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Blood Flow Restriction Exercises for Chronic Kidney Disease: A Systematic Review of Randomized Controlled Trials

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ABSTRACT

Background: Blood flow restriction exercise (BFRE) combines low-intensity exercise with reduced blood flow to muscles; it has emerged as an additional intervention aiming to improve vascular function and muscle strength of patients with chronic kidney disease (CKD).

Objective: This review aimed to summarize the evidence on the effectiveness of BFR exercises in patients with CKD.

Methods: A literature search was conducted across PubMed, Cochrane and PEDro database, lastly updated in January 2025. Search results were limited to RCTs published within the last 10 years investigating BFRE with standard exercises for patients with CKD aged ≥45 years. 3 outcomes were selected; estimated glomerular filtration rate (eGFR), muscle strength, and forearm circumference. Quality of studies was assessed by using PEDro scale, and the level of evidence was determined by the modified Sackett's scale.

Results: Six studies were selected and reviewed; they included 454 patients. The studies had a mean PEDro score of 5.2 and its meta-analysis showed non-significant difference between BFRE and standard training regarding renal function, muscle strength and forearm circumference**.**

Conclusion: Limited evidence is present to support the adding of BFR to standard training for renal function in patients with CKD and strong evidence support its non-significant effect on strength and forearm circumference. Confirmation of this evidence requires more high-quality research.

Keywords: Blood flow restriction, Chronic kidney disease, Meta-analysis, Systematic review.

INTRODUCTION

CKD is an irreversible, degenerative illness marked by a progressive decrease of kidney function over time. Raising awareness of the risk factors and symptoms of this quiet but crippling disease is essential since it frequently remains undiagnosed in its early stages [(1)]. 10% of people worldwide suffer from CKD, which is one of the top ten non-communicable illnesses that cause illness and impairment [(2,3)]. CKD has a substantial financial impact on patients and society; in many affluent nations, chronic dialysis or kidney transplantation account for two to three percent of yearly health care expenditures. Its prevalence is rising globally, and its fatality rate is rising annually [(4)].

A novel method of strength training, BFRE applies external pressure on the limbs to limit blood flow during resistance training. The goal is to increase muscular activation and encourage physiological changes [(5)]. It has an influence on metabolites, which build up during exercise because to the relative ischemia and hypoxia of BFR. These metabolites are also recognized to be mediators of muscle hypertrophy. Because BFR at low loads has similar recruitment to that of high load resistance training [(6)], they are thought to cause early, peripherally mediated exhaustion, which leads to increased motor unit recruitment.

While BFR training appears beneficial for muscle, its impact on renal function and related biomarkers is crucial for CKD patients. Exercise can influence renal hemodynamics and potentially affect disease progression [(7)]. Studies on the effect of BFR training on renal function in CKD patients are limited and still there is debate in its impact as there are several limitations and gaps in the existing research[(8,9)].

Therefore, this systematic review aimed to summarize the evidence on the effectiveness of BFR exercises in patients with CKD based on the best literature.

METHODS

This is a systematic review of randomized clinical studies. This review followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [(10)]. It was also registered with PROSPERO (CRD42024568794).

Search strategy: Beginning in December 2024 and last updated in January 2025, an online literature search was conducted utilizing electronic databases from the Physiotherapy Evidence Database (PEDro), the Cochrane Library (CENTRAL), and PubMed. The following search phrases were used in a computerized search: "Kidney" OR "renal" OR "eGFR or kidney function or dialysis or hemodialysate" AND "blood flow restriction" OR "blood flow occlusion" OR "Kaatsu" OR "vascular occlusion" OR "ischemic" OR "restricted blood flow" OR "occlusion training". The reference lists of the pertinent reviews and research were additional sources of information.

Selection criteria: P: Patients with CKD aged ≥ 45 years; **I:** Intervention of BFRE with standard exercise; **C:** Comparator of standard exercise; **O:** Outcomes of kidney function (eGFR), muscle strength and forearm circumference. The titles, abstracts, and keywords of the publications obtained were screened independently by

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two authors. Relevant studies that met the inclusion criteria were identified and their full-text were retrieved, studies with no full-text available or not published in English studies or different study designs rather than RCT or not including the targeted outcomes were excluded. A third author helped to resolve disagreements between the two researchers throughout the selection process.

