ISSN 2304-3415, Russian Open Medical Journal
2025. Volume 14. Issue 3 (September). Article CID e0307
DOI: 10.15275/rusomj.2025.0307

This article belongs to the Special Topic Collection "Circadian Lighting Hygiene, Health, and Well-being"

Original article

Prognostic Significance of Increased Blood Pressure Variability under Arctic Rotating Shift Work Conditions in Relation to COVID-19

Nina P. Shurkevich [1], Aleksander S. Vetoshkin [1], Maria A. Kareva [1], Lyudmila I. Gapon [1], Denis G. Gubin [1,2,3]

[1] Tomsk National Research Medical Center, Russian Academy of Sciences, Tomsk, Russia
[2] Tyumen State Medical University, Tyumen, Russia
[3] Research Institute of Biomedicine and Biomedical Technologies, Tyumen, Russia

Received 6 February 2025, Revised 23 April 2025, Accepted 8 July 2025

Abstract: This study aimed to investigate the average daily variability of blood pressure (BP) in normotensive men in relation to COVID-19, its effects on the cardiovascular system, and changes in the chronostructure of the daily BP rhythm following infection. Additionally, the prognostic significance of these factors was evaluated under Arctic rotating shift work conditions.

Material and Methods — A one-step retrospective analysis was conducted on the medical records of 517 patients treated at the hospital of the Medical Unit of Gazprom Dobycha Yamburg LLC (Yamburg settlement, Russia; 68°21'40" N). Among these, 310 patients had confirmed COVID-19. From this cohort, 230 men with arterial hypertension (AH) but normal BP, both with and without COVID-19, were selected. Echocardiography (EchoCG) and ambulatory blood pressure monitoring (ABPM) were performed during the "pre-COVID" period. This study is part of a larger project previously published in *RusOMJ* (2024; 4). Here, we present results from normotensive men with (*n*=32) and without COVID-19 (*n*=32), matched for age and shift work experience. Both groups underwent repeated assessments after 15±3 months. At the hospital, 20.6% of patients with COVID-19 experienced a mild disease course, while 73% experienced a moderate course without complications or fatal outcomes. Lung damage assessed by computed tomography (CT) was classified as type "0" in 23%, type "1" in 29.4%, and type "2" in 34.1% of these patients. Ambulatory blood pressure monitoring (ABPM) was performed using the BPLab v.3.2 device (Russia). Chronobiological analysis of BP and chronotype classification followed the method of Cugini *et al*. Echocardiography (EchoCG) was performed with a Philips CX50 scanner (Netherlands).

Results — Logistic regression analysis revealed that a 1 mm increase in the diameter of the inferior vena cava was associated with a twofold increase in the risk of COVID-19. Similarly, a 1.0 mmHg increase in the average daily variability of diastolic blood pressure (DBP) corresponded to a 1.5-fold increase in risk. The area under the receiver operating characteristic (ROC) curve was 0.785 (*p*=0.001). Longitudinal follow-up after COVID-19 revealed that 28.1% of normotensive men developed hypertensive average daily BP levels ≥135/85 mmHg. This increase was accompanied by an increased workload on the right side of the heart. Additionally, concentric left ventricular hypertrophy was detected in 25% of these men. A decrease in the "true normotension" chronotype and an increase in hypertensive chronotypes were observed, including 25.6% of participants exhibiting an atypical arterial hypertension (AH) chronotype characterized by short-term rhythms in daily BP ("aperiodic AH"). An inverse relationship was identified between BP variability and the 24-hour rhythm period, which was associated with a 21.5% increased risk of developing this atypical AH chronotype one year after COVID-19 infection.

Conclusions — Under Arctic rotating shift work conditions, increased blood pressure (BP) variability serves as an indicator of autonomic dysfunction and a marker of disrupted chronostructure in the daily BP rhythm. These findings have prognostic significance for an elevated risk of COVID-19 and subsequent cardiovascular complications.

Keywords: ambulatory blood pressure monitoring (ABPM), chronostructure of blood pressure (BP), echocardiography (EchoCG), shift work, Arctic, COVID-19.

Cite as Shurkevich NP, Vetoshkin AS, Kareva MA, Gapon LI, Gubin DG. Prognostic Significance of Increased Blood Pressure Variability under Arctic Rotating Shift Work Conditions in Relation to COVID-19. *Russian Open Medical Journal* 2025; 14: e0307.

Correspondence to Nina P. Shurkevich. E-mail: Shurkevich@infarkta.net.

Introduction

The recent COVID-19 pandemic remains the subject of extensive research due to numerous unresolved questions. It is well established that increased morbidity and mortality associated with coronavirus infection correlate with age and certain comorbidities, such as arterial hypertension (AH), diabetes mellitus, and obesity, all characterized by elevated sympathetic activity [1]. However, the precise role of the sympathetic nervous system in the pathophysiology of COVID-19 has yet to be fully elucidated. Hyperactivation of the sympathetic nervous system may contribute not only to the development of these

comorbidities but also to increased susceptibility to COVID-19 [2]. The autonomic nervous system (ANS), which regulates the activity of the heart, blood vessels, kidneys, and immune cells, is believed to be involved in this process [3]. Currently, there is growing concern regarding the potential impact of COVID-19 on the cardiovascular system and its association with AH, particularly during the post-COVID period. A meta-analysis of observational studies has provided evidence of an increased risk of hypertension development and progression following COVID-19 infection [4]. Several hypotheses are under investigation to explain the relationship between COVID-19 and elevated blood pressure (BP).

Under Arctic rotating shift work conditions, individuals experience stress related to adverse climatic effects, altered photoperiodism, and frequent translatitudinal movements, all of which place strain on their adaptive mechanisms [5]. This stress may lead to dysregulation of the autonomic nervous system (ANS), characterized by reduced overall tone and parasympathetic activity [6], as well as desynchronization of physiological rhythms [7]. Such alterations have significant clinical implications, including an increased risk of cardiovascular morbidity [8]. A previous study [9] reported increased blood pressure (BP) variability in both hypertensive and normotensive individuals, highlighting this as a characteristic of vascular status among migrants living in the Far North. Numerous studies have identified BP variability as a predictor of cardiovascular complications and a marker of target organ damage in the general population. This variability is closely linked to autonomic nervous system function. However, the potential role of BP variability in patients with COVID-19, especially under Arctic shift work conditions, remains poorly understood [10]. Given the general mechanisms of ANS regulation, including circadian rhythms and immune function [3], it has been hypothesized that autonomic imbalance with sympathetic activation – manifested as increased BP variability – may be associated with disrupted circadian BP rhythms, immune system stress, and heightened susceptibility to COVID-19 infection. Furthermore, this imbalance may contribute to alterations in cardiovascular status during the post-COVID period. This study aimed to investigate these potential associations.

