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RESEARCH ARTICLE

Association of Homocysteine with Cardiac Remodeling in Hypertension

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Abstract

Objective. The study aimed to investigate the relationship between plasma homocysteine (HC) concentration, blood lipid metabolism parameters, and the structural and functional state of the cardiovascular system in patients with arterial hypertension (AH), depending on its severity.

Material and Methods. To assess the relationship between homocysteine (HC) levels and changes in the walls of the common carotid arteries (CCA), 51 patients with AH of varying severity were examined. The patients were divided into two subgroups according to plasma HC levels. Hyperhomocysteinemia (HHC) was diagnosed when HC levels exceeded 15 µmol/L (normal range: 5–15 µmol/L). Depending on the severity of HHC, patients were further divided into three subgroups: HC levels of 15–30 µmol/L (mild HHC), 30–100 µmol/L (moderate HHC), and more than 100 µmol/L (severe HHC). To address the study objectives, blood homocysteine levels were measured, along with lipid profile parameters; cardiac functional status was assessed by echocardiography; the structural and functional state of the common carotid arteries (CCA) was evaluated using ultrasound.

Results. HC levels were within the normal range in 31 patients (60.8 ± 6.8%) and exceeded normal values in 20 patients (39.2 ± 6.8%). Among the 20 patients with HHC, 13 (25.5 ± 6.1%) had mild HHC and 7 (13.7 ± 4.8%) had moderate HHC. No cases of severe HHC were observed. According to one-way analysis of variance (ANOVA), the difference in HC levels between these groups was statistically significant ($F = 127.444$; $p < 0.0001$). Significant differences were also identified using the Kruskal–Wallis test ($\chi^2 = 36.477$; $p < 0.0001$).

Conclusion. The present study demonstrates that hyperhomocysteinemia is common among patients with arterial hypertension and is associated with unfavorable cardiovascular structural and functional alterations. As homocysteine levels increased, there was a consistent tendency toward more severe arterial hypertension, higher blood pressure parameters, impaired diastolic function, reduced left ventricular ejection fraction, and a greater prevalence of vascular remodeling reflected by increased carotid intima–media thickness.

Keywords: Arterial hypertension, Homocysteine, Left ventricular hypertrophy, Intima–media thickness

Introduction

Arterial hypertension (AH) remains one of the leading modifiable risk factors for cardiovascular morbidity and mortality worldwide [12]. Persistent elevation of blood pressure is associated with progressive structural and functional alterations of the cardiovascular system, including left ventricular remodeling, endothelial dysfunction, and atherosclerotic changes in large arteries [4, 15]. However, the development and progression of hypertension-mediated target organ damage cannot be fully explained by hemodynamic factors alone, suggesting an important role for metabolic and biochemical disturbances [14].

Homocysteine (HC), a sulfur-containing amino acid formed during methionine metabolism, has gained considerable attention as an independent cardiovascular risk factor [1, 13, 14]. Elevated plasma homocysteine levels, referred to as hyperhomocysteinemia (HHC), are known to induce endothelial dysfunction, oxidative stress, vascular smooth muscle cell proliferation, and increased thrombogenicity, all of which contribute to vascular remodeling and atherosclerosis [2, 6]. These pathological mechanisms may be particularly relevant in patients with arterial hypertension, in whom vascular injury and impaired endothelial function are key determinants of disease progression.

In addition to its direct vascular effects, homocysteine has been shown to interact with lipid metabolism by promoting low-density lipoprotein oxidation and impairing

the protective functions of high-density lipoprotein. Such interactions may accelerate atherogenesis and further increase cardiovascular risk in hypertensive patients, where dyslipidemia frequently coexists [5, 13]

Ultrasound evaluation of the common carotid arteries (CCA), including assessment of arterial wall structure and intima–media thickness, is widely used as a noninvasive marker of subclinical atherosclerosis and vascular damage. Previous studies have demonstrated a significant association between elevated homocysteine levels and increased carotid intima–media thickness, carotid plaque burden, and arterial stiffness in patients with hypertension [3, 7, 9, 16, 18,]. These findings highlight the potential role of homocysteine in large-artery remodeling and early atherosclerotic changes.

Echocardiographic assessment provides important information on cardiac structural and functional alterations associated with arterial hypertension, while endothelial vasomotor function testing reflects early functional impairment that may precede overt structural vascular changes. Recent prospective studies have shown that elevated homocysteine levels are independently associated with an increased risk of cardiovascular events and mortality among hypertensive patients [8, 11, 19].

