ONLINE VERSION: ISSN 1028-4818
RPNS-1853

Multimed 2024; 28:e3044

Original article

Clinical vascular evaluation of type 2 diabetic patients according to homocysteine levels

Vascular clinical evaluation of type 2 diabetic patients according to homocysteine levels

Clinical vascular assessment of type 2 diabetic patients according to homocysteine levels

Jorge Manuel Gallego Galano I* https://orcid.org/0009-0008-2253-8967
Archimedes Montoya Pedrón I https://orcid.org/0000-0001-9415-4585
Mayelyn Rodríguez Estenger I https://orcid.org/0000-0003-2449-858X
Reynaldo Álvarez Vicario I https://orcid.org/0009-0008-3435-6335
Yindra Bárbara Benítez Casamayor I https://orcid.org/0000-0002-0738-1796

[Yo]Granma University of Medical Sciences. Dr. Juan Bruno Zayas Alfonso General Hospital. Santiago de Cuba, Cuba.

[*]Corresponding author:jorgegallego@infomed.sld.cu

SUMMARY

Introduction: Homocysteine is an additional risk factor for cardiovascular disease in patients with type 2 diabetes mellitus.

Aim: To evaluate type 2 diabetic patients from a clinical vascular point of view according to homocysteine levels.

ONLINE VERSION: ISSN 1028-4818
RPNS-1853

Methods:A descriptive cross-sectional study was conducted at the “Dr. Juan Bruno Zayas” General Hospital from August 2022 to January 2023. The universe consisted of 275 patients and a sample of 53 patients over 30 years of age with type 2 diabetes mellitus who presented cardiovascular risk factors and met the selection criteria. The mean, standard deviation, and percentage were used as summary measures.

Results: increased homocysteine levels were found in 66% of cases,Mild hyperhomocysteinemia predominated in 32.1% of cases, in males (20.6%) and in those over 60 years of age (15.1%). Arterial hypertension was present in 88.7% of cases.%as the most relevant cardiovascular risk factor, LDLhigh cholesterolandLow HDL cholesterolwere the most frequent lipid alterations with 64,2% and 62.3%respectively, both coinciding with the slight elevation of homocysteine in aCarotid intima-media thickness was the most significant vascular wall alteration in 58.5% of cases, as was moderate arterial stiffness in 38.5% of cases, both with mild elevation of homocysteine.

Conclusions: Homocysteine levels allow us to evaluate the vascular status in type 2 diabetic patients, which is why it is considered a biomarker of cardiovascular risk.

Keywords: Homocysteine; Type 2 diabetes mellitus; Cardiovascular risk; Hyperhomocysteinemia.

ABSTRACT

Introduction: Homocysteine is an additional risk factor for cardiovascular diseases in patients with type 2 diabetes mellitus.

Objective:to evaluate type 2 diabetic patients from a vascular clinical point of view according to homocysteine levels.

Methods:a cross-sectional descriptive study was carried out at the Juan Bruno Zayas General Hospital in the period from August 2022 to January 2023. The universe consisted of 275 and a sample of 53 patients over 30 years of age, with type 2 diabetes mellitus who presented cardiovascular risk factors and met the selection criteria. The mean, standard deviation and percentage were used as summary measures.

ONLINE VERSION: ISSN 1028-4818
RPNS-1853

Results: Increased homocysteine levels were found in 66% of cases, with mild hyperhomocysteinemia predominating in 32.1%, in males (20.6%) and in those over 60 years of age (15.1%). High blood pressure was present in 88.7% as the most relevant cardiovascular risk factor, high LDL cholesterol and low HDL cholesterol were the most frequent lipid alterations with 64.2% and 62.3% respectively, both coinciding with the slight elevation of homocysteine by 28.3%. The thickness of the carotid intima media was the most relevant alteration of the vascular wall in 58.5%, as well as moderate arterial stiffness in 38.5%, both with slight elevation of homocysteine.

Conclusions: Homocysteine levels allow us to evaluate the vascular status in type 2 diabetic patients, which is why it is considered a biomarker of cardiovascular risk.

Keywords:homocysteine; Diabetes mellitus type 2; Cardiovascular risk; Hyperhomocysteinemia.