The aim of this study was to investigate the characteristics of average daily blood pressure (BP) variability among normotensive individuals in relation to COVID-19. Additionally, we examined the dynamics of cardiovascular status and the chronostructure of daily BP rhythms following infection, as well as their prognostic significance under Arctic rotating shift work conditions.

Material and Methods

Object and Study Design

A retrospective analysis was conducted on the medical records of 517 patients treated at the hospital of the Medical Unit of Gazprom Dobycha Yamburg LLC, located in the Yamburg settlement (Nadym district, 68°21′40″ N), between June 2020 and February 2021. Among these patients, 310 had confirmed COVID-19. Using random number generation, 230 men with a history of arterial hypertension (AH) but normal blood pressure (BP), both with and without COVID-19, were selected. Inclusion criteria required availability of echocardiography (EchoCG) and ambulatory blood pressure monitoring (ABPM) performed during the "pre-COVID" period (October 2019). This study is part of a larger project previously published in *RusOMJ* (2024; 4). The present paper reports results from a study involving normotensive men with (*n*=32) and without (*n*=32) a history of COVID-19, matched for age and shift work experience. The study design is illustrated in *Figure* 1.

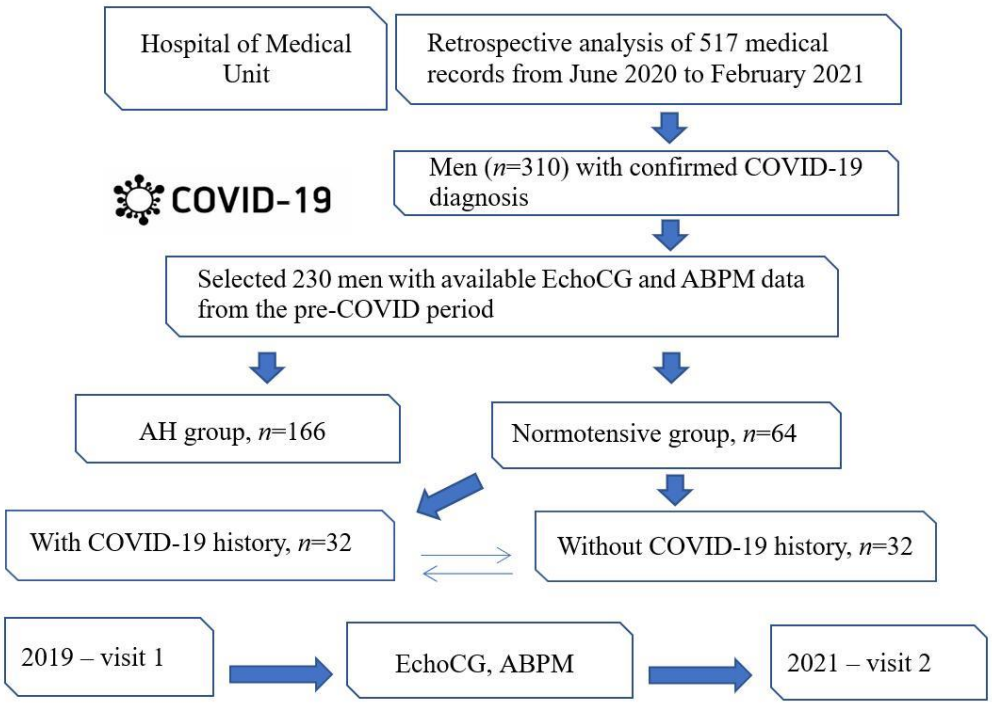

Figure 1. Study design.

Table 1. Main echocardiographic parameters in men with and without COVID-19 and normal blood pressure during the pre-COVID period

Parameter	*With COVID-19 (n=32)*	*Without COVID-19 (n=32)*	*p-value*
LA diameter, cm	36.6±3.6	33.9±4.3	*p*=0.010
Peak velocity E, cm/s	65.6±14.7	64.2±13.2	*p*=0.689
Peak velocity A, cm/s	54.2±19.3	53.3±14.8	*p*=0.845
RA volume, ml	34.3±8.7	34.3±7.9	*p*=0.974
RV diameter, cm	21.2±5.3	23.3±5.6	*p*=0.122
PASP, mmHg	22.5±6	22.8±6.3	*p*=0.855
IVS diastole, cm	1.0±0.1	1.0±0.1	*p*=0.108
LVPW diastole, cm	1.0±0.1	1.0±0.2	*p*=0.500
LVMM, g	188.0±44.5	166.3±36.8	*p*=0.038
LVMMI, g/m²	92.0±17.8	82.1±18.5	*p*=0.033
LVSV, ml	86.3±17.9	76.8±19.3	*p*=0.046
LVEF, %	69.7±6.5	68.1±7.6	*p*=0.361
MV, L/min	6.1±1.4	5.2±1.5	*p*=0.014
E/A ratio	1.3±0.6	1.3±0.4	*p*=0.703
PTR velocity, m/s	172.6±64.1	171.8±62.2	*p*=0.973
IVC collapse, %	35.3±7.3	41.0±6.5	*p*=0.003
IVC diameter, mm	20.8±2.2	19.6±1.5	*p*=0.007

LVPW, left ventricular posterior wall; LV, left ventricular; LA, left atrial; IVS, interventricular septum; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; LVMMI, left ventricular myocardial mass index; LVMM, left ventricular myocardial mass; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; MV, minute volume; IVC, inferior vena cava; RA, right atrial; RV, right ventricular; PASP, pulmonary artery systolic pressure; PTR, peak tricuspid regurgitation; LVSV, left ventricular stroke volume; LVEF, left ventricular ejection fraction. p denotes the significance level of intergroup differences. The nonparametric Mann-Whitney *U* test was employed to compare independent samples.

