

INDICATORS OF ASSOCIATED PULMONARY-CARDIAC PATHOLOGY IN WORKERS WITH HIGH OCCUPATIONAL RISK

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Keywords:

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ABSTRACT

This study focuses on improving the early diagnosis of cardiovascular pathologies in the context of dust-induced lung diseases, which develop due to exposure to occupational hazards. Analysis of humoral aspects of the defense system makes it possible to establish the specifics of the development of professional pathologies. This process underlies the growth of the effectiveness of diagnostics, the modernization of algorithms for the primary and secondary prevention of pathologies, their prognosis and the reduction of the likelihood of loss of working capacity.

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1. INTRODUCTION

The international health care system emphasizes the prevention of occupational pathologies and the protection of workers who have increased risks of exposure to harmful working conditions. Among the most frequently registered occupational pathologies among people whose work activity occurs in the mining industry, silicosis is considered to be developed due to the effect of fibrogenic dust. Various modern treatment approaches have been widely introduced into clinical practice; however, the incidence of silicosis continues to rise. The prevalence of the disease among workers is 15.7% (in the 35–45 age group), with

one-quarter of affected patients experiencing complete occupational disability. As a result, the World Health Organization (WHO) places particular focus on the prevention of this disease, early symptom detection, diagnostics, and treatment coordination [1- 4].

CVD, of which hypertension and ischemic heart disease are the most frequently registered, occupy the leading positions in terms of mortality and loss of working capacity among people of working age [2].

Even with active preventive measures, the development of professional pathologies of the bronchopulmonary system in mine workers is still highly common. It is worth noting that this group of people also has an increased likelihood of developing CVS pathologies. It should be mentioned that the etiological and pathogenetic mechanisms of CVD development as a professional pathology in miners have not been sufficiently studied. [5], [6].

Among the most important issues is the improvement of algorithms for the prediction and development of cardiovascular system pathologies, taking into account production conditions. The development of effective prognostic methodologies remains a challenge. In this context, this study focuses on assessing the medical and biological health indicators of workers in the mining industry and evaluating the probability of adverse cardiovascular effects resulting from prolonged exposure to fibrogenic dust in the workplace.

Today, one of the most important issues in the field of professional pulmonology is the optimization of early detection of respiratory tract pathologies in the etiology of which lies dust, the aerosol effect of which has a tendency to activate fibrotic processes. The systemic vector of detection of respiratory pathologies in the etiology of which lies the effect of dust, which will ensure early detection of pathology, prognosis of respiratory and circulatory deviations, which will provide an optimal surgical approach to the treatment of cardiopulmonary insufficiency and CHF.

Due to these facts, a personal approach should be used to effectively assess the working conditions in mines. Assessment algorithms should cover the actual working conditions and medical status of employees. It is also worth mentioning that in order to develop effective methods for preventing morbidity, it is necessary to rationally assess the harm of working conditions. [1], [2].

Purpose of the study

To evaluate clinical and functional changes caused by coronary heart disease and hypertension in individuals with silicosis.

2. Materials and methods

A total of 126 patients with stage 1, 2, and 3 silicosis were examined, whose work was carried out in various departments of the Altai State Medical University and who were treated at NIISiHiPZMZRUz. The average age of miners in our study was 39.6 ± 1.2 years; it is worth mentioning that the onset of the pathology occurred at least 10 years ago.

The study included 62 miners with stage 1 silicosis, 37 people with stage 2 and 27 subjects with stage 3.

The final results were compared with a control group, which included 20 healthy workers from the mines under study.

In addition to general clinical and instrumental studies (OAC, OAM, ALT, AST, ECG, bilirubin, FEV, rheoencephalography, EEG, X - ray of the chest), we used a set of algorithms for assessing all possible elements of hemodynamics, which include:

Electrophysiological studies (echocardiography)

- **Biochemical analyses** (lipid profile, arterial pressure, creatine kinase-MB)
- **Molecular markers** such as neutrophil elastase, endothelin-1, and tumor necrosis factor-alpha (TNF- α).

Laboratory and Diagnostic Methods

Laboratory studies were carried out at the Central Clinical and Mathematical Center of the TMA. Enzyme-linked immunosorbent assay (ELISA) was performed on a Rayto analyzer, with reagents for endothelin-1, neutrophil elastase and tumor necrosis factor- α (TNF- α). Blood biochemical spectrum study which affected the study of fat background, creatine kinase, was carried out using HUMAN reagents manufactured in Germany, by means of the Midray analyzer. BS -380.

A total of 146 individuals (126 patients from the main study group and 20 healthy volunteers) underwent echocardiography (EchoCG) using an ultrasound system equipped with a sector transducer operating at a frequency of 4.5–7 MHz. Standard echocardiographic positions were used, and examinations were conducted in the morning with participants lying on their left side and back. To ensure accurate results, participants were advised to avoid intense physical activity and heavy meals the day before and on the day of the study.