SUMMARY

Introduction: Homocysteine is an additional risk factor for cardiovascular disease in patients with type 2 diabetes mellitus.

Aim:evaluate type 2 diabetic patients according to homocysteine levels from a clinical vascular point of view.

Methods:A cross-sectional descriptive study was carried out at the General Hospital "Dr. Juan Bruno Zayas" in the period from August 2022 to January 2023. The universe was composed of 275 patients and a sample of 53 patients with more than 30 years of age with type 2 diabetes mellitus that presented cardiovascular risk factors and predefined the criteria of selection. Mean, standard deviation and percentages used as summary measures.

Results: Increased levels of homocysteine were found in 66% of two cases, with mild hyper-homocysteinemia predominating in 32.1% of the male sex (20.6%) in men over 60 years of age (15.1%).Arterial hypertension is present in 88.7% as the most relevant cardiovascular risk factor, or elevated LDL cholesterol and low HDL cholesterol are the most frequent lipid alterations with 64.2% and 62.3% respectively, both coinciding with a discrete elevation of homocysteine in 28.3%.

ONLINE VERSION: ISSN 1028-4818
RPNS-1853

The thickness of the carotid intimate media was the most relevant alteration of the vascular wall in 58.5%, as well as moderate arterial stiffness in 38.5%, both with discrete elevation of homocysteine.

Conclusões: Homocysteine levels allow us to evaluate the vascular status in type 2 diabetic patients, therefore it is considered a biomarker of cardiovascular risk.

Keywords: Homocysteine; Type 2 diabetes mellitus; Cardiovascular risk; Hyperhomocysteinemia.

Received: 07/08/2024

Approved: 10/28/2024

Introduction

Diabetes is one of the fastest growing global health emergencies of the 21st century. According to statistical data from the International Diabetes Federation, (1) in 2021, 537 million people were living with diabetes worldwide and 6.7 million individuals between the ages of 20 and 79 died from complications arising from this disease. In a recent article published in June 2023 in The Lancet journal, (2) it is estimated that by 2050 this figure will increase to more than 1.31 billion people according to data provided at the 83rd Scientific Session of the American Diabetes Association.

Cuba does not escape this health problem, according to the Statistical Health Yearbook, (3) in 2022 the prevalence of DM was 66.5 x 1000 inhabitantswith a mortality rate of 25.8 deaths per 100,000 inhabitants, making it the tenth leading cause of death in the country. In Santiago de Cuba, the prevalence of the disease was 56.1 per 100,000 inhabitants, with a crude mortality rate of 27.6 per 100,000 inhabitants.

In recent decades, the scientific community has made progress in understanding the pathophysiology of diabetes, and new additional risk markers have been identified. One of these is homocysteine, recognized since the 1990s by Framingham, which offers additional

diagnostic and prognostic value to the classic factors known for predicting the risk of atherosclerotic cardiovascular disease in these patients.

Multiple studies show that increased plasma homocysteine levels are associated with an increased risk of coronary artery disease, cerebrovascular disease, and peripheral arterial disease, independently of other conventional risk factors such as smoking, high blood pressure (HBP), and diabetes mellitus (DM), which interact synergistically. [4.5]

It has currently been shown that patients with T2DM have high serum homocysteine concentrations, which participates in the formation of oxidative compounds with atherogenic power, activation of some coagulation factors and inactivation of natural anticoagulants, vasodilatory factors and antiplatelet factors (nitric oxide, prostacyclins), leading to endothelial dysfunction, thrombus formation and development of atherosclerosis; it also causes loss of elasticity and arterial stiffness. The determination of plasma levels of this parameter allows the evaluation of the state of vascular health, an additional tool in the estimation of cardiovascular risk (CVR) in DM for the prevention of complications in the diabetic population. (5,6)

In this context, there are very few studies that evaluate homocysteine levels with alterations of the vascular endothelium, by vascular images such as carotid Doppler ultrasound and vascular hemodynamic parameters by determining the carotid-femoral pulse wave velocity (cfPWV) as an indicator of arterial stiffness (AR), a method that has been performed since the last decade in the province of Santiago de Cuba with the ANGIODIN® PD 3000 equipment, developed at the Medical Biophysics Center of Santiago de Cuba.

