

REVIEW ARTICLE

Prevalence and risk factors of musculoskeletal pain in patients with chronic obstructive pulmonary disease: A systematic review

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Abstract

Objectives: This systematic review aimed to discuss the prevalence and the risk factors of the musculoskeletal pain in chronic obstructive pulmonary disease (COPD).

Data source and study selection: Four databases were analysed (Scopus, PubMed, Cochrane and EMBASE). We excluded systematic reviews, meta-analyses, conference abstracts and case reports. Two authors independently checked for the eligibility of the relevant articles. The risk of bias was evaluated using the Newcastle Ottawa Quality Assessment Scale and the Joanna Briggs Institute critical appraisal checklist. The selection and evaluation of studies followed the PRISMA guidelines.

Results: Twenty studies were retrieved, including from 21 to 7952 patients with COPD. The prevalence of pain was highly heterogeneous across studies: 7–89.7%. Pain was mostly reported in the lumbar (7–69%) and cervical spine (11–48.3%) and the chest (44–82.8%). The main risk factors for developing pain were old age, sex (female), level of physical activity (low) and comorbidities.

Conclusion: Pain is a very common symptom in patients with COPD. Despite this, few clinical trials have investigated the pain. It appears to be located primarily in the lumbar, cervical and thoracic regions and facilitated by being a female, a low level of physical activity, comorbidity(ies) and old age.

KEYWORDS

COPD, pain, prevalence, risk factors

1 | INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is among the four major non-communicable diseases, along with cardiovascular disease, cancer and diabetes,¹ and estimates predict this disease will become the third lead-

ing cause of death in 2020.^{2–4} The main issues are the pulmonary symptoms such as cough, dyspnea and expectoration, but COPD involves also some comorbidities such as diabetes, arthritis and osteoporosis.^{1,2,5}

Pain is defined as ‘an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage; or is described in terms of such damage having physiological

Abbreviations list: COPD, chronic obstructive pulmonary disease.

and psychological consequences'.⁶ It has received increasing attention in the recent years. The prevalence of pain in the general population ranges from 24.4% to 50.4%,⁵ and it was also recognised as an important issue for patients with COPD¹ with prevalence reaching up to 94%.⁷ Pain is even considered as an important determinant of patients' general health and quality of life.³⁻⁵ Moreover, pain was associated to some comorbidities related to COPD, and it can increase the severity of the symptoms in the patients with COPD.^{5,7} However, a better understanding of its characteristics could help to improve pain assessment and management approaches in this specific condition in order to improve the overall condition of the patient with COPD.³

This systematic review aimed to discuss the prevalence and the risk factors of the musculoskeletal pain in chronic obstructive pulmonary disease (COPD).

2 | METHOD

This systematic review was undertaken following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

The selection of articles was performed from inception to June 2020 in four different databases: PubMed, Scopus, Cochrane and EMBASE. The PICO(S) criteria (Table 1) were used to establish the search strategy based on keywords related to the research question of this study associating musculoskeletal pain in patients with COPD. The search equation was initially constructed on EMBASE according to these criteria and adapted for each database syntax. The MESH terms used were pain, chronic pain, pulmonary disease, chronic obstructive, musculoskeletal pain, prevalence, risk factors, epidemiology, causality, incidence, comorbidity and pain measurement.

Articles were only included if they involved all our PICO(S) criteria (Table 1) and were written in French or

English. They were excluded if participants were in acute exacerbation of COPD.

2.1 | Research strategy and selection of studies

The PRISMA flowchart was used to undertake the selection of the articles.⁸ This selection was made by two readers (M.V. and F.L.). At the completion of the search, all references were imported into EndNote X9 software (Thomson Reuter, New York, NY, USA), and duplicates were removed. Titles and/or abstracts of retrieved studies were screened independently by two authors (M.V. and F.L.). Relevant full texts were assessed by the same authors who independently determined if they fulfilled the inclusion criteria. A third reviewer (G.R.) was involved in case of disagreements. In case where an article was not available in full text, an e-mail was sent to the corresponding author in an attempt to retrieve the text.

2.2 | Data extractions

The following information from the selected articles were extracted. These included study details (first author, publication years and study type); sample characteristics (number of participants, age and gender, severity of COPD and smokers status); pain characteristics (prevalence, location, intensity, duration, frequency and risk factors of pain); other assessed outcomes and used measuring tools.

2.3 | Risk of bias of the studies

The methodological quality of the studies included in this review was assessed by the Newcastle-Ottawa Quality Assessment Scale (NOS) for cohort studies⁹ and by the Joanna Briggs Institute (JBI) critical appraisal checklist for analytical cross sectional study.¹⁰ These choices were based on the conclusions of the review of Ma et al.¹¹

The NOS contains eight items, distributed in three dimensions: selection (four items), comparability (one item) and outcome (three items). For each item, a series of answers is proposed, and a star is awarded if the study meets an evaluation criterion. This system allows a maximum of one star per item, except for the comparability item, which allows two stars. The decision of Sharmin et al.¹² to classify the quality of items as follows was adopted in this systematic review: *good quality*: three to four stars for selection, one to two stars for comparability

TABLE 1 PICO selection criterion

Research about: Musculoskeletal pain in patients with COPD	
P	Patients with a confirmed diagnosis of COPD, male or female, 18 to 99 years of age
I	Valid or invalid pain-specific questionnaires, patient interviews or medical record reviews.
C	Non-COPD patient, control group
O	Prevalence, risk factor or epidemiology of musculoskeletal pain

and two to three stars for outcome; *fair quality*: two stars for selection, one to two stars for comparability, and two to three stars for outcome; *poor quality*: zero to one star for selection or zero star for comparability or zero to one star for outcome.

