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The Coexistence of Heart and Lung Diseases in Patients with Chronic Dyspnoea that is Unexplained By Clinical Evaluation

Klinik Olarak Kronik Dispne Nedenine Karar Verilemediği Durumlarda Hem Kalp Hem Akciğer Hastalığının Varlığı

ORIGINAL INVESTIGATION
ÖZGÜN ARAŞTIRMA

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ABSTRACT
ÖZET

Objective: An understanding of the causes of dyspnoea can reduce morbidity and mortality. It may be difficult to decide whether dyspnoea is secondary to heart or lung disease. The objective of this study was to evaluate the coexistence of heart and lung diseases in patients with chronic dyspnoea, when clinical evaluation was not helpful.

Materials and Methods: We conducted a retrospective review of 250 patients with chronic dyspnoea (>1 month). Patients were selected according to the following inclusion criteria: patients presented with a complaint of chronic dyspnoea; clinical evaluation was not sufficient; and both spirometry and TTE had been performed within 1 month.

Results: Eighty-three percent of the patients had a diagnosis of heart and/or lung diseases. Ninety-five (38%) of the 250 patients with chronic dyspnoea had lung and heart diseases concomitantly. Diastolic heart failure was the most common heart disease seen with COPD or asthma. The most common lung diseases were COPD and asthma. One hundred and fifty-five of the patients had a heart disease, with diastolic heart failure being the most common.

Conclusion: When it was unclear whether the chronic dyspnoea was of a heart and/or lung origin based on clinical evaluation, more than one-third of the patients with chronic dyspnoea were shown to have coexisting lung and heart disease.

Key words: Dyspnoea, COPD, asthma, heart failure

Amaç: Dispneli hastalarda olası nedenlerin bilinmesi hastanın mortalite ve morbiditesini azaltabilir. Bazı hastalarda dispne nedeni kalp orijinli mi akciğer orijinli mi karar vermek zor olabilmektedir. Çalışmamızda klinik olarak kronik dispne nedeni kalp orijinli mi akciğer orijinli mi karar verilemeyen hastalarda ekokardiyografi ve spirometri yardımıyla hem kalp hem akciğer hastalığı varlığını değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Kronik dispneli (>1 ay) 250 hastayı içeren retrospektif çalışmadır. Kronik dispne şikayeti olan, klinik değerlendirmeyle kalp ve/veya akciğer hastalığı olup olmadığına karar verilemeyen, 1 ay içinde hem spirometri hem de ekokardiyografik değerlendirilmesi yapılmış olan hastalar çalışmaya dahil edilmiştir.

Bulgular: Hastaların %83'ünün kalp ve/veya akciğer hastalığı mevcuttu. Hastaların 95'inde (38%) kalp ve akciğer hastalığı eş zamanlı izlenmekteydi. Kronik dispne nedeni olarak en sık izlenilen akciğer hastalıkları KOAH ve astımdı. KOAH ve astımlı hastalarda diyastolik kalp yetmezliği en sık izlenilen kalp hastalığıydı. Hastaların 155'i bir kalp hastalığına sahipken en sık izlenilen kalp hastalığı diyastolik kalp yetmezliğiydi.

Sonuç: Kronik dispne nedeni kalp ve/veya akciğer orijinli mi klinik değerlendirmeyle karar verilemediğinde, kronik dispneli hastaların yaklaşık 1/3'ünün hem kalp hem de akciğer hastalığına sahip olduğu görülmüştür.

Anahtar kelimeler: Dispne, KOAH, astım, kalp yetersizliği

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Introduction

Clinicians are often confronted with patients with dyspnoea. Most studies in the literature have evaluated the acute form of dyspnoea, either in the emergency department or in elderly patients (1-4). Little published information is available about patients with chronic dyspnoea. The major causes of this symptom are asthma, chronic obstructive pulmonary disease (COPD), and heart failure (5-7). The most useful tests in distinguishing lung from heart diseases are TTE and spirometry.

