MEDICAL UNIVERSITY – PLEVEN
Faculty of Medicine
Department of Physiology and Pathophysiology

NON-INVASIVE STUDY OF HEMODYNAMICS IN PATIENTS WITH ARTERIAL HYPERTENSION AND OTHER RISK FACTORS

ABSTRACT OF A DISSERTATION
for the acquisition of the educational and scientific degree
"DOCTOR" (PhD)
Professional Field: 7.1. *Medicine*
Doctoral Programme: *Pathophysiology*

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The dissertation contains 150 standard printed pages and is illustrated with 14 tables and 35 figures. The bibliographic list includes 195 literary sources, of which 2 are in Cyrillic and 193 in Latin.

The clinical material related to the dissertation was collected at University Hospital and Medical Center "Prof. Dr. Stoyan Kirkovich" – Stara Zagora. The studies were conducted at the Pathophysiology Section of the Department of Physiology, Pathophysiology and Pharmacology, Faculty of Medicine, Trakia University – Stara Zagora.

The dissertation was discussed, approved and referred for public defense by the Extended Departmental Council of the Department of Physiology and Pathophysiology at the Medical University – Pleven.

The official public defense of the dissertation will take place on 02.10.2026 at 12:30 in Ambroise Paré Hall of the Medical University – Pleven.

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CONTENTS:

I. INTRODUCTION

High cardiovascular risk is clearly indicated as the leading cause of mortality in developed countries by both the World Health Organization and various large studies such as the Framingham Study, the SCORE Study, etc.

The best therapeutic strategy for its reduction and optimization is primary prevention, since patients undergoing secondary prevention already have vascular regions affected by atherosclerotic plaques, and these structures, once they appear, cannot be removed regardless of the good management of modifiable risk factors. In the last decade, multidisciplinary expert groups, including cardiologists, preventive medicine specialists, endocrinologists, gastroenterologists, nephrologists, epidemiologists and public health experts, have developed various recommendations on how to make an exact stratification of cardiovascular risk based on anamnestic data, laboratory and instrumental methods in order to initiate adequate treatment.

Specific risk groups with higher cardiovascular risk stand out, such as patients with arterial hypertension, patients who smoke (two major modifiable risk factors for the development of atherosclerosis), patients with metabolic syndrome and type 2 diabetes mellitus, patients with metabolically active fatty liver disease (as the concept of pathogenesis, complications and especially cardiovascular involvement in this disorder has undergone significant development in the last 5-10 years, the product of which are several multidisciplinary consensuses and several changes in the name of the disease). Faced with a highly contagious viral disease with multisystem involvement such as Covid infection, we understood that methods for individual assessment of cardiovascular risk must be sufficiently flexible and widely available to be of assistance in the prevention and treatment of cardiovascular diseases in patients with Covid infection and post-Covid syndrome, some of whom may already belong to one or more groups of individuals with increased cardiovascular risk.

The constellation theory in pathophysiology, which emerged in the second half of the twentieth century, views each disease as the result of the simultaneous action and mutual potentiation of multiple genetic, molecular, metabolic, hemodynamic, behavioral, environmental, and other factors that form a “constellation” of risk determinants specific to each individual. And if we are not sure that we can capture this “constellation” at a glance, it would be a good idea to take a step further - the development of atherosclerotic disease is a continuum starting with early functional disorders of the vascular endothelium, increased arterial stiffness, and formation and progression of atherosclerotic plaque.

Since increased arterial stiffness is an indispensable and at the same time potentially reversible link in the pathogenetic continuum of atherosclerosis, it would follow that methods for its measurement and have diagnostic significance for patients with subclinical atherosclerosis; prognostic significance - as a method for rapid determination of cardiovascular risk (which takes into account the complex impact of all protective and risk factors - even in cases of borderline values of laboratory tests, belonging to several risk groups or incomplete anamnestic and catamnestic data) as well as significance for monitoring the cardiovascular benefits of various behavioral and therapeutic interventions (as a non-invasive, completely safe and harmless, comfortable for the patient method that can be used as many times as necessary).

Therefore, recently, methods for assessing arterial stiffness and in particular tonometric examination of the brachial artery, have been gaining increasing scientific and clinical significance for diagnosis, stratification and monitoring the dynamics of cardiovascular risk.

II AIMS AND OBJECTIVES

AIM:

To conduct a non-invasive study of hemodynamic indicators of arterial stiffness in patients with arterial hypertension divided into different groups according to the presence of other risk factors.

Objectives

To achieve this aim, the following objectives are defined:

1: Non-invasive study of hemodynamic indicators of arterial stiffness in patients with arterial hypertension, classified based on the questionnaire method as primary smokers, secondary smokers and non-smokers.

1A: Measurement and comparison of augmentation pressure and augmentation index in the three studied groups.

1B: Measurement and comparison of subendocardial viability in the three studied groups.

2: Non-invasive study of hemodynamic indicators of arterial stiffness in patients with newly diagnosed arterial hypertension, after experiencing COVID infection and analysis of their relationship with some demographic, clinical and laboratory parameters:

2A: Study of the distribution by gender and age of indicators of arterial stiffness in patients with newly diagnosed arterial hypertension after experiencing COVID infection.

2B: Study of the difference in indicators of arterial stiffness and vascular inflammation in patients with newly discovered arterial hypertension after a previous Covid infection with and without post-Covid syndrome.

2B: Study of the relationship between arterial stiffness indicators and C-reactive protein levels and platelet-lymphocyte ratio.

2D: Monitoring the dynamics of arterial stiffness indicators - augmentation pressure and augmentation index during recovery from Covid infection at regular intervals for a period of 12 months.

3: Non-invasive study of hemodynamic indicators of arterial stiffness with arterial hypertension of several years of history and newly discovered metabolically associated hepatic steatosis.

3A: Comparison of non-invasively studied arterial stiffness indicators in patients with arterial hypertension of several years of history with and without metabolically associated fatty liver disease.

Subobjective 3B: Monitoring the dynamics of the studied parameters while maintaining the current drug therapy and implementing a hypocaloric Mediterranean-style diet.

IV. MATERIALS AND METHODS

1.Material basis for the implementation of the dissertation work

The present study was conducted entirely in a suitably equipped lab for functional studies and non-invasive monitoring of the cardiovascular system at the Faculty of Medicine of the Thracian University

2. Study Population

Patients included in the study were recruited between January 2018 and November 2020. A total of 729 patients with arterial hypertension were enrolled, comprising 180 participants in the smoker/non-smoker group, 110 patients with newly diagnosed arterial hypertension following COVID-19 infection, and 439 patients with long-standing arterial hypertension with or without metabolic dysfunction-associated steatotic liver disease (MASLD).

Participants were referred by their general practitioners, cardiologists, or other physicians practicing at various healthcare facilities in the city of Stara Zagora. The author gratefully acknowledges the invaluable support and collaboration of these colleagues.

All participants were 18 years of age or older, fully oriented to person, place, and time, and capable of reading, understanding, and personally signing the informed consent. The study was conducted following approval by the Research Ethics Committee of the Faculty of Medicine, Trakia University, Stara Zagora.

3. Inclusion and Exclusion Criteria

Inclusion Criteria

1. Belonging to the predefined age group of 64 ± 15 years.
2. Availability and voluntary provision of detailed medical history and relevant medical documentation regarding arterial hypertension and its management, including disease duration, usual and maximum blood pressure values, antihypertensive medications and dosage regimen, and adherence to both lifestyle recommendations and pharmacological treatment.
3. Adults who were fully oriented to person, place, and time, capable of reading, understanding, and personally signing the informed consent form, as well as completing all questionnaires required for the study.

Exclusion Criteria

I. Cardiac rhythm and conduction disorders

- Persistent atrial fibrillation.
- Persistent first-, second-, or third-degree atrioventricular block.
- Permanent cardiac pacemaker.
- Frequent ventricular premature contractions.

II. Anatomical and vascular abnormalities

- Anatomical or vascular abnormalities affecting the arterial segments examined, leading to inaccurate assessment of arterial stiffness.
- Limb or partial limb amputation.

III. Other exclusion criteria

- Systemic glucocorticoid therapy.
- Active malignant disease.
- Pregnancy.
- Poor patient compliance on the day of examination.
- Smoking or use of nicotine in any form, alcohol consumption, or coffee intake within 4 hours before the examination.
- Inadequate or missed intake of the participant's usual medication on the day of examination, with particular attention to antihypertensive therapy.
- Age below 18 years.
- Individuals who were menthal disoriented.

4. Methods

I. Questionnaire-Based Assessment

A structured face-to-face interview was conducted with all participants to obtain information regarding:

1. Age;
2. Duration and control of arterial hypertension, including usual and maximum blood pressure values, pharmacological and non-pharmacological interventions, and adherence to prescribed treatment;
3. Comorbidities, with particular emphasis on conditions that could influence blood pressure control and atherosclerotic vascular changes;
4. Family history of arterial hypertension, dyslipidaemia, atherosclerosis, and its cardiovascular complications;
5. Tobacco use, classified as current smoker, passive smoker, or non-smoker.

II. Anthropometric Measurements

The following anthropometric parameters were recorded:

1. Height (cm);
2. Body weight (kg);
3. Waist circumference (cm);
4. Measurements required for pulse wave velocity assessment, including the distance from the ramus of the mandible to the sternum (mm) and from the sternum to the inguinal fold.

Body mass index (BMI) was calculated according to the following formula:

BMI = weight (kg) / height^2 (m^2).

The Waist-to-Height Ratio (WHtR) was calculated as the ratio of waist circumference (cm) to height (cm):

WHtR = waist circumference (cm) / height (cm).

III. Laboratory Methods

Serum lipid profile parameters, including total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides, as well as C-reactive protein (CRP), were measured in plasma obtained from fasting venous blood samples collected after a 12-hour overnight fast and, whenever possible, following abstinence from smoking.

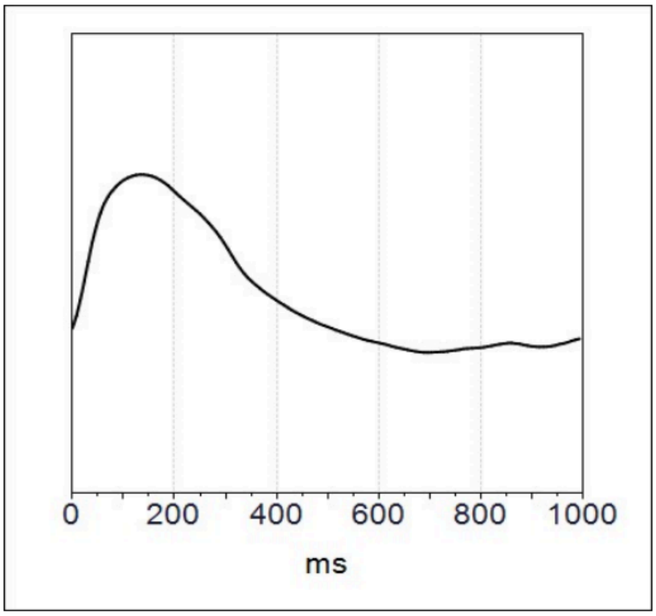
A complete blood count was performed, including erythrocyte, leukocyte, and platelet counts, haemoglobin concentration, haematocrit, differential leukocyte count, erythrocyte indices, and platelet indices. Analyses were carried out using an automated haematology analyser based on the impedance method and flow cytometry.

All laboratory analyses were performed in a certified clinical laboratory.

IV. Instrumental Methods

1. Brachial blood pressure was measured in both arms using the Riva-Rocci auscultatory method after 15 minutes of rest, with the participant in the supine position. The average of three consecutive measurements was used for analysis.
2. Arterial tonometry of the brachial artery was performed using the SphygmoCor XCEL device.

