The Egyptian Journal of Hospital Medicine (April 2024) Vol. 95, Page 1910- 1919

Effect of Intradialytic Cycling Exercises on Functional Performance and Quality of Life in Patients on Hemodialysis: Systematic Review and Meta-Analysis

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ABSTRACT

Background: Intradialytic exercise has emerged as a favorable option for dialysis patients due to its benefits, like enhanced toxin removal, time efficiency, and safety. Previous studies have delved into the effects of such exercises on the quality of life (QOL) in hemodialysis patients. This can also help with improved nutrition, bone density, cardiovascular endurance, and functional ability.

Methods: Relevant electronic databases were searched from 2016 to December 2023. We included randomized controlled trials focusing on intradialytic cycling exercises in patients undergoing hemodialysis. Two review authors independently screened articles and evaluated bias risks. Outcome measures related to intradialytic cycling exercises and hemodialysis patients and their effect on functional performance and QOL were extracted and summarized through qualitative and quantitative methods.

Results: Five trials were selected based on their high-quality methodology. They investigated whether research on intervention techniques were diverse or not. Qualitative analysis was conducted on the findings, which revealed moderate evidence in five articles about the effect of intradialytic cycling exercises on functional performance and QOL in patients undergoing hemodialysis. Meta-analysis was applied, and it showed that, the strategy of performing intradialytic aerobic cycling exercise during the process of dialysis showed higher levels of physical activity and fitness.

Conclusion: Based on our evidence in this systematic review and meta-analysis, this review found moderate evidence that, the intervention of intradialytic aerobic cycling exercise on HD alleviates inflammation, increases bone density, improve nutrition, exercise tolerance and induced higher levels of physical activity and fitness.

Keywords: Intradialytic cycling exercise, Physical activity, Muscle strength, Endurance physical function, CKD, QOL.

INTRODUCTION

For HD patients, an inexpensive, safe method of reducing inflammation is to engage in intradialytic aerobic cycle exercise. This can also help with improved nutrition, bone density, cardiovascular endurance, and functional ability. Numerous research has examined the benefits of intradialytic exercise, and most of them have shown these benefits [(1)].

Even yet, a number of studies have shown that intradialytic exercise can enhance muscle blood flow, which in turn enhances solute elimination during HD. For dialysis patients, QOL is a key indicator of medical treatment results that forecasts hospitalization and death. Enhancing QOL via diverse therapies is essential for dialysis patients [(1)].

ESRD is a case in which the kidneys fail to work properly, necessitating the use of dialysis to get rid of waste products and excess fluids from the body[(2)]. Patients with CKD often have lower activity levels, which leads to functional and physical impairments that mostly show up as a decline in the ability to conduct activities of daily living [(3)].

Renal failure particularly in its advanced stage, profoundly affects the body's health and functioning. The urinary system is essential for maintaining homeostasis by filtering waste items, regulating fluid and electrolyte balance, managing blood pressure, and secreting hormones that encourage red blood cell synthesis. When renal function is compromised, several physiological and biochemical imbalances occur, affecting multiple organ systems [(4)].

Intradialytic exercise has emerged as a favorable option for dialysis patients due to its effects on enhancing toxin removal, time efficiency, and safety. These exercises not only hold the potential for improving cardiovascular outcomes and dialysis effectiveness but also contribute to increased muscle strength, endurance, physical functionality, and lower levels of high-sensitivity C-reactive protein (CRP) in individuals undergoing hemodialysis[(5)].

Prior research has indicated a high correlation between recovery time and health-related QOL in hemodialysis patients. These researchers found that patients' QOL was poorer in those who recovered from their conditions more quickly [(3-5)]. Intradialytic cycling exercise, a rehabilitative strategy to promote functional performance and QOL, was observed to significantly reduce dialysis recovery time [(6)].

When receiving dialysis, the majority of ESRD patients are prone to become sedentary, which lowers their physical activity and fitness levels and ultimately lowers their survival rates compared to healthy populations. To treat these diseases, a number of therapies have been used. Many studies have been carried out in the last ten years to determine the positive benefits of Dual-energy X-ray absorptiometry (DXA) on laboratory markers and physical fitness in ESRD patients receiving HD[(7)].

Received: 02/01/2024
Accepted: 01/03/2024

This study aims to synthesize all the eligible RCTs and systematically analyze the effect of intradialytic cycling exercises on functional performance and QOL in patients on hemodialysis.

1-Methods

The registration for this systematic review is recorded in the PROSPERO review database **(Reference: CRD42023481478).** The study followed the guidelines outlined in PRISMA 2020, which offers a systematic approach to conducting and reporting data in systematic reviews and meta-analyses (PRISMA Statement)[8].

Search strategy and study selection

The identification of records involved searches across several literature databases, including the Cochrane Controlled Trials Register, PubMed, Google Scholar, and PEDro, from 2016 to December 2023. Furthermore, manual searches were conducted using reference lists of relevant papers and reviews. The search strategy utilized a comprehensive approach encompassing search terms associated explicitly with intradialytic aerobic exercises on functional performance and QOL on HD patients. The electronic databases were searched using the following keywords: "intradialytic cycling exercise", “physical activity”, “muscle strength,” “endurance and,” “physical function,” “chronic kidney disease”, “renal failure,” “clinical trial”. The search yielded a total of 226 articles. Screening, initially based on titles and abstracts, followed by subsequent independent full-text screening, was carried out by two authors (SE and MS).

Inclusion and exclusion criteria

An article was **included** if:

(1) Randomized control trials (RCTs) of studies in the last 7 years, from 2016 to 2023.

(2) In the investigations, aerobic intradialytic exercises were utilized as the single intervention or as part of the intervention.

(3) Studies must be in the English language. Studies that were **excluded** from the review:

(1) First, the titles and abstracts were evaluated to find trials that were pertinent, the obvious irrelevant studies were excluded and duplicates were excluded, then the whole texts of pertinent papers were obtained and examined in comparison with this review's qualifying requirements.

(2) Any study other than RCTs (e.g., cross-sectional, cohort studies, case-control, case series, case reports, and review articles).

(3) The studies written in languages other than English.

(4) Articles published before 2016 and after 2023.

