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Modifiable Physical Factors That Influence Physical Function for People Receiving Peritoneal Dialysis

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Introduction: People receiving peritoneal dialysis experience physical function decline, impairing their ability to complete everyday activities, leading to poorer quality of life. Physical factors, including cardiorespiratory fitness, muscle strength, physical activity, and sedentary behavior are associated with physical function. However, little is known about this relationship, or temporal changes of these factors in this cohort. This study aimed to explore modifiable physical factors that are associated with physical function, identify which factor has the strongest influence, and explore temporal changes.

Methods: Adults receiving peritoneal dialysis underwent objective and self-reported physical function, cardiorespiratory fitness, muscle strength, physical activity and sedentary behavior assessments 3 times over a 12-month observation period (at baseline, 6 months, and 12 months).

Results: Eighty-two participants underwent assessments. All modifiable physical factors were predominantly moderate to strongly associated with physical function at baseline. Cardiorespiratory fitness had the strongest and most consistent influence with every meter conferring a 0.08-unit (P < 0.01) and 0.01-unit (P < 0.05) increase in self-report and objective physical function score, respectively. Temporal changes were observed for modifiable physical factors with significant mean changes in cardiorespiratory fitness (-9.8%), quadricep strength (-5%), moderate-to-vigorous (-25.9%) and total (-16.2%) physical activity, and sedentary behavior (+7.1%).

Conclusion: The results of this study indicate that cardiorespiratory fitness could be routinely monitored to detect risk of physical function decline and targeted through intervention to enhance physical function for people receiving peritoneal dialysis. Nevertheless, all factors should be considered when designing interventions to mitigate temporal changes and induce the numerous health benefits offered by being physically active.

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KEYWORDS: cardiorespiratory fitness; muscle strength; peritoneal dialysis; physical activity; physical function; sedentary behavior

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People receiving peritoneal dialysis often experience reduced physical function due to the wide-ranging pathological effects of kidney failure, the comorbid conditions associated, and the burden of treatment for it.^{1,2} Impaired physical function is associated with adverse health outcomes, including a reduced quality of life and increased level of dependency, hospitalizations and mortality risk.³ Physical function refers to an individual's capacity to undertake everyday tasks and is influenced by physical, physiological, psychological, and environmental factors.⁴ The ability to undertake everyday tasks was identified by people receiving peritoneal dialysis at an international consensus meeting as one of the top 3 research priorities.⁵

Factors, including cardiorespiratory fitness, muscle strength, physical activity, and sedentary behavior are associated with physical function and are independently related to outcomes, including morbidity and mortality in dialysis populations.^{6,7} Furthermore, they

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are considered modifiable and can be targeted through movement-based interventions to improve physical function.⁸ Recent reviews addressing physical function have highlighted the higher volume of research focusing on people receiving hemodialysis and consequently, relatively little is known about how these factors and behaviors affect physical function or if they change over time for people receiving peritoneal dialysis.^{7,8} Considering that there are distinct physiological (e.g., mechanism of treatment) and logistical (e.g., venue and timing of treatments) differences between dialysis modalities,⁹ conclusions drawn from hemodialysis populations may not be directly translatable to people receiving peritoneal dialysis.

Longitudinal studies exploring temporal changes to modifiable physical factors associated with physical function are required to quantify functional decline for people receiving peritoneal dialysis. Therefore, the aims of this study were as follows: (i) to explore modifiable physical factors (cardiorespiratory fitness, muscular strength, physical activity, and sedentary behavior) that are associated with physical function, identifying which has the strongest influence; and (ii) to measure temporal changes of modifiable physical factors and physical function over 12 months. Identification of the factors that influence physical function and information about temporal changes could facilitate implementation of specific routine monitoring to identify risk of functional decline and, underpin tailored intervention development to prevent and/or mitigate it for people receiving peritoneal dialysis.

METHODS

This study was reported following the Strengthening the Reporting of Observational Studies in Epidemiology 10 statement.

Study Design

This was a 12-month longitudinal cohort study with participants assessed at the following times: (i) enrollment (baseline data), (ii) follow-up (6 months postbaseline testing), and (iii) study conclusion (12 months postbaseline).

Study Population

Adults aged ≥ 18 years receiving peritoneal dialysis within a local health network in South Australia were invited to participate. The recruitment method has been previously described in full.¹¹ In brief, participants were recruited via flyers, a YouTube video link, and directly by peritoneal dialysis nursing staff during routine patient consultations. All participants received medical clearance from their treating nephrologist prior to testing. Exclusion criteria included inability to give

written consent or understand English (or have adequate translator services available), and any acute medical event or condition precluding safe participation, as determined by their nephrologist.

Study Protocol

Assessments were performed at the participants' choice of a health care setting, scheduled to align their routine clinical care appointment at the site, or during a home visit. Unless requested otherwise by participants, assessments were typically completed in the morning following dialysate "drain out." The time of day that baseline assessment was completed for each participant was maintained in subsequent follow-up assessments to ensure consistency. All assessments were conducted by author BT. Participants were requested to avoid vigorous activity on assessment days. Written informed consent was obtained, and demographic data (age, smoking status, employment status, dialysis vintage, history of hemodialysis [if applicable], medical history, and if hospitalized in previous 3 months) were collected prior to any physical or written assessments. From the reported medical history, participants were asked to identify if any of the reported injuries or medical conditions impacted their physical function. Participants were contacted within a week following each assessment session to check if any adverse events occurred.

Anthropometric Measurements

Waist and hip girth measurements were performed as per published protocol,¹² using a Lufkin W606PM Tape (Apex Tool Group, Sparks, MD). If the 2 measures were within 5%, the mean of the 2 was recorded, and if \geq 5%, a third measurement was taken, and the median value recorded. Bodyweight was measured using electronic scales (Seca 770, Seca Limited, Birmingham, UK) and height was obtained using a wallchart. Both height and weight measures were taken twice and, if within 1% the mean was recorded, and if \geq 1%, a third measure was taken with the median value recorded.