Table 2. Significant differences in ambulatory blood pressure monitoring (ABPM) parameters between men with and without COVID-19 who had normal blood pressure (BP) during the pre-COVID period

Parameter	*With COVID-19 (n=32)*	*Without COVID-19 (n=32)*	*p-value*
DBP24, mmHg	89.6±8.6	82.9±6.8	*p*=0.002
VDBP24, mmHg	11.8±2.8	10.5±1.9	*p*=0.034
VDBP_d, mmHg	10.6±2.7	9.2±2.3	*p*=0.031
DBP_n, mmHg	82.6±12.9	75.4±6.4	*p*=0.007
VDBP_n, mmHg	9.8±2.1	8.5±2.2	*p*=0.053
VHR_d, bpm	14.8±5.5	11.3±4.83	*p*=0.005
VHR24, bpm	15.98±6.36	12.42±5.0	*p*=0.016
HR_d, bpm	86.6±14.8	78.1±13.9	*p*=0.036

DBP, diastolic blood pressure; HR, heart rate; V*** indicates variability of the corresponding parameter; “d” denotes daytime hours; “n” denotes nighttime hours. *p* denotes the significance level of intergroup differences. The nonparametric Mann-Whitney *U* test was employed to compare independent samples.

Table 3. Odds ratio (OR) for COVID-19 in men with normal blood pressure (BP) based on initial inferior vena cava (IVC) diameter and average daily variability of diastolic blood pressure (DBP), as determined by logistic regression analysis

Predictor	*B±SE*	*p-value*	*OR (Exp(B))*	*95% CI*
VDBP24	0.376±0.159	*p*=0.018	1.458	1.068-1.991
IVC diameter	0.729±0.263	*p*=0.006	2.073	1.238-3.471
Constant (intercept)	-19.005±6.246	*p*=0.002	0.000	—

VDBP24, average daily variability of diastolic blood pressure; IVC, inferior vena cava. B represents the regression coefficient ± standard error (SE); P denotes statistical significance according to the Wald test; Exp(B) is the exponentiated coefficient reflecting the change in odds ratio (OR) per unit increase in the predictor, with 95% confidence intervals (CI) provided in parentheses.

COVID-19 diagnosis was confirmed by detecting SARS-CoV-2 RNA using polymerase chain reaction (PCR) performed at the hospital. Approximately one year later (15±3 months), repeated echocardiography (EchoCG) and ambulatory blood pressure monitoring (ABPM) were conducted in both groups. Inclusion criteria required no history of arterial hypertension (AH), coronary artery disease, diabetes mellitus, cardiac arrhythmias, or related complications. This retrospective analysis was conducted as part of routine clinical practice, with all patients providing written informed consent for data processing in accordance with Order No. 36/1 dated January 29, 2020, and the approved consent form. Comprehensive patient examinations adhered to the ethical standards of the Declaration of Helsinki and Russian clinical practice regulations (2005) [“Good Clinical Practice,” GOST R 52379-2005], following a protocol approved by the Academic Council of the Tyumen Cardiology Research Center and the Ethics Committee of the Center (No. 149, dated June 3, 2019). Retrospective analysis of medical records revealed that among normotensive individuals who recovered from COVID-19, 20.6% experienced a mild disease course, while 73% had a moderate course predominantly characterized by lung damage, as evidenced by computed tomography (CT) scans. Specifically, 23.0% of patients exhibited CT type “0,” 29.4% had CT type “1” (0–24.9% lung tissue damage), 34.1% had CT type “2” (25.0–49.9% lung tissue damage), and 10% had CT type “3.” Patients received standard antiviral treatment; 82.9% were administered anticoagulants, and 79.5% received hormonal therapy. No complications or deaths were reported.

Ambulatory blood pressure monitoring (ABPM) was performed using the standard BPLab v.3.2 method (Russia), including chronobiological analysis and determination of predominant circadian blood pressure rhythm chronotypes according to the classification by Cugini P. [11], as detailed in our previous publication [12]. Office blood pressure was measured twice prior to placement of the blood pressure (BP) monitor. The diagnostic and clinical relevance of disturbances in the chronostructure of circadian blood pressure rhythms, including identification of BP chronotypes in individuals with both elevated and normal BP, has been extensively documented [13–15]. Echocardiography (EchoCG) was performed using an expert-class Philips CS 50 ultrasound scanner, following generally accepted protocols [16].

Statistical Analysis

Data analysis was performed using Statistica 8.0 (StatSoft, USA) and IBM SPSS Statistics (version 26.0, release 16.0.0.0, USA). Nonparametric tests, including the Mann–Whitney *U* test, were applied to evaluate quantitative variables. Categorical variables were analyzed using the chi-square (χ^2) test. Correlation analysis was conducted using the nonparametric Spearman rank correlation coefficient. Stepwise logistic regression and receiver operating characteristic (ROC) curve analyses were performed to assess the sensitivity and specificity of the COVID-19 risk model. Wilcoxon signed-rank and McNemar tests were applied to compare the dynamics of continuous and categorical variables, respectively. Statistical significance was defined as a two-tailed *p*-value of less than 0.05.

Results

Among men with normal blood pressure (BP), those who contracted COVID-19 and those who did not were comparable in

age (49.5±8.0 *vs.* 48.7±9.3 years, respectively; p=0.143), duration of shift work (18.4±8.0 *vs.* 17.9±7.5 years; p=0.358), and office systolic BP (SBP) and diastolic BP (DBP) (124.1±7.7 / 83.7±6.9 mmHg *vs.* 123.5±7.7 / 82.6±5.5 mmHg). Significant differences in echocardiographic (EchoCG) parameters between the two groups during the pre-COVID period were observed in left atrial (LA) diameter (p=0.010), left ventricular (LV) myocardial mass (LVMM) (p=0.038), LVMM index (LVMMI) (p=0.033), stroke volume (SV) (p=0.046), minute volume (MV) (p=0.014), and inferior vena cava (IVC) diameter (p=0.007). All these parameters were significantly higher in individuals who subsequently contracted COVID-19 (*Table* 1).

As shown in *Table* 2, men with normal blood pressure (BP) who subsequently contracted COVID-19 initially exhibited significantly higher average daily diastolic blood pressure (DBP24) (p=0.002), including both daytime and nighttime values, along with increased variability across daily, daytime, and nighttime periods. They also demonstrated significantly elevated hypertensive DBP load during average daily, daytime, and nighttime intervals. Furthermore, these individuals exhibited significantly higher daytime heart rate (HRd) (p=0.036), as well as increased average daily and daytime heart rate variability (VHR) (p=0.016 and p=0.005, respectively).

To identify factors associated with COVID-19 risk, we performed stepwise logistic regression analysis using echocardiography (EchoCG) and ambulatory blood pressure monitoring (ABPM) data. The analysis included covariates that significantly differed between men with and without COVID-19 who had normal BP: left atrial diameter (LA), left ventricular myocardial mass index (LVMMI), inferior vena cava (IVC) diameter, minute volume (MV), stroke volume (SV), heart rate variability (VHR24, VHRd), and average daily variability of diastolic blood pressure (VDBP24). The results are summarized in *Table* 3.

