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Interconnection between blood clotting and inflammatory response in patients with acute myocardial infarction

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Abstract

Blood coagulation and inflammation are mutually influenced processes: in the cardiovascular system setting, the inflammatory status following an Acute Myocardial Infarction (AMI) can lead to endothelial dysfunction and activation of the blood coagulation system. This study aimed to evaluate the inflammatory response in AMI and assess its role in predicting prothrombotic state

following primary Percutaneous Coronary Interventions (PCI). Fibrinogen concentration was determined spectrophotometrically with a thrombin-like enzyme. D-dimer and Soluble Fibrin (SF) levels were quantified using enzyme-linked immunosorbent assay ELISA. A semi-automatic hematological analyzer was used to evaluate the blood formula. The lipid profile and C-Reactive Protein (CRP) concentration were analyzed using an automatic biochemical analyzer, the Erythrocyte Sedimentation Rate (ESR) was measured using capillary tubes by standard method. Statistical analysis was performed using the Wilcoxon-Mann-Whitney test. The inflammatory marker CRP, White Blood Cell Count (WBC), ESR, and fibrinogen concentration were used to characterize the intensity of inflammation. Patients with elevated CRP levels before PCI exhibited a significantly increased level of SF on the fifth day after AMI, which can be related to a higher risk of thrombosis than patients with AMI and normal inflammatory marker levels. Our findings highlight the importance of inflammation response assessment before the PCI procedures for accurately diagnosing the prothrombotic state of the hemostasis system, predicting thrombosis, and selecting appropriate therapy.

Introduction

Blood coagulation and inflammation are interconnected processes that influence each other through a reciprocal relationship. Inflammatory mediators play a central role in the disruption of hemostasis, leading to endothelial dysfunction, activation of proenzymes of the blood coagulation cascade, impairment of physiological anticoagulants, and inhibition of fibrinolytic activity.[1,2] Inflammation and hemostasis considerably affect each other, independently of the primary pathological condition, as numerous mediators and cellular factors participate in both processes, creating complex feedback mechanisms.[3]

Acute Myocardial Infarction (AMI) triggers an inflammatory response that manifests both systemically and locally, resulting in the accumulation of acute-phase inflammation proteins.[4-6] The key mediator of the acute phase and a marker of inflammation is C-Reactive Protein (CRP). The study of CRP's role in the development of cardiovascular diseases and its complications has gained particular relevance in recent years. CRP is implicated in various stages of the atherosclerotic process, including activation of the complement system and vascular endothelial cells, thrombosis, lipid accumulation, and apoptosis.[6-8]

Simultaneously with the activation of blood coagulation system components during inflammation, the potential of the Protein C (PC) anticoagulant system diminishes. This reduction is primarily due to decreased regulation of thrombomodulin and reduced expression of the Endothelial Protein C Receptor (EPCR) in endothelial cells, which may lead to thrombotic complications.[9-11]

Despite significant advancements in understanding the molecular mechanisms underlying the interaction between inflammation and hemostasis, many questions remain unanswered. Further research may provide insights that aid in clinical management by identifying new therapeutic targets to prevent complications.

The objective of this research was to determine the extent of the inflammatory process activation and to evaluate the influence of it on markers of blood coagulation system activation in AMI patients. Additionally, the study aimed to identify a clinical predictive indicator of prothrombotic

state to guide the development of novel management strategies for patients after AMI with coronary reperfusion and stenting.

Materials and Methods

Materials

Phosphate Buffered Saline (PBS) tablets and Sodium citrate were purchased from Merck (St. Louis, USA); thrombin-like enzyme from the venom of *Agkistrodon halys halys*, fibrin-specific monoclonal antibody I-3C, biotinilated monoclonal antibody II-4d, monomeric fibrin desAB, D-dimer-specific monoclonal antibody III-3B, D-dimer were obtained from Palladin Institute of Biochemistry of National Academy of Sciences of Ukraine; PC activator, substrate S2236 were from Siemens (Erlangen, Germany).

