

Right heart haemodynamic values and respiratory function test parameters in chronic smokers

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القيم الدينامية الدموية في القلب الأيمن ومتابحات اختبارات الوظيفة التنفسية لدى المدخنين المزمنين
مورات غول باران، تولين كاغاتاي، توفيق غومر، بني كاغاتاي

الخلاصة: أخذت قياسات الوظيفة القلبية أثناء إجراء تصوير الأوعية الإكليلية لدى 24 من المدخنين المزمنين المصابين بمرض القلب الإكليلي، ثم ربطت مع اختبارات الوظيفة التنفسية. وقد كان لدى 14 من المرضى بيانات على مرض رئوي انسدادى مزمن، وكان لنتاج القلب ارتباط مباشر مع السعة الحيوية، ومع السعة الحيوية القسرية، ومع الحجم الزفيري القسري في الثانية الأولى ومع سرعة الجريان للهواء في 25% من السعة الحيوية القسرية. وكانت مقاومة الشريان الرئوي ذات علاقة سلبية مع حصيللة النسبة بين الحجم الزفيري القسري في الثانية الأولى والسعة الحيوية القسرية، كما كان إشباع الأكسجين في الشريان الرئوي ذا علاقة ضعيفة مع مقاومة الشريان الرئوي وذا علاقة متوسطة مع الضغوط في الأذين الأيمن وفي البطين الأيمن. إن التشخيص الباكر والمعالجة الباكرة للمرض الرئوي الانسدادي المزمن لدى المدخنين ممكنان بدون اللجوء إلى طرائق باضعة.

ABSTRACT During coronary angiography in 24 chronic smokers with coronary heart disease, cardiac function measurements were taken and correlated with respiratory function tests. Fourteen patients had evidence of chronic obstructive pulmonary disease. Cardiac output had a direct correlation with vital capacity, forced vital capacity (FVC), forced expiratory volume in 1 s (FEV₁), and velocity at 25% of FVC (Vmax25). Pulmonary artery resistance was inversely correlated with FEV₁/FVC, while pulmonary artery oxygen saturation weakly correlated with FEV₁ and Vmax25. The pulmonary artery pressure had a weak correlation with the pulmonary artery resistance and an intermediate correlation with the right atrium and the right ventricular pressures. Early diagnosis and therapy of chronic obstructive pulmonary disease in smokers may be possible without using invasive methods.

Valeurs hémodynamiques du cœur droit et paramètres du test de la fonction respiratoire chez des fumeurs chroniques

RESUME Lors d'une angiographie coronaire réalisée chez 24 fumeurs chroniques atteints de coronaropathie, des mesures de la fonction cardiaque ont été effectuées et corrélées aux tests de la fonction respiratoire. Quatorze patients présentaient des signes de maladie pulmonaire obstructive chronique. Le débit cardiaque avait une corrélation directe avec la capacité vitale, la capacité vitale forcée (CVF), le volume expiratoire maximum/seconde (VEMS) et le débit expiratoire maximum à 25 % de la capacité vitale forcée (Vmax25). La résistance artérielle pulmonaire était inversement corrélée au rapport de Tiffeneau (VEMS/CVF), tandis que la saturation en oxygène du sang artériel au niveau de l'artère pulmonaire était faiblement corrélée au VEMS et au Vmax25. La pression artérielle pulmonaire était faiblement corrélée à la résistance artérielle pulmonaire et il y avait une corrélation moyenne avec les pressions de l'oreillette droite et du ventricule droit. Le diagnostic précoce et le traitement rapide de la maladie pulmonaire obstructive chronique chez les fumeurs peuvent être possibles sans avoir recours à des méthodes invasives.

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Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by chronic impediment of air circulation in the lungs, which usually has a slow progression and is mostly irreversible. COPD is a complex condition, influenced by multiple genetic and environmental risk factors [1,2].

