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Research

Inspiratory muscle training improves respiratory muscle strength, functional capacity and quality of life in patients with chronic kidney disease: a systematic review

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KEY WORDS

Chronic renal insufficiency
Haemodialysis
Breathing exercises
Respiratory muscle training
Physical therapy

ABSTRACT

Questions: Does inspiratory muscle training improve respiratory muscle strength, functional capacity, lung function and quality of life of patients with chronic kidney disease? Does inspiratory muscle training improve these outcomes more than breathing exercises? **Design**: Systematic review and meta-analysis of randomised trials. **Participants**: People with chronic kidney disease undergoing dialysis treatment. **Intervention**: Inspiratory muscle training versus sham or no inspiratory muscle training, and inspiratory muscle training versus breathing exercises. **Outcome measures**: The primary outcomes were: maximal inspiratory pressure, maximal expiratory pressure, and distance covered on the 6-minute walk test. The secondary outcomes were: forced vital capacity, forced expiratory volume in the first second (FEV_1), and quality of life. **Results**: The search identified four eligible studies. The sample consisted of 110 participants. The inspiratory muscle training used a Threshold® or PowerBreathe® device, with a load ranging from 30 to 60% of the maximal inspiratory pressure and lasting from 6 weeks to 6 months. The studies showed moderate to high risk of bias, and the quality of the evidence was rated low or very low, due to the studies' methodological limitations. The meta-analysis showed that inspiratory muscle training significantly improved maximal inspiratory pressure (MD 23 cmH_2O, 95% CI 16 to 29) and the 6-minute walk test distance (MD 80 m, 95% CI 41 to 119) when compared with controls. Significant benefits in lung function and quality of life were also identified. When compared to breathing exercises, significant benefits were identified in maximal expiratory pressure (MD 6 cmH_2O, 95% CI 2 to 10) and FEV_1 (MD 0.24 litres 95% CI 0.14 to 0.34), but not maximal inspiratory pressure or forced vital capacity. **Conclusion**: In patients with chronic renal failure on dialysis, inspiratory muscle training with a fixed load significantly improves respiratory muscle strength, functional capacity, lung function and quality of life. The evidence for these benefits may be influenced by some sources of bias. **Registration**: PROSPERO CRD42015029986. **[de Medeiros AIC, Fuzari HKB, Rattes C, Brandão DC, de Melo Marinho PÉ (2017) Inspiratory muscle training improves respiratory muscle strength, functional capacity and quality of life in patients with chronic kidney disease: a systematic review. *Journal of Physiotherapy* 63: 76–83]**

Introduction

Chronic kidney disease is characterised by changes in kidney structure or function that are present for > 3 months and classified into different stages that take into account the cause, the glomerular filtration rate and albuminuria.[1] In end-stage kidney disease, renal replacement therapy is required to maintain homeostasis of metabolic function. The most common method of renal replacement is haemodialysis, which is used in the management of over two million people with kidney disease worldwide.[2,3]

People with chronic kidney disease commonly develop uraemic syndrome, which affects multiple systems, including the respiratory system, with complications such as pleural effusion, pulmonary hypertension, calcification of lung parenchyma and respiratory impairment.[4,5] Also as a result of uraemia, myopathy and loss of muscle mass are frequent, due to protein-energy wasting, which affects up to 75% of dialysis patients.[6] An in-vitro study[7] showed decreased strength of the soleus and diaphragm muscles after uraemia induction and an in-vivo study[8] illustrated delay in latency of the phrenic nerve in patients with chronic kidney disease. Thus, people with chronic kidney disease have reduced respiratory and peripheral muscle strength, and low cardiorespiratory conditioning; these complications limit participation in activities of daily living and increase mortality.[9,10]

In order to improve the performance of the respiratory muscles, inspiratory muscle training has been suggested for people with chronic kidney disease.[11] Inspiratory muscle training is helpful in several other patient populations, including: pulmonary and heart disease,[12,13] cardiac surgery,[14] thoracic surgery,[15] multiple sclerosis[16] and stroke.[17] Inspiratory muscle training improves respiratory performance by loading the respiratory system beyond its usual

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level of work.[18] People with chronic obstructive pulmonary disease increase the percentage of type I fibres and size of type II fibres in respiratory muscles after performing inspiratory muscle training.[19]

In people with chronic kidney disease, the benefits of aerobic and resistance exercise are well established in systematic reviews.[20,21] Some individual clinical trials of inspiratory muscle training in haemodialysis patients have identified favourable effects on conditioning and strength of respiratory muscles and a reduction in complications.[10,22] However, no systematic reviews have estimated the effects of inspiratory muscle training on respiratory muscle strength, functional capacity, lung function and quality of life in people with chronic kidney disease.

