International Journal of Medicine and Medical Research

Journal homepage: https://ijmr.com.ua/
Volume 9, No. 1. 2023

UDC 616-018.74-008.6-085.27:616.12-008.331.1:616.441-008.64
DOI: 10.61751/ijmmr.2413-6077.2023.1.24

**Article's History:**
Received: 15.02.2023; Revised: 01.05.2023; Accepted: 30.05.2023

# Endothelial dysfunction correction in patients with hypertension, dyslipidaemia, and decreased thyroid function

**Marta Orel***
Postgraduate Student
I. Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine
46001, 1 Maidan Voli, Ternopil, Ukraine
https://orcid.org/0009-0007-6916-140X

**Larysa Martynyuk**
PhD in Medical Sciences, Associate Professor
I. Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine
46001, 1 Maidan Voli, Ternopil, Ukraine
https://orcid.org/0000-0001-8098-0421

**Abstract.** Endothelial dysfunction is considered a universal predictor of numerous diseases, development of the complications and their adverse course. The study aimed to investigate the endothelium-dependent vasodilation among patients with arterial hypertension, dyslipidemia and different functional state of the thyroid gland and feasibilities of its correction by means of hypolipidaemic and metabolic therapy. 99 patients with arterial hypertension and dyslipidemia were examined, among them were 65 hypothyroid persons (group 1) and 34 individuals with normal thyroid function (group 2). The effects of lipid-lowering combination therapy with ezetimibe and rosuvastatin or monotherapy with statins, and metabolic therapy with L-arginine aspartate during 3 months on endothelium-dependent vasodilation were studied. At the beginning of the study, the values of endothelial-dependent vasodilation in group 1 compared to those in group 2 were reliably smaller by 9.38%. After 3 months of treatment, this indicator in group 1 reliably increased by 11.11%, while 19 (29.23%) patients showed its normalization. The best values of the endothelium-dependent vasodilation was demonstrated by examinees in group 2 – the indicator reliably increased by 15.76 %, while 17 (50%) patients showed its normalization. Together, the greater increase in the percentage of endothelium – dependent vasodilation was observed among subgroups of patients that in complex treatment received combination hypolipidaemic therapy with ezetimibe and rosuvastatin, and metabolic therapy with L-arginine. The best indicators of endothelium-dependent vasodilation were demonstrated by examinees of both groups who, in addition to combination hypolipidaemic therapy, received metabolic therapy. Decreased thyroid gland function negatively affected the values of endothelium-dependent vasodilation and overweighted the possibilities of endothelial dysfunction correction in this cohort of patients. The results of the study can be applied in internal medicine clinic for complex treatment of comorbid hypertensive and hypothyroid patients

**Keywords:** blood pressure; lipid metabolism; hypothyroidism; ezetimibe; vasodilation; L-arginine; thyroid stimulating hormone

## Introduction

Arterial hypertension (AH) is one of the leading causes of cardiovascular morbidity and mortality worldwide [1]. According to the International Society of Hypertension (ISH) over 1.5 billion people suffer from this disease [2]. AH is the cause of 10.4 million deaths annually, while in Ukraine mortality due to elevated systolic blood pressure (BP) is 552.57 per 100,000 population [3, 4]. It is predicted that the number of such patients will increase by 15-20%

**Suggest Citation:**
Orel M, Martynyuk L. Endothelial dysfunction correction in patients with hypertension, dyslipidaemia, and decreased thyroid function. Int J Med Med Res. 2023;9(1):24–31. DOI: 10.61751/ijmmr.2413-6077.2023.1.24

*Corresponding author

by 2025. The World Health Organization (WHO) reported that in 2019 about 10.8 million patients with AH were registered in Ukraine, among them only 14% systematically received antihypertensive therapy, about 30% – periodically [5]. STEPS Survey 2019 revealed that out of one third of the population of Ukraine with AH, 63.3% of respondents were previously unaware of their high BP and only 54.8% of these individuals, who knew, were taking antihypertensive medications [6]. Concurrently, more than 50% of patients with hypertension have additional cardiovascular risk factors, which burden the course of the disease and its prognosis and worsen the quality of life of such patients. Among them are hyperglycaemia, disorders of lipid metabolism, abdominal obesity (waist circumference of above 102 cm in men and 88 cm in women), insulin resistance as the components of metabolic syndrome, sedentary lifestyle, unhealthy diet, smoking, and some others [7].

