

UNIVERSITATEA DE MEDICINĂ, FARMACIE, ȘTIINȚE ȘI TEHNOLOGIE
„GEORGE EMIL PALADE” DIN TÎRGU MUREȘ

ȘCOALA DE STUDII DOCTORALE

Abstract of the doctoral thesis

Evaluation of platelet indices in patients with coronary artery disease

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Introduction

Platelets are essentially involved in atherosclerosis and atherothrombosis from the early stages of atherosclerotic plaque formation to the appearance of thrombotic occlusion at the level of eroded or ruptured plaques. Activation is the response of platelets to a wide variety of stimuli that initiate complex intracellular events that result in platelet shape change and release of substances from α granules. The activation of platelets in this process also increases the size and function heterogeneity of circulating platelets, and the evaluation of these processes by inexpensive and routine determinations, such as platelet indices measured in the blood count, should be attempted.

Beyond the classic cardiovascular risk factors, dyslipidaemia, diabetes, hypertension, there is now a body of experimental and clinical evidence supporting the involvement of inflammation in atherogenesis and the pathophysiology of ischemic events. The inflammatory response mediates the link between risk factors and atherosclerosis. In the last decade, the concept of the involvement of inflammation in atherosclerosis and atherothrombosis has led to the adoption of inflammatory markers for predicting cardiovascular risk, and the development of anti-inflammatory therapies to reduce cardiovascular events and residual risk in patients at high cardiovascular risk.

Objectives

In this study, I aimed to describe platelet parameters and platelets-to-neutrophils and platelets-to-lymphocytes ratios in the context of atherosclerotic coronary disease in all its manifestations, from chronic coronary syndrome to acute coronary syndrome, and in the context of classic cardiovascular risk factors, including their prognostic role, by evaluating mortality at 5 years.

Study 1. Evaluation of platelet indices and platelet/lymphocyte and platelet/neutrophil ratios in patients with acute coronary syndromes

The objective of this study were the compare platelet indices between the three groups of patients studied, namely patients with stable angina pectoris, non-ST segment elevation acute coronary syndromes and ST segment elevation myocardial infarction treated by angioplasty with stent implantation, as well as markers of acute and chronic inflammation such as the platelets-to-lymphocytes and platelets-to-neutrophils ratios. We aimed to evaluate these parameters as diagnostic and prognostic factors in patients who required angioplasty with stent implantation. 719 patients were included in this study, of which 437 (60.8%) patients with chronic coronary syndrome, 151 (21.0%) patients with ST segment elevation myocardial infarction and 131 (18.2%) patients with non-ST segment elevation acute coronary syndrome. Elevated platelets-to-lymphocytes ratio, as a marker of chronic inflammation, has been associated with acute coronary syndrome, particularly STEMI, and is a predictor of 5-year mortality in patients requiring percutaneous coronary angioplasty.

Study 2. Variation of platelet indices during antiplatelet treatment

The objectives of this study were to evaluate and describe the dynamics of platelet indices and platelets-to-lymphocytes and platelets-to-neutrophil ratios on the medium and long term in patients on dual antiplatelet therapy with aspirin and clopidogrel or ticagrelor.

101 patients with chronic coronary syndrome, and 67 patients with acute coronary syndrome followed up to 3 months post-angioplasty, respectively 61 patients with chronic coronary syndrome and 27 patients with acute coronary syndrome followed up to 12 months, were included in the study. The results showed that under dual antiplatelet treatment with aspirin and clopidogrel, platelet indices change differently in stent angioplasty patients depending on its indication. Thus, MPV, PDW and P-LCR decrease in the first 3 months post-angioplasty in patients with chronic coronary syndrome, while the same effect is observed at 12 months in patients with acute coronary syndrome. In addition, the decrease in neutrophil counts after resolution of the acute phenomenon causes the platelets-to-neutrophils ratio to increase 3 months after the acute coronary syndrome. Treatment with ticagrelor does not change platelet parameters, but a study including a larger number of patients would be necessary to confirm this observation.

