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REVIEW



Effect of inspiratory muscle training in hemodialysis patients: a systematic review of randomized controlled trials

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ABSTRACT

Purpose: To clarify the effect of inspiratory muscle training on inspiratory muscle strength, lung function, and functional capacity in hemodialysis patients.

Methods: Randomized controlled trials evaluating inspiratory muscle strength, lung function, and functional capacity in hemodialysis patients were searched. The search was conducted in Medline, Web of Science, and Scopus between August and December 2024. Risk of bias was assessed using the Cochrane Collaboration's risk of bias tool-2.

Results: 316 Studies were analyzed, and 12 were included, involving 460 patients. The intervention consisted of training the respiratory muscles using linear loading devices, varying between 30% and 70% of Maximum Inspiratory Pressure, for 4 to 24 weeks. One study was classified as high risk of bias, three with some concerns, and eight low risk of bias. Inspiratory muscle strength increased significantly in the intervention groups. Significant changes concerning lung function were observed only in some groups. Considerable variations in the distance covered in the 6-MWT test were also found in some studies.

Conclusions: Inspiratory muscle training appears to influence several outcomes. Replicating randomized controlled trials with standardized protocols and robust assessment methods is necessary to more effectively establish their effectiveness.

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KEYWORDS

Hemodialysis; respiratory muscles; breathing exercises; muscle strength; rehabilitation

► IMPLICATIONS FOR REHABILITATION

- Inspiratory muscle training has proven scientific evidence in several chronic diseases, is simple and safe, and has the advantage of being able to be performed during hemodialysis sessions.
- Hemodialysis patients' often show changes in the strength of their inspiratory muscles due to the marked loss of muscle mass to which they are subjected.
- Inspiratory muscle training has been proposed as a non-pharmacological rehabilitation strategy to enhance respiratory muscle strength and lung function, with the clinical goals of reducing dyspnea, improving exercise tolerance, and promoting functional independence.
- A more comprehensive understanding of the multiple variables involved, such as training intensity, session frequency, duration, type of device, respiratory muscle strength, exercise tolerance, and individual clinical factors, is necessary.

Introduction

The gradual and irreversible decline in kidney function defines chronic kidney disease (CKD), and it is expected to be the fifth most common mortality factor among non-communicable diseases by 2040 [1,2]. CKD patients suffer systemic changes due to increased body fluids and the marked loss

of muscle mass [3]. Muscle mass decreases as the glomerular filtration rate decreases and albuminemia increases [4]. Sarcopenia is a frequent diagnosis in CKD patients, and it is associated with chronic kidney inflammation, hormonal changes, lifestyle changes due to reduced appetite, dietary restrictions, restriction of physical activity during dialysis sessions, fatigue after dialysis, and protein loss during dialysis [5].

As with other muscle groups, the function of the inspiratory muscles in CKD patients on a regular hemodialysis program is also compromised, with decreased diaphragm thickness and muscle strength, altered lung volumes, and consequent reduction in lung function [6–9]. Like other skeletal muscles, inspiratory muscles can be strengthened through specific training as a non-pharmacological intervention integrated into a rehabilitation program [9]. Some studies have shown the effectiveness of Inspiratory Muscle Training (IMT) in hemodialysis patients: increased functional capacity, improved inflammatory biomarkers, reduced feelings of dyspnea and fatigue, improved quality of life, improved lung volumes, and increased strength of the inspiratory muscles [7,10–13]. In addition to these benefits, ITM is easy to implement, has a low cost, does not require a specific physical space, and can be implemented in hemodialysis units when other training modalities are impossible [6].

The existing studies in this field are limited by small, heterogeneous samples, varied methodologies, and diverse intervention protocols, which preclude a quantitative synthesis. In this context, a systematic review is particularly valuable as it allows for the rigorous identification, critical evaluation, and synthesis of the available evidence. Beyond summarizing current findings, this approach highlights inconsistencies across studies, uncovers knowledge gaps, and identifies emerging trends that may guide future research. Given the complex clinical needs of patients undergoing hemodialysis, synthesizing the evidence on inspiratory muscle training (IMT) is essential both to evaluate its current potential to improve care and to inform the design of robust, standardized, and replicable intervention protocols.

The following research question emerged: Does inspiratory muscle training improve inspiratory muscle strength, lung function, and functional capacity in patients with chronic kidney disease on a regular hemodialysis program, compared to usual care, or aerobic or resistance training?

