



Dyspnea in relation to symptoms of anxiety and depression: A prospective population study

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KEYWORDS

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Summary

Background: Respiratory symptoms are related to anxiety and depression in several cross-sectional studies but the association has not been explored in longitudinal studies.

Study objectives: To prospectively study the change in dyspnea in relation to symptoms of anxiety and depression over a 9-year time period.

Methods: The study comprised of 515 adults from a population sample who had participated in the European Commission Respiratory Health Survey (ECRHS) I in 1991–1992 and in the ECRHS II in 1999–2000. The questionnaire included a modified British Medical Research Council Scale for dyspnea grading and the Hospital Anxiety and Depression scale questionnaire.

Results: The prevalence of dyspnea was 10.7% in the first and 12.6% in the second survey. Symptoms of depression was an independent determinants for dyspnea in both surveys (OR (95% CI) 3.72 (1.51–9.17) and 3.40 (1.49–7.80), respectively). In subjects that did not have dyspnea at the first survey onset of symptoms of anxiety (OR 3.53 (1.03–12.1)) and depression (OR 12.2 (3.97–37.5)) were significantly related to having dyspnea at the second survey, whereas onset of dyspnea was not significantly associated with developing symptoms of anxiety or depression when each disorder was entered separately.

Conclusion: Our data indicates that there is a causal relationship between development of symptoms of anxiety and depression and dyspnea. Psychological status is therefore an important factor to consider both when evaluating the results

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of epidemiological respiratory studies and in clinical settings when treating patients that have dyspnea.

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Introduction

Dyspnea is a clinical term used to describe the subjective feeling of impaired breathing. The term comprises a wide range of respiratory symptoms such as shortness of breath, increased respiratory rate or altered depth in respiration.¹ Psychiatric comorbidity is common in patients with asthma and chronic obstructive pulmonary disease (COPD)^{2–5} and an association between anxiety and depression and respiratory symptoms has been found in cross-sectional population studies.^{6–8}

The cause and effect relationship between psychological factors and dyspnea is, however, unclear. There are indications that dyspnea may induce psychiatric disorders⁹ while other studies indicate that psychological illnesses intensify the subjective sensation of dyspnea.^{10,11} The European Community Health Survey II (ECRHS II) is a longitudinal population study where adults aged 20–44 years were followed for 9 years.¹² In one of the centres anxiety and depression was assessed at base-line⁶ and the follow-up. This gave us a unique opportunity to study how changes in psychological status affected development of dyspnea over a 9-year follow-up period. The primary aim of the present analysis was therefore to explore the association between change in psychological status and dyspnea.

Population and methods

A postal questionnaire was sent to a randomly selected group of 3600 inhabitants of the municipality of Uppsala, Sweden in the age group 20–44 years within the European Commission Respiratory Health Survey (ECRHS) conducted in 1990–1992.¹³ The questionnaire consisted of 17 questions relating to respiratory symptoms, medication, and smoking. The response rate was 87% ($n = 3145$). A random sample of 800 of the 3145 subjects that answered the questionnaire and 216 subjects that reported asthmatic symptoms or current asthma medication and were not included in the random sample were invited to a clinical examination (Fig. 1). The examination in the ECRHS consisted of a structured interview with questions on respiratory symptoms, current medication and

previous exposure to specific environmental factors and spirometry. The follow-up study, the ECRHS II¹² took place in 1999–2000 and included 679 subjects (response rate 82.4%). The protocol was in general identical to the one used in the previous survey (Fig. 1).

Estimation of dyspnea

Dyspnea was measured using a modification of the British Medical Research Council Scale (the MRC scale) which has been used in epidemiologic surveys since 1960 and provide a sensitive and objective tool in a standardised setting of dyspnea.^{11,14,15} The following categorisation was used: 'No dyspnea' gave nil points, 'feeling short of breath when being in a hurry walking on level ground or up a smaller hill' 1 point, 'feeling short of breath when

