

The presence of respiratory disorders in individuals with low back pain: a systematic review

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TITLE PAGE

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The presence of respiratory disorders in individuals with low back pain: a systematic review

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The study conformed to the principles of the Declaration of Helsinki (1964) and was approved by the Ethics Committee of the University Hospitals Leuven

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ABSTRACT

Background: Inspiratory muscles, such as the diaphragm, play a key role in both respiration and spinal control. Therefore, diaphragm dysfunctions are often related to low back pain (LBP). However, few is known on the association between the presence of LBP and the presence of respiratory disorders (RD).

Objectives: To perform a systematic review on the relation between RD and LBP.

Study Design: Systematic review

Methods: Two reviewers searched on PubMed/MEDLINE for studies concerning LBP and RD, from 1950 up to January 2016. The search string consisted of the following key words: *low back pain, dyspnea, respiratory problems, lung diseases, comorbidity, pulmonary disease, chronic obstructive, smoking, asthma, allergy, sinusitis, respiratory tract infection and hyperventilation*. The aim was to evaluate a potential correlation, co-occurrence or causality between RD and LBP.

Results: A total of 16 articles were included. A significant correlation between the presence of LBP and the presence of RD such as dyspnea, asthma, different forms of allergy, and respiratory

infections was found. No correlation was found between COPD and LBP, and no articles were found on the correlation between hyperventilation and LBP.

Conclusions: This is the first study providing an overview of the literature on the relation between LBP and RD. Immunological, biomechanical, psychosocial and socio-economic factors might explain this correlation. Smoking is likely to contribute. Future studies must reveal the causative relationship.

Key Words: Back pain, comorbidities, smoking, asthma, respiratory disorder

Level of Evidence: Therapy, level 2a

HIGHLIGHTS

The presence of LBP is associated with the presence of respiratory disorders (RD).

These RD include dyspnea, asthma, allergy, and respiratory infections.

The causal link between LBP and RD must be examined by future prospective studies.

The high comorbidity of other disorders in LBP patients must be taken into account.

INTRODUCTION

Low back pain (LBP) is worldwide one of the most important medical conditions in terms of reduced quality of life, disability and socio-economic costs. LBP has a life-time prevalence of 84%. About 10% of all patients with an acute episode of LBP develop chronic LBP (i.e. lasting longer than 3 months). LBP affects men and women equally. The prevalence peaks between 35 and 55 years old and has a complex etiopathogenesis with multiple intrinsic and extrinsic risk factors (Balagué et al., 2012).

Decreased postural control appears to be associated with the presence of LBP (Ruhe et al. 2011).

Although the causal link is not fully clear yet, it is known that dominant use of ankle proprioception during postural control relates to the development and recurrence of LBP (Claeys et al. 2015). The inspiratory muscles (IM), and specifically the diaphragm, have a key role in controlling the spine, which is crucial during postural control (Hodges and Gandevia, 2000). However, during loading of the IM, the use of back proprioceptive signals, necessary for balance control, is reduced in individuals with LBP (Janssens et al., 2010) and in patients with Chronic Obstructive Pulmonary Disease (COPD) (Janssens et al., 2013b). Furthermore, individuals with LBP showed greater susceptibility to diaphragm fatigue compared to healthy controls (Janssens et al., 2013a). Recently, this research group found that targeted training of

the IM in individuals with LBP improved postural control and significantly lowered the severity of LBP (Janssens et al., 2015).

Respiratory muscle weakness and diaphragm fatigue are also found in some patients with COPD during high-intensity exercise (Decramer et al., 1980; Polkey et al., 1996; Bachasson et al., 2013). Patients with more hyperinflation during exercise showed greater diaphragm fatigue.

The latter can be explained by diaphragm flattening and thus an impaired pressure-generating capacity, resulting in a limited contribution of the diaphragm to IM work (McKenzie et al., 1985). Likewise, exacerbations of asthma, airway closure and expiratory airflow limitation can result in hyperinflation. This in turn, compromises the stabilizing function of the diaphragm (Hill, 1991).

Important questions that arise are whether and, if so, to what extent, patients with LBP are susceptible to having a respiratory disorder (RD) and vice versa. To the best of our knowledge, this is the first systematic review providing an overview of the literature on the relation between the presence of RD and the presence of LBP. If there is indeed a correlation, further research must reveal if IM training can be a valuable tool in the rehabilitation of specific subpopulations of individuals with LBP.