The JBI appraisal checklist contains eight questions with four possible answers: 'yes', 'no', 'unclear' and 'not applicable'. The number of positive answers is added together to give a score out of 8. For this scale, the risk of bias was considered as low if they had a positive response to at least 50% of the items (4/8).¹³

3 | RESULTS

3.1 | Selection of articles

The selection process retrieved 5,094 studies in the different database. At the end of the entire process, 20 articles were selected for this systematic review. All these steps of article selection are detailed in the PRISMA flow chart (Figure 1).

3.2 | Quality score of the selected studies

Two out of the 20 retrieved articles were cohort studies.^{14,15} They were rated as 'good quality' with the NOS. The 18 analytical cross-sectional studies^{1-5,16-28} received a total of positive responses to items ranging from five (four studies) to eight (nine studies) on the JBI critical appraisal checklist. All of these studies were therefore considered to be at low risk of bias. Cohort and cross-sectional studies are both observational studies but cohort studies referred to incidence and cross-sectional referred to the prevalence of an outcome.²⁹

Details of the qualitative assessment of the 20 studies are shown in Table 2.

3.3 | Characteristics of the selected studies

The study details, sample characteristics, pain characteristics, additional outcomes and used measuring tools of the selected article are shown in Table 3.

3.4 | Synthesis of results

Eleven studies included both COPD ($n = 21-7952$) and healthy patients ($n = 21-18\,811$)^{1-4,14,15,17-19,21,27} or COPD with other conditions ($n = 1139-8582$), including

six studies incorporating a control population matched in age and sex to the COPD population.^{2-4,15,17,18,27} One of the studies included a qualitative analysis of pain experiences.³

The mean age ranged from 46 to 71.2 years. Sex ratio was well balanced excepted in seven studies.^{1-3,15,16,18,19} The diagnosis of COPD was only confirmed by spirometry in 13 studies,^{4,5,17-27} by completing validated questionnaires^{4,5,17} or by self-reporting^{1,2,14,16} in some studies.

The prevalence of any pain in a population of patients with COPD varies widely, ranging from 7%¹⁴ to 89.7%.¹⁹ Several ways of assessing pain prevalence were used in our studies: filling out a validated questionnaire (25.1-82.1%),^{4,5,17,18,21-26,28} interviewing participants about their pain (7-89.7%),^{1,2,14,16,17,19-21,27} diagnosis from a physician (59.8-60%),^{3,15} request for pain treatment based on a procedure or request for an ambulatory prescription of pain medication (59.8-60%).^{3,15} Five studies mentioned chronic pain. However, the definition of chronic pain varied considerably between studies: equal to or exceeding 42 days,^{3,15} for more than 3 months,^{5,17,18} 6 months¹ or 12 months.² Pain frequency was specified in five studies and was consistently described as having experienced pain at least once a day.^{1,2,5,17,18}

The patients mostly reported lumbar (7-69%),^{2,3,5,14,16-19,22,24-27} or cervical spine pain (11-48.3%)^{2-4,16-19,22,24,26,27} and chest pain (44-82.8%).^{4,17-19,22,24,26,27} Pain intensity was described in 13 studies using a quantitative or qualitative pain scale (e.g., mild, moderate and severe).^{1,2,19,24}

Six studies were matched with non-COPD controls. De Miguel-Diez et al.² showed that pain was higher in COPD patients, in chronic neck pain (+14.4%), chronic low back pain (+16.4%), migraine (+9.3%) and in all the three locations (+6.97%). However, the same distribution of pain was observed in COPD patients and matched control subjects. HajGhanbari et al.⁴ showed that COPD patients had more moderate to very severe pain than control and in more locations of pain (3.1 vs. 1.3; +1.8). The most common location in both groups was the neck and the trunk. Roberts et al.^{3,15} showed that COPD patients had 8.1% more evidence of chronic pain than control (59.8% vs. 51.7%) but the same distribution of pain was observed in both groups. Lee et al.¹⁷ showed that the prevalence of pain was 12% greater in COPD patient and was more common in the chest, the upper back and the upper limb than control patients. Vardar-Yagli et al.²⁷ showed that COPD patients had more neck (+45.5%), chest (+36.4%), back (+18.2%) and head pain (+9.1%).

The main risk factors for developing pain were the following: sex (female),^{1,2,15,17,21,28} level of physical activity (low),^{16,17,27} comorbidities^{1-5,15,19,21,23,25,27} and old age.^{1,2,15,21,28}