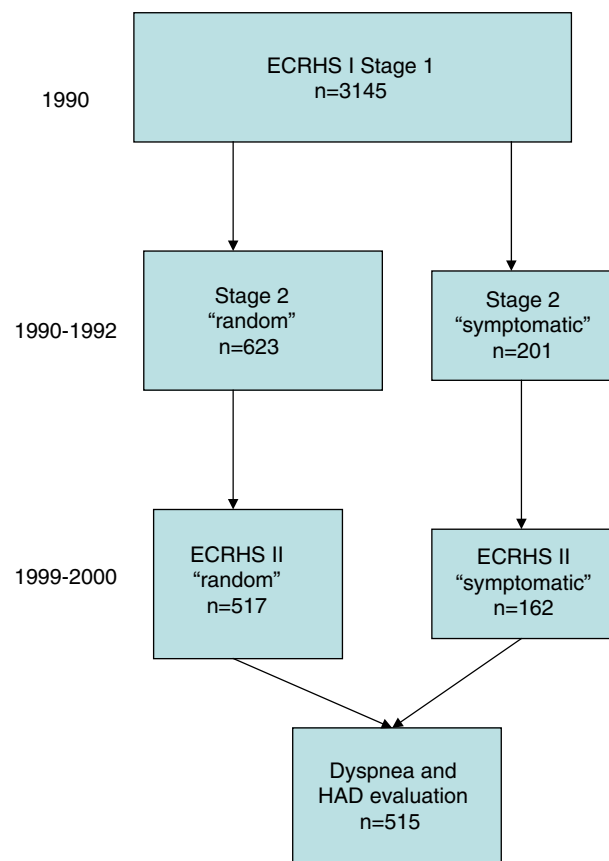


Figure 1 Study design.

walking with other persons of the same age on level ground' two points and 'having to stop to catch once breath when walking at desired speed on level ground?' three points. The original MRC scale includes two more questions that were not included in the ECRHS protocol, given that our population was relatively young and healthy.

Evaluation of psychological status

The Hospital Anxiety and Depression Scale (the HAD scale) was originally developed to detect psychological illness in physically disabled patients admitted in medical clinics.¹⁶ Comparisons with similar scales have shown that the HAD scale is a valid tool for personal screening and for use in outpatient clinics.^{17,18} The HAD scale consists of 14 items with 7 questions of anxiety and 7 questions of depression rated on a four-point scale from 0 to 3. The item scores represent the degree of distress from none, a little, a lot, to unbearably. The items are summed resulting in a maximum of 21 points. Various cut-offs have been applied by investigators. Using psychiatric diagnosis as a gold standard HAD depression ratings of scores of eight and higher indicate the presence of suggested or probable anxiety and depression, respectively.^{16,17}

Asthma

Current asthma was defined as answering yes to the questions: 'Have you ever had asthma?' and 'Have you had an attack of asthma in the last 12 months?'

Smoking

Information on smoking history was collected by administered questionnaire at each occasion. Those who answered 'yes' to the lead question ('Have you ever smoked for as long as one year?') were asked 'Do you smoke now, as of one month ago'. Based on the answer of these questions the subjects were categorised as non-, ex- or current smokers. Four categories were subsequently formed when analysing change in smoking history; non-smokers, smoking debutants, ex-smokers and persistent smokers.

Spirometry

Forced expiratory volume in 1 s (FEV₁) was measured using a dry rolling seal spirometer system (Sensor Medics 2130, Sensor Medics, Anaheim, CA, USA). Up to five technically acceptable blows were

determined. The results were expressed as per cent of predicted using the European Community for Coal and Steel reference values.¹⁹

Body mass index

Body mass index (BMI) was calculated as weight (kg)/[height (m)]².

The study was approved by the Ethical Committee of the Medical Faculty at the University of Uppsala. All subjects gave their permission for utilisation of personal data for this study.

Statistical methods

The statistical analysis was performed using Stat-View 5.0 (SAS Institute Inc., Cary, NC, USA) and Stata 8.0 (Stata Corporation, College Station, Texas). The χ^2 -test and the unpaired *t*-test was used in the univariate comparisons between participants and non-participants and subjects with and without dyspnea, respectively. McNemars-test was used when comparing the prevalence of dyspnea and psychological disorders between the two surveys. Risk factors for dyspnea and anxiety and/or depression were analysed using multiple logistic regression analysis. A *P*-value <0.05 was considered significant. Analyses of interaction were used to study the possibility of a gender difference in the association between dyspnea and psychological status.

Results

Characteristics of the population

The present analysis included subjects that had answered the dyspnea questions and completed the HAD questionnaire in both surveys (*n* = 542). Twenty-seven subjects reported having disabled capability to walk due to non-respiratory causes and were therefore excluded. Of the 515 subjects analysed, 397 were from the random population and 118 from the "symptomatic sample" (Fig. 1). There were 258 men and 257 women, mean age was 33 years (range 20–45 years) in the first survey and 41 years (28–54 years) in the follow-up. The mean follow-up time was 8.6 (range 7.8–9.5) years.

Prevalence of dyspnea, anxiety and depression

There was no significant difference in the prevalence of dyspnea between the two surveys

(Table 1). The prevalence of symptoms of anxiety decreased significantly while there was no significant change in the prevalence of suggested or probable depression (Table 1).

Cross-sectional analyses

Female gender, depression and having a low FEV₁ significantly increased the risk for dyspnea in both

Table 1 Prevalence (%) of dyspnea and symptoms of anxiety and depression in 1991–1992 and 1999–2000 and absolute difference and 95% confidence interval (CI) between the two surveys ($n = 515$).