MATERIAL AND METHODS

Literature Search Strategy

A computerized search in the PubMed/MEDLINE database was conducted independently by two reviewers (A.V. and N.B.) from 1950 up to January 2016. The search string consisted of combinations of the following key words and Medical Subject Headings (MeSH): *low back pain [Mesh], dyspnea [Mesh], respiratory problems, lung diseases [Mesh], comorbidity [Mesh], pulmonary disease, chronic obstructive [Mesh], smoking [Mesh], asthma [Mesh], allergy, sinusitis [Mesh], respiratory tract infection [Mesh] and hyperventilation [Mesh]*. After the computerized search, reference lists of all selected articles were manually checked for additional relevant articles. After de-duplication, the two reviewers independently screened each article to select the potentially relevant studies from titles, abstracts, and keywords. If any of the inclusion criteria were not met, the article was excluded from further consideration. Remaining articles were then screened based on full-text.

Eligibility Criteria for considering studies for this review

Eligibility assessment of the obtained articles was performed independently by the two reviewers (A.V. and N.B) by screening the articles based on predefined in- and exclusion criteria.

a. Eligibility criteria for types of study

The following criteria were used to exclude articles from further consideration: published prior to 1950, not written in Dutch or English, did not include human data, contained no original data, abstract or conference proceeding, no full text available, or article not meeting the topic.

a. Eligibility criteria for types of participants

Study participants had to be female and male adults of at least 18 years old, who reported or had been diagnosed with any type of LBP and any type of RD.

b. Eligibility criteria for outcomes

To be included, articles had to investigate a relation, co-occurrence or causality between LBP and RD.

Risk of bias in included studies

Risk of bias of all included studies was assessed independently by two reviewers (A.V. and N.B.) by using the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement for cohort case-control and cross-sectional studies (von Elm et al., 2008). We used the principles from the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) working group to summarize the body of evidence overall. It was judged that the data were not suitable for statistical pooling due to the heterogeneity of the study designs. Therefore, the results were summarized qualitatively. Disagreements were resolved through consensus with other authors.

Data collection and analysis

After the initial assessment for eligibility, the two reviewers independently extracted the following data from the included studies: study design, sample size, sex, age, type of LBP, type of RD, and main study result.

RESULTS

A flowchart of the literature search is shown in **FIGURE 1**. A total of 16 articles were included.

The results of the quality assessment of each study are shown in **TABLE 1**. Study results are presented in **TABLE 2**. One article described the relation between LBP and dyspnea, six articles investigated the relation of LBP with non-specified RD, five articles with asthma and allergies, three with COPD, and one with respiratory infections.

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Dyspnea

Only one study was found that reported the co-occurrence of dyspnea and LBP. Clark et al., 2014 noted that participants with dyspnea had a considerably higher prevalence of pain (pain interference, chest pain, back pain (BP) (not specified) and arthritis pain) than those without dyspnea (64% vs. 18%). After adjusting for other factors that might cause dyspnea (e.g., emphysema, asthma, COPD, obesity, smoking), or that might influence symptom reporting

(i.e., depression and ADL impairment), the relative risk (RR) for dyspnea was 1.76 (95% confidence interval (CI) 1.71–1.82) for having BP. After adjusting for socio-demographic and health-related variables, the RR for the simultaneous development of dyspnea with BP, compared with developing dyspnea without BP, was 3.26 (95% CI 3.07–3.46).

Non-specified respiratory disorders

Five articles found a positive correlation between LBP and non-specified RD (Heliovaara et al., 1991; Wright et al., 1995; Smith et al., 2006; Smith et al., 2009; Smith et al., 2014). Three articles searched for this correlation among women in three age categories: young, middle-aged and aged (Hurwitz and Morgenstern, 1999; Hestbaek et al., 2004; Hestbaek et al., 2006). They observed a higher risk of developing LBP in women who had an existing or recently developed RD (Odds Ratios (OR) respectively 1.43 and 1.38 in young, 1.13 and 1.63 in middle-aged and 1.09 and 2.11 in aged women). On the other hand, they noted that women with existing or recently developed LBP had a greater probability of developing RD (Hurwitz and Morgenstern, 1999; Hestbaek et al., 2006). Schneider et al., 2007 reported an OR for having unspecified LBP with at least one diagnosis of RD of 1.3 (95% CI 1.0–1.6) (Schneider et al., 2007).

Schäfer et al., 2014 found that chronic LBP had the highest number of associations with a range of medical conditions and was the most important mediator between them. A triad of “chronic LBP + asthma/COPD + allergies” with an observed/expected ratio of 2.4 and a prevalence of 1.4 % was noted in the female subgroup. The prevalence of chronic LBP increased more than expected by chance with the number of comorbidities one person had (Prevalence Observed 79.13; Prevalence Expected 71.55, delta +7.58).

