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# Acute reperfusion treatment in cases with ST-elevation myocardial infarction and peripheral neutrophilia

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***ABSTRACT***

**Objectives:** The study aimed to assess the correlation between neutrophil count at admission and during the short-term follow-up period with clinical outcomes in individuals presenting with ST-elevation myocardial infarction (STEMI).

**Patients and methods:** This prospective study was conducted between March 2010 and September 2010. Seventy-two patients (58 males, 14 females; mean age: 67±12 years; range, 50 to 89 years) diagnosed with acute coronary syndrome presenting with STEMI were included in the study. Complete blood count, serum glucose, urea, creatinine levels, and glomerular filtration rate were assessed in patients at 0, 4, 24, and 48 h. Patients were stratified according to the Killip-Kimball classification. Adverse clinical outcomes were defined as death, reinfarction, and cerebrovascular disease.

**Results:** Adverse clinical outcomes were significantly higher in patients with higher age and Killip-Kimball scores ($p=0.04$, $p<0.01$). A correlation was identified between the white blood cell (WBC) count at 48 h ($p=0.04$) and the neutrophil count at all time points with adverse clinical outcomes ($p<0.05$).

**Conclusion:** In our study, a correlation was determined between WBC and neutrophil counts and the rates of in-hospital mortality and adverse clinical outcomes in individuals presenting with acute STEMI. Elevated neutrophil count assessed upon admission to the hospital and during short-term follow-up may be utilized to identify high-risk patients.

***Keywords:*** Acute coronary syndrome, Killip-Kimball Classification, neutrophil count, ST elevation myocardial infarction.

Acute coronary syndrome (ACS) is a group of clinical syndromes caused by acute myocardial ischemia. It can lead to heart failure, arrhythmias, and even sudden death. It is recognized as a prominent factor contributing to disability and mortality on a global scale.[1] Neutrophils, which are innate immune cells within the body, play a crucial role as the initial barrier of protection against pathogens. Stimulation of neutrophils can trigger various pathological processes, including inflammation.[2] It has been demonstrated that systemic inflammatory mediators play a significant role in atherosclerosis and coronary artery disease.[3] The elevation of circulating white blood cells (WBCs), nonspecific markers of inflammation, can lead to adverse clinical outcomes in coronary artery disease, including ST-elevation myocardial infarction (STEMI).[4] It has been reported that particularly neutrophils are associated with extensive infarct areas, worse angiographic outcomes, and adverse short-term prognosis in STEMI.[5] Neutrophils are known to trigger coagulation, increase microvascular permeability, and mediate ischemia reperfusion injury in ACS.[6]

According to current guidelines, the gold standard treatment following STEMI is percutaneous coronary intervention.[7] Acute reperfusion therapy is preferred in situations where percutaneous coronary intervention cannot be performed. It has been shown that early reperfusion therapy improves outcomes in patients with STEMI.[8]

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The relationship between neutrophil counts and angiographic indexes during reperfusion is not clear. The objective of this study was to assess the correlation between neutrophil count at admission and during the short-term follow-up period with clinical outcomes in patients diagnosed with STEMI.

## PATIENTS AND METHODS

This prospective study was conducted at the Eskişehir Osmangazi University Faculty of Medicine between March 2010 and September 2010. Seventy-two patients (58 males, 14 females; mean age: 67±12 years; range, 50 to 89 years) diagnosed with ACS and presenting with STEMI upon admission to the emergency department were included in the study. A STEMI was defined according to the criteria outlined in the consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction.[9] Patients under 18 years of age, pregnant individuals, those with active malignancy or active infection within the last three months, and patients with multiple organ failure were excluded from the study. Adverse clinical outcomes during follow-up included death, reinfarction, and cerebrovascular disease (CVD).

The Killip-Kimball classification (KC) was developed by Killip and Kimball[10] to stratify patients into four groups according to clinical criteria. In the present study, patients were divided into two groups according to the KC: Group 1 consisted of 60 (83.3%) patients with KC-I (no signs of congestion) or KC-II (S3 heart sound and basal rales on auscultation, and Group 2 consisted of 12 (26.7%) patients with KC-III (acute pulmonary edema) or KC-IV (cardiogenic shock).