The following echocardiographic parameters were recorded:

- Ascending aortic diameter
- Left atrial diameter
- End-diastolic and end-systolic left ventricular dimensions (LVEDD and LVESD, respectively)
- Left ventricular long-axis length
- Left ventricular end-diastolic volume (LVEDV)
- Left ventricular ejection fraction (LVEF)
- Diastolic thickness of the interventricular septum (IVS)
- Diastolic thickness of the posterior wall of the left ventricle (PWLV)
- End-diastolic right ventricular dimension (RVEDD)

Doppler Echocardiography

To assess transpulmonary flow, a left parasternal position was used using a short-axis projection of the LV in the projection of the aortic valve. The maximum blood flow velocity was recorded using pulsed-wave Doppler mode.

For the remaining cardiac valves, Doppler echocardiography was conducted in the apical position, visualizing the valves in four-chamber, five-chamber, and two-chamber projections.

- To determine the maximum systolic velocity of blood flow across the aortic valve, both pulsed-wave and continuous-wave Doppler were utilized.
- For the atrioventricular valves—mitral (MV) and tricuspid (TV)—pulsed-wave Doppler was used, with measurements of the peak early (E-wave) and atrial (A-wave) diastolic filling velocities.

Assessment of Diastolic Myocardial Function

The relaxation capacity of the ventricular heart muscle was evaluated by calculating the ratios of early (E) and atrial (A) ventricular filling in the relaxation phase (E/A). The type of myocardial dysfunction was evaluated based on the Canadian classification of diastole cycle disorders.

- **E/A ratio of 1–2:** indicates optimal relaxation of the heart muscle or the presence of a type 2 diastole disorder. (**pseudonormalization**) in the presence of significant signs of myocardial dysfunction.
- **E/A ratio <1:** Diagnosed as Type 1 diastolic dysfunction (impaired relaxation phase).
- **E/A ratio >2:** Indicative of Type 3 diastolic dysfunction (restrictive filling pattern).

The frequency distribution of diastolic function types among study groups was analyzed.

For transmural blood flow, Doppler echocardiography was performed in the projection of the aortic valve in the left parasternal projection along the short axis of the LV. The maximum blood flow velocity was recorded using pulsed-wave Doppler mode.

For other cardiac valves, Doppler imaging was conducted in the apical position, utilizing four-chamber, five-chamber, and two-chamber projections.

- Maximum systolic velocity across the aortic valve was assessed using both pulsed-wave and

continuous-wave Doppler.

- For the atrioventricular valves (mitral valve [MV] and tricuspid valve [TV]), pulsed-wave Doppler was used to measure early peak velocity (E-wave) and diastolic chamber filling dynamics.

3. Results and Discussion

As the immunological theory of pneumoconiosis states, it is currently accepted to consider that silicosis develops exclusively in the presence of absorption of quartz particles by devourer cells. It has been established that the lifespan of devourer cells is inversely proportional to the toxicity of industrial dust. The death of devourer cells is the main and first step in the formation of silicotic nodules.

Proteolytic enzymes, which include matrix metalloproteinases, elastases neutrophilic type, which are released during the destruction of devourer cells, are the cause of the destruction of lung tissue. The inflammation stage develops simultaneously with recovery, which provokes the formation of mesenchymal cells. Fibrous tissue is also formed due to the uncontrolled formation of vessels and endothelial tissues.

In addition, it has been proven that dust pollution particles have fibrogenic properties and promote the expression of proinflammatory cytokines, among which TNF-alpha and neutrophil are the leaders. elastase in the development of silicosis. It has been shown that elevated levels of TNF- α and neutrophil elastase are characteristic of the immunological profile in silicosis [3], [9], [8], [11], [12].

The analysis of occupational exposure revealed that miners constituted the largest group of patients, making up 28% (Table 1).

Table 1. Distribution of workers diagnosed with silicosis by profession

№	Profession	Number, absolute (abs.)
1	Tunnelers	35
2	Blasters	15
3	Underground mechanics	10
4	Electric locomotive operators	13
5	Drill rig operators	17
6	Support workers	9
7	Haulers	7
8	Underground workers	10
9	Miners	10
	Total:	126

Among the workers examined, the majority were aged 41–50 years, comprising nearly 40% (see Fig. 1).

