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An Evaluation of Chronic Dyspnea in a Chest Disease Clinic

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Abstract

Chronic dyspnea is a frequent cause of applications to pulmonology clinics. Cardiopulmonary diseases represent the most frequent etiological causes of dyspnea. However, studies on this subject are limited. The purpose of this study is to determine the etiological causes in patients who admitted to outpatient clinic with the complaint of chronic dyspnea via specific diagnostic procedures. This prospectively planned study was performed with patients referred to chest disease clinic of Recep Tayyip Erdogan University, Turkey, between 1 July 2012 and 31 May 2013. Patients with a history of shortness of breath that was ongoing more than 1 month were included to study. Causes of dyspnea were investigated by using a 3-stage diagnostic procedure. Four hundred seventy-one patients were enrolled. Specific etiology of dyspnea was identified in 462 patients. The other nine patients could not be diagnosed. Respiratory disease was determined in 101 (22%) patients and non-respiratory disease was found in 361 (78%). Non-respiratory reasons of chronic dyspnea were identified as cardiac disease in 184 (51%), psychiatric diseases in 142 (39%) and other causes in 35 (10%) individuals. The etiology was considerably different between male and female groups. The most common cause of chronic dyspnea was found as respiratory disease (43%) in male group and cardiovascular disease (45%) in female group.

Keywords: Chronic dyspnea; Causes of dyspnea

Introduction

Dyspnea is defined as an uncomfortable sensation of breathing in varying intensity [1]. Ventilation is normally controlled by the autonomic nervous system, with only limited voluntary override [2]. Patients with different disorders use different phrases to describe their breathing discomfort such as air hunger, chest tightness and shortness of breath. The development of dyspnea is complex and multifactorial. The sensation of dyspnea may be developed by any or combination of the sense of respiratory effort, chemoreceptor stimulation, mechanical stimuli arising in lung and chest wall receptors and neuroventilatory dissociation [3]. As an example, in a patient with asthma, vagal stimuli arising from airway inflammation and bronchoconstriction may play role in dyspnea.

Chronic dyspnea is described as shortness of breath lasting longer than 1 month [4]. The most frequent cause is cardiovascular diseases. In cardiac terms, heart failure (HF) and Chronic Ischemic Heart Disease (CIHD) are common causes. The most common respiratory causes are asthma, Chronic Obstructive Pulmonary Disease (COPD), pulmonary embolism, upper respiratory tract infection and Interstitial Pulmonary Disease (IPD) [3]. Psychogenic conditions (e.g., generalized anxiety disorder, panic disorders, post-traumatic stress disorder) can also lead to chronic dyspnea [5]. Obesity can also lead to dyspnea. One study showed that obesity is responsible for dyspnea in 28% of patients [6]. Other causes of dyspnea include anemia, metabolic acidosis, gastro-esophageal reflux, hyperthyroidism and hypothyroidism. Asthma, HF, CIHD, COPD, IPD and psychogenic disorders are responsible for approximately 85% of all dyspnea cases [7]. Cardiac and pulmonary etiologies predominate. A multifactorial etiology applies in one-third of patients [8].

Differential diagnosis in chronic dyspnea generally consists of 4 categories as pulmonary, cardiac, and cardiopulmonary and the others [9]. The disease responsible for chronic dyspnea can usually be determined through history taking of patients, physical examination and a variety of diagnostic tests. Diagnosis can be made on the basis of various multidisciplinary approaches, advanced examinations and invasive techniques. On rare occasions, the etiology behind chronic dyspnea cannot be determined despite the tests performed. As an example, Pratter et al. were able to diagnose only 66% of patients with chronic dyspnea with a single clinical assessment [10].

Our scan of the literature revealed a limited number of studies investigating etiology in patients with chronic dyspnea. The purpose of this study was to use specific diagnostic stages to reveal etiological factors causing chronic dyspnea in patients referred to the pulmonary diseases clinic.

