Canadian Society of Nephrology/ Société canadienne de néphrologie CSN/SCN

CANADIAN JOURNAL OF KIDNEY HEALTH AND DISEASE
Journal canadien de la santé et de la maladie rénale

Narrative Review

Canadian Journal of Kidney Health and Disease
Volume 11: 1–7

DOI: 10.1177/20543581241229253
journals.sagepub.com/home/cjk

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A Current State of the Art and Science of Exercise in Dialysis: A Narrative Review

Megan Borkum[1,2], Adeera Levin[1,2], Joey Ficocelli[1], Lysa Wone[2], and Mercedeh Kiaii[1]

Abstract

Purpose of the review: The purpose of the review is to discuss current proven benefits and problems of integrating exercise in the care of people receiving dialysis by reviewing literature from the last few years and identifying important questions that still need to be asked and answered.

Methods: A focused review and appraisal of the literature were done. Original peer-reviewed articles, review articles, opinion pieces and guidelines were identified from PubMed and Google Scholar databases. Only sources in English were accessed. Search terms "exercise" and "dialysis" were used to find active recruiting randomized trials in various clinical trial registry platforms.

Key findings: Numerous studies have demonstrated the benefits of exercise training in individuals receiving dialysis, limited by factors such as short duration of follow-up and inconsistent adverse event reporting and outcomes selected. Notable gaps in exercise research in dialysis include ways to maintain programs and patient motivation, studies in peritoneal dialysis and home hemodialysis patients, and how best to define and measure outcomes of interest.

Implications: This review summarizes the current state of exercise in people receiving dialysis and serves as a call to action to conduct large, randomized controlled trials to improve the quality of evidence needed to implement and sustain innovative, exercise interventions, and programs for this population.

Abrege

Objectif de la revue: Discuter des bienfaits et problèmes avérés de l'intégration de l'exercice physique dans les soins des personnes dialysées en examinant la littérature des dernières années et en identifiant les questions importantes auxquelles il faut encore répondre.

Méthodologie: Une revue ciblée et une évaluation de la littérature existante. Des articles originaux évalués par des pairs, des articles-synthèses, des articles d'opinion et des lignes directrices ont été répertoriés dans les bases de données Pubmed et Google Scholar. Seuls les articles en anglais ont été consultés. Les termes de recherche « exercice » et « dialyse » ont été utilisés pour rechercher les essais randomisés en cours de recrutement dans diverses plateformes de registres d'essais cliniques.

Principales observations: De nombreuses études ont démontré les bienfaits de l'exercice physique chez les personnes dialysées. Ces études étaient toutefois limitées par des facteurs tels qu'une courte durée du suivi et une incohérence dans le rapport des événements indésirables et la sélection des résultats. Les principales lacunes observées dans les recherches portant sur l'exercice physique en contexte de dialyse concernent les moyens de maintenir les programmes et la motivation des patients, les études sur les patients traités par dialyse péritonéale et hémodialyse à domicile, et les meilleures façons de définir les résultats d'intérêt et de les mesurer.

Conclusion: Cette revue résume la situation actuelle en ce qui concerne l'exercice physique chez les personnes dialysées. Elle constitue un appel à l'action pour la tenue d'essais cliniques de grande envergure visant l'amélioration de la qualité des données nécessaires à la mise en œuvre et au maintien d'interventions et de programmes d'exercice novateurs destinés à cette population.

[1]Division of Nephrology, The University of British Columbia, Vancouver, Canada
[2]BC Renal, Vancouver, BC, Canada

Corresponding Author:
Megan Borkum, Division of Nephrology, The University of British Columbia, Room 5273, 2775 Laurel Street, Vancouver, BC V6Z 1Y6, Canada.
Email: mborkum@gmail.com

Keywords
exercise, peritoneal dialysis, hemodialysis, home hemodialysis, patient-centered outcomes

Received June 15, 2023. Accepted for publication October 31, 2023.

