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Research Article

# Monocyte to high-density lipoprotein and derived neutrophil to lymphocyte ratio in patients with acute pancreatitis are associated with the severity of the disease

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## Abstract

**Objectives:** We aimed to compare the severity of the disease with derived neutrophil to lymphocyte ratio (DNLR) and monocyte to high-density lipoprotein ratio (MHR) in patients with acute pancreatitis (AP).

**Methods:** This retrospective study included 52 patients with Ranson 0, 57 patients with Ranson I, 39 patients with Ranson II, 36 patients with Ranson III–IV, and 20 healthy controls as the control group with similar demographic characteristics to the patient groups. Demographic characteristics, mortality, etiology, and laboratory data of the patients were evaluated from their previous records.

**Results:** The study data were compared in five groups as control and Ranson 0, I, II, III–IV according to their AP stage. MHR values were 9.62±4.25 in the control group and 13.4±5.18, 14.2±4.22, 19.4±10.5, 31.7±26.3 in Ranson 0, I, II, III–IV, respectively ($p<0.001$). DNLR was 1.33±0.45 in the control group and 3.48±2.68, 3.71±2.31, 4.43±2.84, 4.62±3.46 in Ranson 0, I, II, III–IV, respectively ($p<0.001$). MHR and DNLR values were significantly different in patients with AP.

**Conclusion:** The levels of MHR and DNLR evaluated during the follow-up of patients with AP are low-cost and easy to access parameters that may help the clinician in determining the severity of the disease.

**Keywords:** Cholesterol, HDL, lymphocytes, monocytes, neutrophil, pancreatitis

Acute pancreatitis (AP) is a clinical manifestation caused by activation of digestive enzymes and digestion of the pancreatic tissue and surrounding tissues, and consequently leading to widespread inflammation, local, regional, and systemic reflections, and complications in the organism. While most patients have a self-limiting disease, 15%-20% of patients have high morbidity and mortality caused by an exaggerated systemic inflammatory response related to multiorgan failure. AP is seen in 80%-85% as a mild-moderate and 15%-20% as a severe disease [1]. Approximately one-third of AP-related deaths occur in the first week of the disease due to systemic causes leading to progressive organ failure. Deaths after the second week of hospitalization are usually because of local complications [2]. Inflammation and cytokines have an effect on the pathogenesis of the disease. Infected cells and systemic immune cells secrete cytokines such as tumor necrosis factor-alpha, interleukins such as IL-1, IL-2, IL-6, IL-8, IL-10, and platelet-activating factor during inflammation. These cytokines increase capillary permeability, leukocyte adherence, and extravasation, leading to the aggravation of AP and causing systemic complications [3].

During the synthesis and release of proinflammatory and prooxidant cytokines, the monocytes and macrophages play a role. Activation of monocytes is important at the onset of in-

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flammation [4, 5]. High-density lipoprotein (HDL) cholesterol is known to save the endothelium from theharmful effects of low-density lipoprotein (LDL) cholesterol and to inhibit its oxidation [6, 7].

Monocyte to high-density lipoprotein ratio (MHR) and derived neutrophil to lymphocyte ratio (DNLR) are novel indicators of inflammation and oxidative stress and have been shown to be closely related to the presence and prognosis of some inflammatory diseases [8-10]. In some studies on AP, monocyte levels were found to be increased, and in some studies, serum lipid levels were found to be decreased [11-13]. However, there are no studies about MHR.

DNLR is calculated as neutrophil/(leukocyte-lymphocyte) formula and can be interpreted as an indirect indicator of the immune response capacity. So far, its prognostic role in malignancies such as breast, ovary, colon, urothelium, pancreas, and kidney has been discussed [14]. However, no study was conducted on AP severity and DNLR.

In our study, we aimed to compare the severity of the disease, the duration of hospitalization, the treatment modalities, the mortality status, the etiology, biochemical values, DNLR, and MHR of the patients who had been diagnosed with AP.

