Title

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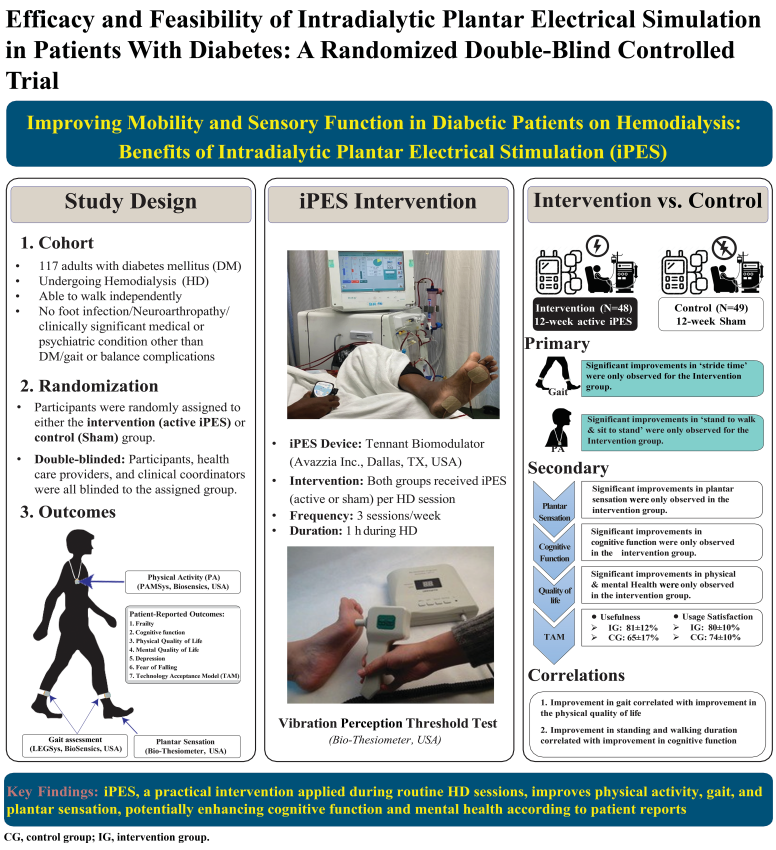

ARTICLE HIGHLIGHTS

- **Why did we undertake this study?**
  Patients undergoing hemodialysis often have reduced gait and physical activity, with low compliance with conventional exercise. Electrical stimulation of the plantar foot during hemodialysis offers a simpler, less demanding alternative.

- **What is the specific question we wanted to answer?**
  Does a 12-week intradialytic plantar electrical stimulation (iPES) program improve gait, physical activity, and patient-reported outcomes in patients undergoing hemodialysis?

- **What did we find?**
  The 12-week iPES program improved gait performance and physical activity, which were linked to better quality of life and cognitive function.

- **What are the implications of our findings?**
  The 12-week iPES therapy enhances mobility, cognitive function, and quality of life in patients undergoing hemodialysis with minimal effort and low risk, providing a practical alternative to regular exercise programs.

Efficacy and Feasibility of Intradialytic Plantar Electrical Stimulation in Patients With Diabetes: A Randomized Double-Blind Controlled Trial

Myeounggon Lee,[1,2] Abdullah Hamad,[3] Mehrnaz Azarian,[2] Jaewon Beom,[4,5] Abderrahman Ouattas,[2] Mohammad Dehghan Rouzi,[1,2] Naima Rodriguez,[2] Nhi Quach,[2] Rania Ibrahim,[3] Mincy Mathew,[3] Talal Talal,[6] Fadwa Al-Ali,[3] and Bijan Najafi[1]

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ORIGINAL ARTICLE

OBJECTIVE

This study investigates the efficacy and feasibility of electrical stimulation (E-Stim) on sensory fibers of the plantar region during hemodialysis sessions, aiming to improve mobility in patients with diabetes by providing a connection between E-Stim and enhanced mobility with minimal patient effort required.

RESEARCH DESIGN AND METHODS

Participants age ≥18 years with diabetes undergoing hemodialysis and able to walk at least 10 m with or without aid were recruited and divided into an intervention group receiving 1-h intradialytic E-Stim three times a week and a control group using an identical nonfunctional device for 12 weeks. Gait, physical activity, patient-reported outcomes, and the technology acceptance model were assessed to evaluate the intervention's effectiveness and acceptance.

RESULTS

Out of 117 initial participants, 97 completed the study. Significant improvements were observed in the intervention group compared with the control group in gait performance (stride time at dual-task and fast walking), physical activity (stand to walk and sit to stand), quality of life, plantar numbness, and cognitive function after 12 weeks. The intervention group showed that magnitudes of improvement on gait performance and physical activity metrics were associated with enhancements in quality of life and cognitive function, respectively. The intervention group also reported higher usefulness and usage satisfaction, with a greater willingness to continue using E-Stim at home.

CONCLUSIONS

The 12-week intradialytic E-Stim intervention is a feasible and effective method to enhance gait performance, physical activity level, cognitive function, and other patient-reported outcomes in patients undergoing hemodialysis, representing a practical, low-risk therapy option for those unable to engage in traditional exercise programs.

