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Effect of an exercise rehabilitation program on physical function over 1 year in chronic kidney disease: an observational study

Nicholas Hargrove[1], Quinn Tays[2], Leroy Storsley[1,3], Paul Komenda[1,2,3,4], Claudio Rigatto[1,2,3,4], Thomas Ferguson[1,2], Navdeep Tangri[1,2,3,4] and Clara Bohm[1,2,3,5]

[1]Max Rady College of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada, [2]Chronic Disease Innovation Centre, Seven Oaks Hospital, Winnipeg, Manitoba, Canada, [3]Manitoba Renal Program, Winnipeg, Manitoba, Canada, [4]Department of Community Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada and [5]Health, Leisure and Human Performance Research Institute, Faculty of Kinesiology and Recreation Management, University of Manitoba, Winnipeg, Manitoba, Canada

Correspondence and offprint requests to: Clara Bohm; E-mail: cbohm@hsc.mb.ca

ABSTRACT

Background. Exercise rehabilitation may help maintain physical function in chronic kidney disease (CKD), but long-term clinical effectiveness is unknown. We evaluated the effect of an exercise rehabilitation program on physical function over 1 year in individuals with CKD.

Methods. This clinical program evaluation included adults with CKD (any stage) registered in a provincial renal program from 1 January 2011 to 31 March 2016. Attenders were referred to and attended a 10-week exercise rehabilitation program ($n = 117$). Nonattenders were referred, but did not attend the program ($n = 133$). Individuals enrolled in a longitudinal frailty study ($n = 318$) composed a second control group. Primary outcome: Change in physical function [short physical performance battery (SPPB) score]. Secondary outcomes included change in health-related quality of life, physical activity, exercise behaviour, hospitalization over 1 year. Predictors of improved SPPB were assessed using logistic regression.

Results. In sum, 53, 40 and 207 participants completed 1-year follow-up in attender, nonattender and second control groups, respectively. Baseline median SPPB [interquartile range (IQR)] scores were 10.5 (9–12), 10 (8–12) and 9 (7–11) in attender, nonattender and second control groups, respectively ($P = 0.02$). Mean change in SPPB score over 1 year was not significantly different between groups ($P = 0.7$). Attenders with baseline SPPB score <12, trended toward increased likelihood of improved SPPB score at 1 year [odds ratio (OR) 2.18; 95% confidence interval (CI) 0.95–5.02; $P = 0.07$]. More attenders (60%) exercised regularly at 1 year than nonattenders (35%) ($P = 0.03$).

Conclusions. The impact of clinical exercise rehabilitation programs on physical function at 1 year needs further delineation. However, our observation of improved exercise behaviour at 1 year suggests sustained benefits with such programs in CKD.

INTRODUCTION

Progression of chronic kidney disease (CKD) is associated with declining physical function [1, 2] and impaired health-related quality of life (HRQOL) [3]. Physical activity levels also decline with the progression of CKD [4, 5], reaching lowest levels in end-stage renal disease (ESRD) [6]. Low levels of physical function and physical activity are associated with an increased risk of all-cause mortality and hospitalization, independent of age and comorbidities in this population [7–9]. In addition, higher rates of physical activity have been associated with slower decline of kidney function [10]. Exercise programming is a strategy to increase physical activity behavior and has been shown to improve physical function and HRQOL in clinical trials in CKD [11, 12]. Based on multiple interventional studies, exercise training and increased physical activity appear to be well tolerated and prove to be safe strategies in improving physical function in the CKD population [11]. However, fatigue, lack of motivation, concerns regarding exercise safety and effectiveness, among other barriers, may limit real-life exercise participation in CKD [13, 14].

Exercise rehabilitation programs, combining lifestyle education and exercise, have the potential to promote habitual exercise by increasing physical activity behavior and facilitating chronic disease self-management [15]. A supervised, outpatient-based exercise rehabilitation program was shown to be more effective in improving exercise capacity and exercise time at 6 months than independent/home-based training [16], and has been shown to be a cost-effective intervention in individuals with cardiac and other chronic diseases [17]. However, few evaluations of exercise rehabilitation have been reported specifically in the CKD population [18–22]. Importantly, while several studies show immediate post-intervention benefits to physical function, the real-world effectiveness of an exercise rehabilitation program in preventing decline of physical function and HRQOL in individuals with CKD over time has not yet been reported [18, 19, 21]. Such evidence is needed to build support for the incorporation of exercise rehabilitation programs into standard clinical care for the CKD population.

Since 2007, our center has offered a 10-week exercise rehabilitation program for individuals with CKD. We evaluated the effect of participation in this clinical exercise program on change in physical function over 1 year. We hypothesized that those who attended the program would maintain or improve physical function over 1 year compared with those who did not attend, in whom physical function would decline.