Complete blood count was performed for all patients at 0, 4, 24, and 48 h after admission. Hemoglobin, hematocrit, WBC count, and neutrophil count data were compared. Analysis was conducted using the Siemens Advia 2120i device (Siemens Healthcare Diagnostics Inc., Tarrytown, USA). Venous blood samples were obtained between 8:00 and 9:00 in the morning following an overnight fasting of 8 to 10 h. Serum glucose, urea, and creatinine levels were analyzed using the Cobas Integra 400 plus device (Roche Diagnostics, Basel, Switzerland). The glomerular filtration rate (GFR) value was determined using the Modification of Diet in Renal Disease criteria.

### Statistical analysis

The data were analyzed using IBM SPSS version 19 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were expressed as frequency. For the comparison of continuous variables showing normal

**Table 1**
Clinical characteristics and risk factors of patients according to adverse clinical outcomes

| | All patients (n=72) | | | Patients without adverse clinical outcome (n=60) | | | Patients with adverse clinical outcome (n=12) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | Mean±SD | n | % | Mean±SD | n | % | Mean±SD | *p* |
| Age (year) | | | 67±12 | | | 58.8±15 | | | 69±10 | **0.01** |
| Sex | | | | | | | | | | |
| Male | 58 | 80.6 | | 50 | 83.3 | | 8 | 66.7 | | 0.386 |
| Hypertension | 35 | 48.6 | | 29 | 48.3 | | 6 | 50 | | 0.579 |
| Family history of coronary artery disease | 15 | 13.9 | | 9 | 15 | | 6 | 26 | | 0.716 |
| Smoke | 31 | 43.1 | | 29 | 48.3 | | 2 | 16.6 | | **0.04** |
| Diabetes mellitus | 28 | 38.9 | | 21 | 35 | | 7 | 58.3 | | 0.435 |
| Hyperlipidemia | 14 | 19.4 | | 13 | 21.6 | | 1 | 8.3 | | 0.835 |
| KC I-II | 60 | 83.3 | | 57 | 95 | | 3 | 25 | | **<0.01** |
| KC III-IV | 12 | 26.7 | | 3 | 5 | | 9 | 75 | | **<0.01** |

SD: Standard deviation; KC: Killip-Kimball classification.

distribution, Student's t-test was used, while for those not showing normal distribution, the Mann-Whitney U test was employed. For the comparison of categorical variables, the chi-square test was used. A *p*-value <0.05 was considered statistically significant.

## RESULTS

Primary percutaneous coronary intervention was performed in 52 (72.2%) of the patients included in the study. Among the patients, 35 (48.6%) had hypertension, 15 (20.83%) had a family history of coronary artery disease, 28 (38.9%) had diabetes mellitus, 31 (43.1%) were smokers, and 14 (19.4%) had hyperlipidemia. Adverse outcomes were identified in 12 (16.7%) patients. Among these, reinfarction occurred in three (4.2%) patients, CVD in two (2.8%) patients, and death in seven (9.7%) patients. In the two patients who developed CVD, the etiology was ischemic in both cases, and no deaths were observed during follow-up (Table 1).

In the evaluation according to the presence of adverse outcomes, A positive relationship was found within the context of age between the two groups (p=0.01), while a negative relationship was observed within the context of smoking status (p=0.04). In patients with KC III-IV upon admission to the coronary intensive care unit, adverse clinical outcomes were significantly higher (p<0.01, Table 1).

White blood cell and neutrophil counts were assessed at 0, 4, 24, and 48 h. A relationship was observed between WBC count at 48 h (p=0.04) and neutrophil count at all time points with adverse clinical outcomes (p<0.05, Table 2).

The relationship between clinical characteristics, hematological parameters, KC scores, and mortality within adverse clinical outcomes was evaluated. A significant relationship was found between advanced age, elevated WBC count at 48 h, elevated neutrophil count at all time points, and mortality (p<0.05). Out of the seven deceased patients, six were in Group 2, while only one patient was in Group 1 (p<0.01, Table 3).

When those with and without adverse clinical outcomes were compared, a positive relationship was observed between elevated blood sugar and creatinine levels, and a negative relationship was observed with GFR (p<0.01, Table 3).

When the patients were compared based on normal and elevated neutrophil levels, neutrophil levels were significantly higher in patients with higher age, creatinine, and KC scores (Table 4).

