Pulmonol. 2019;25(4):236–247

PULMONOLOGY

www.journalpulmonology.org

REVIEW

Effectiveness of manual therapy in COPD: A systematic review of randomised controlled trials

C. Simonelli[a,*], M. Vitacca[b], M. Vignoni[c], N. Ambrosino[c], M. Paneroni[b]

[a] Istituti Clinici Scientifici Maugeri IRCCS, Cardiac Rehabilitation of the Institute of Lumezzane (BS), Italy
[b] Istituti Clinici Scientifici Maugeri IRCCS, Respiratory Rehabilitation of the Institute of Lumezzane (BS), Italy
[c] Istituti Clinici Scientifici Maugeri IRCCS, Respiratory Rehabilitation of the Institute of Montescano (PV), Italy

Received 7 June 2018; accepted 15 December 2018

KEYWORDS
Chronic obstructive pulmonary disease;
Manual therapy;
Manipulation;
Pulmonary rehabilitation;
Physiotherapy

Abstract
Purpose: Manual therapy (MT) has been proposed in pulmonary rehabilitation programmes for patients with chronic obstructive pulmonary disease (COPD), but an updated systematic review of the evidence is lacking. We aimed to systematically review the effectiveness of MT interventions, alone or added to exercise, on lung function, exercise capacity and quality of life in COPD patients, compared to other therapies (e.g. exercise alone) or no treatment.
Materials and methods: We searched MEDLINE, EMBASE, Physiotherapy Evidence Database, and Cochrane Central Register of Controlled Trials databases, using the terms: COPD, manual therapy, manipulation, joint mobilisation, osteopathic manipulation. Only randomised controlled trials (RCT) were considered.
Results: Out of 555 articles screened, 6 fulfilled the inclusion criteria. The study designs were heterogeneous (with different intervention schedules) and there was a high risk of bias. No effect on lung function was found, while results on exercise capacity were contrasting. MT had no effect on quality of life, although valid measures were available only in one study. Only mild adverse events were reported.
Conclusions: Few RCTs of poor methodological quality are available on the effects of MT in COPD. More and better quality RCTs are needed before this technique can be included in rehabilitation programmes for these patients.

Abbreviations: PA, physical activity; PRP, pulmonary rehabilitation programme; HRQL, health-related quality of life; MT, manual therapy; 6MWT, six-minute walking test.

* Corresponding author.
E-mail address: carla.simonelli@icsmaugeri.it (C. Simonelli).

https://doi.org/10.1016/j.pulmoe.2018.12.008
2531-0437/

Introduction

Chronic obstructive pulmonary disease (COPD) is characterised by different phenotypes and often associated with multiple comorbidities contributing to higher mortality rates and reduced physical activity (PA).[1] It has been shown that for these patients pulmonary rehabilitation programmes (PRP) can improve symptoms, exercise capacity and health-related quality of life (HRQL),[2,3] as a consequence, guidelines for management of COPD recommend that PRP including exercise training should be provided for the vast majority of patients.[1]

Despite recommendations that PRP be mainly focused on exercise training,[2] other manoeuvres are used with low level of evidence in some routine settings with the aim of enhancing the effectiveness of PRP.[4] Among these manoeuvres manual therapy (MT) has been proposed also in PRP for COPD patients.[5] Manual Therapy has been defined as a clinical approach utilising skilled, specific hands-on techniques, and is used to treat musculoskeletal, soft tissues and joint dysfunctions, with the aim of improving function, modulating pain, and facilitatin movement.[5–7] The rationale for proposing MT is that there is a high incidence of musculoskeletal disorders,[8] such as cervical and low back pain, and migraine[9] in COPD patients, which may benefit from manual interventions. Musculoskeletal disorders and pain have also been mentioned among the causes of impaired physical performance and reduced physical activity in COPD.[10]

However, there is the need to establish the evidence of effectiveness for MT. A systematic review[5] including only techniques used by the physical therapist and papers published before 1990[9–13] did not find any evidence of effectiveness. Therefore, the aim of this study was to provide a systematic review of randomised controlled trials (RCTs), in order to investigate the effectiveness of MT interventions (alone or added to exercise training), performed by any professional, on lung function, exercise capacity and HRQL in COPD patients. As a secondary aim, we investigated the reported adverse events.

Materials and methods

In this systematic review of RCTs we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[14] For the purposes of this review, MT was defined as ''a clinical approach utilising skilled, specific hands-on techniques'' used to ''diagnose and treat soft tissues and joint structures for the purpose of modulating pain, increasing range of motion, reducing or eliminating soft tissue inflammation, inducing relaxation, improving contractile and non-contractile tissue repair, extensibility and/or stability, facilitating movement, and improving function''.[5]

Data sources and search strategies

The search was conducted from March to September 2017. The following databases were analysed: Medical Literature Analysis and Retrieval System Online (MEDLINE - PubMed), Excerpta Medica dataBASE (EMBASE), Physiotherapy Evidence Database (PEDro) and Cochrane Central Register of Controlled Trials (CENTRAL), from their inception to September 2017. The references of retrieved articles were reviewed for additional studies. The following search terms or medical subject headings (MeSH) were used:

- Chronic obstructive pulmonary disease, chronic obstructive airway disease, chronic obstructive lung disease.
- Manual therapy, manipulation, musculoskeletal manipulation, joint mobilisation, chiropractic, chiropractic manipulation, osteopathic manipulation techniques and stretching.