Modifiable Physical Factors and Measures of Physical Function

A full list and details of assessment protocols is provided in Table 1. The assessments were selected due to their good to excellent validity and reliability, ease to administer, ability to be completed outside a research facility (i.e., field-based) with future potential to be included as part of routine clinical assessment in this cohort.

Data Processing

Accelerometry data were downloaded through GENEActiv PC Software Version 3.2 (ActivInsights,

Table 1. Modifiable physical factors and measures of physical function

| Factor | Test, equipment, and protocol | | | | | |
|--|--|--|--|--|--|--|
| Physical activity and sedentary behavior | Physical activity was captured via a wrist-worn GENEActiv tri-axial accelerometer (ActivInsights, Cambs, UK) at a sampling frequency of 100Hz. The 7-day average of total minutes activity and minutes of moderate-to-vigorous physical activity were used in the analysis. Accelerometers are a highly valid (technical validity, r = 0.98; criterion validity, r = 0.86) and reliable (coefficient of variation (CV) _{intra} = 1.4%; CV _{inter} = 2.1%) objective measures of physical activity. ¹³ Sedentary behavior was assessed using an ActivPAL inclinometer (PAL Technologies Ltd, Glasgow, UK) at a sampling frequency of 20Hz. Inclinometers are highly valid and reliable objective sedentary behavior devices with reported sensitivity of 75% to 99% and specificity of 80% to 91% to distinguish between sit, stand, and lying postures. ¹⁴ The inclinometer was fixed to the front of the upper thigh using waterproofed medical taping. The 7-day average time (min) spent sitting or lying was used in analysis. Participants were given a time recording sheet to document daily; wake up, bedtime, time started and finished work (if applicable), if slept during the day, if the watch was removed during the day and for what reason. | | | | | |
| Cardiorespiratory fitness | The 6-minute walk test was performed according to published protocol. ¹⁵ Where a 30 m track was not available, the track length was altered to the confines presented, but no less than 10 m. Follow-up testing sessions replicated the same track length used at baseline assessment. Assistive walking devices were permitted, and total meters walked recorded. The 6-minute walk test has been shown to be a good predictor of morbidity and mortality in chronically diseased populations with distances \leq 200 m the strongest predictor of mortality (hazard ratio = 2.14) and, reported to be a valid assessment for aerobic capacity (VO ² _{MAX} [r = 0.49]). ^{16,17} | | | | | |
| Muscle strength | Handgrip strength was assessed using an Advanced Hand Dynamometer (TTM, Tokyo, Japan). The quadriceps, bicep and abdominal flexion strength tests were assessed using a hand-held dynamometer (HHD) (Model 01163, Lafayette Instrument Company, Lafayette, IN). The psychometrics presented for these assessments refer to the validity of the HHD when comparing against an isokinetic dynamometer. Handgrip strength was completed with the participant seated, elbow flexed to 90° and wrist in mid pronation. It is identified as a valid assessment for predicting upper and lower body strength (r = 0.47-0.71) with excellent reliability in various clinical cohorts (ICC = 0.95–0.96).^{18,19} Quadricep (knee extension) strength was assessed with the participant seated on a plinth with their feet off the ground and knee flexed to 90°. The HHD was held by the investigator on the anterior, distal part of the lower shank in line with the medial malleolus. The quadricep strength test has been shown to have good to excellent validity (r = 0.43-0.99) and reliability (ICC = 0.70–0.85) as a tool for the assessing lower limb muscle strength.²⁰ Bicep (elbow flexion) strength was assessed with the participant seated with the elbow flexed to 90° and hand supinated, the HHD was placed on the distal part of the forearm between the radial and una head. The bicep strength test has been demonstrated as having good to excellent validity (r = 0.64-0.85) and reliability (ICC = >0.70) as a measure for the assessment of upper limb strength which correlates with upper body strength.^{20,21} Abdominal flexion strength assessment was performed with the participant in a supine position on a plinth. The portion of the upper body from the posterior-superior iliac spine upward was placed on a 25° form wedge with legs parallel to the floor and pillow support under the knees. The HHD was placed in-line with the sternal notch. Participants were asked to, without assistance of the hands, flex their trunk with the objectiv | | | | | |
| Measures of physical function | | | | | | |
| Self-reported | The Short Form- 36^{23} was used as a self-report physical functioning outcome (only the section 'Physical Function' was used for data analysis). The SF-36 (PF) has shown strong internal consistency and validity among older adults with the instrument reporting a moderate relationship with single limb stance (r = 0.42) and strong relationships with gait speed (r = 0.75) and the timed up and go (r = -0.70) and reliability (Cronbach α of .82). ²⁴ Scores ranged from 0 to 100 with lower score reflective of reduced physical function. | | | | | |
| Objective | The Short Physical Performance Battery (SPPB) ²⁵ was employed as a reliable composite objective measure of physical function. The SPPB consisted of 3 components; the ability to balance for up to 10 seconds through 3 stance variations (side-by-side, semi-tandem and tandem), time to complete a 4 m walk and time taken to rise from a chair up to 5 times. A recent review of the psychometric properties of the SPPB to assess physical performance concluded that the battery has good validity and reliability with correlation coefficients (both Pearson and Spearman) ranging between 0.19 to 0.82 when assessed against gait speed (distances ranging 4–50 m), sit to stand, timed up and go, self-report disability questionnaires and balance assessments. ²⁶ Performance is scored from 0 to 12 points with lower score reflective of lower function. A 1 point change is considered clinically significant ²⁷ and was the cut-point used in this study to categorize clinical change. | | | | | |

Cambs, UK) and compressed into 60-second epoch files. The epoch data were then imported into custom software (Cobra) built into MATLAB R2019a (MathWorks, Inc., Natick, MA) for processing (e.g., sleep time and nonwear time removed). Physical activity intensity thresholds established by Esliger et al.¹³ were applied to the period of active wear. Sedentary behavior data were downloaded through activPAL Process and Presentation software Version 7.2.38 (PAL Technologies Ltd, Glasgow, UK) with subsequent processing through activPAL Event Analysis Version 0.5.3.14 (PAL Technologies Ltd, Glasgow, UK) (removing the same time periods mentioned above). All processed data were entered into Microsoft Excel Version 2016 (Microsoft, Redmond, WA) workbooks. Each individual accelerometer and inclinometer session had to capture a minimum of 4 days (with at least 1 being Saturday or Sunday) to be included in the final data set.