Average Peripheral Pulse



SYS
139
mmHg

DIA
73
mmHg

PPP
66
mmHg

MAP
95
mmHg

Overall Quality: **100 %**

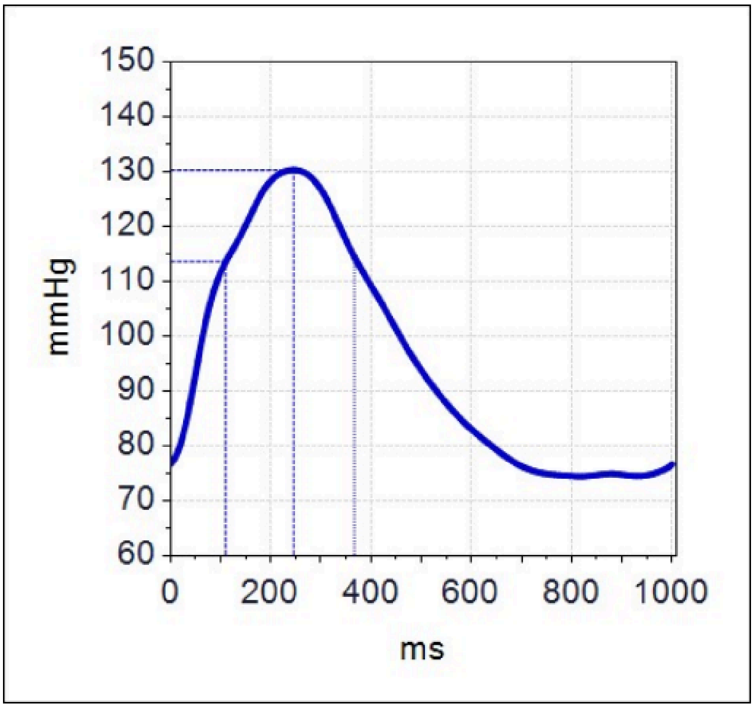
Average Aortic Pressure Pulse

SP
130
mmHg

DP
75
mmHg

PP
55
mmHg

HR
60
bpm



PP Amplification: **119 %**

The time-pressure curve in the brachial artery is measured by applanation of the artery, and depending on the anatomical features and compliance of the patient, the tonometric sensor is attached to the artery using a tonometer pen or a brachial cuff. It is important that the pressure is uniform throughout the examination and allows normal blood flow in the artery. The tonometric sensor works on an oscillometric principle. After registering 10 consecutive time-pressure curves, the device software processes them and creates a model of the aortic time-pressure curve with an appropriate transfer function.

V. Statistical Analysis

Statistical analyses were performed using Microsoft Excel and IBM SPSS Statistics software. Prior to the statistical analyses, the distribution of continuous variables was assessed for normality using tests of Gaussian (normal) distribution.

Descriptive statistics for continuous variables included the calculation of the mean, standard deviation (SD), and 95% confidence interval (95% CI).

Comparisons of mean values between two independent groups were performed using the independent-samples Student's t-test when the data followed a Gaussian distribution. When the assumption of normality was not met, the Mann–Whitney U test was applied.

For comparisons of measurements obtained from the same participants before and after the intervention, the paired Student's t-test was used for normally distributed data, whereas the Wilcoxon signed-rank test was applied when the assumption of normality was not satisfied.

The linear relationship between continuous variables was evaluated using Pearson's correlation analysis, and the Pearson correlation coefficient (r) was calculated.

Statistical significance was defined as a two-sided p-value < 0.05.

V. RESULTS

Results for objective 1: Non-invasive study of hemodynamic indicators of arterial stiffness - augmentation pressure, augmentation index and subendocardial viability in patients with arterial hypertension, classified based on the questionnaire method as primary smokers, secondary smokers and non-smokers

For the first objective , 180 patients with arterial hypertension were included in the study. - 52% men and 48% women. The distribution by gender and according to tobacco consumption habits is presented in Figure 1, with percentages rounded to whole numbers. It is noteworthy that the largest number of male smokers is 24%, the smallest number of female active smokers is 11% and male passive smokers is 12%.

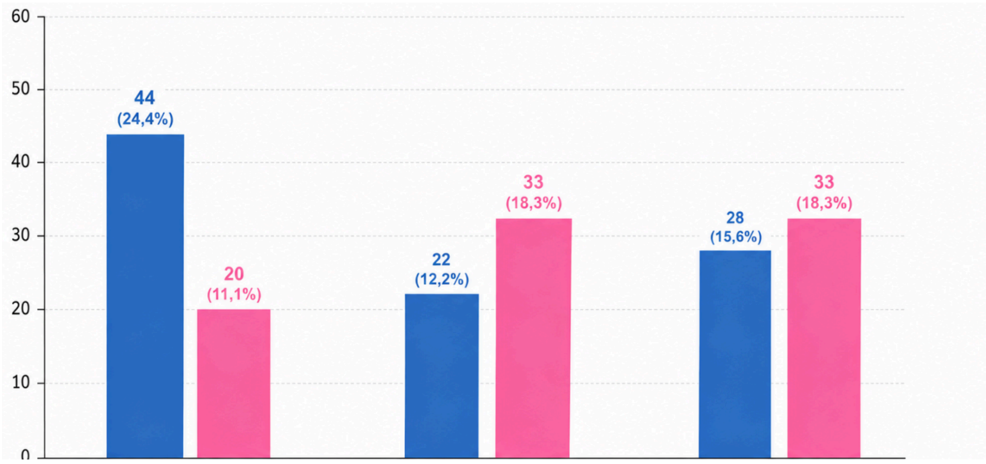


Fig. 1: Distribution by gender and tobacco consumption habits of the studied patients with arterial hypertension

Regarding blood pressure control, the largest proportion of the studied patients had suboptimal blood pressure control – 48% (n=87), and the proportion of patients with poor ABP control was the smallest – 21% (n=38).

Already during the history taking and clinical examination, some differences emerge between active smokers and non-smokers, as presented in Table 1.

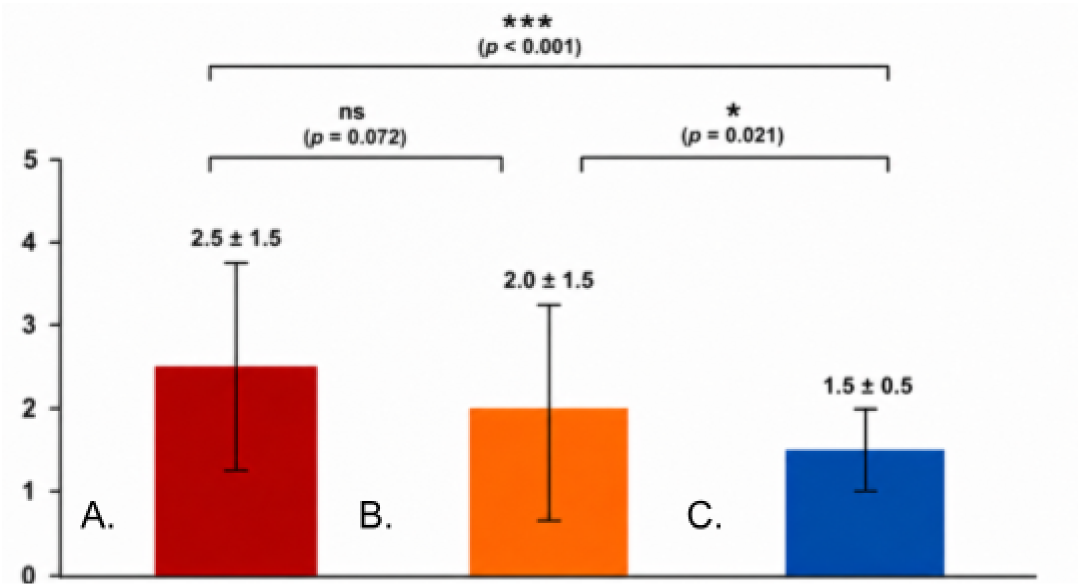


Fig. 2. Antihypertensive therapy in active smokers (A.) , passive smokers (B.) and non-smokers (C.) with arterial hypertension - arithmetic mean and standard deviation. Comparison with Student's T test and Bonferroni correction

**statistically significant difference*

**** statistically significant difference at p<0.001*

	Active smoker +AH	Nonsmoker +AH	p
Medical history			
Age of initiation of antihypertensive therapy	55±6	57±4	0,12
Number of medications used to control BP	2,5±1,5	1,5±0,5	0,001*
Clinical examination			
Brachial SBP	156±11	137±12	0,001*
Ankle-Brachial index	0,8±0,4	1,1±0,2	0,001*
HR	78,7±10,7	76,4±16.8	0,37
Антропометрични размери			
BMI	25±4	27±6	0,02*
Waist circumference	101±11	106±8	0,001*

Table 1 Mean values and standard deviation of anamnestic, clinical and anthropometric data and comparison between the included active smokers and non-smokers.

** statistically significant difference*

1A: Measurement and comparison of augmentation pressure and augmentation index in the three studied groups

Regarding intra-aortic systolic arterial pressure, the indicators of active and passive smokers with AH are similar, but the difference between both active smokers and non-smoking hypertensives is statistically significant, as can be seen in Figure 3.

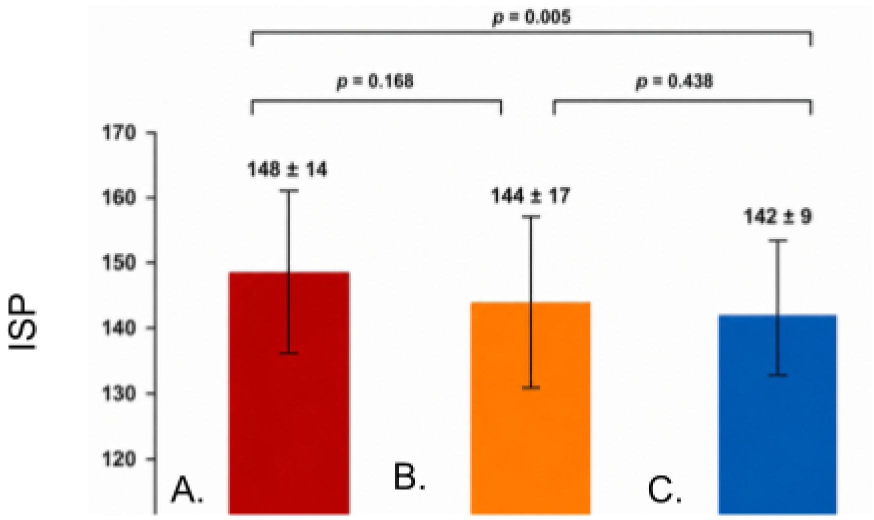


Fig. 3. Intraaortic systolic pressure (ISP) in active smokers (A.) , passive smokers (B.) and non-smokers (C.) with arterial hypertension - mean and standard deviation. Comparison with Student's T test and Bonferroni correction

**statistically significant difference*

**** statistically significant difference at p<0.001*

The values of the augmentation pressure show a statistically significant difference between the three studied groups of patients with arterial hypertension. As can be seen from Figure 4, it is highest in hypertensive active smokers (26mmHg±9,), and lowest - in non-smokers (18mmHg±5) as the level of significance for the difference between active and passive smokers hypertensives is 0.04, and between smokers and non-smokers hypertensives p=0.00.