## Materials and Methods

In our study, patients who were admitted to our clinic and diagnosed with AP between September 2017 and July 2019 were evaluated. Ethical approval was obtained from the ethics committee of Cukurova University, Faculty of Medicine (October 5, 2018, meeting number: 81, decision number: 44). This study was carried out in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. A total of 234 AP patients were reviewed.

The criteria used for the diagnosis of AP are abdominal pain, amylase or lipase levels exceeding 3 times the normal, and ultrasound or computed tomography (CT) with AP-specific findings. Two of these criteria are sufficient for diagnosis. When Ranson criteria are used, 5 criteria are taken into account when in the first 24 h of admission to nonbiliary and biliary AP (Table 1), and each criterion for nonbiliary or biliary AP counts as one point.

Patients with a score of ≥3 are considered to be having severe pancreatitis. Patients with acute and chronic infection, chronic pancreatitis, acute and chronic hepatitis, chronic obstructive pulmonary disease, heart failure, coronary artery disease, malignancy, rheumatic diseases, and patients with thyroid dysfunction before the diagnosis of AP were not included in the study.

The demographic characteristics, length of stay, treatment modalities, mortality, etiology, and laboratory data of the patients with remaining 184 AP patients were analyzed. Laboratory data of blood urea nitrogen (BUN), glucose, creatinine, sodium (Na), calcium (Ca), potassium (K), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), aspartate aminotransferase (AST), gamma glutamyl tranferase (GGT), alkaline phosphatase (ALP), high-sensitivity C-reactive protein (hs-CRP), lipid panel and white blood cell (WBC) and red blood cell from complete blood count, mean corpuscular volume, mean platelet volume, hematocrit (HCT), hemoglobin, platelet (PLT), neutrophil (NE #), lymphocyte (LY #), and monocyte (MON #) levels were evaluated for the study. Complete blood count and biochemical parameters of the patients included in the study were analyzed by the standard automated laboratory method (Abbott Aeroset, MN, USA) and using appropriate commercial kits (Abbott). The scores of the patients according to the Ranson criteria at their admission and their MHR and DNLR in the peripheral blood count were calculated, and participants were divided into two groups as patients who received antibiotics and nonreceivers as treatment, thus divided into subgroups as idiopathic, alcoholic, gallstone, hyperlipidemia, drug-induced cancer, and pancreatic cancer for AP etiology.

**Table 1. Ranson criteria**

| Parameters | Biliary AP | Nonbiliary AP |
|---|---|---|
| Age | >70 | >55 |
| Leukocyte count (µl) | >18 000 | >16 000 |
| Glucose (mg/dL) | >220 | >200 |
| LDH (U/L) | >400 | >350 |
| AST (U/L) | >250 | >250 |

AP: Acute pancreatitis; LDH: Lactate dehydrogenase; AST: Aspartate aminotransferase.

### Statistical analysis

For the statistical analyses SPSS 22.0 statistical software pack (Chicago, IL, USA) was used. Categorical and continuous variables were determined. The Kolmogorov-Smirnov test was used for normal distribution of the continuous variables. Categorical variables were expressed as percentages and numbers, while the continuous variables were expressed as mean±standard deviation. Continuous variables that showed normal distribution were compared using ANOVA, whereas the Kruskal-Wallis test was used for samples without normal distribution. The groups and their statistical comparisons are shown in Tables 1-5. The Chi-squared test was used for the comparison of categorical variables. Except for the parameters used in Ranson criteria, in univariate analyses, in patients with Ranson > 3, to determine the independent markers, a logistic regression analysis was performed. Pearson's and Spearman's correlation analyses were used to determine the parameters associated with MHR. The parameters having the closest association with the MHR were determined using the linear regression analysis. Optimal cutoff points of MHR, DNLR, and hs-CRP were determined using a receiver operator characteristic (ROC) curve analysis. For the statistical significance, a p-value of <0.05 was considered.