Asthma

Five articles investigated the link between asthma and LBP. In all articles, a positive relationship was found between asthma and LBP in young individuals aged 12 to 22 years and 20 to 39 years (Hurwitz and Morgenstern, 1999; Hestbaek et al., 2004; Hestbaek et al., 2006; Smith et al., 2006; Schneider et al., 2007). The probability of having a history of asthma is greater when LBP is reported in the past year ($p < 0.05$). Vice versa, the probability of reporting LBP in the past year is greater in a patient with a history of asthma ($p < 0.05$). The OR of reporting LBP in the past week was 30% higher in patients with asthma compared to patients without a history of asthma ($p < 0.05$) (Schneider et al., 2007).

Allergy

The articles that investigated the link between asthma and LBP also described the correlation between LBP and allergy (Hurwitz and Morgenstern, 1999; Hestbaek et al., 2004; Hestbaek et al., 2006; Smith et al., 2006; Schneider et al., 2007). In two articles, no significant correlation between allergy and LBP was found (Hestbaek et al., 2004; Hestbaek et al., 2006). Schneider et al., 2007 examined the most common comorbidities in patients with LBP, more specifically hay fever and allergic contact dermatitis. Both were significantly more common in patients with LBP than in patients without LBP, with ORs of 1.21 (95% CI 1.06 - 1.38) and 1.47 (95% CI 1.29-1.67), respectively ($p < 0.05$). In addition, allergic urticaria and food allergies were significantly more common in patients with LBP compared to subjects without LBP ($p < 0.05$). Atopic eczema was not associated with a significantly higher risk of LBP ($p > 0.05$).

Moreover, the risk of developing LBP is 50% higher if some form of allergy exists in the past or present (Hurwitz and Morgenstern, 1999). One study found a significant link between LBP and allergy in women of three age cohorts, i.e. 18-23 years, 45-50 years and 70-75 years (Smith et al., 2009).

COPD

The relationship between LBP and COPD has been observed in three studies (Synnot and Williams, 2002; Laban and Kucway, 2003; McIntosh et al., 2006). The prevalence of reporting LBP ever and in the past year was respectively 69% and 58% in subjects with chronic airflow limitation. These patients had a diagnosis of chronic bronchitis, emphysema or asthma, chronic airflow limitation, COPD or chronic obstructive airways disease. The prevalence of reporting LBP ever and in the past year in the general population was respectively 11-84% and 3.9-65% (Balagué et al., 2012). Patients with acute LBP and comorbidities, such as COPD, did not have a significantly longer treatment duration, higher pain score measured by the Visual Analogue Scale (VAS) or worse functional outcome than patients with LBP without comorbidities (McIntosh et al., 2006).

Respiratory infections

Bartholomeeusen et al., 2011 found a significant positive correlation between the incidence of upper respiratory infections in general and the incidence of LBP in a female subgroup aged 25-44 years (OR= 1.31, 95 % CI 1.11 - 1.55, $p < 0.05$), 45-64 years (OR= 1.51, 95% CI 1.30 - 1.76, $p < 0.05$), and 65-74 years (OR= 1.33, 95% CI 1.00 - 1.76, $p < 0.05$), and a male subgroup aged 45-64 years (OR= 1.52, 95% CI 1.3 - 1.78, $p < 0.05$). Also, a correlation between the incidence of specific respiratory infections (i.e. laryngitis) and the incidence of LBP, compared with

patients without LBP, was found in the female subgroup aged 25-44 years (OR= 2.31, 95% CI 1.61 to 3.31, $p < 0.05$).

DISCUSSION

A significant correlation between the presence of LBP and the presence of RD such as dyspnea, asthma, different forms of allergy, and respiratory infections was found. No correlation was found between the presence COPD and the presence of LBP. This is the first study providing an overview of the literature on this particular relation. Different underlying mechanisms might explain this correlation. Immunological, biomechanical, psychosocial and socio-economic factors are purported to contribute to LBP (Balagué et al., 2012). Because these factors may contribute to, or be affected by a RD, the presence of RD may correlate with, and even predispose LBP.