The main investigator (M.Vig.) conducted the search of the bibliographic databases, screening all titles and/or abstracts for the inclusion criteria, and identified and removed duplicates. Titles and abstracts of studies were screened by the main investigator to exclude non-eligible studies. Full-text articles were retrieved where the abstract suggested a potentially eligible study. When details were missing from the abstract, full-texts were retrieved and checked for eligibility. Two independent reviewers (M.Vig., C.S.) assessed full-texts for eligibility. Discrepancies were resolved by discussion. The main investigator maintained records on all studies not meeting inclusion criteria, providing the rationale for their exclusion.

Eligibility criteria

We included RCTs with full-text in English language, according to the following criteria:

Participants: adults with COPD, without any age or disease severity restriction. Studies with mixed population (e.g. combined asthma and COPD) were excluded.

Interventions: RCTs evaluating any form of MT as defined above[5] were eligible. Studies were excluded if MT was not delivered through physical hand contact (e.g. by mechanical tools or devices) or consisted only of treatment with complementary and alternative medicine such as point application, acupressure, acupuncture, reflexology, Chinese herbal medicine, tai-chi, yoga or other traditional Chinese medicine techniques. In addition, studies based on MT interventions consisting uniquely of gentle massage, passive stretching, manual chest physiotherapy (such as chest percussion or vibration), and secretion clearance techniques (such as postural drainage or abdominal thrust) were also excluded. Studies assessing patients during an acute exacerbation were also excluded. No restriction on the professional who carried out the MT was placed.

Comparisons: all RCTs comparing MT to usual care, to sham techniques or light manual interventions (e.g. gentle massage), to PA, exercise alone, or to a combinations of these interventions, were included.

Outcome measures: RCTs assessing any of the following outcome measures: lung function [at least forced expiratory volume at 1st second (FEV_1)], exercise capacity by six-minute walking test (6MWT), and HRQL, were included. Safety of the interventions (Adverse events) was also evaluated.

Data collection and items: using a dedicated electronic database with the use of Microsoft Excel software (2010 version, Microsoft, Redmond, WA, US), the main investigator extracted the data and the second reviewer (C.S.) checked

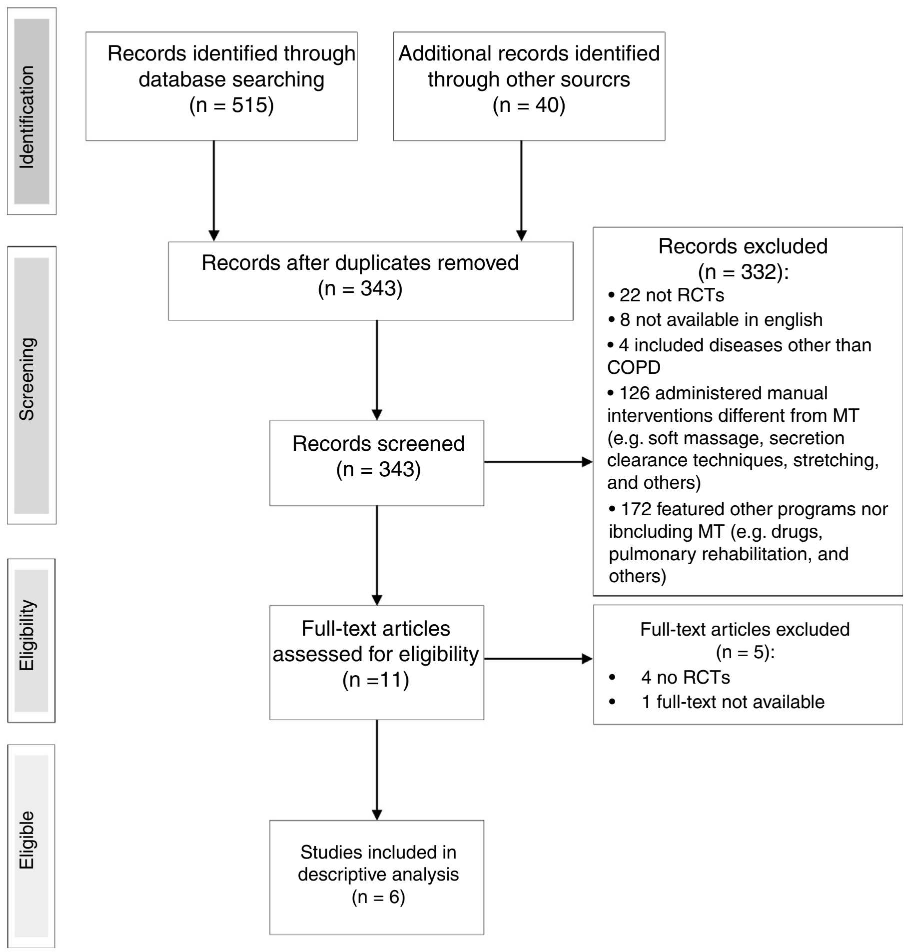

Figure 1 Flow chart of selection of studies for the review.