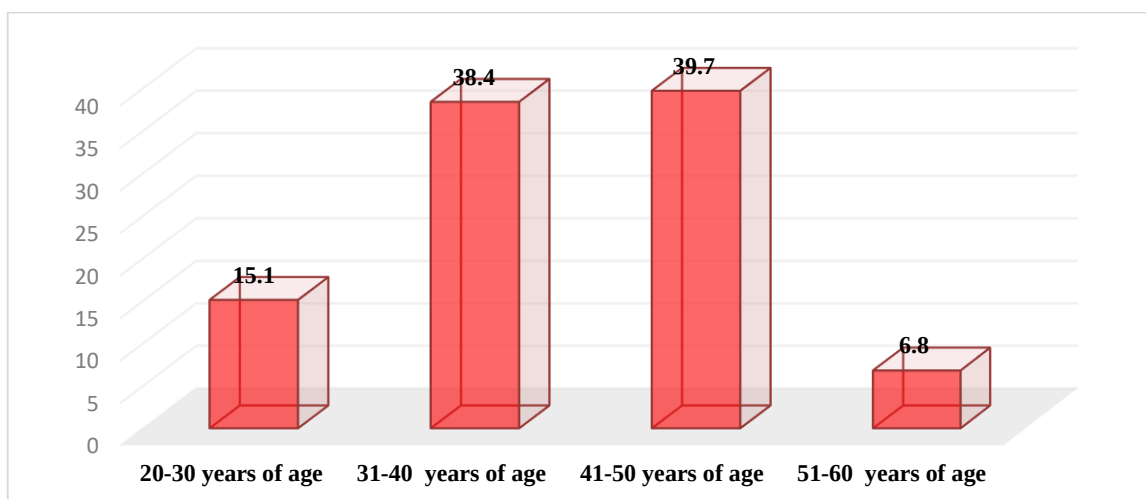


Fig. 1. Age distribution of workers diagnosed with silicosis (%)

Exposure to harmful occupational factors increases the risk of cardiovascular diseases (CVD) by more than twofold (see Fig. 2).

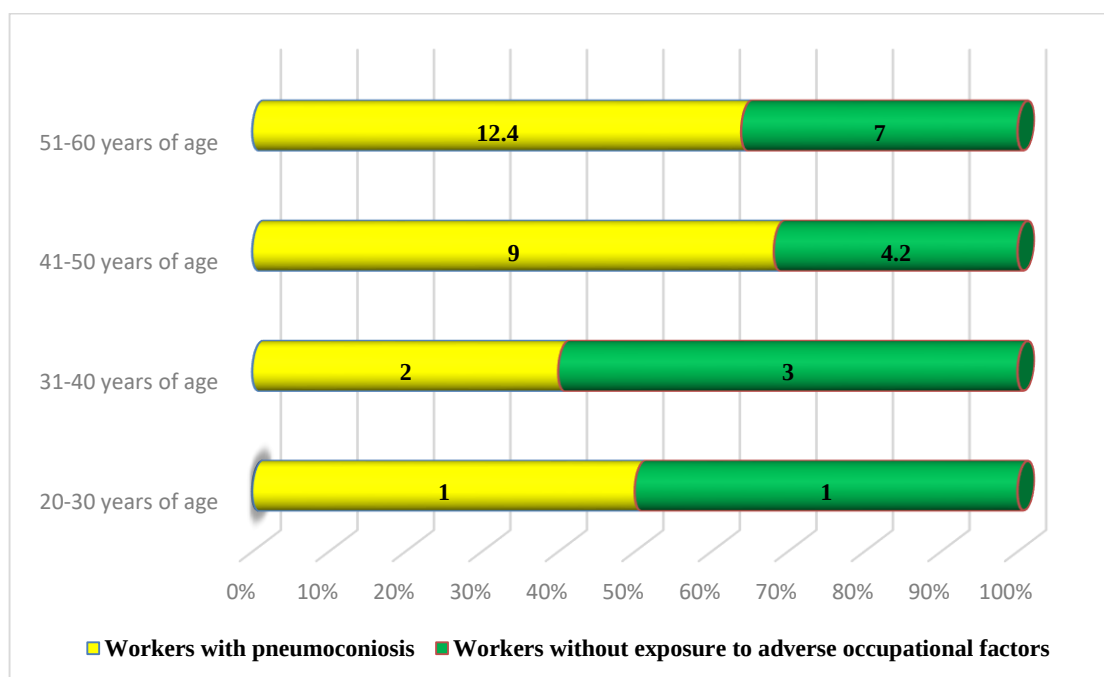


Fig. 2. Prevalence of Cardiovascular Diseases Among Workers With Silicosis and Those Without Exposure to Harmful Occupational Factors (%)

In recent years, CVD pathologies are prone to high frequency and rejuvenation of the covered population. The debut of coronary heart disease and hypertension is often registered in workers who are at least 50 years old. Scientific works prove the high frequency of coronary heart disease development in miners in the age period from 41 to 50 years and with 10 years of work experience, which accounts for 48% of all cases of the disease development. The development of coronary heart disease is positively correlated with age, duration of work, as well as MI and angina. The incidence of hypertension is 69%, which exceeds the prevalence of coronary heart disease by 50% among the number of mine workers of active working age (see Fig. 3).

