

Item S1: Supplemental Methods for Endothelial Function and Heart Rate Variability

Endothelial function

We measured the reactive hyperemia index with peripheral arterial tonometry (RHI-PAT), a non-invasive measure of endothelial function, using the EndoPAT 2000 (Itamar Medical). Patients were asked to avoid caffeine and tobacco for at least 8 hours prior to assessment. The pulse amplitude in the middle fingers of both hands was recorded for five minutes. A blood pressure cuff was then inflated in one arm (which did not have a vascular access in place) to at least 60 mmHg above systolic blood pressure to achieve full occlusion (minimum 200 mmHg, maximum 300 mmHg). After occlusion for 5 minutes, the cuff was deflated, and the device recorded changes in pulse amplitude for an additional 5 minutes and calculated RHI as the ratio of the post to pre occlusion amplitude of the occluded arm relative to the post to pre occlusion amplitude of the control arm, corrected for baseline vascular tone.

Heart Rate Variability

During the five minutes of baseline recording for endothelial function testing, we also assessed time and frequency domain measures of heart rate variability.¹ Specifically, we ascertained the SDNN (standard deviation of NN intervals, the interval between normal R-R peaks on an electrocardiography waveform) and the LF/HF (ratio of low to high frequency power). The LF band primarily represents baroreceptor activity during rest,² whereas the HF band is an indicator of parasympathetic activity and respiratory variation.³ Although these parameters were originally derived from 24-hour recordings, they have been validated over shorter intervals, including 5 minutes.⁴ Patients who had baseline arrhythmia were excluded from analyses of HRV (n=10).

Table S1. Demographics of patients included and excluded from the study

Characteristic	Included (N=60)*	Excluded (N=63)*
Age, years	58 (53, 66)	59 (60, 68)
Sex, % male	78	70
Hispanic, %	17	21
Race, %		
White	15	13
Black	42	30
Asian	20	24
Native Hawaiian/Pacific Islander	8	11
More than one race	7	2
Other/Unreported	8	20
Modality	48 HD, 12 PD	53 HD, 10 PD

*Values Reported as Median (25th, 75th percentile).

Table S2. Step Counts, Physical Function, Questionnaire Scores, Endothelial Function, and Heart Rate Variability in 48 Hemodialysis Patients and 12 Peritoneal Dialysis Patients (raw data and un-modeled, unadjusted differences in change between groups)