Methods

This systematic review used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA 2020) [14]. In the absence of conditions to perform a meta-analysis due to the heterogeneity of the studies, we opted to use the vote counting approach by effect direction, as recommended by the Synthesis Without Meta-analysis guideline (SWiM) [15]. The Direction of Effect was determined by considering the consistency and statistical significance of findings across studies for each outcome domain, categorizing effects as positive, neutral/mixed, or negative. The Confidence in Evidence reflects an evaluation based on risk of bias (assessed using the Revised Cochrane risk-of-bias tool), study design, sample size, consistency of results, and applicability of the evidence to the population and intervention studied. This approach, aligned with SWiM and adapted GRADE principles, provides a transparent synthesis of the available evidence without meta-analysis, facilitating the interpretation of the overall body of evidence. The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO): CRD42024575288.

Eligibility criteria

To select the studies, the PICO-D methodology was used:

- **Patient:**
 - Chronic kidney disease stage 5;
 - > 18 years old;
 - Receiving regular hemodialysis for at least three months;

- **Intervention:**
 - Respiratory muscle training program with devices that provide a linear load;
- **Comparison:**
 - Inspiratory muscle training versus a sham or no intervention;
 - Inspiratory muscle training versus aerobic or resistance training;
- **Outcomes:**
 - Respiratory muscle strength
 - Lung function parameters
 - Functional capacity
- **Design**
 - Randomized controlled trials

Studies were excluded if they did not satisfy the stated selection criteria.

Sources of information

The search was carried out in Medline (accessed by PubMed), Web of Science, and Scopus databases between August and December 2024. Terms related to the research were combined using Mesh Descriptors and Key Concepts (see [Supplementary Appendix 1](#)). Relevant bibliographical references in other systematic review articles were also searched [16–19]. No language or year of publication filters were applied.

Two researchers selected the studies; a third analyzed discrepancies and validated the research.

In the first analysis, duplicate studies were removed. Then, the selection was made after reading the title and abstract. Subsequently, studies such as letters to the editor, cross-sectional studies, and irrelevant or full-text not available were excluded.

A Microsoft Excel® file was created to select studies, compile data, and extract information. The following data were taken from the validated studies: authors, year of publication, country, sample size, age, gender, years on hemodialysis, intervention protocol, device, and linear load of Maximal Inspiratory Pressure (MIP) used, duration of intervention, and main results assessed.

Evaluation of study characteristics

The included studies were assessed using the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) using the Microsoft Excel® macro tool. The risk of bias in the studies is classified as low if the methodological procedure is described in detail and is clear, some concerns if there are doubts about the methodological procedure, and high if the methodological procedure is not described. Two authors independently performed this assessment, discussing any discrepancies until consensus was reached, with the support of a third author. The agreement between the two evaluators was assessed using Cohen's Kappa coefficient. The analysis revealed an observed agreement of 91.67% and the Kappa value obtained was 0.803 (95% CI: 0.434–1.000), representing an “almost perfect agreement” [20].

Results

The search returned 316 studies, and after applying the selection criteria, 12 studies remained, as shown in [Figure 1](#).

The characteristics of the studies are described in [Table 1](#). Eight were conducted in Brazil [6–8,10,12,21–23]. A total of 460 patients were involved: 247 had respiratory muscle training with a device, 66 had another type of intervention, and 147 were in control groups (a sham or no intervention). Inspiratory muscle training was carried out using equipment such as POWERbreathe® or Threshold® with resistance ranging from 30% to 70% of MIP in 11 studies. Another study used the Resp-in-out equipment®, where connectors with different airflow resistances were placed [24]. The number of sets and repetitions was not uniform in the different studies.