Data extraction and quality assessment

This systematic review employed a structured process to include studies, as depicted in **Figure 1**.

Two research team members independently screened articles according to the inclusion criteria at each step, aiming to minimize bias. The title/abstract and full-text screenings were conducted by two reviewers (SE and MS). In cases of discrepancy between the two initial reviewers, a third reviewer was consulted to decide on the inclusion or exclusion of the study. Two independent reviewers scored all the included studies on their methodological accuracy (SE and MS). Using the PEDro scale was more specific to rating RCT quality (Table 2).

The PEDro scale examines 11 criteria of the quality of methodology. Each satisfied item (except the first item, which is related to external validity) adds 1 point to the overall PEDro score within a range of 0 to 10 topics. The study is considered high-quality RCTs when PEDro Scale scores ≥ 6. The methodological quality was graded using the following system: a score of 4 on the PEDro scale denoted poor quality, a score of 4-5 characterized fair rates, a score of 6-8 denoted good quality, and a score of 9–10 denoted excellent quality[9].

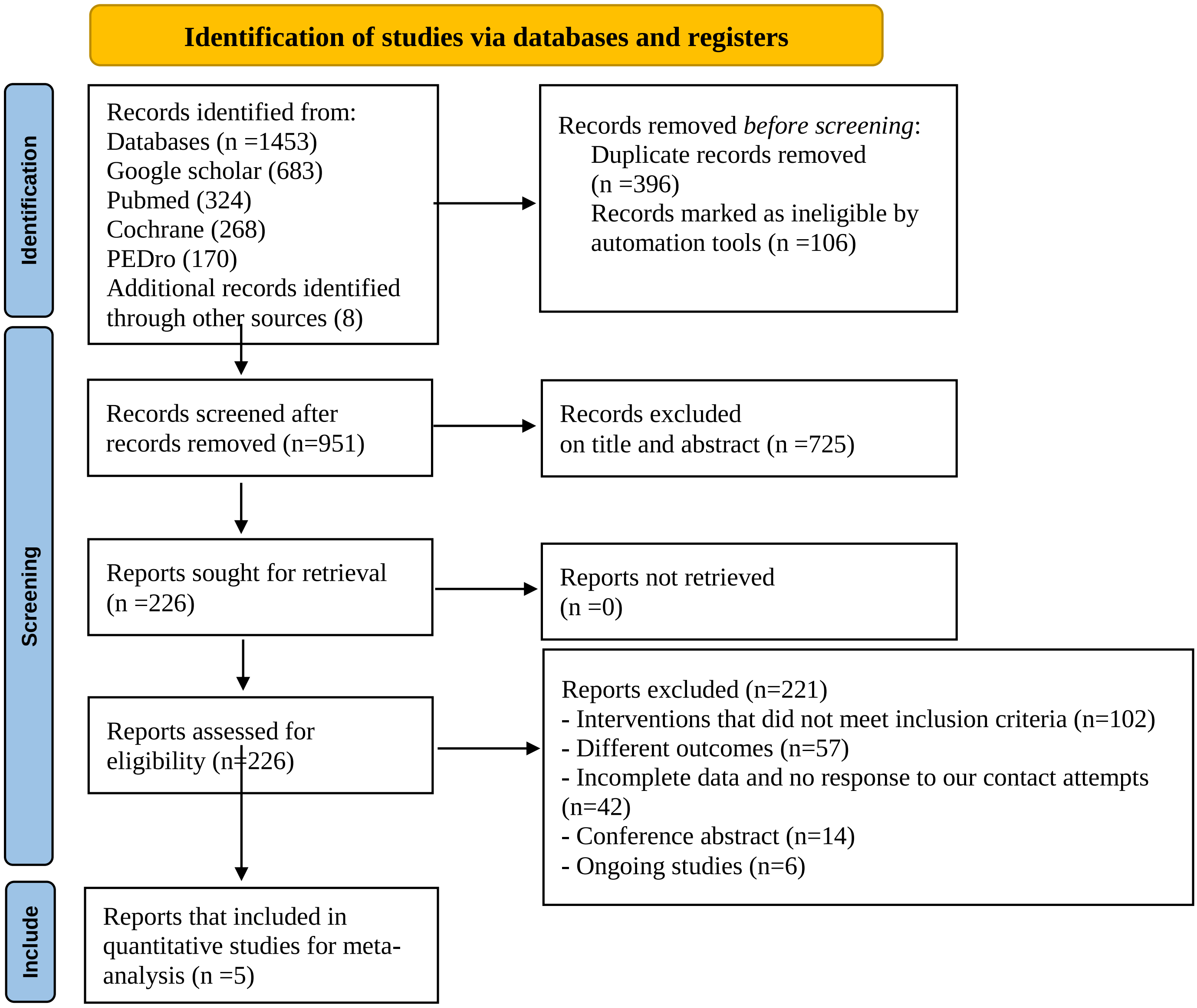


Figure (1): The PRISMA flow chart of the reviewed studies

Quality of evidence

Levels of evidence were defined as follows:

• **High-quality evidence**: It is unlikely that more study will alter the effect estimate's level of confidence. This is given when there are no research design restrictions, at least 75% of RCTs with consistent results, exact and direct data, and no known or suspected publishing biases. Every domain is satisfied.

• **Moderate-quality evidence**: Additional research might alter the evaluation and have a major impact on the confidence in the effect estimate. When one of the domains is not satisfied, this is allocated.

• **Low-quality evidence**: Additional study is anticipated to alter the projection and probably have an impact on the confidence in the effect estimate. When two of the domains are not satisfied, this is allocated.

• **Very–low-quality evidence**: Any effect estimate is highly speculative. When none of the three domains are met, this is assigned.

• **No evidence**: There were no RCTs found that addressed this result.

The level of evidence was reported according to the modified Sackett's scale; levels are listed in the following table:

Level	*Study design*
1	RCT (PEDro score ⩾6)
2	RCT (PEDro score <6), prospective controlled trial, cohort
3	Case control
4	One-group pretest–posttest, case series
5	Case report

Abbreviations: PEDro, Physiotherapy Evidence Database; RCT, randomized controlled trials.

