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Virtual Reality Mindfulness and Personalized Exercise for Patients on Hemodialysis with Depressive Symptoms: A Feasibility Study

Brett T. Burrows [1,*], Ashley M. Morgan [2], Alexis C. King [2], Rosalba Hernandez [3] and Kenneth R. Wilund [2]

[1] Center for the Study of Aging and Human Development, Duke University School of Medicine, Durham, NC 27710, USA
[2] Department of Kinesiology and Community Health, University of Illinois Urbana-Champaign, Urbana, IL 61801, USA
[3] College of Nursing, University of Illinois Chicago, Chicago, IL 60612, USA
* Correspondence: brett.burrows@duke.edu

Abstract: Nonadherence to exercise-related trials in hemodialysis (HD) patients is a significant burden worldwide. To address this issue, we assessed the feasibility and preliminary efficacy of a combined pre-habilitative virtual-reality-based mindfulness (VRM) program and a personalized activity prescription (PARx) in HD patients with elevated depressive symptoms. Ten HD patients (age = 59.60 ± 13.66) with elevated depressive symptoms completed a 10-week intervention. Participants were randomized into either a VRM+PARx (n = 6) or PARx alone (n = 4) group. During the 2-week prehabilitation, the VRM+PARx group completed our VRM program, while the PARx alone group received usual HD care. Post-prehabilitation, both groups began our 8-week PARx program. Feasibility was assessed by rates of recruitment, retention, adherence, and acceptability and adoption. Preliminary efficacy was measured using metrics of depressive symptoms, mindfulness, fatigue, and physical activity (PA) energy expenditure. A 25% recruitment rate was documented, with 90% retention. A 75% exercise adherence rate was observed and PARx demonstrated high perceived autonomy support (M = 27.6 ± 2.1). Post-prehabilitation, the VRM+PARx group showed significant between-group improvement in mindfulness (p = 0.02) and a significant within-group reduction in depressive symptoms (p = 0.05); however, no difference between groups was observed (p = 0.07). Post-PARx, no between-group difference was evident in PA energy expenditure; however, within the VRM+PARx group, a significant increase in PA energy expenditure was observed ($p < 0.01$). Fatigue remained unchanged. Our VRM and PARx programs demonstrated feasibility and potential efficacy for HD patients. However, to validate these findings, future trials should consider a larger sample size and a longer duration.

Keywords: hemodialysis; mindfulness; virtual reality; physical activity; exercise; adherence; depression; patient-reported outcomes

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1. Introduction

Patients on hemodialysis (HD) commonly exhibit high rates of physical inactivity and depression [1,2]. In HD patients, physical inactivity and depression are strongly linked to disease-related declines, exacerbating the risk of hospitalization, morbidity, and mortality [3]. To mitigate disease-related declines in HD patients, researchers and clinicians have historically focused on intradialytic cycling to increase physical activity (PA) levels. However, this "one-size-fits-all" approach to exercise has largely yielded inconsistent and statistically nonsignificant findings [4]. Though the possible reasons for these uninspiring data are indeed multidimensional, nonadherence and dropout have been consistently reported as limitations in HD exercise-related trials [5–7]. Because benefits of exercise are dose-dependent, high levels of nonadherence and dropout may be contributing to the

mixed findings regularly reported by HD exercise-related trials. Although nonadherence and dropout are far too common among HD exercise-related trials, little has been done to combat this global issue. Furthermore, few trials have used personalized medicine for HD patients; therefore, it is unknown to what extent personalizing exercise programs may affect adherence to exercise.

Worldwide, engaging patients has been a significant challenge for HD exercise-related trials. Though patient engagement is multi-faceted and HD patients experience unique barriers to being more active [8], greater patient engagement is critical for improving adherence to healthy behaviors [9,10]. Patient-centered care focuses on engaging the patient by measuring what is most important to the patient [11]. Involving patients in their own care and designing programs that measure what is important to them may help patients understand how their active participation may positively impact health outcomes [9,11]. Currently, however, there is a lack of patient-centeredness in HD exercise-related trials. The "one-sized-fits-all", single mode of exercise (e.g., intradialytic cycling) does not meet the individual needs of a heterogeneous patient population. Eventually, HD patients become increasingly unmotivated, leading to nonadherence and/or dropout [4]. Personalized exercise prescriptions that allow for patient autonomy may lead to greater patient engagement, thus possibly improving adherence and ultimately disease-related outcomes [12].

Co-morbid depression, another factor contributing to exercise nonadherence [13,14], is exceedingly high in HD patients (20–30% compared to 5–10% in primary care settings). Elevated depression is significantly associated with low engagement, exercise nonadherence, and low PA [2,9,15]. While pharmacotherapy remains the primary treatment approach for depression in HD patients, benefits are largely uncertain [16]. Non-pharmacological strategies such as mindfulness therapy, involving the non-judgmental, moment-to-moment awareness of paying attention in the present moment [17], are gaining popularity as a form of depression therapy. While the benefits of mindfulness have been seen in other chronic diseases [18–21], mixed results are evident in HD patients [22]. However, the limited efficacy of mindfulness therapy in HD may be due, in part, to disruptions caused by noises and other distractions in the HD clinics [23]. Implementing alternative modes of delivering mindfulness therapy may be efficacious for in-center HD patients.