Disturbance of the normal functioning of the vessel endothelium – endothelial dysfunction (ED), along with AH, is one of the early stages in the pathogenesis of atherosclerosis and its complications, heart failure. Furthermore, the association of AH with ED is explained by the fact that the latter can be both its cause and consequence [8]. In particular, Y. Li *et al.* [9] have demonstrated the role of ED in the development and progression of AH by reducing the release of nitric oxide (NO) and acceleration of its degradation was proven, in addition to increased activity of angiotensin – converting enzyme on the surface of endothelial cells and increased synthesis of endothelin-1 and other vasoconstrictor substances by endothelial cells in case of their dysfunction. Chronic inhibition of NO in the experiment leads to all organic outcomes of severe long-lasting AH, including atherosclerosis and vascular organ damage [10]. Conversely, according to the research of J. Goodwin [11], high BP potentiates the escalation of oxidative stress and intracellular accumulation of free radicals that adversely affect the function and cohesion of endothelial lining and is one of the pathogenetic links of ED.

Mechanisms of normalization of endothelial function in patients with AH have the objective of lowering BP, regulating lipid profile and providing additional synthesis of NO by endothelial cells. Efforts are aimed towards finding an optimal medication that will not only come up with an endothelium – protective effect, but contribute to the reverse development of ED. The study of D.V.T. da Silva *et al.* [12] revealed that among such agents are some antihypertensive drugs, including angiotensin-converting enzyme inhibitors, dihydropyridine calcium – channel blockers, β-blockers thiazide diuretics and phosphodiesterase type 5 inhibitors, sodium – glucose cotransporter – 2 inhibitors, antioxidants, NO donors and others.

The combination of two and more pathological conditions or diseases in one patient contributes to the formation of new and deepens the existing pathogenetic mechanisms of the disease. The prevalence of hypothyroidism in Ukraine is high and slowly increases, while the deficit of thyroid hormones leads to impairment of lipid metabolism and contributes to cardiovascular morbidity. There is not enough data about the functional state of the vessel endothelium in comorbid patients with hypothyroidism and arterial hypertension. The study aimed to examine the advantages of ezetimibe and L-arginine aspartate use in endothelial dysfunction correction among patients with high blood pressure, dyslipidemia and decreased thyroid gland function.

## Materials and Methods

The research was conducted during the period of 2019-2023 and included 99 patients with stage 2 AH who were treated in the cardiology department of the Ternopil Regional Clinical Hospital. The average age of the patients was 58.62 ± 1.12 years, among them 43 (43.43%) men and 56 (56.57%) women. The diagnosis of AH was made according to the protocol approved by the order of the Ministry of Health of Ukraine dated May 24, 2012 No. 384 [13]. Stage 2 AH was defined as systolic blood pressure (SBP) in values ≥ 140-159 mmHg and/or diastolic blood pressure (DBP) in values ≥ 90-99 mmHg and the presence of asymptomatic hypertension-mediated organ damage, and/or chronic kidney disease stage 3 while glomerular filtration rate within 30-59 mL/min, and/or diabetes mellitus without organ damage and assumed the absence of associated clinical conditions in accordance to national and European Societies of Hypertension and Cardiology (ESH/ESC 2018) requirements [14]. All patients were determined lipid profile indicators and types of dyslipidemia were established in accordance with the classification of *Fredrickson and colleagues* [15]. The functional state of the thyroid gland was evaluated in a laboratory using the enzyme-linked immunosorbent assay by determining the concentration of free thyroxine ($T_4$), general triiodothyronine ($T_3$) and thyroid-stimulating hormone (TSH) in blood serum. Normal values of the free $T_4$ were considered from 12 to 22 pmol/L, general $T_3$ from 1.3 to 3.1 nmol/L and TSH level from 0.270 to 4.20 mIU/L. Primary hypothyroidism was diagnosed when elevated TSH levels, decreased free $T_4$ and normal or decreased general $T_3$ values in blood serum. Subclinical hypothyroidism was diagnosed in the case of TSH levels from 4.21 to 10.00 mIU/L and normal values of thyroid hormones. The exclusion criteria were: stage 1 and stage 3 AH, ischaemic and/or haemorrhagic stroke, myocardial infarction in the anamnesis, diabetes mellitus, chronic kidney disease, other chronic diseases, the patient's refusal to take part or continue to participate in the study.