Patients

Patients with ST-elevation AMI (n = 39, mean age 59.3 years) hospitalized within the first 5 hours from the onset of the pain syndrome were involved in the study. All patients underwent angiography of the coronary arteries and stenting of the infarct-dependent atherosclerotic plaque. They received standard heparin 6,000-10,000 IU to prevent blood clot formation on the background of double antiplatelet therapy (aspirin + ticagrelor or clopidogrel). Anticoagulant was canceled after the procedure, and patients remained on double antiplatelet therapy. Other concomitant medications were guided-recommended and included statins (100%), ACE inhibitors (84,6%), beta-blockers (100%). Patients did not have any chronic inflammatory diseases requiring the use of anti-inflammatory medications such as steroids or immunosuppressants. Patients with known comorbidities (such as chronic kidney disease, chronic obstructive pulmonary disease, or systemic inflammatory diseases) that could cause endothelial damage or increase the level of systemic inflammatory response during the first days after acute myocardial infarction onset were also excluded from the study. The hospital stay was 12-18 days. All patients signed informed consent for enrollment in the study and were discharged from the hospital. Healthy volunteers with no known diseases (n = 19) were used as the reference group.

Blood sampling and collection

Platelet-poor blood plasma was prepared from citrated blood by centrifugation at 1,200 × g for 30 min. Sodium citrate (3.8 %) added immediately after collection to the whole blood at a 1:9 ratio was used as an anticoagulant [12]. Blood samples were collected after admission, before Percutaneous Coronary Interventions (PCI) procedures, and on the 5th day of AMI. All work was conducted under the Declaration of Helsinki.

Blood formula

A semi-automatic hematological analyzer ABX MicrosES 60, company "Horiba Medical" (Montpellier, France) (factory number 907FSOH15623) was used to evaluate the blood formula, specifically for white blood cell count (WBC) measurements.

Lipid profile and C-reactive protein

To assess the lipid profile (total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol) and C-reactive protein, an automatic biochemical analyzer A-25 "Biosystem" (Barcelona, Spain), factory number 831014240) was used.

Erythrocyte sedimentation rate

The Erythrocyte Sedimentation Rate (ESR) was measured using capillary tubes and capillary blood samples. The method involved drawing blood into a capillary tube containing an anticoagulant and placing it vertically. The rate at which erythrocytes settled was recorded after one hour provided a measure of systemic inflammation. This straightforward and effective method facilitated the monitoring of inflammatory responses in AMI patients.

Fibrinogen concentration

Fibrinogen concentration in the blood plasma was determined by the modified spectrophotometric method according to Sokolovska et al. [13]. Blood plasma (0.2 mL) and PBS (1.7 mL) were mixed in a glass tube. Coagulation was initiated by the addition of 0.1 mL of thrombin-like enzyme from the venom of *Agkistrodon halys halys* (1 units/mL) that allowed to avoid fibrin cross-linking. Mixture was incubated during 30 min at 37°C. The fibrin clot was removed and re-solved in 5 mL of 1.5 % acetic acid. The protein concentration was measured using spectrophotometer POP (Optizen, Daejeon, Korea) at 280 nm (ε=1.5).

Soluble fibrin (SF)

SF was detected using sandwich Enzyme-Linked Immunosorbent Assay (ELISA) with monoclonal antibodies produced in Palladin Institute of biochemistry of NAS of Ukraine. Fibrin-specific monoclonal antibody I-3C was used as catch-antibody. Biotinilated monoclonal antibody II-4d that has epitope in NH_2-terminal fragment of γ-chain of D-region of fibrinogen molecule was used as a tag-antibody. Optical density was measured at 492 nm using multiplate reader RT 2100C (Rayto, Shenzhen, China). Monomeric fibrin desAB produced from the human fibrinogen was used for the calibration.[14]

D-dimer

D-dimer was detected using sandwich ELISA as described above for soluble fibrin with modification: biotinilated D-dimer-specific monoclonal antibody III-3B that has epitope in NH_2-terminal fragment of Bβ-chain of D-region of fibrin(ogen) produced in Palladin Institute of biochemistry of NAS of Ukraine was used as the catch-antibody. D-dimer was produced from the human cross-linked fibrin according to the method described in Korolova *et al.*[15]