Data Extraction: The full-texts of the included studies were reviewed and summarized in a table including author, year, patients characteristics, interventions, targeted outcomes, measures and conclusion.

Quality of Studies and Level of Evidence Assessment: Using the PEDro scale, 2 authors independently assess the listed studies' quality [11], which includes 11 items, with each satisfied item contributing one point to the total PEDro score, excluding the first item which specifies to eligibility criteria (external validity) and the other 10 items assess random allocation of participants, hidden distribution, comparability at baseline, participants are blinded, rendering therapists blind, assessor blindness, sufficient follow-up, analysis of intention-to-treat, and statistical comparisons between groups. PEDro score ≤4 = poor, 4-5= fair, 6-8= good and 9-10= excellent quality. The modified Sackett's scale [12] was used to determine the overall level of evidence for each outcome based on the studies methodological rigor and quality.

Ethical approval:
This trial has been approved by the Faculty of Physical Therapy, Cairo University, Faculty of Medicine's Ethics Committee. The study adhered to the Helsinki Declaration throughout its execution.

Data synthesis:
Search results was displayed according to PRISMA flow chart guideline [13], data extracted from the included studies were tabulated and described, and the homogeneity of the studies were reviewed regarding intervention groups, outcomes, and its measures. Level of evidenve for each outcome was analyzed clarified**.** Data were quantitatively synthesized by meta-anlayses using Review Manager software (London, UK) and Microsoft Excel 2010. In the context of effective measure, MD and 95% CI were utilized for each outcome. I^2 test was used for exploration and quantification between-study statistical heterogeneity. The fixed effect model was used in full analyses since heterogeneity was not substantial (I^2< 50%).

RESULTS

The search strategy of this review revealed a total of 55 RCTs on 3 databases; 20 of them were duplicated and removed, then after screening 35 records; only 6 trials were included and reviewed as shown in PRISMA flowchart (**Figure 1**).