Asthma, allergy, chronic bronchitis, COPD and other respiratory conditions involve inflammation and immune reactivity. Asthma and COPD are the two most common chronic inflammatory diseases of the lower airways (Caramori et al., 2015). Hay fever, food allergies and allergic dermatitis may reflect a more broadly reactive immune system. Consequently, it is conceivable that an infectious event (or some other physiological stressor) could induce a perturbation in the immune system towards a more pro-inflammatory state. It is known that pro-inflammatory cytokines play an important role in central and peripheral modulation of nociception. For example, tumor necrosis factor- α (TNF- α) not only plays a role in the

pathophysiology of discogenic LBP and sciatica but also in chronic LBP (Wang et al. 2008).

Therefore, it can be hypothesized that the relationship between RD and LBP can be explained by immunological factors.

Second, the results might be explained through the association between an altered breathing pattern and RD (Hodges and Gandevia, 2000; Synnot and Williams, 2002; Smith et al., 2014).

For example, asthma is associated with functional breathing disorders. One third of women and one fifth of men treated for asthma in a single general practice had symptoms suggestive of dysfunctional breathing (Thomas et al., 2001). Dysfunctional breathing includes the hyperventilation syndrome (with symptoms of breathlessness, chest tightness, chest pain, and non-respiratory symptoms such as anxiety, light headedness and fatigue), unsteady and irregular breathing, frequent sighing and predominantly upper chest rather than diaphragmatic respiratory effort (Folgering, 1999). Roussel et al., 2009 found an altered breathing pattern in patients with chronic LBP during lumbopelvic control tests, and this was not related to pain severity. Thus, when challenging the trunk stabilizing muscles, patients with chronic LBP display an altered breathing pattern. A possible explanation is that some patients with chronic LBP favor the postural function of the diaphragm and thereby disadvantage the respiration,

resulting in an altered breathing pattern with less contribution of the diaphragm (Roussel et al., 2009).

Furthermore, the diaphragm appears to function suboptimally in individuals with LBP. They show a higher diaphragm position and smaller diaphragm excursion during inspiration (Kolar et al., 2012), and more diaphragm fatigability compared to painfree individuals (Janssens et al., 2013a). Therefore, it can be suggested that, when the respiratory muscles are loaded, the diaphragm is less able to contribute to postural control (Hodges et al., 2001). Moreover, individuals with COPD who have IM weakness show a decreased postural stability compared to healthy controls (Janssens et al., 2013b). This impaired postural control may be an important factor in the onset and maintenance of LBP (Claeys et al., 2015). However, a significant correlation between the presence of COPD and LBP was not found. Likewise, exacerbations of asthma result in hyperinflation. Hyperinflation compromises the function of the IM by reducing their force-generating capacity and by impairing their mechanical advantage on the chest wall (Hill, 1991). A recent study regarding IM training in patients with LBP found that, after IM training, inspiratory muscle strength and postural control were significantly improved. During postural control while standing on an unstable support surface, an increased inspiratory muscle strength after IM training was significantly associated with improved postural control (Janssens

et al., 2015). This favors the hypothesis that an impaired stabilizing function of the diaphragm can explain the relationship between RD and LBP. Moreover, this study found a clinically important decrease in LBP severity after IM training (Janssens et al., 2015). Although, this must be interpreted with caution because of the small sample size. Further research is necessary to establish that IM training is effective and if so, to investigate which individuals with LBP in particular may benefit from IM training (e.g., by mediation analyses).

Also, psychosocial components can be underlying the relationship between LBP and RD. Having a RD can result in enhanced anxiety, stress and hypervigilance towards bodily sensations. (Panagioti M et al., 2014). Also, the perception of unpleasantness (i.e., adverse dimension) of both dyspnea and pain are related (von Leupoldt et al., 2009a). This suggestion is based on evidence supporting that the perception of dyspnea and pain share the same emotion-related (para)limbic brain areas such as the insula, anterior cingulate cortex and amygdala. For example, in asthmatic patients lower cortical responses of the insula have been found for both dyspnea and pain stimuli (von Leupoldt et al. 2009b).

An important mediator of the presence of RD is smoking. In this way, smoking history can be another important mechanism explaining the particular relationship with LBP. A meta-analysis showed that both smokers and ex-smokers have a higher incidence and prevalence of LBP in

the past month and in the past year and a higher prevalence of chronic LBP compared to non-smokers. In addition, current smokers have had a higher prevalence of chronic LBP and LBP in the past year than ex-smokers (Shiri et.al, 2010). Smoking does not only influence the onset and maintenance of LBP complaints, it also decelerates recovery of LBP when compared to non-smokers (Behrend et al., 2012). In addition, smoking has a negative effect on the outcome of spinal surgery, as smokers had a higher complication rate and longer hospitalization duration (Stienen et al., 2011). Vice versa, smoking cessation during LBP treatment improved the mean VAS pain rating with more than 15%. The percentage of patients reporting a >30% decrease in LBP was 31% in patients who had never smoked, 29% in ex-smokers and 17% in current smokers (Behrend et al., 2012). This improvement of >30% can be considered as clinically significant (Ostelo et al., 2008).