All examinees were divided into groups according to the functional state of their thyroid gland and methods of treatment (Table 1). Group 1 involved 65 (65.65%) individuals with reduced thyroid function, among them were 34 (34.34%) patients with primary hypothyroidism and 31 (31.31%) patients with subclinical hypothyroidism, who previously received levothyroxine replacement therapy in the dosage of 25-50 mcg daily for the purpose of normalizing the thyroid function. Group 2 included 34 (34.34%) individuals with arterial hypertension with normal thyroid

function. Examinees of both groups were randomly divided into 4 subgroups and each of them was prescribed distinctive treatment. Patients in all subgroups received hypolipidaemic therapy with rosuvastatin; in subgroup 1, individuals were additionally prescribed ezetimibe and metabolic therapy, in subgroup 2 patients received combination lipid-lowering therapy with ezetimibe, and in subgroup 3 – metabolic therapy, besides statins. All examinees received antihypertensive and antiplatelet medicines according to approved national protocol [13].

**Table 1.** Distribution of patients into groups in accordance to the functional state of their thyroid gland and methods of treatment

| Group | Characteristics |
|---|---|
| 1, n = 65 | *Patients with arterial hypertension and reduced thyroid function* |
| *1.1*, n = 16 | Combination: ezetimibe 10 mg + rosuvastatin 10 mg 1 tablet once daily, L-arginine aspartate oral solution 1 measuring spoon (5 mL) 4 times daily |
| *1.2*, n = 16 | C ombination: ezetimibe 10 mg + rosuvastatin 10 mg 1 tablet once daily |
| *1.3*, n = 16 | Rosuvastatin 20 mg 1 tablet once daily, L-arginine aspartate oral solution 1 measuring spoon (5 mL) 4 times daily |
| *1.4*, n = 17 | Rosuvastatin 20 mg, 1 tablet once daily |
| 2, n = 34 | *Patients with arterial hypertension and normal thyroid function* |
| *2.1*, n = 9 | Combination: ezetimibe 10 mg + rosuvastatin 10 mg 1 tablet once daily, L-arginine aspartate oral solution 1 measuring spoon (5 mL) 4 times daily |
| *2.2*, n = 8 | Combination: ezetimibe 10 mg + rosuvastatin 10 mg 1 tablet once daily |
| *2.3*, n = 9 | Rosuvastatin 20 mg 1 tablet once daily, L-arginine aspartate oral solution 1 measuring spoon (5 mL) 4 times daily |
| *2.4*, n = 8 | Rosuvastatin 20 mg, 1 tablet once daily |

**Source:** compiled by the authors

Functional state of vascular endothelium was determined by non-invasive technique of the endothelium-dependent vasodilation (EDV) of the brachial artery (BA) evaluation by the method proposed by D.S. Celermajer *et al.* [16] before and after 3 months of prescribed treatment. All examinees underwent a cuff test while by means of Doppler ultrasound examination the initial diameter (D0) of the BA and diameter of the BA on the fifth minute after distal occlusion of the blood flow (D1) were determined. The response of the vessel endothelium was evaluated as the ratio of the difference between the diameter of the BA on the fifth minute of test and the initial diameter of the BA to its initial diameter:

$$EDV = \frac{(D_1 - D_0)}{D_0} \times 100\%, \quad (1)$$

where *EDV* – endothelium – dependent vasodilation; $D_0$ – initial diameter of the BA; $D_1$ – diameter of the BA on the fifth minute of distal occlusion of the blood flow.

An increase in the BA diameter of less than 8-10% when performing a cuff test was considered a manifestation of ED. Statistical analysis of the obtained data was carried out using MS Excel 2016. The results of the study are presented in the form of arithmetic mean values with the error of the mean square deviation of the sample (M ± m). The probability of data differences in groups was determined using the reliability coefficient P, which was estimated based on Student's t test. The difference in indicators was considered statistically reliable at $P < 0.05$. The strength and direction of the linear relationship between variables was measured by Pearson's pairwise correlation coefficient (R). The study was conducted on the basis of informed consents in accordance with the requirements of bioethics in compliance with the provisions of the e Helsinki Declaration [17].