## DISCUSSION

Acute coronary syndrome is one of the most significant contributors to cardiovascular morbidity and mortality.[11] Inflammation plays a significant role in the development of ACS, according to a study.[12]

**Table 2**
White blood cell and neutrophil parameters of patients according to adverse clinical outcomes

| | Patients without adverse clinical outcome (n=60) | Patients with adverse clinical outcome (n=12) | |
|---|---|---|---|
| | Mean±SD | Mean±SD | *p* |
| 0th hour white blood cell count | 14.400±2.900 | 15.700±6.600 | 0.538 |
| 4th hour white blood cell count | 16.300±3.600 | 15.500±5300 | 0.975 |
| 4th hour white blood cell count | 14.700±3.100 | 16.800±5.900 | 0.753 |
| 48th hour white blood cell count | 11.000±3.980 | 18.800±2.110 | 0.04 |
| 0th hour neutrophil count | 8.988±1.100 | 12.200±1.770 | 0.01 |
| 4th hour neutrophil count | 9.688±528 | 13.100±1.530 | 0.01 |
| 24th hour neutrophil count | 8.510±520 | 14.300±1.570 | 0.04 |
| 48th hour neutrophil count | 7.445±520 | 16.200±1.900 | 0.02 |

SD: Standard deviation.

**Table 3**
Hematological parameters, laboratory data, and KC classification in deceased patients

| | Died (n=7) | | | Alive (n=65) | | | |
|---|---|---|---|---|---|---|---|
| | n | % | Mean±SD | n | % | Mean±SD | *p* |
| Age (year) | | | 71.5±9.8 | | | 59.5±15 | 0.01 |
| Sex | | | | | | | |
| Male | 5 | 71.4 | | 53 | 81.5 | | 0.579 |
| 0th hour white blood cell count | | | 18.400±6.193 | | | 14.193±7.250 | 0.538 |
| 4th hour white blood cell count | | | 17.910±4.410 | | | 15.500±5300 | 0.975 |
| 24th hour white blood cell count | | | 18.328±4.900 | | | 14.680±2.760 | 0.753 |
| 48th hour white blood cell count | | | 21.100±2.455 | | | 11.300±4.470 | 0.007 |
| 0th hour neutrophil count | | | 14.042±2.437 | | | 9.041±3.681 | 0.01 |
| 4th hour neutrophil count | | | 15.428±3.770 | | | 9.681±4.081 | 0.01 |
| 24th hour neutrophil count | | | 15.742±4.663 | | | 8.792±4.362 | <0.01 |
| 48th hour neutrophil count | | | 18.542±5.543 | | | 7.857±4.554 | <0.01 |
| Glukoz (mg/dL) | | | 301±181.2 | | | 166±99.9 | <0.01 |
| Creatinine (mg/dL) | | | 1.90±1.49 | | | 1.03±0.64 | <0.01 |
| eGFR (mL/min/1.73 m$^2$) | | | 65±12 | | | 50±14 | <0.01 |
| KC I-II | 1 | 9.3 | | 59 | 90.7 | | <0.01 |
| KC III-IV | 6 | 85.7 | | 6 | 9.2 | | <0.01 |

KC: Killip-Kimball classification; SD: Standard deviation; eGFR: Estimated glomerular filtration rate.

**Table 4**
Comparison of clinical findings and laboratory values according to neutrophil counts

| | Normal neutrophil count | | | Increased neutrophil count | | | |
|---|---|---|---|---|---|---|---|
| | n | % | Mean±SD | n | % | Mean±SD | *p* |
| Age (year) | | | 59±6.3 | | | 65±8.7 | 0.03 |
| Sex | | | | | | | |
| Male | 26 | | | 32 | | | 0.584 |
| Creatinine (mg/dL) | | | 1.13±0.94 | | | 1.70±1.59 | 0.005 |
| eGFR (mL/min/1.73 m$^2$) | | | 65±7.8 | | | 53±6.4 | 0.003 |
| KC I-II | 35 | 58.3 | | 25 | 41.7 | | 0.384 |
| KC III-IV | 2 | 16.6 | | 10 | 83.4 | | 0.001 |

KC: Killip-Kimball classification; SD: Standard deviation; eGFR: Estimated glomerular filtration rate.