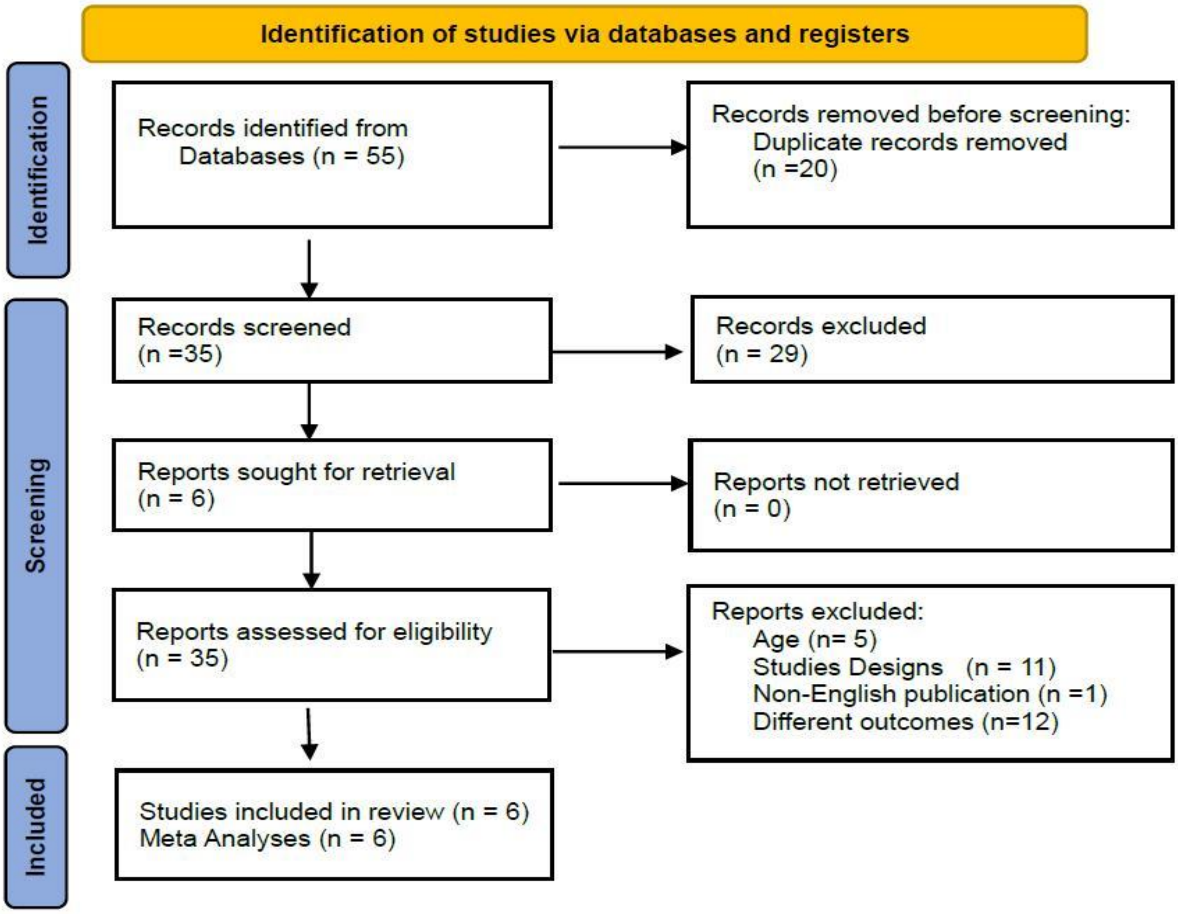

Figure (1): Flowchart of the included studies

The extracted data from the six reviewed studies [14-19] were samurized in **Table (1).**

Table (1): Data of the reviewed studies

Author (Year)	Participants	Interventions	Outcomes (measure)	Authors' Conclusion	Quality
Silva *et al.* (2021) [14]	-**N**= 26 -**Age** ≥45 Y -**CKD**= 4th and 5th stages -On dialysis/not	-**SG**=STE /BFRE VO, 50% LOP -**CG**=STE -8w, 5/w (3 of them at home)	**-Handgrip strength** (Dynamometer) **-Forearm circumference** (Tape) -pre and post 8w.	BFRE was not superior to STE for the outcomes evaluated	**Good**
Deus *et al.* (2021) [15]	-**N**= 141 -**Age** (mean): 58y -**CKD**= 2nd stage	-**SG**=STE +BFRE VO, 50% 1-RM, 50% LOP -**CG**=STE -24 w, 3/w.	**-eGFR** (Blood sample) -pre and post 6 m.	Both groups slowed the decrease in renal function (eGFR).	**Fair**
Corrêa *et al.* (2021) [16]	-**N**= 105 -**Age** (mean): 58y -**CKD**= 2nd stage -Not on dialysis	-**SG=** STE+ BFRE VO, 50% LOP -**CG=** STE -24 w, 3/w	**eGFR** (Blood sample) -pre and post 6 m.	eGFR, was maintained in both groups	**Fair**
Cardoso *et al.* (2020) [17]	-**N**= 59 -**Age** (range): 49.4-59.8 y -On dialysis >6 m (ESKD)	-**SG=** STE + BFRE, 50% LOP -**CG=** STE -12 w, 3/w	-**Muscle strength**, (static test of legs by dynamometer) -pre and post 3 w	No significant change in strength between groups	**Good**
Corrêa *et al.* (2020) [18]	-**N**= 90 -**Age:** 58 y -**CKD**= 2nd stage -Not on dialysis	-**SG**=STE + BFRE (VO, 50% LOP -**CG=** STE -24 w, 3/w	**-GFR (**blood sample) -**Muscle strength** (dynamometer) -pre and post 6 m	Both training attenuated the decline of GFR, and had the similar strength gains.	**Fair**
Barbosa *et al.* (2018) [19]	-**N=** 26 -**Age** > 45 y -**CKD**= 4th and 5th stages -Not on dialysis	-**SG**= STE + BFRE, 50% LOP -**CG=** STE - 8 w, 5/w.	-**Muscle strength** (dynamometer) -**Forearm circumference** (tape) -pre and post 3 w	Physical training associated with BFRE did not demonstrate superiority over STE. Forearms circumference & strength showed no change between groups	**Good**