## Results and Discussion

The mean age of the patients in group 1 was 61 ± 1.38 years, and in group 2, it was 54.06 ± 1.73 years (P = 0.003). There was found no reliable difference in the age of patients between different subgroups of each group. TSH level among patients with AH and hypothyroidism prevailed this indicator among those with normal thyroid function on 3,25 mIU/mL (5.66 ± 0.35 mIU/mL against 2.41 ±v0.18 mIU/mL respectively, P = 0.000).

The study found that the mean value of EDV in patients with AH and decreased thyroid function at the beginning of the study was reliably lower compared with this indicator among patients with AH and normal thyroid function by 9.38% (6.67 ± 0.07% against 7.36 ± 0.13%, P = 0.000) (Fig. 1). According to the results of cuff test among group 1 before and 3 months after the prescribed treatment, the mean value of EDV reliably increased by 11.11% and was 7.41 ± 0.12% (P = 0.000).

The highest indicators of EDV among patients with AH and decreased thyroid function were observed in subgroup 1.1, who, in addition to standard complex treatment, received lipid-lowering combination therapy with ezetimibe and rosuvastatin, and L-arginine aspartate (Table 2). The increase in the percentage of EDV in this subgroup was 16.49%. Together, the reliable improvement of EDV among individuals in subgroup 1.3 by 13.18% was noted, who received therapy with rosuvastatin and L-arginine.

Among patients in subgroups 1.2 and 1.4, who were administered ezetimibe and rosuvastatin, or monotherapy with rosuvastatin without L-arginine, the increase in the percentage of EDV was rather smaller – 8.51% and 6.19% respectively. Normalization of ED was observed among 10 (15.39%) patients in subgroup 1.1 and among 3 (4.62%) and 6 (9.23%) examinees in subgroups 1.2 and 1.3 respectively. No patient in subgroup 1.4 with AH and reduced thyroid function showed normalization of EDV value while taking rosuvastatin.

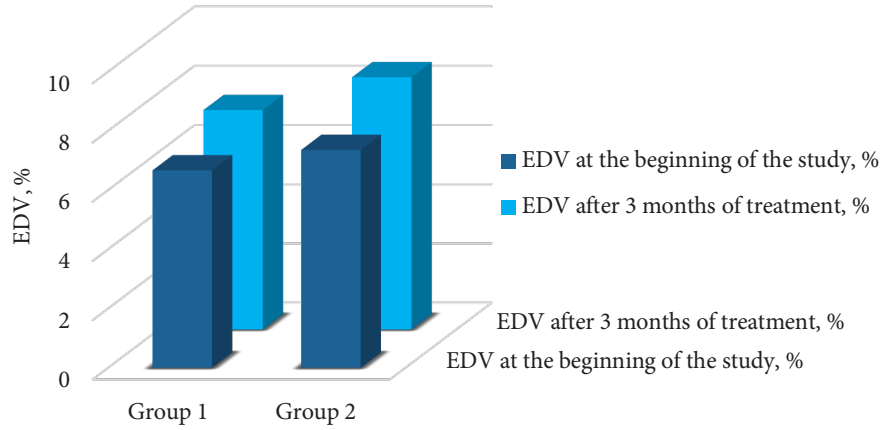


**Figure 1.** The mean values of EDV in patients with decreased and normal thyroid function, %
**Source:** compiled by the authors

**Table 2.** EDV in patients with AH and decreased thyroid function before and after treatment (M ± m)

| Group | EDV at the beginning of the study, % | EDV after 3 months of treatment, % |
|---|---|---|
| *1.1* | 6.95 ± 0.14 | 8.09 ± 0.23*<br>P = 0.000 |
| *1.2* | 6.46 ± 0.17 | 7.01 ± 0.22*<br>P = 0.000 |
| *1.3* | 6.83 ± 0.15 | 7.73 ± 0.25*<br>P = 0.000 |
| *1.4* | 6.46 ± 0.10 | 6.86 ± 0.14*<br>P = 0.000 |

**Notes:** * marked indicators are significantly different from the data at the beginning of the study (P < 0.05)
**Source:** compiled by the authors