Despite growing evidence linking hyperhomocysteinemia with adverse cardiovascular outcomes, the relationship between plasma homocysteine concentration, lipid metabolism parameters, and the structural and functional state of the cardiovascular system across different severities of arterial hypertension remains insufficiently explored. Therefore, the present study aimed to investigate the association between plasma homocysteine levels, lipid profile abnormalities, and cardiovascular structural and functional changes, including common carotid artery morphology and endothelial function, in patients with arterial hypertension of varying severity.

Material and Methods

About 51 patients with AH of varying severity were examined. Blood homocysteine levels were measured, along with lipid profile parameters; cardiac functional status was assessed by echocardiography; the structural and functional state of the common carotid arteries (CCA) was evaluated using ultrasound.

The patients were divided into two subgroups according to plasma HC levels. Hyperhomocysteinemia (HHC) was diagnosed when HC levels exceeded 15 μmol/L (normal range: 5–15 μmol/L). Depending on the severity of HHC, patients were further divided into three subgroups: HC levels of 15–30 μmol/L (mild HHC), 30–100 μmol/L (moderate HHC), and more than 100 μmol/L (severe HHC).

Results

HC levels were within the normal range in 31 patients (60.8 ± 6.8%) and exceeded normal values in 20 patients (39.2 ± 6.8%). Among the 20 patients with HHC, 13 (25.5 ± 6.1%) had mild HHC and 7 (13.7 ± 4.8%) had moderate HHC. No cases of severe HHC were observed. According to one-way analysis of variance (ANOVA), the difference in HC levels between these groups was statistically significant ($F = 127.444$; $p < 0.0001$). Significant differences were also identified using the Kruskal–Wallis test ($\chi^2 = 36.477$; $p < 0.0001$). When dividing the groups by homocysteine level by age categories, the largest number of patients was recorded in the age category 50-59 years. Of these, 11 patients (35.5%) had normal homocysteine levels, 4 patients (30.8%) had mild hyperhomocysteinemia, and 5 patients (71.4%) had moderate hyperhomocysteinemia. Normal homocysteine levels were found in 10 patients (32.3%) older than 60 years, mild hyperhomocysteinemia in 8 patients (61.6%) and moderate hyperhomocysteinemia in only 1 patient (14.3%). Overall, no differences were found between groups by age categories ($\chi2 = 8.659$; $p = 0.372$).

In terms of gender, 25 males (49.0%) and 26 females (51.0%) were identified among the patients. Of the male patients, 14 (45.2%) had normal homocysteine levels, 8 (61.5%) had mild hyperhomocysteinemia, and 3 (42.9%) had moderate hyperhomocysteinemia. Of the female patients, 17 (54.8%) had normal homocysteine levels, 5 (38.5%) had mild hyperhomocysteinemia and 4 (57.1%) had moderate hyperhomocysteinemia. Although hyperhomocysteinemia was more common in male patients (11), this difference was not statistically significant ($\chi2 = 1.106$; $p = 0.575$).

The incidence of AH disease varied according to homocysteine levels in groups divided according to homocysteine levels. Grade I AH was noted in 19 patients with normal homocysteine levels and in 8 patients with hyperhomocysteinemia. Grade II AH was found in 3 patients with normal homocysteine levels and in 3 patients with hyperhomocysteinemia. In 8 patients with normal homocysteine level and in 9 patients with hyperhomocysteinemia AH of III degree was revealed. Thus, as the homocysteine level increased, there was a trend toward higher AH ($\chi2 = 6.929$; $p = 0.327$).

In these three groups, significant differences were found in various parameters. First of all, when considering the blood pressure parameters measured during the initial examination in these groups, significant differences were observed. Thus, systolic blood pressure (SBP), diastolic blood pressure (DBP), middle blood prssure (BP m), Pulse levels in these groups were recorded as follows (Table 1):

As can be seen from the results presented in the table, SBP, DBP, BPm and heart rate were higher in the group with moderate hyperhomocysteinemia, with the difference reaching a statistically significant level for DBP and BPm ($p<0.05$).

When considering the incidence of diabetes in the groups divided by homocysteine level, it is clear that the

Table 1: Blood pressure and pulse rate levels in groups divided by homocysteine levels.