Introduction

The care of people receiving dialysis has traditionally been focused on dialysis adequacy, fluid management, and medical management of laboratory parameters. However, patients often have different priorities to enable them to live well with chronic kidney disease (CKD).[1,2] These include mitigating intolerance of the hemodialysis (HD) treatment due to intradialytic symptoms or feelings of poor productivity and lost time while on dialysis, as well as addressing other symptoms that accompany end-stage kidney disease (ESKD).[1,3-5] Improving levels of physical activity, and associated frailty and sarcopenia, is needed in an aging dialysis population to prevent functional decline, reduced life participation, health care costs, and mortality.[6,7] As such, there is a general movement away from merely targeting the traditional laboratory-based outcome measures in dialysis care and a shift toward more "patient-centered" outcomes. Targeting "what matters to me" in each individual has gained increasing traction in clinical care settings.[1,8,9]

There is a growing body of evidence and interest in the potential for exercise programs to improve patient-centered outcomes, such as physical function and ESKD symptoms, as well as clinical outcomes such as cardiovascular disease and mortality risk.[1,3,10] This article serves to provide an informed review to update knowledge with contemporary data surrounding the proven and suggested benefits of exercise programs for people receiving dialysis. The review further discusses knowledge gaps on the topic as well as the challenges in introducing exercise, motivating patients, and sustaining consistent exercise programs across the spectrum of dialysis modalities. How best to address important unanswered questions in future studies is suggested with the purpose of developing and establishing effective, enduring exercise programs for people living with ESKD.

Methods

A focused narrative review was performed to explore several perspectives of exercise in dialysis, including existing knowledge related to the effect of exercise on various clinical outcomes as well as knowledge gaps and future research required. Relevant literature was searched on PubMed and Google Scholar using "exercise," "peritoneal dialysis," "hemodialysis," "home hemodialysis," and "patient-centered outcomes." The evidence behind the included guidelines was summarized by the authors. Only peer-reviewed and English articles were included. Search terms "exercise" and "dialysis" were used to find active, recruiting randomized control trials (RCTs) from the following clinical trial registries: Clinicaltrials.gov, the Australia and New Zealand Clinical Trials Registry, and the European Union Clinical Trials Register.

Existing Knowledge

Physical Function and End-Stage Kidney Disease Symptoms

A 2022 Cochrane review of exercise interventions in maintenance dialysis patients identified 89 studies (n = 4291), of which 12 were excluded from the meta-analysis due to not reporting either the number of participants in which the outcome was measured or outcomes not relevant to the review. Of the 77 included studies (n = 3846), 70 involved facility-based HD patients and 7 involved peritoneal dialysis (PD) patients. The intervention included any exercise program of 8 weeks or longer (up to 2 years) targeting more than a single muscle group. Of total, 56 studies assessed aerobic exercise (mostly stationary cycling), 21 predominantly assessed resistance exercises, and 19 included both forms of exercise in varying proportions. Exercise programs were mostly 20 to 40 minutes in duration, 3 times a week of medium intensity, and were done during dialysis for a period of 2 to 12 months. Moderate certainty evidence was found for exercise of any time improving the outcomes of depression and functional capacity, measured by the 6-minute walk test (6MWT). Possible improvement in the health-related quality-of-life (HR-QOL) physical component score, pain, and fatigue were found with only low certainty evidence. It is unclear if any exercise training improves the mental component of HR-QOL as the certainty of evidence was very low. Mortality was assessed as an outcome in 1 study with no improvement found; thus, the certainty of the evidence was deemed very low. Adverse events, mainly shortness of breath, soreness and musculoskeletal injuries, were poorly reported and listed as an outcome in only 15% of studies.[11] No studies reported on cardiovascular events which are common in dialysis patients and are a common cause of death in this population and therefore are priority clinical outcomes for both people receiving dialysis and their caregivers.[12-14]

A 2023 multicenter German RCT, DiaTT (Dialysis Training Therapy), used an intervention of 3 times a week, 60-minute sessions of supervised intradialytic cycling and resistance exercises with a 12-month follow-up period.[10] The primary outcome assessed was the change in the 60-second sit-to-stand (STS-60) test used to evaluate lower body strength. A total of 917 patients were included in the final

analysis of the trial. At 12 months, the STS-60 repetitions improved from 16 to 19 in the exercise group but declined from 16 to 15 in the usual care group ($P < .0001$) demonstrating improved physical function in the exercise group. The physical and vitality scores of the 36-item short-form (SF-36) showed a favorable trend in the exercise group compared with the control group. The exercise group spent fewer median days in the hospital per year, 2 in the exercise group and 5 in the usual care group ($P = .036$). Mortality and dialysis-specific adverse events were not affected.[10]

