Relationship between autophagy and complete blood count in patient with acute myocardial infarction

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Abstract

Autophagy is a self-protective mechanism of living cells or organisms under various stress conditions. In this study level of autophagy enzyme in patients with coronary artery disease are measured. Then we investigated to effects of autophagy on the hematologic parameters. 66 patients were included in our study. Participants were separated 2 groups: Group 1- patients with acute myocardial infarction (n=36); and Group 2- normal controls patients (n=30). Blood samples of all patients were collected during coronary angiography process. The enzyme-linked immunosorbent assay (ELISA) kit for autophagy related protein 5(ATG5) in the plasma was studied for these two groups of blood sample. Then autophagy level and complete blood count were compared. Age, gender, prevalence of diabetes mellitus, body-mass-index (BMI) and dyslipidemia were similar between the groups. Autophagy levels are significantly different between the groups (11.7±3.4 ng/ml; 7.5±3ng/ml ; p < 0.001, respectively). Significant positive correlations were found between level of autophagy and white blood cell count (r = 0.491, p < 0.001), neutrophil /lymphocyte ratio ( r=0.287 , p=0.019). Significant negative correlations were found between level of autophagy and ejection fraction (r = -0.427, p < 0.001). In the present study, the autophagy levels were higher in the patients with coronary artery disease than healthy controls. Serum autophagy levels demonstrated a significant positive correlation with white blood cell count and neutrophil/lymphocyte ratio. An increased autophagy level may be considered as an important activator and marker of the atherosclerotic inflammatory process in CAD.

Keywords: Acute myocardial infarction ,autophagy, complete blood count

Introduction

Coronary artery disease (CAD) is a leading cause of death worldwide, which is characterized by different manifestations such as acute myocardial infarction (AMI) and chronic coronary total occlusion.

It is unclear how acute or chronic ischemic events activate and affect autophagy. Previous studies show that autophagy in the ischemic phase is protective because of an adaptive response of the heart [1-4]; these were animal studies and were designed by acute ischemic events. However, a comparison of autophagy levels in patients with AMI has not been studied thoroughly.

Complete blood count (CBC) is the most widespread tests in clinics. Many different studies have demonstrated that the efficiency of CBC parameters to estimate various disease of severity and mortality risk such as neutrophil/lymphocyte ratio(NLR) and platelet /lymphocyte ratio (PLR) [6-10].

In our study, we aimed to investigate the role of autophagy in AMI and we also investigated relationship between autophagy and complete blood count in patient with acute myocardial infarction.

Materials and Methods

Study design
This study was a prospective observational controlled study.

Study populations
66 consecutive patients evaluated at a university hospital and diagnosed as having at least one major acute total occlusion of the coronary artery were included in this study. The number of study participants was based on power analysis. All participants were evaluated during coronary angiography (CAG). Participants were divided into two groups: group 1 included patients with acute myocardial infarction (n = 36); and group 2 included normal controls (n = 30). Participants in groups 2 had a ischemic test result.
Patients in group 1 had ST-segment elevated myocardial infarction and underwent primary percutaneous intervention (PCI). PCI in these patients was performed within 3 hours after the symptoms started, and there were no signs of infection. Furthermore, patients with uncontrolled hypertension, renal dysfunction, autoimmune diseases, thyroid disorders, or history of coronary artery disease (CAD) were not included. The study was performed according to the principles of the Declaration of Helsinki, and its protocol was confirmed by Istanbul Bilim University Ethics Committee. Informed consent forms were taken for all participants.

**Biochemical measurements**

After CAG, approximately 2 mL of blood was drawn from the median cubital veins from each patient and collected into EDTA tubes. In addition, blood samples of all participants were collected during the coronary angiography process. All samples were centrifuged, and plasma samples were stored at −80°C. The enzyme-linked immunosorbent assay (ELISA) kit for autophagy-related protein 5 (ATG5) in the plasma was studied. ATG5 evaluated two times for all samples and we used mean value. Biochemical and hematological parameters were studied on the same day. We measured red blood cell distribution width (RDW), platelet, mean platelet volume (MPV), hemoglobin and some ratios like NLR and PLR.

**Coronary angiography analysis**

All patients underwent CAG by the Judkins technique via a femoral approach. During the procedure, images were recorded at a speed of 15 square/s on a digital angiographic system (ACOM. PC; Siemens AG, Germany). Our contrast agent was Iopromide. The recordings were studied by two cardiologists. CAD severity was determined on the basis of the Gensini score [11].

**Statistical analysis**

SPSS for Windows version 17.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. All continuous variables were defined as mean ± SD, and categorical variables were described as percentages. In addition, categorical data were compared using a chi-square test, and continuous variables were compared between the groups using Student t test, Shapiro–Wilk test was used whether they were distributed normally. Finally, Pearson and Spearman correlation analysis was used to estimate the relationship between the test parameters, and p value of < 0.05 accepted to be statistically significant.

**Results**

Overall, 66 participants were included in our study. Baseline clinical, demographic, and echocardiographic parameters of the participants are listed in Table 1. Age, sex, BMI, smoking, dyslipidemia and type of myocardial infarction were similar among the three groups; however, hypertension was different between the groups (p = 0.026).