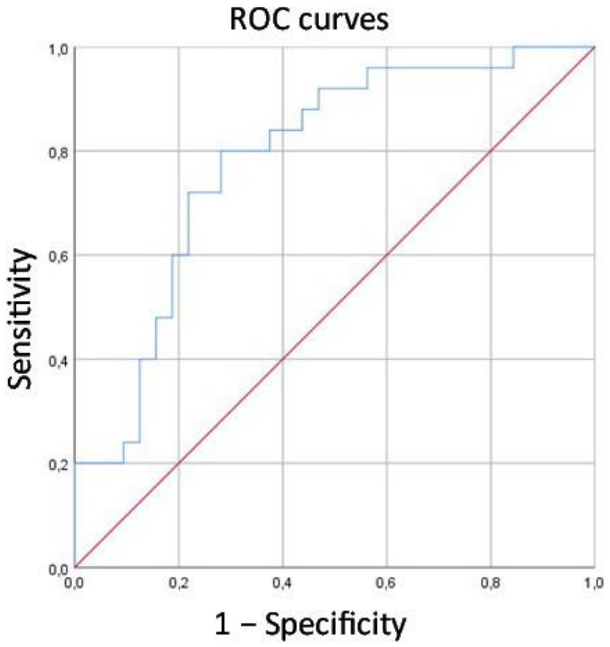

Figure 2. Receiver operating characteristic (ROC) curve analyzing the risk of COVID-19 in men with normal blood pressure (BP) working under Arctic rotating shift work conditions.

Table 4. Dynamics of chronotypes in men with normal blood pressure (BP) who had or had not had COVID-19

Chronotype	*Visit 1*	*Visit 2*	*p-value*
With COVID-19 (n=32)			
Allo-normotension	3 (9.4%)	5 (15.4%)	p=0.453
Aperiodic AH	1 (3.1%)	8 (25.6%)	p=0.016
Iso-normotension	11 (34.4%)	7 (21.9%)	p=0.046
Mesor AH	0 (0.0%)	8 (25.6%)	p=0.019
Normotension	17 (53.1%)	4 (12.5%)	p=0.001
Without COVID-19 (n=32)			
Allo-normotension	4 (12.5%)	4 (12.4%)	p=0.987
Aperiodic AH	0 (0.0%)	0 (0.0%)	—
Iso-normotension	13 (40.6%)	10 (31.3%)	p=0.607
Normotension	15 (46.9%)	18 (56.3%)	p=0.804

AH, arterial hypertension. McNemar's test was used to assess the significance of differences between Visit 1 and Visit 2.

Initially, a 1 mm increase in inferior vena cava (IVC) diameter in normotensive men was associated with a twofold increase in the risk of COVID-19, while a 1.0 mmHg increase in average daily variability of diastolic blood pressure (VDBP) corresponded to a 1.5-fold increase. Sensitivity, specificity, and overall accuracy were 72.0%, 72.4%, and 72.2%, respectively. The area under the receiver operating characteristic (ROC) curve was 0.785 (95% confidence interval [CI], 0.665–0.905; p=0.001) (*Figure* 2).

One year later, among men with normal blood pressure (BP) who had COVID-19, compared to those without the disease, the percentage of inferior vena cava (IVC) collapse during inspiration decreased, approaching statistical significance (p=0.055). Pulmonary artery systolic pressure (PASP) significantly increased (p=0.027). Left ventricular myocardial mass (LVMM) and its index (LVMMI) also significantly increased (p=0.001 for both), driven by thickening of the left ventricular posterior wall (LVPW) (p=0.001), interventricular septum (IVS) (p=0.007), and relative wall thickness (RWT) (p=0.052). Stroke volume (SV) increased significantly (p=0.028), and peak A velocity significantly increased in both groups. The velocity of tricuspid regurgitation (TCR) increased over time only in men who had COVID-19 (p=0.018).

After one year, significant changes in left ventricular (LV) remodeling patterns were observed only in men with COVID-19 and normal blood pressure. The prevalence of normal LV geometry significantly decreased (p=0.031), while concentric LV hypertrophy significantly increased (p=0.023).

Significant longitudinal changes in ambulatory blood pressure monitoring (ABPM) parameters were observed only in men who had COVID-19. These changes included average daily systolic blood pressure (SBP) and diastolic blood pressure (DBP), encompassing daytime and nighttime values; increased variability of nighttime SBP; a significant decrease in daily SBP and DBP indices; and increased average daily, daytime, and nighttime hypertensive loads for both SBP and DBP. Notably, the circadian index (CI) of heart rate (CIHR) decreased following COVID-19 in normotensive men, approaching statistical significance (p=0.053). In men with normal blood pressure who did not contract COVID-19, significant changes in ABPM parameters were limited to increases in average daily diastolic blood pressure (DBP) (p=0.009), average daytime DBP (p=0.031), and average daily DBP hypertensive load (p=0.053). As shown in *Table* 4, among men with normal blood pressure, post-COVID-19 dynamics revealed a significant decrease in the 24-hour circadian blood pressure rhythm, evidenced by a reduction in the "true normotension" chronotype (p=0.001). Concurrently, hypertensive chronotypes emerged, with significant increases in

the “Aperiodic AH” chronotype from 3.1% to 25% (p=0.016) and the “Mesor AH” chronotype from 0% to 25.6% (p=0.019). Among men with normal blood pressure who had not experienced COVID-19, changes in blood pressure chronotype frequencies were not statistically significant.

The dynamics of the “true normotension” and “Aperiodic AH” chronotype frequencies are presented in *Figures* 3 and 4. Marginal means, representing the distribution of the feature within each group, are shown. Specifically, the frequency of the “Aperiodic AH” chronotype during Visit 1 and Visit 2 is illustrated. Frequencies are expressed as proportions per 100 individuals, presented in decimal form (e.g., 0.xx).

Among healthy men who later contracted COVID-19 (n=32), one individual (3.1%) had an average daily blood pressure (BP) of 132/83 mmHg at baseline. One year after COVID-19, 9 of 32 participants (28.1%) exhibited elevated average daily BP ≥135/85 mmHg (p=0.012; McNemar’s test; binomial distribution applied). In contrast, among men who did not contract COVID-19 (n=32), the change in arterial hypertension (AH) prevalence – from 1 (3.1%) to 3 (9.4%) individuals – was not statistically significant (p=0.375) (*Figure* 5).