Statistical Analyses

Descriptive statistics described the cohort demographics. Independent samples t-tests were performed post hoc to explore differences in demographic variables between those that completed all 3 timepoints and those who completed either 1 or 2 (combined to form one group). Pearson correlation tests were used to examine the associations between modifiable physical factors and physical function at baseline. In the event of skewed data, Spearman correlations were used. The strength of the baseline correlation coefficients determined which variables would be included in the primary analysis. Primary analysis employed multivariate linear mixed modelling with participant idenity as the random intercept to explore the influence of modifiable physical factors on physical function. All participants, including those who did not complete assessments at all 3 timepoints, were included in the primary analysis

with linear mixed modelling able to impute missing data. The final model included 3 modifiable physical factors (1 muscle strength, 1 physical activity, and cardiorespiratory fitness) and 3 confounders, all as independent variables with physical function as the dependent variable. All available physical function and modifiable factor data for each timepoint was included in primary analysis. Removal of modifiable physical factor variables from the model illustrated their respective influence via the level of variance explained (i.e., sensitivity analysis). A subsequent completers analysis (participants who completed all 3 time points) was performed following this. All demographic and anthropometric variables were considered as potential confounders in the final model. To explore the effect of conventional biological variables (regardless of baseline correlation strength) age, gender (male or female), body mass index, and weight were used as confounders in additional primary analyses, and the results compared to analyses using confounders selected based on baseline correlation coefficient strength. Secondary analysis employed linear mixed modelling to explore the effect of time (dependent variable) on each of the anthropometric, modifiable physical factor and physical function variables (independent variables). A completers analysis was also employed for secondary analysis. Bonferroni corrections were applied for all secondary analyses. A conservative power calculation suggests 30% power with a sample size of 60 participants based on a 3-predictor and 3-confounder model with $R^2 =$ 0.15, 5% explained variance per predictor. The total peritoneal dialysis population in this catchment during the recruitment period was ~ 208 people.²⁸ All analysis was conducted using SPSS Statistical Software Version 25.0 (IBM Corp. Armonk, NY).

Ethics Approval

The study protocol was approved by the Human Research Ethics Committees of the Central Adelaide Local Health Network (Reference Number R20180810) and the University of South Australia (Protocol Number 201824) and registered on the Australia New Zealand Clinical Trials Registry (Trial ID: ACTRN12620001315909).

RESULTS

Recruitment remained open from April 2019 to March 2022 with 107 ($\sim 51\%$ of the available patient population in the catchment area) participants enrolling in the study and providing informed consent. Eighty-two participants (77% of those initially recruited) underwent baseline assessment and 27 of 82 (33%) underwent assessments at all 3 timepoints (Figure 1). The primary reasons for withdrawal included transition to

hemodialysis, death, and transplant with no participants withdrawing for study-related reasons. Independent samples t-test identified no difference in demographic variables between those who underwent assessments at all 3 time points and those who did not.

Participant Demographics

Descriptive statistics for participants at baseline are presented in Table 2. Two participants were receiving continuous ambulatory peritoneal dialysis only whereas 22 were receiving nocturnal automated peritoneal dialysis with prescribed dialysate in the peritoneal cavity during the day. Two participants had previously received peritoneal dialysis (both prior to previous kidney transplant) and 3 reported currently smoking.

Thirty-three participants previously received hemodialysis for periods ranging 1 week to 3 years (mean [SE] 5.3 [0.8] months) with 3 participants receiving it on-going in addition to peritoneal dialysis. Reasons for hospitalization within the 3 months prior to baseline assessment were predominantly related to fluid removal or catheter complications. No adverse events related to the study protocol were reported throughout the study.

Baseline Modifiable Physical Factor and Physical Function Outcomes

Mean muscular strength, cardiorespiratory fitness, physical activity, sedentary behavior, Short-Form 36-Physical Function (SF-36 PF) and Short Physical Performance Battery (SPPB) findings are presented in Table 2. In subsequent analysis, the cohort was stratified into what would be deemed physical function impairment and mobility limitations according to SF-36 PF score (<75) and the SPPB score (<10).^{1,25} Comparison of the baseline mean scores for modifiable physical factors between these groups are presented in Table 3. Fifty-four percent of participants underwent assessments at their own home and 46% at the dialysis unit. Two participants required a translator. All participants completed the SF-36, handgrip, quadricep, and bicep strength assessments whereas 2 did not complete the abdominal strength assessment due to previous injury concerns and 1 participant did not complete the SPPB due to ambulation issues. Four participants used a walking assistive device (e.g., stick) to complete the 6minute walk test (6MWT) whereas 6 people declined to complete the 6MWT for personal reasons (personal reason: n = 4; pain-related: n = 2). Seventy-two participants completed the sedentary behavior assessment (inclinometer) with 6 instances of technical error (e.g., device malfunction) and 1 that did not meet the data capture threshold (i.e., <4 days data capture). Eight

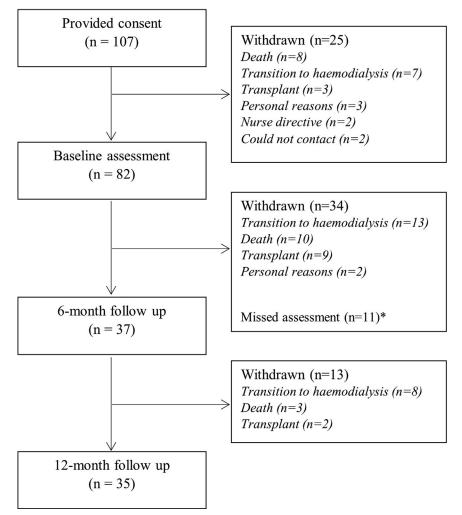


Figure 1. Participant flow. *Missed assessment (however remained enrolled) due to COVID-19-related reasons, including either of the following: (i) participants limiting their exposure to people and/or testing facilities or (ii) state government-imposed restrictions prohibiting nonessential activities (i.e., research activities).

participants declined to complete the assessment (personal reason: n = 6; skin sensitivity: n = 2) and 2 did not return the device. Seventy-four participants completed the physical activity assessment (accelerometer) with 10 instances of technical error and 2 assessments that did not meet the data capture threshold. Six participants declined to complete the assessment (personal reason: n = 5; skin sensitivity: n = 1) and 2 did not return the device. Pearson and Spearman correlation coefficients at baseline were predominantly moderate to strong²⁹ between modifiable physical factors and physical function (Table 4).

