ORIGINAL ARTICLE

IMPACT OF PERCUTANEOUS CORONARY INTERVENTION ON PROTHROMBOGENIC POTENTIAL IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AND DIABETES MELLITUS TYPE 2

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ABSTRACT

The aim: Aim of study is to assess the influence of urgent reperfusion strategy on the levels of vWf, PAI-1 and sCD40L in patients with acute myocardial infarction (AMI) and concomitant diabetes mellitus type 2 (DM2).

Materials and methods: 255 patients with acute myocardial infarction took part in the study, they were divided into four groups depending on the presence of concomitant diabetes mellitus type 2 and performed treatment: I group – 83 diabetic patients who were underwent urgent reperfusion therapy; II group – 60 diabetic patients who received standard anticoagulant therapy; III group – 65 non-diabetic patients who were underwent urgent reperfusion therapy; IV group – 47 non-diabetic patients who received standard anticoagulant therapy. The levels of von Willebrand factor, PAI-1 and sCD40L were determined by enzyme-linked immunosorbent assay. Statistical data were processed using the Mann–Whitney U-test, the Kruskal-Wallis H-test, quantitative variables were described by the following parameters: median (Me), 25th and 75th percentiles (Q1; Q3).

Results: According to obtained data, we can conclude that patients with acute myocardial infarction and concomitant type 2 diabetes mellitus have higher levels of von Willebrand factor, PAI-1 and sCD40L compared to non-diabetic patients with AMI, which leads to the increasing of the platelets adhesion and aggregation and decreasing of fibrinolysis.

Conclusions: Urgent restoration of blood supply in occluded artery contributed to a statistically significant reduction in levels of von Willebrand factor, PAI-1 and sCD40L levels in both diabetics and non-diabetic patients, reducing the risk of thromboembolic complications and thus improving the prognosis.

KEY WORDS: acute myocardial infarction, diabetes mellitus, reperfusion therapy, prothrombogenic potential

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INTRODUCTION

Acute myocardial infarction is one of the leading medical problems currently. Its association with diabetes mellitus type 2 (DM2) is accompanied by higher risk of complications, including thromboembolic ones [1].

It is well known that the main cause of coronary artery occlusion is thrombosis at the site of a ruptured atherosclerotic plaque. The main components of the formed thrombus are blood cells and fibrin. It was found that at the beginning of thrombus formation its main cellular components presented by activated platelets, which are rapidly stabilized by fibrin fibers [2].

The formation of initial thrombi depends mainly on the adhesive and aggregating properties of platelets. Adhesion of activated platelets is initiated by von Willebrand factor (vWF), released from the damaged endothelial cells [3]. Activated platelets express CD40L that being a ligand of glycoprotein IIb/IIIa enhances platelets aggregation [4]. Recent studies showed its association with insulin resistance [5] and complicated course of acute coronary syndrome [6].

Under the normal circumstances, in response to thrombus formation, fibrinolysis is activated due to the synthesis of tPA, aimed at its dissolution. But in patients with type 2 diabetes the balance of these processes is usually disturbed and fibrinolysis inhibitors predominate over its activators [7]. PAI-1 is a major fibrinolysis inhibitor that suppresses the dissolution of fibrin filaments [8]. Increased levels of PAI-1 correlate with degree of insulin resistance [9].

Considering all mentioned above it becomes obvious that presence of diabetes mellitus type 2 (DM2) contributes to the formation of the prothrombogenic status [10] due to enhanced adhesive-aggregation properties of platelets and imbalance between coagulation and fibrinolytic substances.

Given the absolute priority of urgent reperfusion strategy in patients with AMI due to its proven positive effect on short and long-term prognosis [11], we also decided to evaluate its effect on the prothrombotic potential associated with type 2 diabetes.

THE AIM

Aim of study is to evaluate the influence of urgent reperfusion on the levels of vWf, PAI-1 and sCD40L in patients with acute myocardial infarction (AMI) and concomitant diabetes mellitus type 2 (DM2).

