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DYNAMICS OF THE LEVELS OF ASYMMETRIC DIMETHYLARGININE AND PLASMINOGEN ACTIVATOR INHIBITOR TYPE 1 IN PATIENTS WITH ACUTE ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION AND TYPE 2 DIABETES MELLITUS DEPENDING ON THE REPERFUSION STRATEGY

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Summary

Introduction. Despite the major successes achieved in the treatment of acute coronary syndromes (ACS), acute myocardial infarction (AMI) remains the main cause of death among the working-age population of Ukraine. The means of treatment of interventional cardiology can actually reduce the mortality of patients with ACS, improve the course of the acute period of the disease and ensure less reduction in the functional capabilities of the heart in the future. Among the many pathogenetic mechanisms of vascular inflammation in coronary heart disease and type 2 diabetes, endothelial dysfunction is the determining factor.
The aim of the study. To evaluate the levels of plasminogen activator inhibitor type 1, asymmetric dimethylarginine and endothelial nitric oxide synthase on the 10-14th day in patients depending on the presence or absence of concomitant diabetes type 2 and the type of reperfusion therapy.
Materials and methods. 130 patients with acute myocardial infarction were examined, who were divided into 2 groups: 1 group consisted of patients with acute myocardial infarction with accompanying type 2 diabetes (n=73), 2 group – patients with acute myocardial infarction without type 2 diabetes (n =57). The quantitative content of the plasminogen activator inhibitor type 1 (PAI-1) was determined by the immunoenzymatic method using a commercial test system manufactured by Technoclone PAI-1 ELISA Kit (Austria), endothelial nitric oxide synthase (NOS) – Enzyme-Linked Immunosorbent Assay (ELISA) Kit For Nitric Oxide Synthase Endothelial, asymmetric dimethylarginine (ADMA) – Immunodiagnostik ADMA ELISA Kit (Austria).
Results. Percutaneous coronary intervention (PCI) contributes to a more significant decrease in the content of the marker of endothelial dysfunction – ADMA and an increase in NOS on the 10-14th day of acute myocardial infarction in comparison with standard therapy. During PCI, the level of PAI-1 did not reliably change during treatment due to post-inflammatory and post-traumatic activation of platelets in the vascular wall.
Conclusions. In patients with acute myocardial infarction with type 2 diabetes mellitus, percutaneous coronary intervention contributes to a significant decrease in the content of asymmetric dimethylarginine and an increase in NOS on the 10-14th day of acute myocardial infarction, but was not accompanied by a significant decrease in the level of PAI-1, which in general indicates positive effect of performed myocardial revascularization.

Keywords: **acute myocardial infarction, type 2 diabetes mellitus, endothelial dysfunction, asymmetric dimethylarginine, plasminogen activator inhibitor type 1, percutaneous coronary intervention**

INTRODUCTION

Ischemic heart disease (IHD) has always been considered and remains the leading cause of mortality among cardiovascular diseases [1]: in European countries, its share is approximately 38 % in the prevalence structure and 19.5 % among cases of overall mortality [2]. Despite progress in the field of cardiothoracic surgery, including the widespread use of various methods of intracoronary interventions, the mortality rate from IHD, unfortunately, does not significantly decrease. Acute myocardial infarction ranks first among the causes of mortality in the population, even in developed countries.

Diabetes mellitus directly affects not only the quality of life of patients but also complicates the prognosis for the occurrence of unwanted cardiovascular events in this category of patients, making it dangerous to neglect [3].

The imbalance in the NOS-NO system plays a leading role in the development of endothelial damage and inflammation, especially in patients with elevated blood sugar levels [4, 5], which exacerbates the damage to the already compromised vascular wall [6, 7, 8, 9].

According to modern data, in addition to the mentioned factors, a significant role in the development of cardiovascular complications of diabetes mellitus is attributed to the dominance of thrombosis processes over fibrinolysis processes [10, 11], which is associated with an increase in the concentration and activity of the marker of endothelial imbalance and atherothrombosis – plasminogen activator inhibitor type 1 (PAI-1) [12].

Inhibition of fibrinolysis can occur either through direct binding of plasmin or by suppressing the activation of plasminogen. The main factor inhibiting fibrinolysis is PAI-1 (also called endothelial type inhibitor), the production of which is attributed to endothelial cells.