PRISMA 2009 Flow Diagram

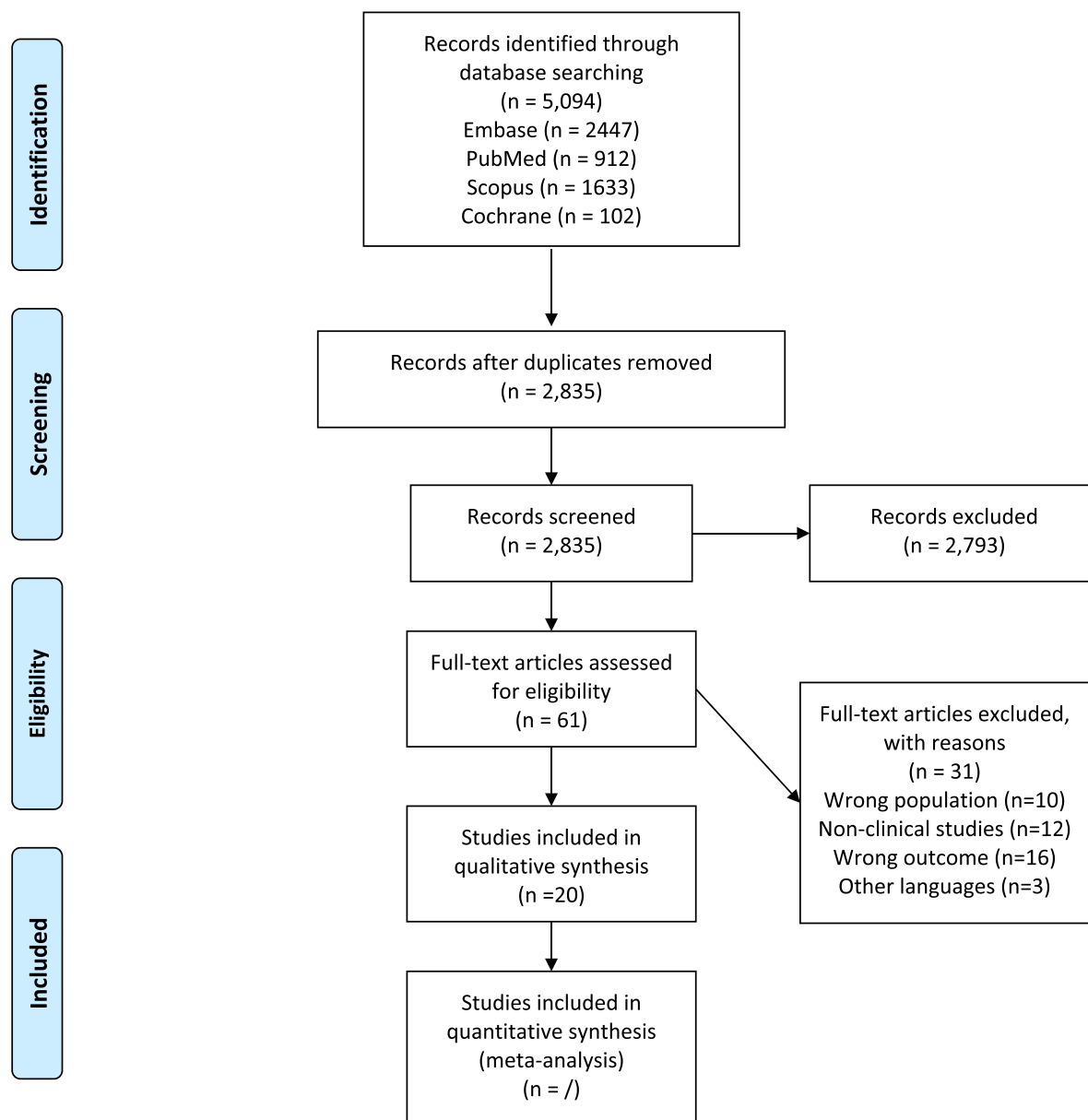


FIGURE 1 PRISMA flow chart of the systematic review

4 | DISCUSSION

The current systematic review showed that there is a wide heterogeneity in the prevalence of pain and its location in patients with COPD. However, the location tends more towards the lumbar and the cervical spine and the chest areas. In addition, several risk factors for the development of pain in COPD were identified such as gender, age, physical activity level and comorbidities.

The heterogeneity in the prevalence of pain (7–89%) can be attributed to the variability in the design and settings of the studies, patient characteristics, measurement instruments used in the studies and pain definition. For example, Roberts et al.^{3,15} were the only ones to have selected their painful patients using an opioid prescription database. However, because opioids may also be prescribed for chronic dyspnea in patients with COPD, the prevalence of pain in these studies may be slightly

TABLE 2 Risk of bias inherent in each study

Newcastle-Ottawa quality assessment scale for cohort study (NOS)											
Studies	Selection		Comparability					Outcomes		Total	
	Representativeness of exposed cohort	Selection of nonexposed cohort	Ascertainment of exposure	Outcome not present at the start of the study			Assessment of outcomes	Length of follow-up	Adequacy of follow-up		
Rasmussen-Barr et al. 2019	*	*	*	*	- *	-	*	*	*	Good quality	
Roberts et al. 2015	*	*	*	-	**	-	*	*	*	Good quality	
Etude	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Total “yes”		
Castillo et al. 2020	Yes	Yes	No	No	Yes	Yes	No	Yes	5		
Cheng et al. 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8		
Vardar-Yagli et al. 2019	Unclear	Yes	Yes	Yes	Yes	No	Unclear	Yes	5		
Vadar-Yagli et al. 2019	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	7		
Andenaes et al. 2018	Yes	Yes	No	No	Yes	Yes	No	Yes	6		
Chen et al. 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8		
De Miguel-Diez et al. 2018	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	7		
Chen et al. 2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8		
Lee et al. 2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8		
Xiao et al. 2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8		
Christensen et al. 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8		
Janssen et al. 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8		
Lee et al. 2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8		
Bentsen et al. 2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8		
Borge et al. 2014	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	7		
Roberts et al. 2013	Yes	Yes	No	No	Yes	Yes	No	Yes	5		
HajGhanbari et al. 2012	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	7		
Bentsen et al. 2011	Yes	No	Yes	Yes	Unclear	Yes	No	Yes	5		

Note: Q1: Were the criteria for inclusion in the sample clearly defined? Q2: Were the study subjects and the setting described in detail? Q3: Was the exposure measured in a valid and reliable way? Q4: Were objective, standard criteria used for measurement of the condition? Q5: Were confounding factors identified? Q6: Were the strategies to deal with confounding factors stated? Q7: Were the outcomes measured in a valid and reliable way? Q8: Was appropriate statistical analysis used?