and revised the database. All entered data were screened for accuracy. Authors of Papers were not asked for missing data. The information included in the database were: study design, setting, sample size, groups, characteristics of participants, details of interventions such as frequency, intensity, time and/or type (FITT), professionals involved, outcome measures and results. Adverse events were classified as 'mild', 'moderate' and 'major', according to the classification described by Carnes et al.[15]

Risk of bias within studies: all included RCTs were assessed using the Cochrane Risk of Bias tool.[16,17] Overall risk of bias for individual studies (low, unclear, high) was assessed by two independent reviewers (M.Vig., C.S.) according to the Cochrane guidelines.[17] Discrepancies had to be solved by consensus with a third reviewer (M.P.).

Results

Study selection

A flow chart of the selection of studies is shown in Fig. 1. From an initial search of databases, 515 potential studies were identified and another 40 studies were identified from the bibliographies of retrieved articles. After removal of duplicates, 343 titles and abstracts were screened for eligibility, of which 332 were excluded as not meeting the eligibility criteria. Out of the remaining 11, four studies were excluded after review of the full-text, one full-text article was not found. Hence, 6 studies fulfilled the criteria for eligibility and were included in the review. The level of agreement between the two main reviewers was always good and the judgement of the third reviewer was not required.

Study characteristics

The main characteristics of the included RCTs are shown in Table 1. All studies contained a similar hypothesis about the physiological effect of MT: to reduce respiratory muscle hyperactivity and increase the mobility of the thoracic structures involved in respiratory mechanics. All subjects in the included papers were outpatients with moderate to very severe COPD.[1] As also shown in Table 1, the intervention schedules varied, consisting of 1–24 sessions lasting 5–45 min. As control treatment, all studies[18–23] administered sham manoeuvres or a technique that the authors deemed as non-therapeutic, and four RCTs[18,22] compared MT also to various exercise programmes or PA.

Table 1 Characteristics of the included studies.

Reference	Setting	Participants	Groups	*n*	Interventions	Intervention schedule	Professional who performed MT
Engel et al.[18] (2013)	Outpatients	15 moderate COPD 9 males age 56.1 (4.2) years FEV_1 61.8 (8.9) % of predicted	Soft tissue therapy	5 (2 males)	Soft tissue therapy: gentle massage (effleurage, friction, cross-fibre friction) applied to intercostal, serratus posterior/anterior, rhomboid, trapezius, latissimus dorsi, erector spinae, quadratus lumborum, levator scapulae muscles	Eight 12–20 min sessions, twice a week for 4 weeks	A clinician
			Soft tissue therapy + Spinal manipulation	5 (4 males)	Soft tissue therapy (same as above) + Spinal manipulation: 2 non-specific, multi-joint HVLA manipulations per session of thoracic and costal joints	Eight 15–20 min sessions	
			Soft tissue therapy + Spinal manipulation + Exercise	5 (3 males)	Soft tissue therapy + Spinal manipulation (same as above) + Exercise consisting in continuous walking on a level surface for 6 min	30-min sessions, before exercise	
Engel et al.[19] (2016)	Outpatients	33 moderate–severe COPD 10 males age 65.5 (4.0) years FEV_1 1.57 (0.47) L 6MWT 479 (97) m	Pulmonary rehabilitation	15 (1 male)	Pulmonary rehabilitation: health education and exercise training	Total duration 24 weeks, with phase 1 (weeks 1–8) consisting of health education and initial exercise training, phase 2 (weeks 9–16) of exercise training with gradual increase of intensity to a level considered suitable for that participant, and phase 3 (weeks 17–24) the indication to continue exercising.	A practitioner

Table 1 (*Continued*)

