International Journal of Medical Sciences And Clinical Research

VOLUME Vol.06 Issue04 2026
PAGE NO. 74-77
DOI 10.37547/ijmscr/Volume06Issue04-14

Assessment of Heart Rate Variability with COPD Associated with Pulmonary and Arterial Hypertension

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Received: 02 March 2026; **Accepted:** 28 March 2026; **Published:** 20 April 2026

Abstract: The work analyzed the heart rate variability of patients with chronic obstructive pulmonary disease with arterial and pulmonary hypertension. The degree of COPD and the determination of disease stages were carried out according to the GOLD recommendations (2011–2019), the severity of dyspnea was assessed using the Modified Medical Research Council Dyspnea Scale (mMRC). The study of heart rate variability (HRV) was carried out using a computer complex with registration of a five-minute ECG recording, with interpretation of the results of temporal and spectral analysis of HRV based on the recommendations of the European Society of Cardiology and the North American Society of Cardiopacing and Electrophysiology (ESC/NASPE, 1996).

Keywords: Chronic obstructive pulmonary disease, arterial hypertension, pulmonary hypertension, heart rate variability indicators.

Introduction: Chronic obstructive pulmonary disease (COPD) is a disease characterized by persistent airflow limitation that is usually progressive and results from a chronic inflammatory response of the airways and lung tissue to exposure to inhaled noxious particles or gases. Exacerbations and comorbid conditions are an integral part of the disease and make a significant contribution to the clinical picture and prognosis [2].

COPD is one of the most common chronic non-communicable diseases. Currently, it is the third cause of morbidity and mortality among adults. Despite the uniform nosological form, COPD is at the same time characterized by significant polymorphism of manifestations, which is obviously associated with the comorbidity of this disease. Comorbidity means the presence in a patient of two or more nosological forms at the same time, which are pathogenetically interrelated. One of the most common comorbid conditions in COPD is arterial hypertension (AH), the so-called cardiorespiratory comorbidity. The prevalence of which is estimated above 40%, which modifies the course of COPD and affects the prognosis. The prevalence of comorbidity in COPD is significant - up to 90% [5,6].

In the pathogenesis of COPD and hypertension, there are some common mechanisms of disease development, which are a key link in the cardiovascular continuum. At the same time, the formation of secondary pulmonary arterial hypertension (PAH) with an increase in the load on the right heart and left atrium

leads to a deterioration of coronary reserve, which increases myocardial ischemia of both ventricles and leads to the progression of both coronary and pulmonary insufficiency [1].

The pathogenetic mechanisms of COPD and hypertension with cardiorespiratory comorbidity, accompanied by a mutual burden syndrome, form certain features of the clinical picture due to the commonality of some links in the pathogenesis, leading to a decrease in the effect of treatment and a worsening prognosis of diseases [4].

Purpose of the study. The study of clinical and laboratory characteristics of COPD and hypertension with cardiorespiratory comorbidity.

METHODS

The study included COPD patients with PH (n=28) and COPD patients with PH and hypertension (n=32). Based on the clinical picture (presence of chronic symptoms - cough, sputum, shortness of breath) and indicators of respiratory function (FEV1/FVC ratio, and FEV1 in % of predicted), patients with COPD stage II, suffering from hypertension in combination with PH were included (recommendations ESC/ERS on the diagnosis and treatment of PH (2015) The control group consisted of 18 relatively healthy individuals.

COPD assessment and disease staging were carried out according to GOLD guidelines (2011–2019). The Modified Medical Research Council Dyspnea Scale (mMRC) was used to assess the severity of dyspnea.

To assess the severity of COPD, the CAT test (COPD Assessment Test) was used; the values of the indicators were determined in points.

The study of mean pressure in the pulmonary artery, right and left parts of the heart was carried out using Doppler echocardiography using a Mindray DC-7 ultrasound scanner (China).

The clinical examination included a standard questionnaire (passport data, education, type of work, smoking, physical activity, etc.), medical history and physical examination.

The blood pressure level was determined by measuring blood pressure three times (according to N.S. Korotkov's method) manually using a standard sphygmomanometer on the patient's right and left arms in a sitting position after five minutes of rest. The average result of three measurements with an interval of 3-5 minutes on the arm with a higher blood pressure level was taken into account.