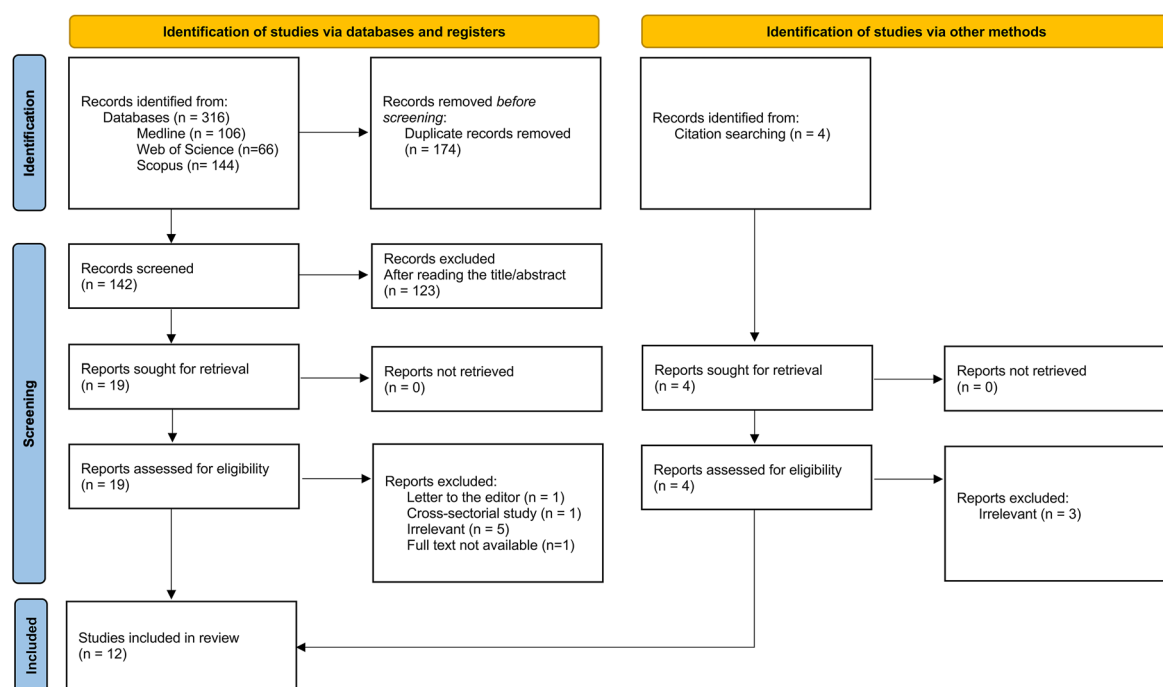


Figure 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources. (From: Page et al. [14]).

The intervention period varied between 4 [24] and 24 weeks [21], with five studies carrying out the intervention for 8 weeks [6,8,11,12,25].

In two studies, the intervention occurred exclusively during the interdialytic period [12,24]; two others were carried out in a mixed context (interdialytic and with supervision during hemodialysis sessions) [7,25], and in the remaining eight studies, the interventions occurred exclusively during hemodialysis sessions.

The sample size ranged from 22 to 64 users, and all patients attended regular hemodialysis programs for stage 5 chronic kidney disease.

Outside the scope of the criteria defined for this systematic review, we want to highlight that quality of life was evaluated in 7 studies [6,10–12,21,25,26]. Diaphragm thickness [12], dyspnea and fatigue [11,25], and biomarkers [6,8,22,26] were also assessed.

The risk of bias analyzed by the Revised Cochrane risk-of-bias tool for randomized trials returned the results shown in Figure 2. As can be seen, one study was classified as having a high risk of bias due to inconsistencies in the measurement of the outcome [23]. Three other studies were evaluated with some concerns [10,11,26]. The remaining studies were assessed as low risk.

Respiratory muscle strength

The included studies assessed the strength of the inspiratory muscles using vacuometry devices. Although the duration in weeks and the timing of the intervention differed between the various studies, the results were similar. In all of them, there were statistically significant changes in the assessment of MIP between the pre-and post-intervention periods. In a study comparing different interventions between groups (IMT, aerobic training, and combined training with the two modalities), there was no difference between the groups [6]. When the intervention with the POWERbreathe devices® with a resistance of 30% of MIP and the incentive spirometer (Respiron®) were compared, both groups significantly increased MIP, but with more significant variation in the group that trained with the incentive spirometer [21]. Patients who underwent IMT with 50% MIP progressing to 70% MIP showed statistically different values at the end of the evaluation period compared to the control group, which maintained the usual care [7]. In another study with three groups (control with 10% MIP, two intervention groups with 30% and 60% MIP, respectively), MIP increased in all three groups but with more significant variation in the intervention groups [25].

Table 1. Characteristics of the studies.