Therefore, the research questions for this systematic review were:

1. Does inspiratory muscle training improve respiratory muscle strength, functional capacity, lung function and quality of life of patients with chronic kidney disease?
2. Does inspiratory muscle training improve these outcomes more than breathing exercises?

Method

Identification and selection of studies

A search was performed in the databases PubMed, CINAHL, CENTRAL, Web of Science, Scopus, LILACS and PEDro. The IBICT bank of theses and dissertations was also searched. No search restrictions were applied regarding year or language of publication. The trial register ClinicalTrials.gov was also accessed to search for relevant studies. The following key words were used: 'Renal Insufficiency; Chronic', 'Kidney disease', 'Hemodialysis', 'Breathing Exercises', 'Inspiratory Muscle Training', 'Respiratory Muscle Training' and 'Clinical Trial', in different combinations (see Appendix 1 on the eAddenda for the full search strategy).

Two independent reviewers evaluated the titles and abstracts of articles found in the searches against the eligibility criteria (Box 1). If there were disagreements between reviewers, a third reviewer arbitrated. All articles that were considered potentially eligible on review of the title and abstract were obtained in full text. Each article that was considered eligible for inclusion in the review had its reference list searched for further eligible publications. Duplicate articles were removed during the assessment of the studies' characteristics.

Assessment of characteristics of studies

Quality

The included studies were assessed using the Cochrane Risk of Bias Tool, which classifies the risk of bias as high, low or unclear.

Box 1. Inclusion criteria.

Design
- Randomised trial

Participants
- Adults (>18 years old)
- Receiving haemodialysis
- Haemodynamically stable

Intervention
- Inspiratory muscle training using linear load

Outcomes
- Primary: pulmonary function, functional capacity
- Secondary: respiratory muscle strength, quality of life

Comparisons
- Inspiratory muscle training versus no or sham intervention
- Inspiratory muscle training versus breathing exercises

Risk of bias was considered: high if a methodological procedure was not described, unclear if the description was unclear, and low if the procedure was described in detail.

The Grading of Recommendations Assessment, Developing and Evaluation (GRADE)[23] tool was used to analyse the quality of the evidence. The GRADE tool considers study limitations, consistency, targeting, precision and publication bias. The assessment of these criteria guides the classification of the evidence into one of four quality levels: high, moderate, low and very low.

Participants

Studies were included if the participants: were > 18 years old, had chronic kidney disease stage 5, and were receiving regular haemodialysis. The data extracted about the participants were age and gender.

Intervention

The experimental intervention of this research was inspiratory muscle training with devices[a,b] that provide a linear load, used in either the intradialytic or interdialytic phase. The data extracted about the intervention were the device used, the load used, and the duration and frequency of training. The control intervention was either no training or sham training. The comparison intervention was another breathing exercise.

Outcome measures

The primary outcome measures in this systematic review were respiratory muscle strength and functional capacity. The measures of respiratory muscle strength were inspiratory and expiratory muscle strength, each assessed using manovacuometry and expressed in cmH_2O. The measure of functional capacity was the distance walked in the 6-minute walk test and expressed in metres.

The secondary outcome measures were lung function and quality of life. The measures of lung function were: forced vital capacity (FVC) and forced expiratory volume in the first second (FEV_1); each was assessed by spirometry and expressed in litres. The measure of quality of life was the Kidney Disease Quality of Life Instrument Short Form questionnaire, which is scored from 0 to 100.

Data analysis

Two reviewers used standard forms to extract data about the characteristics of studies. Data for continuous variables were extracted, pooled using meta-analysis, and expressed as mean difference with a 95% confidence interval. The meta-analyses were performed with standard software[c] and using random effects models.

Results

Identification and selection of studies

The search resulted in 169 potentially relevant articles. After removal of duplicates, 96 articles were screened by title and abstract, of which 90 were excluded and six were assessed in the full-text version. Among the articles obtained in full text, one was excluded due to its ineligible study design and another due to an ineligible intervention (ie, inspiratory muscle training without linear load). The remaining four studies were included in the systematic review (Figure 1).

Characteristics of the included studies

The characteristics of the study are presented in Table 1. The risk of bias analysis is presented in Figure 2.