	Baseline*		3 Months*		6 Months*		Difference in change between groups, from Baseline to 3 months		Difference in change between groups, from Baseline to 6 months		Difference in change between groups, from 3 months to 6 months	
	Control (N=30)	Intervention (N=30)	Control (N=26)	Intervention (N=27)	Control (N=28)	Intervention (N=27)	Difference (95% CI)	p-value*	Difference (95% CI)	p-value**	Difference (95% CI)	p-value*
Primary outcome (±SD)												
Average Daily Step Count ***	3579 (±3680)	3924 (±3422)	3488 (±3292)	5863 (±4019)	4206 (±3736)	4141 (±3737)	2257 (1001, 3513)	<0.01	16 (-1229, 1262)	0.9	-2290 (-1072,-3509)	<0.01
SPPB Score	10.0 (±1.8)	10.0 (±1.8)	9.9 (±2.0)	10.0 (±2.1)	10.5 (±1.5)	9.7 (±2.2)	-0.04 (-0.69, 0.77)	0.9	-0.68 (-1.50, 0.14)	0.1	-0.71 (-1.46, 0.05)	0.07
PF Score	64.3 (±26.6)	61.4 (±28.2)	63.7 (±24.3)	60.2 (±25.4)	64.4 (±29.9)	52.5 (±28.0)	-1.27 (-9.89, 7.34)	0.8	-10.66 (-24.4, 3.04)	0.1	-4.47 (-16.42, 7.47)	0.45
DSI Total Symptom Burden	9.2 (±4.4)	9.3 (±6.2)	9.2 (±5.7)	10.5 (±7.2)	7.1 (±4.8)	11.7 (±6.6)	1.31 (-1.03, 3.66)	0.3	4.98 (2.68, 7.27)	<0.01	2.69 (0.02, 5.37)	0.05
DSI Total Symptom Severity	28.2 (±17.5)	30.9 (±23.0)	29.0 (±20)	34.6 (±26.4)	20.3 (±15.3)	28.4 (±26.7)	2.31 (-6.38, 11.01)	0.6	16.89 (8.16, 25.61)	<0.01	11.29 (3.42, 19.15)	<0.01
CESD Total Score	7.9 (±7.3)	9.0 (±11.9)	6.6 (±6.5)	11.3 (±12.4)	8.2 (±7.8)	13.3 (±10.6)	2.54 (-1.32, 6.40)	0.2	3.27 (-1.96, 8.50)	0.2	0.38 (-4.87, 5.62)	0.89
Vitality Score	52.2 (±26.2)	56.7 (±28.5)	52.7 (±26.3)	55.6 (±25.8)	59.0 (±25.9)	47.8 (±25.6)	2.73 (-9.13, 14.59)	0.65	-13.96 (-26.26,-1.66)	0.03	-13.12 (-26.29, 0.04)	0.05
RHI	1.61 (±0.56)	1.75 (±0.46)	1.54 (±0.51)	1.75 (±0.75)	1.61 (±0.62)	1.59 (±0.78)	0.16 (-0.24, 0.56)	0.4	-0.1 (-0.65, 0.45)	0.71	-0.29 (-0.86, 0.28)	0.3
SDNN	24.71 (±17.19)	19.02 (±17.95)	20.76 (±11.08)	31.31 (±36.14)	27.76 (±19.47)	32.10 (±23.89)	14.97 (1.78, 28.16)	0.03	9.89 (-5.49, 25.3)	0.20	5.15 (-24.14, 13.84)	0.6
LF/HF	0.92 (±0.87)	0.94 (±0.93)	0.98 (±1.19)	1.03 (±1.22)	0.74 (±0.63)	0.92 (±0.93)	-0.11 (-0.96, 0.74)	0.8	0.05 (-0.58, 0.68)	0.9	0.19 (-0.69, 1.08)	0.7

*Values reported as mean ± SD.

**Difference in change calculated by two-sample t test with equal variances, not modeled or adjusted

***Average daily step count was calculated by averaging individual daily step counts over the week prior to each assessment.

†SPPB, Short Physical Performance Battery; PF, Physical Functioning Scale of the SF-36; DSI, Dialysis Symptom Index; CESD, Centers for Epidemiologic Studies Depression Scale.

‡Endothelial Function and Heart Rate Variability recorded in 40 HD patients and 10 PD patients without arrhythmia. RHI, Reactive Hyperemia Index; SDNN, Standard Deviation of N-N intervals; LF/HF, Ratio of Low Frequency Power to High Frequency Power.

Table S3. Activity-Relevant Subset of DSI and Individual Symptoms on the DSI in 48 Hemodialysis Patients and 12 Peritoneal Dialysis Patients (raw data and un-modeled, unadjusted differences in change between groups)