Diabetes and chronic kidney disease (CKD) are significant health concerns, with diabetes affecting >463 million people in 2019 (1). CKD impacts >10% of the global population, leading 2.62 million people to require hemodialysis (2,3). Reduced physical activity and mobility are common in patients requiring hemodialysis,

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worsening through sedentary lifestyles and muscle loss (4,5). Diabetes-related complications, such as peripheral neuropathy, impair exercise tolerance and mobility (6,7). Diminished kidney function correlates with lower muscle strength, slower walking speed, and higher fall risk (8,9). Innovative treatments are needed to enhance physical activity. While intradialytic exercise programs show promise, practical and logistical challenges hinder feasibility (6). Various exercise methods have been tried (10–12), but adherence remains low (13).

Intradialytic plantar electrical stimulation (iPES) is a noninvasive treatment that delivers high-frequency electrical currents to the lower extremities to stimulate sensory and motor nerves (14,15). Previous studies have shown that electrical stimulation (E-Stim) can improve postural control, balance, and gait by stimulating sensory fibers (5,7) and reducing lower-limb pain and numbness in the plantar area (6,16). The iPES is practical and safe for use during hemodialysis sessions as it does not interfere with the process and requires no effort from patients (16).

Given the increasing number of patients with diabetes and CKD and their physical deterioration, this study explores the effect of iPES on improving gait and physical activity. The main target of iPES is afferent plantar sensory fibers. This study is novel in its direct evaluation of gait and physical activity using various methods, unlike previous studies focusing on muscle atrophy prevention and single-task gait assessments (14,15,17). Our prior publication of interim results from the current project found that 12 weeks of iPES improves mobility and plantar sensation in patients with diabetes undergoing hemodialysis (16). We hypothesize that a 12-week iPES program will significantly enhance gait and physical activity in patients undergoing hemodialysis, with improvements in patient-reported outcomes related to these metrics postintervention.

RESEARCH DESIGN AND METHODS

Study Population

This study enrolled adults (≥18 years old) with diabetes undergoing hemodialysis at the Fahad Bin Jassim Kidney Center (Hamad Medical Corporation) who were able to walk a minimum of 10 m independently with or without walking assistance devices and willing to provide informed consent. Patients with active foot ulcers, Charcot neuroarthropathy, major foot amputation, nonambulatory status, severe gait issues, pacemakers, severe cognitive impairment, recent hospitalization, or prior mobility intervention were excluded.

The institutional review boards of Baylor College of Medicine and the Medical Research Center at Hamad Medical Corporation approved the study protocol (protocol nos. H-42315 and MRC-03-17-0010), and the protocol was registered with ClinicalTrials.gov (identifier: NCT05407207; start date: 1 June 2018). The methods used were in accordance with the relevant guidelines and regulations and the Declaration of Helsinki.

The Intervention Program: 12-Week iPES

iPES therapy uses biphasic asymmetrical damped sinusoidal waveforms to alleviate neuropathic pain with a wearable E-Stim device (Tennant Biomodulator; Avazzia), adjusting to tissue properties for stable conductivity and creating a closed-loop system (18). The high-voltage pulsed alternating current mode, set at a power level of 50, results in an intensity of –0.55 mA. Electrical pulses, ranging from 0.3 to 1.3 ms, are grouped into packets of five pulses and delivered at 21–129 Hz. Applications, ranging between 100 to 250 V, last 60 min per session, three times a week, for 12 weeks. This U.S. Food and Drug Administration–cleared regimen provides symptomatic relief for chronic, intractable pain and postsurgical/posttraumatic pain. The intervention group received a functional device, while the control group received a placebo. Electrodes were placed on each foot's calcaneus and metatarsal area, ensuring uniform E-Stim distribution.

Randomization and Double Blinding

This study was conducted as a double-blind randomized controlled trial. Participants, health care providers, and clinical coordinators were blinded to their assigned E-Stim group. A computer-generated list (R2023a; MathWorks, Natick, MA) was used to randomly assign participants to the intervention versus control group by an independent coordinating site at Baylor College of Medicine. To ensure that the correct device was given to participants, devices were labeled with either letter *A* or *B*, and each participant was also assigned a corresponding letter, which had been previously randomized.

Primary Outcome: Gait and Physical Activity Parameters

The primary outcomes of this study were gait (stride time, indicator of slowness [19]) and physical activity (postural transitions, indicator of weakness [20]). These outcomes were measured with validated wearable sensors at baseline and 12 weeks posttherapy during nondialysis clinic days to avoid hemodialysis-related inactivity and fatigue.

For gait assessment, we followed the protocol suggested by Zhou et al. (21). In summary, two wearable sensors (LegSys; BioSensics, Newton, MA) were attached to the lower shins of each participant before conducting gait tests to measure spatiotemporal parameters of gait, with a sampling frequency of 100 Hz. Participants were asked to walk 10 m at their habitual walking speed (single-task walking). Once completed, patients were asked to repeat the previous task while counting down from a given two-digit number verbally and loudly (dual-task walking). Finally, patients were asked to walk 10 m at a quicker pace, as if they were in a rush (fast walking). Stride time, walking speed, and double support phase were calculated to assess the gait performance in each task.

For each visit, physical activity and sleep patterns were recorded using a sensor with a three-axis accelerometer at 50 Hz (PAMSys; BioSensics, Newton, MA). Patients were asked to wear the sensor around their neck for at least 48 consecutive hours during their regular lives. A validated algorithm extracted mobility information, which was quantified by cumulative posture duration (sitting, lying, standing, and walking activities), postural transitions (including sit-to-stand and stand-to-walk occurrences), and locomotion (including step counts and cadence) over 48 h (16,22).