Based on the above, the objective of this study was to evaluate type 2 diabetic patients based on homocysteine levels from a clinical vascular perspective. Our hypothesis is that homocysteine levels correlate with the extent of vascular damage in patients with DM, so its plasma determination allows us to implement predictive, preventive, and personalized medicine, aimed at the targeted intervention of cardiovascular complications.

ONLINE VERSION: ISSN 1028-4818
RPNS-1853

Methods

An observational, descriptive, and cross-sectional study was conducted in patients over 30 years of age diagnosed with type 2 diabetes mellitus and cardiovascular risk factors, treated in the Internal Medicine clinic of the "Dr. Juan Bruno Zayas Alfonso" General Hospital, from August 2022 to January 2023.

Population and sample

The universe consisted of 275 patients who met the selection criteria and consented to participate in the research. The sample consisted of 53 patients who met the selection criteria and consented to participate in the research. The sample size was calculated using the formula for proportions for a finite population:

$$n = \frac{N * (Z\alpha)^2 * p * q}{(d)^2 * (N-1) + (Z\alpha)^2 * p * q}$$

Where:

- N = Total population
- Zα2 = 1.962 (if the certainty is 95%)
- p = expected proportion (in this case 5% = 0.05)
- q = 1 – p (in this case 1-0.05 = 0.95)
- d = precision (in this case we want 3%) whose sample was made up of 52 patients, selected by simple random sampling.

Pregnant women, patients with acute conditions such as infections, anemia, trauma, surgery, cerebrovascular disease, ischemic heart disease, and peripheral arterial disease were excluded, as were those with neoplastic disease undergoing medical treatment with chemotherapy or radiotherapy in the previous six months and those with a history of thyroid, autoimmune, genetic or acquired musculoskeletal diseases, immunodeficiency, or disability.

Variables

Epidemiological and clinical variables:

Sex: male or female.

Age: 30-39, 40-49, 50-59, ≥ 60.

Diabetes onset time: This was defined as years of living with the disease. For the study, the following categories were classified: < 10 years and ≥ 10 years.

Cardiovascular risk factors: high blood pressure (self-reported or confirmed), obesity (BMI ≥ 30 kg/m2), hyperlipidemia, physical inactivity, smoking and alcoholism.

Humoral variables

Homocysteine: it was classified as

- Normal homocysteine: 5-15 µmol/L)
- Mild hyperhomocysteinemia: 16-30 µmol/L
- Moderate hyperhomocysteinemia: 31-100 µmol/L
- Severe hyperhomocysteinemia: greater than 100 µmol/l

Lipidrogram. It was classified according to results in

- Hypercholesterolemia: total cholesterol ≥ 6.5 mmol/l
- Hypertriglyceridemia: triglycerides ≥ 1.70 mmol/l
- High low-density lipoprotein cholesterol (LDLc): 2.6 mmol/l
- High-density lipoprotein cholesterol (HDLc): low: men ≤ 0.92 mmol/l, women ≤ 1.16 mmol/l.

Imaging Variables

Carotid Doppler ultrasound with an ALOKA SSD-α10 device (Mitaka, Tokyo, Japan), in which B-mode and color Doppler images were obtained at the level of both common carotid arteries, the carotid bulb, and the proximal 1.5 cm of the internal carotid artery, where the alterations in the vascular wall were determined:

- Intima media thickness (IMT): classified as normal or increased.
- Atheromatous plaque: classified as present or absent.

Vascular hemodynamic variables

Arterial stiffness: Normal (2.5 to 6 m/s); Mild or moderate: (> 6 and < 10 m/s); Severe: (> 10 m/s).

Techniques and procedures

General information, personal medical history, and cardiovascular risk factors were collected through questionnaires. A data collection form was created to collect these variables. Patients underwent the following biochemical tests: total cholesterol, triglycerides, LDL cholesterol, HDL cholesterol, and fasting homocysteine.

Carotid Doppler ultrasound was performed using an ALOKA SSD-α10 device (Mitaka, Japan), with B-mode and color Doppler images at the level of both common carotid arteries, the carotid bulb, and the proximal 1.5 cm of the internal carotid artery, where vascular wall alterations were determined.