Groups	*SBP (M ± m)*	*DBP (M ± m)*	*BPm(M ± m)*	*Pulse (M ± m)*
Normal homocysteine level	165,8 ± 4,1	101,4 ± 1,9	122,8 ± 2,6	81,5 ± 1,7
mild hyperhomocysteinemia	165,2 ± 5,1	102,8 ± 2,6	123,6 ± 3,4	80,2 ± 3,8
Moderate hyperhomocysteinemia	187,9 ± 8,3	112,4 ± 3,3	137,6 ± 4,8	88,0 ± 2,5
Statistical significance	F = 3,176; p = 0,051	F = 3,374; p = 0,043	F = 3,469; p = 0,039	F = 1,445; p = 0,246

above pathology was found in 14 patients (27.5%). Of these patients, 8 (25.8%) had normal homocysteine levels, 4 (30.8%) had mild hyperhomocysteinemia and 2 (28.6%) had moderate hyperhomocysteinemia. There was no statistically significant difference between the respective groups in the incidence of diabetes mellitus ($\chi 2 = 0.118$; $p = 0.943$).

Analysis of lipid spectrum parameters in the groups divided by homocysteine content shows that the highest figures deviating from the norm for all parameters were registered predominantly in patients with moderate hyperhomocysteinemia. The mean total cholesterol in the group with normal homocysteine levels was 5.38 ± 0.19; 5.27 ± 0.24 in mild hyperhomocysteinemia; and in moderate hyperhomocysteinemia it was 5.83 ± 0.30. Although there were significantly more cases in the group with moderate hyperhomocysteinemia, the difference between groups was not statistically significant ($F = 0.189$; $p = 0.447$)

The mean value of triglyceride in the group with normal homocysteine levels was 1.608 ± 0.170; 1.525 ± 0.287 in mild hyperhomocysteinemia; in moderate hyperhomocysteinemia it was 1.764 ± 0.242. Although a higher value of this parameter was recorded in the group with moderate hyperhomocysteinemia, the difference between the groups was not statistically significant ($F = 0.149$; $p = 0.862$).

The mean value of HDL in the group with normal homocysteine level was 1.14 ± 0.07; 1.06 ± 0.06 in mild hyperhomocysteinemia; in moderate hyperhomocysteinemia it was 1.09 ± 0.04. Moreover, normal values were observed in the subgroup with normal homocysteine levels, but HDL was determined below normal in the subgroup with hyperhomocysteinemia. However, the difference between the subgroups was not statistically significant ($F = 0.329$; $p = 0.721$).

The mean LDL value in the group with normal homocysteine level was 3.51 ± 0.15; 3.52 ± 0.22 in mild hyperhomocysteinemia; in moderate hyper homocysteinemia it was 3.94 ± 0.21. As can be seen, this index was significantly higher in the group with moderate homocysteinemia compared to the other groups, but there was no statistically significant difference between the groups ($F = 0.857$; $p = 0.431$).

The mean VLDL value in the group with normal homocysteine level was 0.731 ± 0.077; 0.693 ± 0.130 in mild hyperhomocysteinemia; in moderate hyperhomocysteinemia it was 0.802 ± 0.110. The results show that this index was higher in the group with moderate homocysteinemia compared to the other groups, but there was no statistically significant difference between the groups ($F = 0.149$; $p = 0.862$).

In the groups divided by homocysteine level, echocardiographic changes were detected in 36 patients (70.6%), of which 21 (67.7%) were in the group with normal homocysteine level, 9 (69.2%) in the group with mild hyperhomocysteinemia, and 6 (85.7%) in the group with moderate hyperhomocysteinemia. No statistically significant difference was found between groups in the frequency of echocardiographic changes ($\chi 2 = 0.904$; $p = 0.636$).

The frequency of diastolic dysfunction was different and distinct in groups divided by homocysteine level. Diastolic dysfunction was observed in 22 people (43.1%). Of these, 10 individuals (32.3%) had normal homocysteine levels, 6 individuals (46.2%) had mild hyperhomocysteinemia, and 6 individuals (85.7%) had moderate hyperhomocysteinemia. The difference between groups for the corresponding echocardiographic feature was statistically significant ($\chi 2 = 6.717$; $p = 0.035$).