One potentially promising strategy for delivering mindfulness-based therapy in HD patients is virtual reality (VR). Many advances in VR technology in recent years have made it a viable platform to deliver mindfulness-based therapy with fewer distractions than traditional approaches [24]. As a therapeutic innovation, full immersive (i.e., head-mounted) VR can offer ultra-realistic imagery and totally immerses the end-user into a virtual world, which has been shown to increase patient engagement, intractability, and motivation compared to conventional treatments [25,26]. VR also has the unique ability to virtually transport users from the confines of their clinical surroundings to a more pleasing setting; therefore, VR has been used as an "active distraction" tool during medical procedures [27]. Currently being used with efficacious results in pain management and cancer treatments, VR has improved acute and chronic pain, anxiety, emotional well-being and reduced psychological symptoms [27,28]. Thus, fully immersive VR, used for "active distraction", may be an effective tool in the delivery of mindfulness-based therapy for in-center HD patients during treatments.

To date, few personalized exercise programs have been delivered to HD patients, and none use a points-based system to track adherence and progression. Additionally, to the best of our knowledge, this is the first study to explore if the use of VR-based mindfulness therapy for reducing depression will increase exercise adherence in HD patients. The primary objective of this pilot study was to assess the feasibility of implementing a pre-habilitative program using VR-based mindfulness (VRM) therapy, coupled with a personalized activity prescription (PARx), designed for HD patients with elevated symptoms of depression. In a secondary analysis, we examined the preliminary efficacy of our VRM

and PARx programs on metrics of depressive symptoms, mindfulness, fatigue, and PA energy expenditure.

2. Materials and Methods

2.1. Population and Study Design

Participants were recruited from a single outpatient HD center. Potential participants were approached by research staff and provided study details. Those interested underwent full screening to determine eligibility. Eligibility criteria included (a) being aged ≥18 years, (b) being on HD for ≥3 months, (c) having elevated symptoms of depression defined using the PROMIS-Depression—Short Form 8a [29], (d) having the visual/audio acuity for VR immersion, (e) physician clearance for involvement in exercise, and (f) speaking English. Exclusion criteria included (a) a history of epilepsy, seizures, or vertigo; (b) congestive heart failure; (c) currently participating in an exercise and/or mindfulness program; (d) having a pacemaker and/or hearing aid; or (e) having a wound/physical limitation restricting the use of a VR headset. Those deemed eligible provided written informed consent, and finally, physician clearance was obtained. Baseline measures were collected before or during each participant's HD treatment session. Following baseline measures, participants were randomized into either a (1) VRM+PARx (treatment) or (2) PARx alone (control) group. Randomization occurred through random allocation using a computer program. See Figure 1 for details of the study timeline. The trial was approved by the Institutional Review Board of the University of Illinois Urbana-Champaign (IRB #21005), and written informed consent was obtained from all enrolled participants.

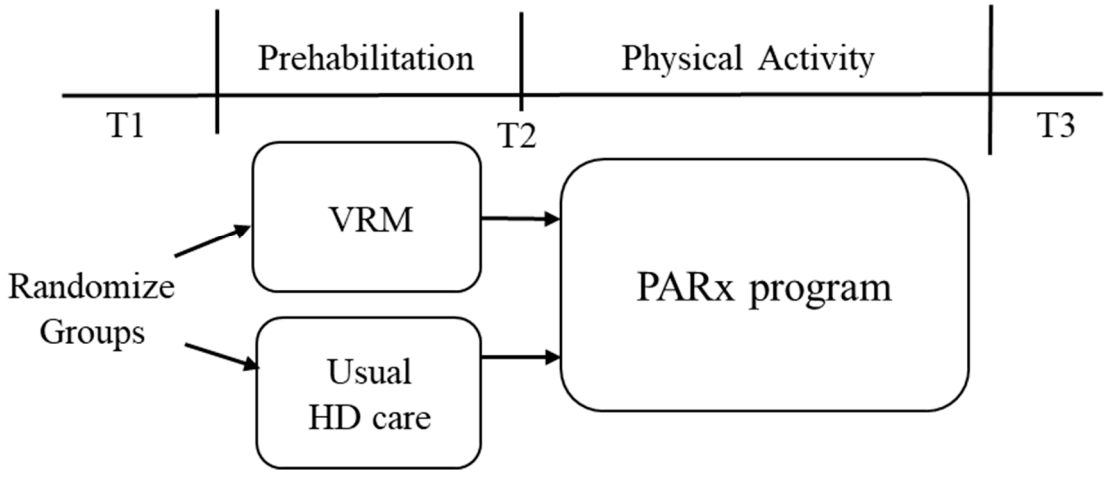

Figure 1. Study flow chart. Randomized groups (VRM+PARx and PA alone) participated in a 2-week prehabilitation phase in which the VRM+PARx group received our virtual-reality-based mindfulness (VRM) program and the PARx alone group received usual hemodialysis (HD) care. Following the prehabilitation, both groups participated in our personalized activity prescription (PARx) for 8 weeks. Note: T1 = baseline testing; T2 = post-prehabilitation testing; T3 = post-PARx testing.