Hemodynamic studies were performed in the vascular hemodynamics laboratory using an ANGIODIN® PD 3000 Digital Plethysmograph, where the RA was determined with the VOPcf (meters/second), which was calculated by computational methods, from a mathematical model of the contour and morphology of the pulse wave obtained by the Photoplethysmography method.

The data were processed computerized on an ASUS computer, in which the Statistical Product and Service Solutions (SPSS) version 25 system was used. The percentage was used as summary measures and for statistical validation the Pearson's $\chi 2$ test of independence was applied to identify any statistically significant association between selected variables of interest, for which a significance level of $\alpha=0.05$ was taken.

Ethical aspects

The study was governed by ethical criteria in accordance with institutional policy and the fundamental principles governing the Declaration of Helsinki. (7) All participants in the research indicated their agreement by signing the informed consent form.

Results

Table 1 shows that the predominant age group was 50-59 years (47.2%), and the female sex predominated (60.4%). Regarding homocysteine determination, 66% of patients had elevated values, with mild hyperhomocysteinemia predominating in 32.1%, followed by moderate hyperhomocysteinemia in 28.3%.

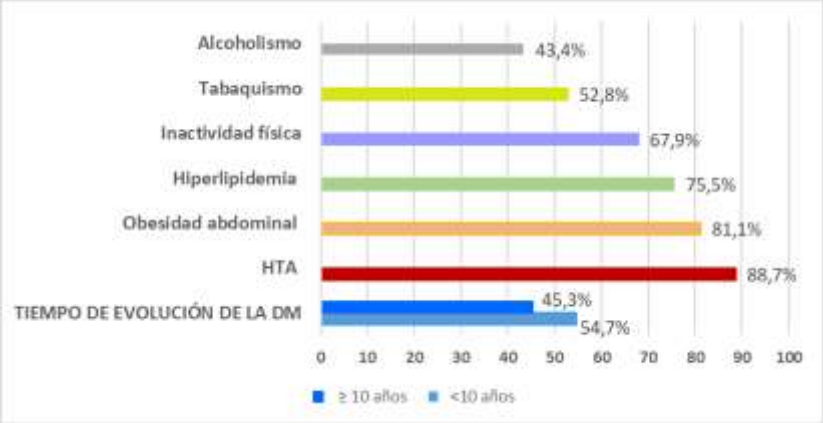
When relating the results of homocysteine determination with the age group, it was found that mild hyperhomocysteinemia prevailed in the group ≥ 60 years (15.1%), coinciding with the female sex (20.8%).

Table 1. Type 2 diabetic patients according to age, sex and homocysteine results.

Epidemiological variables	Homocysteine								Total	
	Normal		Hyperhomocysteinemia (66%)							
			Mild		Moderate		Severe			
	No.	%	No.	%	No.	%	No.	%	No.	%
Age groups (years)										
30 - 39	2	3.8	1	1.9	1	1.9	0	0	4	7.5
40 – 49	3	5.7	3	5.7	1	1.9	0	0	7	13.2
50 - 59	11	20.6	5	9.4	7	13.2	1	1.9	24	45.3
≥ 60	2	3.8	8	15.1	6	11.3	2	3.8	18	34.0
Total	18	34.0	17	32.1	15	28.3	3	5.6	53	100
Sex										
Female	10	18.9	11	20.8	9	17.0	2	3.8	32	60.4
Male	8	15.1	6	11.3	6	11.3	1	1.9	21	39.6
Total	18	34.0	17	32.1	15	28.3	3	5.6	53	100

Regarding cardiovascular risk factors (graph), the most frequent were high blood pressure, followed by abdominal obesity (88.7%) and (81.1%) respectively. It is worth noting that several patients had more than one risk factor. Similarly, in relation to the time of evolution,

there was a predominance in those patients with less than 10 years of disease progression (54.7%).



Graphic. Patients with type 2 diabetes mellitus according to cardiovascular risk factors and disease progression.

*% calculated in relation to the total number of patients

The results in Table 2 show that the most frequently occurring lipid disorder was elevated LDL cholesterol, in 64.2% of patients, followed by low HDL cholesterol in 62.3%. In both lipid disorders, the majority of patients presented mild hyperhomocysteinemia (28.3%), followed by those with moderate hyperhomocysteinemia (26.4%). Furthermore, several patients presented more than one lipid disorder, regardless of homocysteine levels.

