Participant Flow

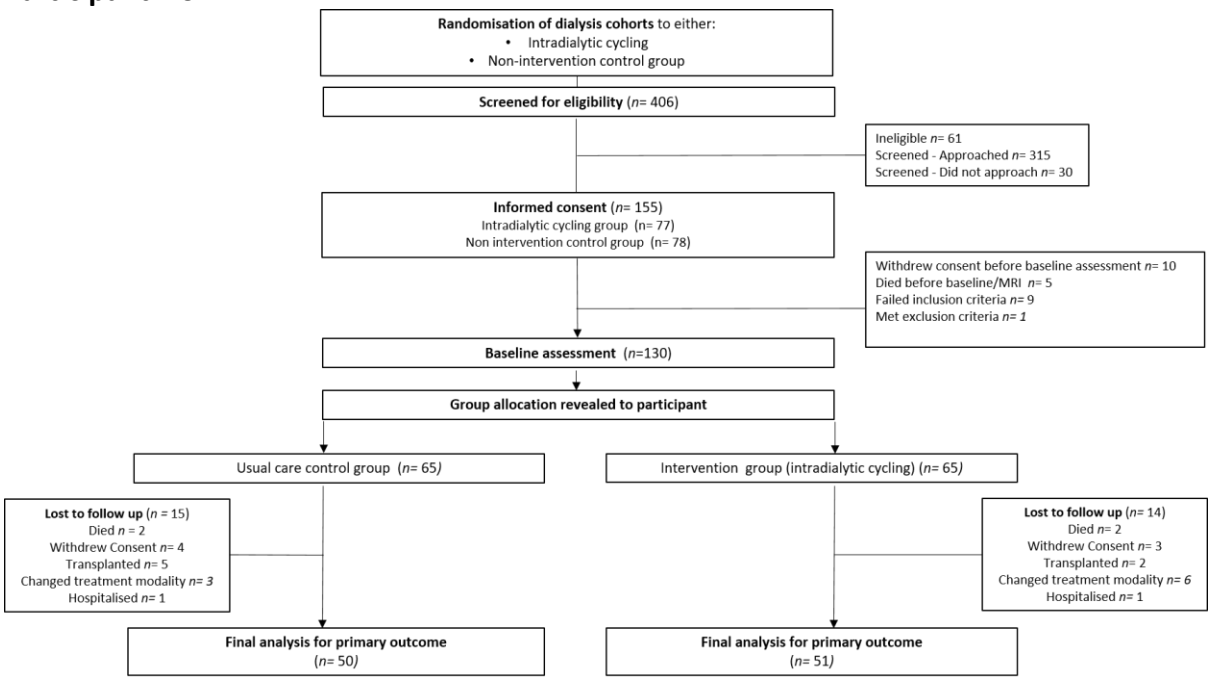

Figure 1. Participant flow through the Cycle-HD trial.

Baseline Characteristics

Table 1.Baseline demographics of Cycle-HD trial population.

	Control group (n=65)	**Intradialytic Exercise Group (n=65)**
Age (years)	58.9 ± 14.9	55.5 ± 15.5
Male sex (%)	53 (81.5%)	42 (64.6%)
Dialysis vintage (years)	1.3 [0.4, 3.2]	1.2 [0.5, 3.7]
Ethnicity?		
White	28 (43.1%)	30 (46.2%)
Mixed	0 (0%)	2(3.1%)
Asian or Asian British	29 (44.6%)	24 (36.9%)
Black or Black British	5 (7.7%)	5 (7.7%)
Other	3 (4.6%)	4 (6.2%)
Inter-dialytic SBP (mm/Hg)	149.3 ± 27.7	140.0 ± 27.8
Inter-dialytic DBP (mm/Hg)	80.8 ± 15.2	80.9 ± 15.5
Predialysis SBP (mmHg)	143.0 ± 20.3	143.1 ± 23.3
Predialysis DBP (mmHg)	75.1 ± 13.6	77.1 ± 14.2
Resting heart rate (bpm)	75.2 ± 11	78.9 ± 12.5
Haemoglobin (g/L)	112 [99, 122]	113 [105, 122]
Ferritin (µg/L)	242 [154, 384] (n=64)	246 [167, 367] (n=64)
Albumin (g/L)	37 (5.2)	36.8 (4.7)
CRP (mg/L)	14 [8, 35] (n=56)	16 [9, 26] (n=48)
Parathyroid hormone (pg/ml)	44.6 [13.9, 77] (n=43)	37.8 [17, 81] (n=41)
Calcium (mmol/L)	2.32 (0.21) (n=64)	2.33 (0.17) (n=65)
Phosphate (mmol/L)	1.55 [1.34, 1.97] (n=65)	1.5 [1.29, 1.96] (n=64)
Total Cholesterol (mmol/L)	3.8 (1.1) (n=50)	4.2 (1.6) (n=52)
Triglycerides (mmol/L)	1.56 [0.97, 2.7] (n=45)	1.46 [0.96, 1.83] (n=38)
HbA1c (%)	5.8 [5.1, 7.1] (n=54)	5.4 [4.9, 6.7] (n=38)
Medications		
Total weekly dose EPO (Units)	7192 (6087)	7179 (7845)
Total weekly dose IV Iron (mg)	228 (782)	212 (659)
ACEi/ARB	12 (18.5%)	16 (24.6%)
Beta-Blocker	35 (53.8%)	37 (56.9%)
Calcium Channel Blockers	29 (44.6%)	29 (44.6%)
Diuretics	17 (26.2%)	10 (15.4%)
Co-morbidities	(n=65)	(n=64)
Ischaemic heart disease	9 (13.8%)	7 (10.9%)
Hypertension	44 (67.7%)	42 (65.6%)
Diabetes mellitus	28 (43.1%)	21 (32.8%)
Atrial Fibrillation	2 (3.1%)	3 (4.7%)
Previous renal transplant	11 (16.9%)	9 (13.8%)