	Baseline*		3 Months*		6 Months*		Difference in change between groups, from Baseline to 3 months		Difference in change between groups, from Baseline to 6 months		Difference in change between groups, from 3 months to 6 months	
	Control (N=30)	Intervention (N=30)	Control (N=26)	Intervention (N=27)	Control (N=28)	Intervention (N=27)	Difference (95% CI)	p-value*	Difference (95% CI)	p-value*	Difference (95% CI)	p-value*
Symptom or Score (±SD) ***												
"Activity-Relevant" DSI Symptom Burden	2.8 (±1.5)	2.6 (±1.9)	3.0 (±1.6)	2.7 (±1.9)	2.3 (±1.5)	3.0 (±1.9)	-0.07 (0.97, 0.83)	0.9	0.99 (-0.03, 2.02)	0.06	0.72 (-0.17, 1.62)	0.1
"Activity-Relevant" DSI Symptom Severity	9.3 (±5.9)	9.5 (±7.5)	9.2 (±5.7)	9.6 (±7.6)	7.1 (±5.4)	10.9 (±7.9)	-0.14 (-3.14, 2.85)	0.9	3.77 (0.47, 7.07)	0.03	2.77 (0.03, 5.51)	0.05
Cramping	2.3 (±1.7)	2.5 (±1.8)	2.4 (±1.6)	2.3 (±1.7)	2.4 (±1.7)	2.4 (±1.8)	-0.15 (-1.07, 0.76)	0.7	-0.08 (1.38, 1.13)	0.9	-0.27 (-1.33, 0.79)	0.6
Muscle Soreness	0.7 (±1.5)	0.9 (±1.7)	0.8 (±1.4)	0.7 (±1.5)	0.8 (±1.6)	1.3 (±1.8)	-0.26 (-1.16, 0.63)	0.6	0.42 (-0.69, 1.54)	0.5	0.46 (-0.69, 1.62)	0.4
Bone and Joint Pain	1.9 (±2.1)	1.7 (±2.2)	1.2 (±1.8)	1.6 (±2.2)	0.8 (±1.5)	1.6 (±2.2)	0.60 (-0.37, 1.55)	0.2	1.08 (0.07, 2.09)	0.04	0.37 (-0.47, 1.20)	0.4
Fatigue (feeling tired or low energy)	2 (±1.6)	1.8 (±1.9)	2.0 (±1.6)	2.3 (±1.6)	1.5 (±1.6)	2.6 (±1.7)	0.31 (0.51, 1.13)	0.45	1.26 (0.40, 2.13)	<0.01	0.70 (-0.14, 1.53)	0.1
Insomnia (Trouble falling or staying asleep)	1.6 (±1.8)	1.6 (±1.8)	1.8 (±1.7)	1.5 (±1.9)	1.3 (±1.5)	2.0 (±1.9)	-0.49 (-1.64, 0.67)	0.40	0.57 (-0.49, 1.62)	0.29	1.01 (-0.01, 2.04)	0.05

* Values reported as mean ± SD.

** Difference in change calculated by two-sample t-test with equal variances, not modeled or adjusted

*** DSI, Dialysis Symptom Index

Table S4. Activity-Relevant Subset of DSI and Individual Symptoms on the DSI in 48 Hemodialysis Patients and 12 Peritoneal Dialysis Patients (modeled through mixed effects linear regression analysis)

	Difference in change between groups, from baseline to 3 months*		Difference in change between groups, from baseline to 6 months*		Difference in change between groups, from 3 to 6 months*	
	Difference (95% CI)	p-value**	Difference (95% CI)	p-value**	Difference (95% CI)	p-value**
Symptom or Score***						
"Activity-Relevant" DSI Symptom Burden	-0.08 (-1.03, 0.88)	0.9	0.74 (-0.14, 1.62)	0.1	0.71 (-0.25, 1.67)	0.2
"Activity-Relevant" DSI Symptom Severity	-0.17 (-3.21, 2.87)	0.9	3.55 (0.68, 6.43)	0.02	2.72 (-0.36, 5.8)	0.08
Cramping	-0.15 (-1.20, 0.90)	0.8	-0.1 (-1.11, 0.91)	0.8	-0.24 (-1.3, 0.83)	0.7
Muscle Soreness	-0.28 (-1.36, 0.80)	0.6	0.39 (-0.60, 1.37)	0.4	0.44 (-0.65, 1.54)	0.4
Bone and Joint Pain	0.58 (-0.37, 1.54)	0.2	1.04 (0.15, 1.92)	0.02	0.36 (-0.60, 1.32)	0.5
Fatigue (feeling tired or low energy)	0.43 (-0.37, 1.23)	0.3	1.52 (0.32, 2.71)	0.01	1.26 (0.46, 2.05)	0.02
Insomnia (Trouble falling or staying asleep)	-0.49 (-1.65, 0.66)	0.4	0.54 (-0.47, 1.55)	0.29	1.01 (-0.17, 2.18)	0.09

* Difference in change between groups modeled through mixed effects linear regression analysis, adjusted for sex and by stratification factor (modality).