The best measures of EDV of the BA were demonstrated by examinees with AH and normal thyroid function. The mean value of EDV in this group of patients significantly increased by 15.76% and was 8.52 ± 0.17% (P = 0.000). Especially, there was noted reliable improvement of EDV by 20.19% in subgroup 2.1 (Table 3). The value of EDV in subgroup 2.3, while taking rosuvastatin and L-arginine, reliably increased by 17.32%, and in subgroups 2.2 and 2.4 among patients, who were administered either combination of ezetimibe and rosuvastatin, or monotherapy with rosuvastatin, by 13.26% and 11.85% respectively. Normalization of ED was observed in 5 (55.56%) individuals in subgroup 2.1, 5 (62.5%) examinees in subgroup 2.2 and among 4 (44.44%) and 3 (37.5%) patients in subgroups 2.3 and 2.4 respectively.

**Table 3.** EDV in patients with AH and normal thyroid function before and after treatment (M ± m)

| Group | EDV at the beginning of the study, % | EDV after 3 months of treatment, % |
|---|---|---|
| *2.1* | 7.58 ± 0.33 | 9.11 ± 0.42*<br>P = 0.000 |
| *2.2* | 7.62 ± 0.26 | 8.63 ± 0.37*<br>P = 0.000 |
| *2.3* | 6.93 ± 0.28 | 8.13 ± 0.29*<br>P = 0.000 |
| *2.4* | 7.34 ± 0.19 | 8.21 ± 0.27*<br>P = 0.001 |

**Notes:** * marked indicators are significantly different from the data at the beginning of the study (P < 0.05)
**Source:** compiled by the authors

The correlation analysis revealed strong negative reliable correlations of EDV with the age of patients (R = -0.6877, P = 0.000) and TSH levels (R = -0.5111, P = 0.000), and weak negative correlations with duration of hypertension (R = -0.1987, P=0.049) and body mass index (R = -0.2074, P = 0.039) among examinees of all groups.

While the primary objective of statin therapy in managing hypertensive patients is traditionally focused on lipid reduction, this study has unveiled a noteworthy improvement in endothelium-dependent vasodilation (EDV) of the brachial artery (BA) following a 3-month course of rosuvastatin in all examined patients. Furthermore, the research by V. Serhiyenko & A. Serhiyenko [18] suggests that the positive impacts of statin therapy on the vascular wall and blood flow stem from an augmentation in the expression of endothelial NO-synthase. This augmentation leads to increased nitric oxide release, enhancing vasodilation in coronary and peripheral arteries, along with the suppression of local inflammation and stabilization of atherosclerotic plaques. The pleiotropic effects of statins on the endothelium encompass a reduction in endothelin-1 synthesis, suppression of angiotensin-1 and tissue plasminogen activator receptors, increased expression of plasminogen activator inhibitor, coupled with a reduction in oxidative stress. These actions collectively enhance neovascularization and reendothelialization processes, inhibit endothelial cell apoptosis, and confer antithrombotic and anti-ischaemic properties [19].

Concurrently, the perspective of Y. Higashi [20] emphasizes the need for more specific and adequate methods to evaluate endothelial function, particularly in patients with dyslipidemia, considering the close association observed between endothelial dysfunction, disturbances in lipid metabolism, and their potential role in cardiovascular complications. Another lipid-lowering agent, ezetimibe, has demonstrated an ability to improve vascular endothelial function. However, the mechanisms underlying this effect remain incompletely understood. It is considered that the reduction of the risk of adverse cardiovascular events when using ezetimibe is a result of blocked activity of cholesterol transport protein Niemann-Pick C1 – Like 1 at the level of the villi of small intestine mucous membrane, which leads to suppression of intestinal absorption and reducing the inlet of low – density lipoproteins (LDL), oxidized LDL and oxysterol, that come with food, into the liver [21]. According to the studies of M. Vavlukis and A. Vavlukis [22] this sequentially leads to the activation of the LDL receptors on the surface of hepatocytes and is accompanied by an increased clearance of the LDL cholesterol from the blood. While this study revealed the highest increase in the percentage of EDV among patients who received combination lipid-lowering therapy with ezetimibe and rosuvastatin compared to patients who received monotherapy with statins, the research of V. Serhiyenko & A. Serhiyenko [23] found that the use of ezetimibe can reduce the levels of LDL cholesterol by 10-18%. In combination with statins, it decreases the level of triglycerides by 10%, insignificantly affects the level of high-density lipoprotein cholesterol in blood, contributes to the regression of atherosclerotic plaques, and improves vasodilation.