Reference	Setting	Participants	Groups	*n*	Interventions	Intervention schedule	Professional who performed MT
			Soft tissue therapy + Pulmonary rehabilitation	9 (4 males)	Pulmonary rehabilitation (same as above) + Soft tissue therapy: gentle massage (effleurage, friction, cross-fibres friction) to intercostal, serratus posterior/anterior, rhomboid, trapezius, latissimus dorsi, erector spinae, quadratus lumborum, levator scapulae muscles	20-min session of soft tissue therapy, administered just before exercise, twice a week, in the 8-week period between week 4 and week 12	
			Soft tissue therapy + Spinal manipulative therapy + Pulmonary rehabilitation	9 (5 males)	Pulmonary rehabilitation + Soft tissue therapy (same as above) + Spinal manipulative therapy: 2 non-specific, multi-joint HVLA manipulations per session of thoracic intervertebral, costovertebral, and costotransverse joints	20-min session including both soft tissue and spinal manipulative therapy administered just before exercise, twice a week, in the 8-week period between week 4 and week 12	
Wada et al.[20] (2016)	Outpatients	30 moderate–severe COPD 15 males age 62.5 (5.5) years FEV_1 44.25 (12.5) % of predicted BMI 25.8 (3.3) kg/m^2 6MWT 456 (85.5) m	Respiratory muscle stretching (hold-relax and passive) + Aerobic training	15 (8 males)	Respiratory muscle stretching: (passive elongation of muscle followed by 3-s isometric contraction) of scalene, sternocleidomastoid, trapezius, pectoralis major and minor, intercostal, serratus anterior, and rectus abdominis muscles + passive elongation sustained for 1 min of muscles that showed limited performance + Aerobic training on a treadmill	24 sessions, twice a week, for 12 weeks. Stretching technique 3 times with 1-min rest between repetitions, before aerobic training. 30-min aerobic training sessions at 60% of average speed achieved during 6MWT, with progression up to 85% according to perceived effort between 4 and 7 on the modified Borg scale	Physiotherapist
			Sham therapy + Aerobic training	15 (7 males)	Sham treatment: active stretching of wrist and ankle flexors and extensors, contraction held for 1 min with 1 min of rest + Aerobic training on a treadmill	30-min stretching sessions before aerobic training. Aerobic training as for the intervention group	

Table 1 (*Continued*)

Reference	Setting	Participants	Groups	*n*	Interventions	Intervention schedule	Professional who performed MT
Rocha et al.[21] (2015)	Outpatients	20 COPD 14 males age 71 (5.5) years FEV_1 34.5 (12.5) % of predicted BMI 25 (3.5) kg/m^2	Manual diaphragm release technique	11 (8 males)	Manual diaphragm release technique 2 sets of 10 deep breaths, with rest interval of 1 min	6 sessions, 2–3 days/week, for 2 weeks	Physiotherapist
			Sham treatment	9 (6 males)	Sham treatment: same manoeuvres executed with light hand touch without any pressure or traction	Same as above	
Zanotti et al.[22] (2012)	Outpatients	20 severe COPD 15 males 63.8 (5.1) years FEV_1 26.9 (6.3) % of predicted RV 190.6 (37) % of predicted BMI 18 (2.8) kg/m^2 6MWT 280 (93) m	Comprehensive pulmonary rehabilitation + OMT	10 (7 males)	Pulmonary rehabilitation (same as below) + Osteopathic manipulation treatment consisting in an initial assessment and treatment of possible restrictions of joint mobility	The same timing and intensity as the other group	Osteopathic practitioner
			Comprehensive pulmonary rehabilitation + Soft manipulation	10 (8 M)	Pulmonary rehabilitation: exercise training (cycle + arm ergometer), educational support, nutritional intervention and psychological counselling + Sham treatment with soft manipulations	Forty 30-min sessions, 5 days/week, for 4 weeks + Forty 45-min soft manipulations	
Noll et al.[23] (2008)	Outpatients	35 COPD 18 males age 70.9 (6.8) years 20 in long-term oxygen therapy	Osteopathic manual therapy (OMT)	18 (8 males)	OMT protocol: 7 standardised techniques + Indirect myofascial release, HVLA manipulation, and muscle-energy techniques	One 20-min session	An operator
			Sham treatment	17 (10 males)	Sham treatment: light hand touch applied to the same anatomic region as the OMT manoeuvre	One 20-min session	

Legend: *n*, number of patients; COPD, chronic obstructive pulmonary disease; OMT, osteopathic manual therapy; HVLA, high velocity low amplitude; FEV1, forced expiratory volume in 1st sec; RV, residual volume; BMI, body mass index; 6MWT, 6-min walking test.

Table 2 Summary of outcome measures assessed in the articles reviewed.

Reference	Dynamic volumes	Static volumes	6MWT	HRQL	AEs	Other outcome measures
Engel et al.[18]	Yes		Yes	Yes (CRQ-SAS)	Yes	
Engel et al.[19]	Yes		Yes	Yes (SGRQ)	Yes	Systolic and diastolic blood pressure; Hospital Anxiety and Depression scale.
Wada et al.[20]			Yes			Chest wall volumes during exercise, expiratory flow and VE by OEP; Borg CR10 dyspnoea at the end of 6MWT; respiratory muscle activity by electromyography and the ratio between respiratory muscle activity and tidal volume.
Rocha et al.[21]			Yes			Chest wall volumes at rest by OEP; inspiratory and vital capacity estimated by OEP; diaphragmatic mobility by echography; maximal inspiratory and expiratory pressures; sniff nasal inspiratory pressure.
Zanotti et al.[22]	Yes	Yes	Yes		Yes	Vital capacity; Borg CR10 dyspnoea at the end of 6MWT
Noll et al.[23]	Yes	Yes			Yes	Forced expiratory flow at 25%, 50%, 75%, and maximum of vital capacity; forced inspiratory volume at 50% and maximum of vital capacity; forced inspiratory vital capacity; expiratory reserve volume; inspiratory capacity; maximum voluntary ventilation; residual volume; slow vital capacity; total gas volume; total lung capacity.