Materials and Methods

Approval was first obtained from the Recep Tayyip Erdogan (RTE) University Faculty of Medicine clinical research ethical committee. A written informed consent of the patients was obtained from the respondents after the purpose of the study had been fully explained to them. The study was planned prospectively. Patients admitted to outpatient clinic of pulmonary disease department with the complaint of dyspnea with unknown etiology and lasting longer than 1 month (between 1 July, 2012, and 31 May, 2013) were included. We excluded

the patients who admitted to emergency department with the symptom of dyspnea. Symptoms such as breathlessness, shortness of breath, feelings of suffocation, insufficient air intake and the need to take deep breaths were regarded as dyspnea. Subjects aged between 20 and 80 were included. Patients with known disease to account for chronic dyspnea were excluded. Patients' age, gender, height, weight, body mass index (BMI), systolic and diastolic blood pressures and cigarette smoking status were recorded.

Patients were administered diagnostic examinations consisting of 3 stages. Patients who could not be diagnosed in the first stage were administered one or more of the second stage examinations. If diagnosis could not be made as a result of second stage examination, third stage examinations were performed.

First stage examinations consisted of anamnesis, physical examination, spirometry [forced expiratory volume percentage in the 1st second (FEV1%), forced vital capacity percentage (FVC%) and [FEV1/FVC], electrocardiography (ECG), chest X-ray, full blood count, thyroid stimulating hormone (TSH), free T4 and oxygen saturation with pulse oxymetry from the fingertip measurement.

Second stage examinations based on examination by a specialist psychiatrist, examination by a specialist cardiologist, Echocardiography (ECO), cardiac exercise test, thoracic Computerized Tomography (CT) (HRCT or CT angiogram with contrast), ventilation/perfusion scintigraphy, bronchial provocation test with histamine and reversibility test (in patients with suspected asthma with normal spirometry values), carbon monoxide diffusion test (DLCO) and pulmonary volumes (in patients with suspected restrictive type pulmonary disease or emphysema) and arterial blood gas (in patients with pulse oxygen saturation below 95%) measurement.

Third stage examinations were coronary angiography, bronchoscopy and right heart catheterization.

Definitions

COPD: Postbronchodilator FEV1/FVC ratio<70% according to global obstructive lung disease (GOLD) [11].

Asthma: Together with appropriate anamnesis and physical examination, an increase of more than 12% or 200 ml in FEV1 compared with basal values following bronchodilator or a increase of greater than 15% in peak expiratory flow (PEF) rate [12].

Systolic heart failure: Left ventricle ejection fraction (EF)<45% with echocardiography in the presence of typical heart failure symptoms and findings (shortness of breath, effort dyspnea, fatigue, swelling in the legs, tachycardia, tachypnea, venous congestion, edema) [13].

Diastolic heart failure: Left ventricle ejection fraction being normal (EF>50%) at echocardiography in the presence of typical heart failure symptoms and findings, no segmental wall motion abnormalities and a rise in diastolic filling with no findings of coronary heart disease, heart valve disease or pulmonary disease[14].

Psychiatric disorders: Diagnosis of psychiatric disorders was performed by a specialist psychiatrist using the SCID-I (Structured Clinical lnterview for DSM-IV) clinical assessment technique.

Obesity: Body mass index>30kg/m^2.

Anemia: For men, anemia is defined as hemoglobin level of less than 13.5 g/dl and in women as hemoglobin of less than 12.0 g/dl.

Blood pressure measurement: Two measurements were performed from the left arm at 5-min intervals after at least 15-min rest using a sphygmomanometer. The mean of the two measurements was recorded as systolic and diastolic blood pressure.

Statistical analysis was performed on the SPSS program (SPSS version 16; SPSS Inc., Chicago, IL, USA). Constant variables were given as mean ± SD and categoric variables as %. Student's t test and ANOVA were applied in the comparison of means and the chi-square test in the comparison of ratios. P<0.05 was regarded as statistically significant.

Results

Four hundred seventy-one patients were included. Stage 1 diagnostic examinations were performed on all patients. In the event that diagnosis could not be made, those stage 2 procedures regarded as necessary based on pre-diagnosis and in the light of history and physical examination were performed. Stage 3 diagnostic procedures were performed with those subjects that could not be diagnosed on the basis of stage 2 procedures. The cause of dyspnea could not be established in 9 patients, despite all these examinations. Diagnosis accounting for dyspnea was established in 462 patients, 290 (63%) women and 172 (37%). Diagnostic procedures performed and rates of diagnosis are shown in Figure 1.