Scientists have proven that plasminogen activator inhibitor type 1 not only promotes thrombosis by disrupting the procoagulant properties of blood but also contributes to the development of carbohydrate metabolism disorders [13, 14]. However, due to conflicting data regarding the concentration of this marker in the dynamics of treatment [15], our study analyzed the dynamics of PAI-1 levels in the presence of combined pathology of acute myocardial infarction and type 2 diabetes mellitus, depending on the therapeutic approach.

The role of endothelial dysfunction cannot be underestimated in the pathogenesis of diabetes mellitus. Impairment of NO-dependent vasodilation is one of the main effects of elevated levels of asymmetric dimethylarginine (ADMA) – an endogenous inhibitor of nitric oxide synthase (NOS), formed during the methylation of the amino acid L-arginine [16, 17].

The study of ADMA as a marker of endothelial dysfunction is ongoing [18].

The development of interventional methods for the treatment of acute coronary syndromes is widely implemented through percutaneous coronary intervention (PCI), which is a life-saving procedure and the best method of reperfusion in acute myocardial infarction with ST-segment elevation [19]. Despite this, there is an ongoing debate among scientists regarding the risks of developing fatal and non-fatal complications after stenting [20, 21].

THE AIM

Depending on the treatment strategy for acute myocardial infarction, analyze how levels of plasminogen activator inhibitor type 1, asymmetric dimethylarginine, and endothelial nitric oxide synthase have changed in patients with impaired carbohydrate metabolism and those without such impairment.

MATERIALS AND METHODS

We conducted a study at the Intensive Care Unit and Cardiology Department of Kharkiv City Clinical Hospital No. 27, the Cardiology Department of Kharkiv Regional Clinical Hospital, and the Department of Interventional Cardiology of the Institute of General and Emergency Surgery named after V. T. Zaytsev, NAMS of Ukraine. We examined 130 patients with acute myocardial infarction.

We divided the patients into two groups: Group 1 consisted of patients with acute myocardial infarction and concomitant type 2 diabetes (n=73), and Group 2 consisted of patients with acute myocardial infarction without type 2 diabetes (n=57). Group 1 included 43 men (41.7 %) and 30 women (58.3 %), while Group 2 included 43 men (70.9 %) and 14 women (29.1 %). The average age of patients in Group 1 was 62.73±1.40 years, and in Group 2, it was 63.98±1.47 years. A control group comprised 20 practically healthy individuals with an average age of 60.85±0.17 years.

The Technoclone PAI-1 ELISA Kit (Austria) was used to determine the content of PAI-1, NOS – Enzyme-Linked Immunosorbent Assay (ELISA) Kit for Nitric Oxide Synthase Endothelial (NOS), and asymmetric dimethylarginine – Immunodiagnostik ADMA ELISA Kit (Austria). In the study, we compared how the levels of markers changed with different approaches to the treatment of AMI, for which we formed 4 subgroups of patients: 1st subgroup of patients with acute myocardial infarction with type 2 diabetes mellitus who underwent PCI (percutaneous coronary intervention) (n=58); 2nd subgroup of patients with AMI with type 2 diabetes mellitus who received standard anticoagulant therapy with enoxaparin/fondaparinux in combination with dual antiplatelet therapy (n=15); 3rd subgroup of patients with AMI without type 2 diabetes mellitus who underwent PCI (n=40); 4th subgroup (n=17) – patients with AMI

without type 2 diabetes mellitus who underwent standard anticoagulant therapy.

Mathematical computer processing of the results was performed using the software package «Statistica 6.0» (StaSoft Inc, USA). Calculations included: mean value (M), variance, standard deviation, median (m), probability, and significance level (p). For comparative analysis of samples with a normal distribution, the validity of differences was confirmed using the Student's t-test. Additionally, a standard correlation analysis program was utilized, calculating means of arithmetic values: M+m, σ, probability, and confidence level (p). For paired comparisons of means in groups, the non-parametric Mann-Whitney test was employed. When analyzing samples not following Gaussian distribution laws, the non-parametric paired Wilcoxon test was used.

RESULTS

It was found that in the presence of type 2 diabetes (table 1), on the 1st day of acute myocardial infarction, the level of PAI-1 significantly exceeded that in patients without concomitant diabetes (62.38±1.83 ng/ml and 50.99±2.01 ng/ml; 66.72±1.63 ng/ml and 51.11±3.03 ng/ml, respectively; p<0.001). This may indicate that patients with insulin resistance have a higher risk of thrombotic complications compared to those with normal carbohydrate metabolism.