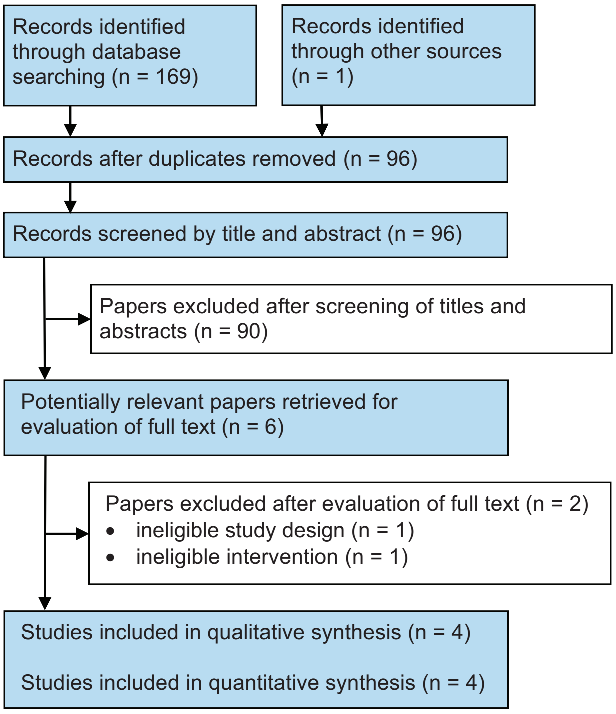

Figure 1. Flow of studies through the review.

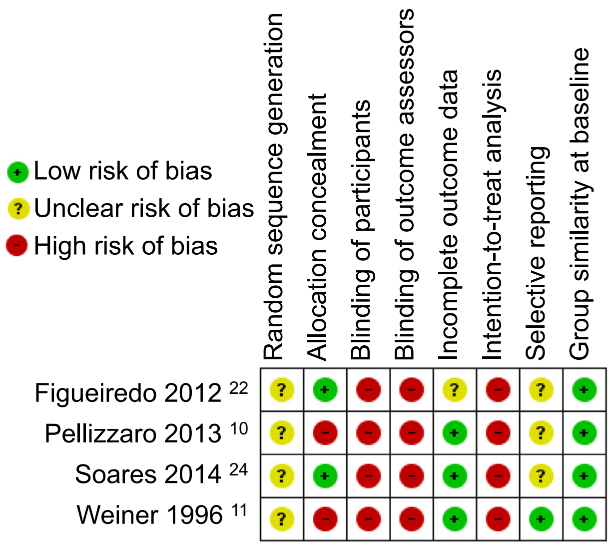

Figure 2. Risk of bias of the included studies assessed using the Cochrane Risk of Bias Tool.

Risk of bias

Regarding *randomisation and allocation*, the main methodological limitation was lack of clarity about whether randomisation was achieved through software, random numbers or other methods, constituting high risk of bias. The use of allocation concealment was clear in two of the four studies by reporting the use of sealed and opaque envelopes. The groups were homogeneous at baseline. Regarding *blinding*, none of the studies mentioned blinding of participants or collaborators, constituting high risk of bias. Regarding *intention-to-treat analysis*, all studies excluded losses in the final analysis and so were considered at high risk of bias. Regarding *selective reporting*, the study by Figueiredo et al[22] was considered to have unclear risk of bias because the control group was only assessed at baseline, preventing comparison with patients in the inspiratory muscle training group at the end of the study; however, the other active intervention group (ie, respiratory biofeedback) was used as a breathing exercise comparison group. The other two studies[10,24] were assessed as having unclear risk of selective reporting bias because the results of the Kidney Disease Quality of Life Instrument questionnaire were only presented as those dimensions that had a statistical difference, and not all the dimensions of the questionnaire.

Participants

The four included studies had a total of 110 participants, including both genders and ages between 19 and 78 years old. All studies were performed in people with chronic kidney disease stage 5 who were receiving regular haemodialysis.

Intervention

Three studies[10,11,22] used a Threshold[a] device and one study[24] used a PowerBreathe[b] device to apply the training load to the respiratory system; all calculated the load in accordance with the value of maximal inspiratory pressure (MIP), which was assessed by manovacuometry. Soares et al[24] used a load of 30% of MIP, Figueiredo et al[22] used 40% of MIP, Pellizzaro et al[10] used 50% of MIP and Weiner et al[11] started with a load of 15% of MIP, gradually increasing up to 60% of MIP, maintaining this percentage to the end of training. The duration of training also varied among the studies: Soares et al[24] used three series of 10 repetitions, Pellizzaro et al[10] used three series of 15 repetitions, Figueiredo et al[22] used

Table 1
Summary of included studies (n = 4).