2.2. Intervention

2.2.1. Prehabilitation

Prior to PARx, both groups participated in 2 weeks of prehabilitation. The VRM+PARx group received six sessions (3x/week) of our VRM program, and the PARx alone group received usual HD care. Utilizing the Oculus Quest 2 (1832 × 1920 resolution per eye at a 120 Hz refresh rate and an 89° field of view) (Facebook Technologies, LLC, Irvine, CA, USA), our VRM program combined our own developed VR-based mindfulness program, Joviality^{TM}, and a commercially available VR app, Guided Meditation VR. The details of Joviality^{TM} are published elsewhere [30]. Briefly, Joviality^{TM} is a 25 min VR-based mindfulness program with didactic material and a 12 min guided meditation. Guided Meditation VR is a VR meditation app where end-users can self-select from 29 virtual

environments (e.g., the beach, mountains, a forest trail, etc.) to meditate. Each of the ten Guided Meditation VR sessions lasted for 10 min and concentrated on learning breathing techniques and being present in the moment. Each of the six VRM exposures occurred chairside during HD treatment sessions and lasted 20–25 min. See Table 1 for a schedule of the six VRM sessions.

Table 1. Virtual reality-based mindfulness program—session schedule.

Session	VR Mindfulness Application	Total VR Exposure (Minutes)
Session 1	Joviality^{TM}	25
Session 2	Guided Meditation VR—Focus 1 and 2	20
Session 3	Guided Meditation VR—Focus 3 and 4	20
Session 4	Guided Meditation VR—Focus 5 and 6	20
Session 5	Guided Meditation VR—Focus 7 and 8	20
Session 6	Guided Meditation VR—Focus 9 and 10	20

VR, virtual reality.

2.2.2. Personalized Activity Prescription (PARx)

Immediately following the prehabilitation, participants in both groups engaged in PARx for 8 weeks. Prior to PARx, research staff provided counseling based on a previously recorded needs analysis, and a collaborative goal was determined between the participant and research staff. Participants were given autonomy to select activities, including intradialytic exercise (cycling and/or resistance exercise) and/or home-based activities, which included lifestyle activities (e.g., house chores, gardening, etc.) and/or structured exercises (resistance, cardiovascular, balance, and/or flexibility exercises). The intradialytic exercise was facilitated and recorded by research staff members. Additionally, participants were given a PA log to record the completion of the home-based activities, which was used to track adherence and progression.

Progression was made on an individual basis and determined through a point-based system. Points were derived from metabolic equivalent (MET) scores based on the PA compendium [31]. Participants accumulated points by completing any activity (e.g., "lifestyle", aerobic, and/or resistance exercises). A total of 500 MET minutes/week is equivalent to the recommended 150 min/week of moderate intensity PA [32]. Accumulating 500 MET minutes/week may be psychologically overwhelming for some patients; therefore, we adjusted the total MET minutes by dividing by 10 to make it less intimidating.

Due to varying degrees of physical function and outcome goals, participants started at differing point goals. However, the overall goal of PARx was the same for each participant: to apply a personalized activity prescription in which weekly activity levels (i.e., points) progressively increased. By the end of the intervention, the goal for each participant was to progress to 50 points/week (500 MET minutes divided by 10 = 50 points). Though this goal may have been unrealistic for some, their goal was to progress as much as possible from their baseline point goal.

2.3. Measures and Assessments

Feasibility, the primary outcome, was assessed by the following metrics: (1) recruitment rates, (2) retention rates, (3) exercise adherence rates, (4) adoption of a personalized PA program, and (5) acceptability, which was determined through subjective ratings and self-reported qualitative measures on whether our VRM and PARx programs, separately, were useful, enjoyable, and beneficial.

In a secondary analysis, preliminary efficacy was assessed through changes in depressive symptoms, mindfulness, fatigue, and PA energy expenditure. Variables were assessed at three separate time points: baseline (T1), post-prehabilitation (T2), and post-PARx (T3).

2.4. Background Measures

Questionnaires gathered socio-demographic information (age, sex, race/ethnicity, marital status, education, household income, and employment) and prevalent medical comorbidities (i.e., hypertension, diabetes, etc.). Body mass index (BMI) was calculated from self-reported measures of height (cm) and weight (kg).

2.5. Primary Outcomes

2.5.1. Recruitment and Retention

Recruitment rates were measured as the proportion of potential enrollees who were approached for recruitment but declined to enroll in the trial. Retention rates were defined as completing post-intervention assessments, categorized as a binary outcome (Y/N).

2.5.2. Exercise Adherence

For the duration of PARx, exercise adherence was calculated as the ratio of each participant's actual weekly accumulated points compared to their prescribed weekly points goal. Only if a participant met and/or exceeded their prescribed weekly points goal were they determined to be adherent for the given week. The number of adherent weeks was summed and divided by the total weeks for an overall adherence rate.

2.5.3. Adoption

The adoption of our PARx program was determined through participants' perceived autonomy. Perceived autonomy was captured through the 6-item Modified Health Care Climate Questionnaire (HCCQ) [33] (Appendix A). Questions are rated on a Likert scale from 1 (strongly disagree) to 5 (strongly agree). Scores range from 6 to 30, with higher scores indicating greater perceived autonomy.

2.5.4. Acceptability

Subjective ratings of our VRM and PARx programs were captured through surveys (Appendices B and C). Participants stated what they liked or disliked most about each program, their experience, and whether either of the programs was enjoyable and/or beneficial.