Shifting focus to L-arginine, a conditionally essential amino acid serving as a substrate for NO synthase, it catalyses the synthesis of NO by endothelial cells. Oral L-arginine selectively enhances EDV in individuals with impaired endothelial function, reducing the aggregation and adhesion of thrombocytes and monocytes to the endothelial wall, and limiting the synthesis of endothelin-1. Several studies have showcased the beneficial effects of L-arginine use in patients with arterial hypertension, ischaemic heart disease, and atherosclerosis, impacting not only endothelial function but also normalizing blood pressure levels, lipid metabolism, LDL oxidation processes, and decreasing markers of cell adhesion and pro-inflammatory cytokines in blood serum. L-arginine has also demonstrated positive effects on the proliferation of vascular smooth muscle cells and an overall enhancement in the quality of life for such patients [24, 25].

Nevertheless, there remains a scarcity of data regarding the outcomes of hypolipidaemic and metabolic therapy in individuals with arterial hypertension and an impaired functional state of their thyroid gland. This study identified the most substantial increase in the percentage of EDV among hypertensive patients who received a combination of lipid-lowering therapy with ezetimibe and rosuvastatin, alongside metabolic therapy involving L-arginine. This increase amounted to 16.49% among individuals with decreased thyroid function and 20.19% among those with normal thyroid function. Additionally, a robust negative correlation was observed between EDV and TSH levels across all examined patients. These findings underscore the potential interplay between metabolic factors, thyroid function, and the efficacy of combined therapeutic approaches in hypertensive individuals.

## Conclusions

Both, arterial hypertension and decreased thyroid gland function, negatively affect the state of the vessel endothelium. While the conducted study aimed to discover the changes of endothelium-dependent vasodilation among patients with hypertension and different thyroid gland function, as well as prospects of its correction, it revealed significantly lower indicators among those with hypothyroidism. Moreover, the study found that decreased levels of thyroid hormones not only had a negative impact on the values of endothelium-dependent vasodilation in hypertensive patients, but burdened the possibilities of endothelial dysfunction correction in this cohort of examinees The mean values of endothelium-dependent vasodilation among patients with hypothyroidism were reliably lower compared with those among patients with arterial hypertension and normal thyroid function both before and after the prescribed treatment – 6.67 ± 0.07% against 7.36 ± 0.13% (P = 0.000) and 7.41 ± 0.12% against

8.52 ± 0.17% (P = 0.000) respectively. The greater increase in the percentage of endothelium-dependent vasodilation indicators was observed among patients of both groups that received lipid-lowering combination therapy with ezetimibe and rosuvastatin, and metabolic therapy with L-arginine aspartate. The use of combination hypolipidaemic and metabolic therapy in the complex treatment of patients with arterial hypertension, dyslipidemia and decreased thyroid function contributed to the reliable improvement of endothelial-dependent vasodilation by 16.40% (P = 0.000). Concomitantly, the strong negative reliable correlation of endothelium-dependent vasodilation with the level of thyroid stimulating hormone was found among all examined individuals (R = -0.5111, P = 0.000). Further studies concerning the effects of the proposed schemes of treatment on lipid metabolism and cardiovascular risk factors modification among patients with AH, depending on the functional state of the thyroid gland, are expected.

## Acknowledgements

None.

## Conflict of Interest

The authors declare no conflict of interest.

## References

[1] Koval SM, Mysnychenko OV. Arterial hypertension and cerebrovascular diseases: Epidemiological, clinical, therapeutic and preventive aspects (a review of the literature and current recommendations). Hypertension. 2020;13(1):10–19. DOI: 10.22141/2224-1485.13.1.2020.197889

[2] Charchar FJ, Prestes PR, Mills C, Ching SM, Neupane D, Marques FZ, et al. Lifestyle management of hypertension: International Society of Hypertension position paper endorsed by the World Hypertension League and European Society of Hypertension. J Hypertens. 2024;42(1):23–49. DOI: 10.1097/HJH.0000000000003563

