

The structure of risk factors of cardiovascular disease and chronic kidney disease in patients with chronic obstructive pulmonary disease

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Summary

Objective

To determine the frequency of risk factors of cardiovascular disease (CVD RF) and chronic kidney disease (CKD) among the patients with chronic obstructive pulmonary disease (COPD).

Materials and methods

We examined 300 patients of the Regional clinical hospital №2 with verified diagnosis of COPD I-IV degree of severity according to the GOLD criteria (2011). We studied the frequency of such RF of CVD and CKD: age > 45 years, male gender, arterial hypertension (AH), impaired glucose metabolism, hypercholesterolemia (level greater than 5.0 mmol/L), body mass index (BMI) > 25 kg/m², and the frequency and intensity of smoking, glomerular filtration rate (GFR) calculated with CKD-EPI.

Results

We identified the high frequency RF of CVD: 100% of patients had RF of CVD, 92,6% of patients had a combination of 3 or more FR, lowered GFR < 89 mL/min/1,73 m² was present in 67,3% patients. 96.4% of patients had age over 45 years, 78,8% of patients were older than 65 years; smoking was detected in 92 % of patients with COPD; hypercho-

lesterolemia - in 70,3% of cases; AG - in 65,6%; hyperglycemia - in 17,6%; BMI > 25 kg/m² - in 38% of patients with COPD. The inverse correlation between BMI and severity of COPD ($r = -0,324, p < 0,05$); and the positive correlation of cholesterol levels with age and severity of COPD ($r = 0,241, r = 0,198, p < 0,05$) have been detected.

Conclusions

Patients with COPD demonstrate the summation of "traditional" RF of CVD, that is determined by COPD on the one hand and on the other - by existing renal dysfunction.

Key words

Chronic obstructive pulmonary disease, risk factors, cardiovascular disease, chronic kidney disease.

Introduction

High occurrence of chronic noninfectious diseases (CNID) during last decades has acquired epidemic sizes and became the leading cause of mortality and disability in population thus defining the priorities of healthcare and preventive medicine [1, 2]. Chronic obstructive pulmonary disease (COPD) has a particular position between these diseases. According with the prognosis of "Global burden of disease" study, COPD will take the third position between mortality causes in population, and nowadays it is the only mortality cause with increasing frequency [3]. It can be explained with the high presence of comorbid pathology in COPD, that is related both to the age of patients and the clinical course of COPD, steadily progressing, chronic disease of respiratory system with proved extrapulmonary effects. Hypoxia, sympathoadrenal system activation, chronic inflammation, oxidative stress and developing endothelial dysfunction, caused by COPD, create the conditions for wide spectrum of comorbid pathologies where cardiovascular diseases (CVD) have their particular position [3, 4]. It is proved that CVD mortality risk in COPD is 2-3 times higher and is the cause of death in 50% of mortality cases. At the same time it had been recently established that chronic kidney disease (CKD) is an independent CVD risk factor (RF) and equivalent of coronary heart disease (CHD) [5]. Taking into account common RF of COPD, CKD and CVD and systemic manifestations of COPD, it is possible to consider the presence of kidney dysfunction that increases cardiovascular risk in patients with COPD due to existence of cardiorenal continuum [5, 6]. At the same time, the question of kidney dysfunction occurrence as an independent CVD RF is poorly studied. The aim of this study is to investigate the occurrence of CVD RF, CKD and frequency of kidney dysfunction in patients with COPD.

Materials and methods

This study involved 300 patient with COPD: 70,4% of all patients were males, with average age of 68,51±9,9

years, average duration of disease 20,9±3,2 years, and 29,6% of patients were females with average age of 65,95±10,1 years and average duration of disease 17,2±2,2 years that were admitted to the Regional hospital №2 in Krasnodar for diagnostics and treatment. COPD diagnosis was established according with the GOLD guidelines (2011). Patients were divided into four groups with comparable age according with the COPD degree of severity: 30 patients with I degree COPD (14 females, 16 males), 64 patients with II degree COPD (24 females, 42 males), 135 patients with III degree COPD (25 females, 110 males), 71 patient with IV degree COPD (10 females, 61 males). Average value of forced expiratory volume in 1 second (FEV₁, % of predicted value) in the I group was 85,3±4,3%, in the II group - 66,7±6,2 %, in the III group - 46,1±4,5 %, in the IV group - 26,5±3,67 %. We performed comparative analysis of CVD and CBP RF: age > 45 years, male gender, arterial hypertension (AH), carbohydrate metabolism disorders, hypercholesterolemia - total cholesterol levels (TC) > 5,0 mmol/L, excessive body weight, including obesity - body mass index (BMI) > 25 kg/m² (WHO, 2004), frequency and intensity of smoking - pack-year index [2]. To identify glomerular filtration rate (GFR) impairment we calculated GFR with CKD-EPI formula (2009, with modifications of 2011) [5, 6, 7].