2.6. Secondary Outcomes

2.6.1. Mindfulness

The Five Facet Mindfulness Questionnaire—Short Form (FFMQ-SF) is a self-reported measurement of the five aspects of mindfulness: (1) observation, (2) description, (3) aware actions, (4) non-judgmental inner experience, and (5) non-reactivity [34]. The 24-item questionnaire is rated on a Likert scale, ranging from 1 (never or very rarely true) to 5 (very often or always true). Each of the five subscales are evaluated separately and totaled, with higher scores reflecting greater mindfulness.

2.6.2. Depressive Symptoms

The PROMIS-Depression—Short Form 8a (Depression-SF8a), validated in individuals with chronic disease, is an 8-item measure of depressive symptoms in the past 7 days [29]. Each item is rated on a Likert scale from 1 (never) to 5 (always), with scores ranging from 37 to 81, with higher scores indicating greater depressive symptoms. A cut-off T-score of $55\leq$ was used to determine mild depressive symptoms.

2.6.3. Fatigue

The Standardized Outcomes in Nephrology-HD (SONG-HD) Fatigue, validated in HD patients, is a 3-item measure of fatigue, including the effect of fatigue on life participation, tiredness, and level of energy from the past week. These dimensions are assessed on a Likert scale indicating increasing severity, ranging from 0 (not at all) to 3 (severely) [35].

2.6.4. Physical Activity Energy Expenditure

Data obtained from the Low Physical Activity Questionnaire (LoPAQ) were computed for MET min/week. The 11-item LoPAQ, designed for HD patients, is a self-reported, validated measure of PA levels from the last 7 days [36]. MET minutes/week were calculated as the MET intensity of an activity multiplied by the total minutes of the activity in the last 7 days [37]. The following equation was used to calculate weekly PA energy expenditure: MET min/week $\times$ 3.5(body weight (kg)/200).

2.7. Statistical Analysis

Data analysis was conducted using SPSS Version 27 (IBM SPSS Statistics 27 for Windows, 2020). Descriptive statistics summarizing baseline characteristics for the total sample are reported for socio-demographic factors and co-morbid diseases (diabetes, hypertension, hypercholesterolemia, and BMI); these are presented as frequencies, percentages, and means as appropriate. An independent sample *t*-test was used to determine group differences in characteristics at baseline. Qualitative data of participants' experiences with the VRM and PARx were analyzed for emergent themes. Due to the pilot nature of this study, intervention effects were examined through exploratory analyses of the impact on outcomes. Between-group differences and group x time differences were assessed using repeated measure ANOVA. Within-group differences were assessed using paired-sample *t*-tests. Significance was recognized as $p \leq 0.05$.

3. Results

3.1. Participant Characteristics

Table 2 presents the baseline characteristics of the participants (n = 10). No significant differences were observed between the treatment or control group. Overall, the mean age was 59.60 ($\pm$13.66) years, 60% were African American, and 70% were female. The mean BMI was 37.55 ($\pm$6.44) kg/m^2, and participants reported a high prevalence of co-morbid disease.

Table 2. Participants' baseline characteristics.

	All Subjects (n = 10)	**VRM+PARx (n = 6)**	**PARx Alone (n = 4)**	***p*-Value**
Age (years)	59.60 $\pm$ 13.66	59.67 $\pm$ 14.12	59.50 $\pm$ 15.07	0.98
Female	7 (70)	4 (66.7)	3 (75)	0.21
Race				0.06
Non-Hispanic White	3 (30)	0 (0)	3 (75)	
African American	6 (60)	5 (83.3)	1 (25)	
Asian	1 (10)	1 (16.7)	0 (0)	
Marital status				0.27
Single	6 (60)	3 (50)	3 (75)	
Married	2 (20)	1 (16.7)	1 (25)	
Divorced	1 (10	1 (16.7)	0 (0)	
Widow(er)	1 (10)	1 (16.7)	0 (0)	
Retired or unable to work	10 (100)	6 (100)	4 (100)	
Schooling (years)	13.40 $\pm$ 1.51	13.67 $\pm$ 1.63	13.00 $\pm$ 1.41	0.53
Income < USD 20,000	6 (60)	4 (66.7)	2 (50)	0.67
BMI kg/m^2	37.55 $\pm$ 6.44	38.62 $\pm$ 7.24	35.94 $\pm$ 5.59	0.55
Hypertension	10 (100)	6 (100)	4 (100)	
Hypercholesterolemia	3 (30)	2 (33.3)	1 (25)	0.81
Diabetes	7 (70)	4 (66.7)	3 (75)	0.81

Data are presented as mean $\pm$ SD or n (%) when appropriate. BMI, body mass index.

3.2. Primary Outcomes

A CONSORT diagram (Figure 2) summarizes recruitment, enrollment, and dropout rates. Of the 14 potential enrollees that did not meet eligibility criteria, 12 self-reported as non-depressed, and 2 had a history of vertigo or seizure. Final enrollment included 10 participants. However, due to medical complications unrelated to the current trial, one

participant in the VRM+PARx group dropped out of the study, resulting in a final analysis of nine participants and a 90% retention rate.