Table I. Levels of vWf, PAI-1, sCD40L measured on the 1st day of AMI depending on the presence of concomitant DM2 (Me [Q1; Q3])

Parameter	Patients with AMI+DM2 (n=73)	Patients with AMI (n=57)	Significance of differences
vWf, AU/ml	1,97 [1,82; 2,18]	1,54 [1,36; 1,72]	U=151,5; p<0,01
PAI-1, ng/ml	68,85 [60,95; 71,1]	53,1 [43,38; 59,6]	U=800,5; p<0,01
sCD40L, ng/ml	3,78 [3,67; 3,9]	3,35 [2,88; 3,63]	U=403; p<0,01

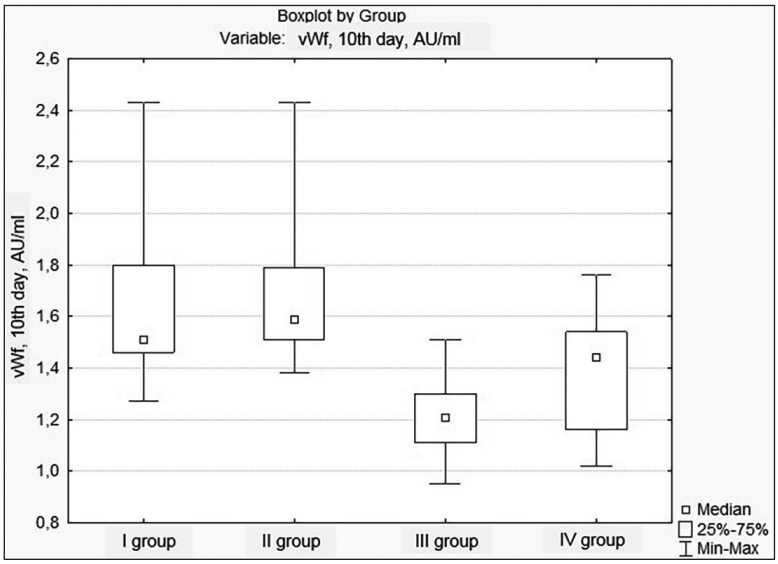

Fig 1. Box graphs of vWf values measured on the 10th day of AMI depending on the presence of concomitant DM2 and performed treatment

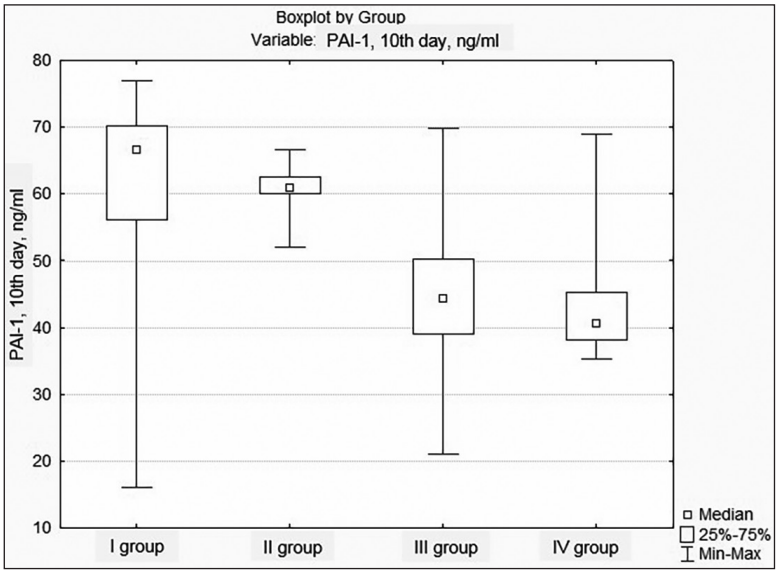

Fig 2. Box graphs of PAI-1 values measured on the 10th day of AMI depending on the presence of concomitant DM2 and performed treatment

MATERIALS AND METHODS

255 patients with acute myocardial infarction were enrolled in the study. They were divided into 4 groups depending on the presence of concomitant diabetes mellitus type 2 and performed treatment: I group – 83 diabetic patients who were underwent urgent reperfusion; II group – 60 diabetic patients who received standard anticoagulant therapy; III group – 65 non-diabetic patients who were underwent urgent reperfusion; IV group – 47 non-diabetic patients who received standard anticoagulant therapy.