Protein C level

The PC level was determined using a PC activator (Siemens, Erlangen, Germany). The generation of activated PC was measured by a chromogenic substrate assay with the specific substrate S2236 (p-Glu-Pro-Arg-pNa). The analysis was conducted in 0.05 M Tris-HCl buffer at pH 7.4, at 37°C. The concentration of the chromogenic substrate was 30 mM. The generation of para-nitroaniline was measured at 405 nm using a microtiter plate reader (Multiscan EX, Thermo Fisher Scientific, Waltham, USA). The results were expressed as the ratio of the PC level in the studied blood plasma compared to the PC level in the blood plasma of a healthy control.[16]

Statistics

Statistical analysis was performed using the Wilcoxon-Mann-Whitney (WMW) test to compare two independent samples. All blood coagulation assays were repeated three times. Results are presented as means ± standard deviation. Data were considered statistically significant when $p<0.05$.

Results

Rising values in CPR levels (over 5 mg/mL),[7,8] in WBC count (over 10.6×10^9/L) and fibrinogen level were selected for the evaluation of the inflammatory process's intensity. An increase in triglycerides levels (over 1.8 mM)[18,18] and in Low-Density Lipoprotein Cholesterol (LDL-C) levels (over 4.5 mM) were chosen as additive secondary parameters. The study population was divided into two groups: Group I included patients with intense inflammatory process, while Group II involved patients in whom inflammation had not presented acutely (Table 1). In detail, with normal CPR levels, other inflammatory markers were not sufficient to classify the patient into group I (the intense inflammatory process group).

The main blood coagulation markers, including D-dimer, SF, and PC, were analyzed and compared in the blood plasma of patients from both groups at baseline (Day 0, prior to stenting) and on Day 5 after the stenting procedure. The data is summarized in Table 2.

Patients in both study groups initially had relatively normal levels of SF, PC, and D-dimer before PCI and stenting (3.15 ± 0.9 μg/mL, 96.1 ± 27.4%, and 73.7 ± 46.5 ng/mL, respectively). However, by the fifth day after the intervention, SF levels in Group I had increased approximately twofold, whereas they remained stable in Group II. In addition, PC levels in Group I decreased by about 50%, and D-dimer concentrations rose to approximately 300 ng/mL following stenting. These changes were not observed in Group II.

Discussion

Epidemiological studies have demonstrated that several pro-inflammatory molecules, including CRP, fibrinogen, and inflammatory cytokines, indirectly activate hemostasis.[7,19] An increase in these pro-inflammatory markers and cytokines contributes to endothelial dysfunction, structural abnormalities of blood vessels, and alterations in lipid levels and oxidative stress.[1-4] Inflammatory processes are also linked to qualitative and quantitative changes in the structure of high-density lipoproteins, which are involved in anti-inflammatory and atheroprotective mechanisms by facilitating reverse cholesterol transport to the liver and preventing low-density lipoprotein oxidation.[18] Disruption of these protective functions can lead to the rapid development of complications.

Patients with AMI were divided into two groups based on their inflammatory process rate, determined mainly by CRP levels. In the two groups there was a remarkable difference in the prothrombotic response of the blood coagulation system within the first days after AMI onset. Lipid profile parameters such as Triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C) were primarily selected to characterize atherosclerotic vascular injury.[19-21]

SF is a highly informative indicator of the process reflecting the activation of the blood coagulation system. Its concentration in blood plasma corresponds to the activity of thrombin generation. It is a specific and reliable marker for identifying thrombophilia, also indicating potential disruptions in the balance between coagulation and fibrinolysis.[22-24] D-dimer is widely recognized as a prognostic indicator for developing thrombosis. However, it's still unknown if the not significant increase in D-dimer levels may be associated positively with the absence of intravascular thrombus or negatively with a reduced effectiveness of fibrinolysis.[25,26] As for PC, this anticoagulant protein

promptly responds to intravascular thrombin generation and inflammatory processes. Its concentration decreases due to consumption, indicating the intensity of coagulation and inflammation.[27,28]

According to our data, patients with AMI and elevated levels of the CRP before the PCI exhibited significantly higher levels of SF 5 days later, more pronounced consumption of PC, and greater accumulation of D-dimer compared to those whose pro-inflammatory markers remained within the normal range. This clearly indicates the prominent increase in the danger of intravascular thrombus formation, particularly for these patients.