MATERIALS AND METHODS

We conducted a program evaluation using a prospective cohort with quasi-experimental pretest–posttest nonequivalent control design. Our eligible population included all adults with CKD (any stage) who were registered in the Manitoba Renal Program (MRP), Manitoba's sole provider of kidney health services (www.kidneyhealth.ca). Manitoba is a province in Canada, and has a population of ∼1.3 million (Figure 1). This study population was divided into three groups as follows:

(i) The 'exposed group (Attenders)' attended the MRP's Exercise Counseling Clinic from 1 January 2011 to 31 March 2016 and were referred to and attended at least 50% of classes in a 10-week exercise rehabilitation session within a year after their initial counseling clinic appointment. Although free to register for classes at any time, the majority of attenders (91%) attended the next available class session within 3 months of the baseline clinic appointment. Once registered, participants were not contacted or stimulated to adhere to the program in any way other than encouragement during the classes themselves.

(ii) The 'first control group (Nonattenders)' attended the MRP's Exercise Counseling Clinic between 1 January 2011 and 31 March 2016 and were referred to, but did not attend the exercise rehabilitation program. Individuals who attended <50% of exercise rehabilitation program classes were also included in this group.

(iii) The 'second control group (CanFIT Controls)' was composed of individuals with CKD enrolled in the Canadian Frailty Observation and Interventions Trial (CanFIT), a concurrent longitudinal observational study of frailty status. Included to account for the threat of self-selection of a motivated sample in the exercise attender and nonattender groups, CanFIT participants underwent similar assessments to the other study groups, but did not attend exercise counseling or exercise rehabilitation [23].

The University of Manitoba Health Research Ethics Board and Manitoba Health Information Privacy Committee approved this study protocol. Study procedures adhered to the Declaration of Helsinki.

Exercise Counseling Clinic

The MRP Exercise Counseling Clinic is an active clinical program [24]. Briefly, individuals with CKD are referred to the clinic by MRP medical staff. At the clinic, attendees complete several self-reported questionnaires, are assessed for medical contraindications to exercise, undergo a brief battery of physical performance measures and subsequently receive an individualized exercise plan taking individual goals, barriers and resources into consideration [24]. Referral to the MRP's 10-week exercise rehabilitation classes may be part of this plan. Voluntary yearly follow-up appointments are scheduled in the counseling clinic. Individuals also provide voluntary consent for inclusion of their visit data in a research database, from which data were obtained for this project.

Exercise rehabilitation program

Supervised by a Certified Exercise Physiologist and open to individuals with all stages of CKD, the exercise rehabilitation program is a 10-week lifestyle education and exercise class program that aims to increase physical activity behavior,
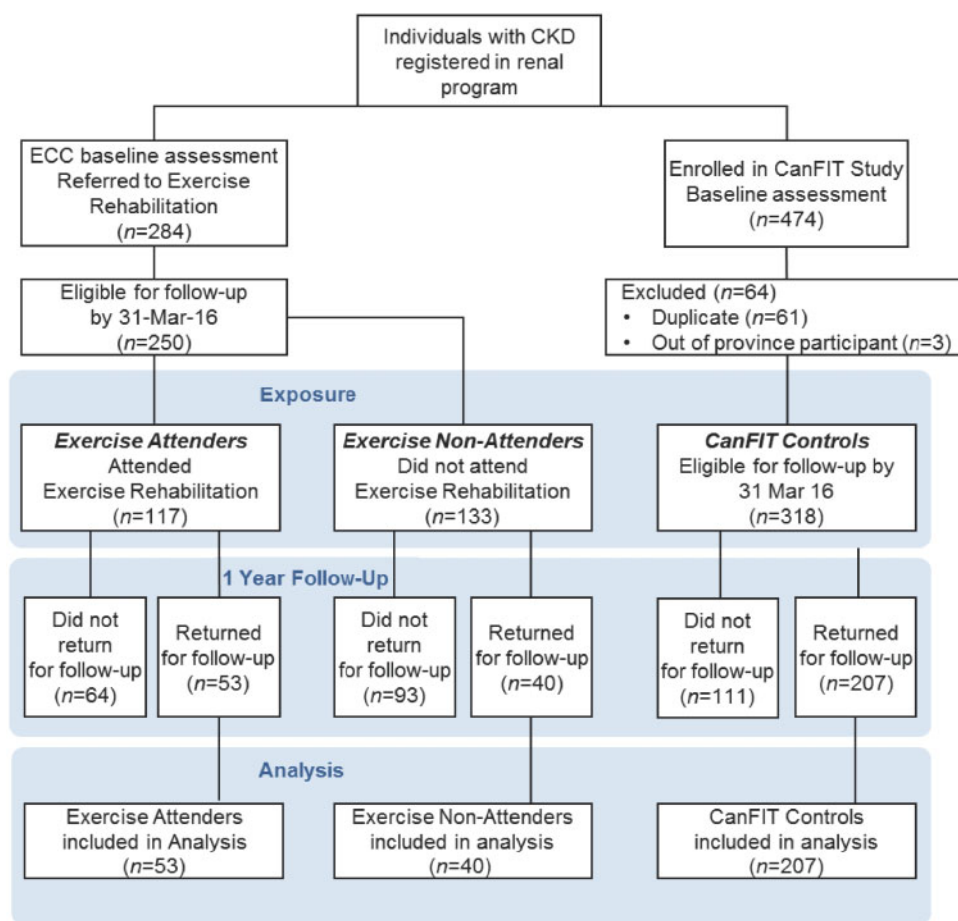
FIGURE 1: Participant flow diagram. Exercise Counseling Clinic (ECC).