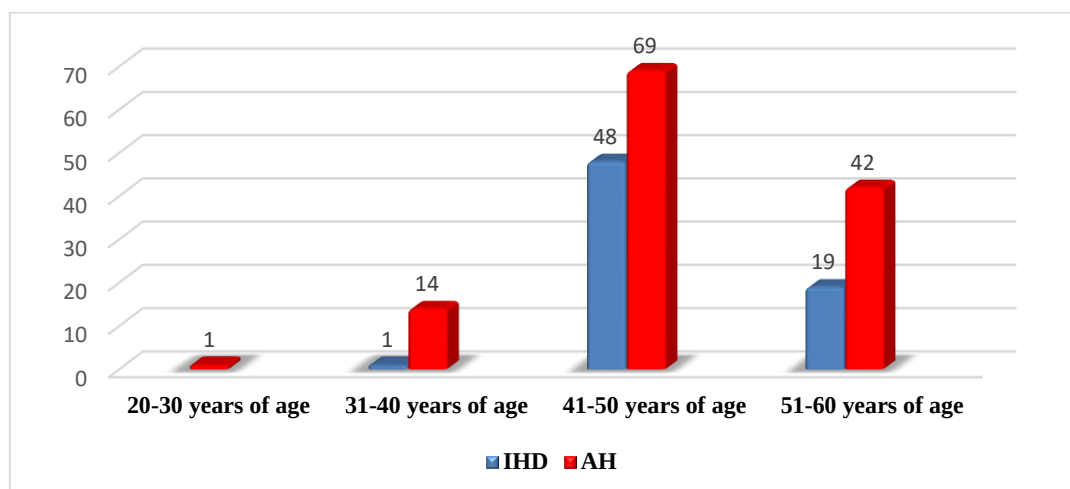


Fig. 3. Distribution of Cardiovascular Disease Patients by Age Group (%)

The presented data prove the frequent development of hypertension and ischemic heart disease among workers of the Almalyk Mining and Processing Plant, which is equal to 40%. It has been proven that hypertension occurs among underground workers from 30 to 39 years of age, which is much more common than among workers on the surface (see Figure 4).

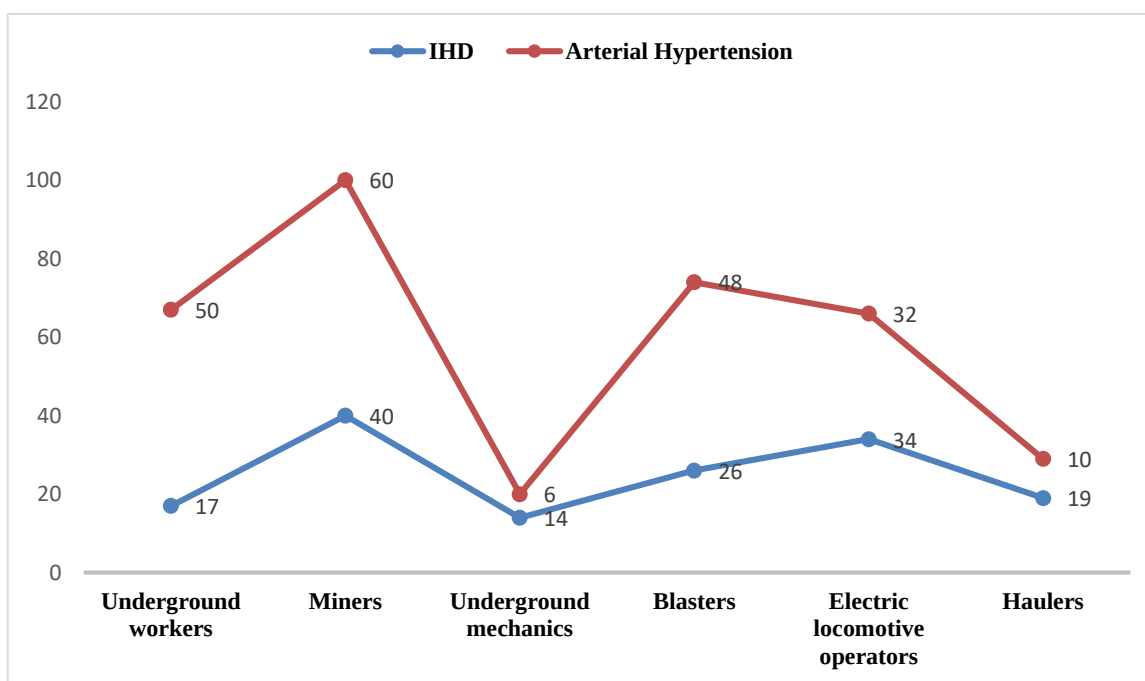


Fig. 4. Distribution of Workers with Diagnosed Ischemic Heart Disease (IHD) and Arterial Hypertension (AH) by Occupation (%)

The clinic of silicosis is burdened with hypertension and CVD pathologies, which leads to disability. During the study of endothelial disorders in patients with CHD and AH silicosis, high values of markers of endothelial damage, including endothelin1, TNF-a, etc., were found (see Fig. 5).