BFRE: Blood Flow Restriction Exercise**; CKD**: chronic kidney diseases; **CG:** control group; **eGFR**: Estimated Glomerular Filtration Rate**; ESKD**: End stage kidney disease**; LOP:** limb occlusion pressure; **m:** month**; N:** number; **STE:** standard exercise; **SG:** Study group; **VO:** vascular occlusion, **w**: week

Participants:
The six studies included a total of 447 participants, primarily adults aged range from 45 years to 70 years with various stages of CKD ranged from the second stage to the end stage kidney disease. These studies utilized BFRE as part of resistance exercises, with outcomes including renal function (eGFR), muscle strength, and forearm circumference.

Intervention and comparator:
Intervention (study) groups received BFRE with STE, while comparator (control) groups received STE only. Blood flow restriction was calculated based on 50% of resting SBP in all included studies. The BFRE was combined with standard exercises in supervised with home-based training [14] or in supervised training only [15-19] from 2 to 6 months, 3 to 5 times/week.

Standard exercise training included the following:
-Training for 8 weeks, 5 times/week, consisted of tennis ball (six sets of ten tennis ball squeezes with one minute of rest and five squeezes added each week); dumbbells (three sets of ten, three sets of twenty dynamic manual handgrip exercises/minute repetitions of elbow flexion with 1 kg over the first two weeks) [14].
-Training for 6 months, 3 times/week, the regimen comprised bench press, seated row, shoulder press, triceps pulley, barbell curls, leg press at 45°, leg extension, and leg curl; the initial two months involved one to three sets of twelve repetitions at thirty percent of one-repetition maximum (1-RM); the subsequent two months entailed two to three sets of ten repetitions at forty percent of 1-RM; the last two months included three sets of eight repetitions at fifty percent of 1-RM[15].

-Training for 6 months, 3 times/weeks consisted three sets of twelve repetitions at thirty percent 1-RM in the first mesocycle, three sets of ten repetitions at forty percent 1-RM in the second, and three sets of eight repetitions at fifty percent 1-RM in the third [16].

-Intradialytic cycling with BFR for 4 months 20 minutes 3 times/week [17].

-Training for 6 months 3 times/week incorporating fixed repetitions and a low cadence, the regimen comprised three sets of twelve repetitions at fifty percent of 1-RM during the initial mesocycle, three sets of ten repetitions at sixty percent of 1-RM in the subsequent mesocycle, and three sets of eight repetitions at seventy percent of 1-RM in the last mesocycle [18].

-Training for 8 months, 5 days/week, consisted of tennis ball: six sets of ten squeezes with a one-minute rest interval, with five squeezes increased per week; Dumbbells: three sets of ten elbow flexion repetitions using 1 kg for the first two weeks, 2 kg for the final two weeks of the first month, and 3 kg for the final four weeks; Handgrip: three sets of twenty contractions with forty percent of the 1-R and one minute of rest interval [19].

Results of methodological quality assessment:
The assessment of the studies' quality by using PEDro scale is presented in **Table (2)**. The total PEDro score of the studies ranged from 4 to 7 with fair to good quality.

Table (2): PEDro quality assesmnet for the included Studies

Study	1*	2	3	4	5	6	7	8	9	10	11	Total Score /10	Quality
Silva et al. (2021) [14]	Y	Y	Y	Y	N	Y	N	N	N	Y	Y	**6**	**Good**
Deus et al. (2021) [15]	Y	Y	N	Y	N	N	N	N	N	Y	Y	**4**	**Fair**
Correa et al. (2021) [16]	Y	Y	N	Y	N	N	N	N	N	Y	Y	**4**	**Fair**
Cardoso et al. (2020) [17]	Y	Y	Y	Y	N	Y	Y	N	N	Y	Y	**7**	**Good**
Correa et al. (2020) [18]	Y	Y	N	Y	N	N	N	N	N	Y	Y	**4**	**Fair**
Barbosa et al. (2018) [19]	Y	Y	Y	Y	N	N	Y	N	N	Y	Y	**6**	**Good**

* This criterion is not counted for the total PEDro score.