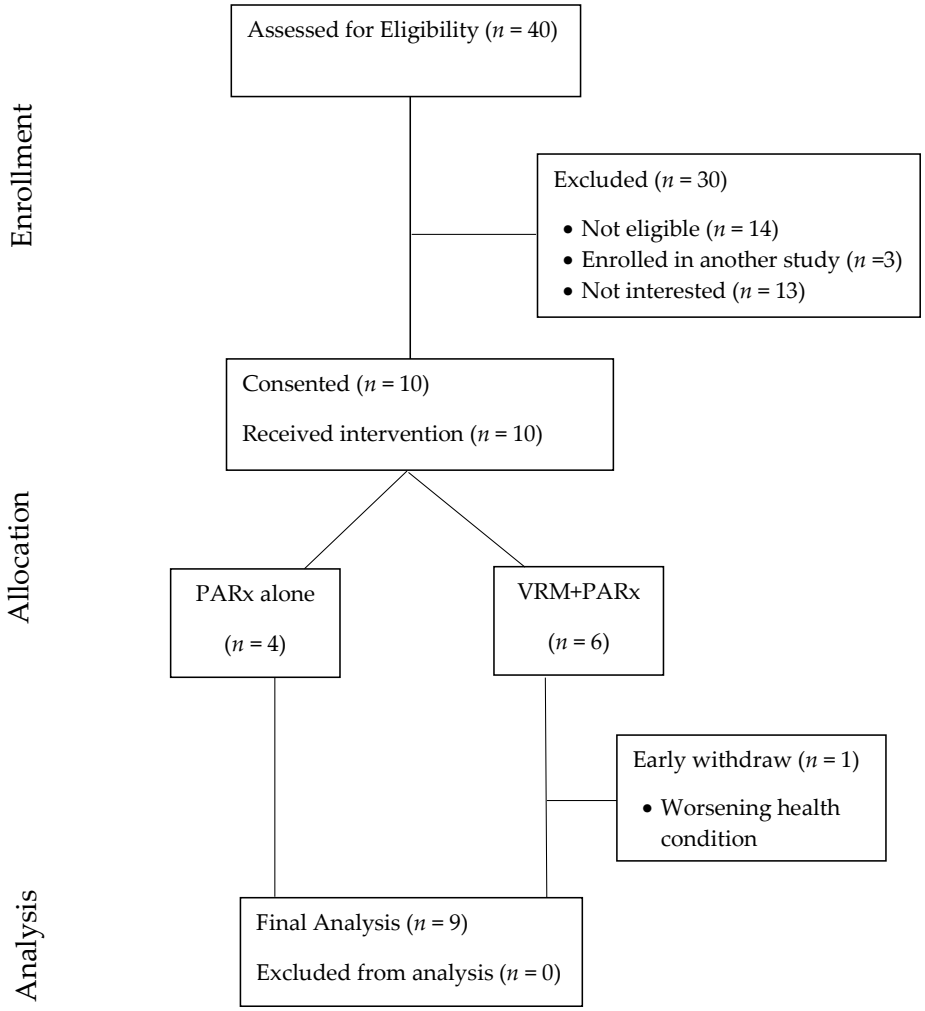

Figure 2. CONSORT diagram.

Overall, participants reported a 75% exercise adherence rate, and the stated PARx was well personalized, as high levels of perceived autonomy ($M = 27.6 \pm 2.12$) were recorded. Both the VRM and PARx programs were well received by participants with high ratings of acceptability. No differences were found in the feasibility of PARx when comparing participants who received our VRM program versus those that did not (exercise adherence: 70.2% vs. 87.8%; $p = 0.14$, adoption (Modified HCCQ): 27.33 vs. 28.00; $p = 0.65$). In total, 100% of the treatment group reported that the VRM program was enjoyable and easy to follow, the virtual environments were relaxing, and the program was a pleasant distraction from their typical HD treatments. In addition, 83% of the treatment group reported that the noise of the clinic did not impact their ability to concentrate on the guided meditation. And 4 weeks post-VRM, 100% of the treatment group reported continued meditation on their own.

Following PARx, 90% of the participants reported it was beneficial, they enjoyed the personalized program, and felt they would continue the program on their own. All participants believed that PARx helped them increase their daily PA. Post-dialysis fatigue and time were reported as the most significant barriers to incorporating more daily PA. When reporting what they felt they improved the most from PARx, 70% indicated feeling stronger and having more energy to do everyday activities.

3.3. Preliminary Efficacy of Secondary Outcomes

Table 3 presents the mean group differences in secondary outcomes. Following prehabilitation (T2), significant between-group differences were seen in the FFMQ-SF subscales of 'observation' (p = 0.04), 'aware actions' (p = 0.03), and "total score" (p = 0.02). The VRM+PARx group saw a 12% reduction in depressive symptoms which strongly trended towards between-group significance (p = 0.07), although a significant within-group change did occur (p = 0.05). After PARx (T3), the VRM+PARx group maintained an increased FFMQ-SF "total score" and a significant between-group difference remained between T2 and T3 (p = 0.04). No between-group difference was evident in depressive symptoms at T3; nevertheless, the VRM+PARx group showed continued lowering of depressive symptoms, and the PA alone group reported a significant within-group reduction in depressive symptoms (p = 0.03) at T3. PARx also generated increases in PA in both groups, though no between-group difference was found. The VRM+PARx group did, however, display a significant within-group change (824 kcals/wk to 2935 kcals/wk; $p < 0.01$). Fatigue was unchanged from the intervention.