Secondary Outcome: Patient-Reported Outcomes and Clinical Assessments

During the baseline visit, research coordinators collected patient and clinical information. At baseline and week 12, validated questionnaires assessed pain (Visual Analog Scale), cognition (Montreal Cognitive Assessment [MoCA]) (23), well-being

(Patient-Reported Outcomes Information System [PROMIS] Global-10) (24), depression (Center for Epidemiologic Studies Depression Scale) (25), and fear of falling (Falls Efficacy Scale-International) (26). Frailty was defined using the Fried frailty criteria (27). Plantar sensory loss was evaluated with the maximum vibration perception threshold (VPT) using a biothesiometer (Bio-Medical Instruments). Peripheral neuropathy was defined as VPT >25 V. We conducted sensory perception tests using monofilaments placed at the following locations: *1*) plantar aspect of the first, third, and fifth toes; *2*) plantar area of first, third, and fifth metatarsals; *3*) plantar midfoot, including medial arch (navicular) and lateral midfoot (cuboid); *4*) plantar central heel; and *5*) dorsal aspect of the first metatarsal. Monofilament tests categorized sensory perception as intact, decreased, or loss of sensation. Patients were interviewed about adverse events (edema, skin breakdown, severe pain, burning during/after therapy) at each visit due to E-Stim (28). Patients were interviewed at each visit about potential adverse experiences defined as edema, skin breakdown, severe pain, or burning during or after E-Stim therapy.

Technology Acceptance Model: Acceptability Outcomes for iPES Intervention

We conducted a technology acceptance model (TAM) survey to prove that the use and preparation of the E-Stim equipment in this study can be performed by patients themselves with minimal effort and training and without medical staff guidance or assistance after the 12-week iPES intervention. The survey included evaluations of perceived usefulness, satisfaction, user friendliness, and changes in balance, foot strength, and sensation. After obtaining scores from all participants, each item and average were converted to percentages (i.e., 0–100%). Furthermore, we asked the participants whether they would be willing to use the E-Stim device at home in the future, and they could answer yes, no, or not sure. The essential items are described in Supplementary Table 1.

Sample Size Justification

The sample size was estimated based on a study by Mishra et al. (16) that showed significant improvement in postural transitions with iPES (Cohen $d = 0.64$). To detect iPES intervention benefits in the intervention group compared with the control group, a power analysis assumed repeated measures with a conservative effect size (Cohen $d = 0.5$), α of 2.5% (i.e., two primary outcomes), two groups, two measurements, and 0.5 correlation. Including a 10% dropout rate, 82 participants were required. The power analysis was performed using G*Power software (version 3.1.9.2).

Statistical Analysis

Descriptive analysis was used to report participant demographics, clinical characteristics, patient-reported outcomes, and acceptability outcomes. The independent *t* test was used for group comparison at baseline for normally distributed continuous demographics, clinical data, patient-reported outcomes, and perception of TAM items. The Mann-Whitney *U* test was used if the assumption of normal distribution was not satisfied. For categorical variables, the χ^2 test was used to compare between-group differences at baseline. This study used intention-to-treat and per-protocol analyses; the intention-to-treat analysis imputed missing follow-up data with baseline values, while the per-protocol analysis included only participants who completed all assessments (Supplementary Table 2).

Differences between the intervention and control groups in primary and secondary outcomes were completed using general linear models. Repeated measures were performed to assess the group × time interaction effect and within-subject time effect. Normality and homogeneity of variances were assessed using the Shapiro-Wilk and Levene tests ($P > 0.05$). The McNemar-Bowker test was used to evaluate monofilament changes within groups (baseline vs. follow-up; χ^2 test used for differences between groups at follow-up).

Effect size was measured using Cohen *d*, and its ranges are as follows: *1*) between 0.20 and 0.49 indicated small effects, *2*) between 0.50 and 0.79 indicated medium effects, and *3*) >0.8 indicated large effects. Pearson product moment correlation analysis was performed to examine the association between changes in gait performance/physical activity and changes in patient-reported outcomes after the 12-week iPES program in the intervention group. All statistical analyses were performed using SPSS for Windows (version 29.0; IBM Corporation, Chicago, IL), and statistical significance was set at $P < 0.05$.

Data and Resource Availability

Data are available upon request of the corresponding author due to privacy concerns.

RESULTS

Clinical Characteristics

Out of the 117 participants who initially met the inclusion and exclusion criteria for this study conducted between 1 June 2018 and 11 November 2023, 97 individuals completed the 12-week iPES treatment, resulting in a completion rate of 83%. Reasons for dropout included death (one each in the control and intervention groups), refusal to participate (three in the control group and one in the intervention group), and loss due to coronavirus disease 2019 (COVID-19) pandemic–related issues (six in the control group and eight in the intervention group) (Fig. 1). When the pandemic-related and unrelated study dropouts were excluded ($n = 16$), the completion rate was 96%. This study's analyses included a total of 97 participants (mean age 53.97 ± 13.04 years, mean BMI 30.96 ± 6.57 kg/m^2, females 32.0%). Table 1 shows no significant baseline differences in demographics, clinical characteristics, and patient-reported outcomes between the intervention and control groups.