Clinicians face difficult issues regarding these diseases. Dyspnoea on exertion is usually the earliest symptom of asthma, COPD, and heart failure. Furthermore, physical examination may be normal at this stage. Therefore, clinical evaluation may not always be sufficient for the diagnosis. In these cases, further diagnostic testing should be performed. Tobacco smoking is an important common aetiological factor in asthma, COPD, and heart failure (8-10). Thus, recognising the recent development of another disease in the presence of a long-standing one may be difficult. Advanced heart failure or advanced COPD is complicated by similarities in symptoms, such as coughing, wheezing, orthopnoea, and dyspnoea during rest, and physical symptoms such as rales and oedema. Such diagnostic complexity has been documented in the prehospital setting (1, 2). It is acknowledged that COPD and asthma can coexist with heart failure. However, the clinician may diagnose the remarkable disease or the disease in his/her own domain of practice.

Coexisting heart and lung diseases can be under-diagnosed and under-treated in patients with chronic dyspnoea, and these problems can lead to increased morbidity and mortality. Therefore, the primary aim of the present study was to evaluate the coexistence of heart and lung diseases in patients with chronic dyspnoea, as diagnosed by TTE and spirometry when clinical evaluation was not helpful. Our second aim was to investigate the demographic and clinical characteristics of these patients.

Materials and Methods

This study was approved by the review boards for human studies of the Hacettepe University Medical School. We conducted a retrospective review of the electronic medical records of 250 individual consecutive patients with chronic dyspnoea seen in the pulmonary diseases clinic. Patients were selected according to the following inclusion criteria: (1) patients presented with a complaint of chronic dyspnoea defined as lasting for more than 1 month; (2) clinical evaluation was not sufficient in the diagnosis of heart and/or lung diseases; and (3) both spirometry and TTE had been performed within 1 month. The records were re-evaluated according to medical history, smoking status, physical examination, and diagnosis from their electronic records. Also, spirometry and TTE laboratory databases were reviewed.

Spirometry was performed using a calibrated flow sensor spirometer (Model D-97204 Jaeger Toennies, Type APS-Pro, Höchberg, Germany) according to the European Respiratory Society Standardization (11). The best of three reproducible maximal flow-volume loops were selected. The spirometric manoeuver comprised the following steps: (a) three normal tidal volume breaths; (b) maximal inhalation; (c) forced maximal exhalation; and (d) maximal inhalation. The principal endpoint was the estimated value of the forced expiratory volume in the first second (FEV_1); in addition, forced vital capacity (FVC) and the FEV_1/FVC ratio were recorded. A diagnosis of COPD was given to patients who presented FEV_1/FVC <70% in spirometry in addition to chronic dyspnoea, cough, and/or sputum production (8). The diagnosis of asthma was based on clinical history, reversibility of FEV_1, or peak expiratory flow >15%, and according to the Global Initiative for Asthma (GINA) criteria (9). Lung diseases represented in small numbers of patients were grouped as 'other lung diseases'. The patients were divided into four groups according to lung diseases: COPD, asthma, other lung diseases, and no obvious lung disease.

TTE reports were assessed for diagnosis. The diagnosis of heart failure was made based on the criteria of the European Society of Cardiology (ESC), i.e. symptoms suggestive of heart failure and objective evidence of cardiac (systolic and/or diastolic) ventricular dysfunction at rest as assessed by TTE. Patients with heart failure were further classified as having 'systolic', 'diastolic', or 'right-sided heart failure'. For systolic heart failure, patients had to have a left ventricular ejection fraction (LVEF) ≤45% in combination with symptoms indicative of heart failure (12). For diastolic heart failure, patients had to have TTE diastolic abnormalities in combination with indicative symptoms and signs of heart failure or indicative symptoms and TTE left ventricular hypertrophy, atrial fibrillation or anginal complaints. We defined four basic TTE patterns of diastolic abnormalities, which were graded I to IV. The mildest form was called an 'abnormal relaxation pattern', or grade I diastolic dysfunction. On the mitral inflow TTE, there was reversal of the normal E/A ratio. Grade II diastolic dysfunction was called 'pseudonormal filling dynamics'. This was considered moderate diastolic dysfunction and associated with elevated left atrial filling pressures. Grade III diastolic dysfunction patients demonstrated reversal of their diastolic abnormalities when they performed the Valsalva manoeuver. This was referred to as 'reversible restrictive diastolic dysfunction'. Grade IV diastolic dysfunction patients did not demonstrate reversibility of their TTE abnormalities, and therefore were said to suffer from 'fixed restrictive diastolic dysfunction'. Patients who had moderate-to-severe mitral or aortic stenosis/insufficiency were termed to have valvular heart disease. Right-sided heart failure was defined as right ventricular hypertrophy and dilatation secondary to pulmonary arterial hypertension caused by lung diseases. Pulmonary artery systolic pressure was estimated from the peak tricuspid regurgitation jet velocities. PH was defined in this study as systolic pulmonary artery pressure (sPAP) ≥40 mmHg based on criteria established by the World Health Organization Symposium on Primary Pulmonary Hypertension (1998). Patients were also divided into five groups according to heart diseases: no obvious heart disease, systolic heart failure, diastolic heart failure, valvular heart disease, and right-sided heart failure.