Authors (year) country	Sample size (intervention group/ control group)	Age/gender	Hemodialysis vintage	Protocol	Device	Duration (weeks/ frequency/sessions)	Main outcomes
De Medeiros et al. (2019) [12] Brazil	Sample size (n=24); IG (n=12); CG (n=12)	Age: IG - 45,50; CG - 47,33. M (n=9); F (n=15)	IG - 76months; CG - 87, 92 months	IG - IMT with 50% MIP, 3 sets of 30 breaths and 1 min rest interval between sets. CG - minimum device load (5 cm H ₂ O) - sham group	POWER-breathe® classic light	8 Weeks / twice a day during 7 days of the week / 112 sessions in the interdialytic period	Primary outcomes: Inspiratory and expiratory muscle strength by a digital manovacuometer; diaphragm thickness using the B mode of the ultrasound apparatus. Secondary outcomes: chest wall regional volumes, diaphragmatic mobility, pulmonary function by spirometry, functional capacity by 6MWT, QoL KDQOL-SF, and treatment satisfaction
Katayıfçı et al. (2024) Turkey [25]	Sample size (n=47); IG1 (n=15); IG2 (n=16); IG3 (n=16)	Age: IG1 - 57; IG2 - 63; IG3 - 55,5. M (n=34); F (n=13)	Not available	IG 1 - IMT with 10% MIP; IG 2 - IMT with 30% MIP; IG 3 - IMT with 60% MIP; 10-15 repetitions followed by 5-10s of rest, 30 min IMT session	POWER-breathe® classic low resistance	8 Weeks / 6 sessions at home (interdialytic period) and 1 session under supervision (intradialytic period) / 56 sessions	Primary outcomes: inspiratory and expiratory muscle strength by respiratory pressure meter. Secondary outcomes: quadriceps femoris muscle strength and handgrip muscle strength by dynamometer, functional capacity by 6MWT, pulmonary function by spirometry, dyspnea by mMRC, fatigue by FSS, QoL by SF36, PA by IPAQ, balance by BBS
Figueiredo et al. (2018) [6] Brazil	Sample size (n=37); IG 1 (n=11); IG 2 (n=13); IG 3 (n=13)	Age: IG1 - 52,8; IG2 - 49,5; IG3 - 45,2. M (n=26); F (n=11)	IG 1-4,4 years; IG 2 - 3,0years; IG 3 - 4,9years	IG 1 - IMT with 50% MIP, 3 sets of 15repetitions and 1min rest interval between sets; IG 2 - AT 40min of cycle-ergometer; IG 3 - combined intervention: IMT was performed immediately before AT	Threshold IMT® or Power-Breathe® light or median resistance	8 Weeks / 3xweek / 24 sessions in the intradialytic period	Primary outcomes: functional capacity by ISWT, MIP by manovacuometer, and lower limbs strength by SST. Secondary outcomes: Plasma levels of interleukin-6, soluble tumor necrosis factor receptor 1, adiponectin, resistin and leptin, redox status parameters and HRQoL (KDQOL-SF)
Campos et al. (2018) [8] Brazil	Sample size (n=41); IG (n=29); CG (n=12)	Age: IG - 48,86; CG - 52,6750; M (n=24); F (n=17)	IG - 29, 97months; CG - 23, 58 months	IG - RMT: 12 sessions lasting 30min each and resistance of 15 cmH2O; the following 12 sessions lasted 40min each and resistance was set at 20 cmH2O. In the first half of each session, the resistance was against breathing in and in the last half, against breathing out. CG - usual care	Threshold PEP®	8 Weeks / 3xweek / 24 sessions in the intradialytic period	Primary outcomes: plasma markers of glycoalkalx derangement. Secondary outcomes: plasma markers of endothelium activation, aberrant angiogenesis and oxidative stress, blood pressure, heart rate; functional capacity by 6MWT; pulmonary function by spimometry; respiratory muscle strength by manovacuometer
Yuenyongchaiwat et al. (2021) [11] Thailand	Sample size (n=50); IG (n=25); CG (n=25)	Age: IG - 54,87; CG - 49,14. M (n=31); F (n=18)	IG - 6,93years; CG - 6,24years	IG - IMT with 40% MIP, 3 sets of 15repetitions and 1min rest interval between sets; CG - IMT with 0% MIP or lowest pressure with MIP - sham group	Power-Breathe K5®	8 Weeks / 3xweek / 24 sessions in the intradialytic period	MIP and MEP by manovacuometer, pulmonary function by spirometry, QoL (KDQoL-SF) and sensation of breathless using a numerical scale (1-5)
Pellizzaro et al. (2012) [10] Brazil	Sample size (n=39); IG 1 (n=11); IG 2 (n=14); CG (n=14)	Age: IG1 43; IG2 48,9; CG - 51,9. M (n=23); F (n=16)	IG 1 - 60months; IG 2-54months; CG - 54months;	IG 1 - IMT with 50% MIP, 3 sets of 15repetitions and 1 min rest interval between sets; IG 2 - 3 sets of 15 knee extension repetitions with free leg weight (50% of 1RM); CG - usual care	Threshold Loader®	10 Weeks / 3xweek / 30 sessions in the intradialytic period	MIP and MEP by manovacuometer, pulmonary function by spirometry, functional capacity by 6MWT and quality of life by KDQoL-SF