engagement in regular exercise and improve CKD self-management practices with the overall goals of improved physical function and better quality of life. Weekly classes consist of 1 h of education (e.g. living with CKD, exercise theory, review of common CKD medications and nutrition, among other topics) and 1 h of group fitness activity. Exercise sessions consist of 30 min of aerobic exercise of the participant's choice, such as fast walking or stationary cycling, targeted to a Borg Rating of Perceived Exertion of 11–13 (somewhat hard) [25] followed by 20 min of strength training using resistance tubing, body weight, free weights or machines and concluding with 10 min of balance exercises and stretching.

Outcome measures

The primary outcome in our study was 'change in physical function' at 1 year as measured by Short Physical Performance Battery (SPPB). The SPPB combines chair stand, balance and 4-m gait speed tests, for a total score ranging from 0 (worst) to 12 (best). [26] The SPPB is a validated measure of lower extremity function in CKD and is predictive of disability, hospitalization and mortality [23, 26–30].

We also included several secondary outcomes as follows:

(i) 'Change in HRQOL' at 1 year measured using the EuroQol™ EQ5D-3L self-reported questionnaire, in which respondents rate their health on a 3-point Likert-type scale across five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression [31]. On the EuroQol Visual Analogue Scale (VAS), respondents report overall perceived health status from 1 ('worst imaginable') to 100 ('best imaginable') [32]. The EQ-5D has been validated in multiple chronic disease populations [31, 33, 34].

(ii) 'Change in self-reported physical activity behavior' at 1 year measured in Attenders and Nonattenders using the Human Activity Profile (HAP). This self-reported 94-item questionnaire identifies activities that the individual is still doing and those that the individual has stopped doing to calculate a Maximal Activity Score (MAS) and Adjusted Activity Score (AAS) [35]. The HAP has been used in CKD and ESRD populations and validated using accelerometry [36, 37]. Additionally, 'the proportion of participants who reported exercising 'regularly' ($\geq$30 min, $\geq$3 times per week) was compared between the exercise attender and exercise nonattender groups at baseline and at 1-year follow-up.

(iii) 'Hospitalization' rate and number of admission days over 1 year were derived from data obtained from the Discharge Admission and Death Hospital Abstracts (Manitoba Health) [38]. The Discharge Admission database contains data on the presenting condition, comorbid conditions, length of stay and outcomes of all hospitalizations in Manitoba.

Data collection and management

Demographic, clinical and outcome data for baseline and 1-year follow-up assessments were obtained from the Exercise Counseling Clinic research database for the exercise attender

Table 1. Comparison of baseline demographics within study group by 1-year follow-up status

Clinical demographics	Exercise attenders			Exercise nonattenders			CanFIT controls		
	Follow-up $n = 53$	No follow-up $n = 64$	P-value	Follow-up $n = 40$	No follow-up $n = 93$	P-value	Follow-up $n = 207$	No follow-up $n = 111$	P-value
Age (years)	63 (12)	67 (12)	0.16	56 (13)	57 (15)	0.7	63 (16)	64 (15)	0.6
BMI (kg/m²)	31.2 (6.5)	30.4 (6.7)	0.5	32.5 (9.2)	30.7 (7.0)	0.3	29.6 (6.1)	29.4 (5.8)	0.8
Race, non-white	23% (10)	19% (11)	0.6	26% (9)	27% (19)	0.9	27% (54)	–	–
Gender, male	51% (27)	58 (37)	0.5	65% (26)	51% (47)	0.1	60% (125)	56% (62)	0.4
Systolic BP (mmHg)	138 (18.2)	143 (23.1)	0.2	138 (23.1)	140 (22.3)	0.6	138 (21.0)	141 (24.0)	0.3
Diastolic BP (mmHg)	75 (12.2)	77 (12.4)	0.4	75 (11.0)	78 (12.7)	0.2	76 (13.3)	74 (12.5)	0.4
Arthritis	38% (20)	39% (25)	0.9	33% (13)	32% (30)	0.9	40% (82)	45% (45)	0.4
Diabetes	57% (30)	45% (29)	0.2	60% (24)	58% (54)	0.8	58% (120)	56% (56)	0.7
High cholesterol	68% (36)	57% (36)	0.2	63% (25)	51% (47)	0.2	61% (126)	55% (55)	0.3
IHD	21% (11)	23% (15)	0.7	23% (9)	35% (33)	0.1	18% (38)	16% (16)	0.6
PVD	13% (7)	9% (6)	0.5	18% (7)	13% (12)	0.5	17% (36)	15% (15)	0.6
Dialysis	25% (13)	30% (19)	0.5	58% (23)	53% (49)	0.6	28% (58)	15% (17)	0.01
Smoker (ever)	34% (18)	41% (26)	0.5	43% (17)	38% (35)	0.6	–	–	–
Walk support	27% (14)	38% (23)	0.2	32% (12)	28% (25)	0.7	28% (21)	38% (15)	0.3
Albumin (g/L)	35 (4.6)	35 (4.8)	0.6	33 (5.8)	33 (5.5)	0.9	36 (5.1)	35 (5.6)	0.3
Calcium corrected (mmol/L)	2.4 (0.2)	2.1 (0.2)	0.9	2.4 (0.2)	2.4 (0.2)	0.3	2.4 (0.2)	2.3 (0.2)	0.7
Creatinine (umol/L)	215 (146–426)	265 (161–469)	0.2	481 (189–785)	445 (181–648)	0.5	306 (210–514)	319 (222–503)	0.4
eGFR—MDRD[a] (mL/min/1.73 m²)	30 (18–40)	24 (18–34)	0.2	24 (16–51)	31 (18–48)	0.8	19 (14–25)	17 (11–22)	0.01
Hemoglobin (g/L)	119 (17.6)	116 (15.1)	0.3	114 (17.9)	113 (18.0)	0.7	114 (15.4)	111 (16.1)	0.09
Phosphate (mmol/L)	1.4 (0.4)	1.4 (0.5)	0.9	1.6 (0.5)	1.5 (0.5)	0.5	1.4 (0.3)	1.5 (0.4)	0.004
PTH (ng/L)	155 (89–236)	168 (76–335)	0.3	176 (118–431)	232 (111–427)	0.7	171 (91–278)	182 (103–335)	0.1