Study	Participants	Intervention	Outcome measures
Weiner[11]	n = 20 Age (yr) = 22 to 78 Gender = not stated	Exp = inspiratory muscle training at 15 to 60% of MIP, 60 mins during 3 haemodialysis/wk x 12 wks, threshold device[a] Con = sham training	• Functional capacity • Respiratory muscle strength
Figueiredo[22]	n = 41 Age *(yr)* = 21 to 60 Gender = 24 M, 17 F	Exp 1 = inspiratory muscle training at 40% of MIP, 20 mins during 3 haemodialysis sessions/wk x 6 wks, threshold device[a] Exp 2 = respiratory biofeedback to generate a target of 30 cmH_2O pressure (about 40% of MIP) during inspiration without resistance, 20 mins during 3 haemodialysis sessions/wk x 6 wks Con = no intervention	• Lung function • Respiratory muscle strength
Pellizzaro[10]	n = 39 Age *(yr)* = 19 to 69 Gender = 23 M, 16 F	Exp 1 = inspiratory muscle training at 50% of MIP, 15 breaths x 3 sets (1-min rests) during 3 haemodialysis sessions/wk x 10 wks, threshold device[a] Exp 2 = peripheral muscle training at 50% of 1RM, knee extensions x 3 sets (1-min rests) during 3 haemodialysis sessions/wk x 10 wks Con = no intervention	• Lung function • Functional capacity • Respiratory muscle strength • Quality of life
Soares[24]	n = 34 Age *(yr)* > 18 Gender = 34 M	Exp 1 = inspiratory muscle training at 30% of MIP, 10 to 14 breaths x 3 sets (1-min rests) during 3 haemodialysis sessions/wk x 6 mths, threshold device[b] Exp 2 = incentive spirometry (2 breathing exercises, diaphragmatic breathing and inspiration) during 3 haemodialysis sessions x 6 mths	• Lung function • Respiratory muscle strength • Quality of life

Con = control group, Exp = experimental group, F = female, M = male, MIP = maximal inspiratory pressure, 1RM = one repetition maximum.
[a] Threshold® inspiratory muscle training device, Respironics, Pittsburgh, PA, USA.
[b] PowerBreathe® inspiratory muscle training device, IMT Technologies Ltd, Birmingham, UK.

20 minutes and Weiner et al[11] used 1 hour. All studies administered the training during dialysis sessions, with a frequency of three times a week. The total duration of the intervention period ranged from 6 weeks to 6 months.

In the two studies that compared inspiratory muscle training to control, one study[11] performed sham inspiratory muscle training, consisting of the same exercise regimen but with an unloaded device[a], and the other study[10] did not provide any intervention to the control group.

The other two studies compared inspiratory muscle training to a form of breathing exercise. One of these studies[22] performed respiratory biofeedback, while the other study[24] performed incentive spirometry.

Outcome measures

The variable inspiratory muscle strength was measured in all studies through manovacuometry.[10,11,22,24] Three studies[10,22,24] measured expiratory muscle strength through manovacuometry and lung function via spirometry as forced vital capacity (FVC) and forced expiratory volume in the first second (FEV_1). Functional capacity was measured in two studies with the 6-minute walk test.[10,11] Quality of life was assessed in two studies using the Kidney Disease Quality of Life Instrument Short Form questionnaire.[10,24] This questionnaire is analysed in four domains (symptoms, sleep, pain and energy), each of which is rated from 0 (worst) to 100 (best).

Effect of inspiratory muscle training

Respiratory muscle strength

Two studies[10,11] reported the effect of inspiratory muscle training on maximal inspiratory pressure, with a pooled sample of 45 participants. When compared to control (sham or no intervention), inspiratory muscle training improved maximal inspiratory pressure by an average of 23 cmH_2O (95% CI 16 to 29), as presented in Figure 3. A more detailed forest plot is available in Figure 4 on the eAddenda.

One study[10] reported the effect of inspiratory muscle training on maximal expiratory pressure (MEP), providing data on 25 participants. MEP improved by an average of 26 cmH_2O more with inspiratory muscle training than control, which was statistically significant (95% CI 21 to 32).

Functional capacity

Two studies,[10,11] both of which compared inspiratory muscle training to control, reported data for the 6-minute walk test as a measure of functional capacity in a total of 45 participants. Inspiratory muscle training caused a significant improvement in functional capacity, with a mean difference of 80 m (95% CI 41 to 119), as presented in Figure 5. A more detailed forest plot is available in Figure 6 on the eAddenda.