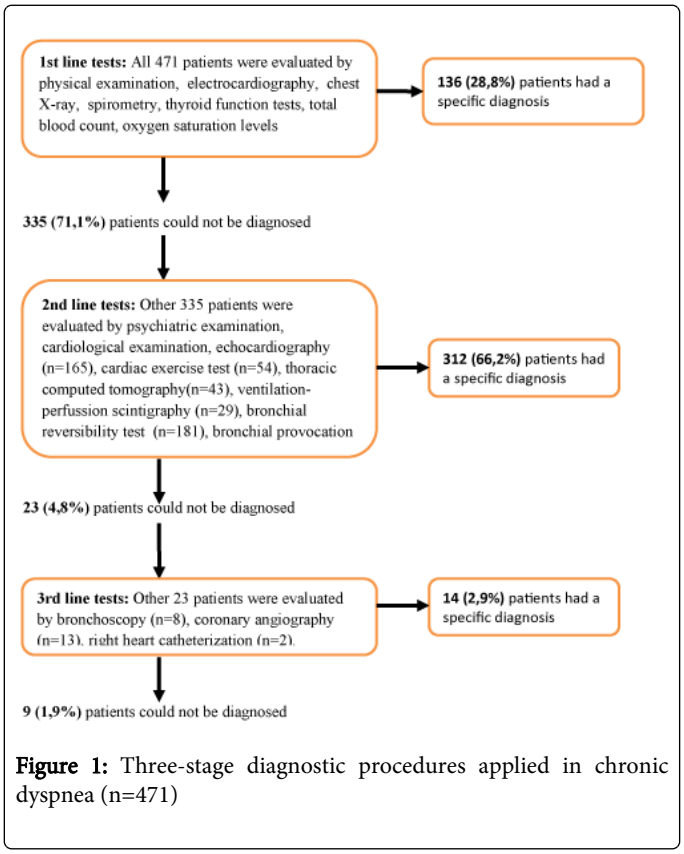

Figure 1: Three-stage diagnostic procedures applied in chronic dyspnea (n=471)

Patients were divided into four categories on the basis of diagnosis; respiratory diseases, cardiac diseases, psychogenic diseases and others. Diagnoses were made of 101 respiratory disease cases (67 COPD, 26 asthma, 6 IPD, 2 primary pulmonary hypertension and 1 lung cancer), 184 cardiac disease cases (83 arterial hypertension, 41 systolic HF, 30 diastolic HF, 16 heart valve disease, 10 CIHD, 3 atrial fibrillation and 1

cardiac tamponade), 142 psychiatric disorder cases (87 generalized anxiety disorder, 33 depression and 22 panic disorder) and 35 other cases (20 obesity, 7 hyperthyroidism, 6 anemia, 1 hypothyroidism and 1 multinodular goiter with tracheal compression). Characteristics of the diagnostic groups are shown in Table 1.

Parameter	Total	Respiratory	Cardiac	Psychiatric	Other	P
Patient (n)	462	101	184	142	35	
M/F (n)	172/290	75/26	53/131	36/106	8/27	<0.001[zx]
Age (years)	53 ± 17	55 ± 15	63 ± 13	37 ± 11	56 ± 17	<0.001[a&]
Smoking (pack-year)	12 ± 19	33 ± 24	5 ± 14	6 ± 12	6 ± 14	<0.001[b&]
DBP (mmHg)	85 ± 17	77 ± 11	99 ± 16	74 ± 8	83 ± 12	<0.001[c&]
SBP (mmHg)	142 ± 32	125 ± 20	170 ± 28	120 ± 13	139 ± 25	<0.001[d&]
BMI (kg/m^2)	29 ± 6	26 ± 4	31 ± 6	25 ± 5	31 ± 7	<0.001[e&]
Hb (gr/dl)	13.9 ± 3.7	14.5 ± 3.1	14.1 ± 2.7	13.6 ± 3.3	13.4 ± 4.2	0.083[&]
TSH (mcg/dl)	2.53 ± 1.40	2.43 ± 1.81	2.54 ± 1.1	2.47 ± 1.34	2.63 ± 1.37	0.114[&]