Table 1

Dynamics of PAI-1 levels on days 1 and 10-14 of acute myocardial infarction depending on the chosen treatment tactics

IPA-1 level, ng/ml	Patients with acute myocardial infarction and concomitant type 2 diabetes mellitus, n=73.		Patients with acute myocardial infarction, n=57.		p
	With coronary artery stenting, n= 58	Without coronary artery stenting, n= 15	With coronary artery stenting, n= 40	Without coronary artery stenting, n= 17	
	1	2	3	4	
The 1st day of acute myocardial infarction.	62,38±1,83*	66,72±1,63**	50,99±2,01^	51,11±3,03»	p_{1-2}>0,05 p_{3-4}>0,05 p_{1-3}<0,001 p_{2-4}<0,001
Days 10-14 of acute myocardial infarction.	61,75±1,81*	60,78±0,90**	45,55±1,88^	42,63±1,94»	p_{1-2}>0,05 p_{3-4}>0,05 p_{1-3}<0,001 p_{2-4}<0,001

Note: *, ** – significance of differences p>0.05; ^, « – significance of differences p<0.05

Ten days after the treatment of acute myocardial infarction in patients with insulin resistance, there was no significant decrease in the level of PAI-1 compared to the results on the 1st day, both with stenting (62.38±1.83 ng/ml and 61.75±1.81 ng/ml, respectively; p>0.05) and with standard antiplatelet therapy (66.72±1.63 ng/ml and 60.78±0.90 ng/ml, respectively; p>0.05). This may indicate a prolonged nature of the thrombotic risk in the context of insulin resistance.

On the contrary, the results of serum in patients without type 2 diabetes on the 10th day of treatment showed a significant decrease in the level of PAI-1 with both treatment tactics: with PCI (50.99±2.01 ng/ml and 45.55±1.88 ng/ml; p<0.05) and with standard antithrombotic therapy (51.11±3.03 ng/ml and 42.63±1.94 ng/ml; p<0.05).

According to the results of our study (table 2), patients with concomitant type 2 diabetes mellitus (T2DM) on the 1st day of acute myocardial infarction had significantly higher levels of ADMA, regardless of the treatment strategy (1.031±0.038 μmol/l and 0.57±0.025 μmol/l; 1.063±0.06 μmol/l and 0.62±0.029 μmol/l, respectively; p<0.001).

ADMA levels significantly decreased after treatment, regardless of the chosen strategy in patients with elevated serum glucose (1.03±0.04 and 0.84±0.03 μmol/l; 1.06±0.06 and 0.87±0.05 μmol/l), as well as without it (0.57±0.03 and 0.51±0.03 μmol/l; 0.62±0.02 and 0.45±0.04 μmol/l, respectively; p<0.05). However, in patients with T2DM, ADMA levels remained significantly higher than in patients without concomitant type 2 diabetes mellitus, regardless of the chosen treatment method (0.84±0.03 μmol/l; 0.87±0.05 μmol/l; 0.51±0.03 μmol/l; 0.45±0.04 μmol/l, respectively; p1-2,3-4>0.05, p1-3<0.001, p2-4<0.05).

The obtained data suggest that both coronary artery stenting and standard antiplatelet therapy positively influence the dynamics of asymmetric dimethylarginine in these patient categories, confirmed by a significant decrease in ADMA during the 10-14 days follow-up after treatment.

Table 2

Dynamics of ADMA levels on days 1 and 10-14 of acute myocardial infarction depending on the chosen treatment tactics

Level of ADMA (Asymmetric Dimethylarginine), μmol/L	Patients with acute myocardial infarction and concomitant type 2 diabetes mellitus, n=73		Patients with acute myocardial infarction, n=57.		p
	With coronary artery stenting, n= 58	Without coronary artery stenting, n= 15	With coronary artery stenting, n= 40	Without coronary artery stenting, n= 17	
	1	2	3	4	
The 1st day of acute myocardial infarction	1,03±0,04*	1,06±0,06**	0,57±0,03 ×	0,62±0,02^	p_{1-2}>0,05 p_{3-4}>0,05 p_{1-3}<0,001 p_{2-4}<0,001
Days 10-14 of acute myocardial infarction	0,84±0,03*	0,87±0,05**	0,51±0,03×	0,45±0,04^	p_{1-2}>0,05 p_{3-4}>0,05 p_{1-3}<0,001 p_{2-4}<0,05

Note: *, **, ″, ×, ^ – significance of differences p<0.05

Oxidative stress directly affects ischemia and endothelial damage in acute myocardial infarction, so the analysis of nitric oxide synthase levels in this cohort of patients was of interest.