RESULTS

Selection of studies

1453 studies were discovered and reviewed; duplicates were deleted, there were 396 studies. Ultimately, 725 studies were excluded after reading title, abstract, and full text resulting in 5 studies meeting the inclusion criteria **(Figure 1).** Descriptions of studies and characteristics of the populations can be found in **(Table 1).**

Table (1): Selection of studies

1	**Liao *et al.*** [10]	Intradialytic aerobic cycling exercise alleviates inflammation and improves endothelial progenitor cell (EPC) count and bone density in hemodialysis patients
2	**Moeinzadeh *et al.*** [11]	Evaluating the effect of intradialytic cycling exercise on QOL and recovery time in hemodialysis patients: a randomized clinical trial
3	**Yeh *et al.*** [12]	Twelve-week intradialytic cycling exercise improves physical functional performance with gain in muscle strength and endurance: a randomized controlled trial
4	**March *et al.*** [13]	Circulating endotoxin and inflammation: associations with fitness, physical activity and the effect of a 6-month programme of cycling exercise during haemodialysis
5	**Assawasaksakul *et al.*** [14]	Effects of intradialytic cycling exercise on daily physical activity, physical fitness, body composition, and clinical parameters in high-volume online hemodiafiltration patients

Column	Liao *et al.* [10]	Moeinzadeh *et al.* [11]	Yeh *et al.* [12]	March *et al.* [13]	Assawasaksakul *et al.* [14]
Research Design	RCT	RCT	RCT	RCT	RCT
Level of Evidence	Level II	Level II	Level II	Level II	Level II
Participant Characteristics	40 ESRD patients on HD, Age 21-65 years, 23 females, 17 males	110 hemodialysis patients, Adults ≥18 years, 50-60% male	76 hemodialysis patients, Mean age 55 years, 52% male	92 hemodialysis patients, Mean age 57 years, 73% male	12 hemodiafiltration patients, Mean age 53 years, 50-67% male
No. of Participants	Exercise group n=20, Control group n=20	Exercise group n=60, Control group n=50	Exercise group n=30, Control group n=32	Exercise group n=46, Control group n=46	Exercise group n=6, Control group n=6
Age Range	21-65 years	≥18 years	Mean age 55 years	Mean age 57 years	Mean age 53 years
Sex	23 females, 17 males	50-60% male	52% male	73% male	50-67% male
Intervention	Intradialytic aerobic cycling exercise during regular dialysis sessions	Intradialytic cycling exercise during dialysis sessions	Twelve-week intradialytic cycling exercise during dialysis	6 months of intradialytic cycling exercise	Intradialytic cycling exercise during high-volume online hemodiafiltration
Control Intervention	Standard hemodialysis treatment	Usual care	Usual care	Usual care	Standard high-volume online hemodiafiltration
Outcome Measures	Inflammation markers, EPC count, Bone density	QOL, recovery time, biochemical measures	6-minute walk distance, sit-to-stand test, muscle strength and endurance	Endotoxin, inflammatory cytokines, physical activity, fitness	Physical activity, fitness, body composition, clinical parameters
Assessment Measures	Blood tests, ELISA, DEXA scans	KDQOL-SF, lab tests	6MWT, sit-to-stand test	Blood tests, accelerometer, ISWT, STS60	Accelerometer, CPET, DXA, blood tests
Main Results	Reduced inflammation markers, Increased EPC count, Improved bone density	Improved QOL and recovery time	Improved physical functional performance, Gains in muscle strength and endurance	Decreased circulating endotoxins, Reduced inflammatory markers, Improved fitness levels	Increased daily physical activity, Improved fitness, Favorable body composition, Improved clinical parameters
Component of Health	Inflammation, Endothelial function, Bone health	Activity and participation	Body functions	Body functions	Activity and participation
Conclusions	Exercise can alleviate inflammation, improve EPC count, and enhance bone density	Exercise improves QOL and recovery time	Twelve-week exercise program improves physical functionality, muscle strength, and endurance	6-month exercise program reduces endotoxins, inflammatory markers, and improves fitness	Exercise impacts daily activity, fitness, body composition, and clinical parameters positively
Reported Adverse Events	Not specified	None	None	None	None

Table (2): Physiotherapy evidence database (PEDro) scores

	Study 1 Liao *et al.* (10)	Study 2 Moeinzadeh *et al.* (11)	Study 3 Yeh *et al.* (12)	Study 4 March *et al.* (13)	Study 5 Assawasaksakul *et al.* (14)
1. Random Allocation	Yes	Yes	Yes	Yes	Yes
2. Concealed Allocation	No	No	yes	No	No
3. Groups Similar at Baseline	Yes	Yes	Yes	Yes	Yes
4. Participant Blinding	No	No	yes	No	No
5. Therapist Blinding	No	No	No	No	No
6. Assessor Blinding	No	No	No	No	No
7. <85% Follow-up	Yes	No	Yes	Yes	Yes
8. Intention-to-Treat Analysis	No	No	No	No	No
9. Between-Group Comparison	Yes	Yes	Yes	Yes	Yes
10. Point Estimates and Variability	Yes	Yes	Yes	Yes	Yes
Total PEDro Score	**6/10**	**5/10**	**7/10**	**6/10**	**6/10**

Study characteristics

The 5 studies examined a total of 330 participants. The five studies divided the hemodialytic patients into two groups (control and study). **Liao *et al.* (10), March *et al.* (13) and Assawasaksakul *et al.* (14)** divided patients into two equal patients in each group. **Moeinzadeh *et al.* (11)** divided participants into 50 patients in control group and 60 patients in exercise group. **Yeh *et al.* (12)** had 76 patients, who were divided into 32 in the control group and 30 in the exercise group. All five studies successfully employed random allocation, which is a good indicator for reducing selection bias. Only one study utilized concealed allocation, a limitation that could introduce allocation bias. All five studies focused on using the cycling exercise through the process of dialysis. After the intervention of cycling exercise, all studies mentioned the significant improvement on reduced inflammation markers, increased EPC count, improved bone density, improved QOL as well as recovery time, increased daily physical activity, improved fitness and favorable body composition.