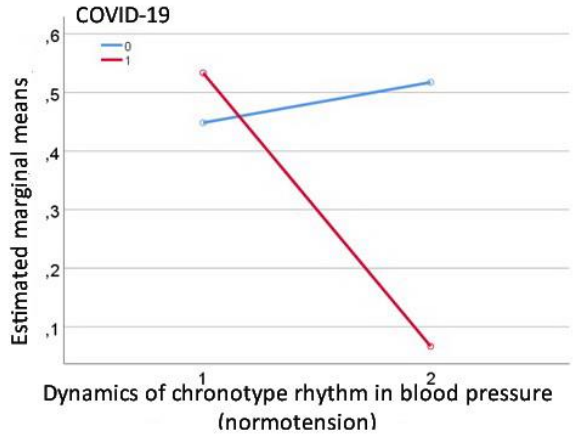

Figure 3. Dynamics of the frequency distribution of the “Normotension” chronotype in men with normal blood pressure who had and did not have COVID-19. Note: Here and below, a two-sided McNemar's p-test was used.

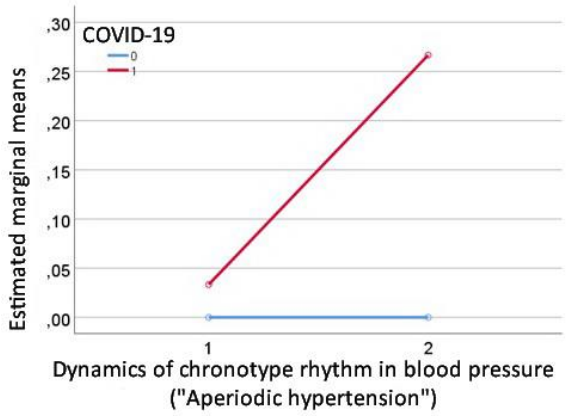

Figure 4. Dynamics of the frequency distribution of the “Aperiodic AH” chronotype in men with normal blood pressure (BP) who had and had not had COVID-19.

Correlation analysis revealed a positive association between initial nighttime diastolic blood pressure variability (VDBPn) before COVID-19 and the presence of the “Aperiodic AH” chronotype after COVID-19 in normotensive individuals (r=0.229, p=0.028).

According to *Table* 5, each 1 mmHg increase in initial nighttime variability of diastolic blood pressure (VDBPn) corresponds to a 21.5% increase in the odds of developing a disrupted daily blood pressure rhythm chronostructure, manifested as the “Aperiodic AH” chronotype, one year after COVID-19.

Discussion

The COVID-19 pandemic has emerged as a global threat, placing substantial pressure on healthcare systems worldwide. Given the current lack of a fully reliable vaccine or definitive cure, protecting individuals at increased risk of COVID-19 remains a critical priority [17].

This study is significant because it compares echocardiography (EchoCG) and ambulatory blood pressure monitoring (ABPM) data from normotensive individuals collected before the COVID-19 pandemic, distinguishing between those who subsequently contracted the disease and those who did not. This approach enabled the identification of potential factors associated with increased susceptibility to COVID-19.

Several factors have been implicated in elevating the risk of COVID-19, including increased expression of angiotensin-converting enzyme 2 (ACE2), reduced sex hormone levels, oxidative stress, mitochondrial dysfunction, a history of arterial hypertension (AH), obesity, and diabetes mellitus [18]. These conditions may promote sympathetic nervous system activation, which plays a key role in modulating immune and inflammatory responses [19].

Blood pressure (BP) variability is an important indicator of cardiovascular health, independent of average BP levels [20]. Although the underlying causes of abnormal BP variability remain under investigation, autonomic factors—particularly sympathetic hyperactivity—have been shown to play a major role [21].

To identify factors potentially increasing disease risk, we conducted a comparative analysis of EchoCG and ABPM data in a cohort of men with normal blood pressure who either developed or did not develop COVID-19 during the pre-pandemic period.

Differences in echocardiographic and ambulatory blood pressure monitoring parameters between men with and without COVID-19, all normotensive in the pre-pandemic period, included significantly higher stroke volume and cardiac minute volume; increased average daily hypertensive diastolic blood pressure (DBP) load during both daytime and nighttime; elevated average daily variability of DBP (VDBP); increased heart rate (HR) values across day and night; and altered indicators of daytime HR variability. These observations suggest heightened sympathetic nervous system activity in men with normal blood pressure who later contracted COVID-19.

Stepwise logistic regression analysis incorporating EchoCG and ABPM variables revealed significant differences between normotensive men with and without COVID-19. Specifically, each 1 mm increase in inferior vena cava (IVC) diameter was associated with a twofold increase in the likelihood of COVID-19, while each 1 mmHg increase in average daily DBP variability over 24 hours (VDBP24) increased the risk by 1.5 times.

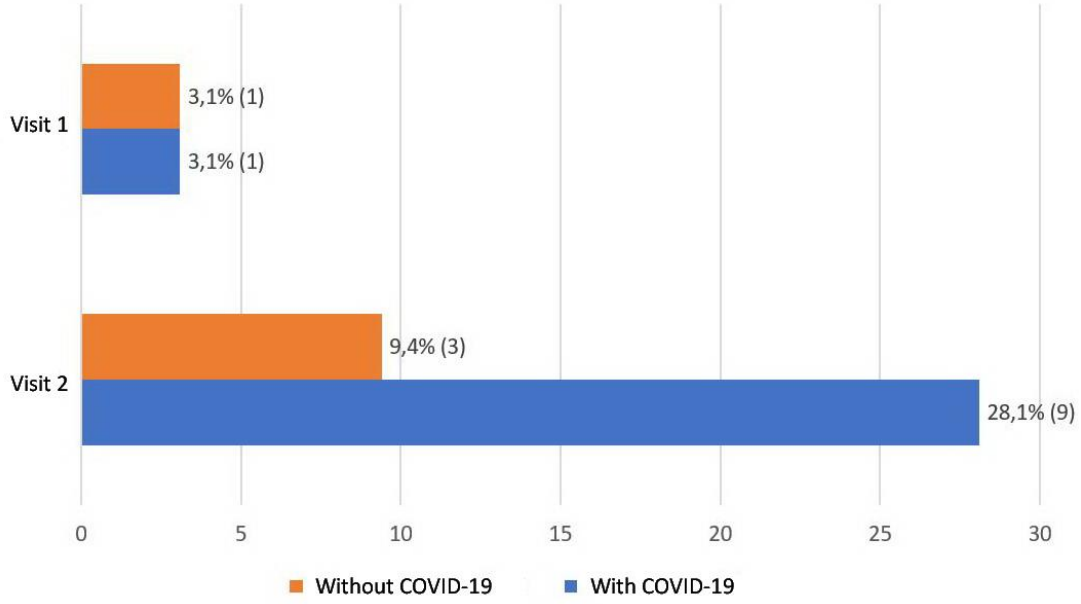

Figure 5. Dynamics of arterial hypertension (AH) frequency based on ambulatory blood pressure monitoring (ABPM) data (average daily BP values ≥135/85 mmHg) in men with normal blood pressure who had and had not had COVID-19.