Table 1: Characteristics of diagnostic groups

F: Female, M: Male, *: packet-year , DBP: Diastolic blood pressure, SBP: Systolic blood pressure, BMI: Body mass index, Hb: Hemoglobin, TSH: Thyroid stimulating hormone, z : male gender was significantly higher in the respiratory group compared to the other 3 groups (p<0.001), while the gender characteristics of the other 3 groups were similar (p:0.797), a : Age was similar between the respiratory group and the other causes group (p:0.945), while the other groups differed significantly from one another, b: Cigarette levels were significantly higher in the respiratory group compared to the other 3 groups. The other 3 groups were similar, c: Diastolic blood pressure was significantly higher in the cardiac disease group compared to the other 3 groups, d: Systolic blood pressure was significantly higher in the cardiac disease group compared to the other 3 groups, e: BMI was significantly high in the cardiac group and other causes group compared to the respiratory and psychiatric diseases groups, &: One-Way ANOVA analysis and post-hoc Tukey-HSD were applied, x: The chi-square test was applied.

Men and women were assessed separately. The causes of chronic shortness of breath between the sexes differed considerably. In women, cardiac diseases were the cause of chronic dyspnea in 45% of cases, psychiatric diseases in 37%, and respiratory diseases in 9% and others in 9%. In men, respiratory diseases were the cause in 43% of cases, cardiac diseases in 30%, and psychiatric diseases in 21% and others in 6%. Levels of diseases causing chronic dyspnea by gender and a comparison of general characteristics are shown in Table 2 and Figure 2.

Respiratory diseases were determined in only 101 (22%) of the 462 patients referred to the pulmonary diseases clinic and investigated for chronic dyspnea. Non-respiratory diseases were responsible for chronic dyspnea in 361 (78%) patients. Patients' ages were a significant guide in the etiology of chronic dyspnea. Psychiatric disorders were the most important cause of chronic dyspnea in 86 (73%) of the 118 patients aged 40 or under. Psychiatric disease was determined in only 2 of the 140 patients aged 65 or above.

Disease	Ratio (%)			Age (year, mean ± SD)			BMI (kg/m^2, mean ± SD)		
	m	f	p	m	f	p	m	f	p
Pulmonary	43	9	<0.001	58 ± 13	45 ± 15	0.008	25.8 ± 3.6	27.4 ± 4.7	<0.001
Cardiac	30	45	0.245	66 ± 14	62 ± 13	0.794	28.3 ± 4.0	32.9 ± 5.4	0.001
Psychogenic	21	37	<0.001	35 ± 12	38 ± 11	0.225	25.7 ± 4.2	25.9 ± 4.7	0.804
Others	6	9	0.347	62 ± 14	55 ± 17	0.290	29.4 ± 5.9	32.1 ± 7.4	0.338
Total	100	100		56 ± 17	51 ± 17	0.004	26.7 ± 4.5	29.8 ± 6.3	<0.001

Table 2: Comparison of diseases causing chronic dyspnea in male and female patients