Continuous variables are expressed as mean (SD) or median (IQR). Categorical variables are expressed as % (*n*). Data not collected in a group is indicated with '–'. Data for CHF, hypertension, lung disease and stroke proportions were analyzed but suppressed due to cell values <6, per the Manitoba Centre for Health Policy [38].

[a]eGFR calculated only for those individuals not on dialysis in each group.

BP, blood pressure; CHF, congestive heart failure; eGFR, estimated glomerular filtration rate; IHD, ischemic heart disease; PTH, parathyroid hormone; PVD, peripheral vascular disease.

and nonattender groups and from the CanFIT study database for the CanFIT control group. To prevent duplication, individuals who were referred to the exercise rehabilitation program and were also enrolled in the CanFIT study were included only in the attender or nonattender groups for analysis, depending on program attendance status.

Sample size

Assuming an SD of 1.7, 46 participants in each study group would provide 80% power to detect a clinically significant difference of 1 point in change in SPPB score over 1 year with alpha of 0.05 [39].

Data analysis

Descriptive statistics and comparisons between primary and secondary outcomes were calculated using *t*-tests, analysis of variance, Mann–Whitney *U*-test, Kruskal–Wallis and chi-squared tests as appropriate, depending on the data type, distribution and number of comparisons. Where differences between multiple groups existed, *post hoc* pairwise comparisons were completed using Tukey's method, or a nonparametric equivalent as described by Brunner and Puri [40]. Similar analyses were performed to compare participants who attended 1-year follow-up with those who did not.

To account for ceiling effect in participants with a perfect SPPB score 12 at baseline, the proportion of individuals with baseline SPPB score <12 who improved by ≥1 was compared between those who attended the exercise rehabilitation program and those who did not. To complement this analysis, a logistic

regression model was constructed using study participants with baseline SPPB score <12, similar to a method used by Hardy *et al.* [41] to determine predictors of improvement in SPPB score over time. The primary predictor was exposure to exercise rehabilitation. Other variables added to the model included age, sex, albumin, hemoglobin, diabetes, CKD category (CKD versus dialysis; CKD versus transplant) and total SPPB score at baseline.

A negative binomial regression model was used to compare rate of hospitalization between groups for the year following baseline assessment.

A P-value of <0.05 was considered statistically significant for all analyses. Analyses were performed using SAS® version 9.4 (Carey, NC, USA).

RESULTS

Of 568 eligible individuals, a total of 300 individuals attended 1-year follow-up. Rates of follow-up varied from 30% in exercise nonattenders to 45% in exercise attenders and 65% in the CanFIT controls group (Figure 1). Characteristics of participants who returned for follow-up and those who did not were similar (Table 1). At baseline, measures of physical function, HRQOL and physical activity behavior between participants who returned for follow-up and those who did not were similar (Table 2).

Comparison of groups at baseline

Study groups were generally similar at baseline (Table 3). Nonattenders were younger: mean age 56 years versus 63 years

Table 2. Comparison of baseline outcome measures within groups by 1-year follow-up status