This study was performed according with the standards of good clinical practice and the Declaration of Helsinki principles. The study's protocol was approved by local ethic committee. All patients gave written informed consent before being included into this study.

Exclusion criteria were the following: decompensation of present chronic diseases and renunciation of participation in the study.

Statistical analysis was performed using variation statistics in statistical software "Statistica 7,0". Kolmogorov-Smirnov test was used to test the normality of characteristic's distribution, distribution was considered normal in case of $p > 0,05$. To study statisti-

cal correlation between different observations we used Spearman's rank correlation coefficient. Student's t-test was used for evaluation of differences between two average values in case of normal distribution, in case of not normal distribution we used Mann-Whitney test. The difference was considered significant if p-value was less than 0,05. Data are present as average value (M) ± standard deviation (SD).

Results

According with our results, 100% of COPD patients had CVD RF, and 92,6% of patients had ≥3 RF (Image 1). Majority of patients was older than 45 years (96,4%, n=289) and 78,8% were considered elderly (> 65 years). Smoking was the second most frequent RF (92% of patients, n=289) (table 1). Average amount of pack-year index was 39,9±6,5 pack-year and it had significant correlation with COPD severity ($r=0,262$, $p<0,05$). Relative number of patients of male gender as an unalterable CVD and CKD RF was 70,4%. Pack-year index, occurrence and duration of smoking were significantly higher in men ($p<0,05$).

Hypercholesterolemia was detected in 70,3% of COPD patients when cholesterol levels >5,0 mmol/L was considered liminal. And TC levels higher than target value of 4,5 mmol/L were detected in 89,6% of patients (n=269). Average TC levels was 5,8±1,1 mmol/L. We found direct correlation of TC levels and patients age and COPD severity ($r=0,241$, $r=0,198$, $p<0,05$).

Lowered GFR was found in 67,3% of COPD patients. 37,3% of patients had mild stage of GFR_{CKD-EPI} reduction

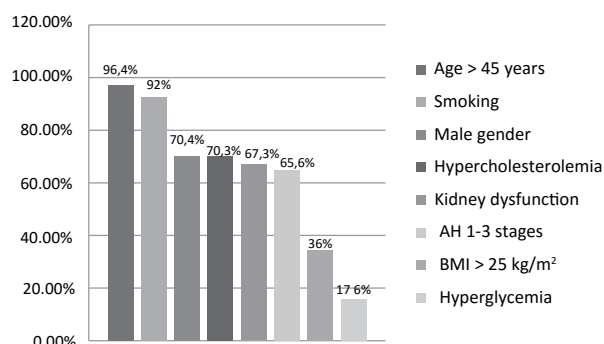


Image 1. CVD RF occurrence in COPD patients

(89-60 mL/min/1,73 m²), 26,7% of patients had moderate GFR_{CKD-EPI} reduction (59-45 mL/min/1,73 m²), 3,3% of patients had prominent GFR_{CKD-EPI} reduction (44-30 mL/min/1,73 m²). Optimal GFR_{CKD-EPI} levels were detected only in 10,7% of COPD patients, hyperfiltration was found in 22% of patients. Together with it, only 28,6% of patients with COPD had hypercreatininemia (creatinine levels > 90 μmol/L), average creatinine levels were around 82,9±22,7 μmol/L.

AH had the six position between RF and it was found in 65,6% of patients. The frequency of concomitant AH was significantly higher in patients with COPD IV severity degree comparing with COPD I severity degree ($p<0,05$), and it had direct correlation with COPD severity degree ($r=0,387$, $p<0,05$) and it had negative correlation with FEV₁ values ($r=-0,362$; $p<0,05$). The frequency of overweight and obesity (BMI > 25 kg/m²) was 36%. We found negative correlation between BMI and COPD severity ($r=-0,324$, $p<0,05$).

Table 1. Clinical and laboratory characteristics of COPD patients

Characteristic	COPD I degree n=30	COPD II degree n=64	COPD III degree n=135	COPD IV degree n=71	Total n=300
Gender male/female	16/14	42/22	110/25	61/10	229/71
Age, years	58,2±12,1	65,1±11,9	69,2±9,2	69,2±9,9	66,3±10,3
Smoking, abs. (%)	26 (86%)	57 (89,1%)	125 (92,6%)	68 (95,7%)	276 (92%)
Pack-year index, «pack-year»	15,3±7,2	28,2±12,35	44,3±9,8**	48,5±12,7***	44,8±19,8
FEV ₁ , % of predicted	85,3±4,3	66,7±6,2	46,1±4,5**	26,5±3,7***	51,5±11,4
BMI, kg/m ²	32,4±7,8	27,9±5,8*	25,1±6,7**	21,2±4,1	26,6±6,1
BMI>25 kg/m ² , abs. (%)	21 (70%)	36 (56,3%)	42 (31,1%)**	15 (21,1%)***	114 (38%)
Creatinine, μmol/L	93,8±21,2	91,2±17,2	82,1±12,5	75,9±16,8	85,7±8,3
TC, mmol/L	5,2±0,9	5,4±0,8	5,5±0,7	5,9±0,9	5,8±1,1
TC>5,0, mmol/L	15 (50%)	39 (60,9%)	95 (70,3%)	62 (87,3%)	211 (70,3%)
GFR, mL/min/1,73 m ²	61,8±18,1	62,9±12,4	69,2±4,3	88,1±6,9	70,2±12,1
DM, IGT, abs. (%)	3 (10%)	8 (12,5%)	22 (16,3%)	22 (26,7%)***	55 (18,3%)
AH I-III st.	12 (40%)	36 (56,25%)	97 (71,8%)	52 (73,2%)***	197 (65,6%)
CHD+AH, abs. (%)	3 (10%)	35 (54,7%)*	104 (77%)**	52 (81,3%)***	144 (48%)