In the research (table 3), it was found that in patients with acute myocardial infarction on the 1st day, concomitant type 2 diabetes mellitus was associated with significantly lower levels of NOS compared to patients without type 2 diabetes, both in subgroups with coronary artery stenting (3.10±0.16 ng/mL and 4.26±0.13 ng/mL, respectively; p<0.001) and in those receiving standard anticoagulant and dual antiplatelet therapy (3.22±0.35 ng/mL and 4.15±0.23 ng/mL, respectively; p<0.05). This suggests endothelial vulnerability under the influence of insulin resistance in the majority of type 2 diabetes patients.

On the 10th day of acute myocardial infarction, NOS levels in the blood serum increased in both patients with concomitant type 2 diabetes mellitus and those without diabetes. However, in patients with type 2 diabetes, the increase was less intense (4.82±0.31 ng/mL and 4.61±0.42 ng/mL; 7.42±0.57 ng/mL and 9.14±1.04 ng/mL, respectively; p1-2>0.05, p3-4>0.05, p1-3,2-4<0.001).

This indicates signs of gradual restoration of anti-ischemic barriers in the intima after revascularization in the studied patients.

Table 3

Dynamics of NOS levels on the 1st and 10-14th day of acute myocardial infarction depending on the chosen treatment strategy

Level of NOS, ng/ml	Patients with acute myocardial infarction and concomitant type 2 diabetes mellitus, n=73		Patients with acute myocardial infarction, n=57		P
	patients with stenting, n= 58	without stenting, n= 15	patients with stenting, n= 40	without stenting, n= 17	
	1	2	3	4	
1st day of AMI	3,10±0,16*	3,22±0,35**	4,26±0,13 ×	4,15±0,23^	p_{1-2}>0,05 p_{3-4}>0,05 p_{1-3}<0,001 p_{2-4} <0,05
10-14th day of AMI	4,81±0,15*	4,61±0,19**	7,42±0,57 ×	9,14±1,04^	p_{1-2}>0,05 p_{3-4}>0,05 p_{1-3}<0,001 p_{2-4}<0,001

Note: *, **, ″, ×, ^ – significance of differences p < 0.05

DISCUSSION

Our study revealed signs of endothelial dysfunction improvement in patients with type 2 diabetes (T2D) and without T2D, as evidenced by a significant decrease in ADMA and an increase in nitric oxide synthase (NOS) concentration on days 10-14 after acute myocardial infarction (AMI) in all examined patients, regardless of the treatment strategy. In patients with T2D, ADMA levels remained significantly higher than in those without T2D,

irrespective of whether it was interventional stenting or dual antiplatelet therapy, indicating the dominance of pathophysiological processes of endothelial dysfunction compared to patients with AMI without T2D in the early post-infarction period.

Regarding the thrombosis marker, PAI-1, in patients with AMI with ST-segment elevation, an increase in PAI-1 concentration was observed in both patient groups. The presence of T2D determined higher values of this marker during the first day after AMI with ST-segment elevation. However, in the early recovery period after AMI, patients without glucose metabolism disorders showed a significant decrease in PAI-1 levels, indicating a reduction in the inhibitory effect of PAI-1 and improvement in blood fibrinolytic activity during treatment. In contrast, patients with T2D maintained significantly higher ($p < 0.001$) PAI-1 levels in the early recovery period after AMI. The results also suggest that patients with AMI with ST-segment elevation may experience a prolonged elevation of PAI-1 concentration in the blood serum for 10-14 days after PCI, leading to disturbances in the coagulation system and inhibition of the natural thrombolytic system.

CONCLUSIONS

1. Coronary artery stenting in patients with type 2 diabetes mellitus (T2D) contributes to a significant decrease in asymmetric dimethylarginine (ADMA) content and an increase in nitric oxide synthase (NOS) on days 10-14 after acute myocardial infarction (AMI), suggesting a positive impact of interventional treatment methods on endothelial dysfunction markers.

2. Coronary artery stenting in patients with type2 diabetes mellitus did not lead to a significant reduction in plasminogen activator inhibitor-1 (PAI-1) levels on days 10-14 after AMI. This suggests the existence of delayed reduction in the concentration of this atherothrombotic marker due to inflammatory consequences of post-procedural platelet activation and reduced functioning of the endogenous thrombolytic system, which may influence the occurrence of adverse cardiovascular events in this category of patients.