The results of the left ventricular (LV) echocardiographic and hematologic parameters were significantly different between the groups (Table 1), particularly LV end-diastolic diameter (50.5 ± 5.1, 47.6 ± 3.5 mm, respectively; p = 0.011), LV end-systolic diameter (36.6 ± 5.7, and 31.7 ± 3.6 mm, respectively; p < 0.001), ejection fraction (46.6 ± 6.7, and 58 ± 1.7, respectively; p < 0.001), left atrial diameter (40.9 ± 3.6 mm, 39.1±2.4 ; p= 0.018) white blood cells counts (11,943 ± 2828, and 7145 ± 1623, respectively; p < 0.001), neutrophil /lymphocyte ratio ( 5±4.2 and 2.1±1.3 ; p< 0.001) and hemoglobin (14.2 ± 1.7, and 12.9 ± 1.1; p < 0.001).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Acute TO (n=36)</th>
<th>Controls (n=30)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>58.6±5.8±5.4</td>
<td>60.1±10</td>
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<td>Gender, female/male</td>
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<td>10/20</td>
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<td>BMI, kg/m2</td>
<td>26.2±2.9</td>
<td>27±1.6</td>
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<td>Dyslipidemia, n (%)</td>
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<td>19(63)</td>
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<td>Hypertension, n (%)</td>
<td>28(77)</td>
<td>29(96)</td>
<td>0.026</td>
</tr>
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<td>Diabetes, n (%)</td>
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<td>12(40)</td>
<td>0.891</td>
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<td>Smokers, n (%)</td>
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<td>17(56)</td>
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<td>WBC</td>
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<td>7145±1623</td>
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</tr>
<tr>
<td>Hemoglobin</td>
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<td>0.001</td>
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<tr>
<td>Platelet</td>
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<td>26000±51652</td>
<td>0.938</td>
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<td>Neutrophil</td>
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<td>4267±1487</td>
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<td>MPV</td>
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<td>10.1±0.6</td>
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<td>124±58</td>
<td>0.689</td>
</tr>
<tr>
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<td>Autophagy</td>
<td>11.7±3.4</td>
<td>7.5±3</td>
<td>0.001</td>
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</table>

BMI, body mass index; IVS, interventricular septum; LA, left atrium; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; MPV; mean platelet volume, RDW; Red Cell Distribution Width; PW, posterior wall; WBC, white blood cell count.

Autophagy levels were significantly different between the groups (11.7 ± 3.4, and 7.5 ± 3 ng/ml; p < 0.001) (Figure 1).

![Figure 1. Autophagy levels of groups](image)
Significant positive correlations were found between level of autophagy and WBC (r = 0.491, p < 0.001), NLR (r = 0.287, p = 0.019). Significant negative correlations were found between level of autophagy and ejection fraction (r = -0.427, p < 0.001).

Discussion

Our study demonstrated that autophagy levels were higher in the CAD. In addition, serum autophagy levels have a significant positive correlation with white blood cell count and neutrophil/lymphocyte ratio. We didn’t find PLR different between the groups. An increased autophagy level may be considered an valuable activator and marker of the atherosclerotic process in CAD.

During the acute myocardial infarction neutrophils secrete inflammatory mediators. Then they may make plaques more vulnerable through the release of proteolytic enzymes, arachidonic acid derivatives, and superoxide radicals [12]. We are not sure about the etiology or significance of autophagy during the acute and chronic stages of CAD. Previously conducted animal studies revealed that autophagy protects the heart during the acute ischemic phase [1-4]. Both previous studies as well as our current study show that autophagy is activated in acute ischemic heart disease, following ischemia-reperfusion injury and in hibernating myocardium [13-17]. In addition, positive correlation between the autophagy and NLR shows that neutrophils work the process of autophagy.

Similar results were seen in other studies, with increased autophagy levels in cases of heart failure [18], cardiac hypertrophy [19], and ischemic cardiomyopathy [13]. In addition, autophagy occurred constitutively in the normal myocardium. Insufficient autophagy or its defects causes the myocardium to perform poorly, and inhibition of starvation-induced autophagy results in cardiac dysfunction and dilatation [20]. We found a significant negative correlations between level of autophagy and ejection fraction. It shows that autophagy may protect the body.

Although neutrophils and platelet have a role during AMI, we found only the relationship of NLR and autophagy in contrast to PLR. Therefore, our study has small population. Because previous studies revealed that PLR and acute coronary syndromes have relationship such as a prognostic factor and severity of coronary artery disease [9,21].

We found that LV echocardiographic and hematologic parameters were significantly different between the groups. Both differences of hematologic parameters and structural parameters of the heart can be responsible for different autophagy levels. In addition, several mechanism may also effect the autophagy levels such as age, diabetes mellitus and hypertension.

Finally, microbiological studies revealed that autophagy is the basic component of the body and its activation is complex and incompletely understood, leading to the activation of a wide range of signaling pathways [22-25].

Study Limitation

Our study was a single-center study that included a small study population. Furthermore, extensive studies with a large patient cohort are warranted in the future to overcome these limitations.

Conclusion

We demonstrated that CAD patients have increased autophagy values. Serum autophagy levels demonstrated a significant positive correlation with white blood cell and neutrophil/lymphocyte ratio. An increased autophagy level may be accepted as an valuable activator and marker of the atherosclerotic process in CAD.

Competing interests

The authors declare that they have no competing interest

Financial Disclosure

The financial support for this study was provided by the investigators themselves.

Ethical approval

Before the study, permissions were obtained from local ethical committee.

Reference