m: male, f: female , BMI: body mass index

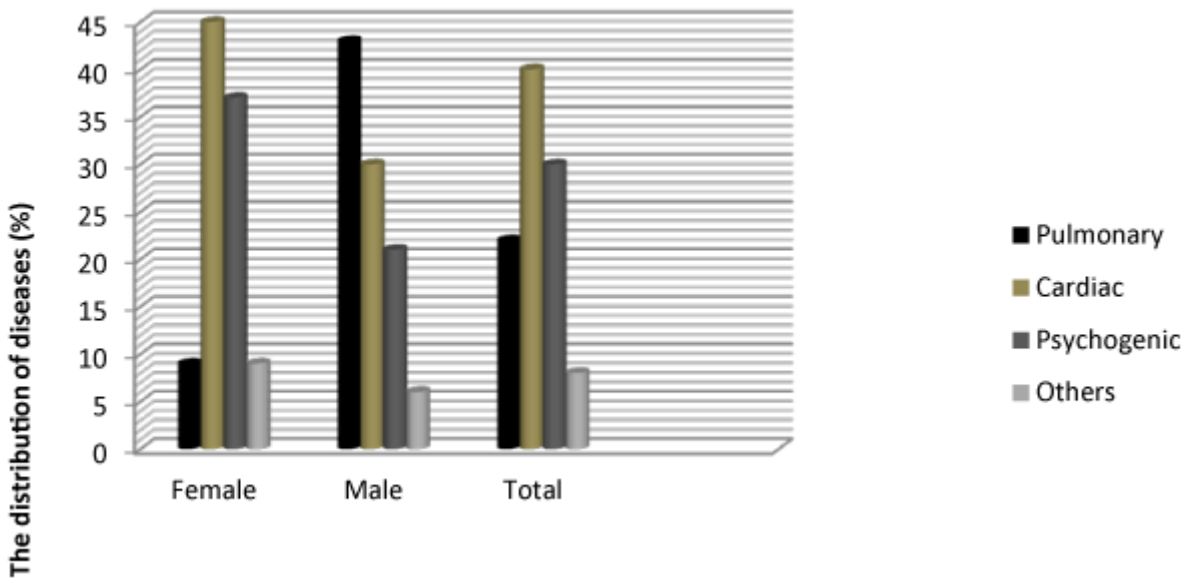

Figure 2: Prevalences of groups of diseases causing dyspnea by gender

Discussion

Although chronic dyspnea represents a significant part of referrals to the pulmonary diseases clinic, the number of studies on the subject is limited. In this study, diseases causing chronic dyspnea were diagnosed using 3-stage diagnostic procedures. Etiological causes were classified under 4 diagnostic groups. Cardiac diseases represented the causes of chronic dyspnea in 40% of the 462 comprising the study population, psychiatric disorders in 30%, respiratory diseases in 22% and others, including obesity, anemia, hypothyroidism and hyperthyroidism in 8%. Hypo or hyperthyroidism causes dyspnea by existence of either cardiomyopathy, atrial fibrillation, peripheral skeletal muscle deconditiong and obesity. But it is not clear the mechanism of dyspnea in the cases of subclinical hypo or hyperthyroidism.

In a recent study of 123 patients with chronic dyspnea, Pratter et al. [15] determined respiratory diseases as responsible in 53% of cases, cardiovascular and circulatory disease in 16%, obesity in 16%, psychogenic disorder in 10% and other causes (fibromyalgia, pregnancy and postnasal drip syndrome) in 5%. The study population consisted of 39% males and 61% females. In that study, respiratory diseases were identified as the cause of chronic dyspnea in more than half of patients. In our study, however, respiratory disease was identified in only 22% of patients. Our study population consisted of 37% males and 63% females. Gender distribution was similar. Significantly high levels of cardiac diseases and psychiatric disorders in our study represent major differences. In a study of 58 patients with chronic dyspnea, DePaso et al. [16] identified pulmonary disease in 36% of patients, cardiac disease in 14%, hyperventilation in 19% and extrathoracic disease in only 3 patients. No diagnosis could be made in 14 patients. In that study, pulmonary disease was observed at a lower level than non-pulmonary diseases. Respiratory diseases were also observed at a low level in our study, 22%. Obesity has been shown as a cause of dyspnea in several studies, although DePaso et al. [16] did not mention it. In our study, obesity represented a cause of dyspnea in 20 (4.3%) cases. Han et al. [17] recently investigated the etiology of chronic dyspnea in 396 patients. Pulmonary disease was diagnosed in 229 (58%) patients and cardiac disease in 62 (16%), while no cause of chronic dyspnea could be determined in 105 (26%) patients. In terms of prevalence of respiratory disease, the results of that study are similar to those of Pratter et al. [15] study. Dyspnea had respiratory causes in more than half of patients. This is one of the rare studies to point to hypertension as a cause of dyspnea. However, only 2 cases of hypertension were reported. In our study, hypertension was shown as the cause of chronic dyspnea in 83 (18%) cases. In a study of 129 patients, Pedersen et al. [18] identified pulmonary disease as a cause of chronic dyspnea in 68 (53%) cases, heart disease in 27 (21%), obesity in 43 (33%), other causes in 20 (16%) and chronic dyspnea in 5 (4%). That study was performed on the 60-79 age groups. The main difference between ours and other studies is that in other studies obesity emerged as a high-level cause of dyspnea. However, we identified obesity as a cause of dyspnea in only 20 (4.3%) cases. In order for obesity to be regarded as a cause of dyspnea, other causes need to be excluded.