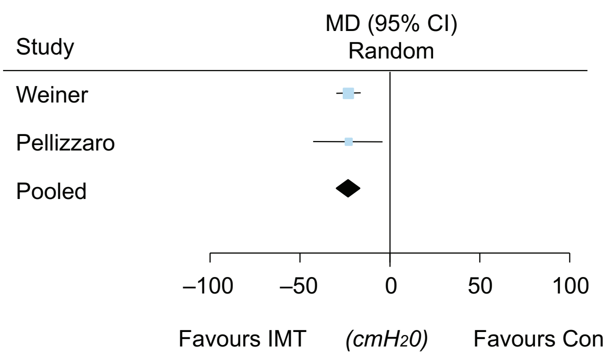

Figure 3. Mean difference (95% CI) in maximal inspiratory pressure (cmH_2O) due to inspiratory muscle training, estimated by pooling data from two studies (n = 45).
Con = control, IMT = inspiratory muscle training.

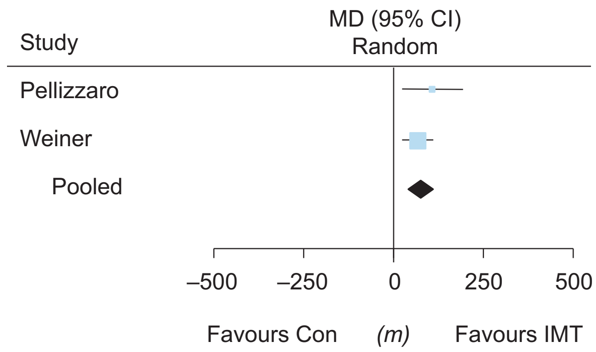

Figure 5. Mean difference (95% CI) in 6-minute walk distance (m) due to inspiratory muscle training, estimated by pooling data from two studies (n = 45).
Con = control, IMT = inspiratory muscle training.

Lung function

Lung function was reported in one study[10] of inspiratory muscle training versus control, providing data on 25 participants. Inspiratory muscle training improved FVC significantly more than control, with a mean difference of 0.70 litres (95% CI 0.53 to 0.87). FEV_1 was not measured in that study.

Quality of life

One study[10] reported the effect of inspiratory muscle training on quality of life, providing data on 25 participants. Three domains of the Kidney Disease Quality of Life Instrument Short Form questionnaire improved significantly more with inspiratory muscle training than with control: sleep ($p < 0.001$), pain ($p < 0.001$), and energy ($p = 0.003$). The data published in the study do not permit calculation of confidence intervals.

Inspiratory muscle training versus breathing exercises

Respiratory muscle strength

Two studies[22,24] reported the effect of inspiratory muscle training on maximal inspiratory pressure, with a pooled sample of 65 participants. When compared to the breathing exercises group (biofeedback or incentive spirometry), inspiratory muscle training did not significantly improve maximal inspiratory pressure, with a mean difference of 1 cmH_2O (95% CI −25 to 26), as presented in Figure 7. A more detailed forest plot is available in Figure 4 on the eAddenda.

Two studies[22,24] reported the effect of inspiratory muscle training on MEP, providing data on 65 participants. Participants who underwent inspiratory muscle training showed a significant increase in MEP after the completion of inspiratory muscle training when compared to breathing exercise, with an average difference of 6 cmH_2O (95% CI 2 to 10), as presented in Figure 8. A more detailed forest plot is available in Figure 9 on the eAddenda.

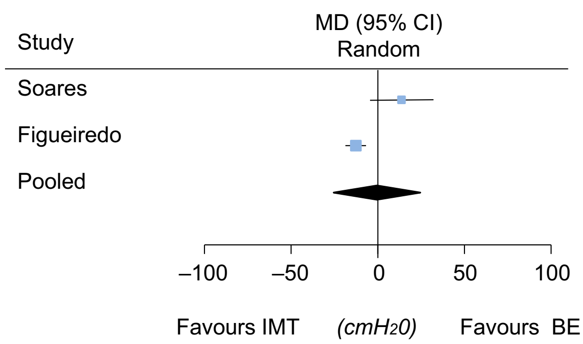

Figure 7. Mean difference (95% CI) in maximal inspiratory pressure (cmH_2O) with inspiratory muscle training versus breathing exercises, estimated by pooling data from two studies (n = 65).
BE = breathing exercises, IMT = inspiratory muscle training.