Level of evidence and quality assessment

The PEDro scale was utilized for the risk of bias assessment, yielding the following results: All five studies successfully employed random allocation, which is a good indicator for reducing selection bias. Only one study utilized concealed allocation, a limitation that could introduce allocation bias. All studies ensured that the groups were homogenous at the baseline, enhancing the studies' internal validity. The I^2 statistics were used to assess heterogeneity; values more than 25 and greater than 50% were regarded as signs of moderate heterogeneity and significant heterogeneity, respectively. Subgroup analysis was done to determine the cause if considerable heterogeneity was found.

None of the studies implemented blinding for participants, therapists, or assessors. Four out of five studies had a follow-up rate greater than 85%, which is generally positive. Study 2 was the exception with less than 85% follow-up. In the five studies there was no drop out, so all the participants were treated.

Total PEDro Score: Every study that was part of the evaluation has a score between five and seven. The more points research receives on the many metrics used to assess its quality, the higher its quality. According to PEDro scale, all the reviewed studies are of good quality. it gives an initial idea of the methodological quality[15].

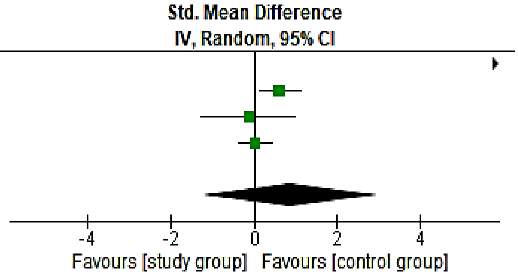
Meta-Analysis: This meta-analysis gathered data at the study-level. At the end of the intervention period, functional performance is evaluated using a 6-minute walking test and sit-to-stand (STS)60. Moreover, QOL outcome measured by CRB taken from blood sample in hemodialysis patients. To facilitate comparison of data from multiple scales, pooled statistics were produced using standardized mean differences (SMDs), which were computed using the Review Manager application **(RevMan software, version 5).** After an initial screening of 1453 papers, 725 papers were excluded (Figure 1). After two reviewers examined the titles and abstracts, 396 papers were later excluded for duplication, 106 incorrect populations, and incorrect treatments. Next, perhaps 226 references were examined during the full-text reviewing phase to see if they met the requirements. Ultimately, 330 people were found in 5 references, which were then included to the study.

1-Effect of intradialytic cycling exercises on functional performance using 6 minutes walking test

Four studies assessed intradialytic cycling exercises on functional performance measurement by 6 minutes walking test between study group and control group to improve functional performance in hemodialysis patients (Forest plot 1). There was considerable heterogeneity in functional performance measurement by 6 minutes walking test between 4 studies (n= 4 studies, n= 208 participants, $P<0.00001$; I^2= 97%). There was no significant difference (P= 0.41) in overall effect of functional performance measurement by 6 minutes walking test (SMD= 0.88; 95% CI, -1.20 to 2.96) between study group and control group. Sensitivity analysis (Forest plot 2) demonstrated that functional performance evaluation by 6 minutes walking test had moderate heterogeneity (I2=44%; P=0.17), except when one trial at a time was excluded from pooled effects to examine if any one research was particularly important. After removing one study, **Liao *et al.* (10),** there was no significant difference (P=0.29) in the overall effect between the study group and the control group in functional performance measurement by the 6-minute walking test (sensitivity 1; SMD= 0.24; 95% CI, -0.21 to 0.70), according to sensitivity analysis matrix.

Study or Subgroup	Study group Mean	SD	Total	Control group Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Liao et al. (2016)	380	0.82	20	290	0.72	20	0.6%	114.32 [87.93, 140.71]	2016
Yeh et al. (2020)	401.97	95.9	30	345	84.43	32	33.9%	0.62 [0.11, 1.13]	2020
Assawasaksakal et al. (2021)	457	30	6	460	2	6	31.4%	-0.13 [-1.26, 1.00]	2021
March et al. (2022)	266	171	46	260	172	46	34.1%	0.03 [-0.37, 0.44]	2021
Total (95% CI)			**102**			**104**	**100.0%**	**0.88 [-1.20, 2.96]**	

Heterogeneity: Tau² = 3.26; Chi² = 75.32, df = 3 (P < 0.00001); I² = 96%
Test for overall effect: Z = 0.83 (P = 0.41)



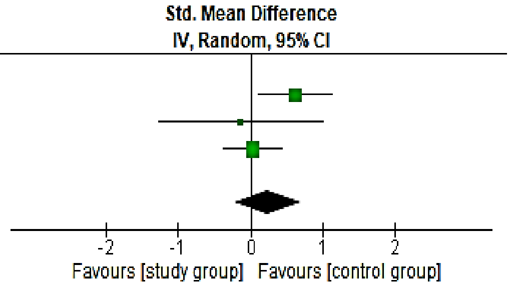
Forest plot (1): Standardized mean differences (95% CI) of intradialytic cycling exercises on functional performance measurement by 6 minutes walking test after assisted as compared with a control from 4 studies.

Sensitivity analysis (Six minutes walking test)

Sensitivity (1)

Study or Subgroup	Study group Mean	SD	Total	Control group Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Liao et al. (2016)	380	0.82	20	290	0.72	20	0.0%	114.32 [87.93, 140.71]	2016
Yeh et al. (2020)	401.97	95.9	30	345	84.43	32	39.1%	0.62 [0.11, 1.13]	2020
Assawasaksakal et al. (2021)	457	30	6	460	2	6	13.3%	-0.13 [-1.26, 1.00]	2021
March et al. (2022)	266	171	46	260	172	46	47.6%	0.03 [-0.37, 0.44]	2021
Total (95% CI)			**82**			**84**	**100.0%**	**0.24 [-0.21, 0.70]**	

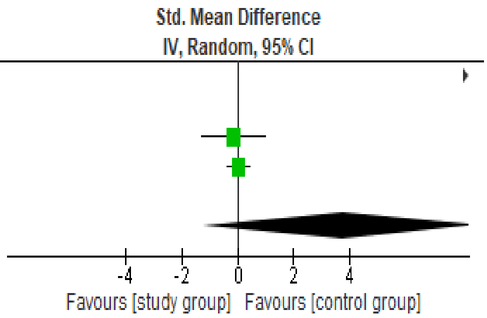
Heterogeneity: Tau² = 0.07; Chi² = 3.55, df = 2 (P = 0.17); I² = 44%
Test for overall effect: Z = 1.05 (P = 0.29)