One of the interesting results of our study is that psychiatric disorders represent the etiological cause in 30% of patients presenting to the pulmonary diseases clinic with chronic dyspnea. Psychiatric disorders were identified as responsible in 73% of cases of chronic dyspnea in the 20-40 age range. These high levels are noteworthy. Generalized anxiety disorder is the most commonly seen psychiatric disorder. These patients were diagnosed using Structured Clinical Interview for DSM-IV (SCID-1) administered by a specialist psychiatrist. The level of psychiatric disease was 10% in Pratter et al. [15] study and 4% in Pedersen F et al. [18] study. The level was significantly higher in our study. The reason why these patients referred to pulmonary diseases clinic before the psychiatry clinic may be that the individuals tend to ascribe their symptoms to an organic disorder or that they tend to reject psychiatric disorders. Additionally, an increase in psychiatric disorders among the young and dyspnea

being one of the predominant symptoms in these patients may also explain the rise in applications to the pulmonary diseases clinic. Furtherly previous studies supported that the anxiety and depressive disorders are found frequently in patients with respiratory impairments and the severity of dyspnea measures does not affect the scores of depression and anxiety [19].

The most interesting finding of our study is the identification of hypertension as a cause of dyspnea. Hypertension was identified as the cause of dyspnea in 18% of our cases. Hypertension was also the highest level cause of dyspnea in the cardiovascular diseases group, in 83 (45%) cases out of 184 HT. Our scan of previous studies revealed no opinions regarding hypertension as a cause of dyspnea. Only Han et al. [17] reported 2 cases of hypertension as a cause of chronic dyspnea. Comparison of hypertension cases with patients with other causes of dyspnea revealed significant differences in terms of gender and obesity. In terms of gender, women were significantly predominant (75 women and men). These patients also had higher BMIs (BMI: 32 ± 5) and obesity levels (BMI>30) (59%). Hypertension cases being more obese may be ascribed to the role of obesity in dyspnea. However, due to a significant decrease or total disappearance of dyspnea symptoms following antihypertensive therapy, obesity was not regarded as a cause of dyspnea. In addition, probably differential diagnoses were excluded by the use of ECG in all these patients. Given the current state of our knowledge it is impossible to state the mechanisms by which hypertension causes dyspnea. Although the mechanism by which dyspnea develops has not been fully explained, different views have been put forward. Mechanoreceptors in the chest wall, chemoreceptors sensitive to hypercapnia and hypoxemia, and sensory receptors transmitted by vagal C fibers in the lung are regarded as peripheral receptors of dyspnea. It has been suggested that the stimulation of these receptors for any reason may lead to the onset of dyspnea [20]. In hypertension, dyspnea may emerge as a result of stimulation with a rise in pressure of chemoreceptors in the aorta and/or carotid body. Alternatively, another mechanism causing a rise in pressure, such as in primary pulmonary hypertension, may give rise to a feeling of shortness of breath. There is a clear need for studies to elucidate the relevant pathophysiology. Dyspnea resolved with the administration of antihypertensive therapy to hypertension patients and their blood pressures returning to normal.

Conclusions

A high level of non-pulmonary diseases was identified in patients presenting to the pulmonary diseases clinic with dyspnea lasting more than 1 month. Significant differences in causes of dyspnea were identified between men and women. Dyspnea was related to non-pulmonary diseases in approximately 90% of women. Cardiac diseases, particularly hypertension, and psychiatric disorders were seen at high levels, 82%, in women. Psychiatric disorders are seen to a noteworthy extent in young patients in particular. Psychiatric disorders should therefore be investigated in young patients presenting with chronic dyspnea. Hypertension was considered as a cause of dyspnea in obese women. Since non-pulmonary diseases are frequently seen, patients with chronic dyspnea should be diagnosed using a multidisciplinary approach. Application of a staged diagnostic algorithm, to the extent of the clinician's means, will greatly assist the diagnostic procedures.

Acknowledgements

The authors declare that there are no competing interests regarding to this study. All authors declare that all the diagnostic procedures have been performed by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in declaration of Helsinki.

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