Table 2. Patients with type 2 diabetes mellitus according to lipid alterations and homocysteine levels.

Lipid disorders	**Homocysteine**								Total*	
	Normal		Hyperhomocysteinemia							
			Light		Moderate		Serious			
	No.	%	No.	%	No.	%	No.	%	No.	%
Hypercholesterolemia	4	7.5	9	17.0	10	18.9	2	3.8	25	47.2
Hypertriglyceridemia	2	3.8	11	20.8	12	22.6	3	5.7	28	52.8
High LDL cholesterol	2	3.8	15	28.3	14	26.4	3	5.7	34	64.2

Low HDL cholesterol	1	1.9	15	28.3	14	26.4	3	5.7	33	62.3

*% calculated in relation to the parameter per row

As shown in Table 3, of the 18 patients with normal homocysteine levels, 30.2% (16 patients) had no vascular wall abnormalities. The most common vascular abnormality was an increased CIMT, in 58.5% of cases, followed by the presence of atheromatous plaques in 52.8%.

The CIMT was predominant in 58.5% of cases, with moderate hyperhomocysteinemia predominating in 24.5%. Of those with atherosclerotic plaques, 22.6% had moderate hyperhomocysteinemia. There was a statistically significant relationship between homocysteine levels and vascular wall abnormalities.

Table 3: Patients with type 2 diabetes mellitus according to vascular wall alterations and homocysteine.

Alterations of the vascular wall	**Homocysteine**								Total	
	Normal		Hyperhomocysteinemia							
			Light	Moderate			Serious			
	No.	%	No.	%	No.	%	No.	%	No.	%
Carotid intima-media thickness	p=0.000									
Increased	2	3.8	13	24.5	13	24.5	3	5.7	31	58.5
Normal	16	30.2	4	7.5	2	3.8	0	0	22	41.5
Atheromatous plaque	p=0.0001									
Present	2	3.8	11	20.8	12	22.6	3	5.7	28	52.8
Absent	16	30.2	6	11.3	3	5.7	0	0	25	47.2
Total	18	34.0	17	32.1	15	28.3	3	5.6	53	100

Positive RA was present in 39 patients (73.6%) with predominanceof the moderate in 35.8% in patients with moderate hyperhomocysteinemia (20.8%) as shown in Table 4. Furthermore, it is striking that 66% of patients with hyperhomocysteinemia, only 1.8% did not present this altered parameter, on the other hand, it was observed that as plasma homocysteine levels increased, they corresponded to the different RA parameters. Statistical

validation showed the existence of a significant relationship between homocysteine levels and RA.

Table 4. Type 2 diabetic patients according to arterial stiffness and homocysteine levels.

Arterial stiffness	Homocysteine								Total	
	Normal		Hyperhomocysteinemia (66%)							
			Light		Moderate		Serious			
	No.	%	No.	%	No.	%	No.	%	No.	%
Normal	10	18.7	3	5.7	1	1.9	0	0	14	26.4
Light	5	9.4	8	15.1	2	37.8	0	0	15	28.3
Moderate	2	37.8	5	9.4	11	20.8	1	1.9	19	35.8
Severe	1	1.9	1	1.9	1	1.9	2	37.8	5	9.4
Total	18	34.0	17	32.1	15	28.3	3	5.6	53	100

p=0.000

Discussion

Homocysteine concentrations rise throughout life in both sexes. Before puberty, all children have low and similar concentrations; at puberty, these values are higher in boys than in girls, so that by age 40, there is a male predominance over female predominance, which equals out at menopause in both sexes equally. (8)

In the diabetic population studied, elevated homocysteine predominated in the age group of 50-59 years and the most frequent sex was female, which may be related to endothelial damage, the onset of atherogenesis which is early in the diabetic population, and on the other hand, the loss of the estrogenic protective effect in the female sex which is involved in its appearance, data consistent with studies by Velarde et al., (9) in Bolivia and Denis et al., (4) in Cuba.