Perspectives for further research. Determination of correlation relationships between markers of endothelial dysfunction in patients with acute myocardial infarction depending on the presence of type 2 diabetes mellitus.

FUNDING AND CONFLICT OF INTEREST

The study was conducted at authors' own expense. The authors report no conflict of interest and any external funding.

COMLIANCE WITH ETHICAL REQUIREMENTS

The research was conducted by the fundamental principles outlined in the «Rules of Ethical Principles for Conducting Medical Research Involving Human Subjects», as stated in the Helsinki Declaration (1964-2013).

LITERATURE

1. Grasgruber P., Sebera M., Hrazdira E., et al. Food consumption and the actual statistics of cardiovascular diseases: an epidemiological comparison of 42 European countries. Food Nutr Res. 2016 Sep 27. 60. 31694. doi: 10.3402/fnr.v60.31694. PMID: 27680091 PMCID: PMC5040825.
2. Timmis A., Townsend N., Gale C., et al. Eur Heart J. 2018 Feb 14. 39(7). 508-579. doi: 10.1093/eurheartj/ehx628. PMID: 29190377.
3. Barkoudah E., Skali H., Uno H., et al. Mortality rates in trials of subjects with type 2 diabetes. J. Am. Heart Assoc. 2012 Feb.1(1).8-15. doi: 10.1161/JAHA.111.000059. PMCID: PMC3487314. PMID: 23130114.
4. Shimizu T., Uematsu M., Yoshizaki T., et al. Myocardial Production of Plasminogen Activator Inhibitor-1 is Associated with Coronary Endothelial and Ventricular Dysfunction after Acute Myocardial Infarction. J Atheroscler Thromb. 2016 May 2. 23(5). 557-66. doi:10.5551/jat.32300. PMID: 26632165.
5. Dong Y., Wu Y., Choi H. C., et al. Diabetic Endothelium Dysfunction, Cardiovascular Complications, and Therapeutics. Diabetes Res. 2016. 5349801. doi: 10.1155/2016/5349801. PMID: 26989698 PMCID: PMC4775813.
6. Степура А. О. Клініко-патогенетичне обгрунтування ранньої інтенсивної гіполіпідемічної терапії у хворих на гострий інфаркт міокарда [дисертація в Інтернеті]. Київ: ДУ «Національний науковий центр «Інститут кардіології ім.акад. М. Д. Стражеска». К.,2019.[цитовано 2019 вер. 22]. Доступно на: https://strazhesko.org.ua ‘ 2019/06 ‘ dys_Stepura.
7. Steg PG, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, Borger MA, et al. Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC); ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2012 Oct. 33(20). 2569-619. doi: 10.1093/eurheartj/ehs215. PMID: 22922416.

8. Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, et al. Authors/Task Force members, 2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J. 2014 Oct 1. 35(37). 2541-619. doi: 10.1093/eurheartj/ehu278. PMID: 25173339.
9. Gaiz A., Mosawy S., Colson N., Singh I. Thrombotic and cardiovascular risks in type two diabetes; Role of platelet hyperactivity. Biomed Pharmacother. 2017 Oct. 94. 679-86. doi: 10.1016/j.biopha.2017.07.121. PubMed PMID: 28787703.
10. Navinan M. R., Mendis S., Wickramasinghe S., et al. Inflammation in ST- elevation myocardial infarction: risk factors, patterns of presentation and association with clinical picture and outcome, an observational study conducted at the Institute of Cardiology-National Hospital of Sri Lanka. BMC Cardiovasc Disord. 2019 May 14.19(1). 111. doi: 10.1186/s12872-019-1104-5. PMCID: PMC6518612. PMID: 31088357.
11. Fonseca V. A. Risk factors for coronary heart disease in diabetes. Ann Intern Med. 2000 Jul 18.133(2).154-6. doi: 10.7326/0003-4819-133-2-200007180-00015. PMID: 10896642.
12. Juhan-Vague I., Alessi M. C., Vague P. Increased plasma plasminogen activator inhibitor 1 levels. A possible link between insulin resistance and atherothrombosis. Diabetologia. 1991 Jul.34. 457-62. doi: 10.1007/bf00403280 PMID: 1916049.
13. Song C., Burgess S., Eicher J. D., et al. Causal Effect of Plasminogen Activator Inhibitor Type 1 on Coronary Heart Disease. J Am Heart Assoc.2017 May 26.6(6). pii: e004918. doi: 10.1161/JAHA.116.004918. PMID: 28550093. PMCID: PMC5669150.
14. Jung R. G., Simard T., Labinaz A., et al. Role of plasminogen activator inhibitor-1 in coronary pathophysiology. Thromb Res. 2018 Apr. 164. 54-62. doi: 10.1016/j.thromres.2018.02.135. PMID: 29494856.
15. Leibundgut G., Lee J. H., Strauss B. H., et al. Acute and Long-Term Effect of Percutaneous Coronary Intervention on Serially-Measured Oxidative, Inflammatory, and Coagulation Biomarkers in Patients with Stable Angina. J Thromb Thrombolysis. 2016 May. 41(4). 569-80. doi:10.1007/s11239-016-1351-6. PMID: 26964999. PMCID: PMC4811750.
16. Xuan C., Tian Q. W., Li H., et al. Levels of asymmetric dimethylarginine (ADMA), an endogenous nitric oxide synthase inhibitor, and risk of coronary artery disease: A meta-analysis based on 4713 participants. Eur J Prev Cardiol 2016 Mar. 23(5).502-10. doi: 10.1177/2047487315586094. PubMed PMID: 25956428.
17. Vallance P. Importance of asymmetrical dimethylarginine in cardiovascular risk. Lancet. 2001 Dec 22-29.358(9299).2096-7. doi: 10.1016/S0140-6736(01)07229-4. PMID: 11784617.
18. Celik M., Cerrah S., Arabul M., et al. Relation of asymmetric dimethylarginine levels to macrovascular disease and inflammation markers in type 2 diabetic patients. J Diabetes Res. 2014. 139215. doi: 10.1155/2014/139215. PMID: 24804267 PMCID: PMC3996885.
19. Sen N., Ozlu M. F., Akgul E. O., et al. Elevated plasma asymmetric dimethylarginine level in acute myocardial infarction patients as a predictor of poor prognosis and angiographic impaired reperfusion. Atherosclerosis. 2011 Nov. 219(1). 304-10. doi: 10.1016/j.atherosclerosis.2011.06.021. PMID: 21726864.
20. Gallo G., Pierelli G., Forte M., et al. Role of oxidative stress in the process of vascular remodeling following coronary revascularization. Int J Cardiol. 2018 Oct 1. 268. 27-33. doi: 10.1016/j.ijcard.2018.05.046. PMID: 29803340.
21. Elgendy I. Y., Jneid H. Microvascular obstruction in ST elevation myocardial infarction patients undergoing primary percutaneous coronary intervention: another frontier to conquer? J Thorac Dis. 2018 Mar. 10(3). 1343-1346. doi: 10.21037/jtd.2018.03.58. PMID: 29708124. PMCID: PMC5906270.

REFERENCES

1. Grasgruber, P., Sebera, M., Hrazdira, E., Hrebickova, S., Cacek, J. (2016). Food consumption and the actual statistics of cardiovascular diseases: an epidemiological comparison of 42 European countries. Food Nutr Res. Sep 27, 60,31694. doi: 10.3402/fnr.v60.31694.
2. Timmis, A., Townsend, N., Gale, C., Grobbee, R., Maniadakis, N., Flather, M., et al. (2018). Eur Heart J. Feb 14. 39(7). 508-579. doi: 10.1093/eurheartj/ehx628.
3. Barkoudah, E., Skali, H., Uno, H., Scott, D. Solomon, Marc A. Pfeffer. (2012). Mortality rates in trials of subjects with type 2 diabetes. J. Am. Heart Assoc. Feb, 1(1), 8-15. doi: 10.1161/JAHA.111.000059.
4. Shimizu, T., Uematsu, M., Yoshizaki, T., Obata, J.E., Nakamura, T., Fujioka, D., et al. (2016). Myocardial Production of Plasminogen Activator Inhibitor-1 is Associated with Coronary Endothelial