Smoking is one of the most common environmental causes of COPD; it increases 10-fold the risk for the disease compared with non-smokers. The dose-response relationship between cigarette smoking and pulmonary function is well-established [1]. Respiratory function tests rapidly worsen over time in smokers. The adverse effect of smoking primarily works by attacking the larger airways and then the small arterioles. The diagnosis of COPD is then easily made after these changes have become irreversible and airways obstruction has occurred [1].

COPD is a major cause of morbidity and mortality worldwide. Thus, early diagnosis and cure of the disease is very important. The gradual increase of airways resistance causes some changes in pulmonary haemodynamics, such as pulmonary hypertension and pathological changes in the right heart. The pulmonary vasoconstriction and hypertension that occurs through alveolar hypoxia leads to deterioration of right heart function. Alveolar hypoxia does not need to be continuous; right ventricular hypertrophy develops with as little as 2 hours a day of hypoxia and abnormal pulmonary haemodynamics have been reported in patients with only nocturnal oxyhaemoglobin desaturation secondary to sleep apnoea [3].

COPD is defined by a reduction of the maximal expiratory flow rate that is progressive and irreversible. Intermediate or high level COPD is determined through the forced expiratory volume in the first sec-

ond (FEV_1). Dividing FEV_1 by the forced vital capacity (FVC) is a sensitive test for mild-degree COPD [1].

Pulmonary hypertension is the most important factor in determining the prognosis of patients with COPD and the measurement is most accurately made during right-heart catheterization [4]. In COPD patients, the right ventricular ejection fraction (RVEF) is often reduced [5]. COPD, combined with deterioration of right ventricular function and pulmonary hypertension, limits peripheral oxygen utilization, reduces exercise capability and increases mortality [6]. Thus, it is necessary to recognize and control pulmonary hypertension as early as possible. The structural and functional adaptations of the right ventricle to the increases in afterload posed by disorders of the respiratory system are commonly referred to as cor pulmonale.

Detailed history taking, physical and X-ray examinations and electrocardiography may be helpful in diagnosing pulmonary hypertension and cor pulmonale, but due to anatomical differences of the thoracic structure it is not always possible to obtain accurate results. In addition, specific examinations such as arterial blood gas measurements, echocardiography, angiography and right-heart catheterization should be undertaken [1,7].

The aim of the study was to investigate whether pulmonary function tests can predict right heart pressure without the need to perform catheterization. It is hoped this will lead to better early diagnosis of deterioration in pulmonary function as well as haemodynamic functions caused by chronic smoking.

Methods

The study was carried out in the Institute of Cardiology of the Cerrahpasa Medical

Faculty at the University of Istanbul. The participants were 24 patients (3 women and 21 men) with known coronary heart disease who were referred for coronary angiography between February and May of 2002. Considering the risk and the cost of the catheterization procedure, we only intervened in patients who were chronic smokers and in need of cardiac catheterization for their coronary problems.

The evaluation of COPD was made by the Department of Bronchopneumology. COPD was evaluated in the patients through detailed history, clinical examinations, chest X-ray and pulmonary function tests. Pulmonary function tests were undertaken with a computerized spirometer (Vitalograph). The following were calculated: peak expiratory flow rate (PEF), vital capacity (VC), FVC, FEV₁, and flow rates at 25%, 50% and 75% lung of FVC (Vmax25, Vmax50 and Vmax75).

After obtaining informed consent from the patients, right-heart catheterization was performed with a 6 F (French) multipurpose catheter via the vena femoralis using the vacuum puncture method. The pressure was measured via liquid filled pressure monitoring sets with an external pressure transducer. Left heart as well as right heart pressures were taken. The following were measured: pulmonary artery pressure (PAP), pulmonary artery resistance (PAR), pulmonary capillary wedge pressure (PCWP), right atrium pressure (RAP) and right ventricle pressure (RVP).

For measurement of arterial partial oxygen pressure (PaO₂) and haemoglobin levels, blood samples (2 mL) were taken from the main pulmonary artery and the aorta using heparinized syringes. PaO₂ was measured through a gas analyser, which calculates oxygen saturation using the Severinghaus equation. The procedure was terminated after removal of the arterial and

venous sheaths and after control of bleeding.