A significantly higher prevalence of smoking was observed in a group of patients with chronic musculoskeletal pain compared to the general population (Orhurhu et al., 2015), although, no difference was observed between fibromyalgia, LBP and headache. The high prevalence of smoking among patients with chronic pain could be partly related to unique factors that exist in this patient population including opioid use and the clustering of addictive behaviors, such as daily smoking (Højsted et al., 2013; Hooten et al., 2009a; Hooten et al., 2009b).

Smoking may induce LBP in different ways (Shiri et al., 2010). It is an important risk factor for osteoporosis. This may lead to LBP due to osteoporotic spinal fracture (Law and Hackshaw, 1997). Furthermore, smoking may reduce the perfusion of the intervertebral discs. This may lead to degenerative lesions in the intervertebral discs (Kauppila et al., 1997; Uematsu et al., 2001). Additionally, smoking may lead to amplification of pain by increasing the level of circulating pro-inflammatory cytokines (O'Loughlin et al., 2008). Moreover, smoking is associated with lower physical fitness, which in turn can lead to higher LBP scores (Heneweer et al., 2012; Mesquita et al., 2015). Finally, smoking enhances expiratory muscle strength, slightly increases IM strength and reduces IM endurance (Chen, 1988), and activates the sympathetic nervous system (Rodrigues et al., 2013). These autonomic changes may influence the breathing pattern, diaphragm function and may also explain the higher incidence of LBP in smokers.

Finally, there might be other contributing factors. It is known that socio-economic disadvantage is associated with general poor health. The association with LBP is less clear. However, patients from a lower socio-economic class are more likely to smoke and could therefore have a greater risk of LBP (Lallukka et al., 2014). Furthermore, gene expressions of an individual's psychological disposition associated with common co-morbidities, such as asthma, may be

involved in the process of pain perception, pain signaling and the psychological process involved in pain, particularly in chronic LBP(Ferreira et al., 2013).

Dyspnea

Individuals who report shortness of breath are more likely to have various types of pain, including LBP. Dyspnea and pain share many features, e.g. similar experienced unpleasantness and intensity (von Leupoldt and Dahme, 2007). The most plausible explanation for the co-occurrence of dyspnea and pain is physical deconditioning (Schäfer et al., 2014). Higher levels of physical fitness, both muscular and aerobic, were strongly associated with having less LBP complaints (OR 0.54, 95% CI 0.34–0.86 and OR 0.59, 95% CI 0.35–0.99 respectively). On the other hand, too much physical activity might as well be hazardous for spinal health (OR 1.60, 95% CI 1.05–2.44). Physical activity at a high enough intensity to improve physical fitness but not too high, may be important in the prevention of LBP (Heneweer et al., 2012). Recognizing and exploring the co-occurrence of dyspnea and pain could help health care providers to better understand patients' experiences, to select appropriate treatments, and possibly to treat both dyspnea and pain simultaneously.

Allergy and asthma

Three articles reported a significant correlation between allergy and LBP (Hurwitz and Morgenstern, 1999; Smith et al, 2006; Schneider et al., 2007), although two studies did not find such a relation (Hestbaek et al., 2004; Hestbaek et al., 2006). In the latter studies, allergy and asthma were completely distinguished from one another, with allergy being defined as ‘atopic dermatitis/hay fever with no evidence of asthma or asthma-like symptoms’ (Hestbaek et al., 2004; Hestbaek et al., 2006). In the three former articles, asthma was not distinguished from allergy. For asthma, more consistent results were found (Hurwitz and Morgenstern, 1999; Hestbaek et al., 2004; Hestbaek et al., 2006; Smith et al., 2006). The chance of reporting LBP is greater for patients suffering from asthma or asthma-like symptoms when compared to patients without asthma. Vice versa, the occurrence of asthma is greater in patients who reported LBP ever or in the past year. Thus, when treating LBP in patients with asthma or asthma-like symptoms, an adequate management of asthma may also be important, together with an optimal LBP treatment. Also, it is known that allergy sufferers release greater amounts of proinflammatory cytokines, including IL-1, IL-8 and TNF- α . These cytokines also play a significant role in chronic LBP (Hurwitz and Morgenstern, 1999; Wang, 2008). Furthermore, dysfunctional breathing may be an important focus in the rehabilitation in patients with asthma

(Thomas et al., 2001), in particular in patients with exercise-induced asthma, where a stress condition (e.g. exercise) may lead to dysfunctional breathing (Barker and Everard, 2015).