Outcome measures	Exercise attenders			Exercise nonattenders			CanFIT controls		
	Follow-up n = 53	No follow-up n = 64	P-value	Follow-up n = 40	No follow-up n = 93	P-value	Follow-up n = 207	No follow-up n = 111	P-value
SPPB score Total	10.5 (9–12) [52]	11 (9–12) [64]	0.6	10 (8–12) [39]	10 (9–12) [93]	0.4	9 (7–11) [207]	8 (5–11) [111]	0.06
SPPB score (baseline <12)	10 (7–11) [35]	9 (8–11) [39]	0.9	9 (8–10) [29]	9 (8–11) [64]	0.3	8 (5–10) [162]	7 (4–10) [83]	0.04
EQ-5D-VAS	62.8 (18.3) [52]	66.0 (16.7) [54]	0.4	59.6 (18.4) [39]	53.9 (18.8) [85]	0.1	62.1 (19.6) [189]	59.5 (20.3) [85]	0.3
HAP MAS	66.9 (13.7) [51]	68.9 (13.3) [62]	0.5	65.3 (16.5) [38]	65.8 (14.8) [92]	0.9	–	–	–
HAP AAS	57.4 (17.0) [49]	56.3 (17.8) [61]	0.8	50.4 (19.9) [37]	50.8 (21.3) [84]	0.9	–	–	–

Continuous variables are expressed as mean (SD) or median (IQR). Number of participants included in analysis indicated by [n]. Data not collected in a group is indicated with '–'.

Table 3. Baseline demographics by study group

Clinical demographics	Exercise attenders n = 53	Exercise nonattenders n = 40	CanFIT controls n = 207	P-value
Age (years)	63 (12)[a]	56 (13)[b]	63 (16)	0.008
BMI (kg/m^2)	31.2 (6.5)	32.5 (9.2)[b]	29.6 (6.1)	0.03
Race, non-white	23% (10)	26% (9)	27% (54)	0.9
Gender, male	51% (27)	65% (26)	60% (125)	0.3
Systolic BP (mmHg)	138 (18.2)	138 (23.1)	138 (21.0)	0.9
Diastolic BP (mmHg)	75 (12.2)	75 (11.0)	76 (13.3)	0.9
Arthritis	38% (20)	33% (13)	40% (82)	0.7
Diabetes	57% (30)	60% (24)	58% (120)	0.9
High cholesterol	68% (36)	63% (25)	61% (126)	0.7
IHD	21% (11)	23% (9)	18% (38)	0.8
PVD	13% (7)	18% (7)	17% (36)	0.8
Dialysis	25% (13)[a]	58% (23)[b]	28% (58)	<0.001
Smoker (ever)	34% (18)	43% (17)		0.4
Walk support	27% (14)	32% (12)	28% (21)	0.9
Albumin (g/L)	35 (4.6)	33 (5.8)[b]	36 (5.1)	0.04
Calcium corrected (mmol/L)	2.4 (0.2)	2.4 (0.2)[b,c]	2.4 (0.2)	0.007
Creatinine (umol/L)	215 (146–426)[a,c]	481 (189–785)	306 (210–514)	0.002
eGFR—MDRD (mL/min/1.73 m^2)	30 (18–40)[d]	24 (16–51)	19 (14–25)	<0.0001
Hemoglobin (g/L)	119 (17.6)	114 (17.9)	114 (15.4)	0.2
Phosphate (mmol/L)	1.4 (0.4)	1.6 (0.5)	1.4 (0.3)	0.03
PTH (ng/L)	155 (89–236)	176 (118–431)	171 (91–278)	0.4

Continuous variables are expressed as mean (SD) or median (IQR). Categorical variables are expressed as % (n). Data not collected in group is indicated with a blank cell. Data for CHF, hypertension, lung disease, and stroke proportions were analyzed but suppressed due to cell values <6, per the Manitoba Centre for Health Policy [36].
Pairwise comparisons (Tukey's):
[a]Attenders versus nonattenders P < 0.05.
[b]Attenders versus CanFIT controls P < 0.05.
[c]Nonattenders versus CanFIT controls P < 0.05.
[d]Attenders versus CanFIT controls P < 0.0001 (eGFR calculated only for those individuals not on dialysis in each group; pairwise comparison).

in attenders (P = 0.008). Nonattenders had a higher mean body mass index than CanFIT controls (32.5 kg/m^2 versus 29.7 kg/m^2). Baseline kidney function in patients not on dialysis, as measured by median estimated glomerular filtration rate (eGFR), was significantly higher in attenders [30 mL/min/1.73 m^2; interquartile range (IQR) 18–40] than in CanFIT Controls (19 mL/min/1.73 m^2; IQR 14–25) (P < 0.001). The proportion of participants on dialysis at baseline was highest in nonattenders (58%) as compared with attenders (25%) and CanFIT controls (28%) groups (P < 0.001). Attenders and nonattenders reported similar proportions exercising regularly at baseline (40% versus 36%, respectively). Baseline lab values for albumin, calcium and phosphate differed statistically between groups, but the magnitudes of differences were not clinically significant.