**p-value for between-group comparison of change, adjusted for sex and by stratification factor (modality).

*** DSI, Dialysis Symptom Index

Table S5. Within-group Changes in Step Counts, Physical Function, Questionnaire Scores, Endothelial Function, and Heart Rate Variability in 48 Hemodialysis Patients and 12 Hemodialysis Patients

	Baseline*		Within-group change from baseline to 3 months*		Within-group change from Baseline to 6 months*		Within-group change from 3 to 6 months*	
	Control (N=30)	Intervention (N=30)	Control (N=26)	Intervention (N=27)	Control (N=28)	Intervention (N=27)	Control (N=28)	Intervention (N=27)
Primary outcome								
Average Daily Step Count **	3579 (±3680)	3924 (±3422)	-125 (±1545)	2132 (±2771)	580 (± 2078)	596 (±2304)	714 (±1741)	-1576 (±2369)
Symptom or Score***								
SPPB Score	10.0 (±1.8)	10.0 (±1.8)	0.1 (±1.1)	0.0 (±1.46)	0.5 (±1.3)	-0.2(±1.6)	0.5 (±1.3)	-0.2 (±1.3)
PF Score	64.3 (±26.6)	61.4 (±28.2)	1.9 (±15.6)	0.7 (± 14.2)	1.8 (±25.8)	-8.9 (±20.0)	-2.9 (±25.2)	-7.4 (±13.2)
DSI Total Symptom Burden	9.2 (±4.4)	9.3 (±6.2)	0.2 (±3.4)	1.5 (±5.0)	-1.9 (±4.6)	3.1 (±3.6)	-1.8 (±4.4)	0.9 (±5.1)
DSI Total Symptom Severity	28.2 (±17.5)	30.9 (±23.0)	2.1 (±16.4)	4.4 (±15.1)	-7.0 (±17.6)	9.9 (±13.5)	-8.0 (±14.3)	3.3 (±13.6)
CESD Total Score	7.9 (±7.3)	9 (±11.9)	-1.0 (±7.7)	1.5 (±5.6)	0.6 (±7.0)	3.8 (±10.8)	1.8 (±9.1)	2.1 (±9.0)
Vitality Score	52.2 (±26.2)	56.7 (±28.5)	0.6 (±23.9)	3.3 (±16.5)	7.7 (±18.5)	-6.3 (±23.5)	4.8 (±20.8)	-8.3 (±24.4)
Surrogate for cardiovascular risk****								
RHI	1.61 (±0.56)	1.75 (±0.46)	-0.03 (±0.62)	0.13 (±0.68)	0.06 (±0.8)	-0.04 (±0.8)	0.12 (±0.58)	-0.17 (±1.06)
SDNN	24.71 (±17.19)	19.02 (±17.95)	-4.10 (±11.93)	10.9 (±38.44)	1.6 (±13.5)	11.5 (±27.2)	6.20 (±14.40)	1.05 (±36.94)
LF/HF	0.92 (±0.87)	0.94 (±0.93)	0.22 (±1.24)	0.11 (±1.26)	-0.06 (±0.65)	-0.01 (±1.00)	-0.33 (±1.21)	-0.14 (±1.40)

*All values reported as mean (±SD)

** Average daily step count was calculated by averaging individual daily step counts over the week prior to each assessment.

*** SPPB, Short Physical Performance Battery; PF, Physical Functioning Scale of the SF-36; DSI, Dialysis Symptom Index; CESD, Centers for Epidemiologic Studies Depression Scale.

****Endothelial Function and Heart Rate Variability recorded in 40 HD patients and 10 PD patients without arrhythmia. RHI, Reactive Hyperemia Index; SDNN, Standard Deviation of N-N intervals; LF/HF, Ratio of Low Frequency Power to High Frequency Power.

Supplementary References

- 1 Linder, J. R. et al. Finger volume pulse waveforms facilitate reliable assessment of heart rate variability, but not blood pressure variability or baroreflex function. *BMC Cardiovascular disorders* 14, 1-8 (2014).
- 2 McCraty, R. & Shaffer, F. Heart Rate Variability: New Perspectives on Physiological Mechanisms, Assessment of Self-regulatory Capacity, and Health risk. *Glob Adv Health Med* 4, 46-61, doi:10.7453/gahmj.2014.073 (2015).
- 3 Quintana, D. S. et al. Resting-state high-frequency heart rate variability is related to respiratory frequency in individuals with severe mental illness but not healthy controls. *Sci Rep* 6, 37212, doi:10.1038/srep37212 (2016).
- 4 Shaffer, F. & Ginsberg, J. P. An Overview of Heart Rate Variability Metrics and Norms. *Front Public Health* 5, 258, doi:10.3389/fpubh.2017.00258 (2017).