Significant associations were observed between the modifiable physical factors, apart from sedentary behavior, which had no association with any muscle strength assessment. Employment status (SF-36 PF r = 0.44; SPPB r = 0.38), age (SF-36 PF r = 0.39; SPPB r = 0.39), and a reported musculoskeletal injury affecting function (SF-36 PF r = 0.35; SPPB r = 0.43), were the 3 demographic factors reporting the strongest relationship

to both physical function outcomes and were included as covariates in the primary analysis. All baseline correlation analyses can be seen in Supplementary Table S1.

Influence of Modifiable Physical Factors on Physical Function

Modifiable physical factors included in the final model with the SF-36 PF included 6MWT, handgrip strength and moderate-to-vigorous physical activity (plus 3 covariates mentioned previously) (Table 5a). The 6MWT was the strongest influence in the final model with every meter conferring between 0.08- and 0.09unit increase in SF-36 PF score across each model it was included (P < 0.01). With the 6MWT removed from the model, handgrip strength became significant. Modifiable physical factors included with SPPB included 6MWT, handgrip strength and moderate-tovigorous physical activity. 6MWT was the strongest influence with every meter conferring a 0.01 unit

Table 2. Participant demographics, mean scores for modifiable physical factors and physical function and change over time (N = 82 at all timepoints unless otherwise stipulated)

| Variable | Baseline mean (SE) | 6-month estimated mean (SE) | 12-month estimated mean (SE) | Change time (p) ^a | Estimated mean change (95% CI) (BL–12 mo) ^b |
|---|------------------------|-----------------------------|------------------------------|------------------------------|---|
| Age (yr) | 61.4 (1.6) | - | - | - | - |
| Gender (% male) | 65.9 | - | - | - | - |
| Dialysis vintage (mo) | 9 (5, 18) ^c | - | - | - | - |
| Previously hemodialysis (% yes) | 40.2 | - | - | - | - |
| Currently employed (% yes) | 31.7 | - | - | - | - |
| Musculoskeletal injury (% yes) ^d | 58.5 | - | - | - | - |
| Medical condition (% yes) ^d | 40.2 | - | - | - | - |
| Hospitalized in <3months (% yes) | 20.7 | - | - | - | - |
| Height (m) | 1.7 (-) | 1.7 (-) | 1.7 (-) | 0.58 | 0 (-0.01, 0.01) |
| Weight (kg) | 83 (2.2) | 81 (2.3) | 80.1 (2.3) | < 0.01 | -3 (-4.6, -1.3) |
| Body mass index (kg/m2) | 28.8 (0.7) | 28.1 (0.72) | 27.9 (0.72) | < 0.01 | -0.9 (-1.5, -0.2) |
| Waist circumference (cm) | 102 (1.6) | 99.5 (1.7) | 100.6 (1.7) | < 0.01 | -1.4 (-3.2, 0.5) |
| Hip circumference (cm) | 105.5 (1.4) | 103.6 (1.6) | 102.7 (1.6) | < 0.01 | -2.8 (-4.9, -0.8) |
| Waist-to-hip ratio | 0.97 (0.01) | 0.96 (0.01) | 0.96 (0.01) | 0.10 | -0.01 (-0.03, 0.08) |
| Handgrip strength (kg) | 27.2 (1) | 27.3 (1.1) | 26.1 (1.1) | 0.05 | -1.1 (-2.3, 0.1) |
| Quadricep strength (kg) | 18.8 (0.8) | 17.1 (0.9) | 17.9 (0.9) | < 0.05 | -0.8 (-2.3, 0.6) |
| Bicep strength (kg) | 13.3 (0.6) | 13 (0.7) | 12.4 (0.66) | 0.07 | -0.8 (-1.7, 0.1) |
| Abdominal strength (kg) ($N = 80$) | 7.7 (0.6) | 8.6 (0.7) | 7.6 (0.7) | 0.12 | -0.1 (-1.2, 1.1) |
| Six-minute walk (m) ($N = 76$) | 332.1 (17.1) | 340.8 (19.8) | 301.2 (19.6) | < 0.05 | -30.9 (-63.1, 1.5) |
| % Day lying/sitting (%) ($N = 65$) | 68.3 (2.1) | 71.2 (3.4) | 73.3 (3.1) | < 0.05 | 4.9 (-3, 13) |
| Daily MVPA (min) ($N = 62$) | 36.2 (25.5) | 34.8 (5.5) | 27.9 (5.4) | < 0.05 | -8.4 (-16.5, -0.3) |
| Daily total activity (min) ($N = 62$) | 213.9 (14) | 201.3 (15.6) | 181.8 (15.3) | < 0.01 | -32.1 (-54.4, -9.8) |
| SPPB (score/12) (N = 81) | 10 (1.3) | 10.2 (1.3) | 9.6 (1.3) | 0.28 | -0.4 (-1.1, 0.4) |
| Short-Form 36 - Physical Function (%) | 48.6 (2.8) | 48.2 (3.5) | 45 (3.5) | 0.41 | -3.6 (-10.1, 3.2) |

BL, baseline; CI, confidence interval; MVPA, moderate-to-vigorous physical activity; SPPB, short physical performance battery.

^aChange over time included all timepoints. ^bMean 12-month change did not include 6-month timepoint data.