Primary Outcomes

Figure 2 summarizes the gait and physical activity parameters. We found a significant group × time interaction effect between the control and intervention groups at follow-up and within each group during baseline and follow-up assessments of stride time at dual-task ($P = 0.031$, $d = 0.449$) and fast ($P = 0.014$, $d = 0.514$) walking (Fig. 2*A*) and from stand to walk ($P = 0.018$, $d = 0.496$) and sit to stand ($P = 0.021$, $d = 0.483$) (Fig. 2*B*). There was no significant group × time interaction effect for the single-task gait parameters and cumulative posture duration and locomotion for the physical activity parameters.

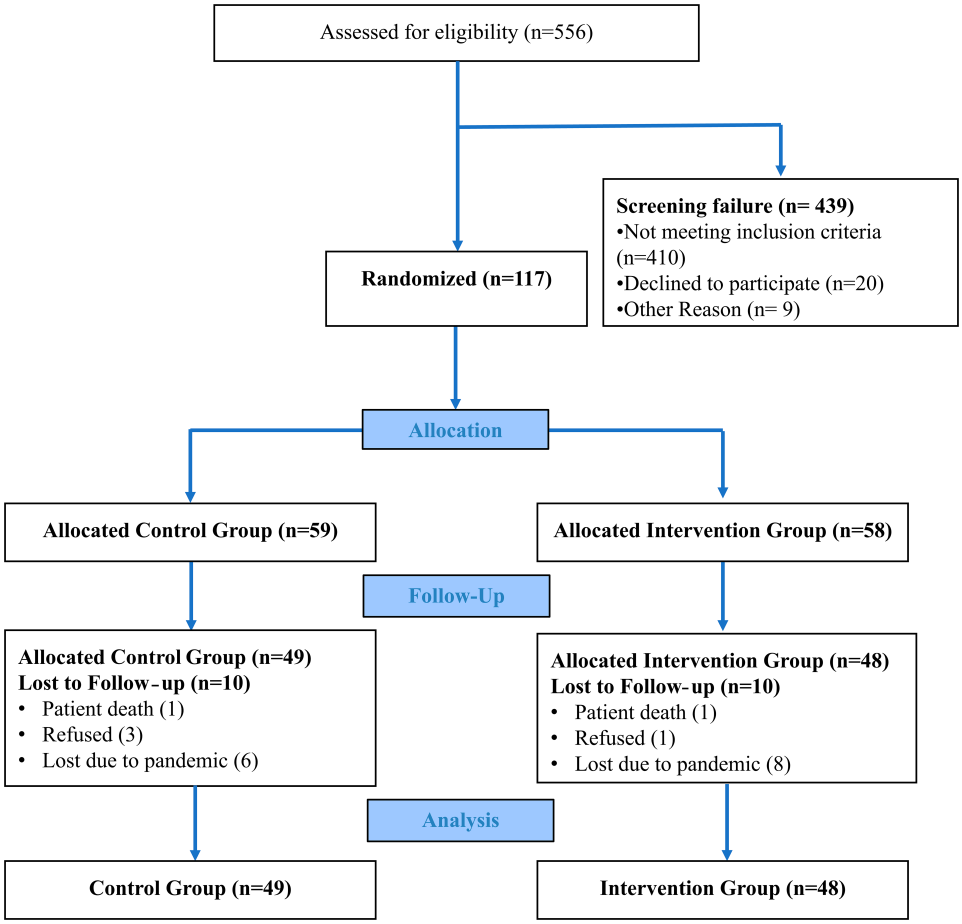

Figure 1—Consolidated Standards of Reporting Trials diagram, providing a comprehensive overview of the study's participants.

Secondary Outcomes

We found a significant time effect on quality of life for physical health (PROMIS: $P < 0.001$, $d = 0.814$) and mental health (PROMIS: $P = 0.005$, $d = 0.598$), sensitivity to plantar sensation (maximum VPT: $P = 0.002$, $d = 0.610$), and cognitive function (MoCA: $P = 0.008$, $d = 0.565$). As for the post hoc analysis for the within-group differences, the intervention group showed significant improvement in cognitive function (MoCA: $P = 0.005$, $d = 0.276$, 4.92% gain), quality of life for physical health (PROMIS: $P = 0.009$, $d = 0.420$, 7.14% gain) and mental health (PROMIS: $P = 0.039$, $d = 0.314$, 5.54% gain), and sensitivity to plantar sensation (maximum VPT: $P = 0.048$, $d = 0.156$, 8.06% decrease). The control group only showed a significant improvement in sensitivity to plantar sensation (maximum VPT: $P = 0.027$, $d = 0.102$, 5.68% decrease) (Supplementary Table 2).

After 12 weeks, monofilament outcomes worsened for six control group participants, while one intervention group participant improved; however, no statistical significance was found (control group: $P = 0.199$, $d = 0.350$; intervention group: $P = 0.910$, $d = 0.144$). Follow-up showed a moderate effect size between the control and intervention groups ($P = 0.114$, $d = 0.634$) (Supplementary Table 3).

Among the significant improvements within baseline and follow-up in the intervention group, we found a significant negative correlation between the magnitude of the reduced double support phase at dual-task walking and the magnitude of improvement in the quality of life for physical health ($r = -0.447$, $P = 0.002$) (Fig. 2*C*). In addition, the magnitude of improvement in standing and walking duration was positively associated with the magnitude of improvement in cognitive function ($r = 0.348$, $P = 0.015$) (Fig. 2*D*).