It is known that inflammation triggers the blood coagulation cascade through highly variable direct and indirect molecular mechanisms.[4,29,30] Notably, activation of the systemic inflammation detected in Group I did not result in an immediate risk of intravascular thrombosis but may lead to it later, following AMI with primary PCI and stenting procedure. Presumably, the balance of the hemostasis system in both patients' groups was maintained for a considerable period but for patients with increased inflammatory process it was ultimately disrupted, resulting in a procoagulant shift. This shift poses a significant danger to patients, increasing the risk of reinfarction, stent thrombosis or other thrombotic complications. Thus, the detection of markers of inflammation is an important issue for accurate diagnostics of thrombosis and prothrombotic states, the prediction of the patient's recovery, and the selection of the appropriate therapy.

Our research revealed that the inflammatory-triggered activation of the blood coagulation system resulted in considerable SF accumulation. However, no significant increase in D-dimer levels was observed, which may suggest not only the absence of intravascular thrombus (which is favorable) but also a reduced effectiveness of fibrinolysis (which is concerning). Only the simultaneous determination of SF and D-dimer for every particular patient is crucial for clarifying the mechanisms underlying the clinical manifestations of the procoagulant shift in the blood coagulation system and assessing the effectiveness of fibrinolysis.[31]

Finally, in our study, CRP was confirmed to be the most reliable clinical marker of the inflammatory process. Recent studies have demonstrated decreasing CRP levels during the standard therapy for cardiovascular diseases,[32] further supporting its role. This has led to the suggestion of CRP as a potential target for therapy. To date, further research is needed not only to understand better the connection between CPR levels and systemic inflammation activity, but also to develop new therapeutic strategies.[33-35]

Conclusions

Our data indicate the significant impact of an elevated inflammatory response on the procoagulant shift in the hemostasis system, which may lead to thrombosis in patients with AMI. We hypothesize that timely suppression of inflammation, along with adequate anticoagulant therapy, could play a crucial role in effectively preventing thrombosis and reinfarction and should be widely considered in patient management.

The main limitation of the present study is the absence of a control group consisting of patients with acute myocardial infarction who did not undergo percutaneous coronary intervention. Such a control group could provide valuable comparative data; however, its inclusion is not feasible for obvious ethical reasons, as withholding a potentially life-saving intervention would be unacceptable. It should also be noted that the relatively small sample size of the study underscores the need for further, larger-scale investigations.