The respiratory function data was linked to the data obtained through catheterization. Cardiac output (CO) was calculated with the direct Fick method [8] and then placed in the PAR formula [9]. The normal range for PAR was taken as 0.9 ± 0.38 mmHg min/L for the 30–49 years age group and 1.0 ± 0.5 mmHg min/L for those aged over 49 years [10].

Statistical evaluation of the data was performed using Pearson correlation and regression analysis.

Results

The mean \pm SD age of the participants was 52.1 ± 10.7 years. All the patients were chronic smokers; 21 had smoked a packet of cigarettes (20 singles) daily for more than 15 years and 3 had smoked a packet daily for about 11–14 years. Of the 24 patients, 14 were diagnosed with mild COPD; none were in the acute exacerbation phase of their disease and none had any cardiac valve disease. The remaining 10 patients did not meet the COPD criteria. Haemoglobin values for the group were 13–16 g/dL (mean 14.1 g/dL).

Cardiac output showed significant ($P < 0.05$) direct correlations with VC ($r = 0.50$), FVC ($r = 0.50$), FEV₁ ($r = 0.47$), Vmax25 ($r = 0.45$), Vmax50 ($r = 0.48$) and PEF ($r = 0.47$).

A weak and direct correlation was found between PAP and PAR ($r = 0.44$, $P < 0.05$). A strong and direct correlation was found between PAP and PCWP ($r = 0.84$, $P < 0.05$), and a medium and direct correlation between PAP and RAP ($r = 0.68$, $P < 0.05$) and RVP ($r = 0.65$, $P < 0.05$) (Table 1).

Table 1 Correlations of cardiac and respiratory function parameters in 24 patients with chronic obstructive pulmonary disease

Parameters compared	Correlation <i>r</i>	<i>P</i> -value
CO and FEV ₁	0.48	<0.05
CO and PEF	0.47	<0.05
CO and VC	0.50	<0.05
CO and FVC	0.50	<0.05
CO and Vmax25	0.45	<0.05
CO and Vmax50	0.48	<0.05
CO and PAR	-0.46	<0.05
PAP and PAR	0.44	<0.05
PAP and PCWP	0.84	<0.05
PAP and RAP	0.68	<0.05
PAP and RVP	0.65	<0.05

CO = cardiac output; FEV₁ = forced expiratory volume in 1 second; PEF = peak expiratory flow rate; Vmax25 = 25% of forced vital capacity; Vmax50 = 50% of forced vital capacity; PAP = pulmonary artery pressure; PAR = pulmonary artery resistance; PCWP = pulmonary capillary wedge pressure; RAP = right atrium pressure; RVP = right ventricle pressure.

There was a very weak and direct correlation between PaO₂ and Vmax25 ($r = 0.40$, $P < 0.05$) and FEV₁ ($r = 0.37$, $P < 0.05$).

A very weak and inverse correlation was found in all patients between PAR and the FEV₁/FVC ratio ($r = -0.35$, $P < 0.05$). In the COPD group of 14 patients, there was a medium strong inverse correlation between PAR and FEV₁/FVC ($r = -0.54$, $P < 0.05$).

Discussion

The pulmonary circulation is a dynamic system that is affected by mechanical, neural and biochemical factors. Beginning

from the response of the pulmonary circulation to these stimuli, researchers are attempting to reverse pulmonary hypertension. Oxygen inhalation, acetylcholine and tolazoline infusions have been tested for their ability to overcome the reflex pulmonary vasoconstriction. A serious pulmonary vasoconstriction may develop in elderly COPD patients with left heart insufficiency due to alveolar hypoventilation and the resultant hypoxia. Inhalation of 100% oxygen in these patients causes PAP and vascular resistance to drop [1].