Acceptability Outcomes

A total of 83 of the 97 participants successfully answered the TAM-categorized usefulness, usage satisfaction, and user-friendly questionnaire after completing the 12-week iPES intervention program (answer rate 85.6%). For usefulness, the intervention group compared with the control group showed significantly higher acceptability for each item (P range $<$ 0.001 to 0.008, d range 0.601–1.016) (Fig. 3*A*) and for the average score (81.46 ± 12.41% vs. 65.60 ± 17.08%, respectively, $P < 0.001$, $d = 1.061$) (Fig. 3*B*, left). For usage satisfaction, the intervention group also showed significantly higher acceptability for each item ($P < 0.001$, d range 0.832–0.928) except for the first item (75.61 ± 9.50% vs. 89.04 ± 16.05%, respectively, $P < 0.001$, $d = 1.016$) (Fig. 3*A*) and for the average score (80.00 ± 10.54% vs. 74.44 ± 10.71%, respectively, $P = 0.020$, $d = 0.523$) (Fig. 3*B*, middle). There was no significant difference for the user-friendly item (Fig. 3*A* and *B*, right). We also asked the participants to answer an additional item about whether they intended to use the E-Stim intervention program at home in the future. As a result,

Table 1—Demographics, clinical characteristics, and patient-reported outcomes at baseline

Variable	Control group (n = 49)	Intervention group (n = 48)	P
Demographics			
Age (years)	54.51 ± 11.95	53.42 ± 14.18	0.682
BMI (kg/m^2)	30.79 ± 6.21	31.14 ± 6.99	0.795
Female sex	30.6	32.7	0.774
Clinical characteristics			
Dialysis period (years)	3.79 ± 3.05	3.70 ± 2.63	0.877
Hemoglobin (g/dL)	11.12 ± 1.05	11.24 ± 1.18	0.609
Calcium (mmol/L)	2.24 ± 0.16	2.19 ± 0.18	0.127
Phosphorus (mmol/L)	1.51 ± 0.44	1.66 ± 0.55	0.131
Sodium (mmol/L)	136.27 ± 2.41	135.27 ± 3.46	0.104
Albumin (g/L)	32.34 ± 3.34	33.34 ± 3.68	0.168
Ferritin (μg/L)	526.12 ± 331.39	549.34 ± 286.13	0.713
Transferrin saturation (%)	27.84 ± 8.63	27.73 ± 8.74	0.952
History of heart failure	18.4	12.5	0.424
History of falls in last year	8.2	10.4	0.702
History of foot ulcer	14.3	14.6	0.796
History of foot surgery	2.0	6.3	0.297
Walking assistance use	18.4	16.67	0.629
Peripheral arterial disease	42.9	43.8	0.662
Diabetic peripheral neuropathy	55.1	58.3	0.748
VPT (V)	27.20 ± 14.80	25.92 ± 13.75	0.658
Monofilament protective sensation			
Intact	65.3	68.8	0.409
Decreased	20.4	25.0	
Complete loss	14.3	6.3	
Diabetes duration (years)	21.04 ± 7.52	18.54 ± 7.56	0.115
HbA_{1c} (%)	7.40 ± 1.68	7.43 ± 1.36	0.937
Grip strength (kg)	19.85 ± 7.35	20.49 ± 7.96	0.685
ABI	1.32 ± 0.46	1.45 ± 0.59	0.245
Patient-reported outcomes			
Cognitive impairment	40.8	27.1	0.271
Depressive symptoms (CES-D score)	10.59 ± 5.92	10.55 ± 7.12	0.976
Depression	18.4	14.6	0.265
Pain (score)	0.56 ± 1.44	0.25 ± 0.96	0.214
Concern for falling (FES-I score)	8.47 ± 1.82	8.57 ± 2.78	0.827
High concern about falling	10.2	18.8	0.265
Physical-related health (PROMIS T score)	49.06 ± 7.23	49.01 ± 8.47	0.973
Mental-related health (PROMIS T score)	48.03 ± 8.65	47.30 ± 8.17	0.674
Screening tools outcomes			
Cognitive function (MoCA score)	25.32 ± 4.66	25.79 ± 4.87	0.635
Frailty (Fried frailty criteria)			
Robust	16.3	14.6	0.881
Prefrail	38.8	35.4	
Frail	44.9	50.00	

Data are mean ± SD or %. ABI, ankle brachial index; CES-D, Center for Epidemiological Studies Depression Scale; FES-I, Falls Efficacy Scale-International.

27 intervention group participants (65.9%) and only 15 control group participants (35.7%) answered yes. However, 9 intervention group participants (22.0%) and 17 control group participants (40.5%) answered no, and 5 (12.2%) and 10 (23.8%) participants, respectively, were not sure (P = 0.023, d = 0.635) (Fig. 3*C*).

CONCLUSIONS

This study examined whether a 12-week E-Stim intervention on the plantar area during hemodialysis could enhance gait performance and physical activity in patients with diabetes. Results showed that the intervention improved gait, physical activity, cognitive function (MoCA score), physical and mental health (PROMIS T scores), and sensory feedback. Improvements in gait and physical activity were linked to better physical health and cognitive function, respectively. The E-Stim intervention also had high acceptability and willingness for home use.