References

1. Esmon CT. New mechanisms for vascular control of inflammation mediated by natural anticoagulant proteins. J Exp Med 2002;196:561-4.
2. Saibeni S, Spina L, Vecchi M. Exploring the relationships between inflammatory response and coagulation cascade in inflammatory bowel disease. Eur Rev Med Pharmacol Sci 2004;8:205-8.
3. Margetic S. Inflammation and haemostasis. Biochem Med (Zagreb) 2012;22:49-62.
4. Stark K, Massberg S. Interplay between inflammation and thrombosis in cardiovascular pathology. Nature reviews. Cardiology 2021;18:666-82.
5. Matter MA, Paneni F, Libby P, et al. Inflammation in acute myocardial infarction: the good, the bad and the ugly. Eur Heart J 2024;45:89-103.
6. Oprescu N, Micheu MM, Scafa-Udriste A, et al. Inflammatory markers in acute myocardial infarction and the correlation with the severity of coronary heart disease. Ann Med 2021;53:1041-7.
7. Schwuchow-Thonke S, Göbel S, et al. Increased C reactive protein, cardiac troponin I and GLS are associated with myocardial inflammation in patients with non-ischemic heart failure. Sci Rep 2021;11:3008.
8. Yi M, Wu L, Ke X, Prognostic value of high-sensitivity C-Reactive Protein in in-stent restenosis: A meta-analysis of clinical trials. J Cardiovasc Dev Dis 2022;9:247.
9. Maas C, Oschatz C, Renné T. The plasma contact system 2.0. Semin Thromb Hemost 2011;37:375-81.
10. Dahlbäck B, Villoutreix BO. Regulation of blood coagulation by the protein C anticoagulant pathway: novel insights into structure-function relationships and molecular recognition. Arterioscler Thromb Vasc Biol 2005;25:1311-20.
11. D'Angelo A, Gerosa S, D'Angelo SV, et al. Protein S and protein C anticoagulant activity in acute and chronic cardiac ischemic syndromes. Relationship to inflammation, complement activation and *in vivo* thrombin activity. Thromb Res 1994;75:133-42.
12. Chernyshenko V, Shteinberg K, Lugovska N, et al. Preparation of highly-concentrated autologous platelet-rich plasma for biomedical use. Ukr Biochem J 2019;91:19-27.
13. Sokolovska AS, Chernyshenko TM, Ivanenko TI, et al. Comparative characteristic of fibrinogen level determination methods in blood plasma. Exp Clin Phys Biochem 2002 3: 82-6.
14. Lugovskoi EV, Kolesnikova IN, Lugovskaia NE, et al. Quantification of D-dimer and soluble fibrin in blood plasma of people with ischemic heart disease and hypertension. Ukr Biochem J 1999;76:136-41.
15. Korolova D, Syrko M, Stohnii Ye, et al. Standardization of the protein calibrators isolation methodology for thrombophilia markers detecting immunodiagnostic test systems. Biotechnol Acta 2022;15:61-9.
16. Korolova DS, Platonova TM, Gornytska OV, et al. Diagnostic value of Protein C depletion in pathologies associated with the activation of the blood coagulation system. Int J Mol Sci 2025;26:6122.
17. Ząbczyk M, Hońdo Ł, Krzek M, Undas A. High-density cholesterol and apolipoprotein AI as modifiers of plasma fibrin clot properties in apparently healthy individuals. Blood Coagul Fibrinolysis 2013;24:50-4.

18. Frangogiannis NG. The inflammatory response in myocardial injury, repair, and remodelling. Nature reviews. Cardiology 2014;11:255-65.
19. Nazir S, Jankowski V, Bender G, et al. Interaction between high-density lipoproteins and inflammation: Function matters more than concentration. Adv Drug Deliv Rev 2020;159:94-119.

20. Kato K, Yokoyama H, Iwasaki T, et al. Impact of triglyceride levels on the long-term clinical outcomes in patients with acute myocardial infarction. In vivo (Athens, Greece) 2024;38:3078-84.

21. Budoff M. Triglycerides and triglyceride-rich lipoproteins in the causal pathway of cardiovascular disease. Am J Cardiol 2016;118:138-45.