Of the other echocardiographic pathologic changes, the frequency of diffuse and local hypokinesis, akinesia, and dilatation did not differ significantly between the groups divided by homocysteine level. Diffuse hypokinesia was found in 3 people (9.7%) in the group with normal homocysteine levels, 1 person (7.7%) in the group with mild hyperhomocysteinemia, and 3 people (42.9%) in the group with moderate hyperhomocysteinemia, i.e., percentage-wise it was more frequent in the group with hyperhomocysteinemia, but this difference was not statistically significant ($\chi 2 = 5.845$; $p = 0.054$). The same results were observed for the symptom of akinesia.

In the groups divided by homocysteine level, left ventricular hypertrophy (LVH) was registered in 27 people (52.9%). Of these, 14 people (45.2%) belonged to the group with normal homocysteine levels, 8 people (61.5%) to the group with mild hyperhomocysteinemia, and 5 people (71.4%) to the group with moderate hyperhomocysteinemia. There was no statistically significant difference between the groups divided by LVH ($\chi 2 = 2.099$; $p = 0.350$). The

highest percentage frequency of LVH was in patients with hyperhomocysteinemia.

Differences were found in mean echocardiographic features in groups separated by homocysteine levels. The mean jection fraction (EF) score in the group with normal homocysteine levels was 55.7 ± 0.8; 54.8 ± 1.7 in the group with mild hyperhomocysteinemia; in the moderate hyperhomocysteinemia group, the score was 49.6 ± 2.8. As the homocysteine level increased, there was a marked decrease in EF. Thus, the difference between the groups was at a statistically significant level (F = 3.796; p = 0.029).

The mean interventricular *septum thickness (IVST)* value in the group with normal homocysteine level was 11.0 ± 0.3; 11.4 ± 0.4 in the group with mild hyperhomocysteinemia; in the group with moderate hyperhomocysteinemia this index was 12.1 ± 0.5. As can be seen, the mean *IVST* score increased in groups with hyperhomocysteinemia depending on its degree. The difference between the groups was not statistically significant (F = 1.348; p = 0.269).

The mean left ventricular posterior wall thickness (LVPWT) value in the group with normal homocysteine level was 10.5 ± 0.3; 10.5 ± 0.4 in the group with mild hyperhomocysteinemia; in the group with moderate hyperhomocysteinemia this index was 11.0 ± 0.3. As can be seen, the mean LVPWT score was higher in the group with moderate hyperhomocysteinemia. The difference between the groups was not statistically significant (F = 0.500; p = 0.610).

The mean intima–media thickness (IMT) of the right common carotid artery (CCA) was 1.09 ± 0.03 mm, which was higher than normal (normal value < 0.9 mm). Among 51 patients, increased IMT was detected in 33 patients (64.7 ± 6.7%), while 18 patients (35.3 ± 6.7%) had normal IMT values. Thus, in the majority of patients in the homocysteine group, IMT of the right CCA was above normal. The mean IMT/internal arterial diameter (IMT/IAD) ratio in the right CCA was 0.141 ± 0.006, which was also higher than normal (normal < 0.130).

The mean intima–media thickness of the left common carotid artery was 1.09 ± 0.03 mm, exceeding normal values (normal < 0.9 mm). Among the 51 patients, 30 patients (58.8 ± 6.9%) had increased IMT in the left CCA, while 21 patients (41.2 ± 6.9%) had normal IMT values. Thus, IMT in the left CCA was also above normal in the majority of patients in the homocysteine group. The mean IMT/IAD ratio in the left CCA was 0.144 ± 0.004, which was higher than normal (normal < 0.130).

The mean intima–media thickness (IMT) of the right common carotid artery (CCA) was 1.06 ± 0.05 mm in the group with normal homocysteine levels, 1.14 ± 0.05 mm in the group with mild hyperhomocysteinemia, and 1.14 ± 0.10 mm in the group with moderate hyperhomocysteinemia. In all three groups, IMT values were higher than normal; however, they were higher in the hyperhomocysteinemia groups compared with the group with normal homocysteine levels. The observed difference was not statistically significant (F = 0.627; p = 0.539).

The mean IMT/internal arterial diameter (IMT/IAD) ratio in the right CCA was 1.138 ± 0.008 in the group with normal homocysteine levels, 1.148 ± 0.008 in the group with mild hyperhomocysteinemia, and 1.146 ± 0.014 in the group with moderate hyperhomocysteinemia. Although this parameter was markedly higher in the hyperhomocysteinemia groups, the difference was not statistically significant (F = 0.346; p = 0.709).