Outcome measures

Table 2. Comparison of changes in primary and secondary outcome measures over time for each treatment group.

	Control Group			Intradialytic Exercise Group			Between group change	
	Baseline	**Follow-up**	**P-value**	**Baseline**	**Follow-up**	**P value**	**Effect (95% CI)**	**P-value**
Cardiac MRI Measures								
Primary Outcome LV Mass (g) (n=101)	116.5 ± 35.9	118.1 ± 37.5	0.40	121.3 ± 45.4	111.3 ± 41	<0.001	-11.1 (-15.8, -6.4)	<0.001
LV Mass (g) (sensitivity) (n=130)	118.8 ± 37.0	123.0 ± 39.2	0.01	123.9 ± 45.5	118.0 ± 43.7	0.002	-9.9 (-14.7, -5.2)	<0.001
LV Mass Index (g/m^2) (n=101)	61.9 ± 18.3	63 ± 18.6	0.38	64.2 ± 22.5	58.7 ± 20.5	<0.001	-6.32 (-9.24, -3.41)	<0.001
LVM/LVEDV (g/ml) (n=101)	0.72 ± 0.15	0.73 ± 0.16	0.60	0.71 ± 0.15	0.65 ± 0.18	0.003	-0.07 (-0.12, -0.02)	0.004
LVEDV (ml) (n=101)	166.7 ± 52	167.6 ± 64	0.8	174.3 ± 61.6	177.3 ± 66.7	0.6	3.49 (-14.22, 21.2)	0.71
LV ejection fraction (%) (n=101)	54.8 ± 80.6	54.9 ± 9.9	0.91	53.1 ± 11.4	55.6 ± 12.2	0.03	2.03 (-0.79, 4.84)	0.16
Additional CMR measures								
aPWV (ms^{-1}) (n=91)	9.13 ± 4.3	9.49 ± 3.8	0.46	9.45 ± 5.4	7.049 ± 2.6	0.01	-2.07 (-3.2, -0.99)	<0.001
Global Native T1 (ms) (n=93)	1268 ± 41	1277 ± 40	0.07	1278 ± 41	1252 ± 46	0.0001	-32.2 (-46.1, -18.3)	<0.001
Septal Native T1 (ms) (n=93)	1288 ± 43	1291 ± 38	0.64	1294 ± 44	1271 ± 48	<0.001	-23.8 (-37.2, -10.3)	<0.001
Non-septal Native T1 (ms) (n=92)	1254 ± 43	1266 ± 46	0.03	1265 ± 39	1235 ± 51	<0.001	-37.5 (-54.3, -20.7)	<0.001
Cardiac biomarkers and blood pressure								
hsTnI (ng/L) (n=96)	20.8 ± 52.2	16.4 ± 28.0	0.59	55.5 ± 190.0	18.2 ± 25.5	0.19	0.86 (-10.8, 12.5)	0.89
NT-ProBNP* (pg/ml) (n=85)	3566.0 [1220.0, 11121.0]	2597.0 [1173.0, 11319.0]	0.44	2515.0 [1015.0, 11443.0]	3721.5.0 [1151.0, 11801.0]	0.46	0.18 (-0.18, 0.54)	0.32
Inter-dialytic SBP (mmHg) (n=89)	153.5 ± 27.5	148.6 ± 31.2	0.26	137.8 ± 27.5	131.8 ± 28.8	0.11	-6.8 (-17.2, 3.6)	0.2
Inter-dialytic DBP (mmHg) (n=89)	79.9 ± 15.9	80.5 ± 16.9	0.8	81.3 ± 15.5	79.3 ± 15.6	0.3	-1.95 (-7.6, 3.7)	0.5
Pre-dialysis SBP (mmHg) (n=107)	142.7 ± 21.4	136.0 ± 34.6	0.12	140.6 ± 21.4	136.6 ± 21.1	0.098	1.32 (-10.5, 13.2)	0.8
Pre-dialysis DBP (mmHg) (n=107)	73.8 ± 14.1	71.3 ± 18.7	0.33	76.4 ± 13.5	73.2 ± 13.0	0.045	0.5 (-5.7, 6.7)	0.9
Measures of physical function and activity								
ISWT (m) (n=77)	271 ± 156	257 ± 170	0.30	278 ± 159	292 ± 176	0.16	28.0 (-3.2, 59.3)	0.08
ESWT (s) (n=74)	510 ± 446	421 ± 448	0.06	410 ± 348	480 ± 420	0.22	136.4	0.06