TABLE 3 Study characteristics and protocol

Study/year	Study design	Participants COPD/control	Pain characteristics COPD/control	Other outcomes	Measuring tools used
Castillo et al. 2020	Cross-sectional analytical	<i>n</i> = 601 52.8 (14.1) years Q: 52.2% COPD severity: NS Smokers: 33.6%	P: 56.2% L: cervical (33.3%) lumbar (38.9%) I: / D: / F: / RF: Low PA associated with chronic lumbar pain (<i>p</i> = 0.0002)	PA Demographics	All participants: COPD: diagnosis? "yes" or "no" Comorbidities: "Have you ever been diagnosed with ... (each comorbidity studied)?" IPAQ form
Cheng et al. 2020	Cross-sectional analytical	<i>N</i> = 901 63.1 (8.5) years Q: <i>n</i> = 109 (12.1%) COPD severity: • FEV1: 45.2 (25.4) % Smokers: <i>n</i> = 726 (80.6%)	P: <i>n</i> = 226 (25.1%) L: • Chest (58.9%) • LBP (19.9%) • Abdomen (15.0%) • Buttocks (3.5%) • Upper limb (2.6%) • Lower limb (6.2%) • Head (4.9%) • Neck (3.5%) I: worst: 3.7 (1.7)/10 • Mild: 69.1% • Moderate: 24.3% • Severe: 6.6% D: / F: / RF: BMI > 24 kg/m ² , high CAT score, high CCQ	Demographics Dyspnea Lung function	mMRC CAT BPI CCQ
Rasmussen-Barr et al. 2019	Cohort	<i>n</i> = 162/1139 46 (10) years/45 (16) years Q: 48% / 59% COPD severity: NS/NS Smokers: 28% / 13%	P: 7%: annoying LBP > 4 years/3%: annoying LBP > 4 years L: Lower back I: / D: / F: / RF: COPD, asthma, asthma + COPD	Demographics Physical Health Psychological Health Social Economic factors Lifestyle Factors of life	All participants: Lumbar pain: < 6 months? Impact work and daily activity? Asthma? "yes" or "no" COPD? "yes" or "no"
Vardar-Yagli et al. 2019	Cross-sectional analytical	<i>n</i> = 29/31 56.59 (8.00) years/54.35 (6.81) years Q: <i>n</i> = 19/20 COPD severity: • FEV ₁ : 50.67 (22.29) % / NS • FVC: 66.69 (20.04) % / NS	P: 89.7% / 19.4% L: • Head: 65.5% / 9.7% • Chest: 82.8% / 0% • LBP: 69.0% / 9.7% • Back pain: 72.4% / 0% • Extremities: 48.3% / 0%	Comorbidity Sensitivity to pain Functional balance Postural aspect at rest	All participants: CCI Algometer Location, causes, severity of pain: self-assessment TUG

(Continues)

TABLE 3 (Continued)

Study/year	Study design	Participants COPD/control	Pain characteristics COPD/control	Other outcomes	Measuring tools used
Vardar-Yagli et al. 2019	Cross-sectional critical	$N = 31/n = 31$ 53.9 (7.4) years/50.6 (7.8) years ♀: $n = 13$ (41.93%) / $n = 12$ (38.71%) COPD severity: • FEV₁: 51.1 (16.7) % / NS • FVC: 66.2 (17.0) % / NS • FEV₁/FVC: 65.3 (17.4) % / NS Smokers: 29.7 (23.3) UPA/NS	• Stomach: 20.7% / 0% • Neck: 48.3% / 0% I: Slight: 48.3% / 16.1% Moderate: 48.3% / 3.2% D: / F: / RF: arthritis, orthopaedic problems, corticosteroid use, excessive walking, lower pressure pain threshold and pain tolerance, posture and functional balance	Demographics Fatigue Lung function Dyspnea Comorbidities Kinesiophobia	All participants: VAS FSS mMRC CCI TSK
Andenaes et al. 2018	Cross-sectional critical	$n = 1199$ (3.5%) / 18.811 (55.4%) 61.6 (13.3) years/51.6 (12.7) years ♀: 51.7% / 48.8% COPD severity: NS Smokers: 75.9% / 45.6%	P: 51.8% / 25.9% L: / I: no pain (19.5% / 42%) very light (9.7% / 13.2%), light (13.9% / 15.2%), moderate (39.3% / 24.2%), severe (15.8% / 4.8%), very severe (1.8% / 0.5%) D: ≥ 6 months F: ≥ 1x/day RF: ♀: higher age, occupation requiring higher education, daily smoking, no PA, comorbidities, anxiety and depression	Demographics Lifestyle Anxiety Depression Comorbidity	All participants: COPD: self-report of medical conditions Pain > 6 months: "yes" or "no" Severity (Last 4 weeks): no pain, very mild, mild, moderate, severe or very severe HUNT questionnaire HADS
De Miguel-Diez et al. 2018	Cross-sectional critical	$n = 2251$ / 2251 66.88 (14.64) years/57.38 (15.15) years ♀: 53.4% / 53.4% COPD severity: NS Smokers: 23.9% / 16.9%	P & L: Chronic neck pain (40.5% / 26.1%), chronic low back pain (44.8% / 28.4%), migraine (22.5% / 13.2%), 3 pain sites (11.86% / 4.89%) I: In the last 4 weeks: light (24.7% / 32%), moderate (37.7% / 39.3%), intense/extreme (37.6% / 28.6%) D: ≥ 12 months	Demographics Self-sufficiency Lifestyle Comorbidities	All participants: BPCO: interview - Diagnosis by a doctor? - Medication? Pain: interview - pain < 12 mois lumbar, cervical ou migraine? - Diagnosis confirmed by a doctor?

