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RESEARCH LETTER

# Adverse Outcomes in Non-ST-Elevation Acute Coronary Syndrome: A Cluster Analysis Study

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Patients with non-ST-elevation acute coronary syndrome (NSTE-ACS) have diverse clinical trajectories and form a heterogeneous group [1]. They exhibit differences in clinical and angiographic findings, laboratory parameters including platelet function, and the severity of concomitant pathology. These variations affect their clinical courses and prognosis [1, 2]. This study examined patients with NSTE-ACS, identified groups with differing laboratory parameters, and performed k-means clustering on clinical, laboratory, and angiographic data.

The study involved 116 patients with NSTE-ACS, primarily with low risk (GRACE 111 ± 25), most of whom were men (64%). The mean age was 64 ± 10 years. Baseline characteristics, including routine laboratory data, were recorded at admission. Platelet reactivity was measured 3–5 days after admission (post-PCI) through detection of p-selectin expression. P-selectin (CD62P) expression on platelet surfaces was measured with a BD FACSCalibur flow cytometer before and after activation with 20 µmol/L ADP, as a percentage of CD62P+ events. The primary outcome was defined as a composite event including all-cause mortality, non-fatal myocardial infarction, or unstable angina recurrence. Follow-up was conducted by telephone 6 months after discharge. Ninety-four clinical and laboratory characteristics were analyzed. Cluster analysis was performed with the k-means method, and a predictive model was developed with logistic regression.

**What is the scientific question being addressed?**

**The heterogeneity of NSTE-ACS and the gaps in the evidence base by investigating patient profiles related to clinical, laboratory, and angiographic factors, and how these profiles affect clinical outcomes.**

**What is the main novel finding?**

**The identification of discrete patient clusters within the NSTE-ACS cohort provides a basis for risk assessment and the development of tailored treatment strategies.**

We evaluated the overall data structure for cluster analysis, examining clinical data, coronary angiography results, and clinical and biochemical blood tests, covering 94 parameters, including platelet functional activity (P-selectin expression). Factors for clustering were chosen according to the highest intragroup variation coefficient values and clinical significance. All indicators were selected to avoid significant correlations. The factors included in the cluster analysis were hemoglobin level, Charlson comorbidity index, platelet function (P-selectin expression), and stent length. Cluster analysis revealed three clusters based on the chosen parameters and containing differing numbers of patients (Figure 1).

The clusters had the following features. The first cluster had a favorable disease course (shortest stent length, low comorbidity, low P-selectin, and high

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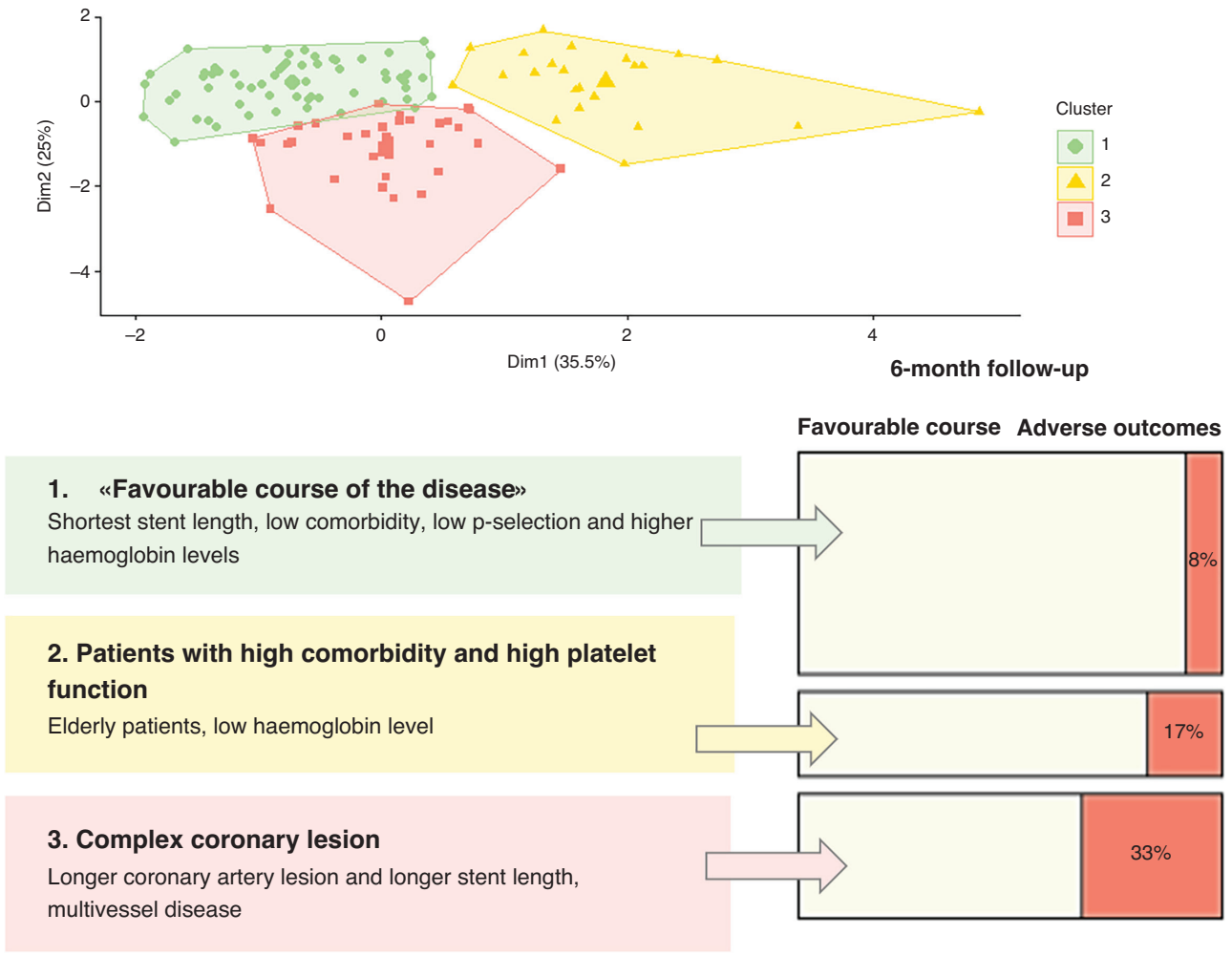