Legend: 6MWT, 6-min walking test; AEs, adverse events; CRQ-SAS, Chronic Respiratory Questionnaire – Self-Administered Standardised; SGRQ, Saint George's Respiratory Questionnaire; VE, minute ventilation; OEP, optoelectronic plethysmography.

Table 2 shows the outcome measures assessed. Most studies assessed 6MWT and reported adverse effects. Few study assessed lung function.

Study quality and risk of bias

Results of the risk of bias analysis are reported in Table 3. All studies were classified as having a high risk of bias. In one study,[18] patients were selected from volunteers recruited through advertisements and newspaper ads, while in another paper[19] a pulmonologist selected patients for the study and referred them to the medical centre where they were then randomised and treated. Fig. 2 provides details of the heterogeneity of the characteristics of the interventions: some studies did not state the duration of the sessions,[20,21] or did not describe the technique.[23] Fig. 3 shows the heterogeneity of study designs, inclusion criteria and outcome measures among the included studies. Study designs and sample sizes were described properly in all studies, COPD was diagnosed according to criteria other than GOLD in two papers[19,23] or without any clear criteria in another.[18]

Outcome measures

Due to the heterogeneity of the included studies, it was not appropriate to conduct a meta-analysis of the results.

A summary of the main results is shown in Table 4. Noll et al.[23] investigated the immediate effects after a single manoeuvre, while all the other studies[18–22] investigated the

Table 3 Risk of bias of included studies based on Cochrane Risk of Bias tool [17]

Domain		References					
		Engel et al. [18]	Engel et al. [19]	Wada et al. [20]	Rocha et al. [21]	Zanotti et al. [22]	Noll et al. [23]
Selection bias	Random sequence generation	?	?	+	+	+	?
	Allocation concealment	+	+	+	+	+	-
Performance bias	Blinding of participants and personnel	-	-	-	+	?	-
Detection bias	Blinding to outcome assessment	+	+	+	-	+	+
Attrition bias	Incomplete outcome data	+	+	+	+	+	+
Reporting bias	Selective reporting	-	+	-	-	?	+
Other bias	Other sources of bias[a]	-	-	-	-	-	-
Sum		-	-	-	-	-	-

Legend: + , low risk of bias; ? , unclear risk of bias; - , high risk of bias.
Note: [a]Other sources of bias include no comparison of baseline data between controls and intervention group, and lack of description of the MT intervention.

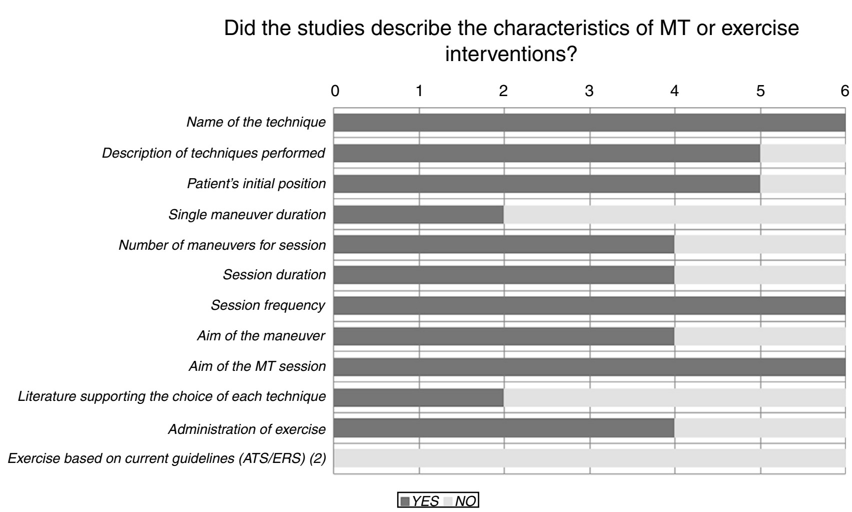

Figure 2 Details of the study protocol as described in the reviewed studies.

effect of a comprehensive programme. No significant effect on FEV_1 was found. Analysing exercise capacity, a significant increase in 6MWT was found in three studies.[18,19,22] In the studies[18,19] assessing HRQL as an outcome measure, an improvement was reported only by Engel et al.[18] who found a reduction in the dyspnoea domain alone. Concerning adverse events, Zanotti et al.[22] reported no adverse events or side-effects from osteopathic manipulative therapy, while three studies[18,19,23] reported mild adverse events after MT (muscle soreness) in 15% and 0.005% of MT sessions in the two studies by Engel et al.,[18,19] respectively, and in two patients out of 35 in the study by Noll et al.[23]

Discussion

Summary of evidence

This systematic review investigated the current evidence for effectiveness of MT interventions targeted at musculoskeletal system in COPD patients. The analysis of the six RCTs included[18–23] show high heterogeneity of study design, patient sample, MT schedule, and outcome measures assessed. All studies showed a high risk of bias. Interventions were feasible, with only mild adverse events. However, the studies showed no effects on airway obstruction and