Another important patient-centered research outcome for patients has been identified as the optimal management of HD-related symptoms. These symptoms are under-recognized with few evidence-based treatments and negatively affect patient well-being and life participation.[1,15-18] In a systematic review and meta-analysis specifically exploring the effect of exercise on HD-related symptoms, only 15 RCTs (n = 508) were included of 3048 studies screened.[3] The intervention in the included studies was aerobic or mixed aerobic and resistance interdialytic or intradialytic exercises compared with non-exercise controls. The exercise intervention was required at least 20 minutes twice a week for a duration of 8 weeks or more. Sample sizes ranged from 17 to 96 participants. Meta-analysis of depressive symptoms demonstrated a clinically significant improvement in the Beck Depression Inventory score with exercise compared to controls (mean difference = −7.57; 95% confidence interval [CI] = −8.25 to −6.89). Other symptoms, the studies were not included in the meta-analysis due to the heterogenicity of symptom assessment tools used and possible risk of bias, such as restless legs, cramping, and fatigue were summarized qualitatively and may improve with exercise. Most studies reported on attrition but lacked reporting on exercise program adherence and the majority did not report adverse events.[3]

Surrogate Cardiovascular Outcomes

Myocardial stunning during HD sessions is associated with intradialytic hypotension-related disturbances in myocardial regional perfusion and transient myocardial dysfunction. Repetitive episodes of myocardial stunning during HD are thought to significantly contribute to the high burden of cardiovascular disease in this population.[19,20] Exercise during dialysis has the potential to mitigate episodes of myocardial stunning during dialysis by reducing episodes of intradialytic hypotension.[21] A French 2023 open-labeled randomized study (n = 60) found that 30 minutes of medium-intensity cycling, 30 minutes after HD onset, significantly improved left ventricular longitudinal and circumferential functioning and torsional mechanics (as measured by speckle tracking echocardiography) compared with non-exercise controls.[22] However, an improvement in myocardial mechanics during HD needs to be studied on a larger scale, and whether these benefits translate into improved long-term clinical outcomes are still to be determined.[22,23]

The CYCLE-HD trial sought to assess the effect of intradialytic exercise on surrogate markers of cardiovascular health. This cluster RCT (n = 130) in 3 centers in the United Kingdom found an 11.1-g decrease in LV mass (95% CI = −15.79 to −6.43 g; $P < .0001$) by cardiac magnetic resonance imaging (MRI) in the intervention arm after 6 months of intradialytic cycling compared with usual care. Most completed the goal of 30 minutes of continuous intradialytic cycling. In addition, other markers of cardiovascular disease including aortic stiffness and potentially myocardial fibrosis improved. There were 51 adverse effects reported (37 in the intradialytic cycling group vs 14 in the control group) but none of them were believed to be related to the intervention. The serious adverse effects in both groups involved cardiovascular causes and dialysis access. The trial was unable to show a statistical difference in physical function or QOL perhaps, despite using validated questionnaires (5Q-5D-5L), attributed to methodological reasons (small sample size, short duration of follow-up) or due to fairly low intensity of exercise (rate of perceived exertion goal of 12-14).[24] This lack of impact of exercise on QOL is consistent with other trials of intradialytic exercise and may also reflect that QOL in dialysis is complex with multiple domains and that exercise alone may not be sufficient to benefit overall QOL.[10,25,26]

Hospitalization and Mortality Risk

The role of home exercise was investigated in multicenter Italian EXerCise Introduction to Enhance Performance in Dialysis (EXCITE) RCT (n = 227). A 6-month home walking program during the non-dialysis days improved functional status and the risk of hospitalization vs normal physical activity controls.[27] In a post-trial observational study, the lower risk for hospitalization from a walking program, registered in the per-protocol analysis of the 6-month EXCITE trial, was maintained for 30 months after the end of the trial, particularly in those with high adherence during the 6-month trial (HR = 0.55; 95% CI = 0.35 to 0.87). The long-term risk reduction occurred despite a minority (30%) of patients in the active arm of the trial maintaining the walking program long-term.[28] Although large trials testing the effect of exercise programs on mortality are lacking, a small Iranian RCT (n = 74) of 3 times weekly intradialytic cycling of at least 60 minutes for a duration of 6 months found that 1-year survival was higher in the intervention group compared with controls (94% vs 73%, $P = .01$).[29] Taken together these findings should lend impetus to conducting further larger-scale trials including hospitalization and mortality outcomes, priority outcomes as identified by the Standardized Outcomes in Nephrology initiative, in addition to patient-centered outcomes of importance such as dialysis-related symptoms.[30]