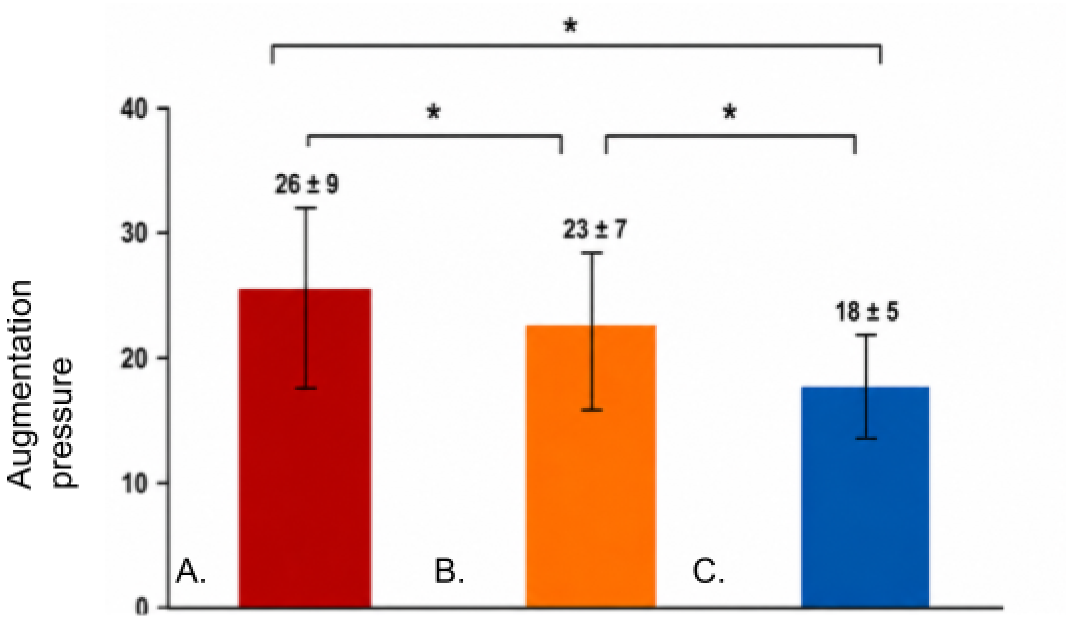


Fig. 4. Augmentation pressure of patients with arterial hypertension - active smokers (A.) , passive smokers (B.) and non-smokers (C.) with arterial hypertension - arithmetic mean and standard deviation. Comparison with Student's T test and Bonferroni correction

**statistically significant difference*

**** statistically significant difference at p<0.001*

The augmentation index depends on the values of the augmentation and pulse pressure, so it is not surprising that similar dependencies are observed with it. The difference in the augmentation index between the studied active smokers and passive smokers with AH is statistically significant, the difference between active smokers and non-smokers is also significant, but not the difference between passive smokers and non-smokers. The observed trends are illustrated in Figure 5

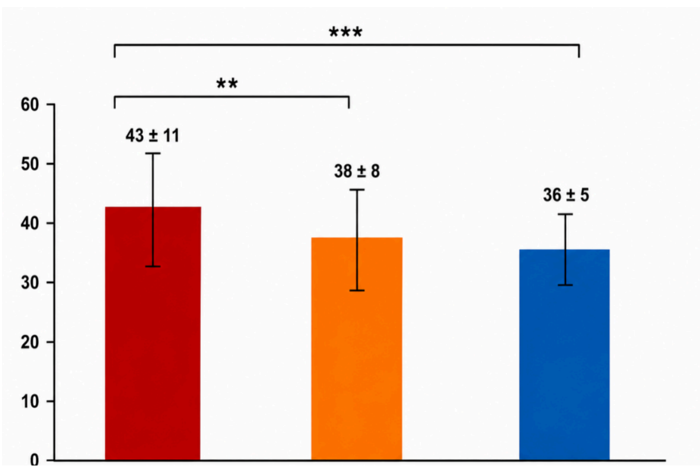


Fig. 5. Augmentation index of patients with arterial hypertension - iactive smokers (A.) , passive smokers (B.) and non-smokers (C.) - arithmetic mean and standard deviation. Comparison with Student's T test and Bonferroni correction

**statistically significant difference*

**** statistically significant difference at p<0.001*

1B: Measurement and comparison of subendocardial viability in the three studied groups

Regarding subendocardial viability, only SEVR significantly differs in active smokers versus non-smokers. There is a tendency (figure 6) for the Bookberg index to be lowest (i.e. most unfavorable) in active smokers with AH, higher in passive smokers with AH and highest in non-smokers with AH.

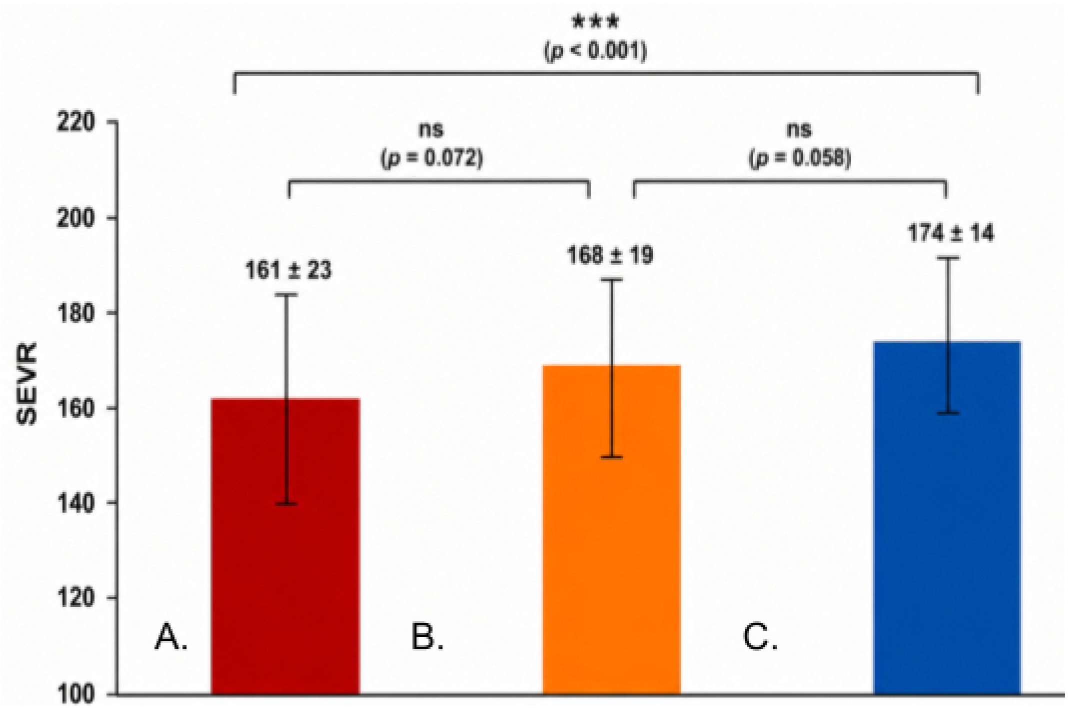


Fig. 6. Subendocardial viability of patients with arterial hypertension - *in active smokers (A.) , passive smokers (B.) and non-smokers (C.)* - arithmetic mean and standard deviation. Comparison with Student's T test and Bonferroni correction

*statistically significant difference

*** statistically significant difference at p<0.001

Discussion on objective 1

The established higher values of AIx and AP in active smokers can be explained by the direct vasoconstrictor effect of nicotine on the sympathetic nervous system. In addition to acute functional changes, chronic smoking is also associated with structural changes in the arterial wall, including increased collagen deposition and destruction of elastic fibers. The role of smoking as a predisposing factor for the development of atherosclerosis is also indisputable.

Of particular interest is the fact that similar, although less pronounced, changes are also observed in individuals exposed to passive smoking.

According to literature data, short-term exposure to tobacco smoke leads to measurable impairments in endothelial function and increased arterial stiffness, with effects comparable to those observed in active smokers (Barnoya & Glantz, 2005; Argacha et al., 2008).

The observed changes in AIx in second-hand smokers are likely the result of the same pathophysiological mechanisms that operate in active smokers, although with lower intensity.

The results obtained are in accordance with the studies of Mahmud and Feely (2003), which demonstrated a significant increase in the augmentation index immediately after smoking.

Of particular importance is the fact that the augmentation index is considered a sensitive and dynamic marker of early vascular changes. Therefore, its increase in smokers can be considered as an early sign of subclinical vascular damage, preceding the development of clinically apparent cardiovascular disease.

Conclusions on sub-objective 1A:

1. A significant difference in the augmentation index was observed in the three studied groups ($p<0.001$).
2. A significant difference in the augmentation pressure was observed in the three studied groups ($p<0.05$).

Conclusions on sub-objective 1B:

1. A significant difference in subendocardial viability was observed between active smokers and non-smokers with AH ($p<0.001$).
2. There was no significant difference in subendocardial viability between active smokers and passive smokers as well as between passive smokers and non-smokers.

Results for objective2: Non-invasive study of hemodynamic indicators of arterial stiffness in patients with newly diagnosed arterial hypertension after experiencing COVID infection and study of their relationship with age, gender and some inflammatory markers.

2A: Study of the distribution by gender and age of indicators of arterial stiffness in patients with newly diagnosed arterial hypertension after experiencing COVID infection.

The descriptive analysis of the indicators of arterial stiffness, measured by non-invasive examination of the reflected pulse wave, shows relatively similar values in men and women, with some differences observed both in terms of average values and in terms of variability of measurements.

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	Female (n = 43) Mean ± SD	95% CI	Male(n = 67) Mean ± SD	95% CI
PP (mmHg)	54,74 ± 12,67	50,85–58,64	56,69 ± 7,55	54,84–58,53
AP (mmHg)	36,35 ± 5,26	34,73–37,97	37,19 ± 3,20	36,41–37,97
AI (%)	67,33 ± 6,89	65,21–69,45	66,43 ± 3,67	65,53–67,32
AI75 (%)	52,46 ± 4,95	50,94–53,99	51,55 ± 2,52	50,94–52,17

Table 2. Arterial stiffness indicators in patients who have survived COVID infection - descriptive characteristics of the studied indicators by gender

Abbreviations: PP – pulse pressure; AP – augmentation pressure; AI – augmentation index; AI75 – augmentation index, corrected for heart rate 75 beats/min;

Data are presented as mean ± standard deviation (SD) and 95% confidence interval (95% CI).

	All patients (N=110)	**95% CI**	**Female (n=43)**	**Male (n=67)**
AI75	.604**	[.47, .71]	.708**	.603**
AI	.710**	[.60, .79]	.755**	.678**
AP	.890**	[.84, .92]	.924**	.879**

Table 3. Correlations between age and reflected pulse wave parameters in the total sample and by gender in patients with newly diagnosed arterial hypertension after a previous COVID infection, Pearson correlation coefficients (r) are presented. p < .001 for all correlations.

Analysis by gender shows a similar trend for both men and women. In women, the correlations between age and AI75 ($r = .708$, $p < .001$), AI ($r = .755$, $p < .001$) and AP ($r = .924$, $p < .001$) are strong to very strong. In men, statistically significant positive relationships are also found between age and AI75 ($r = .603$, $p < .001$), AI ($r = .678$, $p < .001$) and AP ($r = .879$, $p < .001$). Although the coefficients in men are slightly higher, the dependence pattern is similar in both groups, suggesting a universal effect of age on the characteristics of the reflected pulse wave in patients with newly diagnosed arterial hypertension after COVID infection.

The high correlation between age and augmentation pressure deserves special attention. The value of the coefficient ($r = .890$) shows that age explains a significant part of the variation of this indicator in the studied population.

The results of the conducted correlation analysis show the presence of statistically significant positive relationships between age and the studied indicators of the reflected pulse wave in patients who have experienced COVID infection. The established correlation dependencies are of moderate to very strong degree and confirm the significant role of age as a factor related to changes in arterial function and hemodynamics after experiencing COVID.

In the general sample, a moderate to strong positive correlation was observed between age and the AI75 index ($r = .604$, $p < .001$), as well as a strong positive correlation between age and AI ($r = .710$, $p < .001$). The highest value of the correlation coefficient was found between age and AP ($r = .890$, $p < .001$), which indicates an extremely strong relationship between advancing age and an increase in the amplitude of the reflected pulse wave.

Discussion on sub-objective 2A:

According to our data, the significant importance of age for the parameters of the reflected pulse wave known from literature data in the general population is also preserved in patients with newly diagnosed arterial hypertension after a previous COVID infection. In addition to vascular aging, the observed results may also be due to changes in reactivity and resistance in older patients. As a rule, viral infections can be more severe in them, and COVID infection.

Conclusions on sub-objective 2A:

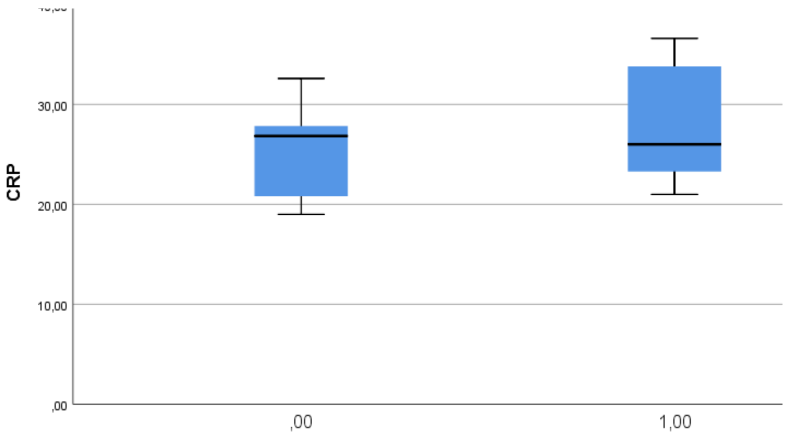
1. In patients with newly diagnosed arterial hypertension, after experiencing COVID infection, significantly higher values of augmentation pressure and augmentation index and AI75 are observed compared to literature data and compared to other groups of patients with arterial hypertension observed by us.