Table 5. Odds ratio (OR) for detection of the "Aperiodic AH" chronotype one year after COVID-19 according to initial nighttime variability of diastolic blood pressure (VDBPn) in normotensive individuals working under Arctic rotating shift work conditions

Covariate	*B±SE*	*p-value*	*OR*	*95% CI Lower*	*95% CI Upper*
VDBPn	0.195±0.092	*p*=0.033	1.215	1.016	1.454

VDBPn, nighttime variability of diastolic blood pressure. B, regression coefficient ± standard error (SE); *P*, statistical significance according to the Wald test; Exp(B), exponentiated coefficient representing the change in odds ratio (OR) per unit increase in the predictor. Values in parentheses indicate 95% confidence intervals (CI) for Exp(B).

Our findings indicate that increased inferior vena cava (IVC) diameter correlates with elevated risk of COVID-19. The IVC diameter reflects moderate increases in right atrial (RA) pressure [22], which serves as an indicator of intracardiac and systemic hemodynamics. RA pressure depends on cardiac output and venous return and is modulated by the sympathetic branch of the autonomic nervous system (ANS) [23].

These data indirectly support the role of sympathetic activation of the autonomic nervous system and increased blood pressure variability in susceptibility to COVID-19. Bellocchi et al. (2022) demonstrated a close interaction between the autonomic nervous system and the immune system. The ANS regulates both innate and adaptive immunity via sympathetic and parasympathetic pathways, and dysregulation of this balance may alter immune responses and promote inflammation [24, 25].

Longitudinally, one year post-infection, normotensive men who had COVID-19 exhibited increases in average daily systolic blood pressure (SBP), diastolic blood pressure (DBP), and SBP variability, alongside reductions in circadian heart rate indices compared to those who remained uninfected. These changes suggest worsening autonomic imbalance and align with findings from other studies.

Jatiya *et al*. (2024) reported autonomic dysfunction in patients three months post-COVID-19 infection, which correlated with inflammatory markers, autonomic function test results, and heart rate variability parameters [26].

In our cohort, 28.1% of normotensive men who subsequently developed COVID-19 exhibited elevated average daily systolic and diastolic blood pressure (SBP and DBP) one year post-infection compared to those who remained uninfected. These changes were accompanied by increased right heart workload and left ventricular (LV) wall thickening, culminating in concentric LV hypertrophy in 25% of affected individuals. Furthermore, initial average daily and nighttime variability of SBP and DBP correlated with interventricular septum (IVS) thickness in normotensive men following COVID-19.

The association between COVID-19 and the long-term risk of hypertension development and progression remains incompletely understood. Wasim *et al.* (2021) reported that approximately 16% of patients developed newly diagnosed arterial hypertension (AH) post-infection. Proposed mechanisms include activation of the renin-angiotensin-aldosterone system, volume overload, hyperreninemia, cytokine storm, and sympathetic nervous system activation [27].

Our study investigated the relationship between circadian rhythm disturbances, blood pressure (BP) chronostructure, and variability of blood pressure (VBP) indices, aiming to elucidate regulatory mechanisms contributing to heightened cardiovascular responses in normotensive individuals following COVID-19.

Circadian rhythms of the cardiovascular system, including blood pressure, are orchestrated by the biological clock located in the suprachiasmatic nucleus of the hypothalamus. These rhythms are modulated via humoral mediators of the autonomic nervous system (ANS), which exert effects on vascular structures and immune cells, indicating shared regulatory mechanisms of the ANS for both circadian rhythms and immune function [28, 29].

The circadian rhythm of the human body is well characterized and plays a pivotal role in regulating neuroendocrine and immune system functions that maintain physiological homeostasis [30].

A key finding of our study is that, beyond the observed increase in average daily blood pressure (BP) values among normotensive individuals following COVID-19, there was a notable disruption in the chronostructure of daily BP patterns. This disruption manifested as a reduction in the typical 24-hour rhythm—referred to as the "true normotension" chronotype—and a corresponding increase in abnormal hypertensive patterns characterized by shorter rhythms within the daily spectrum, termed "aperiodic arterial hypertension (AH)." This atypical chronotype was identified in 25.6% of infected individuals.

Previous research has established that an atypical circadian BP chronotype constitutes an independent risk factor for the development of arterial hypertension. This chronotype is associated with more pronounced structural alterations in the myocardium, exacerbated autonomic symptoms, and frequent atherosclerotic lesions in the brachiocephalic arteries [15].

In our prior study [12], we were the first to evaluate the impact of circadian blood pressure (BP) chronoperiodicity disturbances on COVID-19 risk among hypertensive patients working Arctic shift schedules. Chronobiological analysis revealed that the presence of the "aperiodic arterial hypertension (AH)" chronotype increased the risk of contracting COVID-19 threefold. Moreover, in hypertensive patients, initial replacement of the normal 24-hour BP rhythm by short-duration fluctuations within the daily spectrum prior to COVID-19 infection correlated with more pronounced echocardiographic changes post-infection.

In the present study, correlation analysis demonstrated an inverse relationship between blood pressure (BP) variability indices and the integrity of the normal 24-hour rhythm. Elevated BP variability thus serves as a marker of disturbed chronostructure in the daily BP rhythm, likely driven by generalized dysregulation of autonomic nervous system (ANS) function in both hypertensive and normotensive individuals.

Consequently, longitudinal assessment of cardiovascular status via ambulatory blood pressure monitoring (ABPM) and echocardiography (EchoCG) in normotensive men one year post-COVID-19 revealed that approximately one-third of infected subjects exhibited hypertensive average daily systolic and diastolic BP values and developed concentric left ventricular (LV) hypertrophy. Furthermore, increased average daily BP variability was linked to a heightened risk of COVID-19 and to more pronounced echocardiographic alterations, including a significant increase in interventricular septum (IVS) thickness following infection. This elevated BP variability was also associated with disruption of the normal 24-hour BP chronostructure and the emergence of an atypical "aperiodic" hypertension chronotype in 21% of normotensive men after COVID-19.