(Continues)

TABLE 3 (Continued)

Study/year	Study design	Participants COPD/control	Pain characteristics COPD/control	Other outcomes	Measuring tools used
Lee et al. 2018	Cross-sectional critical	n = 21/21 70 (1) years/68 (11) years ♀: 62% /62% COPD severity: • FEV1 = 36.4 (19.8) % /89.5 (13.9) % • FVC = 75.9 (29.7) % /104 (20.9) % Smokers: 24 (29) UPA/0 UPA	P: n=11//NS L: • Lower back (n = 5), //NS • Upper back (n = 1) //NS • Cervical region (n = 1) //NS • Chest and shoulders (n = 4) //NS I: 2,3 (1.9) /10//NS D: / F: / RF: no relationship between thoracic cyphosis or scapula orientation deviations and D+ intensity.	Postural parameters Lung function Comorbidities (COPD=control)	All participants: 41 adhesive reflective markers Motion Tracking Technology (9 Camera Vicon Mx Ultramet HD) Spirometry Cumulative illness rating scale Groupe COPD: BPI Spirometry (FEV1/FVC < 0.70)
Chen et al. 2017	Cross-sectional critical	n = 96 71.2 (9.6) years ♀: n = 39 (40.6%) COPD severity: • FEV1 (% predicted): 51.3 ± 20.8 Smokers: 4.2% (40.3 ± 25.8 UPA)	P: 71% L: 156 different locations. Lower back (41.2%), knees (25%), shoulders (23.5%) I: 4.0 (1.7) /10 D: ≥ 3 months F: ≥ 1x/day RF: a low GSE score, renting one's house rather than owning it, co-morbidities	Demographics Comorbidities Dyspnea Fatigue Perceived self-efficacy	All participants: BPI List of health conditions that might contribute to pain and medication record DI BFI CCQ GSE
Chen et al. 2017	Cross-sectional critical	N = 91 70.7 (9.5) years ♀: n = 39 (43%) BPCO severity: • FEV1: 51.1 (21.1) % Smokers: 41.5 (25.9) UPA	P: 74% L: / I: 4.0 (2.0)/10 D: / F: / RF: dyspnea, comorbidities	Demographics Lung function Dyspnea Fatigue	All participants: BPI DI BFI CCQ
Lee et al. 2017	Cross-sectional critical	n = 64/64 71 (10) years/67 (13) years ♀: 43% /43% COPD severity: • FEV1: 37.9 (14.9) % /91.3 (16.2) % • FVC: 61.6 (21.2) % /99.8 (15.3) %	P: 41% /29% L: 7 regions (neck, chest ++, lower back, upper back ++, buttocks, MI et MS) I: 3.8(2.4)/10/2.7 (1.7)/10 D: <3 months: Control ++ 3–12 months: COPD ++ >12 months: COPD ++ F: daily pain (definition chronic pain)	Depression Anxiety Physical Activity Catastrophication of pain Dyspnea Sensory perception Lung function Fatigue	All participants: BPI (long version) Duration and frequency of pain: • Total duration? • Chronic pain (>3months)? • Duration of episodes over the last 7 days? EABPS S-LANSS PCS

(Continues)

TABLE 3 (Continued)

Study/year	Study design	Participants COPD/control	Pain characteristics COPD/control	Other outcomes	Measuring tools used
Xiao et al. 2017	Cross-sectional critical	N = 282 61.5 (6.0) years ♀: n = 147 (51.9%) COPD severity: NS Smokers: n = 113 (83.1%)	P: 37% L: / I: 0.9 (1.5) / 10 D: / F: / RF: <65 years, ♀, exacerbation <12 months, COPD >10 years, CAT score >10, moderate COPD > mild	Demographics Lung function	Spirometry Groupe COPD: CRQ HADS MDP SAM All participants: MPQ short form CAT
Christensen et al. 2016	Cross-sectional critical	N total = 258 <i>COPD pain vs. COPD no pain:</i> N = 157 vs. n = 101 63.42 (9.44) years vs. 62.36 (8.51) years ♀: n = 96 (61.1%) vs. n = 41 (40.6%) COPD severity: • FEV ₁ : 40.93 (19.22) % vs. 34.69 (18.68) % • FEV ₁ /FVC: 0.41 (0.13) vs. 0.45 (0.12) Smokers: n = 41 (26.1%) vs. 21 (20.8%)	P: 61% L: average no. of locations: 5.50 (4.93), LBP = 47.4% I: 3.91 (2.35) / 10 D: F: RF: higher FEV ₁ %, comorbidities, depression, sleep disturbance, fatigue	Demographics Comorbidities Lung function Anxiety Depression Sleep Disruption Fatigue	All participants: SCQ-19 mMRC BPI-short form STAI-S CES-D GSDS LFS
Janssen et al. 2016	Cross-sectional critical	N = 67 64.9 (10.2%) years ♀: n = 27 (40.3%) COPD severity: • FEV ₁ : 50.0 (20.3) % Smokers: n = 8 (11.9%)	P: 82.1% L: Chest pain: n = 36 (53.7%) Neck, shoulders, lower back I: D: F: RF: young people, ♀, no correlation with hyperinflation	Demographics Dyspnea Lung function Anxiety Depression	All participants: mMRC 6MWT CAT HADS MPQ BPI
Roberts et al. 2015	Cohort	n = 7,952/15,904 69.3 (11.7) years/68.4 (11.6) years	P: 59.8% // 51.7% L: / I: /	Comorbidity Direct cost Insurance	All participants: COPD:

(Continues)

TABLE 3 (Continued)

Study/year	Study design	Participants COPD/control	Pain characteristics COPD//control	Other outcomes	Measuring tools used
Bentsen et al. 2014	Cross-sectional critical	<i>N</i> = 100 66.1 (18.3) years Q: <i>n</i> = 49 (49%) COPD severity: • FEV ₁ : 46 (15) % Smokers: NS	P: 45% L: / I: worst (0–10): 7.3 (1.6) D: / F: / RF: /	Demographics Anxiety and depression QOL Lung fonction Physical function	All participants: HADS NRS SGRQ QOLS ISWT All participants: Pain: diagnostic code ICD-9-CM or request for procedure-based pain treatment or request for ambulatory prescription of pain medication CMS morbidities Elixhauser morbidities
Roberts et al. 2013	Cross-sectional critical	<i>n</i> = 7 952/15 904 69.3 years/68.4 years Q: 58% /58% COPD severity: NS/NS Smokers: NS/NS	P: chronic pain: 59.8% /51.7% Neuropathic pain: 26.5% /20.9% Inflammatory pain: 70.1% /64.7% Mechanical/compressive pain (back): 35.9% /26.7% Mechanical/compressive pain (neck): 13.0% /9.9% Mechanical/compressive pain (other location): 49.1% /32.1% Muscular pain: 15.3% /12.8% Injury: 22.3% /19.2% L: back, neck, other I: / D: between 42 and 60 days (definition chronic pain) F: / RF: COPD, Osteoarthritis, rheumatoid arthritis, comorbidities	Comorbidities Medication Type of meeting at the selection event	All participants: Pain: diagnostic code ICD-9-CM or request for procedure-based pain treatment or request for ambulatory prescription of pain medication CMS morbidities Elixhauser morbidities
HajGhanbari et al. 2012	Cross-sectional critical	<i>n</i> = 47/47 70 (6.7) years/68.2 (8.8) years Q: <i>n</i> = 20 (42.55%) / <i>n</i> = 20 (42.55%) COPD severity: FEV ₁ : 44.7 (19.2) % Smokers: NS/NS	P: 7.5x and 2.2x more COPD with moderate to very severe pain than control (QPM and BPI respectively) L: average no. of locations: 3.1 (0.4) /1.3 (0.2) Neck + trunk = most common I: • MPQ: 10.0 (1.4) /3.8 (0.7) • BPI: 28.5 (3.5) /12.5 (3.5) D: /	Physical Activity Quality of life Comorbidity Medication Kinesiophobia	All participants: Spirometry SF-36 Medication formulary + comorbidities Chart review COPD MPQ BPI TSK CHAMPS

(Continues)

TABLE 3 (Continued)

Study/year	Study design	Participants COPD/control	Pain characteristics COPD//control	Other outcomes	Measuring tools used
Bentsen et al. 2011	Cross-sectional critical	N total = 100/993 <i>Pain group:</i> N = 45/n = 333 65.0 (9.2) years/57.8 (10.5) years Q: n = 24 (53%)/n = 193 COPD severity: • FEV ₁ : 48 (16) % Smokers: NS	P: 45% /34% L: average no. of locations: 5.6 (5.5) /7.4 (6.5) I: no difference between the two groups D: 18 (17.3) years/15.8 (13.6) years F: / RF: advanced age, comorbidities	Demographics Lung function	All participants: Demographic Questionnaire Vitalograph Alpha spirometer 9-item questionnaire for pain
Borge et al. 2011	Cross-sectional critical	N = 154 64.6 (10.2) years Q: 48.7% COPD severity: • FEV ₁ : 1.6 (0.7) % Smokers: n = 68 (44.2%)	P: 72.1% L: • Shoulders 33.1% • Lumbar spine 29.2% • Legs 26.6 % • Back 21.4% • Chest 17.5% • Neck 16.9% • Hips 16.2% • Head 12.3% I: 3.7 (1.9) /10 D: / F: / RF: BMI	Lung function Demographics	All participants Demographic questionnaire BPI RQLQ QOLS