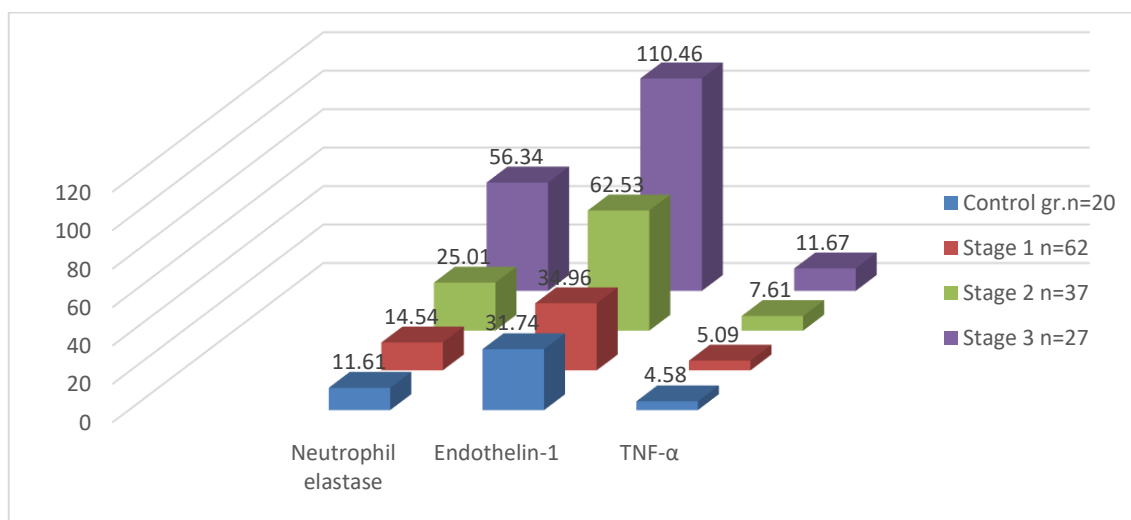


Fig. 5. Indicators of Endothelial Dysfunction in Patients with Silicosis Combined with Ischemic Heart Disease (IHD) and Arterial Hypertension (AH) (pg)

Note: $P < 0.05$; * - compared to the control group.

In individuals with silicosis and hypertension, a high concentration of endothelin1 is detected, which indicates deviations in the vasoconstrictor activity of the vascular bed. An increase in this marker, as well as TNF- α in this group of individuals, proves damage to the vascular endothelium. These criteria indicate the release of proteases that destroy the vascular endothelium and express local inflammatory processes with the formation of a fibrous layer and, as a result, reducing the elasticity of the vessels, which leads to an increase in the risk of developing cardiovascular pathologies [7], [8].

The study of neutrophil elastase plays a crucial role in the development of respiratory diseases, particularly in silicosis caused by exposure to silica-containing dust. Neutrophil elastase serves as a marker of lung fibrosis, and its detection in the bloodstream enables the early diagnosis of fibrotic processes in lung tissue, helping to prevent severe complications of the disease [9], [10].

Analysis of lipid metabolism disorders in patients with silicosis in combination with coronary heart disease and hypertension revealed a significant increase in the concentration of fats, creatine kinase, TC, TG, LDL-C, VLDL-C, AI, and the creatine kinase-MB fraction (CK-MB) ($P < 0.05$) (see Fig. 6).

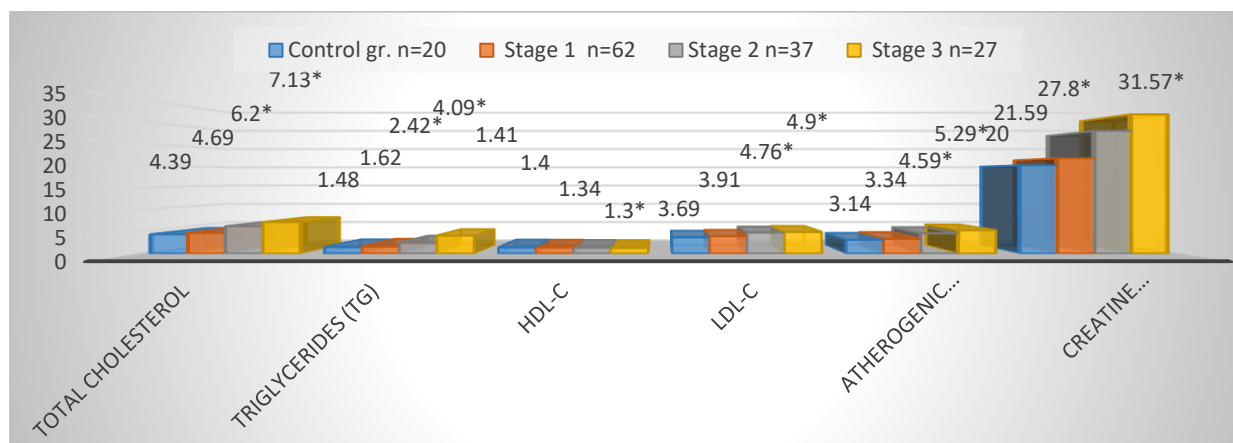


Fig. 6. Indicators of Lipid Metabolism Disorders in Patients with Silicosis Combined with Ischemic Heart Disease (IHD) and Arterial Hypertension (AH) (pg)

Note: $P < 0.05$; * - compared to the control group.

Echocardiographic examination results indicated that the heart rate in patients with stage 1 silicosis was significantly higher than in the control group ($P<0.01$). However, no significant difference in heart rate was observed between patients with silicosis and the control group (Table 2).