Conclusion

In the context of Arctic rotating shift work, elevated blood pressure (BP) variability reflects autonomic dysfunction and serves as a marker of disrupted chronostructure in the circadian BP rhythm. This disruption has prognostic significance, being associated with an increased risk of COVID-19 infection and subsequent cardiovascular complications in both hypertensive and normotensive individuals. These findings underscore the importance of identifying patients with heightened BP variability as a high-risk subgroup warranting intensified monitoring and management within shift-based occupational health settings.

Limitations

This study is limited by a relatively small sample size, restricted to normotensive individuals. Additionally, the investigation primarily focuses on autonomic imbalance and the interplay between blood pressure variability and circadian rhythms among hypertensive patients exposed to desynchronized environmental conditions in the Far North and engaged in rotating shift work. These factors may limit the generalizability of the findings to broader populations.

Authors' contributions

Conceptualization and study design: Shurkevich N.P., Vetoshkin A.S., Kareva M.A. Data processing and analysis: Shurkevich N.P., Vetoshkin A.S., Kareva M.A., Gubin D.G. Manuscript drafting: Shurkevich N.P., Vetoshkin A.S. Manuscript editing and revision: Shurkevich N.P., Vetoshkin A.S., Gapon L.I., Gubin D.G.

Ethical Approval

This retrospective analysis was performed as part of routine clinical practice. All patients provided written informed consent for the use and processing of their data in accordance with Order No. 36/1 dated January 29, 2020, and the approved consent form. Comprehensive patient examinations adhered to the ethical standards of the Declaration of Helsinki and the clinical practice guidelines of the Russian Federation ("Good Clinical Practice," GOST R 52379-2005), following protocol No. 149 dated June 3, 2019, which was approved by the Academic Council of the Tyumen Cardiology Research Center and its Ethics Committee.

Participants were invited to participate in the research project and, upon consenting, signed voluntary informed consent forms. The cross-sectional "Light Arctic" study was conducted in accordance with the Declaration of Helsinki principles and received approval from the Ethics Committee of Tyumen State Medical University (Protocol No. 101, dated September 13, 2021). All participants provided written informed consent prior to inclusion.

Conflict of Interest

The authors declare that they have no competing interests.

Funding

This study was supported by the West Siberian Science and Education Center, Government of Tyumen District (Decree No. 928-rp, dated November 20, 2020).

References

1. Korostovtseva LS, Rotar OP, Konradi AO. COVID-19: what are the risks in hypertensive patients? *Arterial Hypertension* 2020; 26(2): 124-132. Russian. https://doi.org/10.18705/1607-419X-2020-26-2-124-132.
2. Porzionato A, Emmi A, Barbon S, Boscolo-Berto R, Stecco C, Stocco E et al. Sympathetic activation: a potential link between comorbidities and COVID-19. *FEBS J* 2020; 287(17): 3681-3688. https://doi.org/10.1111/febs.15481.
3. Chacón F, Cano P, Lopez-Varela S. Chronobiological features of the immune system. Effect of calorie restriction. *Eur J Clin Nutr* 2002; 56(3): 69-72. https://doi.org/10.1038/sj.ejcn.1601491.
4. Daodu TB, Rugel EJ, Lear SA. Impact of Long COVID-19 on Health Outcomes Among Adults with Preexisting Cardiovascular Disease and Hypertension: A Systematic Review. *CJC Open* 2024; 6(8): 939-950. https://doi.org/10.1016/j.cjco.2024.03.003.
5. Korneeva YaA, Simonova NN, Degteva GN, Dubinina NI. Shift workers adaptation strategies in the Far North. *Human ecology* 2013; 20(9): 9-16. Russian. https://doi.org/10.17816/humeco17305.
6. Merkulov YuA, Pyatkov AA, Gorokhova SG, Merkulova DM, Atkov OYu. Disturbances of Autonomic Regulation of Cardiovascular System at

Different Working Regimes with Night Shifts. *Kardiologiia* 2020; 60(9): 62-67. Russian. https://doi.org/10.18087/cardio.2020.9.n1134.