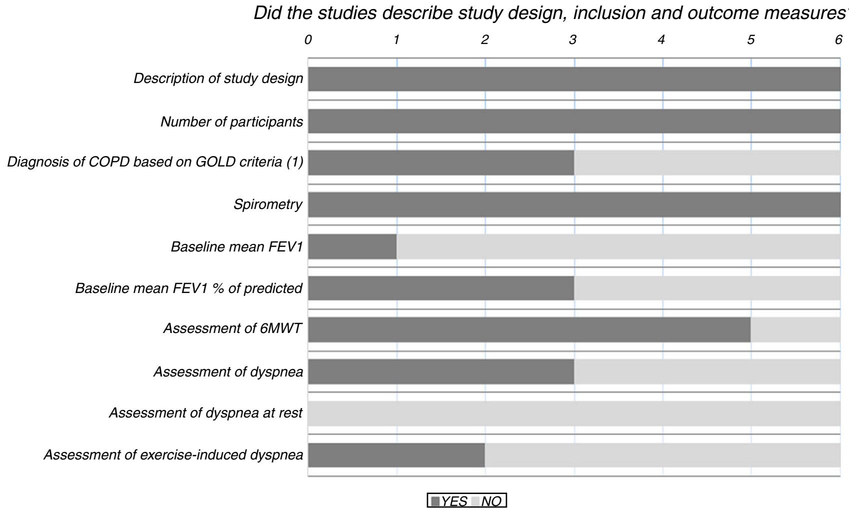

Figure 3 Details of study design, inclusion criteria and outcome measures across the reviewed studies.

inconclusive results in static volumes. Inconclusive results were found concerning exercise capacity and only one study showed benefit in HRQL. As a consequence, at present there is no evidence to support the inclusion of MT interventions in standard PRP for patients with COPD.

Our results confirm those by Heneghan et al.,[5] which found that pulmonary function change minimally after MT and stated that evidence supporting MT is lacking. Wearing et al.[24] instead found that MT, administered in addition to exercise, increased forced vital capacity and functional capacity, but that review[24] was focused only on joint manipulation techniques, whereas our review and that by Heneghan et al.[5] included a wider variety of techniques. However, that review[5] included only MT techniques performed by physical therapists, while we did not limit the search in relation to the professional carrying out MT.

Variability of interventions

The MT techniques evaluated in the included studies[18–23] were either patient- or therapist-dependent. The assumption that a reduction in muscular stiffness and an improvement in joint mobility could produce a COPD-associated decrease of rib cage rigidity was not supported in these studies.[18–23] It is unclear whether these manoeuvres may really increase chest wall motion. It has been shown that thoracic high velocity low amplitude techniques improve pain and function in some syndromes such as neck pain,[25] shoulder impingement[26] and low back pain,[27] but effects on chest wall mechanics have not been demonstrated in either healthy or patients with COPD.

The intervention schedules as well as the operator performing them varied among studies. Therefore, it is difficult to compare the interventions, and the contribution of each individual technique to the outcome measures is unknown.

Study quality

The small sample size of the studies is a serious methodological limitation. It was not clear whether the diagnosis of COPD followed accepted guidelines[1] or whether lung function assessments were performed according to standardised methods, which puts into question the comparability of the outcome measures of the studies. No study assessed the specific outcome measures for which MT techniques were aimed at, such as pain. Furthermore, disease-specific HRQL questionnaires were used only in two studies.[18,19] Manual therapy was compared to different exercise modalities and schedules but no studies compared MT to a standardised multidisciplinary PRP including high-intensity exercise training.[2]

No study showed significant effects of MT on airway obstruction. In addition, as a potential adverse effect, in one study[23] MT resulted in an immediate increase in static volumes confirming a previous report by the same authors[28] but in contrast to another study showing a reduction in static volumes.[22] Despite the fact that exercise capacity, as assessed by 6MWT, improved significantly in 3 out of 5 studies[18,19,22] the related mechanisms such as a reduction in dyspnoea were assessed only in one study.[18] The HRQL did not significantly improve in any study.

Limitations

Missing data were not requested from the authors of papers. Gathering more specific data on the applied technique and on the diagnostic criteria of COPD used, could have reduced the level of bias. Furthermore, the inclusion of RCTs only, and the exclusion of non-English language articles may have induced a publication bias. Another limitation may be due to the fact that various professionals, with different educational paths and different experience, performed MT. Limiting the search to MT manoeuvres performed by specific professionals (e.g. physical therapists) can lead to different results.

Practical implication and future studies

The present evidence does not support the inclusion of MT in PRP in COPD patients. A standardisation of MT techniques,

Table 4 Synthesis of results of outcome measures.