Abbreviations: BFI, Brief Fatigue Inventory; BPI, brief pain inventory; CAT, COPD assessment test; CCI, Charlson Comorbidity Index; CCQ, Clinical COPD Questionnaire; CES-D, Center for Epidemiologic Studies Depression scale; CHAMPS, The Community Health Activities Model Program for Seniors; COPD: chronic obstructive pulmonary disease; CRQ, Chronic Respiratory Questionnaire; D, duration; DI, Dyspnea Inventory; EABPS, Extended Aberdeen Back Pain Scale; F, frequency; FEV₁, forced expiratory volume in one second; FSS, Fatigue Severity Scale; FVC, forced vital capacity; GSE, general self-efficacy scale; GSDS, General Sleep Disturbance Scale; HADS, Hospital Anxiety and Depression Scale; HUNT, Health Study in Nord-Trøndelag; I, intensity; ICD-9-CM, pain-related International Classification of Diseases, Ninth Revision, Clinical Modification; IPAQ, International Physical Activity Questionnaire; ISWT, Incremental shuttle walking test; L, location; LFS, Lee Fatigue Scale; MDP, Multidimensional Dyspnea Profile; mMRC, modified medical research council dyspnea scale; MPQ, McGill pain questionnaire short form; n, number of; no., number; nLBP, low back pain; NS, non-specified; NRS, numeric rating scales; P, prevalence; PA, physical activity; PCS, Pain Catastrophizing Scale; PEF, peak expiratory flow; QOL, quality of life; QOLS, Quality of Life Scale; RF, risk factors; RQLQ, Respiratory Quality of Life Questionnaire; S-LANSS, Self-reported Leeds Assessment of Neuropathic Symptoms and Signs pain scale; SAM, StepWatch Activity Monitor; SCQ-19, Self-Administered Comorbidity Questionnaire; SF-36, the Medical Outcomes Study Short Form-36; SGRQ, St. George's Respiratory Questionnaire; STAI-S, State-Trait Anxiety Inventory for Y; TSK, modified Tampa Scale of Kinesiophobia; TUG, Time Up and Go test; UPA, unity pack-years; VAS, Visual Analog Scale; 6MWT, 6 minute walk test.

overestimated.^{2,30} Moreover, divergent definitions of pain adopted in validated or non-validated questionnaires or simple interviews were used to establish the presence of pain in subjects. These differences in study methods influenced the prevalence of reported pain and make it difficult to draw conclusions from the six matched studies. Indeed, Lee et al.¹⁷ used the BPI questionnaire containing a body chart to assess the main locations of pain in COPD patients. Similarly, HajGhanbari et al.⁴ also used the BPI but they did not discuss the location of the pain. On the other hand, the other four studies assessed the prevalence of pain in predefined locations.^{2,3,15,27} In addition, cultural differences between countries may have also influenced the findings about prevalence or intensity of pain.³¹ Pain behaviour is influenced by social, cultural and psychological factors, and a similar pain can be then reported differently.³²

It is interesting to interpret the prevalence of reported pain in COPD in relation to the prevalence of pain found in the general population or in other chronic condition such as cancer. For example, O'Brien et al.³³ showed that chronic pain was present in 20% of European citizens. Concerning people suffering from cancer, the systematic review of Van den Beuken-van Everdingen et al.³⁴ indicated that the prevalence of pain was 50.7% in studies including all stages of cancer. Thus, the literature indicates that the prevalence of pain in patients with COPD is generally higher than in the general population or cancer patients.³⁵

Pain in the neck, chest and lower back was more common than in other parts of the body. This may be due in part to the location of the primary respiratory muscles (such as the diaphragm and intercostal muscles), as well as a series of accessory muscles located in the neck (sternocleidomastoid and scalene muscles), the posterior part of the shoulder (major and minor pectorals) and the back (spinal erectors and costarum levators). These muscles may be overused due to the modified breathing pattern in COPD^{21,36} or cough resulting in a feeling of muscle fatigue³⁷ and therefore lead to the development of pain symptoms.

In addition to the muscular aspect, chest pain could also be caused by pulmonary hyperventilation, loss of elasticity of the parietal pleura, pathological bronchial fibrosis, deformation of the thoracic or costotransverse vertebrae, intervertebral arthropathy or cardiovascular comorbidity.^{23,38} Lumbar pain may be related to rib cage remodelling, diaphragm fatigue and increased lung volume in patients with COPD.^{39,40}

Several comorbidities associated to COPD also lead to pain. It was shown that patients with COPD who experienced pain reported a higher number of co-morbidities compared to those without pain.⁵ This is consistent with

our findings that co-morbidities are a recurrent risk factor for the development of musculoskeletal pain in patients with COPD.

The women are more likely to experience pain and to report a higher intensity, frequency and number of pain sites compared to male both in the general population^{41–43} and in the COPD population.^{25,44} This may be caused by differences in sex-related biological (hormones or physiology), social or psychological factors or because women are more likely to have risk factors for musculoskeletal pain.⁴³ Another possible explanation for a higher degree of pain in women refers to the symptoms accompanying their illness. For a similar degree of lung damage, women experience more severe dyspnea and hyperinflation, poorer health status,^{45,46} higher levels of anxiety and depression, poorer symptom-related quality of life and it negatively influences the pain experience.^{45,47,48}

Physical activity can be a risk factor as it significantly decreases in COPD over time, regardless of the basic severity of the disease.⁴⁹ The inactivity is linked to systemic inflammation, caused by a lack of muscle use^{49,50} and predisposes to the development of chronic conditions such as musculoskeletal disorders.^{50,51} Castillo et al.¹⁶ showed that low levels of physical activity were associated with chronic neck pain in COPD subjects. In addition, lower level of physical activity in patients with COPD may be associated with higher risks of co-morbidities that can lead to pain such as osteoporosis or osteopenia.⁴⁹ More recently, Lee et al.¹⁷ showed that patients with COPD and pain had a lower level of physical activity than those who did not have pain. According to Vlaeyen et al.,⁵² the vicious circle of deconditioning begins with an attempt to avoid pain by reducing daily physical activity. While avoidance may lead to a decrease in pain in the short term, the reduction of activity may lead to greater deconditioning, which may then lead to an increase in their baseline pain.