Criteria of PEDro Scale: 1=eligibility specified; 2=random allocation; 3=concealed allocation; 4=prognostic similarity at baseline; 5=subject blinding; 6=therapist blinding; 7=assessor blinding; 8=85% follow-up of at least 1 key outcome; 9= treatment and control subjects received treatment as allocated; 10=between group statistical comparison for at least 1 key outcome; and 11=point estimates and measures of variability provided for at least 1 key outcome. **Scoring:** N= no (absent/unclear) = 0, Y=yes (present) =1.

Overall Level of Evidence:
After scoring the studies quality according to PEDro scale; the overall level of evidence for each outcome was described according to the modified Sackett's scale[12] as summarized in table (3).

Table (3): Overall evidence according to the modified Sackett's scale

Outcome (measure)	No of studies	PEDro score	Level of evidence	Overall evidence
Renal Function/ eGFR (blood sample)	3 (15,16,18)	4,4,4	2a	Limited evidence that " BRFE was not superior to STE in slowing the decrease in renal function (eGFR)"
Muscle Strength (dynamometer)	4 (14,17-19)	6,7,4,6	1a	Strong evidence that "BRFE was not superior to STE in strength gain"
Forearm Circumference (tape)	2 (14,19)	6,6	1a	Strong evidence that "BRFE was not superior to STE in forearm circumference change"

Outcomes

1. Renal function (eGFR)

The first analysis compared the effects of BFRE+STE compared to STE on renal function; it included 3 studies [15,16,18] with a total of 100 patients in the BFRE group and a total of 100 patients in the control group. The study analysis level revealed that the 95% confidence interval (CI) of the three studies overlapped the null effect value so there was no significant difference between both groups. I^2 is shown as a percentage and shows the overall variability in the studies' effect measure that is related to heterogeneity. When the P value is >0.05, there is no heterogeneity between the studies, the I^2statistic (I^2=0 %, P=0.89) indicated that the studies are more suitable to be pooled in to meta-analysis. The 95% CI of the overall estimate (the overall effect z=0.65 (p=0.52) overlapped the null effect value so there was not significant (statistical) difference between both groups regarding eGFR.

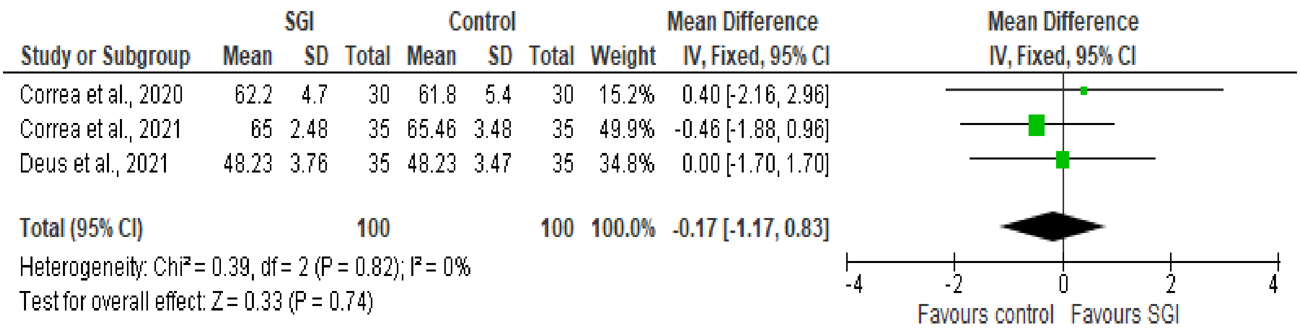

Figure (2): Forest plot of comparison between SGI (BFRE) and control (STE) groups for eGFR.