2. In patients with newly diagnosed arterial hypertension, after experiencing COVID infection, higher augmentation pressure and augmentation index and AI75 are observed in women. Higher variability of the studied parameters in female patients.

3. Strong correlation of augmentation pressure, augmentation index and AI75 with age, especially after distribution by gender.

Results on sub-objective 2B: Study of the difference in indicators of arterial stiffness and vascular inflammation in patients with newly diagnosed arterial hypertension after experiencing COVID infection with and without post-covid syndrome.

The mean CRP concentration was higher in patients with Long COVID (28.19 ± 5.37) compared to patients without Long COVID (25.92 ± 4.43). The Levene's test performed showed a statistically significant difference in the variances between the two groups ($F = 11.649$; $p = 0.001$), therefore the interpretation was based on the results of the t-test with unequal variances. The analysis found a statistically significant difference between the groups ($t = -2.381$; $df = 94,900$; $p = 0.019$), with the mean difference amounting to -2.26 units (95% CI: -4.15 to -0.38). The effect size was small to medium (Cohen's $d = 0.46$; Hedges' $g = 0.46$). The results obtained show that patients with Long COVID have significantly higher CRP values, which supports the assumption of persistent systemic inflammatory activity in this condition. The results are presented as a boxplot in Figure 7.



*p < .001**

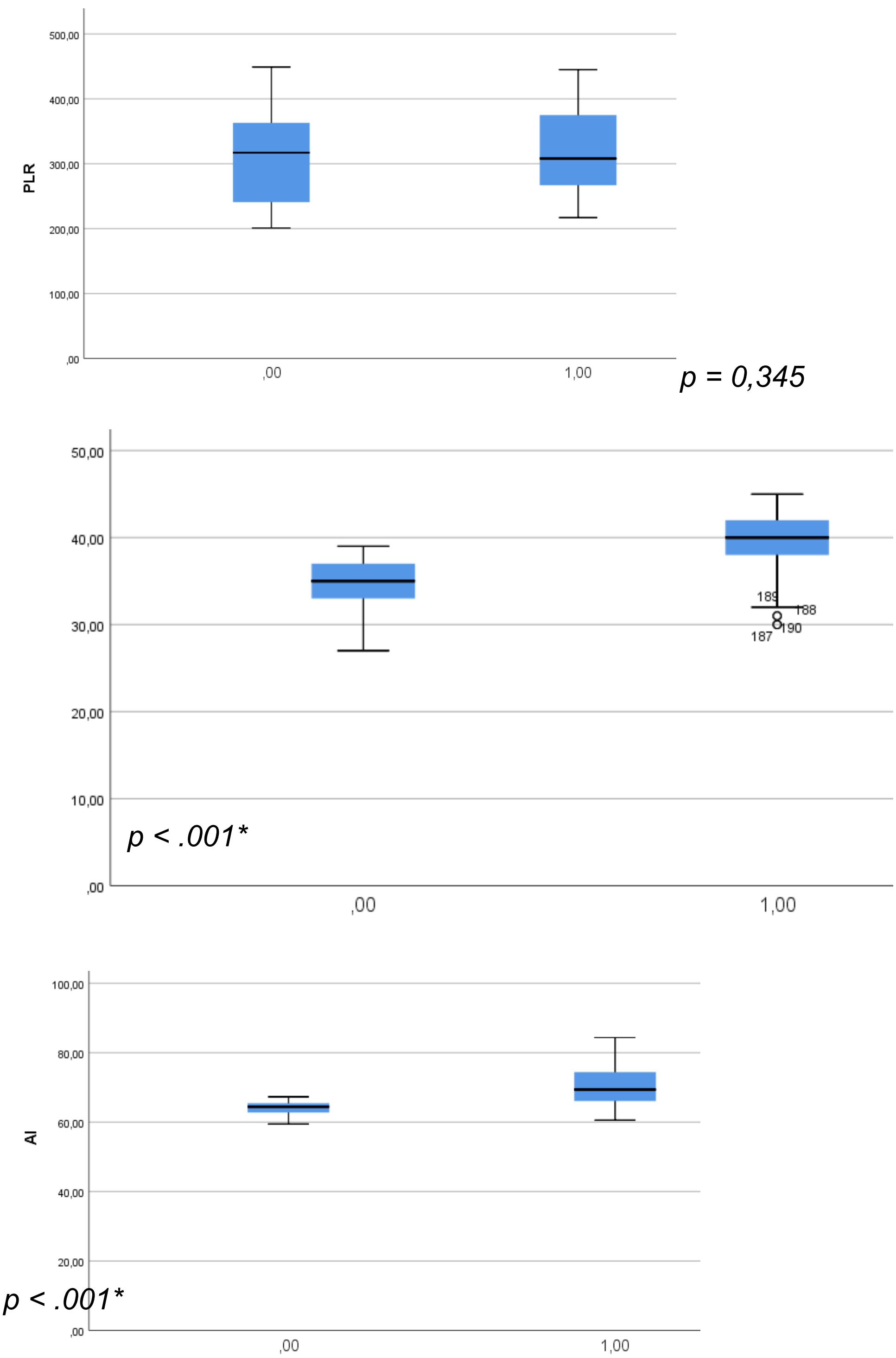


Fig. 7. Distribution of values of vascular inflammation and arterial stiffness indicators in patients with newly diagnosed arterial hypertension with and without post-covid syndrome.

7A. C-reactive protein (CRP)

7B. Platelet-lymphocyte ratio

7C. Augmentation pressure

7D. Augmentation index (AI)

Legend:

1 - patients with newly diagnosed arterial hypertension with post-covid syndrome;

2 - patients with newly diagnosed arterial hypertension without post-covid syndrome

* - statistically significant difference

The mean value of PLR (Figure 7B.) is higher in patients with postcovid syndrome (321.00 ± 63.70) compared to patients who did not develop this complication (308.67 ± 71.24). Levene's test did not establish a statistically significant difference in the variances between the groups ($F = 1.113$; $p = 0.294$), therefore we compare them with independent Student's t-test. The latter did not show a statistically significant difference between the two groups ($t = -0.948$; $df = 108$; $p = 0.345$). The effect size was small (Cohen's $d = 0.18$; Hedges' $g = 0.18$). Therefore, despite the trend towards higher mean PLR values in Long COVID patients, it cannot be considered a reliable marker for distinguishing patients from the two groups.

The results of the t-test for equal variances (after checking with the Levene test) for independent samples showed a statistically significant difference in AP values between the studied groups - $t(110) = -7.26$, $p < 0.001$. Patients with post-COVID syndrome had higher mean AP values ($M = 39.44$, $SD = 3.74$) compared to participants without post-COVID syndrome ($M = 34.72$, $SD = 3.09$) (Figure 7C). The effect size was very large (Cohen's $d = 1.39$), indicating that patients who developed post-COVID syndrome had higher augmentation pressure. In light of these results, AP is presented as a suitable marker for the diagnosis and prognosis of post-COVID syndrome.

The analysis by t-test for independent samples with unequal variances showed a statistically significant difference in AI values (Figure 7D) between patients with newly diagnosed arterial hypertension after COVID infection with and without postcovid syndrome $t= -7.36$, $p < .001$, 95% CI [-7.95; -4.55]. Patients with newly diagnosed arterial hypertension with post-covid syndrome demonstrated higher mean AI values ($M = 70.19$, $SD = 5.73$). The effect size was very large (Cohen's $d = 1.52$; Hedges' $g = 1.50$). In light of these results , AP is presented as a suitable marker for the diagnosis and prognosis of post-covid syndrome.

Conclusions on 2 B:

1. In patients with newly diagnosed arterial hypertension, after experiencing COVID infection, a significant difference is observed between the indicators of arterial stiffness and vascular inflammation in patients with and without postcovid syndrome.

Results on sub-objective 2C: Study of the relationship between the indicators of arterial stiffness and the levels of C-reactive protein and the platelet-lymphocyte ratio in the patient sample.

To assess the relationship between systemic inflammation and indicators of arterial function, a correlation analysis was performed between C-reactive protein (CRP) values and reflected pulse wave parameters.

	r	**95% CI**	**p**
AP	.563	[.420; .679]	< .001
AI	.373	[.200; .524]	< .001
AI75	.322	[.143; .480]	.001

Table 4. Correlations between CRP and reflected pulse wave parameters (N = 110)Pearson correlation coefficients (r) and 95% confidence intervals (CI) are presented.

The results showed statistically significant positive correlations between CRP and all parameters studied. The strongest relationship was found between CRP and augmentation pressure (AP) (r = .563, p < .001), which corresponds to a moderate to strong positive correlation. This indicates that higher values of the inflammatory marker are associated with higher values of augmentation pressure.

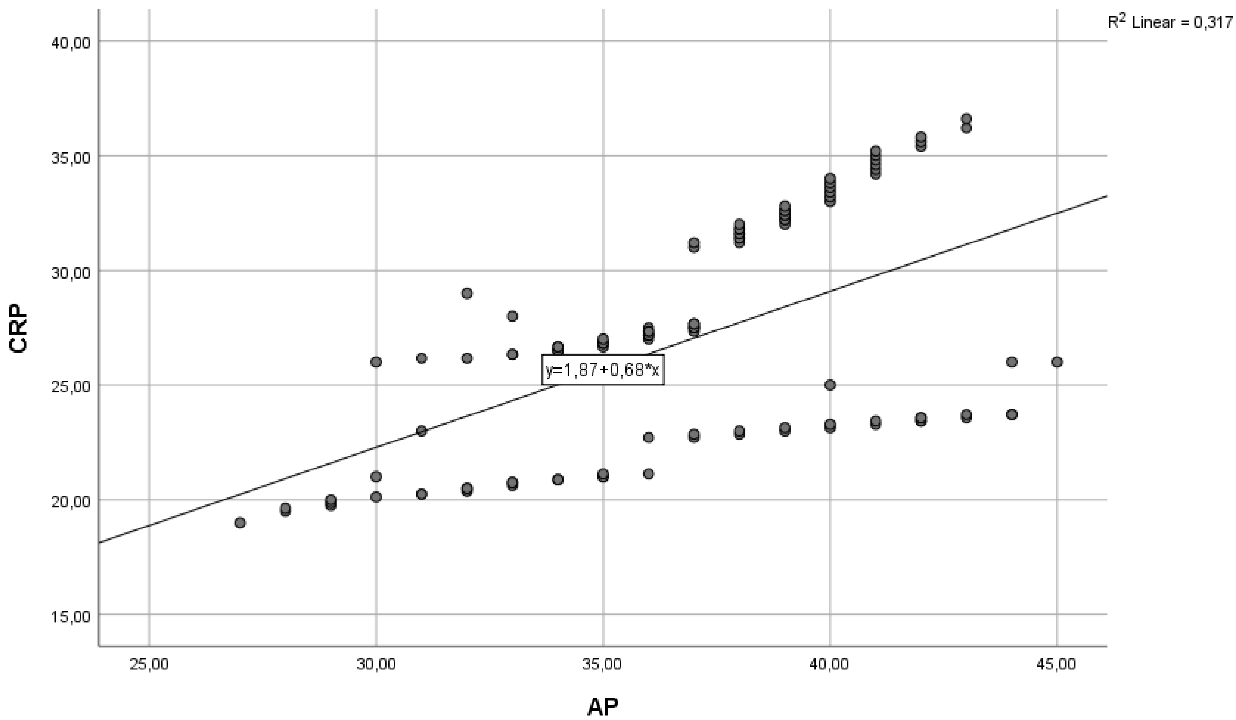


Fig. 8 Linear correlation between augmentation pressure and C-reactive protein in patients with newly diagnosed arterial hypertension after a previous COVID infection

Statistically significant positive correlations were also found between CRP and the augmentation index (AI) ($r = .373$, $p < .001$), as well as between CRP and the standardized augmentation index at a heart rate of 75 beats/min (AI75) ($r = .322$, $p = .001$). Although these relationships are weaker compared to the relationship between CRP and AP, they also show a consistent trend for an increase in reflected pulse wave parameters with more severe systemic inflammation.