Hemodialysis is usually conducted while sitting or lying down, which accelerates loss of amino acid and protein in patients with diabetes (29), reducing physical activity (30) and gait speed (31). In a systematic review of exercise-based intervention programs to improve gait performance, however, the effectiveness of the intervention programs for improved habitual walking was not consistent because of differences in essential components (i.e., frequency, intensity, duration, and type) (31), making

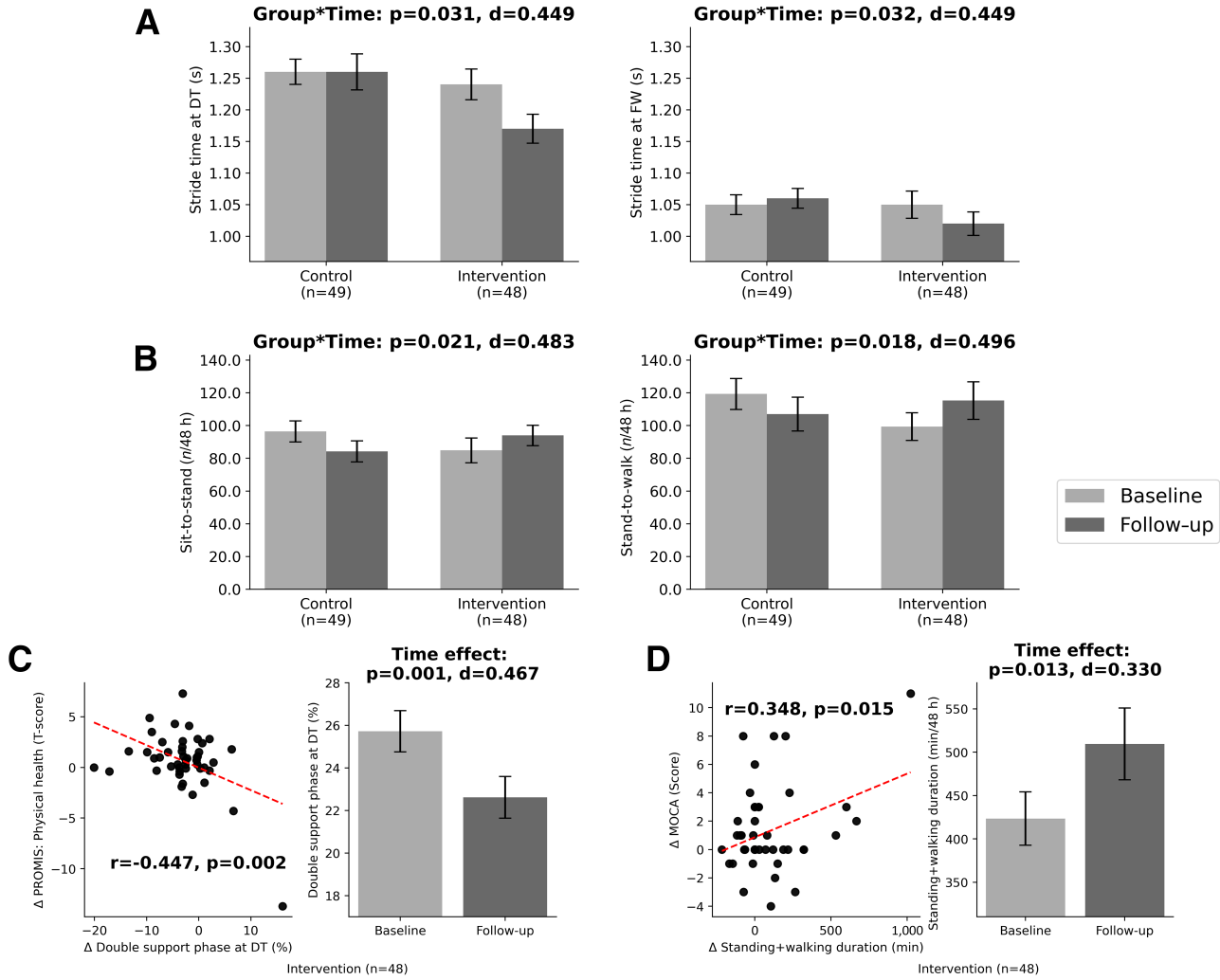

Figure 2—Group × time interaction results for physical activity and gait parameters after 12-week iPES intervention ($P < 0.05$): *A*: Gait parameters. *B*: Physical activity parameters. There were significant associations between improvement in gait/physical activity parameters and other metrics in the intervention group only ($n = 48$): *C*: The magnitude of the double support phase at dual-task (DT) walking was negatively correlated with the magnitude of quality of life for physical health. *D*: The magnitude of standing and walking duration was correlated with the magnitude of cognitive function. FW, fast walking.

it difficult to determine whether gait performance in patients undergoing hemodialysis declines. Our study also indicated no significant improvements in the habitual walking. Few studies conducted an advanced gait task, such as dual-task walking, using an objective gait analysis system, and Shin et al. (32) reported that patients undergoing hemodialysis showed poor gait characteristics, such as slower walking speed with a compensation strategy. In addition, Finco et al. (33) conducted a 12-week game-based intradialytic exercise improvement program focusing on ankle strength and reported that the intervention group showed improvement in gait performance, including fast walking speed and longer stride length after the 12-week intervention compared with the control group. In our study, we confirm that the improvement of gait parameters in the intervention group after the 12-week iPES, such as shortened stride time (dual-task walking: Δ −0.09 s, −7.14%; fast walking: Δ −0.03 s, −2.86%), reflects increased walking speed patterns (34). The intervention group showed improved walking speed in both the dual-task walking (Δ 0.13 m/s, 15.48%) and fast walking (Δ 0.05 m/s, 3.51%) parameters. These results suggest that changes in gait speed within the range of 0.1–0.2 m/s indicate a significant improvement based on the minimal clinically important difference, similar to findings reported in previous studies (35). However, these improvements were not statistically significant ($P > 0.05$). The results make sense because walking speed and stride length depend on lower-limb muscle strength, particularly ankle joint power at pushoff (34). The primary aim of the iPES intervention in this study was to improve afferent plantar sensory function rather than to strengthen foot muscle or to improve function-related ankle strength as in the Finco et al. (33) study, although iPES might also stimulate motor fibers. Thus, iPES may not have a direct effect on improving lower-extremity muscle strength, but it may be able to improve sensory function considering the mechanism of action, which may improve gait performance in patients undergoing hemodialysis.