(Continued)

Table 1. Continued.

Authors (year) country	Sample size (intervention group/ control group)	Age/gender	Hemodialysis vintage	Protocol	Device	Duration (weeks/ frequency/sessions)	Main outcomes
Dipp et al. (2020) [7] Brazil	Sample size (n=25) IG (n=14); CG (n=11)	Age: IG - 60; CG - 55. M (n=19); F (n=6)	IG - 48 months; CG - 36 months	IG 1 - IMT with 50% MIP progressing to 70%, 5 sets of 10 repetitions and 2 min rest interval between sets; CG - usual care	POWERbreathe Plus Light Resistance®	5 Weeks / 6xweek (three times a week with supervision during the hemodialysis session and three other times at home monitored by a home-based diary) / 30 sessions	Primary outcome: inspiratory muscle strength by manovacuometer. Secondary outcomes: functional capacity (6MWR, and STST) and endothelial function
Soares et al. (2020) [21] Brazil	Sample size (n=64) IG1 (n=23) IG2 (n=24) CG (n=17)	Age: IG1 - 54,7; IG2 - 49,5; CG - 49,3. M (n=64)	IG1 - 44, 16 months; IG2 - 57, 3 months; CG - 55, 1 month	IG1 - IMT with 30% of MIP, 3 sets of 10 repetitions and 1 min rest interval between sets, during 11 min; IG2 - diaphragmatic breathing and inspiration in times; CG - usual care	IG1 - Power breathe; IG2 - incentive spirometer	24 Weeks / 3xweek / 72 sessions in the intradialytic period	Respiratory muscle strength by manovacuometer; pulmonary function by spirometry; QoL (KDQoL-SF)
Defi et al. (2023) [26] Indonesia	Sample size (n=32) IG (n=16); CG (n=16)	Age: IG - 45,13; CG - 45,69. M (n=9); F (n=23)	IG - 40,94 months; CG - 32 months	IG - IMT with 50% MIP 5 sets of 10 repetitions during 20 min; CG - IMT with 10% MIP 5 sets of 10 repetitions	Threshold IMT equipment	12 Weeks / 3xweek / 36 sessions in the intradialytic period	Maximal inspiratory pressure by vacuometer, inflammatory cytokine IL-6, Serum urea, creatinine levels, and QoL by KDQoL-SF
Lamberti et al. (2023) [24] Italy	Sample size (n=22); IG (n=11); CG (n=11)	Age: IG - 62; CG - 65. M (n=13); F (n=9)	IG - 3 years; CG - 4 years	IG - 5 sets of 8 repetitions (8 complete respiratory cycles per min and 1 min rest interval between sets); CG - usual care	Resp-in-out, Medinet	4 Weeks / 2xday / 48 sessions in the interdialytic period	Primary outcomes: maximal inspiratory and expiratory pressure by vacuometer; secondary outcomes: pulmonary function by spirometry; functional capacity by 6MWT
Barbosa et al. (2023) [22] Brazil	Sample size (n=38) IG (n=19) CG (n=19)	Age: IG 49,7; CG 62,08; M (n=19); F (n=19)	IG - 45,57 months; CG - 28,92 months	IG - AT with cycle-ermometer progression from 10 min to 36 min; IMT with progression from 10% to 40% MIP; RT exercises for the muscle groups, progressing from 1 set of 10-15 repetition to 3 sets of 10-15 repetitions; 1 type per session; CG - usual care	Threshold IMT®	12 Weeks / 3xweek / 36 sessions in the intradialytic period	Respiratory muscle strength by manovacuometer; physical capacity by maximum handgrip strength test, 30-s sit-to-stand test, Timed Up and Go Test and 6MWT; inflammatory markers
Figueiredo et al. (2012) [23] Brazil	Sample size (n=41); IG1 (n=16) IG2 (n=15) CG (n=10);	Age: IG1 40,46; IG2 41,20; CG 50; M (n=24); F (n=17)	CG 64 months; IG1 57,94 months; IG2 - 47,33 months	IG1 - IMT with 40% MIP for 20 min, 1 min of breathing effort and 1 min of rest; IG2 - respiratory biofeedback system 40% MIP for 20 min, 1 min of breathing effort and 1 min of rest; CG - usual care	Threshold IMT	6 Weeks / 3xweek / 18 sessions in the intradialytic period	MIP and MEP by manovacuometer, pulmonary function by spirometry