Key Knowledge Gaps and Future Direction

Implementing and Sustaining Exercise Programs

It is well recognized, in studies of exercise programs for people on dialysis, that participation, motivation, and adherence to exercise programs wane over time.[9,31-33] "Gamification" of exercise in dialysis and the application of wearable technologies have been suggested as effective tools to maintain patient interest.[31,34] A 12-week trial of an intradialytic nonimmersive (video game format) virtual reality exercise program improved patient physical function (gait speed and 6MWT) with adherence rates exceeding 70%.[35]

Exercise professionals (such as physiotherapists or kinesiologists) are important in motivating patients and establishing and supporting exercise interventions yet their availability is limited as part of multidisciplinary kidney care teams.[9,32,36-43] Conventional kidney care team members, such as nurses, are excellent "exercise champions" in centers participating in exercise programs during dialysis; however, staff workload frequently and lack of comfort in prescribing or monitoring exercise intervention arise as barriers to their continued role in these programs.[36,38,41,44] Recognizing that resources will always be a limitation, there is a need to investigate the cost-benefit of exercise professionals in order to advocate for their integration into kidney care teams. Proposed interim pragmatic solutions to the lack of direct access to exercise professionals include using widely available online or digital resources to improve patient's access to care and upskilling current kidney care team members to recognize frailty and act as first responders in discussing physical activity with patients.[45]

Limited Evidence for Home Dialysis Modalities

Individuals dialyzing at home have consistently been excluded from exercise studies despite also struggling with ESKD symptoms and the sequelae of inactivity. Unlike those dialyzing in facilities, those dialyzing at home traditionally find it harder to engage in studies.[44] The International Society for PD and the Global Renal Exercise (GREX) network developed a set of practice points regarding physical activity specifically in PD.[46] Most guidance is derived from the expert opinion of PD clinicians, exercise professionals, and patients. Despite recognizing its importance, and previously overstated belief of possible harm (eg, exercises that increase intrabdominal pressure can cause hernias), there is little evidence-based data to support recommendations.[47,48] A 2022 systematic review of exercise studies in PD patients, aimed to explore data on adverse events experienced by people receiving PD while undertaking an exercise or physical activity intervention. Of total, 25 studies were found and, of the 17 that provided adverse event data, no serious adverse events (eg, death, hospitalization) were attributable to the intervention.[49] Of reported adverse events, 32 were attributable to the exercise intervention, most being musculoskeletal discomfort followed by fatigue. Events were mild to moderate in severity and were resolved by exercise program modification, education, rest, or medication.

We are unaware of exercise studies in home hemodialysis (HHD) patients, presumably also due to safety concerns. Although guidelines and protocols may vary, in a survey to assess perceived benefits and barriers to exercise, similar barriers to exercise and desired outcomes were found across all modalities.[31] With this in mind, future studies including both PD and HHD cohorts with improved adverse events reporting are recommended.

Defining Outcomes of Interest in Clinical Research

On review of active, RCTs in ESKD listed study outcomes are heterogeneous (Table 1). Improvement in patient-reported fatigue, as a primary outcome, was identified in 2 trials. The Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) assesses multiple dimensions of fatigue and is validated in people receiving kidney replacement therapy.[9,50] Simple, inexpensive markers used for muscle mass and function assessment have established prognostic value, including isometric manual handgrip strength and the STS test.[51] Similarly, the 6MWT has proven reliable to assess cardiorespiratory fitness and physical function in kidney patients with mortality implications.[52,53]

A 2023 systematic review of measures to assess physical function in CKD, in an attempt to promote consistency and accuracy in clinical settings and in research, included 50 studies with 21 315 participants. A total of 22 physical function tests were reviewed, and the short physical performance battery (SPPB), timed-up-and-go, STS-5, and STS-60 had good evidence to support their use in CKD.[54] Although there remains a need for consensus in the application of standardized, validated outcome measures in exercise research in kidney disease for maximal impact these recommendations should be considered in future trials on the topic.

Discussion and Conclusions

With an increasing interest in exercise as part of CKD management, several online exercise initiatives and resources for patients, caregivers, and providers are being developed. These include the GREX Network (https://grexercise.kch.illinois.edu/), an international and multidisciplinary group working to foster research, awareness, and innovation to increase physical activity and improve health outcomes, and Kidney BEAM which offers a paid online program with on-demand and live exercise classes (https://beamfeelgood.com/on-demand/kidney%20disease). Recognizing challenges for providers the UK Kidney Association published

Table 1. Active Recruiting Randomized Control Trials in ESKD.