Chi-square test was used for comparison of discrete variables and analysis of variance (ANOVA) test was used for comparison of continuous variables. Whenever the difference was found to be statistically significant, Tukey's honestly significant difference (HSD) test was used to test pairwise comparisons. If the data were not normally distributed (for continuous variables), one-way Kruskal-Wallis analysis of variance test was used instead of ANOVA. Whenever differences were statistically significant, Mann-Whitney U test (with Bonferroni correction) was used.

Results

The study included 250 patients with chronic dyspnoea, with a mean age of 59.4±13.2 years. The female-male ratio was 1.0 (51% female). Cigarette smoking was recorded in approximately 9% of female patients with chronic dyspnoea, whereas approximately 90% of male patients with this symptom had a history of cigarette smoking.

As shown in Table 1, approximately 83% of the patients had a diagnosis of heart and/or lung disease, while the remaining approximately 17% did not have any obvious lung or heart disease. There was a statistically significant difference between lung and heart diseases (χ^2=46.135, p=0.0001). Ninety-five (38%) of the 250 patients with chronic dyspnoea had lung and heart diseases concomitantly. Diastolic heart failure was the most common heart disease seen with COPD or asthma. One hundred and forty-eight (59.2%) of the 250 patients had a lung disease. The most common causes of chronic dyspnoea resulting from lung diseases were COPD and asthma. One hundred and fifty-five (62%) of the 250 patients had a heart disease, with diastolic heart failure being the most common.

The characteristics of patients according to lung and heart diseases are shown in Tables 2 and 3. The characteristics were somewhat different among the four lung disease groups. While male gender was more prevalent in the COPD group, female gender was

Table 1. Distribution of lung diseases according to heart diseases

		No obvious heart disease	Heart diseases Systolic heart failure	Diastolic heart failure	Valvular heart disease	Right-sided heart failure	Total
	No obvious lung disease n (%)	42 (41.2)	19 (18.6)	30 (29.4)	11 (10.8)	0 (0.0)	102 (100.0)
	COPD n (%)	15 (25.4)	7 (11.9)	23 (39.0)	7 (11.9)	7 (11.9)	59 (100.0)
	Asthma n (%)	30 (45.5)	4 (6.1)	22 (33.3)	6 (9.1)	4 (6.1)	66 (100.0)
	Other lung n (%) diseases	8 (34.8)	0 (0.0)	5 (21.7)	2 (8.7)	8 (34.8)	23 (100.0)
	Total n (%)	95 (100.0)	30 (100.0)	80 (100.0)	26 (100.0)	19 (100.0)	250 (100.0)
Lung diseases		**No obvious heart disease**	**Any heart disease**				**Total**
	No obvious lung disease n (%)	42 (41.2)	60 (58.8)				102 (100.0)
	Any lung disease n (%)	53 (35.8)	95 (64.2)				148 (100.0)
	Total n (%)	95 (100.0)	155 (100)				250 (100.0)

X^2 = 46.135, p=0.0001

Table 2. Characteristics of patients according to lung diseases

		Lung diseases No obvious lung disease		COPD		Asthma		Other lung diseases		$\chi 2$	p	F	P
		N	%	n	%	n	%	n	%				
Gender	Female	55	43.3	10	7.9	44	34.6	18	14.2	41.035	0.001	-	-
	Male	47	38.2	49	39.8	22	17.9	5	4.1				
Smoking History	No	70	47.0	12	8.1	48	32.2	19	12.8	51.003	0.0001	-	-
	Yes	32	31.7	47	46.5	18	17.8	4	4.0				
		Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**				
FEV_1		95.8	21.6	60.7	24.7	75.5	23.3	69.3	25.0	-	-	26.917	0.0001
FVC		97.6	20.2	76.5	25.5	87.7	18.1	72.2	25.8	-	-	13.578	0.0001
FEV_1/FVC		81.3	6.9	61.5	11.0	71.8	11.3	80.8	14.5	88.840	0.0001	-	-
Age		58.0	13.5	65.0	9.7	55.6	13.5	61.7	14.4	-	-	6.324	0.0001