Note: AT: aerobic training; BBS: Berg Balance Scale; CG: control group; EMS: expiratory muscle strength; F: female; FSS: Fatigue Severity Scale; FVC: forced vital capacity; HGS: handgrip muscle strength; HROol: health-related quality of life; IG: intervention group; IMEP: intradialytic multicomponent exercise program; IMT: inspiratory muscle training; IMS: inspiratory muscle strength; IPAQ: Physical Activity Questionnaire; IS: incentive spirometry; ISWT: Incremental Shuttle Walk Test; KDQoL-SF: Kidney Disease Quality of Life Short Form; M: male; MEP: maximal expiratory pressure; MIP: maximal inspiratory pressure; mMRC: Modified Medical Research Council; PA: physical activity; PMT: peripheral muscle training; QMS: quadriceps femoris muscle strength; QoL: quality of life; RMT: respiratory muscle training; RT: resistance training; SSI: sit to stand test; 6MWT: 6 min walk test.

Unique ID	D1	D2	D3	D4	D5	Overall
Lamberti 2023	+	+	+	+	+	-
Pellizzaro 2012	-	+	+	!	+	!
Katayifçı 2024	+	+	+	+	+	-
Figueiredo 2018	+	+	+	+	+	-
Campos 2018	+	+	+	+	+	-
Yuenyongchaiwat 2021	!	+	+	+	+	!
Barbosa 2023	+	+	+	+	+	-
Figueiredo 2012	+	+	+	-	+	-
Sousa 2017	+	+	+	+	+	-
Medeiros 2019	+	+	+	+	+	-
Dipp 2020	+	+	+	!	+	-
Defi 2023	!	+	+	+	-	!

+ Low risk
! Some concerns
- High risk

D1 Randomisation process
D2 Deviations from the intended interventions
D3 Missing outcome data
D4 Measurement of the outcome
D5 Selection of the reported result

Figure 2. Risk of bias of the included studies.

Lung function

Pulmonary function assessed by spirometry was performed in 8 studies [8,10–12,21,23–25]. Katayifçı et al. [25] reported that only in the group that had IMT with 30% MIP were there statistically significant changes for Peak Expiratory Flow (PEF), Forced Expiratory Volume in 1s (FEV₁), and Forced Vital Capacity (FVC). Campos et al. [8] reported statistically significant changes for FVC and FEV₁. In the remaining six studies [10–12,21,23,24], there were changes in the variables under study, but without statistical significance, between the pre-and post-intervention moments of the same group or between the intervention and control groups.

Functional capacity

Concerning functional capacity, seven studies [7,8,10,12,21,22,25] used the 6-Minute Walk Test (6-MWT) to assess walking distance. There were no significant changes in walking distance in 3 studies [7,12,21]. However, other studies have shown statistically significant changes [8,22]. In a study in which 11 patients underwent IMT with 50% MIP and 14 patients underwent resistance training of the lower limbs, both groups showed statistically significant variations compared to the control group. This variation was more significant in the IMT group than in the lower limb resistance training group. It should also be noted that a positive and significant relationship was found between the variation in distance covered and the variation in MIP [10]. Patients who underwent IMT with 30% or 60% MIP achieved statistically and clinically significant gains in the 6-MWT [25].

In another study, using the Incremental Shuttle Walk Test (ISWT), all patients in the three groups (IMT with 50% MIP, aerobic training with a cycle ergometer, and combined training) had gained functional capacity, but without statistical significance [6].