[3] GBD 2017 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: A systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1923–94. DOI: 10.1016/S0140-6736(18)32225-6

[4] Poliakova D. Equator: Contemporary and future management of cardiovascular risk factors. Ukr Med J. 2023; 1(153):3–6. DOI: 10.32471/umj.1680-3051.153.238822

[5] Hypertension Ukraine 2020 country profile [document on the Internet]. World Health Organization; 2021 [cited 2023 Dec 5]. Available from: https://www.who.int/publications/m/item/hypertension-ukr-country-profile-ukraine-2020

[6] STEPS: Prevalence of non-communicable disease risk factors in Ukraine, 2019. Copenhagen: WHO Regional Office for Europe; 2020. Available from: https://apps.who.int/iris/handle/10665/336642

[7] Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension global hypertension practice guidelines. Hypertension. 2020;75(6):1334–57. DOI: 10.1161/HYPERTENSIONAHA.120.15026

[8] Mishchenko LA, Ovdienko TM, Matova OO, Talaieva TV, Tretyak IV, Vasilinchuk NM, Vavilova LL. Functional state of endothelium and additional possibilities of its correction with the use of ethylmethylhydroxypyridine succinate in patients with arterial hypertension. Ukr Med J. 2021;4(144):2–5. DOI: 10.32471/umj.1680-3051.144.213876

[9] Li Y, Srivastava AK, Anand-Srivastava MB. Nitric oxide and cardiovascular health. In: Ray A, Gulati K, editors. Nitric Oxide: From Research to Therapeutics. Advances in Biochemistry in Health and Disease, Volume 22. Springer, Cham; 2023. P. 15–39. DOI: 10.1007/978-3-031-24778-1_2

[10] Smiyan S, Koshak B, Bilukha A, Koshak D. The role of endothelial dysfunction in the development of arterial hypertension in patients with ankylosing spondylarthritis. Bull Soc Hyg Health Prot Org Ukraine. 2018; 2(76):54–58. DOI: 10.61751/1681-2786.2018.2.9371

[11] Goodwin, J. Endothelial dysfunction and vascular remodelling in hypertension. In: Flynn JT, Ingelfinger JR, Brady TM, editors. Paediatric Hypertension. Springer; 2023. P. 195–15. DOI: 10.1007/978-3-031-06231-5_41

[12] da Silva DVT, Baião DdS, Almeida CC, Paschoalin VMF. A critical review on vasoactive nutrients for the management of endothelial dysfunction and arterial stiffness in individuals under cardiovascular risk. Nutrients. 2023; 15(11):e2618. DOI: 10.3390/nu15112618

[13] Ministry of Health of Ukraine. On approval and implementation of medical-technological documents for standardization of medical care in arterial hypertension [Internet]. 2012 [cited 2023 Dec 5]. Order No 384/2012. 2012 May 24. Available from: https://zakon.rada.gov.ua/rada/show/v0384282-12#Text

[14] Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Cardiology and the European Society of Hypertension. J Hypertens. 2018;36(10):1953–41. DOI: 10.1097/HJH.0000000000001940

[15] Beaumont JL, Carlson LA, Cooper GR, Fejfar Z, Fredrickson DS, Strasser T. Classification of hyperlipidaemias and hyperlipoproteinaemias. Bull World Health Organ. 1970;43(6):891–15.