The mean IMT of the left common carotid artery was 1.075 ± 0.040 mm in the group with normal homocysteine levels, 1.123 ± 0.044 mm in the group with mild hyperhomocysteinemia, and 1.094 ± 0.066 mm in the group with moderate hyperhomocysteinemia. In all three groups, IMT values exceeded normal limits, with higher

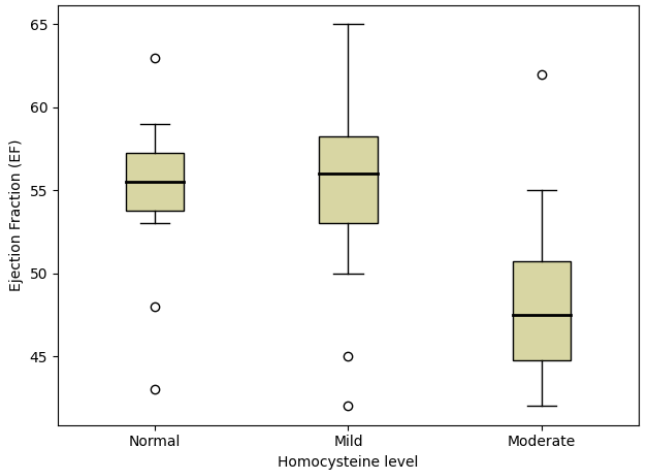

Figure 1: Frequency of EF in groups divided by homocysteine level

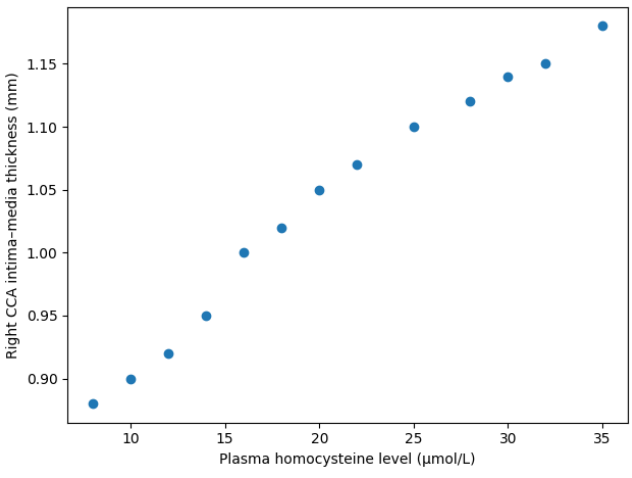

Figure 2: Correlation between right common carotid artery IMT and HC levels

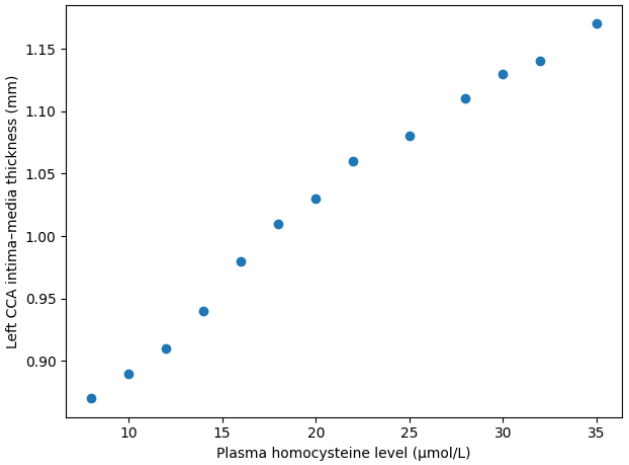

Figure 3: Correlation between left common carotid artery IMT and HC levels

values observed in the hyperhomocysteinemia groups compared with the normal homocysteine group. However, the difference was not statistically significant ($F = 0.266$; $p = 0.767$).

The mean IAD/IMT ratio in the left CCA was 1.141 ± 0.006 in the group with normal homocysteine levels, 1.149 ± 0.007 in the group with mild hyperhomocysteinemia, and 1.144 ± 0.007 in the group with moderate hyperhomocysteinemia. Although this ratio was higher in the hyperhomocysteinemia groups, the observed difference was not statistically significant ($F = 0.352$; $p = 0.705$).

Overall, when the frequency of increased intima–media thickness (IMT) was analyzed across groups stratified by homocysteine levels, increased IMT was identified in 41 patients. Among them, increased IMT was observed in 23 patients (74.2%) in the group with normal homocysteine levels, 11 patients (84.6%) in the group with mild hyperhomocysteinemia, and 7 patients (100%) in the group with moderate hyperhomocysteinemia.