**Figure 1** Clusters of Patients with Non-ST Segment Elevation Acute Coronary Syndrome.

hemoglobin levels). The second cluster had high comorbidity, high platelet function, and low hemoglobin levels. The third cluster had relatively longer, more complex coronary artery lesions and longer stent lengths. The three clusters did not differ in NSTE-ACS structure (ratio of myocardial infarction and unstable angina) or initial severity, measured according to the GRACE score as follows: 102 (88; 110) vs. 125 (119; 141) vs. 116 (102; 133). Platelet counts were within reference values and did not differ among clusters, as follows: 218 (192; 248) vs. 200 (180; 233) vs. 236 (184; 257). However, differences were observed in platelet function, and P-selectin expression was significantly elevated in the second cluster, as follows: 4.1 (1.6; 7.9) vs. 17.6 (9.2; 22.6) vs. 3.6 (2.6; 8.5), $P < 0.05$. During the 6-month follow-up, 20 adverse outcomes were recorded. Six events occurred during hospitalization and were classified as myocardial infarction type 4A. The remaining 14 events were cardiovascular events (myocardial infarction or unstable angina) occurring during follow-up. No cases of cardiac death, including sudden death, were reported. Adverse outcomes were more frequent in the second (17%) and third (33%) clusters ($P = 0.008$) than the first cluster (8%).

A logistic regression model was developed to predict adverse outcomes according to the results of the analysis. The model included hemoglobin level, P-selectin expression, Charlson comorbidity index, stent length, and the presence of multivessel coronary lesions. ROC analysis revealed an AUC of 0.80, indicating sufficient accuracy, and a sensitivity of 80% and specificity of 78%.

NSTE-ACS encompasses a broad range of clinical conditions with multiple pathogenetic variants, thus resulting in various clinical manifestations. Prognosis varies and is influenced by clinical

manifestations, angiographic features, and comorbid conditions. Several studies have shown the benefits of using combined risk scales integrating clinical, laboratory, and instrumental parameters for comprehensive prognosis assessment [1].

The pathogenesis and clinical course of NSTE-ACS are due primarily to coronary artery lesions, associated with lipid metabolism disorders, chronic inflammation, oxidative stress, and endothelial dysfunction. These pathophysiologic changes are reflected in clinical and biochemical blood tests. Anemia, dyslipidemia, and prothrombotic states are associated with poor prognosis. Severe arterial lesions indicate a less favorable prognosis. Thus, multivessel disease in ACS is associated with poorer outcomes [3]. Comorbidities also significantly influence prognosis. In a Swedish cohort study, cardiovascular and non-cardiovascular multimorbidity have been found to double the risk of cardiovascular events in the year following an acute coronary syndrome [4]. Recurrent ischemic events, stent thrombosis, and bleeding are common ACS complications occurring both early and over the long term. Thus, prognosis substantially depends on the condition of the platelet hemostasis system. Changes in platelet function in people with cardiovascular disease are often caused by metabolic disorders, such as obesity, insulin resistance, dyslipidemia, and hyperglycemia. These comorbidities are associated with increased cardiovascular disease risk factors. Thus, a potential link between comorbid pathology and thrombosis has been suggested in these individuals [5].

Understanding the variability in clinical outcomes and identifying key prognostic factors are crucial for personalized care. Forming distinct clusters and analyzing their outcomes can improve risk stratification and aid in the development of more targeted therapeutic strategies for patients with NSTE-ACS. This approach is aimed at enhancing prognostic accuracy and optimizing clinical management, and ultimately improving patient outcomes.

## Data Availability Statement

The data presented in this study are available from the corresponding author upon reasonable request.

## Ethics Statement

The study was approved by the local ethics committee under ethical approval No. 2312-21-02. All patients provided informed consent before participating in the study.

## Author Contributions

D. N. Nedbaeva collected and provided clinical information, conducted statistical analysis, and wrote the original draft. V. S. Mikhaleva contributed to data collection and patient follow-up. G. A. Kukharchik designed the study, reviewed and edited the manuscript, and performed critical revision. All authors have read and approved the final manuscript.

## Conflicts of Interest

All authors declare that they have no competing interests.

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