**Table 2. Comparison of clinical, demographic, and laboratory values according to study groups**

| Variable | Control (n=20) | | RANSON 0 (n=52) | | RANSON I (n=57) | | RANSON II (n=39) | | RANSON III-IV (n=36) | | p |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % | n | % | |
| Age (years) | 53.2±10.9 | | 39.2±13.7$^{\alpha,\beta,*}$ | | 54.7±13.1 | | 55.1±20.6 | | 59.2±15.7 | | **<0.001** |
| Sex (male/female) | 8/12 | | 26/26 | | 24/33 | | 20/19 | | 13/23 | | 0.336 |
| Hospitalization (days) | - | | 4.3±2.8α | | 4.9±3.1 | | 5.4±4.5 | | 7.8±7.9 | | **<0.001** |
| Antibiotherapy | - | | 25 | 48$^{\alpha}$ | 36 | 63 | 25 | 64 | 27 | 75 | **0.031** |
| Mortality | - | | 1 | 2 | 0 | 0 | 3 | 8 | 1 | 3 | 0.858 |
| Etiology | | | | | | | | | | | |
| Idiopathic | - | | 17 | 33 | 16 | 28 | 9 | 23 | 8 | 22 | 0.318 |
| Stone | - | | 24 | 46 | 36 | 63 | 21 | 54 | 20 | 56 | |
| Pancreas cancer | - | | 1 | 2 | 1 | 2 | 2 | 5 | 1 | 3 | |
| Alcohol | - | | 5 | 10 | 1 | 2 | 0 | 0 | 3 | 8 | |
| Hyperlipidemia | - | | 3 | 6 | 2 | 4 | 6 | 15 | 4 | 11 | |
| Drug | - | | 2 | 4 | 1 | 2 | 1 | 2 | 0 | 0 | |
| Glucose (mg/dL) | 89±5.9$^{\&}$ | | 112±24$^{\alpha,\beta}$ | | 125±47 | | 147±50 | | 155±65 | | **<0.001** |
| BUN (mg/dL) | 25.9±4.6$^{\&}$ | | 25.5±9.9$^{\alpha,\beta}$ | | 30.2±13.7 | | 38.0±21.6 | | 42.9±38.3 | | **0.001** |
| Creatinine (mg/dL) | 0.56±0.08$^{\&}$ | | 0.65±0.17$^{\alpha,\beta}$ | | 0.72±0.28 | | 0.98±0.56 | | 1.22±1.12 | | **0.003** |
| Na (mmol/L) | 140±3.3 | | 139±2.9 | | 140±5.5 | | 138±4.7 | | 137±3.5 | | 0.164 |
| K (mmol/L) | 4.2±0.3 | | 4.1±0.5 | | 4.2±0.6 | | 4.2±0.5 | | 4.4±0.5 | | 0.115 |
| LDH (U/L) | 119±51$^{\&}$ | | 179±54$^{\alpha,\beta}$ | | 204±118 | | 260±130 | | 317±165 | | **<0.001** |
| AST (U/L) | 28.9±5.2$^{\&}$ | | 78.7±82.4$^{\alpha}$ | | 108±132$^{¥}$ | | 169±171 | | 289±418 | | **<0.001** |
| ALT (U/L) | 24.0±4.9$^{\&}$ | | 96.2±143$^{\alpha}$ | | 120±217 | | 165±222 | | 203±247 | | **0.006** |
| GGT (U/L) | 27.4±6.2$^{\&}$ | | 155±204$^{\alpha}$ | | 188±276 | | 264±322 | | 286±309 | | **0.003** |
| ALP (U/L) | 64.9±18.4$^{\&}$ | | 112±57.2 | | 129±98.1 | | 135±77.4 | | 155±95.2 | | **0.001** |
| HDL (mg/dL) | 56.1±7.7$^{\&}$ | | 47.6±12.8 | | 43.2±13.2 | | 41.9±12.7 | | 37.0±11.1 | | **0.001** |
| hs-CRP (mg/dL) | 0.20±1.6$^{\&}$ | | 2.15±3.12$^{\alpha,\beta,*}$ | | 4.53±6.5$^{¥}$ | | 5.16±5.92$^{:}$ | | 5.98±4.50 | | **<0.001** |