The anthropometric parameters of the study included determination of body weight (BW), height, and calculation of body mass index (BMI). To diagnose obesity, BMI was used, defined as the ratio of body weight in kilograms to the square of height in meters: BMI = weight (kg)/height (m)2.

Determination of biochemical parameters was carried out on a biochemical analyzer "Konelab 30i" (Finland).

A study was carried out on the content of total cholesterol (TC), high-density lipoproteins (HDL), low-density lipoproteins (LDL), very low-density lipoproteins (VLDL), and triglycerides (TG). The studies of biochemical blood parameters also included determination of blood serum glucose levels on an empty stomach and after exercise, urea, creatinine, bilirubin, ALT, AST.

Instrumental research methods included radiography, spirometry, ECG, echocardiography.

The study of the functional state of the ventilation capacity of the lungs was based on measuring the speed indicators of bronchial patency using a microprocessor spirograph "SMP-21/01-"R-D". When assessing the results of spirometry, the following indicators were assessed: FVC, FEV1, FEV1/FVC, total lung capacity (TLC), residual lung volume (RLV).

The modified Medical Research Council Dyspnea Scale (mMRC) was used to quantify the severity of dyspnea.

Cardiological examination included ECG and EchoCG for all patients using Doppler modes on a Vingmed - 800SV device (General Electric, USA) with a sectoral sensor with a scanning frequency of 2.5 MHz. The condition of the cavities and valves of the heart, contractility of the left ventricle, and intracardiac flows were assessed using pulsed Dopplerography and color Doppler mapping.

The study of heart rate variability (HRV) was carried out using a computer complex with the registration of a five-minute ECG recording that did not contain extrasystoles and artifacts. Interpretation of the results of temporal and spectral analysis of HRV was based on the recommendations of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (ESC/NASPE, 1996).

To determine the quantitative assessment, statistical analysis indicators were used:

- SDNN – standard deviation (SD) of the normal R-R (N-N) intervals; CV - coefficient of variation; pNN50% – percentage (proportion) of consecutive N-N intervals, the difference between which does not exceed 50 ms;
- when analyzing HRV, the histogram indicators were used to distribute the values of cardiointervals:

Mo (mode) – the value of the most common duration of R-R cardiointervals (ms); AMo (mode amplitude) – the number of values corresponding to the mode,

which is expressed as a percentage of the total number of cardiointervals (%); MxDMn - variation range or difference between the longest and shortest duration of cardiointervals (ms).

In the spectral analysis of HRV with an assessment of the distribution of the studied oscillations by frequency and power, the following indicators were assessed: TP - the total power of the spectrum of oscillations of the duration of RR intervals in the range of up to 0.4 Hz; HF - power of high-frequency oscillations of the duration of RR intervals in the frequency range 0.15-0.4 Hz; LF - power of low-frequency oscillations of the duration of RR intervals in the range of 0.04-0.15 Hz; VLF is the power of ultra-low frequency oscillations, which are considered in the range from 0.003 to 0.04 Hz. To assess the degree of tension in regulatory systems, the tension index of regulatory systems, the stress index - Si (a.u.) and the centralization index (IC), reflecting the influence of cerebral ergotropic structures, were determined.

To carry out statistical processing of the factual material, the statistical packages Stat Soft Statistica 10.0 (2011) and SPSS Statistic version 23 were used. The material was processed using variational statistical methods by calculating the arithmetic mean (M), its standard deviation (±σ), error (±m). Statistical comparison of mean values between two parallel groups with a normal distribution of the trait was carried out using a two-sided Student's t test at different significance levels (p). Results were considered reliable at $p<0.05$.

RESULTS

A study of the vegetative status of patients with COPD with PH and hypertension revealed significant changes in the sympathetic division of the autonomic nervous system with increased activity of the brainstem center, which regulates vascular tone.

Among COPD patients with PH, a decrease in SDDN to 44.9±2.52 ms was detected compared with the control group - 61.7±4.75 ms, which reflects moderate activation of the sympathetic division of the autonomic nervous system.