Sensitivity (2)

Study or Subgroup	Study group Mean	SD	Total	Control group Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Liao et al. (2016)	380	0.82	20	290	0.72	20	3.3%	114.32 [87.93, 140.71]	2016
Yeh et al. (2020)	401.97	95.9	30	345	84.43	32	0.0%	0.62 [0.11, 1.13]	2020
Assawasaksakal et al. (2021)	457	30	6	460	2	6	47.8%	-0.13 [-1.26, 1.00]	2021
March et al. (2022)	266	171	46	260	172	46	48.9%	0.03 [-0.37, 0.44]	2021
Total (95% CI)			72			72	100.0%	3.76 [-1.23, 8.75]	

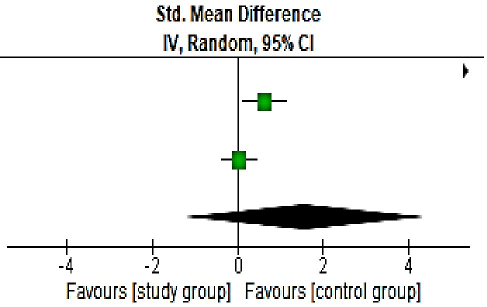
Heterogeneity: Tau² = 13.22; Chi² = 72.12, df = 2 (P < 0.00001); I² = 97%
Test for overall effect: Z = 1.48 (P = 0.14)



Sensitivity (3)

Study or Subgroup	Study group Mean	SD	Total	Control group Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Liao et al. (2016)	380	0.82	20	290	0.72	20	1.1%	114.32 [87.93, 140.71]	2016
Yeh et al. (2020)	401.97	95.9	30	345	84.43	32	49.3%	0.62 [0.11, 1.13]	2020
Assawasaksakal et al. (2021)	457	30	6	460	2	6	0.0%	-0.13 [-1.26, 1.00]	2021
March et al. (2022)	266	171	46	260	172	46	49.6%	0.03 [-0.37, 0.44]	2021
Total (95% CI)			**96**			**98**	**100.0%**	**1.58 [-1.22, 4.37]**	

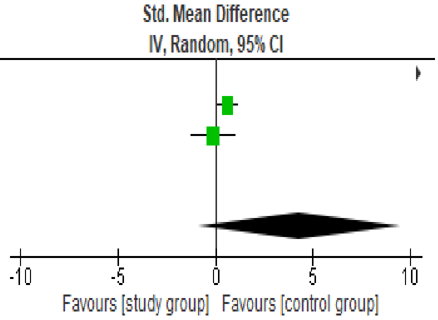
Heterogeneity: Tau² = 4.06; Chi² = 74.85, df = 2 (P < 0.00001); I² = 97%
Test for overall effect: Z = 1.11 (P = 0.27)



Sensitivity (4)

Study or Subgroup	Study group Mean	SD	Total	Control group Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Liao et al. (2016)	380	0.82	20	290	0.72	20	3.6%	114.32 [87.93, 140.71]	2016
Yeh et al. (2020)	401.97	95.9	30	345	84.43	32	48.7%	0.62 [0.11, 1.13]	2020
Assawasaksakal et al. (2021)	457	30	6	460	2	6	47.8%	-0.13 [-1.26, 1.00]	2021
March et al. (2022)	266	171	46	260	172	46	0.0%	0.03 [-0.37, 0.44]	2021
Total (95% CI)			56			58	100.0%	4.31 [-0.86, 9.48]	

Heterogeneity: Tau² = 14.22; Chi² = 72.85, df = 2 (P < 0.00001); I² = 97%
Test for overall effect: Z = 1.63 (P = 0.10)

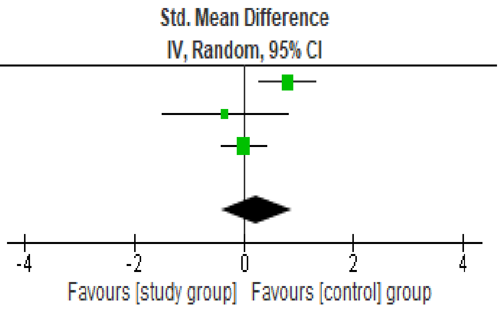


Forest plot (2): Sensitivity analysis showed that intradialytic cycling exercises on functional performance measurement by 6 minutes walking test was significant, except when one experiment, **Liao *et al.* [10],** was excluded from pooled effects to assess if any one research was particularly important. Susceptibility analysis revealed that the meta-analysis's results were stable.

2-Effect of intradialytic cycling exercises on functional performance using sit to stand (STS 60)

Three studies assessed intradialytic cycling exercises on functional performance measurement by STS 60 between study group and control group to improve functional performance in hemodialysis patients (Forest plot 3). There was substantial heterogeneity in functional performance measurement by STS 60 between three studies (n= 3 studies, n= 164 participants, P=0.04; I^2= 70%). There was no significant difference (P= 0.48) in overall effect of functional performance measurement by STS 60 (SMD= 0.23; 95% CI, -0.41 to 0.88) between study group and control group. Sensitivity analysis (Forest plot 4) showed that functional performance measurement by STS 60 was no heterogeneity (I^2=0%; P=0.58) except for eliminating one experiment at a time from pooled effects to assess whether a single research was highly important. After excluding one research, **Yeh *et al.*** **[12],** there was no significant difference (P=0.84) in the overall effect between the study and control groups in functional performance measurement by STS 60 (sensitivity 1; SMD= -0.04; 95% CI, -0.42 to 0.35), according to the sensitivity analysis matrix.