^cMedian (25th percentile). ^dParticipants answered 'yes' if they had a musculoskeletal injury or medical condition (aside from kidney failure) that affected their physical function.

increase in SPPB score (P < 0.05) across each model it was included. No other modifiable physical factors met the level of conventional significance, even with removal of the 6MWT from the model. Exploring of the variance inflation factor between predictor variables confirmed that collinearity was unlikely to have impacted results. Primary analyses with conventional biological variables (age, gender, body mass index, and weight) used in lieu of the confounders selected for the primary analysis did not impact the pattern of results.

These results were consistent with the completers analysis (Table 5c).

Temporal Changes in Anthropometric Measures, Modifiable Physical Factors and **Physical Function**

Mixed model analysis with time as the fixed factor found significant declines in weight, body mass index, waist circumference, hip circumference, quadricep strength, 6MWT, moderate-to-vigorous physical

| Table 3. Mean baseline modifiable | physical factor scores stratified by | y thresholds deemed physica | al function impairment and mobility limitations |
|-----------------------------------|--------------------------------------|-----------------------------|---|
| | | | |

| | Short Form-36 (P | hysical Function) | Short Physical Performance Battery | | |
|---------------------------------------|---|------------------------------------|---------------------------------------|------------------------------------|--|
| Variable | <75/100 ^a (<i>n</i> = 62) mean (SE) | ≥75/100 (<i>n</i> = 20) mean (SE) | $<10/12^{a}$ (n = 45) mean (SE) | ≥ 10/12 (<i>n</i> = 36) mean (SE) | |
| Handgrip strength (kg) | 25.6 (1.0) | 32.1 (2) | 24.2 (1.2) | 31.2 (1.4) | |
| Quadricep strength (kg) | 16.2 (0.9) | 19.5 (1.5) | 15.1 (1.1) | 19.7 (1) | |
| Bicep strength (kg) | 12.4 (0.6) | 15.3 (1.5) | 11.8 (0.8) | 15.1 (0.9) | |
| Abdominal strength (kg) | 7 (0.7) | 9.8 (0.9) | 6.1 (0.7) | 9.8 (0.8) | |
| Six-minute walk (m) | 291.2 (17.8) | 443.6 (19.2) | 244.8 (18.5) | 427.3 (15.2) | |
| % Day lying/sitting (%) | 71 (2) | 61.2 (4) | 74.1 (2) | 60.7 (2.7) | |
| Daily MVPA (min) | 26.7 (4.2) | 63.4 (14.1) | 20.4 (3.3) | 57.8 (10.1) | |
| Daily total activity (min) | 191.2 (14.7) | 269.3 (30.3) | 171.7 (15.4) | 267.3 (21.6) | |
| SPPB (score/12) | 8 (0.4) | 11 (0.3) | 6.7 (0.4) | 11.3 (0.1) | |
| Short-Form 36 - Physical Function (%) | 37 (2.3) | 84.5 (1.7) | 36.1 (3.3) | 64.2 (3.7) | |

MVPA, moderate-to-vigorous physical activity; SPPB, short physical performance battery.

^aSF-36 Score of <75¹ and Short Physical Performance Battery score of <10²⁵ are reported as thresholds to indicate physical function impairment and mobility limitations.

| Table 4. Correlation coefficient matrix between modifiable physical factors and physical function measures at baseline ($N = 82$) |
|---|
|---|

| Variable | QuadS | BicS | AbS | 6MWT | %SIT | MVPA | TOTAL | SPPB ^a | SF-36 PF |
|----------|-------------------|-------------------|-------------------|-------------------|--------------------|--------------------|--------------------|--------------------|--------------------|
| HGS | 0.59 ^b | 0.79 ^b | 0.53 ^b | 0.54 ^b | -0.22 | 0.47 ^b | 0.49 ^b | 0.47 ^b | 0.43 ^b |
| QuadS | | 0.78 ^b | 0.47 ^b | 0.50 ^b | -0.20 | 0.39 ^b | 0.45 ^b | 0.44 ^b | 0.38 ^b |
| BicS | | | 0.56 ^b | 0.44 ^b | -0.20 | 0.39 ^b | 0.41 ^b | 0.39 ^b | 0.33 ^b |
| AbS | | | | 0.38 ^b | -0.14 | 0.46 ^b | 0.37 ^b | 0.46 ^b | 0.35 ^b |
| 6MWT | | | | | -0.37 ^b | 0.47 ^b | 0.52 ^b | 0.79 ^b | 0.62 ^b |
| % SIT | | | | | | -0.52 ^b | -0.64 ^b | -0.43 ^b | -0.45 ^b |
| MVPA | | | | | | | 0.87 ^b | 0.51 ^b | 0.50 ^b |
| TOTAL | | | | | | | | 0.47 ^b | 0.45 ^b |

% SIT, percent of day sitting; 6MWT, 6-minute walk test; AbS, abdominal strength; BicS, bicep strength; HGS, handgrip strength; MVPA, moderate-to-vigorous physical activity; NS, not significant; QuadS, quadricep strength; SF-36 PF, Short-Form 36 Physical Function; SPPB, short physical performance battery; TOTAL, total physical activity. ^aSpearman correlation.

^bCorrelation is significant at the <0.01 level.

activity, total activity, and an increase in average percentage of day lying or sitting. Mean changes between baseline to 12 months are presented in Table 2. Completers' analysis (n = 27) results were consistent, replicating the significant shifts presented in Table 2, apart from waist and hip circumference which showed a trend for a decline that did not meet conventional significance (Supplementary Table S2).

DISCUSSION

Our study is the first to report that for people receiving peritoneal dialysis, of the 3 modifiable physical factors explored (cardiorespiratory fitness, muscle strength, physical activity), 6MWT (cardiorespiratory fitness) appears to influence self-reported and objective physical function most strongly. All modifiable physical factors were associated with physical function at baseline and significant temporal changes were observed, with declines in 6MWT distance, quadricep strength, physical activity levels, and an increase in sedentary behavior. The results indicate that cardiorespiratory fitness could potentially be routinely monitored to detect risk of physical function decline and targeted through intervention.