22. Elged AA, El-Gamal RA, Bastawy SA, Moselhy MS. Soluble fibrin monomer complex assay enhances early and accurate diagnosis of acute myocardial infarction. Int J Clin Exp Pathol 2016;9:5801-9.
23. Zhao X, Yang S, Lei R, et al. Clinical study on the feasibility of new thrombus markers in predicting massive cerebral infarction. Front Neurol 2023;13:942887.
24. Ieko M, Naito S, Yoshida M, et al. Plasma soluble fibrin monomer complex as a marker of coronary thrombotic events in patients with acute myocardial infarction. Tohoku J Exp Med 2009;219:25-31.
25. Schafer K, Goldschmidt E, Oostra D, et al. The clinical significance of ultra-high D-dimer levels. J Vasc Surg Venous Lymphat Disord 2022;10:8-13.
26. Yan W, Liu J, Liu H, Lu J, et al. Elevated D-dimer levels predict adverse outcomes in hospitalised elderly patients with chronic heart failure. Intern Med J 2019;49:1299-306.
27. Stankovic S, Obradovic S, Dzudovic B., et al. Lower plasma protein C activity is associated with early myocardial necrosis and no-reflow phenomenon in patients with ST elevation myocardial infarction. Acta Cardiologica 2019;74:331-9.
28. Al Sulaiman K, Alsuwayyid F, Alrashidi A, et al. Apixaban use in patients with Protein C and S deficiency: A case series and review of literature. J Blood Med 2022;13:105-11.
29. Jennewein C, Tran N, Paulus P, et al. Novel aspects of fibrin(ogen) fragments during inflammation. Mol Med 2011;17:568-73.
30. Rudez G, Meijer P, Spronk HM, et al. Biological variation in inflammatory and hemostatic markers. JTH 2009;7:1247-55.
31. Udovenko A, Makogonenko Y, Korolova D, et al. Formation and elimination of soluble fibrin and D-dimer in the bloodstream. CMJ 2023;64:421-9.
32. Ridker PM, MacFadyen JG, Everett BM, et al. CANTOS Trial Group, Relationship of C-reactive protein reduction to cardiovascular event reduction following treatment with canakinumab: a secondary analysis from the CANTOS randomised controlled trial. Lancet 2018;391:319-28.
33. Šilhavý J, Zídek V, Landa V, et al. Rosuvastatin can block pro-inflammatory actions of transgenic human C-reactive protein without reducing its circulating levels. Cardiovasc Ther 2014;32:59-65.
34. Caprio V, Badimon L, Di Napoli M, et al. pCRP-mCRP dissociation mechanisms as potential targets for the development of small-molecule anti-inflammatory chemotherapeutics. Front Immunol 2018;9:1089.
35. McFadyen JD, Kiefer J, Braig D, et al. Dissociation of C-Reactive Protein localizes and amplifies inflammation: Evidence for a direct biological role of C-Reactive Protein and its conformational changes. Front Immunol 2018;9:1351.

Table 1. Characteristics of the groups of patients divided according to the content of pro-inflammatory markers. CRP, C-reactive protein; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; WBC, white blood cells; ESR, erythrocytes sedimentation rate.

Parameter	CRP, mg/mL	TG, mM	LDL-C, mM	WBC, $\times 10^9$/L	ESR, mm/hour	Fibrinogen, mg/mL
Group I (n = 23)	**5.85**# (0.9-11.1)	**1.95**# (1.07-8.00)	**4.11**# (2.5-6.4)	10.0 (6.8-13.7)	6.0 (3-18)	3.0 (1.7-6.1)
Group II (n = 16)	3.9 (0.8-4.8)	1.21 (0.47-3.02)	2.93 (2.13-5.6)	9.5 (7-14.1)	7.0 (3-31)	2.8 (1.6-5.3)
Control	≤5.0	≤1.8	≤4.5	≤10.6	≤10.0	2.6 (2.2-3.1)

# p<0.05 according to the Mann-Whitney U test, compared to Group II.

Table 2. Blood coagulation system parameters of the groups of patients divided according to the content of pro-inflammatory markers. SF, soluble fibrin, PC, protein C.

Parameter	SF, μg/mL		PC, %		D-dimer, ng/mL	
Time of analysis	**Day 0**	**Day 5**	**Day 0**	**Day 5**	**Day 0**	**Day 5**
Group I (n = 23)	3.1 (1.4-5.6)	**6.35*** (1.9-9.6)	98 (65-121)	91 (51-115)	57 (12-125)	90 (32-308)
Group II (n = 16)	3.1 (1.7-4.6)	3.3 (2.2-5.0)	97 (68-120)	100 (55-110)	63 (20-103)	51 (13-117)
Control	3 (1-9)		100 (90-110)		47 (20-100)	

* p<0.05 according to the Mann-Whitney U test, compared to Group II on the Day 5.