	Study group			Control group				Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Yeh et al. (2020)	24.67	7.27	30	19.59	5.2	30	38.1%	0.79 [0.27, 1.32]	2020
Assawasaksakal et al. (2021)	9.47	1.98	6	10.33	2.58	6	19.6%	-0.35 [-1.49, 0.80]	2021
March et al. (2022)	16	12	46	16	12	46	42.3%	0.00 [-0.41, 0.41]	2021
Total (95% CI)			**82**			**82**	**100.0%**	**0.23 [-0.41, 0.88]**	
Heterogeneity: Tau² = 0.21; Chi² = 6.56, df = 2 (P = 0.04); I² = 70%									
Test for overall effect: Z = 0.71 (P = 0.48)									

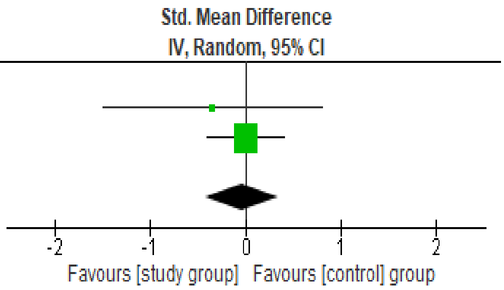


Forest plot (3): Standardized mean differences (95% CI) of intradialytic cycling exercises on functional performance measurement by STS 60 after assisted as compared with a control from three studies.

Sensitivity analysis (STS 60)

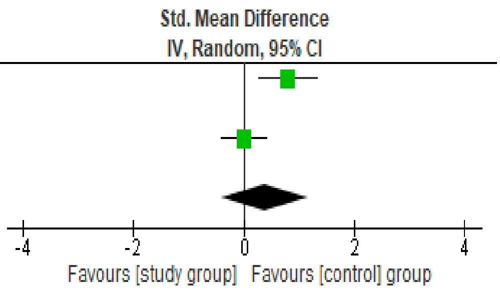
Sensitivity (1)

	Study group			Control group				Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Yeh et al. (2020)	24.67	7.27	30	19.59	5.2	30	0.0%	0.79 [0.27, 1.32]	2020
Assawasaksakal et al. (2021)	9.47	1.98	6	10.33	2.58	6	11.3%	-0.35 [-1.49, 0.80]	2021
March et al. (2022)	16	12	46	16	12	46	88.7%	0.00 [-0.41, 0.41]	2021
Total (95% CI)			**52**			**52**	**100.0%**	**-0.04 [-0.42, 0.35]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.31, df = 1 (P = 0.58); I² = 0%									
Test for overall effect: Z = 0.20 (P = 0.84)									



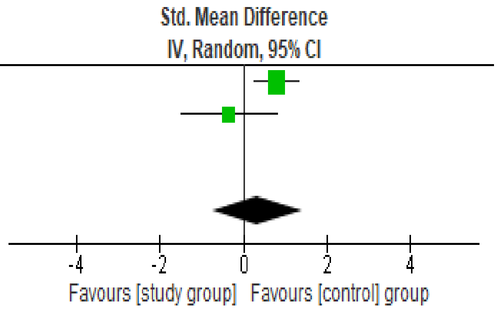
Sensitivity (2)

	Study group			Control group				Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Yeh et al. (2020)	24.67	7.27	30	19.59	5.2	30	47.7%	0.79 [0.27, 1.32]	2020
Assawasaksakal et al. (2021)	9.47	1.98	6	10.33	2.58	6	0.0%	-0.35 [-1.49, 0.80]	2021
March et al. (2022)	16	12	46	16	12	46	52.3%	0.00 [-0.41, 0.41]	2021
Total (95% CI)			**76**			**76**	**100.0%**	**0.38 [-0.40, 1.16]**	
Heterogeneity: Tau² = 0.26; Chi² = 5.44, df = 1 (P = 0.02); I² = 82%									
Test for overall effect: Z = 0.96 (P = 0.34)									



Sensitivity (3)

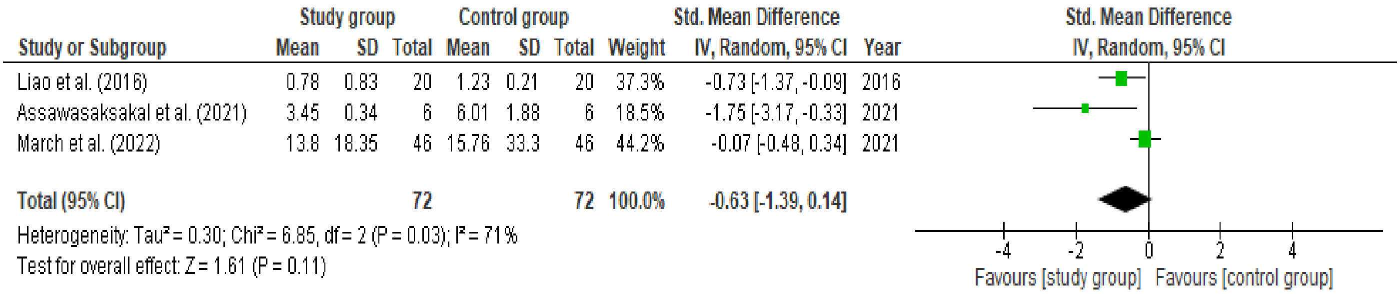
	Study group			Control group				Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Yeh et al. (2020)	24.67	7.27	30	19.59	5.2	30	60.4%	0.79 [0.27, 1.32]	2020
Assawasaksakal et al. (2021)	9.47	1.98	6	10.33	2.58	6	39.6%	-0.35 [-1.49, 0.80]	2021
March et al. (2022)	16	12	46	16	12	46	0.0%	0.00 [-0.41, 0.41]	2021
Total (95% CI)			**36**			**36**	**100.0%**	**0.34 [-0.75, 1.43]**	
Heterogeneity: Tau² = 0.44; Chi² = 3.14, df = 1 (P = 0.08); I² = 68%									
Test for overall effect: Z = 0.61 (P = 0.54)									



Forest plot (4): Sensitivity analysis showed that intradialytic cycling exercises on functional performance measurement by STS 60 was significant except when one experiment was excluded, **Yeh *et al.*** **[12]**, at a time from pooled effects to investigate if any one research was particularly important. Susceptibility analysis revealed that the meta-analysis's results were stable.