Change in physical function

Baseline median SPPB (IQR) scores were 10.5 (9–12), 10 (8–12) and 9 (7–11) in the attender, nonattender and CanFIT control groups, respectively (P = 0.02). These differences persisted at

Table 4. Outcome measures over time by study group

Outcome measures	Baseline				One year				Mean change over 1 year			
	Exercise attenders n = 53	Exercise nonattenders n = 40	CanFIT controls n = 207	P-value	Exercise attenders n = 53	Exercise nonattenders n = 40	CanFIT controls n = 207	P-value	Exercise attenders n = 53	Exercise nonattenders n = 40	CanFIT controls n = 207	P-value
SPPB score Total	10.5[a] (9–12) [52]	10 (8–12) [39]	9[b] (7–11) [207]	0.02	11[c] (9–11) [49]	9 (7–12) [37]	9 (6–11) [204]	0.02	−0.06 (2.30) [48]	−0.38 (1.75) [37]	−0.33 (2.33) [204]	0.7
SPPB score (baseline <12)	10 (7–11) [35]	9 (8–10) [29]	8 (5–10) [162]	0.05	10[b] (9–11) [33]	9 (7–11) [27]	8 (5–10.5) [160]	0.01	0.31 (2.61) [32]	−0.26 (1.83) [27]	−0.23 (2.52) [160]	0.5
EQ-5D-VAS	62.8 (18.3) [52]	59.6 (18.4) [39]	62.1 (19.6) [189]	0.7	62.2 (20.0) [52]	61.3 (20.3) [35]	66.3 (17.9) [202]	0.2	−0.5 (21.3) [51]	0.8 (22.0) [34]	4.4 (21.5) [184]	0.3
HAP MAS	66.9 (13.7) [51]	65.3 (16.5) [38]	X	0.6	69.0 (11.7) [51]	65.1 (17.2) [34]	X	0.2	1.5 (8.4) [49]	0.2 (10.7) [33]	X	0.5
HAP AAS	57.4 (17.0) [49]	50.4 (19.9) [37]	X	0.08	55.2 (17.3) [51]	52.3 (19.9) [33]	X	0.5	−3.0 (9.5) [47]	0.5 (9.2) [31]	X	0.1

Continuous variables are expressed as mean (SD) if normally distributed, or expressed median (IQR) if not normally distributed. X = not measured in CanFIT control group.

Number of participants included in analysis indicated by [n].

Pairwise comparisons:

[a]Exercise attenders versus CanFIT controls P <0.001.

[b]Exercise nonattenders versus CanFIT controls P <0.001.

[c]Exercise attenders versus CanFIT controls P <0.004.

1 year. There was no significant difference in mean change in SPPB score over 1 year between study groups (Table 4).

In the 219 individuals with reduced baseline function (SPPB score <12), 18 of 32 individuals (56%) who attended the exercise program had a clinically significant improvement (1 point) in SPPB score over 1 year, in contrast to 69 of 187 individuals (37%) who did not attend exercise rehabilitation (P = 0.04). Similarly, attenders with low baseline function (SPPB <12) showed a trend to be more likely [odds ratio (OR) 2.18; 95% confidence interval (CI) 0.95–5.02; P = 0.067] to have any improvement in SPPB over 1 year than nonattenders and CanFIT controls (pooled sample) after adjustment for relevant covariates (Table 5).

HRQOL

There was no significant difference between groups in mean EQ-VAS score at baseline and 1 year. Mean change in EQ-VAS score at 1 year did not differ significantly between the exposed and control groups (Table 4). Due to small numbers in cells, a comparison of proportions improving, maintaining or declining in EQ-5D-3L domains between groups could not be completed [38]. Proportion of individuals endorsing any impairment in EQ5D-3L domains was similar in all study groups at baseline and follow-up (Table 6).

Physical activity behavior

Although the proportion of individuals exercising regularly was similar at baseline, a significantly higher proportion of attenders reported regular exercise (59%) at 1 year, as compared with nonattenders (41%) (P = 0.03; Figure 2). There was no significant difference between the attender and nonattender groups in mean HAP MAS or HAP AAS at baseline and 1 year, nor was there any significant difference in mean change in HAP MAS or HAP AAS over 1 year (Table 4).

Hospitalization

No significant difference between study groups in mean number of hospital admission days over 1 year was observed; attenders = 2.1 (SD 5.4); nonattenders = 4.5 (SD 10.0); CanFIT controls = 5.2 (SD 18.9) (P = 0.5). No differences in hospitalization rates over 1 year were noted between study groups (P = 0.6).

DISCUSSION

This pragmatic evaluation of a 10-week clinical exercise rehabilitation program demonstrated no significant difference between study groups in our primary outcome, i.e. mean change in SPPB over 1 year. However, exercise rehabilitation program attendance was associated with a significant increase in exercise participation at 1 year as compared with controls. In addition, subgroup analysis showed a strong signal in individuals with CKD and reduced baseline physical function (SPPB <12), suggesting that participation in a 10-week exercise rehabilitation program may be associated with a clinically meaningful improvement in physical function (SPPB change ≥1 point) compared with those who do not attend the program [39]. Using distribution and anchor-based methods, clinically meaningful change in SPPB has been shown to be in the range 0.5–1.0 [39]. This finding was adjusted for age, sex, baseline physical function and category of CKD, and suggests that structured exercise rehabilitation may improve physical function and exercise participation in older adults with CKD.