In addition to influencing physical function, this study found a significant decline in 6MWT distance after 12 months with the estimated mean change (-30.8 m)or -9.7% relative to baseline) considered clinically meaningful.³⁰ This is of concern because declining 6MWT distance associates with an exponential risk of all-cause mortality.³¹ The 6MWT is considered a valid proxy of cardiorespiratory fitness in clinical populations and identified as a key contributor to physical function capacity.^{32,33} Cardiorespiratory fitness reflects the capacity of the circulatory and respiratory systems to supply oxygen to skeletal muscle, in turn enabling the muscle to contract and facilitate an instant, continuous and/or repetitive movement.^{34,35} Therefore, on a practical level, activities of daily living such as walking, lifting, or carrying items require the ability to sustain

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movements. Hence, cardiorespiratory fitness translates directly into the ability to complete activities of daily living.³⁵ People receiving peritoneal dialysis suffer from negative alterations in cardiac function and/or structure as a result of kidney failure and dialysis that would invariably affect performance of the 6MWT.³⁶ Results of the current study indicate that continual declines in cardiorespiratory fitness would likely contribute to reduced distances in the 6MWT and physical function decline. This highlights that both monitoring and intervention should be an important consideration as part of routine care in this cohort.

Physical decline and increased sedentary levels that we observed have been independently documented in studies involving people receiving peritoneal³⁷ or hemodialysis,³⁸ and are identified as factors associated with physical function for people receiving dialysis.⁷ Indeed, with the 6MWT removed from the final model, muscle strength was significantly associated with self-reported physical function. Muscle wasting and sarcopenia (characterized by loss of muscle strength and mass), is a significant problem for people receiving dialysis, with strength decline also increasing the incidence and risk of falls and fractures.³⁹ Therefore, in addition to physical function decline, the results suggest that the declines in muscle strength may translate to increased risk of falls or fractures.⁴⁰ The reduction in muscle strength is a likely contributor to reports that <50% of people receiving peritoneal dialysis complete adequate physical activity (i.e., 150 minutes of moderate intensity activity per week).¹ Indeed, according to baseline measurements of those who completed the physical activity assessment, 44% achieved adequate physical activity levels. Kidney failure and dialysis-specific alterations that may underpin, in part, loss of muscle strength and physical inactivity can include negative protein balance, malnutrition, chronic inflammation, metabolic acidosis, insulin resistance, and hormonal derangements.^{39,41,42} Consequently, in addition to reduced physical function, declining strength

Table 5. Final mixed model analysis between modifiable physical factors and physical function including all participants (n = 82) (a), those that completed both baseline and 6-month follow-up (n = 37) (b) and, completers only (n = 27) (c)