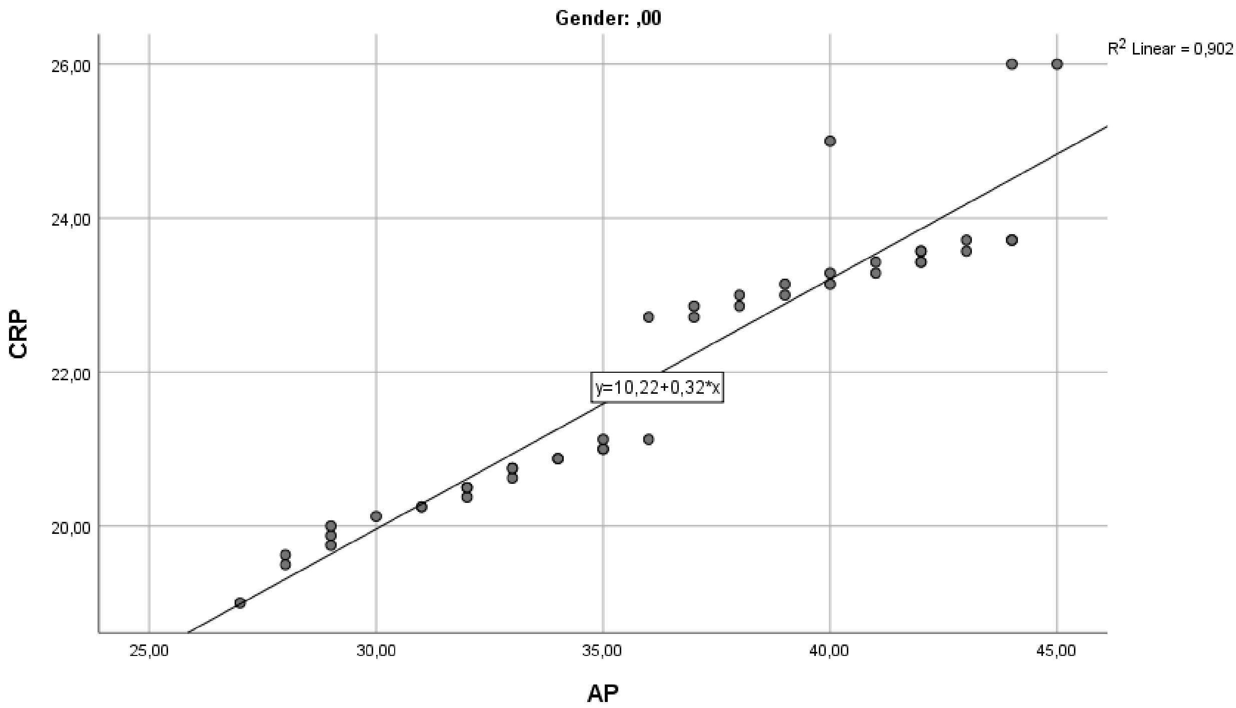


Figure 9: Linear correlation between C-reactive protein and augmentation pressure in women with newly diagnosed arterial hypertension after COVID infection

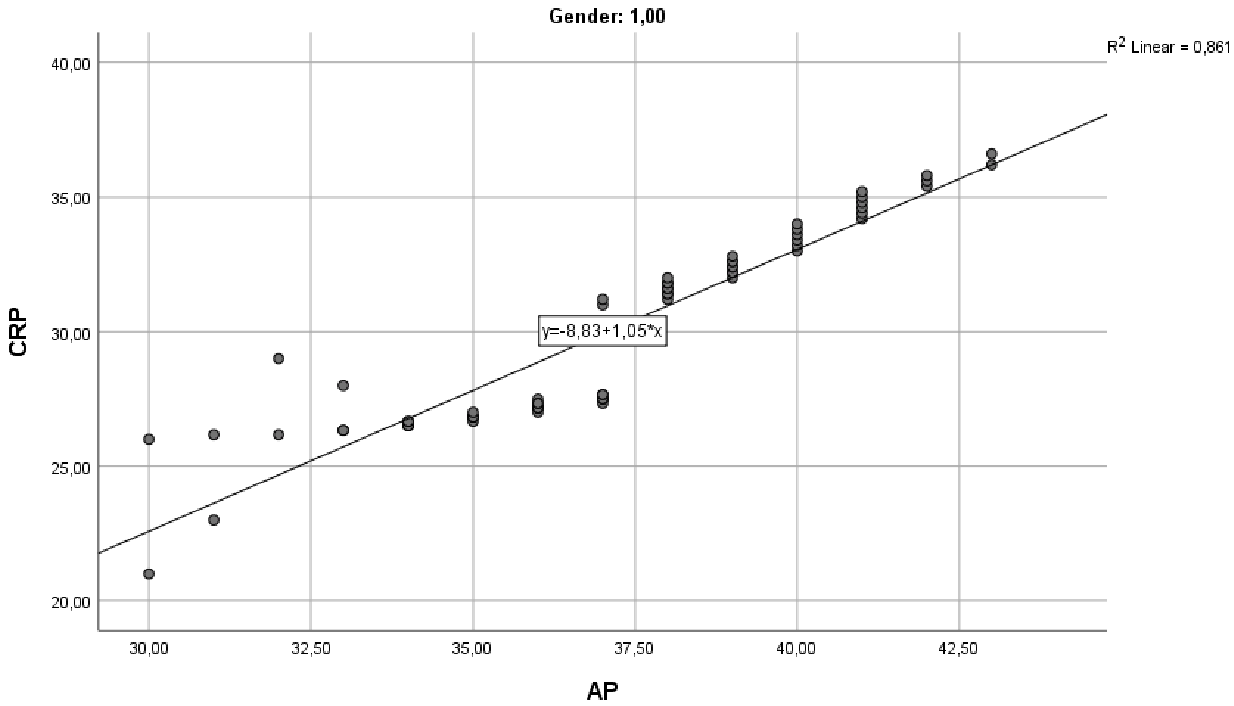


Figure 10: Linear correlation between C-reactive protein and augmentation pressure in men with newly diagnosed arterial hypertension after COVID infection

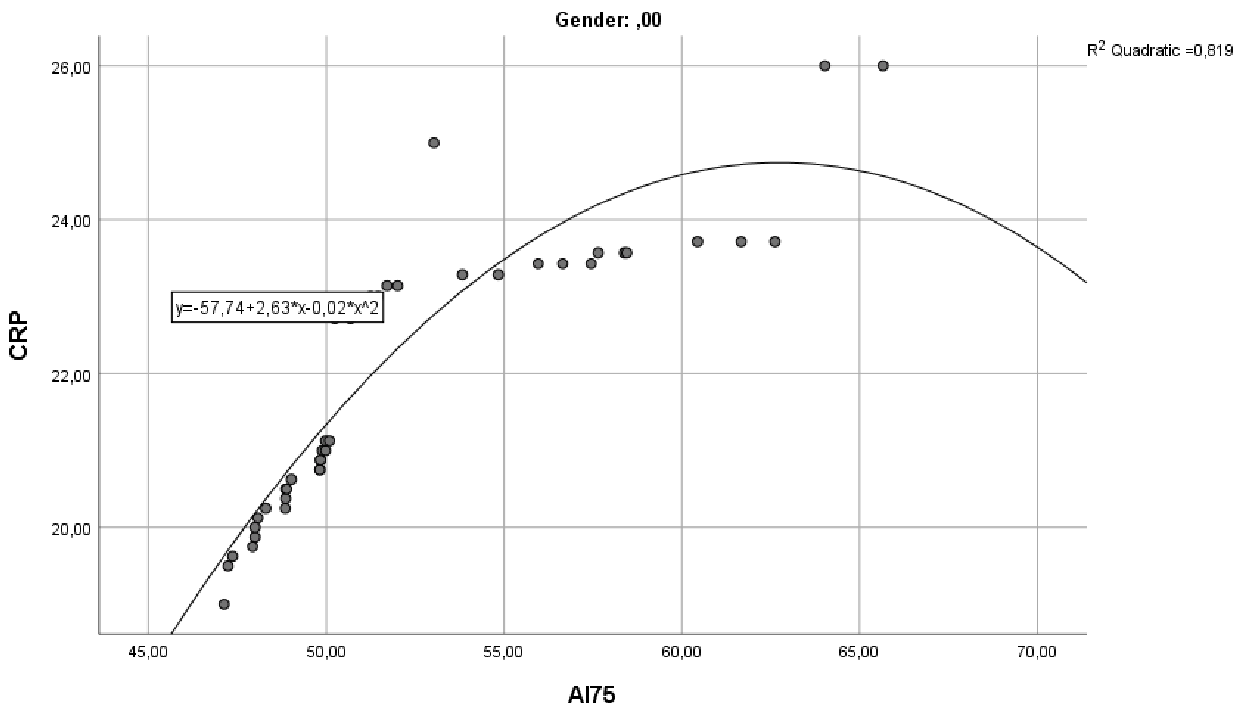


Figure 11: Linear correlation between C-reactive protein and AI75 in women with newly diagnosed arterial hypertension after COVID infection

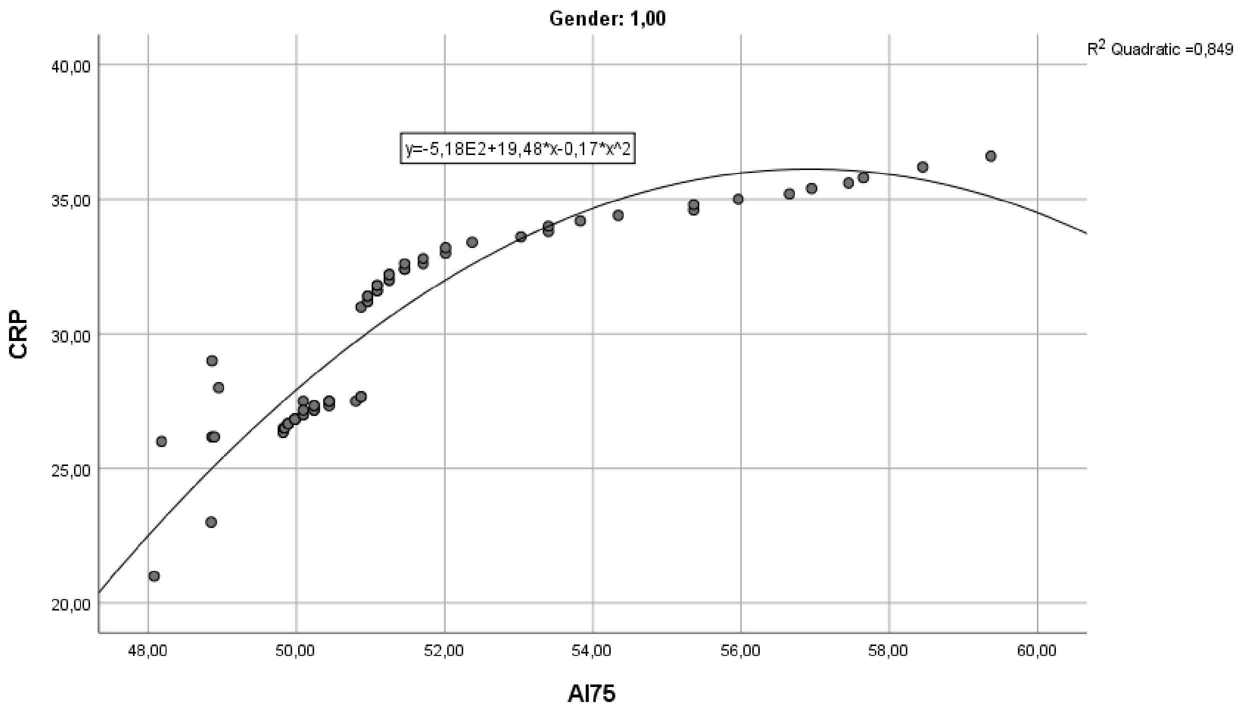


Figure 12: Linear correlation between C-reactive protein and AI75 in men with newly diagnosed arterial hypertension after COVID infection

The analysis of the relationship between CRP and augmentation index (AIx) revealed a better fit of the quadratic model compared to the linear regression (R^2 = 0.84 and 0.81, respectively, in the analyzed subgroups). This indicates the presence of a nonlinear, accelerating relationship between systemic inflammation and arterial stiffness.