Table 3. Between-group mean changes in secondary outcome measures.

Outcomes	VRM+PARx (n = 5)			PARx Alone (n = 4)				
	T1	T2	T3	T1	T2	T3	p-Value [a]	p-Value [b]
FFMQ-SF								
Non-reactivity	16.00 ± 3.54	16.40 ± 4.62	16.80 ± 3.63	15.75 ± 5.62	15.25 ± 2.06	18.50 ± 0.58	0.60	0.96
Observation	15.80 ± 1.10	15.00 ± 1.58	13.20 ± 2.77	10.00 ± 5.48	10.75 ± 5.44	13.00 ± 6.00 †	0.04	0.20
Aware actions	20.40 ± 4.16	21.80 ± 3.03	23.00 ± 2.12	18.00 ± 4.08	13.75 ± 2.50	14.00 ± 4.08	0.03	<0.01
Description	19.80 ± 3.96	21.00 ± 4.36	21.40 ± 4.04 †	18.50 ± 3.11	16.50 ± 3.11	17.00 ± 4.55	0.19	0.21
Non-judgmental	17.20 ± 3.35	18.40 ± 3.36	18.40 ± 3.44	21.25 ± 3.78	16.75 ± 6.60	17.25 ± 5.62 †	0.85	0.88
Total score	89.20 ± 8.58	92.60 ± 11.44	92.80 ± 10.38	83.50 ± 9.26	73.00 ± 6.16	79.75 ± 8.58	0.02	0.04
Depression-SF8a	56.72 ± 1.33	49.48 ± 6.94 *	45.42 ± 6.20 †	57.10 ± 3.03	57.50 ± 3.35	41.43 ± 5.38 **†	0.07	0.51
SONG-HD Fatigue	4.40 ± 2.20	3.40 ± 1.67	4.00 ± 2.24	3.50 ± 1.92	3.25 ± 1.26	4.25 ± 2.75	0.41	0.81
Weekly PA energy expenditure (kcals)	1042.05 ± 661.39	823.70 ± 1001.10	2935.32 ± 1496.43 **†	615.57 ± 791.91	792.14 ± 1204.80	1740.20 ± 690.17	0.87	0.37

Data are presented as mean ± SD. * Within-group change $p < 0.05$ between T1 and T2; ** within-group change $p < 0.05$ between T2 and T3; † within-group change $p < 0.05$ between T1 and T3. [a] Between-group change from T1 to T2. [b] Between-group change from T1 to T3. Bold indicates significance at $p < 0.05$. FFMQ-SF, five facet mindfulness questionnaire—short form; Depression-SF8a, PROMIS-Depression—Short Form 8a; PA, physical activity.

4. Discussion

The primary finding in this study was that both our VRM and PARx programs were feasible for in-center HD patients. Participants self-reported both programs as enjoyable and beneficial, and participants reported high adherence to PARx. In a secondary analysis, we found that our VRM program enhanced mindfulness and reduced depressive symptoms, which were associated with a significant increase in PA levels. Though these data are promising, more robust data are needed to fully determine the additive benefits of a prehabilitative VRM program and personalized activity in HD patients with elevated depressive symptoms.

In the last decade, personalized medicine has become a focal point in the nephrology community [11,38]. Unfortunately, this has not translated to the exercise community in HD patients. Currently, a "one-size-fits-all" approach (e.g., intradialytic cycling) is the standard of exercise programming for in-center HD patients. However, the "one-size-fits-all" approach does not align with each patient's individual needs, abilities, and goals. Though many HD patients have impaired physical function, there are indeed HD patients that do not. Not only does intradialytic cycling lack personalization, but it may not be challenging enough for high-functioning HD patients. On the other hand, it may be too challenging for very low-functioning/disabled HD patients. As such, patients may lose interest or be unable to participate, both of which affect adherence and dropout rates.

Compared to conventional exercise programs, personalized approaches can help motivate HD patients to be more active by designing programs around what they enjoy and can complete. Tawney et al. [39] highlighted a patient-centered approach by allowing HD patients to self-select leisure activities (e.g., housework or walking). This autonomous approach led to a significant improvement in PA levels and physical function compared

to the control group. We found similar results in this study, as high perceived autonomy led to more than a doubling of PA levels. Allowing participants to choose their own activities motivated them to engage in their own care, resulting in adherent participants, and improved outcomes.

While HD patients face exceedingly high rates of co-morbid depression, there is a lack of effective treatment strategies. To date, few trials have explored nonpharmacological strategies such as exercise or mindfulness therapy to reduce depressive symptoms in HD patients. Previous research has shown therapeutic effects of exercise [13], similar to results from PARx. Though exercise seemingly has therapeutic effects, the benefits of mindfulness therapy are still in question. Possibly impacting the effectiveness of mindfulness therapy is the mode of delivery. HD clinics are known to be loud and distracting [23], which may limit the therapeutic effects of traditional mindfulness therapy. Full immersive VR has the ability to "actively distract" HD patients, which has been suggested as one possible mechanism for VR's therapeutic effect [27]. In this current study, by utilizing full immersive VR, the treatment group was less distracted by the noises and activities of the HD clinic, and thus were able to engage more fully in the VRM content. Greater engagement improved mindfulness and depressive symptoms, suggesting a therapeutic effect of our VRM program. However, we cannot fully determine that the benefits of our VRM program are entirely the result of the VRM content. It is possible that therapeutic effects occurred, in part, from participants being virtually transported out of the HD clinic and not solely from the VRM content. Further research is needed to clearly determine the therapeutic effects of VRM.