3-Effect of intradialytic cycling exercises on QOL measured by CRB

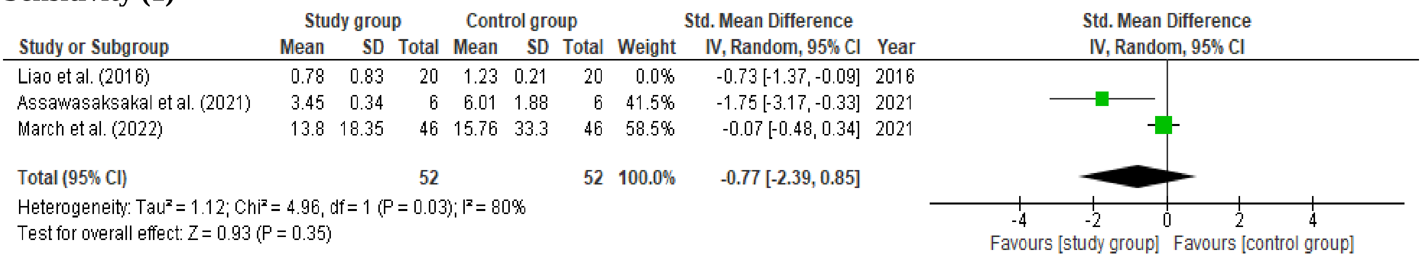
Three studies assessed intradialytic cycling exercises on QOL measured by CRB between study group and control group to improve functional performance in hemodialysis patients (Forest plot 5). There was significant variability in QOL evaluated by CRB across three trials (n= 3 studies, 144 individuals, P=0.03; I2=71%). There was no significant difference (P= 0.11) in the overall effect of QOL as evaluated by CRB (SMD= -0.63; 95% CI, -1.39 to 0.14) between the study and control groups. Sensitivity analysis (Forest plot 6) revealed that QOL assessed by CRB had moderate heterogeneity (I2=39%; P=0.20), unless one experiment at a time was excluded from pooled effects to evaluate whether any single study was particularly important. There was a significant variance (P=0.03) in overall effect between study and control groups in QOL evaluated by CRB (sensitivity 3; SMD= -1.04; 95% CI, -1.95 to -0.12) was noted following the removal of one research, **March *et al.*** [13], in accordance with the sensitivity analysis matrix.



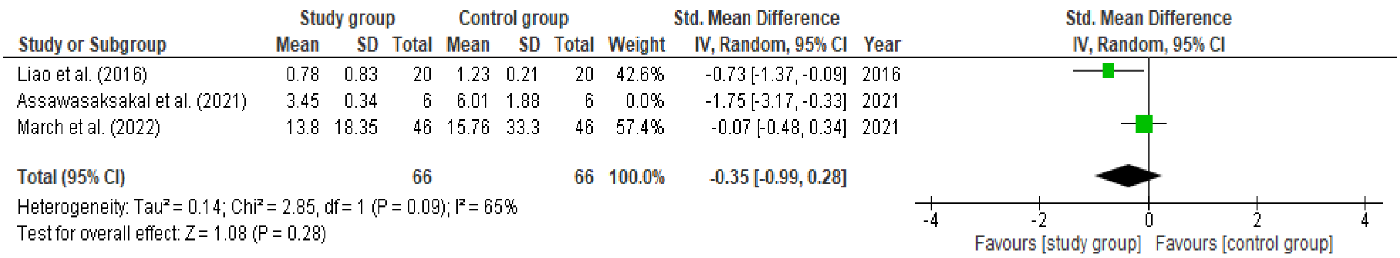
Forest plot (5): Standardized mean differences (95% CI) of intradialytic cycling exercises on QOL measured by CRB after assisted as compared with a control from three studies.

Sensitivity analysis (Quality of life)

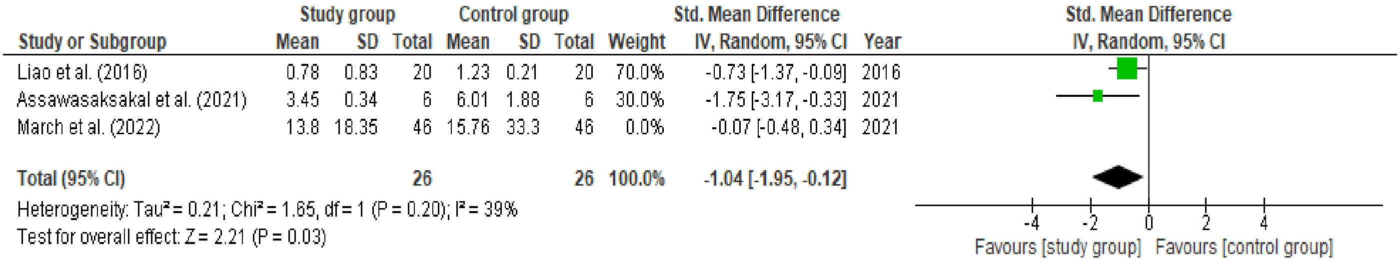
Sensitivity (1)



Sensitivity (2)



Sensitivity (3)



Forest plot (6): Sensitivity analysis showed that intradialytic cycling exercises on QOL measured by CRB was significant except when excluded one experiment, March *et al.* [13]**, at a time from pooled effects to evaluate if any single research was particularly influential. Susceptibility analysis revealed that the meta-analysis's results were stable.**

DISCUSSION

The purpose of the current systematic review (SR) was to evaluate the effectiveness of intradialytic cycling exercises on functional performance and QOL in patients undergoing hemodialysis. The studies vary in terms of their sample size, duration of intervention, and outcome measures, providing a diverse overview of the available evidence in this domain. This review included RCTs studies published from 2016 to 2023. The PEDro scale criteria of sufficient randomization, allocation concealment, participant, therapist, and research personnel blinding, inadequate outcome data, baseline similarity, and intention to treat analysis were employed to assess the included studies' internal validity. Every study participant received a random assignment, reported the findings of statistical comparisons between groups, and supplied measures of variability for a minimum of one outcome. All of the studies included groups with comparable baselines and detailed the qualifying requirements. The PEDro ratings of the evaluated studies ranged from 6 to 8, indicating high quality evidence supporting the use of intradialytic cycling workouts in hemodialysis patients.