COPD

The prevalence of having an episode of LBP (69%) or reporting LBP (58%) in the past year in subjects with chronic airflow limitation is comparable to the prevalence of LBP in the general population (respectively 11-84% and 3.9-65%) (Synnot and Williams, 2002). For acute LBP, a statistically significant although not clinically significant difference in VAS pain (0.5 points) and in total number of treatment days (2 days difference) was found in individuals with COPD compared to individuals without COPD (McIntosh et al., 2006). Thus, patients with COPD will likely recover from LBP at the same rate as individuals without COPD. A possible explanation for these results may be that patients with COPD have difficulty to differentiate pain caused by LBP from pain caused by COPD, and thus report less LBP (Synnot and Williams, 2002). On the other hand, patients with COPD do have an impaired balance control (Janssens et al., 2013b). The latter may play a key role in the onset and maintenance of LBP (Claeys et al., 2015). Therefore, future studies should investigate (low back) pain symptoms in patients with COPD in more detail, to distinguish different pain sources.

Hyperventilation

No articles on the link between hyperventilation and LBP were found. It is known that hyperventilation can be a reaction to pain. Thus, one may theoretically expect a higher prevalence of hyperventilation in patients with LBP (Glynn et al., 1981). Moreover, psychosocial factors, negative pain beliefs and job dissatisfaction are associated with the development of chronic LBP (Nicholas et al., 2011). Subjects with panic disorder show a condition of baseline hyperventilation (Glynn et al., 1981). During such dysfunctional breathing in pain, stress and emotional states, the diaphragm becomes more flattened, hypertonic and relatively immobile (Courtney, 2009). As mentioned before, an altered functioning of the diaphragm can be an important factor in postural control impairments and the maintenance of LBP (Janssens et al., 2013b). However, these potential mechanisms must be investigated in future studies examining the correlation between LBP and hyperventilation.

Clinical implications

In patients with LBP, health care providers need to take into account the potential history of RD including asthma, different kinds of allergy, frequent respiratory infections and smoking status. Further research is necessary to determine whether the relationship between LBP and

RD is causative. If so, future studies must reveal whether IM training or treatment of relevant RD would be beneficial for individuals with LBP who also report RD. Finally, an altered breathing pattern is associated with RD, and this latter can be related to LBP. As a consequence, we can hypothesize that a correction of an altered breathing pattern could be a target of treatment.

Limitations

There are limitations to this study. First, the results were summarized qualitatively due to the heterogeneity of the study designs. Different study designs, outcome variables, measures and data analyses were found. Examples are the broad differences in sample size, age, and type of LBP. Bias in setting and participants (as presented in Table 1) needs consideration when indirectly comparing results across studies. Second, it must be kept in mind that apart from RD, other diseases are more frequently seen in individuals with LBP compared to individuals without LBP. Chronic LBP was found to be strongly associated with other chronic conditions that may cluster in a frail subgroup of the population (Hestbaek et al., 2003). Also, the prevalence of chronic LBP increases more than expected by chance with the number of comorbidities one person has (Schäfer, 2012). For this reason, chronic LBP might be the result of and not the cause of having other diseases. Third, none of the included designs could confirm

a causative relationship between the presence of LBP and RD. Therefore, we recommend future studies to observe the onset, development and maintenance of LBP on the one hand and RD on the other hand in a prospective study design with a long-term follow-up. Risk factors can be calculated using logistic regression analysis. Mediation analyses can for example elucidate the underlying mechanisms of IM training.

CONCLUSION

A significant correlation between the presence of LBP and the presence of RD such as dyspnea, asthma, different forms of allergy, and respiratory infections was found. This review of the literature showed that individuals with a particular RD report higher rates of LBP and vice versa. However, mechanisms to explain this association are inconclusive at this point. No correlation was found between the presence COPD and the presence of LBP, and no articles were found on the correlation between hyperventilation and LBP. Based on this systematic review, further research is necessary to investigate which individuals with LBP in particular may benefit from IM training and whether history taking of RD will help practitioners to select these patients.

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FIGURE 1. PRISMA flow chart of study-selection process

Table 1. Risk of bias (STROBE) and level of evidence (GRADE) assessment.