	1991–1992	1999–2000	Difference % (95% CI)
Dyspnea grades 1–3	10.7	12.6	1.9 (–0.9, 4.8)
Dyspnea grades 2–3	2.8	3.5	0.8 (–1.0, 2.6)
Dyspnea grade 3	0.8	0.6	–0.2 (–1.2, 0.8)
Anxiety	26.4	18.5	–7.9 (–11.5, –3.8)
Depression	7.4	8.6	1.2 (–1.5, 4.2)
Anxiety and/or depression	28.5	20.6	–8.0 (–12.1, –3.9)

Table 2 Determinants of dyspnea at the first and second survey.

Risk factor	N	Dyspnea			
		1991–1992		1999–2000	
		OR*	95% CI	OR*	95% CI
Women	257	3.82	1.86–7.81	2.99	1.59–5.63
Age 1991–1992 (10-year increase)		1.65	1.04–2.63	1.67	1.10–2.54
FEV ₁ 1991–1992 (10% increase)		0.74	0.57–0.95	0.77	0.61–0.96
BMI 1991–1992 (5 units increase)		1.85	1.19–2.88	1.51	0.98–2.31
<i>Current asthma</i>					
1991–1992	71	2.99	1.31–6.47		
1999–2000	54			1.88	0.86–4.13
<i>Smoking habits 1991–1992</i>					
Non-smoker	267	1			
Ex-smoker	124	1.11	0.49–2.50		
Smoker	124	0.82	0.38–1.81		
<i>Smoking habits 1991–2000</i>					
Persistent non-smoker	376			1	
Started to smoke	10			3.24	0.55–19.0
Stopped smoking	56			1.33	0.55–3.22
Persistent smoker	68			2.13	1.03–4.39
<i>Psychological status 1991–1992†</i>					
No disorder	368	1			
Anxiety	136	2.76	1.41–5.42		
Depression	38	3.72	1.51–9.17		
Anxiety and/or depression	147	2.38	1.22–4.65		
<i>Psychological status 1999–2000†</i>					
No disorder	409			1	
Anxiety	95			1.90	0.96–3.74
Depression	44			3.40	1.49–7.80
Anxiety and/or depression	106			1.80	0.93–3.50

*Adjusted for sample (random or symptomatic) and all the variables in the table.

†Each type of psychological symptom was entered separately.

surveys, while asthma, a high BMI and anxiety were related to dyspnea in the first survey and being a persistent smoker during the study period significantly increased the risk of dyspnea at follow-up (Table 2).

Longitudinal analyses

Onset of symptoms of anxiety and depression was significantly related to having dyspnea in the ECRHS II among subjects that did not have dyspnea in ECRHS I (Table 3). No significant association was found between symptoms of anxiety and or depression at baseline and onset of dyspnea (adjusted OR (95% CI) 1.38 (0.65–2.93)).

Onset of dyspnea was not significantly associated with symptoms of anxiety or depression in the ECRHS II among subjects without anxiety and depression symptoms in the ECRHS I (Table 4). A significant association between onset of dyspnea and psychological status was, however, found when anxiety and depression were combined.

There was no significant difference between men and women in the association between psychological status and dyspnea, when this was analysed by interaction analyses.

Non-responders

Subjects that did not participated in the present investigation were more often smokers (35.6% vs. 24.1%, $P = 0.003$) and had a higher prevalence of anxiety (39.6% vs. 26.4%) and dyspnea (19.3% vs. 10.7%) ($P < 0.001$) in the ECRHS I than the participants. No significant differences were found regarding age, sex, asthma or depression between the participants and non-participants.

Discussion

The main findings of this study are that symptoms related to anxiety and especially depression are important determinants for the development of dyspnea, while there was less evidences that dyspnea induces psychological symptoms.

A significant relation between respiratory symptoms and anxiety and depression has been found in many previous cross-sectional studies,^{6–8,11,20} but to our best knowledge the associations between psychological status and dyspnea have not previously been investigated in a longitudinal population study. In the present study, the risk of developing dyspnea was increased in subjects that developed symptoms of anxiety and depression during the follow-up. No significant association between persistent psychological symptoms and onset of dyspnea was found.