For the majority of ESRD patients receiving dialysis, the main goal of traditional therapy is likely to make them inactive, which will eventually lead to decreased physical activity and fitness and shorter survival rates than in healthy populations. Current nonsurgical approach has been utilized to overcome these conditions. Cycling exercise, in particular, has gained attention as a potential intervention for hemodialysis patients. Intradialytic cycling, a form of exercise performed during hemodialysis sessions, involves engaging in moderate-intensity cycling using specially designed stationary bikes. This exercise modality offers several advantages for individuals undergoing hemodialysis; including enhanced cardiovascular fitness, increased muscle strength, improved psychological well-being, and an overall enhancement in QOL **(16).**

The papers included in this review are distinguished by offering immediate and follow up results, which help in determining the immediate and long- term effect of intradialytic cycling exercises in patients on hemodialysis.

Moreover, the current systematic review examined RCTs using stringent selection criteria for inclusion. Meta-analysis was used to 5 studies, including **[Liao *et al.* (10), Moeinzadeh *et al.* (11), Yeh *et al.* (12), March *et al.* (13) and Assawasaksakul *et al.* (14)]**.

In the study by **Liao *et al.* (10)** the intervention of intradialytic aerobic cycling exercise on HD alleviates inflammation and increases bone density. A control group and an exercise group were randomly allocated to forty ESRD patients receiving HD. During three HD sessions per week for three months, the patients in the exercise group cycled according to a protocol that included a five-minute warm-up, twenty minutes of cycling at the target workload, and a five-minute cool-down. An analysis was conducted on biochemical indicators, inflammatory cytokines, nutritional state, bone mineral density, serum EPC count, and functional capability. Following three months of physical activity, the patients in the exercise group had noteworthy increases in their body mass index, serum albumin levels, and levels of inflammatory cytokines. Patients in the control group had no increases in EPCs and a decrease of bone density at the femoral neck when compared to the exercise group. After finishing the exercise program, the patients in the exercise group also had a substantially longer 6-minute walk distance. Additionally, both before and after the three-month program, there was a strong correlation between the number of EPCs and the 6-minute walk distance. Exercise regimens using intradialytic aerobic cycling have been shown to significantly reduce inflammation and enhance diet, bone density, and exercise tolerance in persons with Huntington's disease. These strategies were in line with the study conducted by **March *et al.* (13)** who used intradialytic aerobic cycling exercise to study at the impact of an IDC program lasting six months on endotoxin levels in circulation. The secondary objectives were examining alterations in the levels of circulating cytokines, including interleukin-6 (IL-6), IL-10, tumor necrosis factor-a, C-RP, and the IL-6:IL-10 ratio, and their correlations with cardiovascular outcomes, physical activity, and fitness. After the 6-month IDC program, there were no discernible variations in any circulating cytokine between the groups. Lower levels of endotoxin, IL-6, CRP, and the IL-6:IL-10 ratio were linked to higher levels of fitness and physical activity.

Regarding **Yeh *et al.* (12)**, the results were measured using a 6-minute walk distance, the amount of time needed to complete 10 sit-to-stand-to-sit cycles, and the total number of sit-to-stand-to-sit cycles following a 12-week period of intradialytic cycling exercise that included warm-up, main, and cool-down phases. There was stationary cycling equipment that included resistance and aerobic training. The level of effort was kept at a somewhat high level. Beginning in the second hour of therapy, each intradialytic cycling exercise was performed for thirty minutes. As a result, in week eight, the exercise group's 6-minute walk distance differed considerably from the control group's baseline measurement. Notably, the exercise group's sit-to-stand-to-sit results improved dramatically. Another study by **Moeinzadeh *et al.* (11)** aimed to evaluate the impact of intradialytic exercise on recovery time during a dialysis session and QOL. Random assignments were used to place patients in the intervention and control groups. For twelve weeks, patients in the intervention group exercised for thirty minutes three times a week on a stationary cycle; in contrast, patients in the control group got standard hemodialysis. QOL was measured using the kidney disease QOL short form version 1.3. To gauge recovery time, patients were asked to respond to the question, "How long does it take to recover from a dialysis session?". 110 hemodialysis patients in all were examined, 60 of whom were in the intervention group and 50 of whom were in the control group. After 12 weeks of intradialytic cycling exercise in the intervention group, there was a significant increase in the generic (MD ± SE: 1.50 ± 0.44, P = 0.001), kidney disease (MD ± SE: 0.84 ± 0.28, P = 0.004), and overall QOL (MD ± SE: 1.18 ± 0.33, P = 0.001) scores. Additionally, the mean difference of all QOL ratings after the intervention showed a significant difference between the intervention and the control group.

Moreover, **Assawasaksakul *et al.*** [(14)] stated that, the members of the IDX group were required to work out for 60 minutes on a cycle ergometer at each session. Using DXA to calculate lean body mass, a wrist-worn triaxial accelerometer was used to measure physical activity. VO_2max and other physical performance tests were used to assess physical fitness or cardiorespiratory fitness, and QOL was used to compare various parameters between baseline and six months. Results from the initial physical exercise state were comparable. After six months of IDX, physical fitness and QOL were comparable, but the IDX group's physical activity significantly increased. While the IDX group's lean body mass metrics appeared to be declining, they were maintained in the control group.

STUDY STRENGTHS AND LIMITATIONS

It included only the studies of RCT design, the included studies in this systematic review had a moderate quality of PEDro score, in addition to having descriptive analysis as well as meta-analysis.

The main limitation in our systematic review was the sample size of participants and the number of included studies is relatively small, which may affect the generalizability of the findings.

CONCLUSION

This review found moderate-quality evidence that the intervention of intradialytic cycling exercise in hemodialysis patients is utterly effective in improving the inflammatory markers, increased EPC count, bone density, QOL, recovery time, increased daily physical activity, improved fitness and favorable body composition. However, additional clinical trials are necessary to clinically support this combined intervention's impact, specifically in alleviating inflammation, and improving functional performance and QOL.

IMPLICATION FOR PHYSIOTHERAPY PRACTICE

This approach may prove advantageous in the management of hemodialysis patients potentially resulting in improved outcomes such as QOL, increased daily physical activity. Additionally, the combined therapy could potentially optimize dialysis efficiency, requiring fewer time and satisfactory results. Physiotherapists should consider incorporating this combined approach into their treatment protocols for hemodialysis patients.

Conflict of interest: none declared.
Fund: non-fundable.

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