$^{\alpha}$: Significant association between the Ranson 0 group and Ranson III–IV group (p<0.05); $^{\beta}$: Significant association between the Ranson 0 group and Ranson II group (p<0.05); *: Significant association between the Ranson 0 group and Ranson I group (p<0.05); $^{:}$: Significant association between the Ranson II group and Ranson III–IV group (p<0.05); $^{\&}$: Significant association between the control group and acute pancreatic groups (p<0.05); $^{¥}$: Significant association between the Ranson I group and Ranson III–IV group (p<0.05). BUN: Blood urea nitrogen; LDH: Lactate dehydrogenase; Na: Sodium; K: Potassium; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; GGT: Gamma glutamyl tranferase; ALP: Alkaline phosphatase; HDL: High-density lipoprotein; hs-CRP: high-sensitivity C-reactive protein.

## Results

The study data were compared in five groups as control and Ranson 0, I, II, III-IV groups according to their AP stage. In the same analysis, subgroup analysis values were determined separately for the parameters that were different according to the AP stage.

When AP patients were compared among themselves, the mean age was found to be the lowest in the Ranson 0 patient group, and it was found to be significantly different from all other stages (p<0.001, Table 2). Ranson III-IV patients were found to be more frequently treated with antibiotics and hospitalized for a longer period of time. Glucose, BUN, creatinine, LDH, and hs-CRP levels increased from Ranson 0 group to Ranson III-IV group, and it was significantly higher in Ranson II and III-IV groups than Ranson 0 group. AST, ALT, and GGT levels were also increased in Ranson III-IV group, and a significant difference was detected between Ranson III-IV and Ranson 0 groups. Serum HDL levels decreased with increasing Ranson stage (Table 2).

In our study, gender, mortality, and etiology parameters of the control and AP groups were similar. All parameters except the Na and K values were different between the two groups (Table 2).

In patients with AP, hematologic parameters WBC, NE #, MON # values, and MHR and DNLR levels were higher. The MON # level was only different between the Ranson III-IV and Ranson 0 groups (Table 3). MHR and DNLR were significantly higher in the Ranson III-IV patient group, and there was a significant difference between all other Ranson stages (0-I-II) (p<0.001, for each, Table 3).

Except for the parameters used in the Ranson criteria, logistic regression analysis was performed for the parameters that were significant in the univariate analysis of the AP patients. As a result of this analysis, it was found that MHR, DNLR, and hs-CRP levels independently determined the presence of AP (p<0.001, p=0.014, and p=0.010, respectively, Table 4). According to this analysis, it was found that odds ratios were 1.136, 0.126, and 1.107 in MHR, hs-CRP, and DNLR, respectively

**Table 3. Comparison of laboratory values according to study groups**

| Variable | Control (n=20) | RANSON 0 (n=52) | RANSON I (n=57) | RANSON II (n=39) | RANSON III–IV (n=36) | p |
|---|---|---|---|---|---|---|
| WBC ($\times10^3$ $\mu L^{-1}$) | 6.5±1.6[&] | 10.8±2.8 | 11.3±3.9 | 12.9±5.6 | 11.8±4.6 | **<0.001** |
| RBC ($\times10^6$ $\mu L^{-1}$) | 4.5±0.41 | 4.7±0.62 | 4.7±0.7 | 4.9±0.8 | 4.8±0.8 | 0.386 |
| HGB (g/dL) | 12.9±0.9 | 13.6±2.0 | 12.9±1.9 | 13.5±2.1 | 13.5±2.3 | 0.309 |
| HCT (%) | 40.0±5.6 | 41.0±5.5 | 39.7±5.4 | 41.0±5.8 | 40.7±6.7 | 0.517 |
| MCV (fL) | 86.5±3.2 | 87.5±7.3 | 86.1±9.6 | 85.6±10.4 | 87.3±9.8 | 0.849 |
| PLT ($10^3$ $\mu L^{-1}$) | 284±35 | 257±66 | 260±87 | 296±170 | 252±84 | 0.257 |
| NE# ($10^3$ $\mu L^{-1}$) | 3.6±1.1[&] | 7.9±3.0 | 8.7±3.8 | 10.1±5.1 | 9.3±4.7 | **<0.001** |
| LY# ($10^3$ $\mu L^{-1}$) | 2.11±0.62 | 1.96±0.81 | 1.74±0.80 | 1.91±1.31 | 1.74±0.98 | 0.465 |
| MON# ($10^3$ $\mu L^{-1}$) | 0.52±0.20[&] | 0.61±0.21[α] | 0.64±0.24 | 0.76±0.35 | 0.97±0.51 | **<0.001** |
| MPV (fL) | 8.2±0.65 | 8.8±1.01 | 8.8±0.88 | 8.8±1.1 | 8.8±1.11 | 0.284 |
| MHR (µL/mg/dL) | 9.62±4.25[&] | 13.4±5.18[α] | 14.2±4.22[¥] | 19.4±10.5[‡] | 31.7±26.3 | **<0.001** |
| DNLR | 1.33±0.45[&] | 3.48±2.68[α] | 3.71±2.31[¥] | 4.43±2.84[‡] | 4.62±3.46 | **<0.001** |