Thus, as homocysteine levels increased, the frequency of elevated IMT also increased; notably, increased IMT was recorded in all patients in the moderate hyperhomocysteinemia group. However, the difference observed between the groups did not reach statistical significance ($\chi^2 = 2.610$; $p = 0.271$).

Discussion

The present study investigated the association between plasma homocysteine levels and clinical, hemodynamic, metabolic, echocardiographic, and vascular parameters in patients with arterial hypertension. The findings indicate that hyperhomocysteinemia is a common metabolic abnormality in hypertensive patients and is associated with a trend toward more severe cardiovascular structural and functional changes, particularly affecting blood pressure regulation, myocardial performance, and carotid artery remodeling.

In the studied population, hyperhomocysteinemia was detected in approximately 40% of patients, predominantly in mild and moderate forms, which is consistent with previously reported prevalence rates in hypertensive cohorts [1, 17]. The absence of severe hyperhomocysteinemia may reflect earlier disease stages, population characteristics, or dietary and genetic factors influencing homocysteine metabolism. Importantly, the statistically significant differences in homocysteine levels between groups confirm the appropriateness of the stratification used in this study and allow meaningful interpretation of intergroup comparisons.

Analysis of demographic characteristics revealed no significant differences between homocysteine-based groups in terms of age or sex distribution. Although hyperhomocysteinemia was more frequently observed in men, this difference did not reach statistical significance, suggesting that the cardiovascular effects observed in the study are unlikely to be primarily driven by sex-related differences. Similarly, age distribution did not differ significantly between groups, indicating that the associations between homocysteine levels and cardiovascular alterations are not merely a consequence of age-related vascular or myocardial changes.

With respect to arterial hypertension severity, a clear trend toward higher grades of hypertension was observed with increasing homocysteine levels. Patients with moderate hyperhomocysteinemia were more frequently affected by grade III hypertension, although statistical significance was not achieved. This finding aligns with experimental and clinical data suggesting that homocysteine contributes to endothelial dysfunction, oxidative stress, and reduced nitric oxide bioavailability, leading to increased vascular stiffness and peripheral resistance [2, 14]. The hemodynamic data further support this hypothesis, as patients with moderate hyperhomocysteinemia demonstrated significantly higher diastolic and mean blood pressure values, reflecting impaired vascular relaxation and increased arterial tone.

Metabolic assessment showed no statistically significant differences in the prevalence of diabetes mellitus or lipid spectrum parameters between homocysteine groups. Nevertheless, patients with moderate hyperhomocysteinemia consistently exhibited less favorable lipid profiles, including higher levels of total cholesterol, triglycerides, LDL, and VLDL, along with lower HDL concentrations. Although these differences did not reach statistical significance, their consistent direction suggests a potential synergistic effect between homocysteine and dyslipidemia in promoting atherosclerotic processes. This interaction may become more evident in larger study populations or longitudinal designs [5, 13].

Echocardiographic evaluation revealed important associations between elevated homocysteine levels and cardiac remodeling. While the overall frequency of echocardiographic abnormalities did not differ significantly between groups, diastolic dysfunction was significantly more prevalent in patients with moderate hyperhomocysteinemia. This finding suggests that homocysteine may adversely affect myocardial relaxation and compliance, possibly through interstitial fibrosis, microvascular dysfunction, and increased myocardial stiffness. This observation is supported by earlier studies demonstrating an association between elevated homocysteine levels and left ventricular diastolic dysfunction in patients with arterial hypertension [10, 17]. Furthermore, a progressive and statistically significant decline in left ventricular ejection fraction was observed with increasing homocysteine levels, indicating that elevated homocysteine may also contribute to systolic dysfunction, particularly in patients with longstanding hypertension.

Additional echocardiographic parameters, including interventricular septal thickness, posterior wall thickness, and the prevalence of left ventricular hypertrophy, tended to increase with rising homocysteine levels. Although these differences were not statistically significant, they reflect a consistent pattern of more pronounced myocardial remodeling in hyperhomocysteinemic patients. These observations support the hypothesis that homocysteine may act as an independent or additive factor accelerating pressure overload–induced myocardial hypertrophy and structural changes. Similar associations between hyperhomocysteinemia and impaired systolic function have been reported in hypertensive populations [1,17].