Hypertension, abdominal obesity and hyperlipidemia were the risk factors that predominated in diabetic patients regardless of the time of evolution. On the other hand,

the presence of an increase in homocysteine in plasma speaks in favor of endothelial dysfunction, increased thrombogenicity, increased permeability of lipid and inflammatory cells, lipoprotein oxidation, vascular inflammation and abnormalities in the coagulation cascade, which is why the determination of this biomarker is a tool to evaluate in the prediction of cardiovascular risk in these patients.

Shih et al., (10) showed in a middle-aged and elderly population that high plasma homocysteine levels were independently associated with hypertension, diabetes mellitus and dyslipidemia components of the cardiometabolic syndrome, while Zhang et al., (11) in a prospective cohort study in China found a significant association in patients with intermediate to severe hyperhomocysteinemia with cardiovascular events (HR 2.07, 95% CI 1.01–4.26) and death from all causes (HR 3.08, 95% CI 1.56–6.07) in the elderly population without a history of cardiovascular disease, with a positive association in the female sex, not the same in the male.

Clinical epidemiological studies have shown that homocysteine increases secretion with the biosynthesis and secretion of cholesterol (low-density lipoproteins), triglycerides, with a decrease in protein synthesis of apolipoprotein A1, therefore, decreasing HDL-C levels, which coincide with the findings of this study, in the same way with the study of Zhou L and collaborators, (12) in China showed that plasma homocysteine was significantly associated with conventional atherogenic lipids, in the same way it was independently correlated with the levels of remaining cholesterol beyond other lipids.

The alterations of the arterial wall evidenced by carotid Doppler ultrasound are a method that allows for a more precise evaluation of the presence of subclinical atherosclerosis demonstrated at its onset by IMT, up to the presence of atheromatous plaque, which is demonstrated in this study where both alterations were present and were more evident in those patients with moderate and severe hyperhomocysteinemia.

Laverde, (13) in a bibliographic review about homocysteine and cardiovascular disease noted that the thickness of the intima media was related to high levels of homocysteine, consistent with the findings found, where patients with mild and moderate hyperhomocysteinemia

showed an increase in the CIMT, followed by those with atheromatous plaques and in all patients with severe hyperhomocysteinemia both alterations were found, similar results found in other studies, (14,15) similar to studies carried out where the relationship of homocysteine levels with the CIMT and the presence of atheromatous plaque in vascular complications mainly stroke and coronary artery disease is demonstrated.

Hyperhomocysteinemia has been linked to alterations between collagen and elastin that cause stiffness and loss of arterial distensibility, which is consistent with this study where it was found that the degree of arterial stiffness was related to homocysteine levels.

Sheng et al., (16) in an analytical study in China, found that plasma homocysteine levels are independently associated with alterations in large artery stiffness in men, but not in women; while Shindo et al., (17) found that higher plasma homocysteine levels are related to greater stiffness in adult women, associated with cognitive impairment.

The results obtained in this study show that homocysteine is a risk biomarker for assessing the vascular status of patients with type 2 diabetes. Despite its relationship with vascular endothelial alterations demonstrated in vascular hemodynamic studies, it is an additional tool for cardiovascular risk stratification, enabling vigorous, personalized, multidisciplinary therapeutic action to prevent vascular complications in patients with type 2 diabetes.

Among the study's weaknesses is its descriptive, monocentric nature with a small population, so the authors recommend conducting analytical studies that can demonstrate the causal relationship between the variables studied.

Conclusions

Homocysteine levels allow us to evaluate vascular status in patients with type 2 diabetes, which is why it is considered a risk biomarker to consider in the prevention of cardiovascular events.

ONLINE VERSION: ISSN 1028-4818
RPNS-1853

Bibliographic references

1. International Diabetes Federation [Internet]. Brussels: IDF; 2023 [cited 22/11/2023]; Available at:https://idf.org/es/

2. Diabetes: a defining disease of the 21st century. [Internet]. Lancet. 2023; 401(10394):2087.

3. Cuba. National Office of Statistics and Information. Health Statistical Yearbook [Online]. Havana: ONEI; 2023 [cited 11/20/2023]. Available at: https://www.onei.gob.cu/sites/default/files/publicaciones/2023-08/19_salud_publica-_asistencia-social-2022-edicion-2023

4. Denis de Armas R, Torres Yribar W, CeperoLlauger K, Alonso Rodríguez CA. Hyperhomocysteinemia as a risk factor for obstructive vascular disease. Cuban Journal of Medicine. 2024;63:e3373.