Sensitivity to pain increases due to age-related brain plasticity and a number of anatomical, physiological, immune, neuroendocrine, inflammatory and autonomic mechanisms. Therefore, it seems evident to state that older COPD patients are at greater risk of experiencing pain than younger subjects.⁵³

Systemic corticosteroids used in the treatment of COPD as anti-inflammatory drugs, increased the risk of osteoporosis and their use has been associated with a higher incidence of fractures, which can lead to pain.⁵⁴ This is also true for inhaled corticosteroids, where the association is dose-dependent.⁵⁵ Similar results were shown in patients with asthma^{54,55} and cystic fibrosis.⁵⁶

It appears that patients with moderate COPD reported a higher prevalence of pain than patients with severe to very severe COPD. Groenewegen-Sipkema

et al.⁵⁷ found a strong inverse relationship between lung function and the prevalence of pain. One explanation could be that the patients with severe COPD had pain for a longer period of time and experienced a 'change of response' in their perception of the severity of the pain.²⁵ Also, a very severe patient may neglect pain due to the presence of other more important symptoms such as coughing, shortness of breath and wheezing.³⁶

Smoking has been considered for a long time to be the main cause of COPD,⁵⁸ and it is also a known risk factor for developing chronic pain.⁵⁹ Indeed, the prevalence and intensity of pain were greater in smokers than in non-smokers.⁶⁰ Given that the COPD population has a higher prevalence of smokers than the general population (75.9% vs. 45.6%), it is therefore possible to state that a greater number of patients with COPD develops pain compared to healthy subjects.¹

There are several pain treatments that can be used for patients with COPD. The most common option is the use of painkillers. These are widely used by patients with COPD, and even more by people without COPD.⁶¹ Bentsen et al.²¹ reported that 49% of COPD participants with pain were receiving analgesic therapy. Since cardiovascular co-morbidities are one of the most common co-morbidity in patients with COPD, these patients frequently have background antiplatelet therapy (Aspirin) that also has an analgesic effect.^{62,63}

Andenaes et al.¹ stated that physical activity and exercise can improve the severity of pain. However, people with pain may also lack the energy to exercise or may find that exercise may exacerbate their pain. Recio Iglesias et al.⁶¹ reported that patients undergoing pulmonary rehabilitation programmes have shown no improvement in pain. It can be surprising because pain decreased with regular exercise in the general population.⁶⁴

As pain has a significant impact on the daily lives of patients, adequate recognition of pain and its treatment should be incorporated into the management of patients with COPD and included in the COPD guidelines.

As such, further studies are needed to determine the optimal tools to assess pain. Dansie and Turk⁶⁵ have published a list of validated questionnaires most commonly used in the evaluation of chronic pain but they are not validated in patients with COPD, except the Brief Pain Inventory.⁶⁶ This questionnaire provides information on the location and intensity of pain and how it interferes with aspects of daily life.

Only 6 of the 20 studies selected in this review include matched COPD patients with a control population. Comparing the prevalence of pain in the healthy population allows for a better assessment of the relevance of the presence of pain in the COPD population. Future studies should include this in their methodology

to better understand the differences in pain with the COPD population.

It would also be important to inspect all components of pain, such as type of pain, duration, frequency and intensity, too often neglected in the literature, in order to better understand the epidemiology of pain in patients with COPD. It would also be relevant to assess the optimal treatment of pain. We know that chronic pain is complex and multimodal. It can come from many different sources and be influenced by many biological, psychological and social factors.⁶⁷

The impact of acetylsalicylic acid use in patients with COPD with cardiovascular co-morbidities should be explored. When used as an antiplatelet agent, its analgesic action could modify the pain prevalence and intensity.

5 | CONCLUSION

Pain is a very common symptom in COPD. Despite this, few clinical trials have investigated the pain. The factors associated with pain are poorly understood. Pain appears to be more prevalent in patients with moderate COPD, located primarily in the lumbar, cervical and thoracic regions and facilitated by being a female, a low level of physical activity, co-morbidity(ies) and old age. Future studies will need to agree on a common methodology and reliable measurement tools in order to provide comparable results.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

Latiers Fabien has contributed substantially to the conception, the design of the work and the acquisition, the analysis and interpretation of data for the work; to drafting the work and revising it critically for important intellectual content and to the final approval of the version to be published. He agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Vandenabeele Marie has contributed substantially to the conception, the design of the work and the

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Reychler Gregory has contributed substantially to the conception, the design of the work and the acquisition, the analysis and interpretation of data for the work; to drafting the work and revising it critically for important intellectual content; and to the final approval of the version to be published. He agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Poncin William has contributed substantially to the conception; to drafting the work and revising it critically for important intellectual content; and to the final approval of the version to be published. He agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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