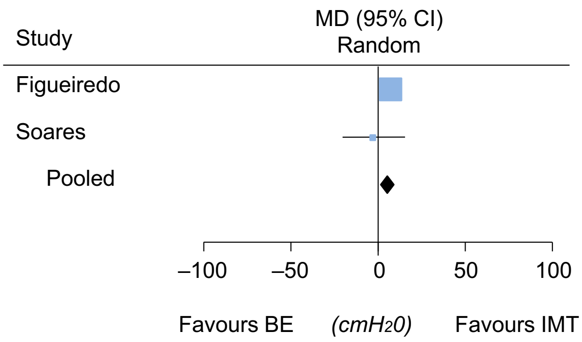

Figure 8. Mean difference (95% CI) in maximal expiratory pressure (cmH_2O) due to inspiratory muscle training, estimated by pooling data from two studies (n = 65). BE = breathing exercises, IMT = inspiratory muscle training.

Lung function

Lung function was reported in two studies[22,24] of inspiratory muscle training versus breathing exercises. These studies reported data for FVC and FEV_1 in 65 participants. FVC did not increase in the inspiratory muscle training group compared to breathing exercises, with a mean difference of 0.24 litres (95% CI –0.01 to 0.49), as presented in Figure 10. A more detailed forest plot is available in Figure 11 on the eAddenda. However, FEV_1 did increase in the inspiratory muscle training group compared to breathing exercises, with a mean difference of 0.24 litres (95% CI 0.14 to 0.34), as presented in Figure 12. A more detailed forest plot is available in Figure 13 on the eAddenda.

Quality of life

One study[24] reported the effect of inspiratory muscle training on quality of life, providing data on 34 participants. The data published in the study do not include or permit calculation of the between-group difference.

GRADE assessment

According to the GRADE assessment, the outcomes functional capacity, MEP and lung function showed low-quality evidence, due to limitations in the studies and 'no directionality'. The MIP outcome showed very low quality of evidence because it lost an additional point due to inconsistency (Tables 2 and 3).

Discussion

This review identified that in patients with chronic renal failure on haemodialysis, inspiratory muscle training induces significant benefits in respiratory muscle strength, functional capacity, lung function and quality of life. The four studies included in this systematic review showed important methodological limitations and heterogeneity among studies (such as the training load and duration of the sessions). The evidence for those benefits is therefore low or very low quality. Although this is the first systematic review evaluating the use of inspiratory muscle training in this population, reviews on inspiratory muscle training in patients with COPD[12] and congestive heart failure[13] populations, who also develop weakness in respiratory muscles, have already identified benefits of inspiratory muscle training. Therefore, recognising that the evidence is low quality, the substantial effect sizes noted in the present review suggest that inspiratory muscle training may be worthwhile for people with chronic kidney disease.

In chronic kidney disease, loss of muscle mass is a significant and common problem that affects activities of daily life, and is associated with quality of life and mortality rate.[25] The loss of muscle mass is due to the protein-energy wasting, which includes systemic protein reduction and reductions in skeletal muscle mass and body mass.[6] Among the factors that are associated with muscle weakness in this population are: vitamin D deficiency, anaemia, hypophosphatemia and malnutrition.[26] Sarcopenia is considered a predictor of morbidity and mortality in patients with chronic kidney disease; the reduced muscle strength becomes a debilitating symptom in chronic kidney disease and a sedentary lifestyle acts as a determining factor of the disease.[9,27] Thus, exercise is an effective alternative for reducing the potentially negative effects of dialysis.[28]

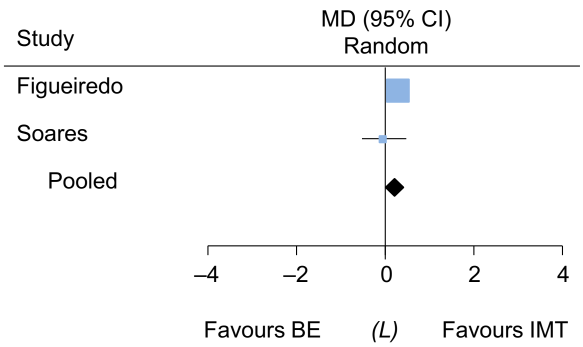

Figure 10. Mean difference (95% CI) in forced vital capacity (L) due to inspiratory muscle training, estimated by pooling data from two studies (n = 65).
BE = breathing exercises, IMT = inspiratory muscle training.

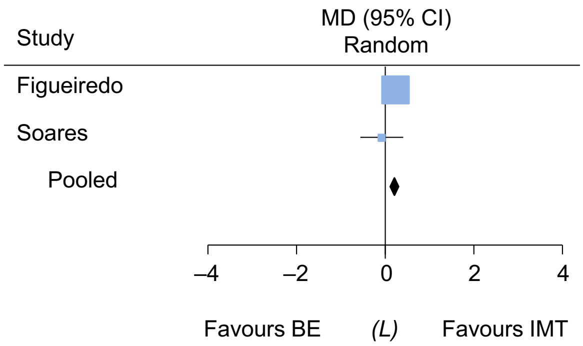

Figure 12. Mean difference (95% CI) in forced expiratory volume in the first second (FEV_1) (L) due to inspiratory muscle training, estimated by pooling data from two studies (n = 65).
BE = breathing exercises, IMT = inspiratory muscle training.