Patients undergoing hemodialysis often experience decreased physical activity and mobility affected by poor walking balance and coordination and fatigue after sessions (4,5), contributing to a higher

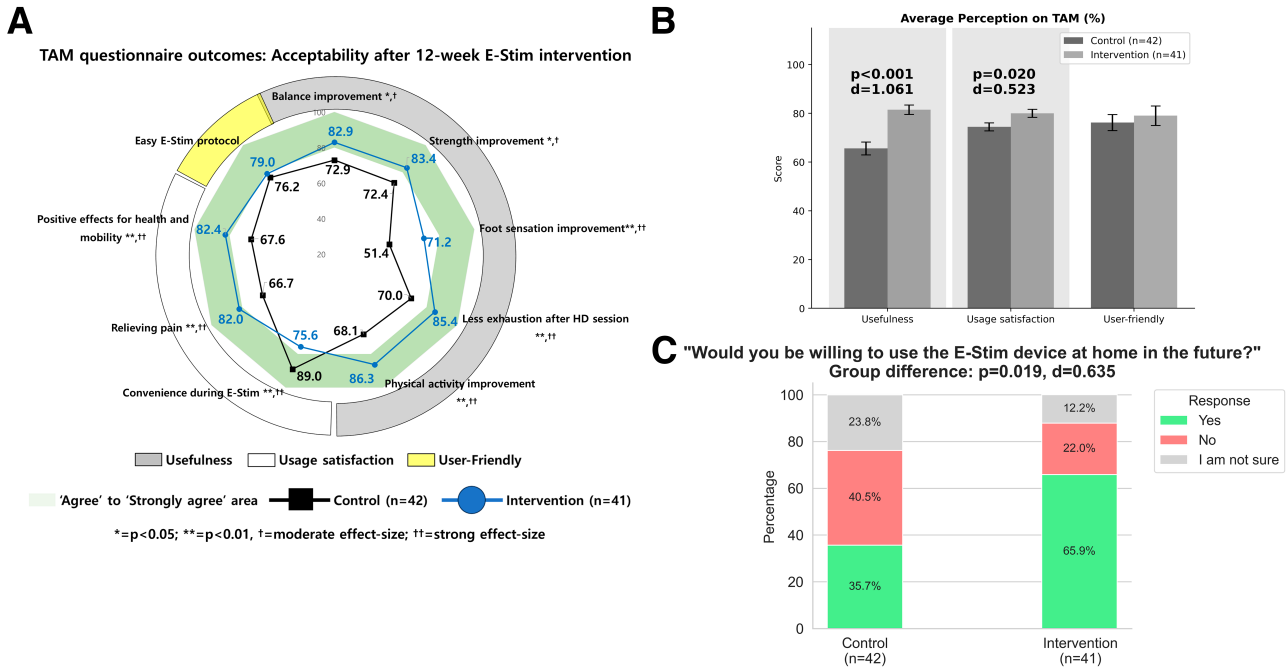

Figure 3—Acceptability outcomes regarding the TAM questionnaire. *A*: Overall item, including usefulness, usage satisfaction, and user-friendly. *B*: Average perceptions for usefulness, usage satisfaction, and user friendliness. *C*: Willingness to use the E-Stim intervention program at home, including yes, no, and not sure. HD, hemodialysis.

risk of falls (36). In daily living, sit to walk is a sequential postural locomotor task consisting of sit to stand and stand to walk (36). Sit to stand is influenced by a multitude of factors, such as sensorimotor control, balance, psychological factors, and combined measures of lower-limb muscle strength (36). Hemodialysis sessions affect sit-to-walk performance due to slower postural transition speed, which can attribute to an inability to maintain the timing sequence in postural transitions, and this pattern is more clear in patients undergoing hemodialysis (36). Interestingly, the control group in this study demonstrated reduced trends in sit to stand (Δ −12.20 *n*/48 h, −12.63%) and stand to walk (Δ −12.29 *n*/48 h,−10.30), whereas improved trends were found in the intervention group (sit to stand: Δ 9.09 *n*/48 h, 10.71%; stand to walk: Δ 15.96 *n*/48 h, 16.07%) based on the group × time interaction effect. In other words, the frequencies of sit to stand and stand to walk in the intervention group increased by 4.55 and 7.98 times per day, respectively, after 12 weeks of the iPES program. In contrast, the control group showed decreases of 6.1 and 6.15 times, respectively. Since postural transitions in daily activities affect subsequent movements and have a direct impact on physical activity levels (36), the increased number of postural transitions is considered to indicate an improvement in physical activity function. Our prior publication of interim results from the current project found reduced postural transitions in the control group, while the intervention group showed increases after the 12-week E-Stim intervention (16). The results indicate that E-Stim therapy improves cutaneous perfusion by possibly producing vascular endothelial growth factor (37), and it has been shown to stimulate axonal outgrowth, allow neurons and Schwann cells to survive, and promote neuron and Schwann cell proliferation in cultured animal cells (38). Therefore, our findings suggest that regular iPES therapy could improve mobility-related postural transitions, such as sit to stand and stand to walk, in daily life.