The results obtained suggest that at low CRP values, changes in AIx are relatively limited, while at higher levels of inflammation, a proportionally more pronounced increase in the augmentation index is observed. This can be explained by threshold activation of endothelial dysfunction, increased oxidative activity and progressive decrease in nitric oxide, leading to accelerated deterioration of arterial elasticity in patients with post-covid syndrome.

We can summarize that elevated CRP values are associated with adverse changes in pulse wave characteristics, which further supports the role of inflammation as an important factor in the pathogenesis of post-covid syndrome.

Показатели	**Female r (95% CI)**	**p**	**Male r (95% CI)**	**p**
AP – Tr	0,211 (-0,10 до 0,49)	0,175	-0,158 (-0,39 до 0,09)	0,201
AP – PLR	0,693	<0,001	0,495	<0,001

Показатели	**Female** **r (95% CI)**	**p**	**Male** **r (95% CI)**	**p**
	(0,50 до 0,82)		(0,28 до 0,67)	
AI – Tr	0,237 (-0,08 до 0,51)	0,126	-0,170 (-0,40 до 0,07)	0,170
AI – PLR	0,676 (0,48 до 0,81)	<0,001	0,480 (0,26 до 0,66)	<0,001
AI75 – Tr	0,235 (-0,08 до 0,51)	0,129	-0,174 (-0,40 до 0,07)	0,160
AI75 – PLR	0,659 (0,46 до 0,80)	<0,001	0,456 (0,23 до 0,64)	<0,001

Table 5. Correlations between platelet count and inflammatory index platelet/lymphocyte ratio and reflected pulse wave parameters standardized by gender in patients with newly diagnosed arterial hypertension after COVID infection

Abbreviations: AP – augmentation pressure; AI – augmentation index; AI75 – augmentation index, corrected for heart rate 75 beats/min; PLR – platelet-to-leukocyte ratio; CI – confidence interval.

Note: Pearson correlation coefficients (r) with 95% confidence intervals are presented. Statistically significant values are considered at $p < 0.05$.

Regarding the other group of inflammatory markers (Table 5), the most significant finding is the presence of statistically significant positive correlations between PLR and all reflected wave parameters (AP, AI and AI75) in both women and men. The strength of these relationships was higher in women (r = 0.659–0.693) than in men (r = 0.456–0.495). This suggests that a higher platelet/leukocyte ratio is associated with more pronounced pulse wave amplification and reflection, with this relationship being more pronounced in women.

On the other hand, the absolute platelet count did not show a statistically significant relationship with any of the reflected wave parameters. In women, weak positive correlations were observed between platelets and AP, AI, and AI75 (r = 0.211–0.237), while in men the correlations were weak and negative (r = –0.158 to –0.174). In all cases, the confidence intervals included zero, and the p values were above 0.05, which does not allow us to assume the presence of a statistically significant association.

These data support the role of low-grade inflammation, but not platelet activation, in changes in vascular stiffness in patients with newly diagnosed arterial hypertension after experiencing COVID infection.

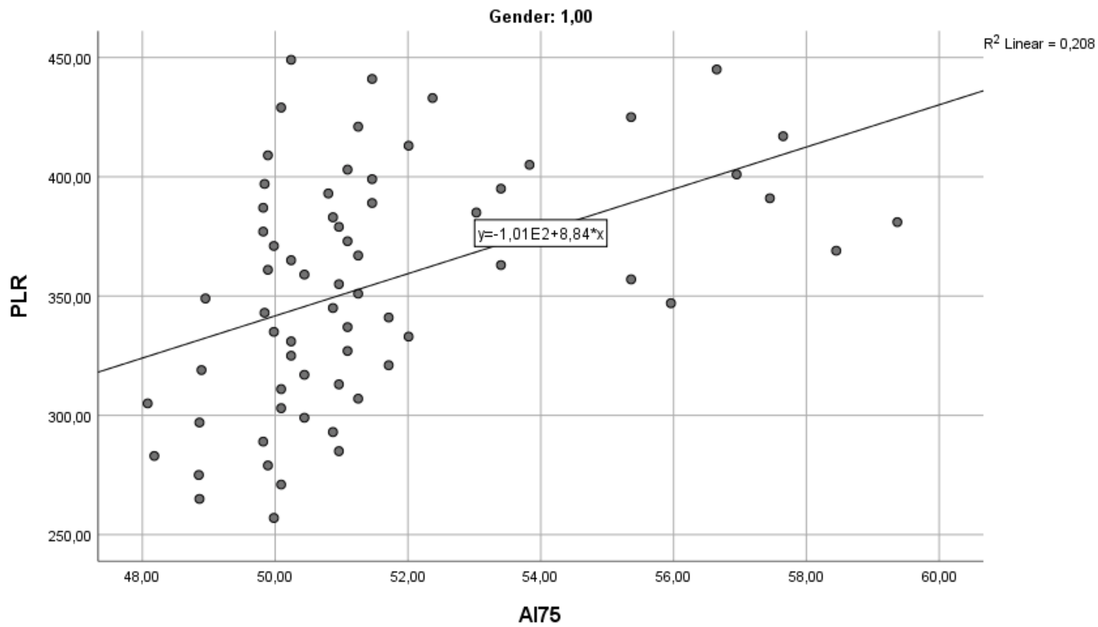


Figure 13: Correlation between platelet-lymphocyte ratio and augmentation index 75 in men with newly diagnosed arterial hypertension after COVID infection

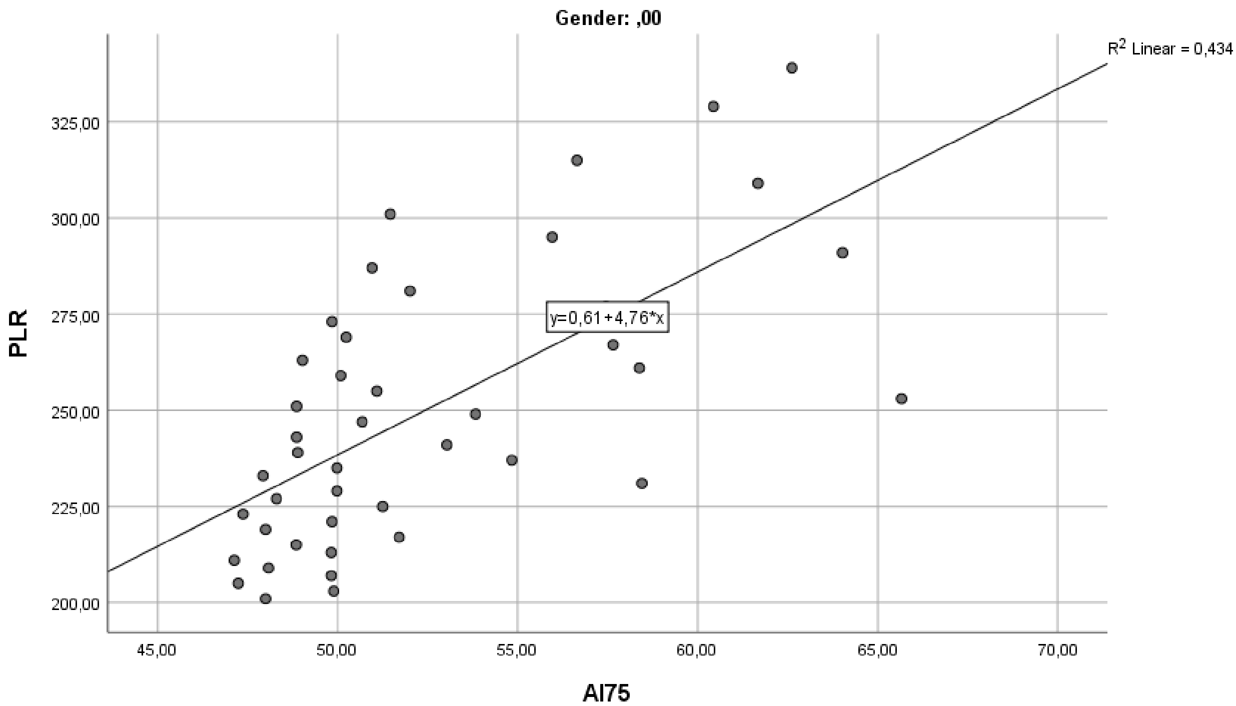


Figure 14: Correlation between platelet-lymphocyte ratio and augmentation index 75 in women with newly diagnosed arterial hypertension after COVID infection

Conclusion:

1. In patients with newly diagnosed arterial hypertension, after experiencing COVID infection, a moderate correlation of augmentation pressure, augmentation index and AI75 with C-reactive protein levels and platelet/leukocyte ratio is observed.

Results on sub-objective 2D: Monitoring the dynamics of arterial stiffness indicators - augmentation pressure and augmentation index during recovery from COVID infection at regular intervals for a period of 12 months

When following up the patients, a consistent decrease in all studied arterial stiffness indicators was found. The least pronounced change was observed during the first three months, after which the trend towards improvement became increasingly clear. The lowest mean values of augmentation pressure, augmentation index and augmentation index standardized to heart rate 75 beats/min were recorded at the 12th month of follow-up. The results obtained show a steady improvement in the parameters characterizing arterial stiffness throughout the entire observation period. Despite the downward trend, the arterial stiffness indicators did not normalize.

The estimated standard errors of the mean values are low for all indicators and all follow-up periods. Accordingly, the 95% confidence intervals are relatively narrow, which indicates a high reliability of the calculated mean values. Despite the gradual decrease in the mean values over time, the standard deviations remain relatively constant, which suggests that the improvement is observed in the entire study group, without a significant increase in variability between patients.

The assessment of the effect size using the Cohen's d indicator shows a gradual increase in the strength of the observed effect during the follow-up period. A relatively small effect size was found during the first three months, while it increased significantly at the sixth and ninth months. The highest Cohen's d values were recorded at the 12th month for all studied indicators, which indicates a clear departure of the mean values from the baseline level. According to the results obtained, the observed changes are not only statistically, but also clinically significant.

Conclusions on subobjective 2 D:

1. In patients with newly diagnosed arterial hypertension, after experienced COVID infection, a gradual improvement of arterial stiffness is observed in the course of recovery from the infection and against the background of standard antihypertensive therapy. The reduction is most pronounced in the first six-month period.