5. Rodríguez Perón JM. Cardiac biomarkers of atherothrombosis and their implications for cardiovascular disease risk estimation. Cuban Journal of Military Medicine. 2021;50(2):e0210766.

6. Zhou L, Liu J, An Y, Wang Y, Wang G. Plasma Homocysteine Level Is Independently Associated With Conventional Atherogenic Lipid Profile and Remnant Cholesterol in Adults. Front Cardiovasc Med. 2022; 9:898305.

7. The World Medical Association. Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013; 310(20):2191-4.

8. Rosabal-Nieves E. On homocysteine metabolism. Implications for nutrition. Cuban Journal of Food and Nutrition. 2016;26(1):157-71.

9. Velarde Negrete J, Hidalgo Filipovich RA, Martinez Eid G, Coloccini MA, Uriona Trigo MC. Relationship between plasma homocysteine and apolipoprotein b-100 levels and cardiovascular risk. Rev Cient Cienc Méd. 2022; 25(2): 18-24.

10. Shih YL, Shih CC, Huang TC, Chen JY. The Relationship between Elevated Homocysteine and Metabolic Syndrome in a Community-Dwelling Middle-Aged and Elderly Population in Taiwan. Biomedicines. 2023;11(2):378.

11. Zhang Z, Gu X, Fang X, Tang Z, Guan S, Liu H, et al. Homocysteine and the Risk of Cardiovascular Events and All-Cause Death in Elderly Population: A Community-Based Prospective Cohort Study. Ther Clin Risk Manag. 2020;16:471-81.

12. Zhou L, Liu J, An Y, Wang Y, Wang G. Plasma Homocysteine Level Is Independently Associated With Conventional Atherogenic Lipid Profile and Remnant Cholesterol in Adults. Front Cardiovasc Med. 2022; 9:898305.

13. Laverde G. Homocysteine and cardiovascular disease. Perspect Nut Hum. 2013;(16):53-66.

14. Yanli L, Yi Z, Huarong X, Yuxiao W. Relationship between plasma homocysteine, serum 25-hydroxyvitamin D 3 levels and carotid intima-media thickness in young diabetic patients [J]. JCMP. 2020; 24(10): 45-8.

15. Momin M, Fan F, Yang Y, Li J, Jia J, Zhang Y. Additive effect between homocysteine and low-density-lipoprotein cholesterol upon incidence of novel carotid plaque formation: data from a Chinese community-based cohort. BMC Cardiovasc Disord.2023; 23:332.

16. Sheng L, Wu C, Bai YY, Xiao WK, Feng D, Ye P. Plasma homocysteine levels are independently associated with alterations of large artery stiffness in men but not in women. J Geriatr Cardiol. 2015; 12(3):251-6.

17. Shindo-Hamasaki A, Akazawa N, Momma R, Maeda S. The Association between Homocysteine, Arterial Stiffness and Executive Function Middle-aged and Older Women. Artery Res. 2021; 27(1):32-7.

Conflict of interest

The authors declare that there is no conflict of interest.

Authorship contribution

Conceptualization and Data Curation: Jorge Manuel Gallego Galano, Reynaldo Álvarez Vicario, Yindra Bárbara Benítez Casamayor, Arquímedes Montoya Pedrón.

Formal Analysis: Mayelyn Rodríguez Estenger, Jorge Manuel Gallego Galano.

Research: Jorge Manuel Gallego Galano, Reynaldo Álvarez Vicario, Yindra Bárbara Benítez Casamayor.

Methodology: Mayelyn Rodríguez Estenger.

Project Management: Jorge Manuel Gallego Galano, Arquímedes Montoya Pedrón.

Software: Mayelyn Rodríguez Estenger.

Validation: Mayelyn Rodríguez Estenger, Jorge Manuel Gallego Galano, Arquímedes Montoya Pedrón.

Original draft written by: Jorge Manuel Gallego Galano.

Writing – review and editing: Jorge Manuel Gallego Galano, Arquímedes Montoya Pedrón.