following dialysis initiation, objective physical performance does not increase in parallel. There is a compelling need for further research to better define the spectrum of changes in symptom burden and physical performance among patients started on maintenance dialysis. Such research will crucially inform the discussion between clinicians and patients in the shared-decision making process around the timing of dialysis initiation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of study participants at study visit prior to dialysis initiation

Age (yr)	55 ± 13
Male Sex	34 (75)
Race, n (%)	
White	15 (47)
Black	12 (38)
Asian/Pacific Islander	2 (6)
American Indian/Native Alaskan	1 (3)
Other	2 (6)
Current smoking	4 (13)
Body mass index (kg/m ²)	32 ± 7
Systolic BP (mmHg)	142 ± 20
Blood laboratory results	
Potassium (mmol/l)	4.7 ± 0.7
Calcium (mg/dl)	8.6 ± 1.2
Phosphorus (mg/dl)	5.1 ± 1.2
Creatinine (mg/dl)	5.1 ± 2.2
C-reactive protein (mg/L)	1.5 (0.6, 4.6)
Urine laboratory results	
Albumin to creatinine ratio (mg/g)	1614 (163, 3417)
Kidney function (eGFR ml/min/1.73m²)	
CKD-EPI Creatinine	14 ± 7
CKD-EPI Cystatin C	20 ± 7
Medications	
Angiotensin-converting enzyme inhibitor	12 (38)
Angiotensin II receptor blocker	11 (34)
Statin	18 (56)
Antidepressant medication	9 (28)
Prevalent disease	
Coronary artery disease	12 (38)
Cerebrovascular disease	3 (9)
Diabetes	19 (59)
Hypertension	32 (100)

* Values for categorical variables given as *n* (%), whereas values for continuous variables given as mean ±SD or median (IQR) as appropriate

Table 2

KDQOL scores, physical performance, and lung function pre- and post-initiation of dialysis

Outcome	Pre-initiation	Post-initiation	Change score	P value ^a
KDQOL Subscores^b (n=32)				
Symptom/Problem Score	64.6 ± 19.6	66.5 ± 17.9	1.9 ± 19.9	0.60
Cognition score	71.0 ± 26.5	69.4 ± 21.2	-1.7 ± 24.9	0.71
Sleep score	51.1 ± 18.9	48.8 ± 23.6	-2.3 ± 21.7	0.57
SF-36 Subscores^b (n=29)				
General health score	38.1 ± 21.2	35.5 ± 21.0	-2.5 ± 19.4	0.49
Energy-fatigue score	37.0 ± 21.7	38.4 ± 22.7	1.4 ± 25.3	0.77
Physical functioning score	42.6 ± 27.8	53.5 ± 27.3	10.9 ± 25.9	0.03
Pain score	53.3 ± 32.1	57.3 ± 28.8	3.9 ± 25.4	0.41
Specific symptoms^c (n=32)				
Muscle soreness	2.7 ± 1.2	2.5 ± 1.1	-0.2 ± 1.3	0.51
Chest pain	1.6 ± 0.8	1.5 ± 0.9	-0.03 ± 1.1	0.88
Cramps	2.3 ± 1.3	2.8 ± 1.2	0.5 ± 1.6	0.07
Itchy skin	2.7 ± 1.5	2.7 ± 1.4	0.06 ± 1.5	0.82
Dry skin	2.8 ± 1.4	2.7 ± 1.3	-0.1 ± 1.4	0.62
Shortness of breath	2.6 ± 1.2	2.0 ± 0.9	-0.6 ± 1.4	0.01
Faintness or dizziness	1.9 ± 1.1	2.0 ± 1.2	0.06 ± 1.5	0.81
Lack of appetite	2.0 ± 0.9	2.2 ± 1.3	0.2 ± 1.3	0.42
Feeling washed out	3.1 ± 1.3	2.7 ± 1.4	-0.4 ± 1.8	0.19
Numbness	2.7 ± 1.6	2.4 ± 1.3	-0.31 ± 1.2	0.16
Nausea	2.1 ± 1.3	2.2 ± 1.1	0.03 ± 1.3	0.89
Physical performance scores				
SPPB total score ^d (n=27)	9.0 ± 3.2	7.6 ± 4.4	-1.4 ± 3.9	0.08
TUAG (seconds) (n=17)	10.0 ± 2.7	10.7 ± 2.3	0.7 ± 1.7	0.11
6 minute walk (meters) (n=12)	394 ± 67	402 ± 103	7.5 ± 57	0.66
Lung function scores (n=29)				
FEV1 (L)	2.1 ± 0.8	2.2 ± 0.6	0.09 ± 0.6	0.43
FVC (L)	2.8 ± 1.1	2.8 ± 1.0	0.05 ± 0.6	0.64

* Data are reported as mean ±SD; abbreviations: SPPB, short physical performance battery; TUAG, timed-up-and-go; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity

^aP value for two sided paired t test

^bScale 0-100, with higher score representing better quality of life

^cScale 1-5, with higher scores representing more burdensome symptoms

^dScore range 0 (worst performance) to 12 (best performance)