Table 2. Comparative Characteristics of Central and Intracardiac Hemodynamic Parameters in Patients with Silicosis Depending on the Disease Stage

Parameter	Stage 1 (n=62)	Stage 2 (n=37)	Stage 3 (n=27)	Control gr. (n=20)	
HR, bpm	80,61±1,83**	80,84±2,26	78,67±3,14	72,90±1,19	-0,064
Aorta, mm	29,69±0,11***	32,62±0,86^***	32,44±0,36^^^***	27,10±0,16	-0,281
LA, mm	30,39±0,22	30,81±0,35	33,96±0,68^^^###***	28,50±0,78	-0,595
LV EDD, mm	47,29±0,49	47,97±0,72	53,26±1,40^^#**	47,30±0,91	-0,634
LV ESD, mm	29,73±0,40	30,27±0,63	39,78±1,58^^^####***	29,75±0,75	-0,908
LV EDV, mL	107,37±2,64	103,19±3,11	140,93±8,23^^^####***	107,55±4,93	-0,665
LV EF, %	67,42±0,70	65,11±0,86	50,59±1,89^^^####***	65,35±1,26	1,000
IVS, mm	10,89±0,14***	11,14±0,22***	10,41±0,27	9,75±0,16	0,308
LVPW, mm	10,60±0,15***	10,73±0,24***	10,04±0,11^**	9,20±0,19	0,373
RV, mm	29,00±0,18***	27,89±0,34^***	28,89±0,76***	19,20±0,40	0,273
Ao, m/sec	137,08±1,61	114,57±2,10^^^***	121,67±3,66^^*	136,65±2,96	0,284
PA Vmax, m/sec	93,51±1,75	88,95±0,93	82,33±2,03^^^	92,47±3,04	0,146
E MV, m/sec	86,24±3,59	63,54±2,28^^^*	66,48±3,02^^^*	87,25±6,54	0,206
A MV, m/sec	71,08±1,75	70,68±2,99	84,19±4,61**	64,15±1,89	-0,380
E TV, m/sec	67,63±2,50	52,38±1,77^^^*	50,48±3,93^^*	67,45±4,66	0,255
A TV, m/sec	46,71±1,53	47,59±1,57	50,37±0,42**	43,45±1,78	-0,373

Note: - Significant difference compared to the control group (CG);

^ - Significant difference compared to patients with stage 1 silicosis;

-Significant difference compared to patients with stage 2 silicosis;

-One symbol – $p < 0.05$, two symbols – $p < 0.01$, three symbols – $p < 0.001$.

Echocardiographic (EchoCG) examination demonstrated that in all clinical subgroups of the main study group, the ascending aorta diameter was significantly larger than in the control group (CG) ($p < 0.001$ for all comparisons). Furthermore, in patients with stage 1 silicosis, this parameter was considerably smaller than in those with more advanced stages of the disease ($p < 0.05$ vs. stage 2; $p < 0.001$ vs. stage 3).

Likewise, the left atrium (LA) diameter increased with disease progression, showing significant differences compared to the CG and stage 1 silicosis patients ($p < 0.001$), as well as stage 2 patients ($p < 0.01$). Left ventricular (LV) size was increased in stage 3 silicosis patients ($p < 0.01$ compared to CG and stage 1 patients, and $p < 0.05$ compared to stage 2 patients). Consequently, the calculated LV chamber volume was highest in this group ($p < 0.001$ difference from stage 2 patients and $p < 0.01$ compared to stage 1 patients and CG). The sizes and volumes of the left heart chambers in stage 1 and 2 silicosis patients were comparable to each other and to CG.

The right ventricular (RV) diameter was significantly larger in all silicosis stages compared to CG ($p < 0.001$ for all three comparisons). Diastolic wall thickness of the LV was increased in silicosis patients compared to CG, with a tendency to decrease as the disease stage progressed: the thickness of the interventricular septum (IVS) was significantly greater in stage 1 and 2 silicosis patients compared to CG, but similar in stage 3 patients and CG. The thickness of the posterior wall of the left ventricle (PWL) was significantly higher in stage 1 and 2 silicosis patients compared to CG ($p < 0.001$) and in stage 3 patients compared to CG ($p < 0.01$). However, PWLV thickness in stage 3 patients was significantly lower compared to stage 1 patients ($p < 0.05$).

Left ventricular systolic function (Fig. 7) was reduced in stage 3 silicosis patients (50.59%) relative to the reference norm (55%) and compared to CG (65.35%) and stage 2 and 1 silicosis patients (67.42% and 65.11%, respectively). Since the main criterion of cardiotoxicity is a reduction in LV ejection fraction (LVEF), patients with an LVEF below the reference norm of 55% were identified. A total of 18 such patients were found, all of whom had stage 3 silicosis (66.67% of this group). Regional dyskinesia was detected in 12 stage 3 silicosis patients (44.44%), in 5 stage 2 silicosis patients (13.51%), and in none of the CG or stage 1 silicosis patients ($\chi^2 = 39.17$, $p < 0.001$).