							(-2.5, 275.2)	
SPPB (n=78)	8.3 ± 3.0	7.7 ± 2.9	0.06	9.6 ± 2.6	9.5 ± 2.9	0.72	0.6 (-0.1, 1.3)	0.08
Step count per day** (n=66)	3514 ± 4099	3080 ± 3445	0.26	2710 ± 1945	3175 ± 2610	0.07	732 (-75, 1539)	0.08
Average METs per day** (n=73)	1.2 ± 0.3	1.2 ± 0.3	0.29	1.2 ± 0.3	1.2 ± 0.3	0.73	0.02 (-0.05, 0.09)	0.58
Measures of quality of life								
EQ5D (n=89)	0.686 (0.292)	0.630 (0.278)	0.08	0.667 (0.292)	0.738 (0.248)	0.04	0.12 (0.01, 0.23)	0.07
SF-12 PCS (n=91)	37.3 ± 10.6	38.0 ± 9.3	0.97	38.3 ± 11.6	38.1 ± 10.5	0.92	0.2 (-3.0, 3.4)	0.9
SF-12 MCS (n=90)	45.8 ± 11.8	46.1 ± 11.3	0.83	46.0 ± 11.3	47.4 ± 12.0	0.33	1.2 (-2.5, 5.0)	0.52

*NT-ProBNP data summarised as median and quartiles; p-values from analysis of log-transformed values; estimated treatment effect reported as the between-group ratio, with 95% CI.

**measured by accelerometer.

g, grams; m, metre; ml, millilitre; ms^{-1}, metre per second; ms, millisecond; ng, nanogram; L, litre; pg, picagram; mmHG, millimetre of mercury; m, metre; s, second.

Adverse Events

Table 3. Serious Adverse Events, where N represents the number of events

	Statistic	All (n=51)	Control Group (n=14)	Intradialytic Exercise Group (n=37)
Event in a subject from baseline population	N_{obs} (N_{miss})	51 (0)	14 (0)	37 (0)
Yes	N (%)	44 (86.3%)	12 (85.7%)	32 (86.5%)
No	N (%)	7 (13.7%)	2 (14.3%)	5 (13.5%)
Event in a subject from the per-protocol population	N_{obs} (N_{miss})	51 (0)	14 (0)	37 (0)
Yes	N (%)	26 (51.0%)	8 (57.1%)	18 (48.6%)
No	N (%)	25 (49.0%)	6 (42.9%)	19 (51.4%)
Seriousness criterion	N_{obs} (N_{miss})	51 (0)	14 (0)	37 (0)
Resulted in death	N (%)	8 (15.7%)	3 (21.4%)	5 (13.5%)
In-patient hospitalisation or prolongation of existing hospitalisation	N (%)	43 (84.3%)	11 (78.6%)	32 (86.5%)
Death	N_{obs} (N_{miss})	51 (0)	14 (0)	37 (0)
Yes	N (%)	9 (17.6%)	4 (28.6%)	5 (13.5%)
No	N (%)	42 (82.4%)	10 (71.4%)	32 (86.5%)
Outcome	N_{obs} (N_{miss})	51 (0)	14 (0)	37 (0)
Resolved	N (%)	41 (80.4%)	10 (71.4%)	31 (83.8%)
Resolved with sequelae	N (%)	1 (2.0%)	0 (0.0%)	1 (2.7%)
Fatal	N (%)	9 (17.6%)	4 (28.6%)	5 (13.5%)
Relation to study	N_{obs} (N_{miss})	51 (0)	14 (0)	37 (0)

Related	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Not related to a trial procedure or intervention	N (%)	51 (100.0%)	14 (100.0%)	37 (100.0%)
Major cardiovascular event	N_{obs} (N_{miss})	51 (0)	14 (0)	37 (0)
No	N (%)	45 (88.2%)	12 (85.7%)	33 (89.2%)
Cardiovascular death	N (%)	1 (2.0%)	0 (0.0%)	1 (2.7%)
Non-fatal myocardial death	N (%)	2 (3.9%)	1 (7.1%)	1 (2.7%)
Non-fatal cerebro-vascular event	N (%)	3 (5.9%)	1 (7.1%)	2 (5.4%)
Days in hospital	N_{obs} (N_{miss})	51 (0)	14 (0)	37 (0)
	Mean (SD)	19.3 (27.9)	23.8 (36.7)	17.5 (24.2)
	Median (IQR)	11.0 [4.0, 18.0]	12.0 [2.0, 18.0]	10.0 [5.0, 18.0]
	Range	(0.0, 136.0)	(0.0, 136.0)	(1.0, 128.0)