Comment: * — significance of differences between I and II groups; ** — significance of differences between I and III groups; *** — significance of differences between I and IV groups.

Diabetes mellitus (DM) and impaired glucose tolerance (IGT) had 8th rank position, their frequency was 17,6% in total group. We detected significant differences in blood glucose levels between analyzed groups, maximal average values ($7,5\pm 2,3$ mmol/L) were found in IV group.

We analyzed also the frequency of concomitant diseases that have strong influence on COPD patients' prognosis. The AH+CHD combination (64,6% of patients) was more frequently registered in groups of severe and very severe COPD ($\chi^2=19,5$; $p<0,05$), in males significantly more frequently than in females ($\chi^2=12,3$; $p<0,05$). The evidences of myocardial infarction (MI) were present in 16% of patients ($n=48$), MI was significantly more frequent in IV group's patients ($\chi^2=18,5$; $p<0,05$). Cardiac rhythm abnormalities were found in 51 patients (17%) including 25 persons (8,3%) with atrial fibrillation, the frequency of which correlated with the age ($r=0,241$; $p<0,05$) and COPD severity ($r=0,241$; $p<0,05$). Previous pulmonary embolism was reported in 16 (5,3%) of patients, acute arrest of cerebral circulation was reported in 2 patients with COPD.

Discussion

High occurrence of CVD and CKD RF in COPD patients that reaches 100% is expectable because of systemic COPD manifestations [4, 5, 8]. This study demonstrated the prevalence of people above 45 years (96,4%) among these patients that goes along with modern ideas about COPD as the disease of the second half of life [4, 9]. High percentage of male patients (70,4%) is comparable with existing data about higher occurrence of COPD in men [4, 9]. The frequency of smoking in this study was higher than average frequency in population (92% and 70,5% respectively) of comparable age (>40 years) and the results of GATS (Global Adult Tobacco Survey) (39,1%), (Global Adult Tobacco Survey) (39,1%), that was done in 2009 [10]. At the same time, these results go along with the data about smoking frequency in COPD patients that reaches 89,6% [11]. Extremely high frequency of this RF is explained with the fact that smoking, being one of the most aggressive CVD RF, is the most significant etiological factor of COPD [4, 9].

AH occurrence in COPD patients reaches 65,5% and it corresponds results of other studies (34-76%), demonstrating the influence of systemic COPD manifestations on cardiovascular system [4, 9, 12, 13]. High frequency of hypercholesterolemia according with the results of this study (70,3%) can be indirectly

indicate the presence of endothelial dysfunction in majority of COPD patients, developing as the consequence of smoking or chronic inflammation [4, 9]. The occurrence of hypercholesterolemia in healthy able-bodied population of Krasnodar was 51,5% that is evidently lower than its occurrence in COPD patients (70,3%) [14]. The frequency of body overweight and obesity in studied group of patients was 36% with expected minimum of BMI in patients with IV COPD degree ($21,2\pm 4,1$ kg/m²), that is explained with protein and energetic insufficiency in patients with severe and very severe COPD [15, 16]. The highest number of IGT and DM cases was found in patients with IV grade COPD (26,7%), here we identified also the highest average levels of glycemia ($7,5\pm 2,3$ mmol/L). These numbers are slightly lower than the ones found in other studies (46-57%) [17]. The frequency of GFR reduction less than 89 mL/min/1,73 m² (67,3%) in COPD patients is higher than the same characteristic in able-bodied population of Krasnodar (46,1%). Possibly it can be explained with systemic effects of COPD [14].

Conclusions

High prevalence of main CVD and CKD RF in COPD patients was detected in up to 100% of patients, 92,6% of patients have combination of ≥ 3 RF.

Typical cardiovascular RF accumulate during COPD progression and it leads to increased frequency and severity of cardiac pathology in patients with severe and very severe COPD.

Considering the majority of CVD and CKD RF as potentially modifiable, their opportune correction in order to improve cardiovascular prognosis is highly relevant.

Conflict of interest: None declared

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