	Astrand, 1987	Bartholomeusen et al., 2011	Clark et al, 2014	Heliovaara et al., 1991	Hestbaek et al., 2004	Hestbaek et al., 2006	Hurwitz and Morgenstern, 1999	Laban and Kucway, 2003	McIntosh et al., 2006	Schäfer, 2014	Schneider et al., 2007	Synnott and Williams, 2002	Smith et al., 2006	Smith et al., 2009	Smith et al., 2014	Wright et al., 1995
1a	+	-	-	-	+	+	+	+	+	-	-	+	+	+	+	-
1b	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
3	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
4	+	-	+	-	-	-	-	+	+	-	-	+	-	-	-	-
5	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
6a	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
6b	n/a	+	n/a	n/a	n/a	n/a	n/a	+	+	n/a	n/a	n/a	n/a	+	+	n/a
7	+	+	+	+	-	-	-	-	+	-	+	+	+	-	-	+
8	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
9	+	-	+	-	-	+	-	-	-	-	+	-	-	-	-	+
10	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
11	+	-	+	+	-	-	-	-	-	-	-	-	-	-	-	+
12a	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+
12b	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
12c	+	-	+	-	-	-	-	-	-	-	-	-	+	-	+	-
12d	+	-	-	+	-	-	-	n/a	+	+	+	+	+	-	+	-
12e	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
13a	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
13b	-	-	+	-	-	-	-	-	-	n/a	+	-	+	-	+	-
13c	-	-	-	-	-	-	-	-	-	n/a	+	-	-	-	-	-
14a	+	-	+	+	-	-	+	-	+	-	+	-	-	-	-	-

14b	+	-	-	-	-	-	-	-	+	-	-	-	+	+	+	-
14c	n/a	+	n/a	n/a	n/a	+	n/a	n/a	+	n/a	n/a	n/a	n/a	+	+	n/a
15	+	+	+	+	+	-	+	+	+	+	+	+	+	-	-	+
16a	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+
16b	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-
16c	n/a	n/a	n/a	n/a	n/a	n/a	na	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
17	+	+	+	+	+	+	+	-	+	+	+	+	-	-	-	+
18	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
19	+	+	+	+	+	-	+	-	+	+	+	-	+	+	+	+
20	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
21	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
22	+	+	+	-	+	+	-	-	-	+	+	-	+	+	+	-
Total (STROBE)	87%	64%	81%	68%	58%	59%	61%	45%	76%	66%	77%	65%	74%	61%	70%	65%
GRADE score	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B

STROBE checklist: STrengthening the Reporting of OBservational studies in Epidemiology. The checklist consists of 22 items. The total score (%) is based on the amount of + scored on each individual (sub)item of the STROBE checklist.

GRADE: Grading of Recommendations Assessment, Development, and Evaluation. Scores range from A (highest level of evidence) to D (lowest level of evidence).

n/a: not applicable

Table 2. Results on the association between the presence of low back pain and the presence of respiratory disorders.

Study	Design	Sample size	Sex	Age	Type of low back pain (LBP)	Type of respiratory disorder (RD)	Main study result	Funding sources
Astrand (1987)	Cross-sectional	391	M	35-65	Self-reported LBP	Breathlessness in smokers, asthmatics and on exertion	- OR for breathlessness in case of LBP is 2.5 - No association between LBP and frequent cough or asthma	Not available
Bartholomee usen et al. (2012)	Cohort	160000	M+F	25-44 45-64 65-74	LBP with and without radiculopathy	- Acute upper respiratory infection - Flu -Acute bronchitis/ bronchiolitis -Acute Laryngitis/ tracheitis	- Correlation between the incidence of upper respiratory infections in general and LBP in all female age groups and a male subgroup aged 45-64. - Correlation between the incidence of specific respiratory infections (i.e laryngitis) and LBP in female aged 25-44.	Non-industry
Clark et al. (2014)	Longitudinal	266000	M+F	<75>	Back pain (non-specified) - Most of the time in past 4 weeks - All the time in past 4 weeks	Dyspnea	- Prevalence of back pain with dyspnea is 64% - Prevalence of back pain without dyspnea is 18%	Non-industry