Although there were no significant between-group differences in symptoms of depression at T2, there was a significant within-group reduction of ~13% in the treatment group. Our sample size was limited due to the COVID-19 pandemic; thus, our study was not powered (observed 1-β = 0.332) to detect between-group changes, though this was a secondary outcome. Based on a post hoc power analysis, we would require at least a total of 47 subjects to detect a significant between-group change in depressive symptoms, given our observed effect size (Cohen's *d*) of 0.386. Our limited sample and modest effect size may explain the decrease in the FFMQ-SF subscale "observation" between T1 and T2 by the treatment group. Despite the treatment group declining and the control group increasing in the FFMQ-SF subscale "observation" between T1 and T2, a statistically significant between-group difference remained. However, this may reflect the difference in baseline values between the groups.

The theoretical framework (Figure 3) for this intervention borrows from the Stress and Coping Theory [40], the Broaden-and-Build Theory [41], and the Self-Determination Theory [42]. Though the treatment group displayed increased mindfulness and reduced depressive symptoms at the onset of PARx, both groups had high exercise adherence with no between-group difference. This suggests that despite elevated symptoms of depression at the onset of activity, providing HD patients with autonomy to self-select activities (i.e., autonomous motivation) may be enough to elicit an increase in exercise adherence. However, future trials should examine this relationship further.

Given the pilot nature of this intervention, several limitations should be noted—namely, our small sample size. Due to complications related to COVID-19, we were limited in our recruitment and sample size; therefore, efficacy analysis was limited to detecting intervention effects. However, this was our secondary analysis. Our primary outcome, feasibility, was the development of two novel approaches (VRM and PARx), which we determined to be feasible for HD patients. Due to the nature of self-reports, we are uncertain of participants' adherence to the home-based portion of PARx. Furthermore, due to the study design, it is unknown which positively impacted exercise adherence, the VRM or PARx. While the majority of participants self-reported improvement in energy levels from PARx, fatigue was unchanged. Thus, SONG-HD Fatigue may not be sensitive enough to detect changes in fatigue over time. Lastly, the long-term sustainability of the improvements of PARx is uncertain. Future trials will need to conduct follow-up testing to

determine if PARx has lasting effects or whether there is a return to baseline values over time.

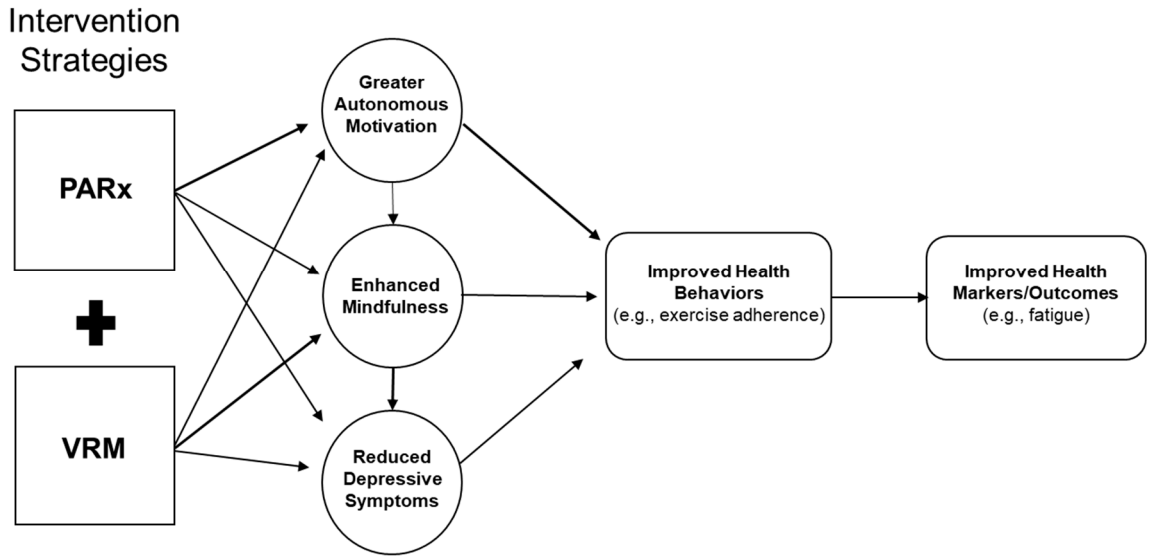

Figure 3. Hypothesized framework. Intervention strategies such as virtual-reality-based mindfulness (VRM) and personalized activity prescription (PARx) potentially have therapeutic effects alone. It was hypothesized that when intervention strategies are combined (treatment group), greater intervention effects would be evident compared to PARx alone (control group). Multiple pathways could occur in reverse; however, pathways have been omitted to simplify the figure.