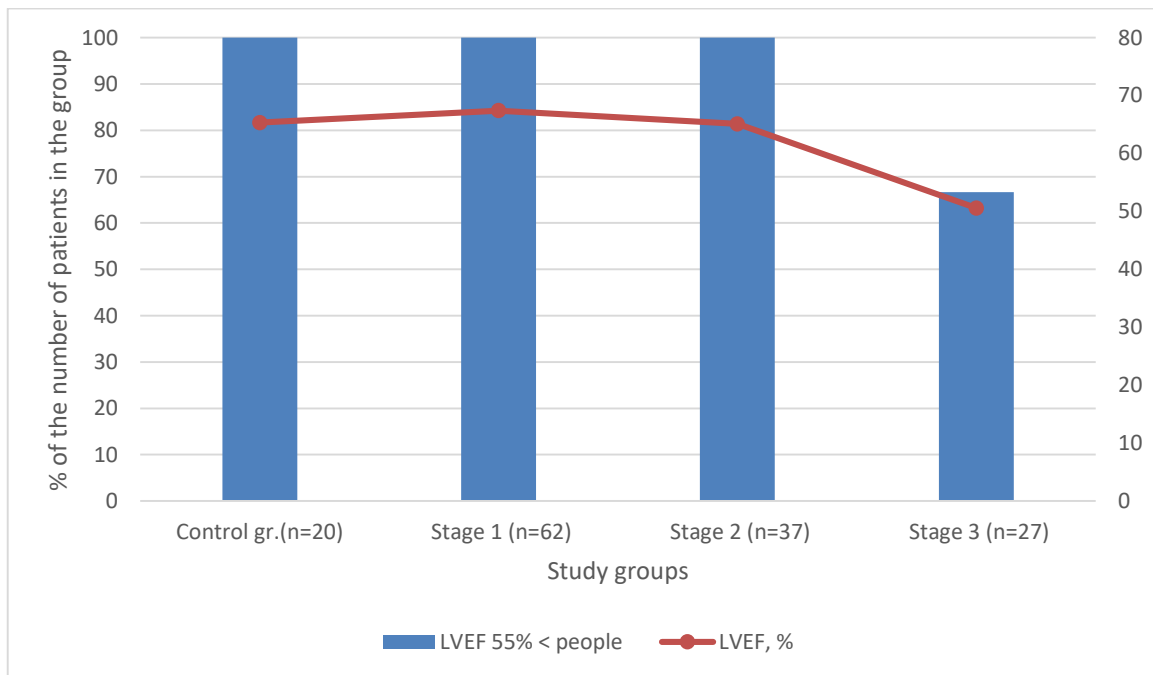


Fig.7. Left Ventricular Ejection Fraction in the Study Groups.

Assessment of diastolic function demonstrated that the number of patients with left ventricular diastolic dysfunction (LVDD) increased with the progression of silicosis (Figure 8). In the control group (CG), all individuals exhibited normal diastolic function of both ventricles. In contrast, 29.03% of patients with stage 1 silicosis showed evidence of LVDD1, while the prevalence of LVDD1 in patients with stage 2 and stage 3 silicosis was 56.76% and 85.19%, respectively ($\chi^2 = 68.25$, $p < 0.001$). Additionally, four patients (14.81%) with stage 3 silicosis were diagnosed with grade 2 diastolic dysfunction.

For the right ventricle (RV), the prevalence of diastolic dysfunction was 14.52%, 43.24%, and 66.67% in patients with stage 1, stage 2, and stage 3 silicosis, respectively ($\chi^2 = 36.39$, $p < 0.001$) (Figure 9).

A hallmark of diastolic dysfunction was the progressive decline in early diastolic filling velocity. Significant differences in the transmitral flow were recorded in individuals with stage 2 and 3 silicosis, relative to the control group ($p < 0.05$) and the group of individuals with stage 1 silicosis ($p < 0.001$). Similar differences were observed in the translucus flow between patients with stage 2 and 3 silicosis relative to the control group ($p < 0.05$), and relative to stage 1 and 2 ($p < 0.001$).

Furthermore, atrial filling flow velocity was elevated, with significant differences in both transmitral and transtricuspid flows between patients with stage 3 silicosis and the control group ($p < 0.05$).