7. Durov AM, Gubin DG, Denezhkina VL, Nazarenko MA. Comparative analysis of circadian rhythms of cardiorespiratory system and the biological age of inhabitants of the south and the north of the Tyumen Region. *Fundamental research* 2015; (1 Pt 4): 730-734. Russian. https://www.elibrary.ru/twtopf.
8. Baschieri F, Cortelli P. Circadian rhythms of cardiovascular autonomic function: Physiology and clinical implications in neurodegenerative diseases. *Auton Neurosci* 2019; 217: 91-101. https://doi.org/10.1016/j.autneu.2019.01.009.
9. Shurkevich NP, Vetoshkin AS, Gubin DG, Gapon LI. Arterial hypertension in the Far North. Desynchronosis and hyperreactivity of the body as factors in the development of the disease. Moscow: Medical book, 2009; 208 p. Russian. https://www.elibrary.ru/QLTUPN.
10. Morin CM, Carrier J, Bastien C, Godbout R. Canadian Sleep and Circadian Network. Sleep and circadian rhythm in response to the COVID-19 pandemic. *Can J Public Health* 2020; 111(5): 654-657. https://doi.org/10.17269/s41997-020-00382-7.
11. Cugini P, Kawasaki L, Palma D. Arterial hypertension: diagnostic optimization using chronobiologic analysis of blood pressure monitoring in a cybernetic view. In: Halberg F, Watanabe H, Eds Workshop on Computer Methods on Chronobiology and Chronomedicine: 20th International Congress of Neurovegetative Research. Tokyo: Medical Review, 1992; 38: 69-88.
12. Shurkevich NP, Vetoshkin AS, Kareva MA, Gubin DG. Arterial hypertension and COVID-19 in Arctic rotating shift work: the impact of chronostructure disruptions on circadian blood pressure rhythm in relation to echocardiographic parameters. *Russi Open Med J* 2024; 13: e0408. https://doi.org/10.15275/rusomj.2024.0408.
13. Gapon LI, Shurkevich NP, Vetoshkin AS, Gubin DG, Belozerova NB. Orcadian profile and chrono-structure of blood pressure in patients with arterial hypertension: desynchronosis as a risk factor in Far North shift workers. *Cardiovascular Therapy and Prevention* 2011; 10(1): 38-46. Russian. https://www.elibrary.ru/ntjhxx.
14. Gubin DG, Cornelissen G, Weinert D, Vetoshkin A, Gapon L, Shurkevich N, et al. Circadian disruption and vascular variability disorders (VVD): Mechanisms linking aging, disease state and Arctic shift work: Applications for chronotherapy. *World Heart Journal* 2013; 5(4): 285-306. https://www.elibrary.ru/tqhvwj.
15. Vetoshkin AS, Shurkevitch NP, Gubin DG, Poshinov FA, Belozyorova NV, Gapon LI. Desynchronosis in the form of a typical chronotypes of daily rhythms of arterial pressure in healthy persons as an arterial hypertension risk factor in transpolar rotational working system conditions. *Therapist* 2013; (9): 46-55. Russian. https://www.elibrary.ru/rjluhf.
16. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015; 28(1): 1-39.e14. https://doi.org/10.1016/j.echo.2014.10.003.
17. Wolff D, Nee S, Hickey NS, Marschollek M. Risk factors for Covid-19 severity and fatality: a structured literature review. *Infection* 2021; 49(1): 15-28. https://doi.org/10.1007/s15010-020-01509-1.
18. Farshbafnadi M, Kamali Zonouzi S, Sabahi M, Dolatshahi M, Aarabi MH. Aging & COVID-19 susceptibility, disease severity, and clinical outcomes: The role of entangled risk factors. *Exp Gerontol* 2021; 154: 111507. https://doi.org/10.1016/j.exger.2021.111507.
19. Giunta S, Giordani C, De Luca M, Olivieri F. Long-COVID-19 autonomic dysfunction: An integrated view in the framework of inflammaging. *Mech Ageing Dev* 2024; 218: 111915. https://doi.org/10.1016/j.mad.2024.111915.
20. Hoshide S, Yano Y, Mizuno H, Kanegae H, Kario K. Day-by-day variability of home blood pressure and incident cardiovascular disease in clinical practice: The J-HOP study (Japan Morning surge-home blood pressure). *Hypertension* 2018; 71(1): 177-184. https://doi.org/10.1161/hypertensionaha.117.10385.
21. Mancia G, Di Rienzo M, Parati G, Grassi G. Sympathetic activity, blood pressure variability and end organ damage in hypertension. *J Hum Hypertens* 1997; 11 Suppl 1: S3-8. https://pubmed.ncbi.nlm.nih.gov/9321734.
22. Alekhin MN, Zateischikova AA, Kiselev DG, Shavrin IV, Privalov DV, Vtorushkin DV. Importance of echocardiographic postcava evaluation for calculations of average pressure in the pulmonary artery in patients with chronic obstructive lung disease. *Kremlin Medicine Journal* 2010; (2): 64-67. Russian. https://www.elibrary.ru/mwpkwd.
23. Bruno RM, Ghiadoni L, Seravalle G, Raffaella D, Taddei S. Sympathetic nervous system activity in health and disease – advances with microneurographic recordings. Front. Physiol. 2012; 3: 284. https://doi.org/10.3389/fphys.2012.00284.
24. Bellocchi C, Carandina A, Montinaro B, Targetti E, Furlan L, Rodrigues GD et al. The Interplay between Autonomic Nervous System and Inflammation across Systemic Autoimmune Diseases. *Int J Mol Sci* 2022; 23(5): 2449. https://doi.org/10.3390/ijms23052449.
25. Datta K., Tripathi M. Sleep and Covid-19. *Neurol India* 2021; 69(1): 26-31. https://doi.org/10.4103/0028-3886.310073.
26. Jatiya L, Feula JM, Latha R, Vidhyalakshmi R, Rajesh J. Autonomic Imbalance and Elevated Inflammatory Cytokines in Long COVID: A Cross-Sectional Study. *Cureus* 2024; 16(8): e66971. https://doi.org/10.7759/cureus.66971.
27. Wasim D, Alme B, Jordal S, Lind Eagan TM, Tadic M, Mancia G, et al. Characteristics of 24-hour ambulatory blood pressure monitoring in a COVID-19 survivor. *Future Cardiol* 2021; 17(8): 1321-1326. https://doi.org/10.2217/fca-2020-0235.
28. Yamakawa GR, Brady RD, Sun M, McDonald SJ, Shultz SR, Mychasiuk R. The interaction of the circadian and immune system: Desynchrony as a pathological outcome to traumatic brain injury. *Neurobiol Sleep Circadian Rhythms* 2020; 9: 100058. https://doi.org/10.1016/j.nbscr.2020.100058.
29. Adrover JM, Del Fresno C, Crainiciuc G, Cuartero M, Casanova-Acebes M, Weiss LA, et al. A Neutrophil Timer Coordinates Immune Defense and Vascular Protection. *Immunity* 2019; 50(2): 390-402.e10. https://doi.org/10.1016/j.immuni.2019.01.002.
30. Huang H, Mehta A, Kalmanovich J, Anand A, Bejarano MC, Garg T, Khan N, et al. Immunological and inflammatory effects of infectious diseases in circadian rhythm disruption and future therapeutic directions. *Mol Biol Rep* 2023; 50(4): 3739-3753. https://doi.org/10.1007/s11033-023-08276-w.

Authors:

Nina P. Shurkevich – MD, PhD, Leading Researcher, Department of Arterial Hypertension and Coronary Insufficiency, Scientific Division of Clinical Cardiology, Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Russian Academy of Sciences, Tomsk, Russia. http://orcid.org/0000-0003-3038-6445.

Aleksander S. Vetoshkin – MD, PhD, Senior Researcher, Department of Arterial Hypertension and Coronary Insufficiency, Scientific Division of Clinical Cardiology, Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Russian Academy of Sciences, Tomsk, Russia. http://orcid.org/0000-0002-9802-2632.

Maria A. Kareva – MD, Cardiologist, Department of Arterial Hypertension and Coronary Insufficiency, Scientific Division of Clinical Cardiology, Tyumen Cardiology Research Center; Tomsk National Research Medical Center, Russian Academy of Sciences, Tomsk, Russia. http://orcid.org/0000-0002-7200-8111.

Lyudmila I. Gapon – MD, PhD, Professor, Honored Scientist of the Russian Federation, Head of the Scientific Division of Clinical Cardiology, Tyumen Cardiology Research Center; Tomsk National Research Medical Center, Russian Academy of Sciences, Tomsk, Russia. http://orcid.org/0000-0002-3620-0659.

Denis G. Gubin – MD, PhD, Professor, Department of Biology, Tyumen State Medical University; Head of the Laboratory of Chronobiology and Chronomedicine, University Research Institute of Medical Biotechnology and Biomedicine, Tyumen State Medical University; Senior Researcher, Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Russian Academy of Sciences, Tomsk, Russia. http://orcid.org/0000-0003-2028-1033.