An aggregated summary of the findings across included studies is presented in Table 2. This narrative synthesis table organizes outcomes by the number of studies reporting each outcome, the overall direction of effect, and the assessed confidence in the evidence.

Discussion

This systematic review suggests that IMT significantly increased the strength of the inspiratory muscles in the patients studied. Some studies also indicated potential benefits in lung function and functional capacity following the interventions, although the evidence remains limited. Although most of the included studies were classified as having a low risk of bias according to the Revised Cochrane Risk-of-Bias tool, the overall quality of the evidence remains somewhat limited. In addition, the interventions were heterogeneous in terms of duration, intensity, and context, and the sample sizes were generally small. These factors may have influenced the consistency of the findings and should be taken into account when interpreting the results of this review.

Table 2. SWiM narrative synthesis table: summary of findings by outcome.

Outcome	Number of studies	Direction of effect	Confidence in evidence	Summary of main findings
Inspiratory muscle strength (MIP)	12	Consistently positive	Moderate (majority RCTs, low risk of bias)	IMT consistently improves inspiratory muscle strength compared to control/usual care. Variation in training loads (30–70% MIP) did not clarify the optimal protocol.
Lung function (spirometry)	8	Mixed: significant in some, no effect in others	Low to moderate (heterogeneous protocols, small sample sizes)	Statistically significant improvements reported in some studies; overall evidence limited and variable depending on the intervention details.
Functional capacity (6MWT, ISWT, SST)	7	Mixed: clinically significant improvements in some, no change in others	Low to moderate (heterogeneity in samples and interventions)	Some studies showed meaningful gains in functional capacity; others showed no statistical change. Positive correlation noted between MIP improvement and walking distance.
Safety/adverse events	12	No adverse events reported	Moderate (consistent reporting, but small samples)	IMT appears safe with no reported adverse effects across included studies.

Note: IMT: inspiratory muscle training; ISWT: Incremental Shuttle Walk Test; MIP: maximal inspiratory pressure; RCT: randomized controlled trial; SST: sit to stand test; 6MWT: 6 min walk test.

Changes in lung function, such as restrictive and mixed pathologies, are frequent findings in patients with CKD on hemodialysis [27]. There are various reasons for this type of pattern, such as respiratory muscle dysfunction, a drop in glomerular filtration rate, pulmonary edema, pulmonary fibrosis, pulmonary calcification, pulmonary hypertension, and pleural fibrosis [28]. The presence of uremic toxins, dialysis procedures, and inflammatory states also affects CKD patients on a regular hemodialysis program, with consequences such as cardiovascular disease, depression, and frailty [29]. In hemodialysis patients, type 2 muscle fibers are predominant, with increased intramuscular fat content and decreased capillary density. These structural changes are not as pronounced in patients with CKD who are not yet on a regular hemodialysis program [30]. Recent studies have shown that muscle strength and physical performance are associated with the risk of mortality in these populations [31–33]. Given the available evidence, it is essential for rehabilitation professionals to be interested in this subject. Although the percentage of MIP with which better results are obtained is still unclear, this intervention has an essential impact on managing CKD. Other systematic reviews have also concluded that IMT is effective and recommended for hemodialysis patients [18,19]. However, the load, number of sets and repetitions, and the length of time for which this intervention should be carried out remain to be defined. Any type of training must comply with certain general principles: the principles of overload, specificity, reversibility, and individuality [34]. Regarding the principle of overload, some guidelines recommend working with loads above 30% of the patient's MIP for the training to be effective. The patient should train at a level where they feel they can only complete the full 30-breath session and should feel that the training is difficult [35]. When we analyzed the studies included here, it was found that this load (percentage above the patient's MIP) varied between 30 [25] and 70% [7], and it was not clear which protocol achieved the best results. However, the benefits of IMT are already well documented in pathologies such as COPD and asthma, increasing the strength of the inspiratory muscles, improving respiratory symptoms, and increasing exercise capacity [36]. This training has also shown benefits in heart failure [37], chronic venous insufficiency [38], and adults with obesity [39].