COPD patients with PH had a moderate decrease in the spectrum of HF equal to 0.65±0.13 ms ($p<0.05$) and LF - 0.59±0.05 ($p<0.05$) in the frequency range, compared with the values in control group HF - 1.98±0.59 ms ($p<0.05$) and LF - 1.94±0.33, respectively.

Indicators Mo, Amo, MxDMn, reflecting the interaction of the sympathetic and parasympathetic parts of the autonomic system, revealed an increase in the tone of the sympathetic nervous system, which was expressed in a decrease in the value of Mo (823.4 ± 18.23) and MxDMn (349.3 ± 32.0), and the mode amplitude increases significantly (49.01±1.92), compared to the control group 847.9±26.2; 661.1±60.7 and 33.9±2.27, respectively.

Patients suffering from COPD with PH and hypertension had more pronounced changes in terms of increased activity of the sympathetic part of the nervous regulation, so the SDDN indicator was equal to 30.1 ± 0.31 ms compared to the control group, in which SDDN was 61.7 ± 4.75 ms ($p<0.05$), this indicator among COPD patients with PH was 44.9±2.52 ms.

Along with this, COPD patients with PH and hypertension had a significant increase in Amo ($p<0.01$), with a tendency for the MxDMn indicator to decrease by more than 3 times (207.2±1.25), pNN50% - by 9 times (2 .77±0.35), a decrease in the coefficient of variation CV (4.1±0.1) compared to the control group. These data also reflect the increased influence of the sympathetic nervous system.

Indicators of heart rate variability in patients with COPD with PH and hypertension revealed a significant decrease in the total power of the TR spectrum equal to 1.6±0.17 ms ($p<0.01$) and the power of high-frequency oscillations HF - 0.21±0.02 ms ($p< 0.05$) and the power of low-frequency oscillations LF - 0.24±0.05 ($p<0.01$), compared with indicators in the control group (4.46±0.1; 1.98±0.59 and 1.94±0.33, respectively). A decrease in the power of high-frequency HF oscillations by more than 1.5 times among COPD patients with PH and hypertension indicates a decrease in the proportion of the parasympathetic division of autonomic nervous regulation.

The percentage contribution of high-, low- and ultra-low-frequency oscillations to the total spectrum power of COPD patients with PH and hypertension revealed a significant decrease in low-frequency LF oscillations (28.01±0.89%) with a predominance of ultra-low-frequency oscillations (48.4±1.42%) , which indicates activation of the subcortical cardiovascular center.

The stress index SI, indicating the tension of regulatory systems, was significantly increased among patients with COPD with PH and hypertension (SI equal to 174.8 ± 6.0 a.u.) compared to the control group (SI - 70.7 ± 10, 6 USD).

A comparative analysis of heart rate variability, reflecting the state of autonomic nervous regulation, revealed unidirectional changes in the state of regulatory systems among COPD patients of both groups. At the same time, the share of LF frequencies was 35.7±1.31% among COPD with PH and 28.01±0.89% ($p<0.05$) among COPD with PH and hypertension, which is reflected in an increase in the activity of the central regulatory circuit , more

pronounced in COPD with PH and hypertension.

The changes in the spectral parameters of heart rate variability in patients with COPD, determined during the study, showed an increase in the activity of the sympathetic division of the autonomic nervous system, which was more detected among patients with COPD in combination with pulmonary and arterial hypertension, i.e. vascular hypertension in the pulmonary and systemic circulation.

CONCLUSIONS

1. The SDNN indicator, which is an integral indicator of HRV and depends on the influence on the sinus node of the sympathetic and parasympathetic divisions of the autonomic nervous system, revealed increased activity of the sympathetic division of the autonomic nervous system in patients with COPD with PH and hypertension.

2. When stimulated from the receptors of the lungs during their stretching during inspiration, as well as the direct transmission of excitation from the respiratory center to the centers of the vagus nerve, they activate the parasympathetic nervous system, which slows down the heart rate, which is manifested by an increase in the duration of cardio intervals.

3. Indicators Mo, AMo, MxDMn reflecting the interaction of the sympathetic and parasympathetic parts of the autonomic nervous system in the case of increased tone of the sympathetic nervous system, the values of cardio intervals became more uniform, the spread of their values decreased, while the magnitude of the mode in the variation range decreased, and the amplitude of the mode increased.

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