[16] Celermajer DS, Sorensen KE, Gooch VM, Spiegelhalter DJ, Miller OI, Sullivan ID, et al. Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. Lancet. 1992;340(8828):1111–15. DOI: 10.1016/0140-6736(92)93147-f
[17] The World Medical Association. Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects [Internet]. Available from: https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/
[18] Serhiyenko V, Serhiyenko A. Diabetes, dyslipoproteinemia and statins. Endokrynologia. 2021;27(1):29–42. DOI: 10.31793/1680-1466.2021.27-1.29
[19] German CA, Liao JK. Understanding the molecular mechanisms of statin pleiotropic effects. Arch Toxicol. 2023;97:1529–45. DOI: 10.1007/s00204-023-03492-6
[20] Higashi Y. Endothelial function in dyslipidemia: Roles of LDL-cholesterol, HDL-cholesterol, and triglycerides. Cells. 2023;12(9):e1293. DOI: 10.3390/cells12091293
[21] Di Costanzo A, Indolfi C, Sorrentino S, Esposito G, Spaccarotella CAM. The effects of statins, ezetimibe, PCSK9-inhibitors, inclisiran, and icosapent ethyl on platelet function. Int J Mol Sci. 2023;24(14):e11739. DOI: 10.3390/ijms241411739
[22] Vavlukis M, Vavlukis A. Adding ezetimibe to statin therapy: Latest evidence and clinical implications. Drugs Context. 2018:7:e212534. DOI: 10.7573/dic.212534
[23] Serhiyenko V, Serhiyenko A. Ezetimibe and diabetes mellitus: A new strategy for lowering cholesterol. Int J Endocrinol. 2022;18(5):302–14. DOI: 10.22141/2224-0721.18.5.2022.1190
[24] Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. Eur Heart J. 2020;41(2):255–23. DOI: 10.1093/eurheartj/ehz486
[25] Szlas A, Kurek JM, Krejpcio Z. The potential of l-arginine in prevention and treatment of disturbed carbohydrate and lipid metabolism – a review. Nutrients. 2022;14(5):961. DOI: 10.3390/nu14050961

# Корекція ендотеліальної дисфункції у пацієнтів із гіпертензією, дисліпідемією та зниженою тиреоїдною функцією

**Марта Андріївна Орел**

Аспірант
Тернопільський національний медичний університет ім. І. Я. Горбачевського МОЗ України
46001, майдан Волі, 1, м. Тернопіль, Україна
https://orcid.org/0009-0007-6916-140X

**Лариса Петрівна Мартинюк**

Кандидат медичних наук, доцент
Тернопільський національний медичний університет ім. І. Я. Горбачевського МОЗ України
46001, майдан Волі, 1, м. Тернопіль, Україна
https://orcid.org/0000-0001-8098-0421

**Анотація.** Ендотеліальна дисфункція вважається універсальним предиктором багатьох захворювань, розвитку їх ускладнень та несприятливого перебігу. Метою роботи було дослідити ендотелій-залежну вазодилятацію плечової артерії у хворих на артеріальну гіпертензію та дисліпідемію із різним тиреоїдним статусом та можливості її корекції із застосуванням гіполіпідемічної та метаболічної терапії. Обстежено 99 осіб із артеріальною гіпертензією та дисліпідемією, серед них 65 пацієнтів із зниженою функцією щитоподібної залози (група 1) та 34 пацієнти із нормальним тиреоїдним статусом (група 2). Вивчено вплив гіполіпідемічної терапії із застосуванням комбінації езтимібу та розувастатину або монотерапії статинами, а також метаболічної терапії із використанням L-аргініну аспартату протягом трьох місяців на ендотелій-залежну вазодилятацію. Показник ендотелій-залежної вазодилятації у групі 1 на початку дослідження був вірогідно меншим від даного показника у групі 2 на 9,38 %. Через 3 місяці призначеного лікування показник ендотелій-залежної вазодилятації у групі 1 достовірно покращився на 11,11 %, водночас у 19 (29,23 %) осіб спостерігали його нормалізацію. Найкращі показники ендотелій-залежної вазодилятації продемонстрували обстежені групи 2 – середній показник вірогідно зріс на 15,76 %, а його нормалізацію продемонстрували 17 (50 %) пацієнтів. Більший приріст відсотка ендотелій-залежної вазодилятації спостерігався у підгрупах пацієнтів, які отримували у складі комплексної терапії комбіновану гіполіпідемічну терапію езетимібу та розувастатину, та метаболічну терапію із застосуванням L – аргініну. Найкращі показники ендотелій-залежної вазодилятації продемонстрували обстежені обох груп, які, окрім комбінованої гіполіпідемічної терапіїї, додатково отримували метаболічну терапію. Гіпотиреоїдний статус пацієнтів негативно впливав на показники ендотелій-залежної вазодилятації та обтяжував можливості корекції ендотеліальної дисфункції у даній когорті осіб. Результати дослідження можуть бути використані у клініці внутрішніх хвороб у комплексному лікуванні хворих із коморбідною патологією – артеріальною гіпертензією та гіпотиреозом

**Ключові слова:** кров'яний тиск; обмін ліпідів; гіпотиреоз; езетиміб; вазодилятація; L-аргінін; тиреотропний гормон