[&]: Significant association between the control group and acute pancreatic groups (p<0.05); [α]: Significant association between the RANSON 0 group and RANSON III–IV group (p<0.05); [¥]: Significant association between the RANSON I group and RANSON III–IV group (p<0.05); [‡]: Significant association between the RANSON II group and RANSON III–IV group (p<0.05). WBC: White blood cell; RBC: Red blood cell; HGB: Hemoglobin; HCT: Hematocrit; MCV: Mean corpuscular volume; PLT: Platelet; NE#: Neutrophil; LY#: Lymphocyte; MON#: Monocyte; MPV: Mean platelet volume; MHR: Monocyte to HDL ratio; DNLR: Derived neutrophil to lymphocyte ratio.

(Table 4). A similar analysis was found with the ROC curve, and the area under the ROC curve was 0.682, 0.595, and 0.552 in MHR, hs-CRP, and DNLR, respectively ($p < 0.001$, $p = 0.006$, $p = 0.007$, respectively, Table 5 and Fig. 1). When the cutoff values of MHR, hs-CRP, and DNLR were taken as 17 µL/mg/dL, 5.90 mg/dL, and 6.30, respectively, Ranson III-IV patients were identified with a sensitivity/specificity of 75.0%/72.0%, 65.0%/62.0%, and 41.0%/34.0%, respectively (Table 5).

**Table 4. Independent parameters for the occurrence of Ranson III–IV**

| Ranson III–IV | Odds ratio | 95% confidence interval | p |
|---|---|---|---|
| MHR | 1.136 | 1.065-1.212 | <0.001 |
| hs-CRP | 0.126 | 0.055-0.221 | 0.014 |
| DNLR | 1.107 | 1.103-1.115 | 0.010 |

MHR: Monocyte to HDL ratio; hs-CRP: High-sensitive C-reactive protein; DNLR: Derived neutrophil to lymphocyte ratio.

## Discussion

Our study showed that in patients with severe AP, MHR and DNLR levels are independent predictors of the severity of the disease. The levels of MHR, DNLR, and hs-CRP evaluated during the follow-up of patients with AP are markers to help the clinician in determining the severity of the disease.

The major pathological event initiating AP is the conversion of trypsinogen into trypsin and that trypsin causes inappropriate intracellular proteolytic activation of other digestive enzymes. Activated pancreatic enzymes, microcirculation, and release of inflammatory mediators can cause pancreatic damage, necrosis, and rapid deterioration of the clinic [15, 16]. Monocytes/macrophages have been implicated as the main inflammatory cell population involved in the pathogenesis of the early and late disease. For the severity of AP, the degree of proteolytic activation might be one of the most important factors. In addition to monocyte/macrophages in the pancreas, monocyte/macrophages in distant organs may contribute to the progression of AP and multiorgan disease [11, 17]. Apolipoprotein-A1 (APO A-I), a major component of HDL cholesterol, has been shown to create anti-inflammatory effects by inhibiting CD11b activation in monocytes [6]. Due to the increased cytokines in AP, the synthesis of APO A-I required for HDL synthesis and transport in the liver may have decreased, and ultimately the blood levels of HDL are found to be decreased [18]. Decreased HDL ratios induce hemopoietic