As the first study to investigate the long-term 'real-world' effects of a single 10-week exercise rehabilitation program in individuals with CKD, our findings add to existing knowledge. Previous studies investigating the effect of exercise rehabilitation on physical function in CKD have focused on immediate postprogram effects in clinical trials. A randomized controlled trial (RCT) of 94 individuals with CKD Stages 3 or 4 demonstrated that a 12-week exercise intervention, consisting of 60 min of aerobic, resistance and stretching exercises two times per week, significantly improved exercise capacity and lower extremity function as compared with standard care [21]. A study in the UK randomized individuals with CKD Stages 3 and 4 to 12-month, thrice-weekly exercise rehabilitation program versus

Table 5. Predictors of improvement in SPPB over time in those with Baseline SPPB <12 (n = 218)

Variable	OR (95% CI)	P-value
Exercise rehabilitation attendance	2.18 (0.95–5.02)	0.07
Age	0.99 (0.96–1.01)	0.2
Sex	0.91 (0.50–1.64)	0.2
Albumin	0.97 (0.91–1.03)	0.3
Hemoglobin	1.00 (0.98–1.02)	0.9
Diabetes	0.79 (0.43–1.46)	0.5
SPPB total score at baseline	0.96 (0.86–1.06)	0.4
Dialysis versus CKD	0.72 (0.36–1.46)	0.3
Transplant versus CKD	1.42 (0.28–7.23)	0.5

Logistic regression model included: age, sex, serum albumin, hemoglobin, presence of diabetes, baseline SPPB score and category of CKD (CKD versus dialysis; CKD versus transplant).

Table 6. Proportion of participants endorsing any impairment in EQ-5D-3L domains over time by study group

	Baseline				One-year follow-up			
	Exercise attenders n = 53	Exercise nonattenders n = 40	CanFIT controls n = 207	P-value	Exercise attenders n = 53	Exercise nonattenders n = 40	CanFIT controls n = 207	P-value
Mobility	40.4 (21)	62.5 (25)	47.4 (91)	0.1	46.2 (24)	61.1 (22)	51.7 (106)	0.4
Self-care	23.1 (12)	20.0 (8)	9.9 (19)	0.02	17.3 (9)	21.6 (8)	8.3 (17)	0.02
Usual activities	44.2 (23)	52.5 (21)	22.4 (43)	<0.001	41.2 (21)	50.0 (18)	25.9 (53)	0.004
Pain/discomfort	63.5 (33)	74.4 (29)	55.2 (106)	0.07	71.2 (37)	77.8 (28)	50.2 (103)	<0.001
Anxiety/depression	37.3 (19)	50.0 (20)	29.7 (57)	0.04	43.1 (22)	38.9 (14)	28.3 (58)	0.08

Proportions are represented as % (n) endorsing any disability in that dimension, i.e. domain score >1. Proportions compared between groups using chi-square testing.

standard care and demonstrated increased exercise capacity in the exercise group [20]. Similarly, investigators in Australia studied the effects of a 12-month exercise rehabilitation program incorporating aerobic and resistance exercise and lifestyle education consisting of 8 weeks of supervised exercise, and a subsequent 10-month home-based program, which demonstrated improved exercise capacity and increased active and walking minutes per week at 6 months as compared with standard care control. Interestingly, the observed benefits of the intervention declined at 1 year in this study, despite an ongoing exercise intervention [19]. While immediate postprogram physical function was not assessed in our study, our findings are the first to suggest that a short duration exercise rehabilitation program may be associated with sustained benefits to physical function and exercise participation following completion of the intervention.

Interestingly, although exposure to the exercise rehabilitation program was associated with a higher proportion of individuals exercising at 1 year, we did not observe a change in physical activity behavior between groups as measured by the HAP. Similarly, previous investigators did not report a significant change in self-reported physical activity level at completion of the intervention in their RCT despite showing improvements in physical function [21]. An Australian study investigating a 12-month exercise intervention demonstrated a 50% increase in physical activity, as measured by weekly walking minutes, after 6 months of exercise rehabilitation, which decreased to baseline levels at 12 months despite an ongoing exercise intervention during the latter 6 months [19]. In contrast, a single-arm pre–post 6-month exercise rehabilitation intervention demonstrated increased self-reported physical activity and increased physical function as measured by the International Physical Activity Questionnaire and Sit-Stand and 6-min walk testing in 47 participants with CKD living in Japan [22]. Our lack of observed change in self-reported physical activity may be due to lack of intervention effect. However, another contributing factor is likely the HAP's ability to report changes in the intensity of activities that the individual is doing on a regular basis, but its lack of sensitivity to changes in duration/frequency of weekly exercise sessions that are not associated with changes in intensity level [42]. In addition, despite demonstrated reliability and validity, there have been no a priori studies on the HAP's responsiveness to change [37].

Our study also demonstrated no significant change in HRQOL as measured by EQ-5D-3L/VAS between exercise and control groups over time. Use of a generic, rather than disease-specific measure may have limited the ability to detect subtle differences in this outcome. However, our findings are consistent with those in the literature, which have shown a varied effect of exercise programming on HRQOL measures [11, 43].