There are two possible ways to interpret our results. The first is that the increased dyspnea is the cause of psychological symptoms which is in accordance with what was found in a study of patients with severe COPD. In that study, van Manen et al. found that the risk for depression was 2.5 times greater compared to controls.⁹ Likewise, Goodwin et al. found that asthma was associated with a significantly increased likelihood of having anxiety disorder, panic disorder, social phobia, generalised anxiety disorder, and bipolar disorder.^{21,22} The second interpretation is that psychological symptoms is the causes of dyspnea by intensifying the subjective sensation of dyspnea.¹¹ This is in accordance with the results of Tiller and co-workers, who found that correlations between estimates of resistive loads and peak inspiratory mouth pressure were significantly less for the anxious patients than for normal subjects.¹⁰

Table 3 Dyspnea at follow-up in subjects without dyspnea at baseline in relation to change in psychological status ($n = 441$).*

	Onset of dyspnea		
	N	OR [†]	95% CI
Onset of anxiety	34	3.53	1.03–12.1
Onset of depression	29	12.2	3.97–37.5
Onset of anxiety or depression	39	4.35	1.38–13.7
Persistent anxiety	51	2.30	0.73–7.28
Persistent anxiety or depression	58	2.08	0.66–6.53

Each type of psychological symptom was entered separately.

[†]Adjusted for sample (random or symptomatic), age, gender, change in asthma status, baseline FEV₁, baseline BMI and change in smoking status.

*Too few subjects to analyse the relationship between persistent depression and onset of dyspnea.

Table 4 Psychological disorders at follow up in subjects without disorders at baseline in relation to change in dyspnea status (*n* = 354).

	<i>N</i>	Psychological status*					
		Anxiety		Depression		Anxiety and/or depression	
		OR [†]	95% CI	OR [†]	95% CI	OR [†]	95% CI
No dyspnea	348	1		1		1	
Onset of dyspnea	25	3.01	0.81–11.1	5.00	0.73–34.4	3.93	1.12–13.8
Persistent dyspnea	16	0.38	0.03–4.45	—	—	0.42	0.04–4.41

*Each type of psychological symptom was entered separately.

†Adjusted for sample (random or symptomatic), age, gender, change in asthma status, baseline FEV₁, baseline BMI and change in smoking status.

The results of the present study gives more support for psychological symptoms being the cause of dyspnea than the opposite. Onset of suggested or probable anxiety and depression increased the risk of developing dyspnea among subjects that did not have dyspnea in the first survey. On the other hand the onset of dyspnea was not significantly associated with developing symptoms of anxiety or depression when each condition was analysed separately. There are two known conditions in which emotional breathing patterns can cause dyspnea. The former is dyspnea in patients with panic disorder and hyperventilation.^{22–24} The latter occurs when emotional breathing turns into excessive inspiration. This will lead to a hyperinflation of the airways that evokes a sense of dyspnea.²⁵ There was, however, no significant relationship between psychological status at baseline and onset of dyspnea. It is therefore not possible to draw a firm conclusion on the cause effect relationship between psychological status and dyspnea.

No significant gender difference was found in the association between psychological status and dyspnea but in accordance with other studies the prevalence of dyspnea was higher among women than men.^{26,27} There are several possible explanations for these results. There is for instance the difference in anatomy, with women having smaller lungs than men. Hormonal differences may also be part of the explanation, as progesterone is a recognised respiratory stimulant. The age group mainly includes females in their fertile period who probably are more susceptible to dyspnea due to the cyclical hormonal variations.^{27,28}

A higher BMI was related to increased dyspnea. In some studies, obese subjects report more asthma-like symptoms and a higher usage of asthma medication but have the same level of airway

hyperresponsiveness and airflow obstruction as subjects with normal body weight.^{29,30} Another study has, however, found a significant relationship between a higher BMI and bronchial hyperresponsiveness.³¹ Obesity has been shown to adversely affect respiratory mechanisms and gas exchange, decrease respiratory muscle function and lung volumes, and increase the effort of breathing.^{28,29} As expected from previous studies, ageing, smoking and low lung function was also found to be determinants of dyspnea.²⁶

Some methodological issues are worth discussing. The response rate was relatively high but we did find that the non-participants differed from the participants in several aspects. The non-participants were more often smokers and had a higher prevalence of dyspnea and anxiety in the ECRHS I than the participants. This may have reduced the possibility of finding a significant association between persistent anxiety symptoms and dyspnea. It is also possible that the results may have been affected by other exposures not controlled for in the present study such as marital and socioeconomic status. The MRC scale has been widely used in epidemiologic surveys and has been shown to be a sensitive and valid tool in a standardised setting.¹⁵ The scale has been modified in our study since the last two steps of the scales are not included. The prevalence of dyspnea grade 3 was low. Omitting the two last steps ('having to stop for breath after walking 100 yards' and 'being too breathless to leave the house') has therefore probably not affected our results. The HAD scale has proven to correspond well with established scales currently used in the field of psychiatry, such as the American Psychiatric Association's Diagnostic and statistical Manual (DSM-3), Beck Depression Inventory (BDI) and Spielberger's State Trait Anxiety inventory (STAI).^{17,18}

Our data indicates that there is a causal relationship between development of psychological symptoms and dyspnea. Psychological status is therefore an important factor to consider both when evaluating the results of epidemiological respiratory studies and in clinical settings when treating patients that have dyspnea.

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