Heliovaara et al. (1991)	Cross-sectional	5673	M+F	30-64	- Chronic LBP - Sciatica - Non-specified LBP	- Non- specified RD - Smoking	Smokers have an increased risk of having LBP	Not available
Hestbaek et al. (2004)	Cross-sectional	9567	M+F	12-22	- Ever - 1-30 days last year - >30 days last year	- Atopic dermatitis/ Hay fever - Asthma	- Positive associations between LBP and asthma - No association between LBP and atopic dermatitis/hay fever	Non-industry
Hestbaek et al. (2006)	Cross-sectional	10000	M+F	20-30	Persistent LBP	- Asthma - Allergy	- LBP and asthma in adolescence are positively associated with future LBP - No association between atopic disease and future LBP - Large degree of clustering of these disorders, except for atopic disease	Non-industry
Hurwitz et al. (1999)	Cross-sectional	6836	M+F	20-39	In last year	- Asthma - Hay fever - Insect reaction - Food allergy - Animal allergy - Other forms of allergy	Subjects with a history of any allergy are more likely to report LBP (OR 1.51)	Not available

Laban et al. (2003)	Case-control	69	M+F	67-83	Spinal canal stenosis with night time sacro-lumbalgia	Endstage COPD with pulmonary hypertension	Pulmonary hypertension in those with COPD and nocturnal lumbosacral radiculopathy	Not available
McIntosh et al. (2006)	Cohort	7077	M+F	18-65	(Sub)acute LBP with or without comorbidity	COPD (and/or other conditions)	No differences LBP intensity and duration between LBP group with comorbidities and LBP group without comorbidities	Not available
Schäfer et al. (2014)	Cross-sectional	98619	M+F	>64	Chronic LBP	Astma/COPD + Allergy	- Chronic LBP + asthma/COPD + allergies triad Observed/Expected ratio: 2.4 - Prevalence of chronic LBP increases more than expected by chance with the number of comorbidities	Non-industry + industry (health insurance company BARMER/GEK)
Schneider et al. (2007)	Cross-sectional	7124	M+F	18-79	In last 7 days	-Allergic contact dermatitis ¹ -Atopic eczema ² - Food allergy - Hay fever (allergic rhinitis / conjunctivitis) - Allergic urticaria ³ - Chronic bronchitis ⁴ - Asthma (Bronchial asthma, Asthma	All the investigated morbidities are more common in subjects with LBP, except for atopic eczema	Non-industry

						pulmonale, Allergic asthma) ⁵		
Smith et al. (2006)	Cross-sectional	38050	F	18-23 45-50 70-75	In last year	<ul style="list-style-type: none"> - Breathing difficulties / RD - Asthma - Allergy (incl. hay fever and sinusitis) 	<ul style="list-style-type: none"> - Allergy associated with LBP among 3 age cohorts - RD associated with LBP among mid-age and older women - Asthma associated with LBP among younger women 	Non-industry
Smith et al. (2009)	Cohort	7499	F	18-23 45-50 70-75	<ul style="list-style-type: none"> - In last year - Pre-existing and newly developed 	<ul style="list-style-type: none"> - Pre-existing RD - Newly developed RD 	<ul style="list-style-type: none"> - Women with pre-existing or newly developed RD have an increased risk for the development of LBP (OR⁷ 2.11) - Women with LBP or newly developed LBP are more likely to develop RD - Allergy is associated with LBP development 	Non-industry

Smith et al. (2014)	Cohort	58458	F	18-23 45-50 70-75	- In last year - Pre-existing and newly developed	- Pre-existing RD - Newly developed RD	- Women with pre-existing or newly developed RD had an increased risk for LBP development (OR ⁷ 2.11) - Women with pre-existing and newly developed LBP were more likely to develop RD (OR: 2.62)	Non-industry
Synnot et al. (2002)	Cross-sectional	60	M+F	71+/-8	- Ever - In the past year - In the past 7 days	- Chronic bronchitis - Emphysema- chronic airflow limitation COPD ⁶	Lifetime, 12-month and 7day prevalence of LBP in patients with chronic airflow limitation is 69%, 58% and 31% (comparable to the general population)	Not available
Wright et al. (1995)	Cross-sectional	34000	M+F	18-39 >65	Non-specified LBP	Non- specified RD	LBP is associated with smoking (OR 1.52) at all ages	Not available

¹ Allergic contact dermatitis: ‘‘a rash caused by detergents, cosmetic agents, nickel, etc.’

² Atopic eczema: ‘‘itchy eczema, mainly at the level of the elbows and knees’

³ Allergic urticaria: ‘transient, very itchy lesions’

⁴ Chronic bronchitis: ‘nocturnal cough without cold, with productive cough in the morning for at least three months per year in two consecutive years’

⁵ Asthma: ‘the diagnosis of asthma or having asthma-like symptoms, such as wheezing during cold weather or contact with animals or pollen, shortness of breath on exertion, more than one month cough, dry cough independently of colds’

⁶ COPD: chronic obstructive pulmonary disease

⁷ OR: odds ratio