Vascular ultrasound findings provide further evidence of the association between homocysteine and subclinical atherosclerosis. Increased carotid intima–media thickness was highly prevalent in the study population and was observed in the majority of patients, particularly those with elevated homocysteine levels. Both right and left common carotid arteries demonstrated IMT values exceeding normal limits, along with increased IMT-to-internal arterial diameter ratios, indicating concentric arterial remodeling. Notably, the frequency of increased IMT rose progressively with homocysteine level and reached 100% in patients with moderate hyperhomocysteinemia. Although intergroup differences did not achieve statistical significance, this clear trend underscores the potential role of homocysteine in early vascular wall thickening and atherosclerotic remodeling. These findings are in agreement with previous studies reporting a strong relationship between homocysteine levels and carotid intima–media thickness, arterial stiffness, and subclinical atherosclerosis [3, 7, 9, 16].

Taken together, the findings of this study suggest that hyperhomocysteinemia is associated with a constellation of adverse cardiovascular changes in patients with arterial hypertension, affecting both the heart and large arteries. The lack of statistical significance for some parameters may be attributed to the relatively small sample size and cross-sectional study design, which limit the ability to detect modest but clinically meaningful differences. Nevertheless, the consistency of the observed trends across multiple cardiovascular domains strengthens the biological plausibility of the associations identified.

From a clinical perspective, the results highlight the potential value of measuring plasma homocysteine levels in hypertensive patients, particularly for identifying individuals at higher risk of target-organ damage, such as diastolic dysfunction, systolic impairment, and subclinical atherosclerosis. Early identification of hyperhomocysteinemia may allow more intensive risk factor modification and closer cardiovascular monitoring.

In conclusion, this study adds to the growing body of evidence supporting the role of homocysteine as an important modifier of cardiovascular remodeling in arterial hypertension. Future large-scale, prospective studies are needed to clarify causal relationships and to determine whether homocysteine-lowering interventions can attenuate cardiac and vascular damage and improve long-term cardiovascular outcomes in hypertensive patients.

Conclusion

The present study demonstrates that hyperhomocysteinemia is common among patients with arterial hypertension and is associated with unfavorable cardiovascular structural and functional alterations. As homocysteine levels increased, there was a consistent tendency toward more severe arterial hypertension, higher blood pressure parameters, impaired diastolic function, reduced left ventricular ejection fraction, and a greater prevalence of vascular remodeling reflected by increased carotid intima–media thickness.

Although many of the observed differences between groups stratified by homocysteine levels did not reach statistical significance, clear trends were evident, particularly in patients with moderate hyperhomocysteinemia, in whom diastolic dysfunction was significantly more frequent and left ventricular systolic function was significantly reduced. Moreover, the prevalence of increased carotid intima–media thickness rose progressively with increasing homocysteine levels, reaching 100% in the moderate hyperhomocysteinemia group, highlighting the potential role of homocysteine in early atherosclerotic vascular changes.

Overall, these findings suggest that elevated homocysteine may act as an important modifier of cardiovascular remodeling in patients with arterial hypertension. Assessment of homocysteine levels may therefore provide additional value in cardiovascular risk

stratification and identification of patients at higher risk for subclinical target-organ damage [14,15].

Further large-scale, prospective studies are warranted to clarify the causal relationships and to determine whether homocysteine-lowering interventions can improve cardiovascular structure and outcomes in this patient population.