and Ventricular Dysfunction after Acute Myocardial Infarction. J Atheroscler Thromb. May 2, 23(5), 557-66. doi:10.5551/jat.32300. PMID: 26632165.
5. Dong, Y., Wu, Y., Choi, H.C., Wang, S. (2016). Diabetic Endothelium Dysfunction, Cardiovascular Complications, and Therapeutics. Diabetes Res., 5349801. doi: 10.1155/2016/5349801.
6. Stepura, A. O. Kliniko-patohenetychne obhruntuvannia rannoi intensyvnoi hipolipidemichnoi terapii u khvorykh na hostryi infarkt miokarda [dysertatsiia v Interneti]. Kyiv: DU «Natsionalnyi naukovyi tsentr «Instytut kardiolohii im.akad. M. D. Strazheska»; 2019.[tsytovano 2023 zhov. 20] Available from: https://strazhesko.org.ua ‘ 2019/06 ‘ dys_Stepura.
7. Steg, P.G, James, S.K., Atar, D., Badano, L.P., Blömstrom-Lundqvist, C., Borger M. A., et al. (2012). Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC), ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. Oct, 33(20), 2569-619. doi: 10.1093/eurheartj/ehs215.
8. Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, et al. (2014). Authors/Task Force members, 2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J., Oct 1,35(37),2541-619. doi: 10.1093/eurheartj/ehu278.
9. Gaiz, A., Mosawy, S ., Colson N., Singh I. (2017). Thrombotic and cardiovascular risks in type two diabetes; Role of platelet hyperactivity. Biomed Pharmacother, Oct 94, 679-86. doi: 10.1016/j.biopha.2017.07.121.
10. Navinan, M.R., Mendis, S., Wickramasinghe, S., Kathirgamanathan, A., Fernando, T., Yudhisdran, J. (2019). Inflammation in ST- elevation myocardial infarction: risk factors, patterns of presentation and association with clinical picture and outcome, an observational study conducted at the Institute of Cardiology-National Hospital of Sri Lanka. BMC Cardiovasc Disord., May 14,19(1),111. doi: 10.1186/s12872-019-1104-5.
11. Fonseca, V.A. (2000). Risk factors for coronary heart disease in diabetes. Ann Intern Med. Jul 18, 133(2), 154-6. doi: 10.7326/0003-4819-133-2-200007180-00015.
12. Juhan-Vague, I., Alessi, M.C., Vague, P. (1991). Increased plasma plasminogen activator inhibitor 1 levels. A possible link between insulin resistance and atherothrombosis. Diabetologia., Jul,34,457-62. doi: 10.1007/bf00403280.
13. Song, C., Burgess, S., Eicher, J.D., O’Donnell, C.J., Johnson, A.D. (2017). Causal Effect of Plasminogen Activator Inhibitor Type 1 on Coronary Heart Disease. J Am Heart Assoc., May 26, 6(6). pii: e004918. doi: 10.1161/JAHA.116.004918.
14. Jung, R.G., Simard, T., Labinaz, A., Ramirez, F.D., Di Santo, P., Motazedian, P., et al. (2018). Role of plasminogen activator inhibitor-1 in coronary pathophysiology. Thromb Res. Apr, 164, 54-62. doi: 10.1016/j.thromres.2018.02.135.
15. Leibundgut, G., Lee, J.H., Strauss, B.H., Segev, A., Tsimikas, S. (2016). Acute and Long-Term Effect of Percutaneous Coronary Intervention on Serially-Measured Oxidative, Inflammatory, and Coagulation Biomarkers in Patients with Stable Angina. J Thromb Thrombolysis, May, 41(4), 569-80. doi:10.1007/s11239-016-1351-6.
16. Xuan, C., Tian, Q.W., Li, H., Zhang, B.B., He, G.W., Lun, L.M. (2016). Levels of asymmetric dimethylarginine (ADMA), an endogenous nitric oxide synthase inhibitor, and risk of coronary artery disease: A meta-analysis based on 4713 participants. Eur J Prev Cardiol., Mar, 23(5), 502-10. doi: 10.1177/2047487315586094.
17. Vallance, P. (2001). Importance of asymmetrical dimethylarginine in cardiovascular risk. Lancet., Dec 22-29, 358(9299), 2096-7. doi: 10.1016/S0140-6736(01)07229-4.
18. Celik, M., Cerrah, S., Arabul, M., Akalin, A. (2014). Relation of asymmetric dimethylarginine levels to macrovascular disease and inflammation markers in type 2 diabetic patients. J Diabetes Res., 139215. doi: 10.1155/2014/139215.
19. Sen, N., Ozlu, M.F., Akgul, E.O., Kanat, S., Cayci, T., Turak, O., et al. (2011). Elevated plasma asymmetric dimethylarginine level in acute myocardial infarction patients as a predictor of poor prognosis and angiographic impaired reperfusion. Atherosclerosis. 2011 Nov, 219(1), 304-10. doi: 10.1016/j.atherosclerosis.2011.06.021.
20. Gallo, G., Pierelli, G., Forte, M., Coluccia, R., Volpe, M., Rubattu, S. (2018). Role of oxidative stress in the process of vascular remodeling following coronary revascularization. Int J Cardiol. Oct 1, 268, 27-33. doi: 10.1016/j.ijcard.2018.05.046.
21. Elgendy, I.Y., Jneid, H. (2018). Microvascular obstruction in ST elevation myocardial infarction patients undergoing primary percutaneous coronary intervention: another frontier to conquer? J Thorac Dis., Mar, 10(3), 1343-1346. doi: 10.21037/jtd.2018.03.58.