| | | | Adjusted ^a | | | | |
|------------------------------|--------------------------------|------------------------------------|--------------------------------|-----------------------------------|------------------------------------|--------------------------------|--|
| | | Unadjusted | 1 | 2 | 3 | 4 | |
| Physical function measure | Predictor variables (unit) | Estimate (95% CI) ^d | Estimate (95% CI) ^d | Estimate (95% CI) ^d | Estimate (95% CI) ^d | Estimate (95% CI) ^d | |
| (a) SF-36 (/100) | Employed (if yes) | 26.22 (16.1, 36.23) ^b | 10.44 (-1.43, 22.31) | 10.19 (-1.79, 22.17) | 17.13 (4.98, 29.28) ^b | 6.51 (-3.68, 16.70) | |
| 51-50 (100) | Injury (if yes) | -19.50 (-29.6, -9.41) ^b | -1.75 (-11.84, 8.34) | -2.71 (-12.8, 7.38) | -6.79 (-16.51, 2.93) | -5.77 (-14.88, 3.34) | |
| | Age (per year) | $-0.70 (-1.05, -0.36)^{b}$ | -0.04 (-0.47, 0.39) | -0.10 (-0.53, 0.33) | -0.09 (-0.54, 0.36) | -0.04 (-0.47, 0.39) | |
| | Hand Grip Strength (per kg) | 1.35 (0.86, 1.83) ^b | 0.44 (-0.12, 1.01) | | 0.84 (0.29, 1.39) ^c | 0.37 (-0.14, 0.88) | |
| | 6MWT (per metre) | 0.11 (0.08, 0.13) ^b | 0.08 (0.04, 0.11) ^b | 0.09 (0.05, 0.13) ^b | | 0.08 (0.04, 0.12) ^b | |
| | MVPA (per minute) | 0.30 (0.18, 0.42) ^b | 0.06 (-0.08, 0.20) | 0.08 (-0.06, 0.22) | 0.12 (-0.02, 0.26) | | |
| SPPB (/12) | Employed (if yes) | 6.38 (0.98, 11.77) ^c | 1.84 (-6.50, 10.17) | 1.85 (-6.47, 10.17) | 2.40 (-5.70, 10.50) | 1.12 (-5.29, 7.54) | |
| | Injury (if yes) | -5.72 (-10.9, -0.47) ^c | -4.11 (-11.20, 2.98) | -4.17 (-11.19, 2.86) | -4.68 (-11.43, 2.06) | -3.20 (-11.41, 1.87) | |
| | Age (per year) | -0.23 (-0.40, -0.06)° | -0.20 (-0.47, 0.09) | -0.20 (-0.47, 0.08) | -0.24 (-0.51, 0.04) | -0.25 (-0.52, 0.02) | |
| | Hand Grip Strength (per kg) | 0.17 (0.04, 0.29) ^c | 0.01 (-0.17, 0.19) | | 0.05 (-0.12, 0.22) | 0.07 (-0.05, 0.19) | |
| | 6MWT (per metre) | 0.01 (0.01, 0.02) ^b | 0.01 (0.00, 0.02) ^c | 0.01 (0.00, 0.02) ^b | | 0.01 (0.00, 0.02) ^b | |
| | MVPA (per minute) | 0.02 (-0.01, 0.04) | 0.00 (-0.03, 0.03) | 0.01 (-0.03, 0.03) | 0.01 (-0.03, 0.04) | | |
| (b) SF-36 (/100) | Employed (if yes) | 27.7 (9.93, 45.47) ^b | 14.07 (-4.56, 32.7) | 13.33 (-6.25, 32.91) | 18.91 (0.09, 37.73) ^c | 10.22 (-5.01, 22.26) | |
| | Injury (if yes) | -26.75 (-42.54, -11) ^b | , | | -18.82 (-32.9, -4.66) ^c | , , , | |
| | Age (per year) | -0.70 (-1.53, 0.31) | 0.08 (-0.69, 0.85) | 0.03 (-0.78, 0.84) | -0.08 (-0.84, 0.68) | -0.09 (-0.72, 0.54) | |
| | Hand Grip Strength (per kg) | 1.73 (0.98, 2.47) ^b | 1.11 (0.3, 1.91) ^b | | 1.28 (0.04, 1.71) ^b | 1.05 (0.33, 1.78) ^b | |
| | 6MWT (per metre) | 0.1 (0.06, 0.14) ^b | 0.06 (0.00, 0.11) ^c | 0.08 (0.01, 0.14) ^b | | 0.06 (0.00, 0.1) ^c | |
| | MVPA (per minute) | 0.26 (0.07, 0.45) ^c | -0.03 (-0.22, 0.17) | 0.03 (-0.18, 0.23) | 0.07 (-0.18, 0.19) | | |
| SPPB (/12) | Employed (if yes) | 2.29 (0.1, 4.47) ^c | 0.46 (-1.6, 2.52) | 0.45 (-1.57, 2.48) | 1.48 (-0.86, 3.82) | -0.02 (-1.81, 1.76) | |
| | Injury (if yes) | -3.18 (-4.97, -1.39) ^b | -1.52 (-3.16, 0.11) | -1.52 (-3.13, 0.09) | -2.84 (-4.61, -1.06) ^b | -1.24 (-2.77, 0.29) | |
| | Age (per year) | -0.08 (-0.17, 0.02) | -0.07 (-0.1, 0.07) | -0.2 (-0.1, 0.07) | -0.04 (-0.14, 0.05) | -0.01 (-0.09, 0.06) | |
| | Hand Grip Strength (per kg) | 0.13 (0.03, 0.22) ^c | 0.01 (-0.08, 0.1) | | 0.08 (-0.1, 0.17) | 0.03 (-0.06, 0.11) | |
| | 6MWT (per metre) | 0.01 (0.01, 0.02) ^b | 0.01 (0.00, 0.02) ^b | 0.01 (0.00, 0.02) ^b | | 0.01 (0.01, 0.02) ^b | |
| | MVPA (per minute) | 0.03 (0.01, 0.06) ^b | -0.00 (-0.02, 0.02) | -0.00 (-0.02, 0.02) | 0.01 (-0.02, 0.03) | | |
| (c) SF-36 (/100) | Employed (if yes) | 23.62 (6.67, 40.57) ^b | -0.08 (-21.07, 20.91) | -0.90 (-22.03, 20.22) | 15.78 (-2.71, 34.27) | 4.29 (-13.68, 22.26) | |
| | Injury (if yes) | -18.78 (-35.21, -2.3)° | 0.39 (-16.12, 16.90) | -0.09 (-16.71, 16.52) | -13.00 (-26.80, 0.81) | -6.81 (-22.08, 8.46) | |
| | Age (per year) | -1.06 (-1.75, -0.37) ^b | 0.43 (-0.42, 1.29) | 0.25 (-0.58, 1.08) | -0.06 (-0.86, 0.74) | -0.03 (-0.80, 0.73) | |
| | Hand Grip Strength (per kg) | 1.54 (0.83, 2.25) ^b | 0.75 (-0.13, 1.63) | | 0.88 (0.04, 1.71) ^c | 0.85 (0.02, 1.69)° | |
| | 6MWT (per metre) | 0.11 (0.07, 0.14) ^b | 0.1 (0.04, 0.17) ^b | 0.11 (0.05, 0.18) ^b | | 0.09 (0.02, 0.15) ^b | |
| | MVPA (per minute) | 0.27 (0.11, 0.42) ^b | 0.10 (-0.06, 0.27) | 0.13 (-0.04, 0.30) | 0.11 (-0.06, 0.27) | | |
| SPPB (/12) | Employed (if yes) | 2.13 (-0.11, 4.37) | 0.61 (-1.45, 2.67) | 0.64 (-1.39, 2.68) | 1.59 (-0.41, 3.58) | -0.52 (-2.44, 1.40) | |
| | Injury (if yes) | $-2.84 \ (-4.75, \ -0.94)^{b}$ | -1.91 (-3.53, -0.29)° | -1.90 (-3.50, -0.30) ^c | -2.95 (-4.47, -1.42) ^b | -1.54 (-3.16, 0.09) | |
| | Age (per year) | $-0.12 (-0.21, -0.04)^{b}$ | -0.07 (-0.16, 0.01) | -0.07 (-0.15, 0.01) | -0.11 (-0.19, -0.02) ^c | -0.04 (-0.13, 0.04) | |
| | Hand Grip Strength (per kg) | 0.14 (0.05, 0.23) ^b | -0.02 (-0.11, 0.06) | | -0.02 (-0.11, 0.07) | 0.01 (-0.08, 0.09) | |
| | 6MWT (per metre) | 0.01 (0.01, 0.02) ^b | 0.01 (0.00, 0.01) ^c | 0.01 (0.00, 0.01) ^c | | 0.01 (0.00, 0.01) ^b | |
| | MVPA (per minute) | 0.02 (0.00, 0.04) ^c | 0.00 (-0.01, 0.02) | 0.00 (-0.02, 0.02) | 0.00 (-0.02, 0.02) | | |

^aInfluence of modifiable physical factors explored by removal from model (description of models below) Model 1–all variables included; Model 2–hand-grip strength removed; Model 3– 6MWT removed; Model 4-MVPA removed 6MWT-six-minute walk test; MVPA-moderate-vigorous physical activity; SF-36-short-form 36 (Physical Function); SPPB-short physical performance battery. $^{\rm b} {\rm Estimate}$ is significant at $\it P < 0.01$ level.

^cEstimate is significant at P < 0.05 level.