2. Muscle Strength

The second analysis compared the effects of BFRE+STE compared to STE on muscle strength; it included 4 studies [14,17-19] with a total of 76 patients in the BFRE group and a total of 80 patients in the control group. The study analysis level revealed that the 95% confidence interval (CI) of the four studies overlapped the null effect value so there was no significant difference between both groups. I^2 presented as a percentage % and represents the total variability in the studies effect measure, which is due to heterogeneity, when the P value is >0.05 then no heterogeneity is between the studies, the I^2statistic (I^2=0 %, P=0.96) indicated that the studies are more suitable to be pooled in to meta-analysis. The 95% CI of the overall estimate (the overall effect z=1.37 (p=0.17) overlapped the null effect value so there was not significant (statistical) difference between both group regarding muscle strength.

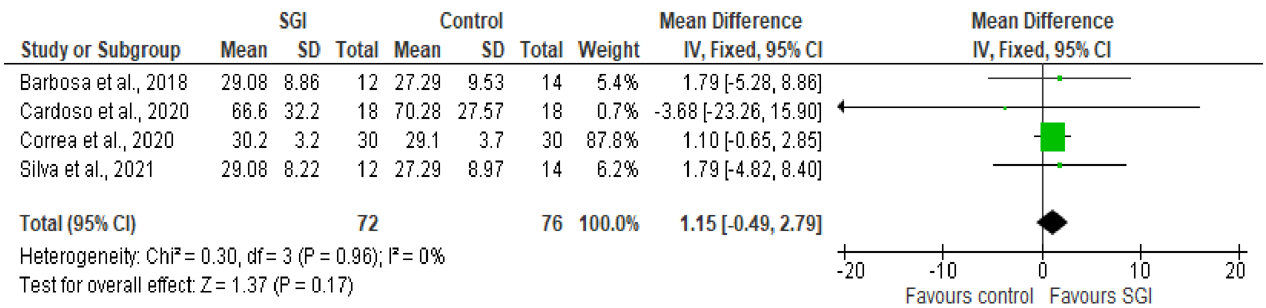

Figure (3): Forest plot of comparison between SGI (BFRE) and control (STE) groups for muscle strength.

3. Forearm Circumference

The third analysis compared the effects of BFRE+STE compared to STE on forearm circumference; it included 2 studies [(14,19)] with a total of 24 patients in the BFRE group and a total of 28 patients in the control group. The study analysis level found that the two studies' 95% confidence intervals (CIs) overlapped the null effect value, indicating that there was no meaningful difference between the groups. I^2 is shown as a percentage and shows the overall variability in the studies' effect measure that is related to heterogeneity. When the P value is >0.05, there is no heterogeneity between the studies, the I^2statistic (I^2=0 %, P=1) indicated that the studies are more suitable to be pooled in to meta-analysis. The 95% CI of the overall estimate (the overall effect z=0.88 (p=0.38) overlapped the null effect value so there was not significant (statistical) difference between both group regarding forearm circumference.

	SGI			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Barbosa et al., 2018	26.49	2.31	12	25.84	3.19	14	46.7%	0.65 [-1.47, 2.77]
Silva et al., 2021	26.49	2.14	12	25.84	3	14	53.3%	0.65 [-1.33, 2.63]
Total (95% CI)			**24**			**28**	**100.0%**	**0.65 [-0.80, 2.10]**

Heterogeneity: Chi² = 0.00, df = 1 (P = 1.00); I² = 0%
Test for overall effect: Z = 0.88 (P = 0.38)

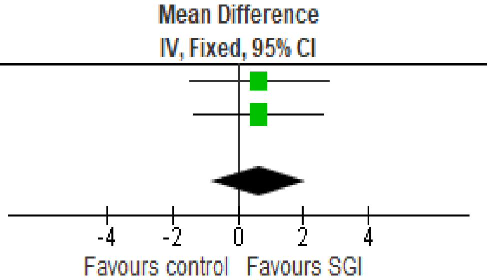

Figure (4): Forest plot of comparison between SGI (BFRE) and control (STE) groups for forearm circumference

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DISCUSSION

This review aimed to summarize the evidence on the effectiveness of BFR exercises on renal function, muscle strength and forearm circumferences in patients with CKD. It focused on analysing RCTs to evaluate whether adding BFRE to the standard resistive exercises could serve as a feasible therapeutic modality in this population. Meta-analysis revealed non-significant difference between the BFRE and the STE for the whole outcomes evaluated, which means that it was not superior to the standard training. According to the modified Sackett's scale[(12)]; limited evidence was found to the superiority of BRFE to STE in slowing the decrease in renal function (eGFR), while strong evidence supported that BRFE was not superior to STE in strength gain or forearm circumference change.