Резюме

ДИНАМІКА РІВНІВ АСИМЕТРИЧНОГО ДІМЕТІЛАРГІНІНУ ТА ІНГІБІТОРА АКТИВАТОРА ПЛАЗМІНОГЕНУ 1 ТИПУ У ХВОРИХ НА ГОСТРИЙ ІНФАРКТ МІОКАРДА З ЕЛЕВАЦІЄЮ СЕГМЕНТА ST ТА ЦУКРОВИМ ДІАБЕТОМ 2 ТИПУ В ЗАЛЕЖНОСТІ ВІД ТАКТИКИ РЕПЕРФУЗІЙНОЇ ТЕРАПІЇ

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Вступ. Незважаючи на серйозні успіхи, досягнуті у лікуванні гострих коронарних синдромів (ГКС), гострий інфаркт міокарда (ГІМ) залишається основною причиною смертності працездатного населення України. Засоби лікування інтервенційної кардіології дозволяють фактично знизити смертність хворих з ГКС, покращити перебіг гострого періоду захворювання та забезпечити менше зниження функціональних можливостей серця в майбутньому. Серед багатьох патогенетичних механізмів запалення судин при ішемічній хворобі серця та цукровому діабеті 2 типу визначальним є ендотеліальна дисфункція.
Мета. Оцінити рівні інгібітора активатора плазміногену 1 типу, асиметричного діметіларгінину та ендотеліальної синтази оксиду азоту на 10-14-й день у хворих в залежності від наявності або відсутності супутнього цукрового діабету 2 типу та виду репер фузійної терапії.
Матеріали та методи. Обстежено 130 хворих на гострий інфаркт міокарда, яких було розподілено на 2 групи: 1 групу склали хворі на гострий інфаркт міокарда з супутнім цукровим діабетом 2 типу (n=73), 2 групу – хворі на гострий інфаркт міокарда без цукрового діабету 2 типу (n=57). Кількісний вміст інгібітора активатора плазміногену 1 типу (ІАП-1) визначали імуноферментним методом з використанням комерційної тест-системи виробництва фірми Technoclone PAI-1 ELISA Kit (Австрія), ендотнліальної синтази оксиду азоту (NOS) – Enzyme-Linked Imunosorbent Assay (ELISA) Kit For Nitric Oxide Synthase Endothelial, асиметричного діметіларгінину (АДМА) – Immunodiagnostik ADMA ELISA Kit (Австрія).
Результати. Проведення черезшкірного коронарного втручання сприяє більш значному зниженню вмісту маркеру ендотеліальної дисфункції – АДМА та підвищенню NOS на 10-14-й день гострого інфаркта міокарда у порівнянні зі стандартною терапією. При проведенні ЧКВ рівень ІАП-1 достовірно не змінювався у динаміці лікування за рахунок постзапальної та посттравматичної активації тромбоцитів у судинній стінці.
Висновки. У хворих на гострий інфаркт міокарда з цукровим діабетом 2 типу проведення черезшкірного коронарного втручання сприяє достовірному зниженню вмісту асиметричного діметіларгінину та підвищенню NOS на 10-14-й день гострого інфаркту міокарда, але не супроводжувалось достовірним зниженням рівню ІАП-1, що в цілому свідчить про позитивний вплив проведеної реваскулярізації міокарда.

Ключові слова: **гострий інфаркт міокарда, цукровий діабет 2 типу, ендотеліальна дисфункція, асиметричний діметіларгінін, інгібітор активатора плазміногену 1 типу, черезшкірне коронарне втручання**