In a cross-sectional study evaluating pre-dialysis and hemodialysis patients with CKD [40], there was a decrease in respiratory muscle strength (MIP and MEP) in both groups, but with a more significant impact on the group already on hemodialysis. Specifically, in patients on a regular hemodialysis program, there was a decrease in MIP with values 70% lower than predicted [40]. All studies included in this systematic review found patients with pre-intervention MIP values lower than those expected for age and sex. It seems essential that more clinical trials be carried out to clarify the best protocol to follow and optimize respiratory function in these patients.

Although IMT translates into gains in lung function, in the study conducted by Arazi et al. [41], there was no significant change in the distance covered in the 6-MWT. The authors justify these findings by the fact that uremic myopathy, anemia, and malnutrition are known to affect the results of the 6-MWT in hemodialysis patients. Another study [42] confirmed that mitochondrial dysfunction was associated with the severity of CKD, lower physical function (measured by the 6-MWT), higher intermuscular fat, and higher markers of inflammation and oxidative stress, which reinforces its influence on functional capacity.

The multifactorial causes of CKD (baseline kidney issue, an inflammatory or immune-mediated cause, or a toxic insult) have a direct impact on the health status and baseline functional status of participants [43], which may also hinder the generalization of results in this type of intervention. In addition, the simple randomization that was performed in all studies may cause patients with very different characteristics to be compared, once again hindering the interpretation of the results.

The timing of IMT (intradialytic or interdialytic) was not significant. Because of this finding, the intradialytic period should be considered to promote this type of training. Even so, if there are resources for IMT to be carried out in an interdialytic or mixed context, this opportunity should be explored since it is effective [7,12,24,25]. It is unclear whether shorter or longer periods translate into different results: one study in which IMT was carried out for 4 weeks showed a significant increase in MIP values [24]; similar results were obtained in another study that ran for 24 weeks [21]. Although there is no consensus on the ideal duration of training programs, but it seems that longer programs tend to produce health gains with greater impact [34]. However, none of the studies carried out long-term evaluations. Assessments of the variables under study were limited to the intervention period. Thus, and in accordance with the principle of training reversibility [34], it remains unclear whether the effect of IMT in hemodialysis patients is maintained over time or tends to diminish, as is the case with the same type of training in other chronic diseases [44]. It would be interesting to understand how the inspiratory muscles would evolve and what impact this would have on these patients after 3, 6, and 12 months.

None of the studies considered in this systematic review showed any adverse effects, so IMT in hemodialysis patients seems to be a safe intervention. However, there may be some limitations. Although there is evidence of the impact of CKD on inspiratory muscle strength, the number of studies on the effect of IMT is still limited. The studies included in this systematic review mostly have small and heterogeneous samples and varying interventions, so it is not easy to draw consistent conclusions. The fact that most of the studies were conducted in the same country (Brazil) may limit the generalizability of the findings. Demographic variables, the etiology of the diseases in question with an impact on the clinical condition of patients, socioeconomic conditions, and health policies vary considerably from country to country, and it may therefore be unwise to extrapolate the results.

Some studies have compared IMT using linear loading devices with control groups that only received maintenance or usual care. However, others have compared it with other breathing exercises or training types, such as aerobic or muscle-strengthening training. In addition, the variables under study and how the results are presented are diverse, making comparative analysis between studies complex. It would also be interesting to explore other ways of assessing the inspiratory muscles, such as surface electromyography, since this is recommended in research and clinical practice for evaluating the respiratory muscles [13], with a proven correlation between the neural respiratory impulse and the sensation of dyspnea, respiratory load, exacerbations, and mortality [45].

The findings of the studies included in this systematic review suggest that IMT may improve inspiratory muscle strength in hemodialyzed patients. Concerning lung function and functional capacity, study results are heterogeneous. It seems essential that more randomized controlled trials are carried out to clarify the variables in the intervention protocol. Other forms of assessment could also add crucial data to help explain the impact of IMT on these patients.

Author contributions

CRedit: **Sônia Alexandra Claro Casado**: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Validation, Writing – original draft; **Maria Eugénia Rodrigues Mendes**: Conceptualization, Formal analysis, Methodology, Validation; **Leonel São Romão Preto**: Formal analysis, Methodology, Software, Validation; **Carolina Júlia Félix Vila-Chã**: Formal analysis, Methodology, Resources, Visualization, Writing – review & editing; **André Filipe Morais Pinto Novo**: Conceptualization, Data curation, Investigation, Methodology, Project administration, Supervision, Writing – review & editing.

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