Table 3. Characteristics of patients according to heart diseases

		Heart diseases No obvious heart disease		Systolic heart failure		Diastolic heart failure		Valvular heart diseases		Right-sided heart failure		$\chi 2$	p	F	P
		n	%	n	%	n	%	n	%	n	%				
Gender	Female	53	41.7	10	7.9	43	33.9	14	11.0	7	5.5	6.464	0.617	-	-
	Male	42	34.1	20	16.3	37	30.1	12	9.8	12	9.8				
Smoking History	No	62	41.6	16	10.7	44	29.5	19	12.8	8	5.4	6.834	0.145	-	-
	Yes	33	32.7	13.9	5.6	35.6	14.4	7	6.9	11	10.9				
		Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**				
FEV_1		87.4	27.5	69.9	20.2	76.5	26.5	80.8	23.3	70.0	31.8	-	-	3.508	0.009
FVC		94.0	23.3	79.4	20.0	86.0	21.4	87.0	19.0	79.3	31.8	-	-	3.165	0.015
FEV_1/FVC		76.8	12.1	71.7	11.5	72.0	13.4	75.2	11.6	70.4	13.4	-	-	2.077	0.085
Age		52.9	13.6	60.4	8.7	65.7	9.6	63.2	12.9	58.1	15.9	42.472	0.0001	-	-

more prevalent in the asthma group. Patients with COPD had a higher prevalence of smoking than those with asthma. There was a statistically significant difference between the COPD and asthma groups in terms of FEV_1, FVC, FEV_1/FVC, and age. Patients with COPD had a lower FEV_1 (p=0.007), FVC (p=0.039), and FEV_1/FVC (z=-4.867 p=0.001), and were significantly older (p=0.0001) than patients with asthma. There were no statistically significant differences among the five heart disease groups with respect to gender, history of smoking, and FEV_1/FVC. There was a statistically significant difference between the systolic heart failure group and the no obvious heart disease group in terms of FEV_1 (p=0.031) and FVC (p=0.04); the systolic heart failure group had a lower FEV_1 and FVC than the no obvious heart disease group. There were statistically significant differences between the no obvious heart disease group, systolic heart failure group (z=-2.938, p=0.003), diastolic heart failure group (z=-6.335, p=0.0001), and valvular heart disease group (z=-3.090, p=0.002) in terms of age. Patients in the heart failure and valvular heart disease groups, but not in the right-sided heart failure group, were older than patients with no obvious heart disease. Patients in the systolic heart failure group were significantly younger than patients with diastolic heart failure (z=-2.667, p=0.008). When comparing other groups, no significant differences were found. Among patients with heart failure, four had a right-sided heart failure (i.e. cor pulmonale).

Discussion

In patients with chronic dyspnoea, the differentiation of heart and lung causes is essential for proper management. In some patients, this may be difficult based on clinical evaluation alone. Pratter et al. reported that objective testing was more accurate than clinical impression alone (the cause of dyspnoea identified in 100% vs. 66%) (6). This is the first study to evaluate lung and heart disease causes of chronic dyspnoea when it is unclear whether the chronic dyspnoea is of heart and/or lung origin. Furthermore, this study included only patients with chronic dyspnoea and evaluated the presence of both heart and lung disease in the same patient group. It appears important to point out that in this study, more than one-third of all patients had coexisting lung and heart disease. We believe that the coexistence of chronic lung and heart disease in patients with chronic dyspnoea remains frequently unrecognised.