As much as 75% of patients undergoing hemodialysis have cognitive impairments due to CKD-related comorbidities, such as inflammation, oxidative stress, diabetes, malnutrition, and hypertension (39), which contribute not only to a reduction in cognition but also to worse dual-task walking performance (32). Our intervention group had significantly improved gait performance by reducing double support phase at the dual task (−12.02%) and improved physical health quality of life (7.14%); these improvements showed significant correlations (r = −0.447). They also demonstrated improvements in mental health and foot numbness after the intervention, and these findings are supported by previous studies (5,17). A slower walking speed leads to an increased double support phase to improve gait stability as a compensation strategy (34). Consequently, the iPES therapy can improve dual-task walking performance, which reflects improved cognitive and physical health quality of life in patients undergoing hemodialysis. In addition, the intervention group showed significant improvements for standing and walking duration in daily life (20.34%) and cognitive function (4.92%) after 12 weeks of iPES, with a significant correlation between them (r = 0.348). The effect of iPES on these participants' cognitive functioning might be related to the change in cognition-related blood parameters, such as brain-derived neurotrophic factor (40). The patients undergoing hemodialysis who did not use a walking aid showed higher numbers of walking bouts in daily life compared with those who used a walking aid; thus, assessment of participants' mobility function and level of physical activity should consider the number of walking bouts (22). These findings suggest that even though the

iPES intervention was focused on improving afferent plantar sensory dysfunction, it can also improve overall mobility function and physical activity, as well as patients' quality of life through improved physical health and cognitive function.

According to the TAM analysis, the intervention group demonstrated significantly higher scores in usefulness and usage satisfaction compared with the control group, with acceptance levels corresponding to strongly agree. Although no statistically significant difference was observed between the two groups, both groups exhibited strongly agree levels for user friendliness, suggesting that iPES could be a safer and more effective intervention program requiring minimal effort compared with traditional exercise-based intradialytic interventions. Since nurses positioned the E-Stim pads and activated the device, the TAM items related to user friendliness may not be entirely pertinent. However, as participants observed the process of positioning the pads and operating the E-Stim device, their perception of ease of use regarding self-administration remains relevant. This insight could inform the potential application of the intervention as a home-based or self-administered therapy. In the TAM survey, 65.9% of intervention group participants showed a willingness to use E-Stim therapy at home compared with 35.7% in the control group, explaining the intervention group's strongly agree responses. The demand for home-based treatments, including telemedicine, has risen since the COVID-19 pandemic. Given these trends and benefits for patients with diabetes, iPES therapy is recommended during dialysis to maintain/improve patient function.

We recognize several limitations in this study. First, although the study considered a total of 117 participants, ∼14.56% were inevitably excluded (12.00% due to COVID-19 and 2.56% due to death). This resulted in challenges in the progress of the experiment over a certain period, but ultimately, 97 participants were successfully analyzed. We observed improvements in sensory feedback in patients undergoing active iPES therapy during hemodialysis compared to shame iPES therapy, with medium effect size, as measured by monofilament outcomes. However, the results were not statistically significant in our sample. We anticipate that a longer-term or more frequent application of iPES or an increase in sample size, may yield significant results in verifying this sensory recovery in response to iPES therapy. Moreover, perfusion measurements could provide important insights into evaluating physiological improvements through the iPES intervention. Additionally, it has been reported that most patients undergoing hemodialysis exhibit a loss of balance ability (5), but this study did not consider balance evaluation following the intervention. To determine which parameters of balance are improved after an iPES intervention, future research should examine the balance metrics. Finally, we believe that the exercise is one of the most effective and recommended interventions; however, it may not be feasible for patients undergoing hemodialysis based on low compliance due to fatigue after the dialysis session (4,5). Even the 12-week iPES intervention had an impact on physical function in this study, but iPES is merely one method to help maintain and improve the physical function of patients undergoing hemodialysis, and we do not believe it can replace exercise interventions. Therefore, future research should not only consider a longer intervention period but also incorporate suitable exercise programs for these patients to confirm whether their overall physical function can be maintained or improved.

In conclusion, patients with diabetes undergoing hemodialysis experience a decrease in physical function, including diminished plantar sensation, cognitive function, and quality of life due to their comorbid conditions. This study demonstrated that a 12-week intervention using iPES could improve walking ability, increase physical activity, enhance plantar sensation, and improve cognitive function and quality of life. Notably, the improvements in gait function and physical activity level through the 12-week iPES intervention were significantly associated with enhancements in cognitive function and physical quality of life among patients undergoing hemodialysis. The iPES intervention program proved convenient and required minimal effort on the part of patients, resulting in high adherence rates without adverse events and high satisfaction levels. As such, iPES therapy is suggested for the improvement of physical capabilities, clinical characteristics, and overall function in patients undergoing hemodialysis. Future studies should explore the impact of its medium- to long-term application on the preservation or enhancement of patients' functions.

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Duality of Interest. B.N. serves as a consultant for BioSensics, the manufacturer of the wearable devices used in this study to assess gait and balance. However, his consultancy role was not related to the scope of this study and he did not participate in the data analysis for this study. No other potential conflicts of interest relevant to this article were reported.

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