The trial does have strengths. Most notably, the treatment group significantly improved their mindfulness from six sessions of VRM therapy. Further, 100% of the treatment group reported practicing meditation on their own 4 weeks after exposure to our VRM program. In addition, over half the participants exceeded the minimum recommended 500 MET/min/week of moderate intensity PA and went from being classified as "low" at baseline to "moderately" active at the conclusion of PARx [37]. Importantly, the treatment group had a statistically and clinically significant within-group reduction in depressive symptoms at T2, which was sustained at T3. The control group also had a statistically and clinically significant with-group reduction in depressive symptoms at T3, indicating that both VRM and PARx have therapeutic effects in reducing depressive symptoms. Finally, no adverse events were reported during the intervention.

5. Conclusions

We determined that our VRM and PARx programs were feasible for in-center HD patients. Despite the small sample size, preliminary efficacy is promising, though future trials should examine the intervention effects with a larger sample and longer duration to validate these findings.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

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Appendix A

Modified Health Care Climate Questionnaire (HCCQ)
Item Response Options
Strongly disagree = 1, Disagree = 2, Somewhat agree = 3, Agree = 4, Strongly agree = 5

Modified HCCQ Questions
1. I feel that my exercise leader provided me with choices and options for my physical activity program.
2. I feel that my exercise leader understood and respected how I saw things.
3. I feel that my exercise leader expressed confidence in my ability to increase my physical activity.
4. I feel that my exercise leader listened to how I wanted to personalize my physical activity program.
5. I feel that my exercise leader encouraged me to ask questions.
6. I feel that my exercise leader tried to understand how I saw things before offering an opinion.

Appendix B

Post-Virtual Reality Mindfulness Participant Feedback Questionnaire

Questions	Strongly Disagree		Neutral		Strongly Agree
1. Do you feel you had an enjoyable experience with the VR mindfulness program?	1	2	3	4	5
2. Do you feel you were able to follow along/keep up with the VR mindfulness program?	1	2	3	4	5
3. Do you feel the guided meditation was clear and easy to follow?	1	2	3	4	5
4. Do you feel the virtual environments were pleasing/calming?	1	2	3	4	5
5. Do you feel the realistic nature of the virtual environments distracted you from listening to the guided meditation and/or performing the assigned tasks?	1	2	3	4	5
6. While using the VR mindfulness program, were you still aware of events occurring in the real world around you?	1	2	3	4	5
7. Do you feel the noise of the clinic negatively impacted your ability to listen to the VR mindfulness program?	1	2	3	4	5
8. Do you feel the VR mindfulness program was a positive distraction from your dialysis treatments?	1	2	3	4	5
9. Would you like to continue using a similar VR mindfulness program in the future?	1	2	3	4	5
10. Did having multiple virtual environments to choose from improve your experience?	1	2	3	4	5
11. Do you feel the VR mindfulness program was beneficial to you?	1	2	3	4	5
12. Do you feel that other individuals on hemodialysis would benefit from a VR mindfulness program like this?	1	2	3	4	5
13. Did you feel discomfort at any time during your VR experience?	Not at all 1	2	Neutral 3	4	Very much 5
14. How easy or difficult was it to use the VR remote controller?	Very easy 1	2	Neutral 3	4	Very difficult 5
15. How easy or difficult was using head movement to control the virtual environment?	Very easy 1	2	Neutral 3	4	Very difficult 5

16. Did you prefer controlling the VR program via the handheld controllers or using head movements? Why?
17. What did you like the most about the VR mindfulness program? Why?
18. What did you like least about the VR mindfulness program? Why?
19. What would you most like to change about the VR mindfulness program to improve it?

20. What was your favorite virtual environment scene and was there an environment that was not offered that you would like to add for a future version?

Appendix C

Post-PARx Participant Feedback Questionnaire

Question	Not at All–Very Much				
1. Did you enjoy your experience with the physical activity program?	1	2	3	4	5
2. Were you successful meeting your goals?	1	2	3	4	5
3. Did you feel that the physical activity program was personalized to your ability and wants?	1	2	3	4	5
4. Was the information provided clear?	1	2	3	4	5
5. Did you ever feel you couldn't complete the tasks assigned?	1	2	3	4	5
6. Did the physical activity program meet your expectations?	1	2	3	4	5
7. Do you feel the physical activity program was beneficial for you?	1	2	3	4	5
8. Do you feel the physical activity program was difficult to understand?	1	2	3	4	5
9. Were the research staff's expectations of your involvement clear?	1	2	3	4	5
10. Do you feel the physical activity program helped you incorporate more activity into your daily life?	1	2	3	4	5
11. Did you enjoy the personalized nature of the physical activityprogram over a traditional exercise program like intradialytic cycling?	1	2	3	4	5
12. Do you feel most people would like the personalized nature of the physical activity program?	1	2	3	4	5
13. Do you feel you will continue the physical activity program on your own?	1	2	3	4	5
14. Do you feel the different aspects of the physical activity program were well integrated?	1	2	3	4	5
15. Do you feel it was difficult to incorporate more activity into your daily life?	1	2	3	4	5

16. What did you like most about the physical activity program?
17. What did you like least about the physical activity program?
18. What was your biggest barrier to incorporating more physical activity into your daily life?
19. What do you feel was your biggest improvement from the physical activity program?
20. What recommendations would you make to improve the physical activity program?

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