This research was carried out in compliance with all relevant diagnostic and treatment standards of the requirements for the ethical component of clinical trials (GCP, 1997). Before the study, patients were informed about the essence of the study, its purpose and possible results. All participants signed up the informed agreement. This study was approved by the local ethics committee in accordance to the recommendations of the ethical committees for biomedical research, Ukrainian legislation on health protection, the 2000 Helsinki Declaration and the directives

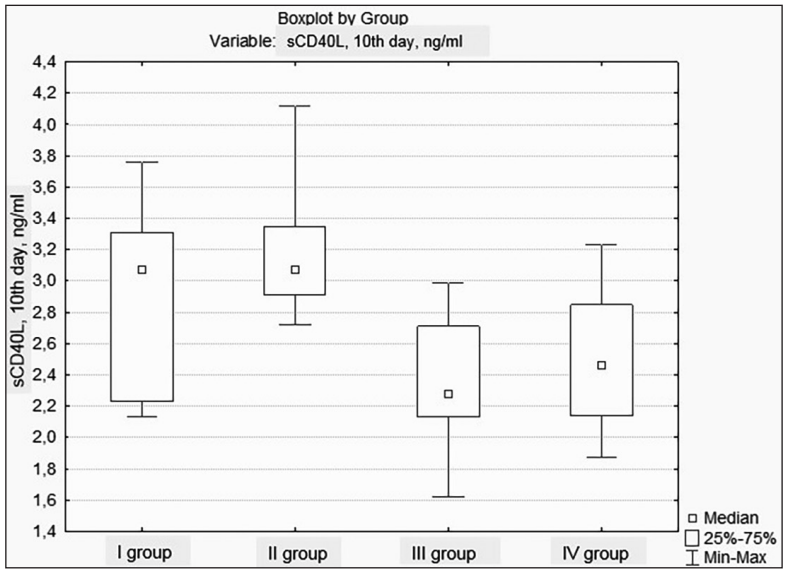

Fig 3. Box graphs of sCD40L values measured on the 10th day of AMI depending on the presence of concomitant DM2 and performed treatment

of the European Partnership 86/609 on the participation of people in biomedical research.

Acute myocardial infarction was diagnosed according to the Order of the Ministry of Health of Ukraine №455 dated 02.07.2014 «Unified clinical protocol of emergent, primary, secondary (specialized) and tertiary (highly specialized) medical aid and medical rehabilitation of the patients with acute coronary syndrome with elevated ST segment» on the basis of clinical, echocardiographic and biochemical criteria. Type 2 DM was diagnosed according to the Order of the Ministry of Health of Ukraine № 1118 dated 21.12.2012 «Standardized Clinical Protocol «Diabetes Mellitus Type 2».

Blood samples were obtained on the 1st and 10th days of AMI under the basal conditions, vWf blood serum levels were determined with commercial enzyme linked immunosorbent assay ELISA kit (Technoclone GmbH, Austria), PAI-1 blood serum levels were determined with commercial enzyme linked immunosorbent assay ELISA kit (Technoclone GmbH, Austria), sCD40-ligand blood serum levels were determined with commercial enzyme linked immunosorbent assay ELISA kit (YH Biosearch Laboratory, China) on the Automated EIA Analyzer "LabLine-90" (Austria). Statistical processing of results was performed using IBM SPSS Statistics software: quantitative variables were described by the following parameters: median (Me), 25th and 75th percentiles (Q1; Q3), the Mann–Whitney U-test was used for the assessment of the differences between two independent groups, the Kruskal-Wallis H-test was used for the assessment of the differences between four independent groups, p-statistical significance ($p<0,05$ is considered statistically significant).