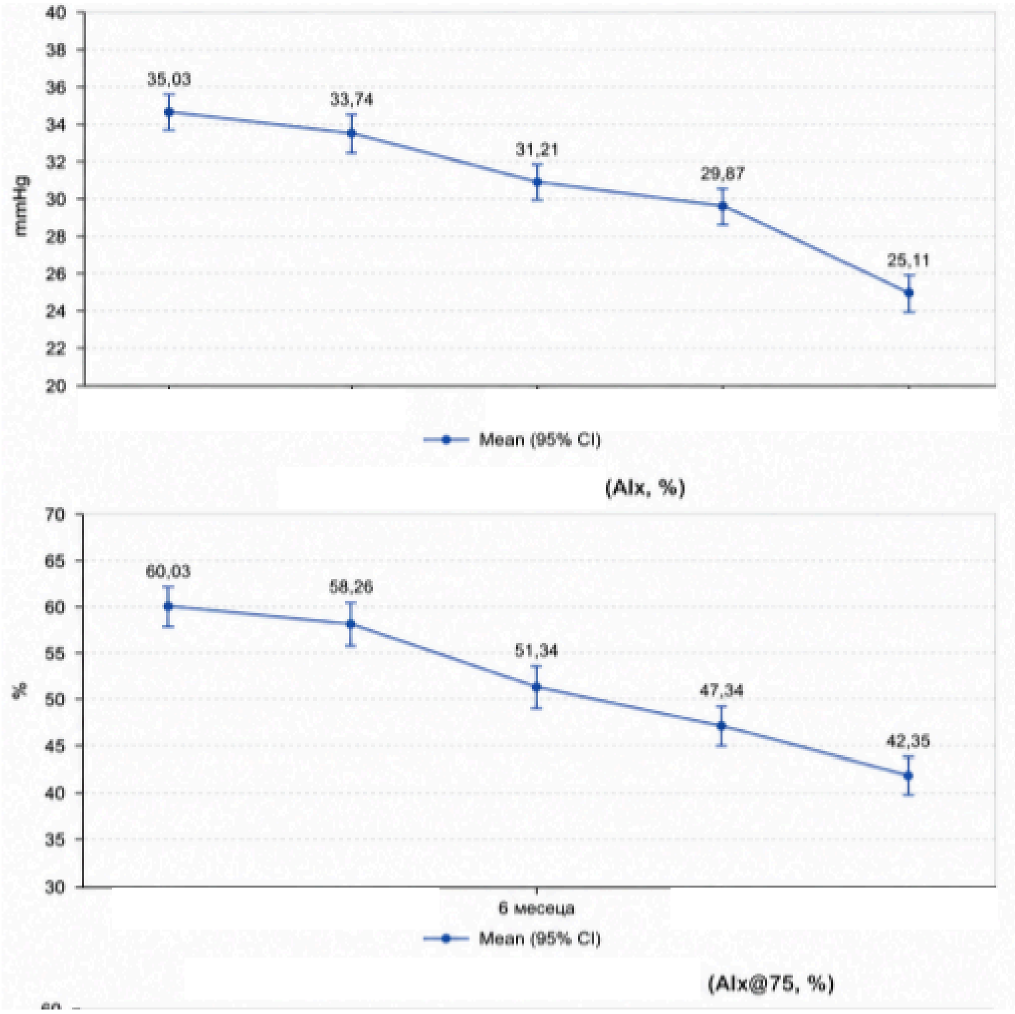


Figure 15: Change in arterial stiffness indicators – augmentation pressure, augmentation index and augmentation index 75 in patients with newly diagnosed arterial hypertension after COVID infection during recovery from the infection and on the background of standard antihypertensive therapy.

Objective 3: Non-invasive study of hemodynamic indicators of arterial stiffness in patients with arterial hypertension of several years of history and newly discovered metabolically associated hepatic steatosis.

Results on subobjective 3A: Comparison of non-invasively studied indicators of arterial stiffness in patients with arterial hypertension of several years of history with and without metabolically associated fatty liver disease.

	No MASLD (n=219) **M±SD**	**MASLD (n=220)** **M±SD**	**t**	**p**
AP (mmHg)	19.81 ± 7.16	21.43 ± 3.65	2,75	0.006
PP (mmHg)	40.17 ± 4.86	39.33 ± 5.36	-1,7	0.09
AI(%)	47.61 ± 5.92	53.90 ± 4.50	11,64	<0.001

Table 8: Comparison of arterial stiffness indices between patients without MASLD and patients with MASLD using Student's t-test for independent samples

Comparison between patients with arterial hypertension and metabolically active liver disease and patients with arterial hypertension without metabolically active liver disease (excluded by ultrasound). Patients in both groups were referred by a gastroenterologist after a diagnostic examination for another reason. Inclusion criteria were: based on ultrasound, laboratory and other data, the gastroenterologist could unambiguously assess whether the patient suffered from MSLD; the patient suffered from arterial hypertension and regularly received antihypertensive therapy for many years; all other inclusion and exclusion criteria relevant to the patients in the three tasks.

Patients with MASLD demonstrated statistically significantly higher values of augmentation pressure compared to individuals without MASLD (21.43 ± 3.65 vs. 19.81 ± 7.16 mmHg, p=0.006). The most pronounced difference was observed in the augmentation index, which was significantly higher in patients with MASLD (53.90 ± 4.50% vs. 47.61 ± 5.92%, p<0.001). No statistically significant difference was found in pulse pressure between the two groups (39.33 ± 5.36 vs. 40.17 ± 4.86 mmHg, p=0.09).

Conclusions on task 3A: In patients with arterial hypertension of several years' duration and newly discovered metabolically associated fatty liver disease, increased augmentation pressure and augmentation index are observed compared to patients with arterial hypertension without metabolically associated fatty liver disease.

Results on subtask 3B: Monitoring the dynamics of the studied parameters while maintaining the current drug therapy and implementing a hypocaloric Mediterranean-style diet in patients with arterial hypertension of several years' duration with metabolically associated fatty liver disease.

In order to study the changes in arterial stiffness in patients with metabolically associated fatty liver disease and arterial hypertension, we followed a group of 115 patients newly diagnosed by a gastroenterologist MASLD and AH of more than 5 years' duration. All patients were given general recommendations and an appropriate hygienic dietary regimen in accordance with their primary and concomitant disease, but the intervention group, consisting of 125 patients, followed a reducing diet proposed by a dietician for 2 years, and the patients in the control group - 130 people, were not given specific calorie restrictions.

During the study, the dynamics of anthropometric characteristics, lipid metabolism and arterial stiffness indicators were monitored.

Not all patients included in the intervention group completed the study - due to failure to achieve a reduction in serum lipids and the need to include antilipemic therapy, 3 women and 2 men dropped out in the first 6-month period, 1 woman and 7 men in the period from the 6th to the 12th month, after which no patients dropped out. During the first 6 months of follow-up, one woman was also excluded due to her own desire. Thus, the reduced composition of the intervention group remains at 111 patients.

	Interventional group Mean ± SD	Control group Mean ± SD	p
High (sm)	166.4 ± 6.1	166.9 ± 6.3	0.98
Weigh(kg)	97.0 ± 11.6	96.0 ± 10.9	0.62
WC (sm)	95.5 ± 8.3	96.0 ± 8.3	0.71
BMI (kg/m²)	33.9 ± 4.7	34.6 ± 4.7	0.74
WHtR	0.574 ± 0.055	0.576 ± 0.053	0.82

Table 9: Anthropometric characteristics in patients with metabolically active liver disease and arterial hypertension with long-standing history distributed into control and intervention groups

Regarding the control group, in the first period of 6 months, 8 women and 14 men dropped out due to failure to achieve a reduction in serum lipids and the need to include antilipemic therapy, in the period from the 6th to the 12th month, 2 more men dropped out for the same reason, as well as 6 women and 4 men because they started to follow different dietary regimens of their own free will. After that, no patients dropped out. Thus, the reduced composition of the intervention group remains 106 patients.

In the intervention group, the average height values were 166.5 ± 6.1 cm, body mass 97.0 ± 11.6 kg, and waist circumference 95.5 ± 8.3 cm. Accordingly, the calculated mean body mass index was 34.9 ± 4.7 kg/m², which falls within the range of obesity grade II according to standard classifications. The waist-to-height ratio (WHtR) was 0.574 ± 0.055, which exceeds the threshold value of 0.5 and is an indicator of increased cardiometabolic risk associated with central adipose tissue accumulation.

In the control group, the corresponding values were extremely similar: height 166.5 ± 6.3 cm, body mass 96.0 ± 10.9 kg and waist circumference 96.0 ± 8.3 cm. The mean body mass index was 34.6 ± 4.7 kg/m², and WHtR was 0.576 ± 0.053. A similar degree of obesity and a similar pattern of fat distribution were also observed in this group.

The mean values of triglycerides, total cholesterol, LDL-cholesterol, HDL-cholesterol, pulse pressure, augmentation pressure, augmentation index, as well as the CRI-I and CRI-II indices were similar between the two groups. In none of them was a significant difference observed according to the Student's T test.

The intervention and control groups were homogeneous with respect to all studied indicators. The obtained results show good comparability of the participants at the beginning of the study. Therefore, any changes found in the subsequent analyses could be more related to the effect of the intervention, and not to pre-existing differences between the groups.

	Interventional group Mean ± SD	Control group Mean ± SD	t	p-value
Tg	3.04 ± 0.70	3.15 ± 0.54	-1.83	0.07
Total Cholesterol	6.08 ± 0.51	6.11 ± 0.63	-0.39	0.70
LDL	3.71 ± 0.22	3.70 ± 0.23	0.33	0.74
HDL	1.54 ± 0.23	1.58 ± 0.21	-1.34	0.18
Ap	21.77 ± 3.77	21.11 ± 3.52	1.33	0.19
PP	39.21 ± 5.42	39.45 ± 5.31	-0.33	0.74
AI	53.44 ± 4.72	54.35 ± 4.28	-1.48	0.14
CRI-I	4.02 ± 0.67	4.04 ± 0.54	-0.24	0.81
CRI-II	2.46 ± 0.39	2.52 ± 0.37	-1.16	0.25

Table 10: Serum lipids, reflected pulse wave indices and cholesterol risk index 1 and 2 in patients with metabolically active liver disease and long-standing arterial hypertension divided into control and intervention groups

After following a hypocaloric Mediterranean-style diet for 18 months, statistically significant improvements were observed in all major components of the lipid profile. Triglyceride levels decreased from 3.04 ± 0.70 to 2.25 ± 0.54 mmol/L. The observed difference was statistically significant ($t = 17.41$, $p < 0.001$). Total cholesterol also demonstrated a significant decrease – from 6.08 ± 0.51 to 5.02 ± 0.75 mmol/L ($\Delta = 1.06$ mmol/L; $t = 16.99$; $p < 0.001$). LDL-cholesterol levels, which are considered the main atherogenic lipoprotein, decreased from 3.71 ± 0.22 to 3.50 ± 0.22 mmol/L ($\Delta = 0.21$ mmol/L; $t = 24.02$; $p < 0.001$). Although the absolute change was relatively smaller compared to triglycerides and total cholesterol, it was statistically significant. HDL-cholesterol increased from 1.54 ± 0.23 to 1.68 ± 0.24 mmol/L ($\Delta = +0.14$ mmol/L; $t = -16.81$; $p < 0.001$).

All observed changes in the lipid profile are significant, and some of them - the reduction of triglycerides and total cholesterol - may be associated with an improvement in the patients' condition - a decrease in insulin resistance and an improvement in lipid metabolism. The changes in LDL and HDL are too small to be clinically significant.

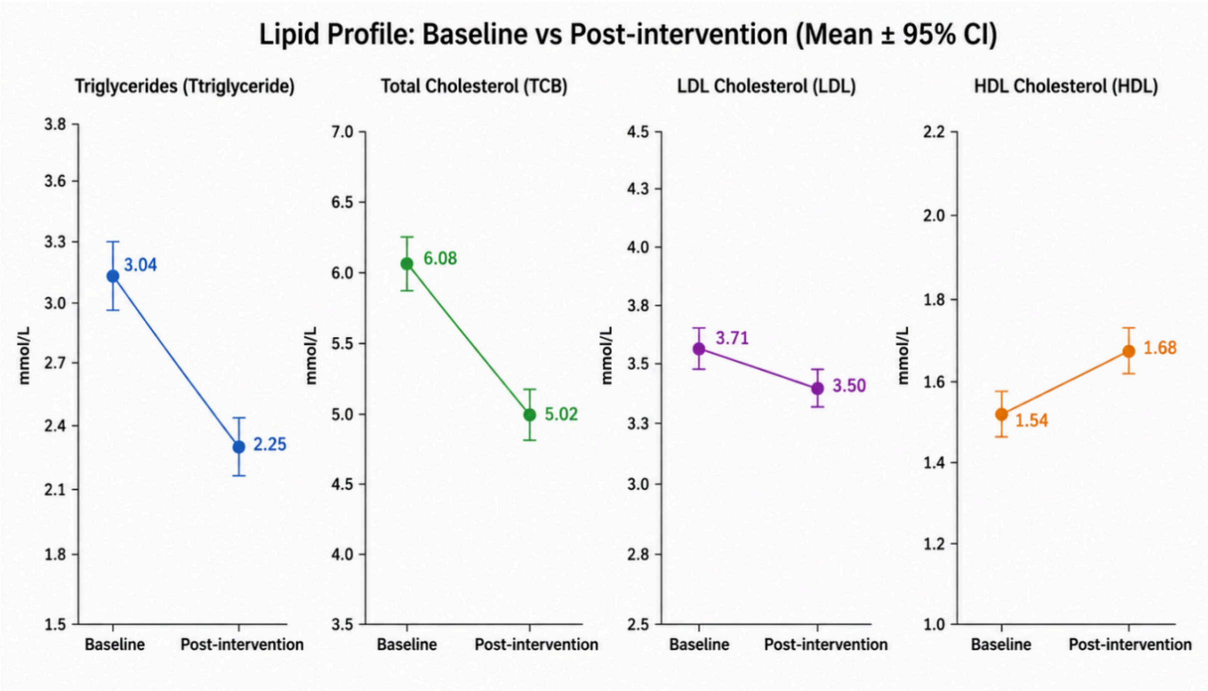


Figure 16: Changes in serum lipids in patients with metabolically active liver disease and arterial hypertension after 18 months of adherence to a hypocaloric Mediterranean-style diet