Reference	MT intervention	Control	FEV_1	RV	6MWT	HRQL	Adverse effects (AEs)
Engel et al.[18]	Massage + 2 HVLA + Exercise	Massage	=		↑ [+168 (12.0) m]	↑ [+0.44 (0.10) points][a]	No major, 18 mild AEs (muscle soreness) after MT
	Massage + 2 HVLA	Massage	=		↑ [+120 (26.3) m]	↑ [+0.64 (0.22) points][a]	
	Massage + 2 HVLA + Exercise	Massage + 2 HVLA	=		↑ [+48.0 (18.5) m]	=	
Engel et al.[19]	Massage + 2 HVLA + Exercise	Exercise	=		=	=	No major, 2 mild AEs (muscle soreness) after MT
		Massage + exercise	=		↑ [+48.3 m (98.33% CI 8.9 to 87.69)+ and +58.4 m (98.33% CI 4.70 to 112.2)][b]	=	
Wada et al.[20]	Respiratory muscle stretching + aerobic training	Wrist and ankle muscle stretching + aerobic training			=		Not investigated
Rocha et al.[21]	Manual diaphragmatic release techniques	Manual contact			=		Not investigated
Zanotti et al.[22]	Pulmonary rehabilitation + OMT	Pulmonary rehabilitation + Soft manipulation	=	↓ [-0.44 L (95% CI −0.26 to −0−62)]	↑ [+48.8 m (95% CI 17–80.6)]		No AEs reported
Noll et al.[23]	7 standardised OMT + myofascial release, HVLA and muscle-energy techniques	Light touch	=	↑ [from 4.37 (2.09) to 5.02 (3.06) L in OMT; ↓ from 5.03 (1.68) to 4.84 (1.84) L in controls]			No major, 2 mild AEs (muscle soreness) after MT, 4 mild AEs in controls (elevated blood pressure, heart palpitations, muscle and back soreness)

Note: [a]Chronic Respiratory Questionnaire – Self-Administered Standardised, domain Dyspnoea; [b]FVC and 6MWT were collected at a 24-week follow-up, 12 weeks after the conclusion of an 8-week MT intervention; 6MWT was collected at a 16-week follow-up, 4 weeks after the conclusion of an 8-week MT intervention. In brackets are reported the mean improvement of the intervention group ($p < 0.05$) compared to controls.
Legend: ↑, significant increase; ↓, significant decrease; =, no significant change; FEV_1, forced expiratory volume at 1st sec; RV, residual volume; 6MWT, 6-min walking test; HRQL, health-related quality of life; AEs, adverse effects; OMT, osteopathic manipulation treatment; HVLA, high velocity low amplitude; CI, confidence interval.

methods and schedules as well as of outcome measures is necessary to provide a common language, which may be shared across different countries.[29] Also the professional carrying out the MT should be always clearly specified. An effort should be made to tailor these techniques to the individual patient,[30] and to different COPD phenotypes.[31] Future studies should also investigate the effects of MT on symptoms, such as pain, and disability related to musculoskeletal disorders in COPD.

Conclusions

This systematic review has provided low-quality evidence showing that a variety of MT techniques and programmes, although feasible, have no effects on lung function in COPD patients. Contrasting results have been found regarding the effects on exercise capacity and HRQL. Further studies with better standardisation and scientific validity are needed to assess the effects of MT on exercise capacity, symptoms, disability and quality of life.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or non-for-profit sectors.

Conflicts of interest

The authors report no conflict of interest.

Acknowledgements

The Authors thank Rosemary Allpress for the English revision of the manuscript and Laura Comini for editing and technical assistance.