Study 3. The impact of cardiovascular risk factors on platelet indices

The hypothesis of our study was that, given that cardiovascular risk factors influence not only thrombopoiesis, but also platelet function and cells involved in inflammation and atherosclerosis, platelet size parameters and the ratio of platelets to inflammatory cells will be different depending on the presence or the absence of certain risk factors.

The first objective of this study was to evaluate the differences between platelet indices of patients with and without diabetes, hypertension, and dyslipidaemia who required percutaneous angioplasty with stenting for chronic coronary syndrome, non-ST-segment elevation acute coronary syndrome, and ST segment elevation myocardial infarction. At the same time, we aimed to evaluate the clinical significance of the association between platelet indices and cardiovascular risk factors by evaluating the 5-year mortality of these patients.

719 patients were included in the study, of which 222 (30.8%) had diabetes, 564 (78.4%) had hypertension and 391 (54.3%) were dyslipidaemic. In our study, platelet indices were not significantly influenced by the presence of risk factors, but a low platelet/neutrophil ratio was predictive of 5-year mortality in patients with diabetes, dyslipidaemia, or hypertension treated with percutaneous angioplasty for chronic coronary syndrome or ST segment elevation myocardial infarction.

General conclusions

In this study including patients with significant atherosclerotic coronary artery disease who required percutaneous stenting in the setting of stable coronary artery disease, non-ST-

segment elevation acute coronary syndrome, and ST-segment elevation myocardial infarction, platelet indices represented by MPV, PDW and P-LCR did not differ by patient presentation, but correlated positively with the severity of coronary artery disease. In the long-term post-angioplasty, a tendency to a decrease of platelet indices was observed both in patients with chronic coronary syndrome and in those with acute coronary syndromes, without differences in patients treated with clopidogrel compared to those treated with ticagrelor, and without significant differences in association with the major cardiovascular risk factors represented by diabetes, hypertension and dyslipidaemia.

The platelets-to-neutrophils ratio, lower in patients with acute coronary syndromes, was a prognostic factor for 5-year mortality in patients with diabetes, dyslipidaemia, or hypertension.

Elevated platelet/lymphocyte ratio is associated with acute coronary syndrome and is predictive of 5-year mortality for patients treated with percutaneous coronary angioplasty.

The originality of the thesis

Although at the time of the initiation of this research project, data on platelet indices and platelets-to-lymphocyte ratio in patients with atherosclerotic coronary artery disease were not abundant, and rather focused on the differences between healthy patients and those with atherosclerotic disease, in recent years more and more data have appeared in the attempt to explain the pathophysiology and predictive role of these factors.

However, our study presents a comprehensive analysis of platelet indices covering the entire spectrum of manifestations of coronary atherosclerotic disease, following patients from the time of percutaneous angioplasty up to one year from the hemogram point of view, and up to 5 years to be able to evaluate the their clinical significance.

Our study includes several analyses not explored in other studies, such as the relevance of the platelets-to-neutrophils ratio in the context of cardiovascular risk factors and under long-term treatment with clopidogrel and ticagrelor, the long-term variation of platelet indices under dual antiplatelet therapy and the relevance of variation for the long-term prognosis not only of patients with acute myocardial infarction, but also with chronic coronary syndrome.

In this context, I consider these results to complement the already published information regarding the possibility of using platelet indices and platelets-to-lymphocytes or neutrophils ratios in different subpopulations of patients with atherosclerotic coronary artery disease.

The results may be useful in the context of the current trend of identifying therapies that target atherosclerosis and atherothrombosis beyond the modulation of platelet function. Thus, for the complex evaluation of the effect of these treatments, the identification of predictive or treatment follow-up parameters will be useful, and the relationship between platelet function and markers of inflammation could be interesting to explore.