In this study, we determined oxygen saturation of the aorta and the pulmonary artery as well as PCWP, PAP, RVP and RAP, cardiac output and especially PAR. PAR gives the resistance pressures of the main pulmonary artery, the arterioles and the precapillary and pulmonary capillary beds. In comparison with PAP, PAR is a better way to determine the presence and the severity of pulmonary vascular disease [11]. We therefore investigated the relation between PAR and the pulmonary function test parameters, and revealed that there was an inverse correlation between PAR and FEV₁/FVC.

In the study of Wolf et al. with krypton-81m perfusion, the RVEF was investigated in COPD patients and in healthy individuals [12]. The RVEF was distinctly low in COPD patients and there was a linear inverse correlation between PAP and RVEF. In COPD patients with pulmonary hypertension, RVEF was clearly lower than in COPD patients without pulmonary hypertension. Concerning RVEF, they again found a weak positive correlation with the PaO₂ and FEV₁, but no correlation with partial CO₂ pressure, pulmonary hypertension or FEV₁/FVC.

The data of Wright et al. show that PAP and pulmonary artery wedge pressures and cardiac output were normal at rest [13].

However, patients with more severe disease showed greater increases in PAP and pulmonary artery wedge pressures with exercise than did patients with minimal or no disease. Oxygen breathing had no effect at rest but it lowered PAP and PCWP during exercise in the patients with more severe disease. Histological studies showed that patients with moderate obstructive lung disease have structural changes in the pulmonary arteries consistent with pulmonary hypertension when compared with patients with minimal or no disease. Zhang et al. showed that exercise testing can identify the early phase of latent pulmonary hypertension and that in cor pulmonale patients PAP rises after exercise [14].

The criteria for pulmonary hypertension are a mean PAP greater than 20 mmHg resting and greater than 30 mmHg on exercise. The RVP increase cannot be determined for these criteria. PAR is more sensitive in showing the right ventricular load in conjunction with PAP [9]. In 14 of our patients, PAP was greater than 20 mmHg. There was a direct correlation between PAR and PAP.

According to the Fick formula, cardiac output is equal to the right ventricular flow, assuming that there are no intracardiac shunts [8]. It is thus useful to note that we found a direct correlation between cardiac output and FEV₁, PEF, VC, FVC and the Vmax25. As COPD develops, the parameters above and the right ventricular output deteriorate. Furthermore, it seems consistent that there is an inverse correlation between the cardiac output and PAR and a direct correlation between the PAP and the PCWP and the RAP as well. PEF is a useful measure of pulmonary health status. In a study of van Helden et al., a trend towards reduced peak flow was already evident in teenagers who smoked and whose parents were smoking [15]. In a similar study, the

results showed that, even for younger people, cigarette smoking is associated with significant detrimental effects on cardiopulmonary function and exercise tolerance. Objective evidence of an effect of smoking on cardiopulmonary function and exercise tolerance in this age group may assist educators and health care professionals in convincing teenagers to quit smoking [16].

Pulmonary function testing, at least the measurement of FEV₁, in all middle-aged smokers has been recommended. The smokers with abnormal FEV₁ should be advised to quit smoking [17]. Further investigations are needed to understand the relationship of oxygen saturation to Vmax25 and FEV₁ values, although we found a correlation between these parameters and PaO₂.

Finally, we could have obtained results that are more reliable if we had focused on COPD patients and compared their right heart pressures according to disease severity. Our study evaluated right heart function for patients who primarily came for coronary angiography and then we looked for COPD. Since we had no severe COPD patients, right heart function did not show deterioration. Invasive diagnostic procedures are usually unnecessary if non-invasive studies indicate mild to moderate pulmonary hypertension in chronically hypoxaemic patients with severe airways obstruction. We should keep in mind that there is an inverse correlation between the FEV₁/FVC ratio and PAR, and a direct correlation between the Vmax25 and FEV₁, which are indicators of a mild to moderate degree of COPD. We believe that this approach may be useful for estimating deterioration of right heart parameters without using invasive methods and thus improving the early diagnosis and therapy of chronic obstructive pulmonary disease in smokers.

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