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# No-reflow Phenomenon After Primary Percutaneous Coronary Intervention: To Reflow or not to Reflow?

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## *Dear Editor,*

We have read with great interest the recently published article by Abdi et al. entitled evaluation of the clinical and procedural predictive factors of no-reflow phenomenon Following Primary Percutaneous coronary intervention (1). In this well-designed article, the authors evaluated clinical predictors of the no-reflow phenomenon after primary percutaneous coronary intervention (pPCI) in 438 patients with acute ST segment elevation myocardial infarction (STEMI). In that study, they found that the white blood cell (WBC) count and thrombus grade are strong, independent predictive factors of developing the no-reflow phenomenon in STEMI patients undergoing pPCI. There is also an association between the no-reflow phenomenon and pain duration, maximal ST-change, left ventricle function, high sensitivity C-reactive protein (hs-CRP), bifurcation, eccentricity, and coronary anatomy.

Despite achievement of optimal epicardial coronary flow in the majority of patients treated for STEMI by pPCI, myocardial no-reflow is a commonly encountered phenomenon occurring in 5% - 50% of these patients (2). The no-reflow phenomenon in patients with STEMI is associated with a worse prognosis during short and long-term follow-up periods (3). The pathophysiological mechanisms responsible for the no-reflow phenomenon are very complex and poorly explained. The pathophysiology of the no-reflow phenomenon includes a combination of mechanisms, including distal atherothrombotic embolisation, ischemic injury, reperfusion injury, and heightened susceptibility of the coronary microcirculation to injury (3).

Inflammation is known to play a critical role in the initiation and progression of the atherosclerotic process (4). The complete blood count (CBC) is one of the most frequently ordered laboratory tests in clinical practice. Various studies have evaluated the performance of these hematological CBC parameters to predict disease severity and mortality risk. Automated cell counters are routinely available in many clinical laboratories and can be used to determine red cell distribution width (RDW), platecrit, platelet count, platelet distribution width (PDW), mean platelet volume (MPV), and some ratios such as the neutrophil-lymphocyte ratio (NLR) and the RDW-platelet ratio (RPR). We previously demonstrated that admission NLR, platecrit, and RPR are independent correlates of no-reflow and in-hospital major adverse cardiovascular events (MACEs) among 580 patients with STEMI undergoing pPCI (5). On the other hand, we also showed that admission PDW and MPV are independent correlates of no-reflow and in-hospital MACEs among patients with STEMI undergoing pPCI (6).

We also found that female gender, pain to balloon time, high TIMI thrombus grade, tirofiban, MPV, and PLR were independent predictors of no-reflow in young patients with STEMI after pPCI (7). Moreover, it has been shown that admission biluribin, plasma gamma glutamyl transferase (GGT), and N/L ratio levels are independent predictors of the no-reflow phenomenon in patients with STEMI undergoing pPCI (8-10). Admission renal functions are very important for prediction of no-reflow in this patient group. We previously showed that decreased glomerular filtration rate (GFR) upon admission in patients with STEMI is independently associated with risk of poor myocardial perfusion following pPCI (11). Moreover, it is well known that metabolic syndrome, with its associated cardiovascular risks and its detrimental effects on coronary microcirculation, may play a role in poor myocardial perfusion after pPCI in patients with AMI. Concordantly, we have shown a significant association between metabolic syndrome and impaired myocardial perfusion after pPCI in patients with STEMI undergoing pPCI (12).

C-reactive protein, an acute-phase reactant, plays an important role in innate immune response, and it is now recognized to be a mediator of atherothrombotic disease (13). C-reactive protein is not only a marker of the amount and activity of circulating proinflammatory cytokines; in fact, this protein may also contribute to inflammation in ischemic myocardia by activating the complement system (14, 15).

In this recently published article, we aimed to investigate the impact of CRP levels on the development of poor myocardial perfusion after pPCI in patients with STEMI (16). Our study population consisted of 75 patients admitted to

our hospital with acute anterior MI, who underwent pPCI in the left anterior descending coronary artery. Patients were divided into two groups according to TIMI myocardial perfusion grade (TMPG) after pPCI. Group 1 consisted of 25 patients with TMPG 0 - 1, and Group 2 consisted of 50 patients with TMPG 2 - 3. Admission hs-CRP levels of the patients in Group 1 were significantly higher than those of the patients in Group 2 ($28.67 \pm 8.31$ $\mu$g/dL versus $12.03 \pm 3.95$ $\mu$g/dL, respectively, $P < 0.001$). Moreover, we detected a significant independent association between CRP levels and the development of poor myocardial perfusion (OR = 1.85). We also found a significant independent association between pain to balloon time and poor myocardial perfusion (OR = 5.49). These findings have suggested that high CRP levels measured upon admission in patients with AMI undergoing pPCI are likely to participate in the causal pathway leading to the development of poor myocardial perfusion, especially when combined with prolonged pain to balloon time.

In conclusion, the no-reflow phenomenon is the Achilles' heel of treatment of patients with STEMI. Because the main pathophysiological mechanisms underlying that phenomenon are very complex, understanding these interrelated mechanisms is the most critical step in treatment. Therefore, we strongly believe that the use of simple bedside laboratory markers may play a significant role in identifying patients at high risk for no-reflow phenomenon development.

## Footnote

**Authors' Contribution:** Turgay Celik, study concept and design, analysis and interpretation of data; Cengiz Ozturk, drafting of the manuscript; Sevket Balta, critical revision of the manuscript for important intellectual content; Atila Iyisoy, study supervision.

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