This review had a prospective protocol registered on PROSPERO; it followed a comprehensive literature search across PubMed, Cochrane Library (CENTRAL), and PEDro databases, and it was restricted to the published RCTs as it is considered the gold standard type of primary researches for interventions.

The mean of the total PEDro score for the reviewed trials was 5.2 indicating fair quality; The inclusion requirements, participant randomization, baseline similarity, between-group statistical comparison, and both point measurements and measures of variability for at least one important outcome were all disclosed in the included studies. Allocation concealment was reported in 3 studies [(14,17,19)]. Blinding of therapist was stated in two studies [(14,17)], blinding of the assessors was stated in two studies [(17,19)], while the 3 criteria of blinding of subjects, 85% follow-up of at least one key outcome and also the intention to treat criteria were not achieved in any of the included studies. Of the six studies included; three studies [(14,17,19)] graded score (6-8) and were of good quality, while the other three [(15,16,18)] graded score (4–5) and were of fair quality. The quality of the investigations affect the reliability of the meta-analysis and strength of evidence, which was determined by the modified Sackett's scale[(12)]. Studies that reported benefits of combining BFRE with standard training in improving muscle strength among CKD patients; as enhanced grip strength, lower limb functionality, and overall physical capacity; the improvements were attributed to the increased recruitment of motor units and the metabolic stress induced by the occlusive effects of BFR. While BFR was not always superior to standard training, it offered a viable alternative for patients unable to tolerate high-intensity exercises, achieving similar strength gains with reduced strain [(16,17)]. Other studies reported a neutral impact of BFRE on eGFR levels [(14,15,17)].

Previous brief review by **Rolnick *et al.*** [(20)] on BFR training in CKD patients highlighted its efficacy and safety, and suggested that it may maintain muscle strength, GFR, and improve uremic parameters, inflammatory profiles, and glucose homeostasis. It included only narrative synthesis and was not restricted to RCTs while the current review followed systematic review design and excluded non-randomized and crossover studies [(21-23)] to decrease the bias of evidence.

Several strength points present in this systematic review, which included specificity of the PICO model that search for the evidence of specific age (>45 years), specific intervention (BFRE added to STE) and comparator (Standard resistive training) and specific outcomes (eGFR, muscle strength and forearm circumference) and focusing on RCT design only. The homogeneity of the included studies regarding the PICO made meta-analysis applicable for all targeted outcomes. On the other hand, some outcomes were not included in this systematic review due to limited number of the studies having same outcomes as oxidative stress, cytokine profiles, antioxidant defences and D-dimer level.

LIMITATIONS

The small number of studies it covered, the relatively small sample size, and the generally poor quality of its methodology, which restrict the conclusions' generalizability and somewhat undermine the strength of the evidence it draws. Therefore, future well-designed high quality studies are still needed with larger sample to obtain high reliability results and to establish clear guidelines for clinical practice. Future studies should focus on investigating BFR exercise for CKD patients, including determining the ideal occlusion pressure, exercise intensity, and session frequency. Follow-up are necessary to explore the long-term effects of BFR on renal function, cardiovascular health, and overall patient quality of life.

CONCLUTION

Adding BFRE to the standard training was not significantly effective in comparison with using the standard training alone for improving renal function, muscle strength or forearm circumference in patients with CKD. Limited evidence was found to the superiority of BRFE to STE in slowing the decrease in renal function (eGFR), and strong evidence supported that BRFE was not superior to STE in strength gain or forearm circumference change. Further well designed research may confirm the efficacy and safety of BFR training.

Conflict of Interest: Nil
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