Systematic reviews[20,21,29] evaluating aerobic and resistance exercise in patients with chronic kidney disease have demonstrated its benefits in improving strength, exercise capacity, functional capacity, cardiac dimensions and quality of life. This evidence suggests that exercise should be undertaken for > 30 minutes per session and three times per week[20] moreover, if used during haemodialysis, the exercise should be performed in the first two hours.[21] A randomised, controlled trial also illustrated that exercise, in addition to being effective, is safe in this population, with no major adverse events reported in 12 months of training.[9] However, many of these aspects of using inspiratory muscle training have not yet been evaluated.

The specific training of respiratory muscles may be a useful alternative for patients with chronic kidney disease because the conditioning and strengthening of respiratory muscles can delay the complications of loss of muscle mass.[22] Inspiratory muscle training should be delivered with a fixed load (ie, flow is dependent upon a pre-set pressure being achieved) to ensure strong activation of the inspiratory muscles.[30] Its achievement may result in effects like phenotype modification of the respiratory muscles, increased respiratory muscle strength and endurance.[31]

This review identified that inspiratory muscle training improves inspiratory muscle strength when compared to the non-performance of exercises (sham or control), with an important effect (MD 22 cmH_2O, 95% CI 16 to 29), corroborating the results of systematic reviews in COPD.[13,32] However, when the inspiratory muscle training was compared to breathing exercises, there was no

Table 2
Quality of evidence using the GRADE approach (inspiratory muscle training versus control/sham).

Quality assessment							Participants		Effect	Quality	Importance
Studies (n)	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	IMT (n)	Con (n)	Absolute effect (95% CI)		
Inspiratory muscle strength (follow-up mean 11 weeks; measured with manuvacuometer; range of scores 0 to 300; better indicated by lower values)											
2	RCTs	serious[a]	no serious inconsistency	serious[b]	no serious imprecision	none	21	24	MD 22.53 lower (28.75 to 16.31 lower)	⊕⊕⊝⊝ low	important
Functional capacity (follow-up mean 11 weeks; measured with 6-minute walk test; range of scores 0 to 700; better indicated by higher values)											
2	RCTs	serious[a]	no serious inconsistency	serious[b]	no serious imprecision	none	21	24	MD 80.06 higher (41.18 lower to 118.95 higher)	⊕⊕⊝⊝ low	important

Con = no-intervention, IMT = inspiratory muscle training.
[a] Limitations of randomisation, allocation, blinding and intention-to-treat.
[b] Differences in training (load and duration).

Table 3
Quality of evidence using the GRADE approach (inspiratory muscle training versus breathing exercises).

Quality assessment							Participants		Effect	Quality	Importance
Studies (n)	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	IMT (n)	BE (n)	Absolute effect (95% CI)		
Inspiratory muscle strength (follow-up mean 15 weeks; measured with manuvacuometer; range of scores 0 to 300; better indicated by lower values)											
2	RCTs	serious[a]	very serious[b]	serious[c]	serious[d]	none	35	30	MD 0.56 lower (26.38 lower to 25.27 higher)	⊕⊝⊝⊝ very low	important
Expiratory muscle strength (follow-up mean 15 weeks; measured with manuvacuometer; range of scores 0 to 300; better indicated by higher values)											
2	RCTs	serious[a]	no serious inconsistency	serious[c]	no serious imprecision	none	35	30	MD 6.07 higher (2.26 lower to 9.89 higher)	⊕⊕⊝⊝ low	important
Forced vital capacity (follow-up mean 15 weeks; measured with spirometer; range of scores 0 to 5; better indicated by higher values)											
2	RCTs	serious[a]	no serious inconsistency	serious[c]	no serious imprecision	none	35	30	MD 0.24 higher (0.01 lower to 0.49 higher)	⊕⊕⊝⊝ low	important
Forced expiratory volume in 1 second (follow-up mean 15 weeks; measured with spirometer; range of scores 0 to 4; better indicated by higher values)											
2	RCTs	serious[a]	serious[e]	serious[c]	no serious imprecision	none	35	30	MD 0.24 higher (0.01 lower to 0.49 higher)	⊕⊝⊝⊝ very low	important

BE = breathing exercises, IMT = inspiratory muscle training.
[a] Limitations of randomisation, blinding and intention-to-treat.
[b] Heterogeneity is considerable ($I^2 = 87\%$).
[c] Differences in training (load and duration) and breathing exercises (incentive spirometer or respiratory biofeedback).
[d] Wide confidence interval.
[e] Heterogeneity is moderate ($I^2 = 52\%$).

significant difference in their effects on MIP. There was high heterogeneity for this outcome (I^2 = 87%), which was probably due to different interventions used in the breathing exercise groups.