Title and clinical trial registration	Sites	Population, estimated enrollment	Intervention type and duration	Primary outcome measure(s)
Exercise and Cardiac Stunning During HD (TICKERS_HD) (NCT04877041)	Canada, the United States, Australia	Adults, maintenance HD (n = 160)	Standard care with intradialytic cycling (60 minutes, 3×/week) vs a non-intervention control Duration: 12 weeks	Change in the number of cardiac RWMA at peak HD stress (last 30 minutes of HD) using echocardiography
Physical Activity in Dialysis: Clinical and Biological Impact (NCT04525196)	France	Adults, maintenance HD (n = 250)	2 to 3 sessions (~25 minutes) of intradialytic exercise/week in the first 2 hours of the HD session vs a non-intervention control Duration: 12 months	Change in 6MWT
A Simple Exercise Program for Patients With End-Stage Kidney Disease to Improve Strength and Quality of Life: A Feasibility Study (NCT03787589)	Canada	Adults, maintenance HD (n = 90)	Prescribed use of Nordic Walking poles, online home exercise, regular use of a pedometer and regular verbal encouragement to exercise by dialysis unit staff vs a non-intervention control Duration: 12 months	Recruitment feasibility and adherence
Intradialytic Yoga Resistance Exercise for Hemo dialysis Patients (NCT05535114)	Vietnam	Adults, maintenance HD (n = 72)	Intradialytic yoga- resistance exercises (breathing, flexibility and resistance exercises, relaxation with meditation) in the first 2 hours of each HD, 3×/week vs non-intervention control Duration: 12 weeks	Fatigue (FACIT-Fatigue), depression (PHQ-9), sleep quality (Pittsburgh Sleep Quality Index), and muscle strength (handgrip dynamometer and STS-60)
Virtual Reality Intradialysis: Last vs. First Part of the Session (NCT04046042)	Spain	Adults, maintenance dialysis (n = 43)	Virtual reality exercise during the first 2 hours of the HD session vs virtual reality exercise during the last 2 hours of the HD session Duration: 9 months	Episodes of intradialytic hypotension
Structured Exercise Program to Reduce Fatigue in Patients Receiving Dialysis: An Adaptive Trial (M-FIT) (ACTRN12620000408987)	Australia	Adults, maintenance HD and PD (n = unavailable)	Three structured exercise programs and a non-intervention control in patients receiving HD Duration: 12 weeks	Fatigue as measured by FACIT-Fatigue at 12 weeks

Note. ESKD = end-stage kidney disease; HD = hemodialysis; RWMA = regional wall motion abnormality; 6MWT = 6-minute walk test; FACIT-Fatigue = functional assessment of chronic illness therapy – fatigue; PHQ-9 = Patient Health Questionnaire, STS-60 = 60 second sit-to-stand; PD = peritoneal dialysis.

the first-ever clinical practice guidelines in 2021 for exercise and lifestyle in CKD. These include points for implementation and recommendations and integrate the latest evidence.[55] It is hoped that these resources will equip clinical teams to understand and assist their dialysis patients concerning lifestyle interventions.

Evidence supports that exercise improves physical function and fitness as well as some common and often debilitating symptoms (particularly restless legs and depression) for dialysis patients. However, important gaps in evidence remain such as identifying the best ways to quantify the effect of exercise, the minimum effort needed to have an impact on patient well-being, and the overall effect on patient morbidity and mortality.

If the community desires more robust data, then large pragmatic trials should be developed to support the value of exercise programs and the cost benefits of exercise professionals. The assessment of the value of different exercise strategies could be tested across all dialysis modalities and the use of consistent, relevant, and validated outcome measures is essential in the conduct of such clinical trials in kidney disease. A concerted effort to overcome well-recognized barriers to implementation and sustainability would then follow. Ultimately, it is hoped that kidney care teams will be equipped with the knowledge and resources to practice the art of prescribing exercise, incorporating exercise science with behavioral techniques to achieve the desired outcomes.

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

The authors have consented publication of this article.

Availability of Data and Materials

Not applicable.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Megan Borkum https://orcid.org/0000-0003-0082-554X

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