RESULTS

Analyzing the levels of vWf on the first day of myocardial infarction (table I), we detected that in the group of diabetic patients the median vWf was considerably higher than in the group of non-diabetic – 1,97 AU/ml and 1,54 AU/ml respectively ($U=151,5$; $p<0,01$), that indicates significantly more intense processes of platelets adhesion under conditions of concomitant disorders of carbohydrate metabolism.

Similar statistically significant differences between the study groups were found for the level of PAI-1: the median PAI-1 in diabetic patients was 68,85 ng/ml while in non-diabetic patients – 53,1 ng/ml respectively ($U=800,5$; $p<0,01$) which can contribute to inhibition of lysis of blood clots.

A similar trend was found for sCD40L, the median of which was significantly higher in the group of patients with concomitant type 2 diabetes compared to patients without concomitant type 2 diabetes – 3,78 ng/ml and 3,35 ng/ml respectively ($U=403$; $p<0,01$), indicating a high platelet aggregation potential.

Taking into account these results, it can be established that patients with acute myocardial infarction and concomitant type 2 diabetes mellitus experience prothrombotic status due to increased adhesion and aggregation properties of platelets on the background of inhibited fibrinolysis.

Urgent reperfusion strategy helps to improve outcomes for patients due to its positive impact on short and long-term prognosis [11]. However, it is interesting to note that in patients with AMI with concomitant DM2, urgent endovascular intervention is performed significantly less often than in patients without diabetes, although, according to modern guidelines for high-risk patients, tactics require greater determination aimed at reduction of the incidence of complications, including thromboembolic complications, to which these patients are prone [12]. We decided to analyze how PCI affects the mediators of thrombosis studied by us and whether there are differences depending on the co-existing DM2.

According to obtained data, we can conclude that urgent reperfusion had a positive impact on the dynamics of the studied indicators, determined on the 10th day of

AMI: reperfusion therapy contributed to a statistically significant reduction in the levels of vWf (H=60,421; p<0,01) (fig.1), PAI-1 (H=48,434; p<0,01) (fig.2), sCD40L (H=47,614; p<0,01) (fig.3) in the groups of diabetic and non-diabetic patients.

DISCUSSION

Obtained results correlate with recent studies that showed positive impact of PCI on the vWF dynamics and significantly higher risk of development of major adverse cardiovascular events in patients with increased residual levels of vWF after performed PCI due to myocardial infarction. The authors confidently call the Willebrand factor an essential risk marker in patients with acute coronary syndrome and offer to use it for the assessment of long-term prognosis after acute coronary events [13].

The positive effect of percutaneous coronary intervention on the marker of platelet aggregation activity-sCD40L was demonstrated in several recent investigations where invasive approach to the treatment of acute coronary syndrome also contributed to a more significant reduction in sCD40L compared with conservative therapy in diabetic [12] and non-diabetic patients [14].

PCI was also accompanied by a decrease in the level of PAI-1 in the dynamics of patients with and without disorders of carbohydrate metabolism, but still in the literature there are conflicting data on its prognostic value in predicting of adverse cardiovascular events [15].

Given the results, it can be argued that urgent reperfusion strategy reduces the prothrombotic potential in patients with acute myocardial infarction, regardless of concomitant insulin resistance by reducing the adhesive-aggregation properties of platelets and inhibition of antifibrinolytic effects.

CONCLUSIONS

Patients with acute myocardial infarction and concomitant type 2 diabetes mellitus have higher levels of von Willebrand factor, PAI-1 and sCD40L compared to non-diabetic patients with AMI, which contributes to the formation of prothrombotic potential.

Reperfusion therapy has significantly reduced levels of von Willebrand factor, PAI-1 and sCD40L levels in both diabetics and non-diabetic patients with acute myocardial infarction, reducing the risk of thromboembolic complications and thus improving the prognosis.

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Conflict of interest:

The Authors declare no conflict of interest.

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