References

1. Global strategy for prevention, diagnosis and management of COPD. http://goldcopd.org/gold-reports/ [accessed 04.06.18].
2. Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, et al. ATS/ERS Task Force on Pulmonary Rehabilitation. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. Am J Respir Crit Care Med. 2013;188:e13–64.
3. Paneroni M, Simonelli C, Vitacca M, Ambrosino N. Aerobic exercise training in very severe chronic obstructive pulmonary disease: a systematic review and meta-analysis. Am J Phys Med Rehabil. 2017;96:541–8.
4. Hill CJ, Lazzeri M, D'Abrosca F. Breathing exercises and mucus clearance techniques in pulmonary rehabilitation. In: Clini E, Holland AE, Pitta F, Troosters T, editors. Textbook of pulmonary rehabilitation. Cham, Switzerland: Springer pub; 2018. p. 205–16.
5. Heneghan NR, Adab P, Balanos GM, Jordan RE. Manual therapy for chronic obstructive pulmonary disease: a systematic review of current evidence. Man Ther. 2012;17:507–18.
6. Bokarius AV, Bokarius V. Evidence-based review of manual therapy efficacy in treatment of chronic musculoskeletal pain. Pain Pract. 2010;10:451–8.
7. Southerst D, Yu H, Randhawa K, Côté P, D'Angelo K, Shearer HM, et al. The effectiveness of manual therapy for the management of musculoskeletal disorders of the upper and lower extremities: a systematic review by the Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration. Chiropr Man Therap. 2015;23:30.
8. Chen YW, Camp PG, Coxson HO, Road JD, Guenette JA, Hunt MA, et al. Comorbidities that cause pain and the contributors to pain in individuals with chronic obstructive pulmonary disease. Arch Phys Med Rehabil. 2017;98:1535–43.
9. de Miguel-Díez J, López-de-Andrés A, Hernandez-Barrera V, Jimenez-Trujillo I, Del Barrio JL, Puente-Maestu L, et al. Prevalence of pain in COPD patients and associated factors: report from a population-based study. Clin J Pain. 2018;34: 787–94.
10. HajGhanbari B, Garland SJ, Road JD, Reid WD. Pain and physical performance in people with COPD. Respir Med. 2013;107:1692–9.
11. Howell RK, Allen TW, Kappler RE. The influence of osteopathic manipulative therapy in the management of patients with chronic obstructive lung disease. J Am Optom Assoc. 1975;74:757–60.
12. Miller WD. In: Bethesda, editor. The research status of spinal manipulative therapy: a workshop held at the National Institutes of Health, February 2–4. Washington (US): U.S. Dept. of Health, Education, and Welfare, Public Health Service, National Institutes of Health, National Institute of Neurological and Communicative Disorders and Stroke; 1975.
13. Witt PL, MacKinnon J. Trager psychophysical integration (TPI); a method to improve chest mobility of patients with chronic lung disease. Phys Ther. 1986;66:214–7.
14. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med. 2009;151:264–9.
15. Carnes D, Mullinger B, Underwood M. Defining adverse events in manual therapies: a modified Delphi consensus study. Man Ther. 2010;15:2–6.
16. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al., Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomized trials. BMJ. 2011;343, d5928.
17. Jørgensen L, Paludan-Müller AS, Laursen DR, Savović J, Boutron I, Sterne JA, et al. Evaluation of the Cochrane tool for assessing risk of bias in randomized clinical trials: overview of published comments and analysis of user practice in Cochrane and non-Cochrane reviews. Syst Rev. 2016;5:80.
18. Engel RM, Vemulpad SR, Beath K. Short-term effects of a course of manual therapy and exercise in people with moderate chronic obstructive pulmonary disease: a preliminary clinical trial. J Manipulat Physiol Ther. 2013;36:490–6.
19. Engel RM, Gonski P, Beath K, Vemulpad S. Medium term effects of including manual therapy in a pulmonary rehabilitation program for chronic obstructive pulmonary disease (COPD): a randomized controlled pilot trial. J Man Manip Ther. 2016;24:80–9.
20. Wada JT, Borges-Santos E, Porras DC, et al. Effects of aerobic training combined with respiratory muscle stretching on the functional exercise capacity and thoracoabdominal kinematics in patients with COPD: a randomized and controlled trial. Int J Chron Obstruct Pulmon Dis. 2016;11:2691–700.
21. Rocha T, Souza H, Brandão DC, et al. The manual diaphragmatic release technique improves diaphragmatic mobility, inspiratory capacity and exercise capacity in people with chronic obstructive pulmonary disease: a randomized trial. J Physiother. 2015;61:182–9.
22. Zanotti E, Berardinelli P, Bizzarri C, et al. Osteopathic manipulative treatment effectiveness in severe chronic obstructive

pulmonary disease: a pilot study. Complement Ther Med. 2012;20:16–22.
23. Noll DR, Degenhardt BF, Johnson JC, Burt SA. Immediate effects of osteopathic manipulation treatment in elderly patients with chronic obstructive pulmonary disease. J Am Osteopath Assoc. 2008;108:251–9.
24. Wearing J, Beaumont S, Forbes D, Brown B, Engel R. The use of spinal manipulative therapy in the management of chronic obstructive pulmonary disease: a systematic review. J Altern Complement Med. 2016;22:108–14.
25. Cross KM, Kuenze C, Grindstaff TL, Hertel J. Thoracic spine thrust manipulation improves pain, range of motion, and self-reported function in patients with mechanical neck pain: a systematic review. J Orthop Sports Phys Ther. 2011;41:633–42.
26. Bizzarri P, Buzzatti L, Cattrysse E, Scafoglieri A. Thoracic manual therapy is not more effective than placebo thoracic manual therapy in patients with shoulder dysfunctions: a systematic review with meta-analysis. Musculoskelet Sci Pract. 2017;33:1–10.
27. De Oliveira RF, Liebano RE, Costa Lda C, Rissato LL, Costa LO, et al. Immediate effects of region-specific and non-region specific spinal manipulative therapy in patients with chronic low back pain: a randomized controlled trial. Phys Ther. 2013;93:748–56.
28. Noll DR, Johnson JC, Baer RW, Snider EJ. The immediate effect of individual manipulation techniques on pulmonary function measures in persons with chronic obstructive pulmonary disease. Osteopath Med Prim Care. 2009;3:9.
29. Mintken PE, DeRosa C, Little T, Smith B. American Academy of Orthopaedic Manual Physical Therapists AAOMPT clinical guidelines: a model for standardizing manipulation terminology in physical therapy practice. J Orthop Sports Phys Ther. 2008;38:A1–6.
30. Ambrosino N, Clini EM. Response to pulmonary rehabilitation: toward personalised programmes? Eur Respir J. 2015;46:1538–40.
31. Ambrosino N, Venturelli E, de Blasio F, Paggiaro P, Pasqua F, Vitacca M, et al. Respiration. 2015;89:141–7.