	Baseline Mean± SD	After 18 m.diet Mean ± SD	Δ	t (df=110)	p-value
Tg	3.04 ± 0.70	2.25 ± 0.54	0.79 ↓	17.41	<0.001
Total Cholesterol	6.08 ± 0.51	5.02 ± 0.75	1.06 ↓	16.99	<0.001
LDL	3.71 ± 0.22	3.50 ± 0.22	0.21 ↓	24.02	<0.001
HDL	1.54 ± 0.23	1.68 ± 0.24	0.14 ↑	-16.81	<0.001

Table 11: Changes in serum lipids in patients with AH+MALD after 18 months of adherence to a hypocaloric Mediterranean-style diet

	Baseline Mean± SD	After 18 m.diet Mean ± SD	Δ	t (df=110)	p-value
CRI-I	4.02 ± 0.67	3.14 ± 0.24	0,88	13.4	<0.001

	Baseline Mean± SD	After 18 m.diet Mean ± SD	Δ	t (df=110)	p-value
CRI-II	2.46 ± 0.39	2.12 ± 0.33	0.33	17.95	<0.001

Table 12: Changes in cholesterol risk index 1 and 2 in patients with AH+MALD after 18 months of adherence to a hypocaloric Mediterranean-style diet

Cholesterol Risk Index I (CRI-I) decreased from 4.02 ± 0.67 to 1.44 ± 0.24 (Δ = 2.58; t = 40.40; $p < 0.001$), which represents a significant reduction in atherogenic risk. CRI-II also demonstrated a statistically significant decrease – from 2.46 ± 0.39 to 2.12 ± 0.33 (Δ = 0.33; t = 17.95; $p < 0.001$).

Dietary intervention also led to significant changes in indicators related to arterial stiffness and central hemodynamics.

Augmentation pressure (AP) decreased from 21.77 ± 3.77 to 16.16 ± 3.93 mmHg (Δ = 5.61 mmHg; t = 49.12; $p < 0.001$), and augmentation index from 53.44 ± 4.72% to 44.35 ± 4.48% (Δ = 9.09%; t = 43.79; $p < 0.001$).

In the control group, we observed a slight increase in serum lipids and cholesterol risk index one and two as well as an increase in augmentation pressure and augmentation index. The differences are not statistically significant, but the observed upward trend is alarming because it suggests an increase in arterial stiffness with persistent upper limit values of the components of the atherogenic lipid fraction.

	Baseline Mean± SD	**After 18 m.diet Mean ± SD**	**Δ**	**t (df=110)**	**p-value**
AP	21.77 ± 3.77	16.16 ± 3.93	5.61 ↓	49.12	<0.001
PP	39.21 ± 5.42	36.35 ± 5.39	2.86 ↓	39.86	<0.001
AI	53.44± 4.72	44.35 ± 4.48	9.09	43,79	<0.001

Table 13: Changes in reflected pulse wave parameters in patients with AH+MASLD after 18 months of adherence to a hypocaloric diet

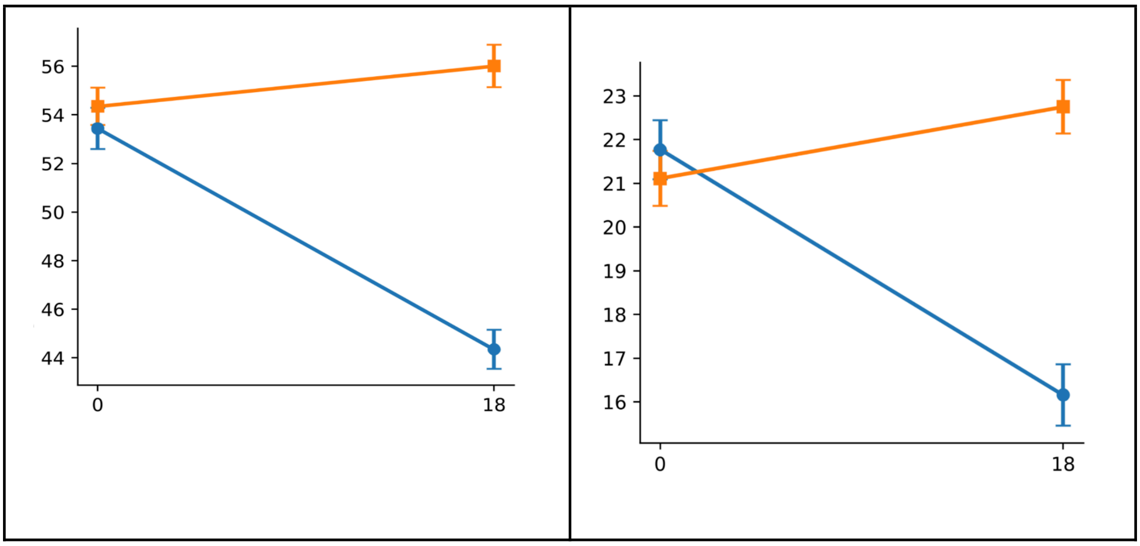


Figure 17: Changes in arterial stiffness parameters in patients with AH+MALD after 18 months of adherence to a hypocaloric diet.

Conclusions on sub-objective 3B:

In patients with arterial hypertension of several years' duration and newly discovered metabolically associated fatty liver disease, following a hypocaloric Mediterranean-style diet, the following are observed:

1. Significant reduction in augmentation pressure and augmentation index
2. Small but significant reduction in cholesterol index 1 and 2

CONCLUSIONS

From the implementation of the set goal and tasks in the dissertation work, the following conclusions can be drawn

Conclusions on task 1

Conclusions on task 1A:

A significant difference in the augmentation index was observed in the three studied groups ($p<0.001$).

A significant difference in the augmentation pressure was observed in the three studied groups ($p<0.05$).

Conclusions on task 1B:

A significant difference in subendocardial viability was observed between active smokers and non-smokers with AH ($p<0.001$).

There was no significant difference in subendocardial viability between active smokers and passive smokers as well as between passive smokers and non-smokers.

Conclusions on task 2

Conclusions on task 2 A: In patients with newly diagnosed arterial hypertension, after experiencing COVID infection,

1. Significantly higher values of the reflected pulse wave indicators are observed compared to the other groups of patients with arterial hypertension observed by us.

2. Strong correlation of the augmentation pressure, the augmentation index and AI75 with age after distribution by gender.

Conclusions on task 2 B:

1. In patients with newly diagnosed arterial hypertension, after experiencing COVID infection, a significant difference is observed between the indicators of arterial stiffness and vascular inflammation in patients with and without post-covid syndrome.

Conclusions on task 2 B:

1. In patients with newly diagnosed arterial hypertension, after experiencing COVID infection, a moderate correlation of the augmentation pressure, the

augmentation index and AI75 with the levels of C-reactive protein and the platelet/leukocyte ratio is observed.

Conclusions on task 2 D:

1. In patients with newly diagnosed arterial hypertension, after experiencing COVID infection, a gradual improvement in arterial stiffness is observed during the course of recovery from the infection and against the background of standard antihypertensive therapy. The reduction is most pronounced in the first six-month period.

Conclusions on task 3

Conclusions on task 3A: In patients with arterial hypertension of several years' duration and newly discovered metabolically associated fatty liver disease, increased augmentation pressure and augmentation index are observed compared to patients with arterial hypertension without liver involvement

Conclusions on task 3B:

In patients with arterial hypertension of several years' duration and newly discovered metabolically associated fatty liver disease, when following a hypocaloric Mediterranean-style diet, the following are observed:

1. Significant reduction in augmentation pressure and augmentation index

2. Small but significant reduction in cholesterol index 1 and 2

CONTRIBUTIONS

1. For the first time in Bulgaria, we have determined how the indicators of arterial stiffness - augmentation pressure, augmentation index and augmentation index 75 - change in patients with newly diagnosed arterial hypertension after a previous covid infection depending on gender, age, inflammatory markers, and manifestation of post-covid syndrome.

2. We observed a progressive decline in augmentation pressure and augmentation index 12 months after the acute phase of covid infection.

3. We have determined increased augmentation pressure and augmentation index in patients with arterial hypertension and metabolically associated fatty liver disease compared to patients with AH and a healthy liver.

4. We observed a significant reduction in augmentation pressure and augmentation index as well as cholesterol risk index 1 and 2 in patients with arterial hypertension and metabolically associated fatty liver disease after 18 months of hypocaloric dietary regimen.

5. We found significantly higher augmentation pressure and augmentation index as well as lower subendocardial viability in patients with long-standing arterial hypertension who are active or passive smokers, compared to non-smokers.

Scientifically applied

6. We proved the capabilities of arterial tonometry as an important diagnostic method in patients with arterial hypertension and other risk factors to assess and monitor changes in arterial stiffness that occur in various pathological conditions.

7. We proved that arterial tonometry reliably assesses the patient's benefit from various therapeutic interventions.

LIST OF SCIENTIFIC PUBLICATIONS RELATED TO THE DISSERTATION

Articles:

1. Georgieva V., Dimitrova A., Tolekova A. Hypocaloric Diet in Arterial Hypertension and MASLD: Metabolic and Vascular Benefits. Journal of IMAB, 2026, 32(4);

2. Georgieva V., Dimitrova A., Tolekova A. Noninvasive hemodynamic monitoring and pulse wave analysis in patients with arterial hypertension and type 2 diabetes with and without hypertriglyceridemia. Jubilee scientific conference with international participation "50 years of medical education and science in Pleven", November 1–3, 2024. Collection of reports. Medical University – Pleven, 2024; pp. 19–21; ISBN: 978-954-756-346-9

3. Georgieva V., Dimitrova A., Tolekova A., Darko S. Heart Rate Variability after Coronavirus Disease. Thrace Journal of Sciences, 2021, 19(Suppl. 2): 7–13; ISSN: 1312-1723

4. Georgieva V., Dimitrova A. Applanation Arterial Tonometry Assessment of Arterial Stiffness. Varna Medical Forum, 2021, 10(Suppl. 3): 14–18; ISSN: 1314-3425

Participation in national and international forums:

1. Georgieva, V.; Dimitrova, A.; Tolekova, A. Noninvasive Hemodynamic Monitoring and Pulse Wave Analysis in Patients with Arterial Hypertension and Metabolic Associated Fatty Liver Disease. Jubilee Scientific Conference with International Participation "50 Years of Medical Education and Science in Pleven", Pleven, Bulgaria, 1–3 November 2024.

2. Georgieva, V.; Dimitrova, A.; Tolekova, A. Noninvasive Hemodynamic Monitoring and Pulse Wave Analysis in Patients with Arterial Hypertension and Type 2 Diabetes Mellitus with and without Hypertriglyceridemia. Jubilee Scientific Conference with International Participation "50 Years of Medical Education and Science in Pleven", Pleven, Bulgaria, 1–3 November 2024.

3. Georgieva, V.; Simonov, D.; Dimitrova, A.; Tolekova, A. Heart Rate Variability after Coronavirus Disease. Scientific conference "COVID-19 - multidisciplinary scientific review", College of Medicine, Thrace University, Stara Zagora, October 1-2, 2021.

4. Georgieva, V.; Dimitrova, A. Applanation arterial tonometry to measure cardiovascular risk. Anniversary scientific conference "60 years Department of Pathophysiology", Medical University - Varna, September 24-25, 2021.