Our results suggest that in patients with chronic dyspnoea, diastolic heart failure often coexists with COPD and asthma. While these obstructive lung diseases were frequently complicated by the development of left-sided heart failure, right-sided heart failure was rare in this condition. Actually, COPD and asthma may lead to left ventricular dysfunction and heart failure. However, studies on the prevalence of left ventricular dysfunction in COPD and asthma patients, or vice versa, are scarce. Elderly patients with coexisting COPD and chronic heart failure are hospitalised more frequently and are at a greater risk of death than age-matched controls with either COPD or chronic heart failure alone (13). We believe that the failure to diagnose lung and heart disease may be deleterious if this results in misguided therapy.

It is well known that asthma and COPD are the most common chronic lung diseases in developed and developing countries. Not surprisingly, these obstructive lung diseases were implicated in half of our patients presenting with chronic dyspnoea. We included interstitial lung disease (ILD) in the 'other lung diseases' group, as the frequency of patients with ILD was much lower than that of patients with COPD and asthma. There are no data in the medical literature with which to compare our results. A previous study reported that the most common causes of dyspnoea were asthma, COPD, and ILD in an unselected patient population (29%, 14%, and 14%, respectively) (6). In other studies of patients with chronic dyspnoea that was unexplained despite a basic evaluation, the most common pulmonary cause was asthma/hyperactive airways disease. These studies are not directly comparable with ours because they excluded COPD and recognised asthma easily as determined by spirometry (7, 14). Interestingly, in our study population, more than half of the patients with COPD and asthma who presented with chronic dyspnoea had a cardiac cause of this symptom.

In this study, about 60% of all patients had a cardiac cause on TTE. As previous investigators performed TTE in selected patients – only in patients with clinical suspicion of heart failure, they found a lower rate of cardiac causes compared with our study (6,7). Diastolic heart failure was the most common cardiac cause that led to chronic dyspnoea. This result is not surprising, since dyspnoea is the most common manifestation of diastolic dysfunction (15). Compared with right-sided heart failure, systolic and diastolic heart failure occurred more often. In fact, some have suggested that under-diagnosed heart failure among the patients with chronic dyspnoea may be high; however, until now, there have been no studies to quantify this prevalence.

COPD and asthma were the most common causes of an obstructive spirometry pattern. Not unexpectedly, while patients with asthma had a mild obstructive pattern and those with COPD had a moderate or severe obstructive pattern on spirometry, interestingly, they all sensed dyspnoea (16). Patients with chronic, predominantly non-valvular, congestive heart failure frequently exhibit a restrictive pattern on spirometry due to an enlarged heart size, increased intrathoracic fluids, and impaired inspiratory muscle strength (17). While restrictive defect may be seen in patients with heart failure, significant airflow obstruction is more likely to occur in the latter (18). Airway obstruction can occur during congestive heart failure through various mechanisms and with varying degrees of severity. Our patients with systolic heart failure had a lower FEV_1 and FVC than patients with no obvious heart disease; i.e., they had a restrictive defect. Patients in the heart failure and valvular heart disease groups, but not in the right-sided heart failure group, were slightly older than patients with no obvious heart disease. We know that heart failure is the more common form in the elderly and is expected to increase as the population ages (19). Patients with systolic heart failure were younger than patients with diastolic heart failure. Advanced age can be associated with increased extracellular matrix fibrillar collagen content and abnormal diastolic function (20). However, the mechanisms that underlie diastolic dysfunction are not well understood.

Study Limitations

This study has several inherent limitations. Because it is a retrospective review of a prescreened population, the results may be skewed by selection bias and should not be extended to unselected patients without considering this constraint. However, the hard cri-

teria used for the diagnosis of COPD, asthma, and chronic heart failure, and our detailed review of the spirometry and TTE reports for the same period provide a solid basis for our findings. In this study, we focused on the most common causes of chronic dyspnoea among heart and lung diseases. Chronic dyspnoea most often has a cardiac and/or pulmonary aetiology, although occasionally other causes, such as anaemia, acidosis or neuromuscular diseases, must be considered. We do agree that a prospective analysis might shed light on referral patterns, test selection, and the influence of policies on healthcare practice.

Conclusion

A better understanding of the causes of dyspnoea can potentially reduce morbidity and mortality. In some patients, it may be difficult to decide whether dyspnoea is secondary to heart or lung disease. Our results showed that when it was unclear whether the chronic dyspnoea was of heart and/or lung origin based on clinical evaluation, more than one-third of the patients with chronic dyspnoea were shown to have coexisting lung and heart disease.

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