^dEstimate indicates the amount of change in SF-36 or SPPB score per unit change in predictor variable.

and activity levels increase the risk for poor health outcomes, enhancing the clinical urgency for routine monitoring and intervention.43,44

The mean self-report (48.6) and objective (10) physical function scores at baseline in the current study fall within or close to ranges reported with other peritoneal dialysis (self-report score range 44.4-56.4; objective score range 9-9.8) and hemodialysis (self-report score range 41.4- 59.4; objective score range 7-9.4) populations using the same assessments.^{1,45-49} These data suggest that physical function levels may vary between cohorts of the same modality, and dialysis modalities

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may have similar functional capacity. People receiving both modalities of dialysis require urgent support and research regarding their physical function, because the data typically fall below the self-report scores of 75 and objective scores 10 reported as the thresholds for physical impairment and mobility limitations.^{1,25,50}

However, these modalities are distinct treatments with people receiving peritoneal dialysis experiencing unique physical and physiological changes such as weight gain due to the dialysate containing glucose and accelerated protein loss induced by the dialysate leading to muscle degradation.⁵¹ Therefore, though physical function levels may appear similar, the factors that underpin the impairment and potential decline are likely different; thus, the need for peritoneal-dialysis-specific research.

This study reported associations between cardiorespiratory fitness, muscle strength, physical activity, and sedentary behavior in people receiving peritoneal dialysis, suggesting that an interrelationship exists in addition to each outcome being independently related to physical function. The literature supports that movement-based interventions (e.g., exercise therapy) targeting these factors can enhance physical function.^{52,53} This is evident for people receiving dialysis from a review exploring exercise-based interventions to improve objective physical function concluding that exercise, regardless of modality, improved physical function.⁸ However, from 27 included studies, only 2 involved people receiving peritoneal dialysis. These 2 studies employed aerobic training reporting that increases in cardiorespiratory fitness led to improvements in physical function; however, both studies also involved people receiving hemodialysis with the results not stratified by dialysis modality.54,55 More recently, interventional studies involving people receiving peritoneal dialysis have reported on exercise programs involving aerobic and resistance training, finding that they led to improved markers of physical function.^{56,57} Although the results of the current study suggest that interventions targeting cardiorespiratory fitness may result in greater improvements in physical function, the literature supports that targeting improvements in muscle strength and physical activity levels may also confer benefit and should be considered when developing programs.⁸ Further interventional data are required to explore the efficacy of exercise therapy on physical function in this population group; however, it should be considered as a management option due to the numerous health benefits that can be induced by participation.

The study was strengthened by the robust protocol development involving the authors and wider dialysis staff community (e.g., nurses, occupational therapists, and researchers) to identify the priority clinical need and subsequent development of the assessment battery, recruiting protocols, and strategies. Furthermore, it is the first study to report the relationship between cardiorespiratory fitness and physical function in this population. In addition, it is the first study to quantify the changes in physical function and modifiable physical factors over a 12-month period and include an objectively assessed abdominal flexion muscle strength test. The selection of field-based assessments for modifiable physical factors and physical function employed in this study could be employed in health care settings to routinely screen people receiving peritoneal dialysis. This would enable early identification of those experiencing physical function decline warranting intervention. Indeed, it is feasible that the 6MWT, the strongest influence on physical function in the current study, with good reliability and sensitivity to detect change in clinical populations,⁵⁸⁻⁶⁰ could be prioritized. The 6MWT requires minimal time, equipment, and knowledge, with this study highlighting the flexibility of this assessment to be completed at alternate settings, such as a person's home.

The study was limited by the relatively high proportion of participants who could not undertake assessment at all 3 timepoints (67%), which may have potentially resulted in residual confounding between those who underwent all assessments and those who did not. However, these withdrawals were for reasons unrelated to the study (e.g., transition to hemodialysis, death, and transplant) with the primary reasons for withdrawal potentially a reflection of the longitudinal clinical picture for this cohort. Therefore, it is possible that nonrandom attrition effects may explain the absence of temporal changes in physical function and modifiable physical factors. Nevertheless, this limitation accounted for, at least in part, using mixed model analysis and the overall pattern of results confirmed by the completers analysis. Despite having results that may be relatively generalizable to state and national populations within Australia, the demographic characteristics may not be consistent with other countries. Factors such as age, dialysis vintage, and comorbidity profile often vary among countries; thus, the results may not be fully translatable to all peritoneal dialysis populations. Limited biochemistry data were collected to enhance the focus on factors that had been previously underreported and minimize burden to participants. Consequently, biochemical data were not available to be included as confounders. Six-minute walk distances were also completed using various track lengths based on individual household layout. It has been suggested that shorter track lengths may reduce the total distance walked; thus, some totals

reported in this study may underestimate the actual figures. $^{\rm 61}$

Conclusion

This study found that people receiving peritoneal dialysis experience declines in cardiorespiratory fitness, quadricep strength, physical activity; and increase in sedentary behavior over time. Consequently, these changes can contribute to functional decline and poor health outcomes, highlighting the need for monitoring and intervention to be included in routine care. The current study suggests that cardiorespiratory fitness may have the strongest influence on physical function and could be the focus of both monitoring and a potential target for interventions (e.g., exercise therapy). Accordingly, exercise or physical activitybased interventions should be considered as a management option to not only prevent or mitigate physical function decline but to allow people receiving peritoneal dialysis to receive the many health benefits offered by engaging in an active lifestyle.

DISCLOSURE

All the authors declared no competing interests.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, (BT), upon reasonable request.

AUTHOR CONTRIBUTIONS

Study protocol and design was done by BT, KEF, TPW, PNB, and SJ. Data acquisition was done by BT. Data analysis and interpretation was done by BT, KEF, TPW, PNB, and SJ; Statistical analysis was done by BT. Supervision or mentorship was done by KEF, TPW, PNB, and SJ. Each author contributed important intellectual content during manuscript drafting or revision and has approved the final version. Furthermore, each author agrees to be personally accountable for the individual's own contributions and to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated, and resolved, including with documentation in the literature if appropriate.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Pearson correlations between demographic, modifiable physical factors, and physical function at baseline.

Table S2. Temporal changes in participants that completedall 3 timepoints (i.e., completers).**STROBE statement** (PDF)

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