In this study, a direct correlation was observed between an increase in the WBC, particularly neutrophil count, at the time of diagnosis and during follow-up and adverse clinical outcomes in patients presenting to our emergency department due to STEMI. Adverse clinical outcomes were characterized as mortality, recurrent infarction, and CVD. In our study, the neutrophil count was significantly higher in those who were older and had high KC scores and creatinine levels. Patients with adverse clinical outcomes were older and had higher KC scores. In this group of patients, the neutrophil count was significantly elevated at the time of diagnosis and throughout the short follow-up period. Similarly, when it comes to their relationship with mortality, mortality was higher in those with high neutrophil counts, KC scores, and creatinine.

Acute myocardial infarction (AMI) is a systemic inflammatory disease triggered by acute inflammation. The severity of inflammation correlates with the extent of myocardial infarction. In patients with elevated WBC and neutrophil counts during the course of AMI, a larger infarct size was observed.[13] In the study conducted by Tavares et al.,[14] individuals with higher neutrophil ratios were found to be older, had higher KC scores, had a higher rate of smoking, exhibited more impaired renal function, and experienced a higher rate of hospitalization for all causes. On the other hand, according to a study comparing neutrophil counts and infarct size in patients with AMI, individuals with high neutrophil counts at admission statistically had a significantly larger infarct area.[15] In another study involving 363 patients with AMI, it was observed that individuals with high neutrophil and WBC counts had significantly more extensive infarct areas along with a higher incidence of adverse cardiac endpoints.[16] In our study, adverse clinical outcomes were more prevalent in elderly patients and those with KC scores of III-IV. Similar to the study conducted by Mello et al.,[17] it was observed that mortality rates increased with higher KC scores and age following ACS. The reason for the association between elevated neutrophil counts post STEMI and adverse clinical outcomes may be attributed, as demonstrated in previous studies, to the role of leukocytes, particularly neutrophils, in plaque rupture, reperfusion injury, and remodeling processes in ACS.[18] Furthermore, neutrophils may trigger the occurrence of reinfarction by facilitating platelet neutrophil interactions, thrombus formation, and the continuation of coagulation through the membrane attack complex-1 (CD11b-CD18) pathway.[19] The high neutrophil percentage may also be independently associated with damage occurring in microvascular perfusion. Interactions between neutrophils, platelets, and endothelium in ACS can also lead to cytokine release, which may contribute to microvascular dysfunction.[20] In a study involving 160 patients with non-ST-elevation ACS, it was found that cases with high neutrophil counts upon admission to the hospital had a statistically higher incidence of death, acute heart failure, and recurrent myocardial infarction.[21] In our study, patients in the group with high neutrophil counts had higher creatinine levels and lower GFR. Similar to our study, in a study conducted, impaired renal function resulted in increased mortality and prolonged intensive care unit stay in patients undergoing reperfusion therapy after STEMI.[22]

The most significant limitation of the study is the small number of participants. Additionally, two different reperfusion strategies were applied to the patients. Pharmacological reperfusion was attained through the administration of thrombolytic therapy, whereas mechanical reperfusion was achieved through primary percutaneous coronary intervention. These two methods have different effects on systemic inflammation. In our study, the majority of patients underwent primary percutaneous coronary intervention treatment.

In conclusion, a correlation was determined between WBC and neutrophil counts and the rates of in-hospital mortality and adverse clinical consequences in individuals presenting with acute STEMI. There are numerous studies conducted on the WBC count in patients diagnosed with ACS, including AMI. However, the number of studies examining the relationship between neutrophil count and adverse clinical outcomes is limited. Elevated neutrophil count assessed upon admission to the hospital and during short-term follow-up may be utilized to identify high-risk patients.

**Ethics Committee Approval:** The study protocol was approved by the Eskişehir Osmangazi University Faculty of Medicine Ethics Committee (date: 21.05.2010, no: PR-10-03-19-09). The study was conducted in accordance with the principles of the Declaration of Helsinki.

**Patient Consent for Publication:** A written informed consent was obtained from each patient.

**Data Sharing Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Author Contributions:** Idea/concept, data collection and/or processing, literature review, writing the article, critical review, references and fundings, materials: M.İ.D.; Design, control/supervision, analysis and/or interpretation: M.İ.D., A.Ü.

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