This study has several limitations. First, low follow-up rates increase the risk of attrition bias. However, there were no meaningful differences in baseline characteristics and baseline outcome measures were similar between those who returned for follow-up and those who did not. Second, participant self-selection to attend exercise counseling and exercise rehabilitation programs raises the threat of a healthier and more motivated intervention group as compared with controls. The CanFIT control group was included to help mitigate a motivated control group as a source of selection bias. We acknowledge that fitness for exercise was not an inclusion criterion for the CanFIT study. This introduces the potential bias of a more sick and lower functioning control group. However, even low functioning individuals on hemodialysis are able to improve
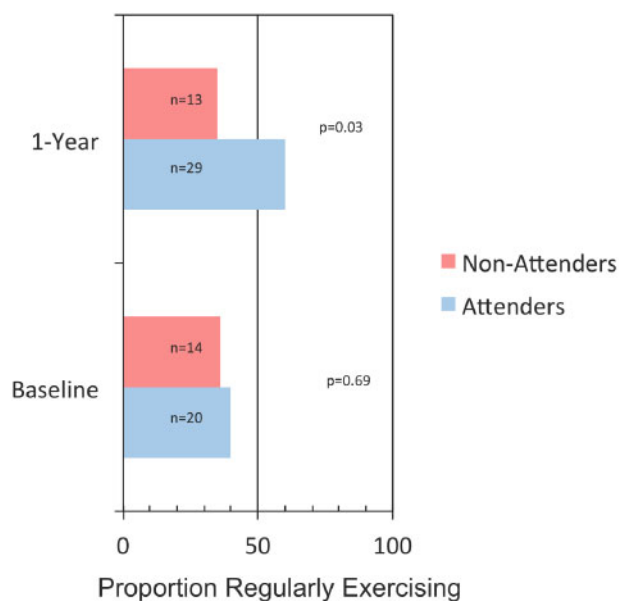

FIGURE 2: Proportion of participants reporting regular exercise at baseline and 1 year.
Proportions are percentage reporting they are currently exercising ≥30 min at least three times weekly at specified time period. Proportions exercising compared between attenders and nonattenders at specified time period using chi-square test.

physical function with exercise programming [44]. Due to the pragmatic nature of this study, we were unable to assess the effect of contamination due to participation in other exercise activities in the study groups. Also, the small sample size gave us limited power to detect a statistically significant difference in both mean change in SPPB and the association of exercise program participation and change in SPPB over 1 year. Lastly, a ceiling effect has been reported as a limitation of the SPPB in diverse and higher functioning populations [41, 45, 46]. Approximately 33% of the participants in the exercise rehabilitation group had a perfect baseline SPPB score of 12. Exercise nonattender and CanFIT control groups had 27% and 21% of individuals with baseline SPPB scores of 12. Thus, these individuals may have been misclassified as having no improvement in physical function in our study. Analysis of the subitems contained within the SPPB (chair-stand and gait speed) as continuous variables would mitigate this issue, but these data were not available.

To our knowledge, this is the first study to evaluate the long-term effect of a clinical exercise rehabilitation program on physical function in individuals with CKD. In addition, the diversity of the study population in terms of age, sex, race, CKD stage and comorbidities resulted in a sample that was more characteristic of the general CKD population [47] than previous investigations, which were predominantly focused on CKD Stages 3 and 4 [19–21], maximizing generalizability. Lastly, as an evaluation of a preexisting clinical exercise rehabilitation program, this study addresses the effectiveness of exercise rehabilitation for CKD patients seen in a clinical setting.

Future investigations with a larger study sample should confirm our observations and determine whether or not the effects of exercise rehabilitation on physical function persist for >1 year, if repeat attendance at exercise rehabilitation sessions has added benefits and if observed benefits to physical function translate into long-term decreases in adverse outcomes such as

hospitalization and mortality. In addition, in view of relatively low rates of adherence to an exercise prescription (41% in this study), particularly in the dialysis population, there is a need to investigate how barriers to attending such programs can be overcome. Finally, although incorporation of measures of physical function less prone to ceiling effects than the SPPB is important, in light of recent initiatives such as Standardized Outcomes in Nephrology – Hemodialysis (SONG-HD), future studies should focus on characterizing the effect of exercise on clinically- and patient-important outcomes in CKD [48, 49].

This pragmatic evaluation demonstrated that participation in a 10-week clinical exercise rehabilitation program may be associated with improved physical function over 1 year among individuals with CKD who had reduced baseline physical function. In addition, a larger proportion of individuals who attended the exercise rehabilitation program reported exercising regularly at 1 year. Although confirmatory studies are necessary, these results suggest that attendance at a single, 10-week exercise rehabilitation program may have sustained beneficial effects on exercise participation and physical function in CKD.

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AUTHORS' CONTRIBUTIONS

Research idea and study design were provided by C.B., L.S. and C.R.; C.B., N.H. and Q.T. participated in data acquisition; data analysis/interpretation was done by N.H., C.B., T.F., Q.T., N.T. and C.R.; statistical analysis was made by N.H. and T.F.; and supervision or mentorship was given by C.B., N.T. and C.R. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST STATEMENT

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