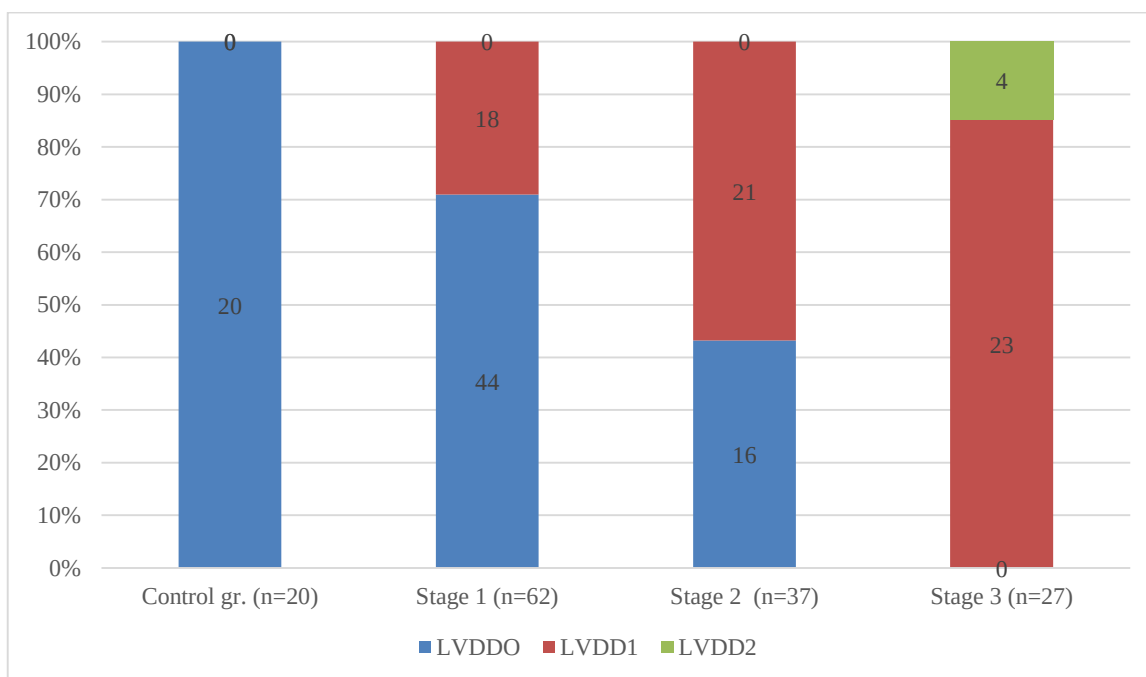


Fig.8. Distribution of Patients Included in the Study by Type of Left Ventricular Diastolic Filling, Depending on the Stage of Silicosis ($\chi^2=68.25$, $p<0.001$)

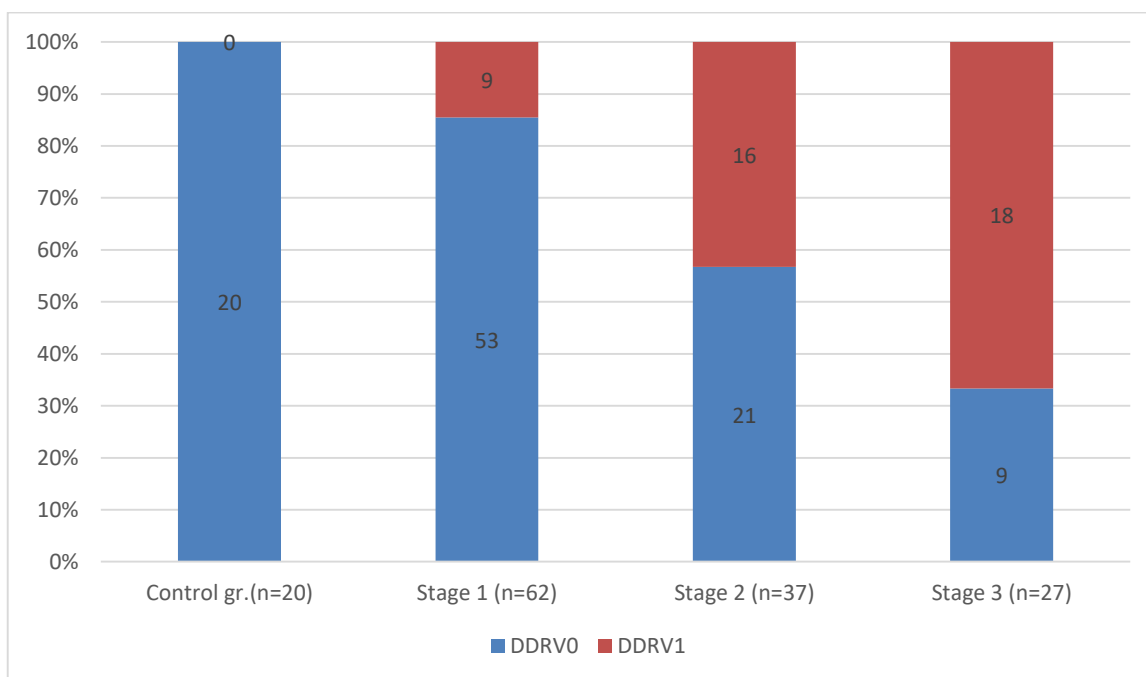


Fig. 9. Distribution of Individuals Included in the Study by Types of Right Ventricular Diastolic Filling, Depending on the Stage of Silicosis ($\chi^2=36.39$, $p<0.001$)

4. Conclusions

Most often, coronary heart disease and hypertension are registered in miners, whose average age is 39.6 ± 1.2 years. It has been proven that the influence of dust, noise, and vibration, physical exertion, and adverse microclimatic conditions are significant risk factors for cardiovascular diseases among workers

with 10 or more years of occupational experience.

A general assessment of the clinical, functional, and protective indicators established that silicosis with the parallel presence of coronary heart disease and hypertension entails changes in hemodynamics, in the activity of the endothelial layer of blood vessels, and leads to an increase in the concentration of TNF- α , endothelin-1, and non-neutrophilic elastase. Additionally, an increase in Ox, Tr, LDL-C, VLDL-C, AT, CK-MB and a decrease in HDL-C were observed.

Thus, the early detection of cardiovascular changes in patients with silicosis complicated by IHD and AH has enabled the monitoring of cardiovascular function in workers with prolonged industrial aerosol exposure. The presence of systemic inflammatory markers (elevated neutrophil elastase and TNF- α) and atherogenic dyslipidemia allows for a reliable prediction of cardiovascular dysfunction risk, serving as a key indicator of the cardiotoxic effects of occupational exposure.

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