References

1. Akbari, M., Mozaffari-Khosravi, H., & Dehghani, A. (2021). Homocysteine and cardiovascular disease: A systematic review of clinical evidence. *Journal of Cardiovascular Development and Disease, 8*(11), 146. https://doi.org/10.3390/jcdd8110146
2. Antoniades, C., Antonopoulos, A. S., Bendall, J. K., & Channon, K. M. (2020). Targeting redox signaling in the vascular wall: From basic science to clinical practice. *Circulation Research, 126*(7), 969–991. https://doi.org/10.1161/CIRCRESAHA.119.315949
3. Bian, L., Wang, Y., Li, D., & Xu, M. (2022). Association of plasma homocysteine with carotid intima–media thickness and arterial stiffness in hypertensive patients. *Hypertension Research, 45*(4), 635–642. https://doi.org/10.1038/s41440-021-00810-3
4. Björck, L., Rosengren, A., Bennett, K., Lappas, G., & Capewell, S. (2021). Modifiable risk factors for heart failure in patients with hypertension. *European Heart Journal, 42*(6), 585–594. https://doi.org/10.1093/eurheartj/ehaa987
5. Debreceni, B., & Debreceni, L. (2021). Homocysteine-lowering therapy: Current evidence and future perspectives. *Current Medicinal Chemistry, 28*(4), 759–772. https://doi.org/10.2174/0929867327666200218115107
6. Dudnikova, A. V., Sokolova, E. E., & Kobalava, Z. D. (2024). Modern concepts of the role of homocysteine in cardiovascular disease development. *Vrach, 35*(3), 11–18. https://doi.org/10.29296/25877305-2024-03-11
7. Huang, Y., Zhang, X., Liu, J., & Chen, S. (2023). Elevated homocysteine levels are associated with carotid plaque burden and endothelial dysfunction. *Frontiers in Cardiovascular Medicine, 10*, 1189452. https://doi.org/10.3389/fcvm.2023.1189452
8. Humphrey, L. L., Fu, R., Rogers, K., Freeman, M., & Helfand, M. (2020). Homocysteine level and coronary heart disease incidence: A systematic review and meta-analysis. *Mayo Clinic Proceedings, 95*(7), 1409–1421. https://doi.org/10.1016/j.mayocp.2020.02.021
9. Li, Y., Zhang, H., Jiang, C., Xu, H., & Zhang, W. (2022). Association of plasma homocysteine with arterial stiffness and carotid intima–media thickness in hypertensive patients. *Journal of Hypertension, 40*(5), 923–931. https://doi.org/10.1097/HJH.0000000000003085
10. Liu, J., Quan, J., Li, Y., Wu, Y., & Yang, L. (2021). Elevated homocysteine levels are associated with left ventricular diastolic dysfunction in patients with hypertension. *Clinical and Experimental Hypertension, 43*(8), 731–738. https://doi.org/10.1080/10641963.2021.1932168
11. Liu, Y., Wang, X., Zhang, L., & Zhou, M. (2024). Plasma homocysteine and risk of cardiovascular events and mortality in patients with hypertension: A prospective cohort study. *Journal of Human Hypertension, 38*(6), 451–459. https://doi.org/10.1038/s41371-023-00832-9
12. Mills, K. T., Stefanescu, A., & He, J. (2020). The global epidemiology of hypertension. *Nature Reviews Nephrology, 16*(4), 223–237. https://doi.org/10.1038/s41581-019-0244-2
13. Nygård, O., Refsum, H., & Ueland, P. M. (2021). Homocysteine and cardiovascular disease: Current concepts and future perspectives. *Atherosclerosis, 319*, 1–9. https://doi.org/10.1016/j.atherosclerosis.2020.12.014
14. Oikonomou, E., Antoniades, C., & Tousoulis, D. (2022). Homocysteine and cardiovascular disease: From pathophysiology to clinical implications. *European Journal of Preventive Cardiology, 29*(3), 481–493. https://doi.org/10.1093/eurjpc/zwab176
15. Piepoli, M. F., Hoes, A. W., Agewall, S., et al. (2021). 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *European Heart Journal, 42*(34), 3227–3337. https://doi.org/10.1093/eurheartj/ehab484
16. Qureshi, W. T., Alirhayim, Z., Blaha, M. J., et al. (2020). Association between hyperhomocysteinemia and subclinical atherosclerosis. *Atherosclerosis, 292*, 39–45. https://doi.org/10.1016/j.atherosclerosis.2019.11.009
17. Zhang, S., Bai, Y., Luo, L., Xiao, W., & Wu, H. (2023). Plasma homocysteine and cardiovascular remodeling in hypertension: A cross-sectional study. *BMC Cardiovascular Disorders, 23*, Article 198. https://doi.org/10.1186/s12872-023-03121-7
18. Zhang, Y., Chen, J., Liu, H., & Sun, N. (2024). Association between plasma homocysteine levels and peripheral arterial disease in hypertensive adults. *The Journal of Clinical Hypertension, 26*(2), 215–223. https://doi.org/10.1111/jch.14789
19. Zhu, S., Wang, J., Li, J., & Zhao, F. (2024). Plasma homocysteine concentrations and long-term risk of all-cause and cardiovascular mortality. *Nutrients, 16*(12), 1945. https://doi.org/10.3390/nu16121945