Although it does not apply a load to the expiratory muscles, inspiratory muscle training significantly increased MEP by 26 cmH_2O more than control (95% CI 21 to 32). This may reflect that stronger inspiratory muscles are able to bring the thorax to a more expanded position in preparation for the MEP measurement manoeuvre. This more expanded position would mean greater elastic recoil of the lungs and chest wall, which may have boosted the MEP data. This does not explain the greater MEP in the trials where inspiratory muscle training was compared to breathing exercises because in these trials, the effects on MIP did not significantly differ between the groups. Although statistically significant, the difference in MEP was much smaller (MD 6 cmH_2O, 95% CI 2 to 10), so this may be a Type I error.

Studies in COPD[13,33] show that, in addition to increasing respiratory muscle strength, inspiratory muscle training improved functional capacity, exercise capacity, dyspnoea and quality of life. A similar broad range of benefits was also apparent in the present review, where there was improvement in functional capacity assessed by the 6-minute walk test (MD 80 m, 95% CI 41 to 119) and FVC (MD 0.70 litres, 95% CI 0.53 to 0.87). A significant effect on FEV_1 was only seen in the trials with breathing exercises as the comparison intervention.

The 6-minute walk test is a submaximal exercise test of low cost and easy application that has been widely used in patients with chronic diseases as a predictor of mortality or to evaluate an intervention. In chronic kidney disease, there have been no reports of the minimum clinically important difference for the 6-minute walk test. However, a cohort study with 52 chronic renal patients illustrated that survival increased approximately 5% for every 100 m walked in the 6-minute walk test.[34,35] Although difference in the distance walked in this study was 80 m, the lack of studies evaluating the minimum clinically important difference in this population make it difficult to conclude that this difference has a clinical impact on kidney patients. Conversely, the magnitude is also much larger than the effects of whole-body exercise training studies in other chronic disease populations, which seems counterintuitive.

Although clinical trials in other populations[36–38] have reported benefits from daily inspiratory muscle training, the studies in the present review opted for completion of the training only in the intradialytic period (ie, a frequency of three times a week). Therefore, there is a gap in the literature on the benefits of increased training frequency in this population.

Regarding the limitations of the included studies, moderate to high risk of bias was observed. Factors that contributed to the risk of bias were the unspecified randomisation procedures, no mention of allocation concealment in some studies, and no use of blinding. The small number of participants in the analysed studies also limited the results of this review. Other important limitations were due to the implementation of inspiratory muscle training (duration and training load) and different control groups or breathing exercises, which may have justified the heterogeneity of results in inspiratory muscle strength outcome.

It is recommended that further clinical trials investigate inspiratory muscle training in chronic renal failure patients, with improved methodological rigor. Such trials could also help to refine how inspiratory muscle training should be prescribed.

Low-quality evidence suggests that inspiratory muscle training can provide strengthening of respiratory muscles, improving functional capacity and lung function in chronic renal failure patients on dialysis. Due to the low number of included articles and the variation in interventions used, current evidence shows a limited guide to this physical therapy practice.

In conclusion, inspiratory muscle training improves maximal respiratory pressures, lung function, functional capacity and quality of life in patients with chronic renal failure who are receiving haemodialysis. However, these promising findings are based on evidence that is limited in its amount and quality. New clinical trials should be conducted with larger sample size, more rigorous control of source of potential bias, and the inclusion of other outcomes such as adverse effects.

What is already known on this topic: Inspiratory muscle training improves inspiratory muscle strength and functional capacity of patients with chronic diseases such as heart failure and chronic obstructive pulmonary disease.
What this study adds: Inspiratory muscle training improves maximal respiratory pressures, lung function, functional capacity and quality of life in people with chronic renal failure who are receiving haemodialysis. However, these promising findings are based on evidence that is limited in its amount and quality.

Footnotes: [a]Threshold®, Healthscan Products Inc, Cedar Grove, USA, [b]PowerBreathe®, HaB International Ltd, Southam, UK, [c]RevMan 5.3, Nordic Cochrane Centre, Copenhagen, Sweden.

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