**Table 5. ROC analysis for MHO, hs-CRP, and DNLR to detect patients with Ranson III–IV**

| Variable | Area under the ROC curve | p | Cutoff | Sensitivity, % | Specificity, % |
|---|---|---|---|---|---|
| MHR | 0.682 (0.593-0.778) | <0.001 | 17 | 75.0 | 72.0 |
| hs-CRP | 0.595 (0.496-0.696) | 0.006 | 5.90 | 65.0 | 62.0 |
| DNLR | 0.552 (0.435-0.677) | 0.007 | 6.30 | 41.0 | 34.0 |

MHR: Monocyte to HDL ratio; hs-CRP: High-sensitive C-reactive protein; DNLR: Derived neutrophil to lymphocyte ratio; ROC: Receiver operating characteristic.

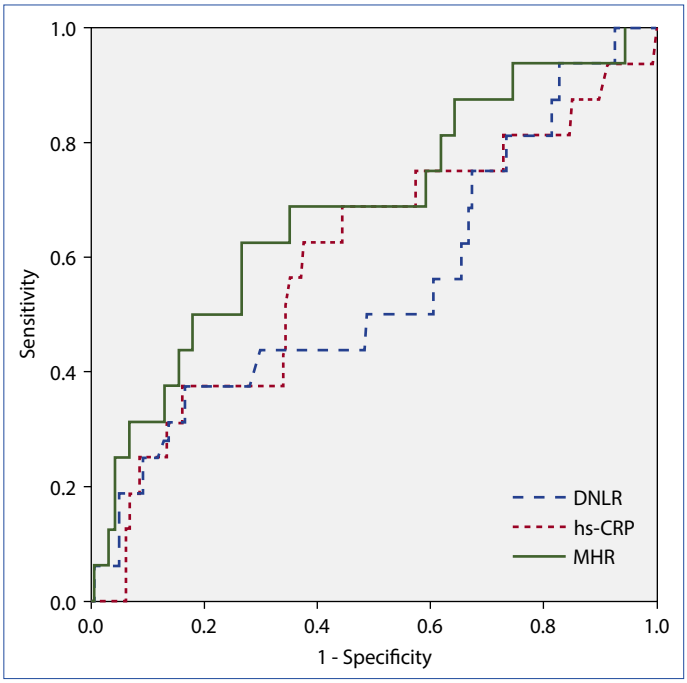


**Figure 1.** Receiver operating characteristic curves with monocyte to HDL ratio (MHR), high-sensitive C-reactive protein (hs-CRP), and derived neutrophil to lymphocyte ratio (DNLR).

stem cell proliferation, especially monocytosis [19]. Therefore, low HDL levels may break the normal systemic response at the acute stage due to overproduced inflammatory factors. In the literature, there are several articles that pay attention to the change in the function of HDL rather than the level of HDL in acute disease development [7, 12].

Various scoring systems such as Ranson criteria, Atlanta classification, APACHE (acute physiology and chronic health examination) II score, BISAP (Bedside index of severity in acute pancreatitis), HAPS (harmless acute pancreatitis score), Imrie's score (modified Glasgow II scoring), and Balthazar scoring are used to determine the severity of AP and to suggest its prognosis. However, none of these are excellent and easy to use in terms of predicting the prognosis [20, 21].

Recent studies have shown that MHR may be a new marker of inflammation and oxidative stress. A low HDL value and a high monocyte cell count appear to be an indirect indicator of inflammation [9, 22-24]. However, there are no studies associated with MHR and AP. Cetin et al. [22] showed that MHR as a novel inflammation-based marker seemed to be an independent predictor of the severity of coronary artery disease. In this study, 2661 patients with acute coronary syndrome were enrolled. MHR was significantly positively correlated with CRP (r=0.394). During in-hospital and long-term follow-up, stent thrombosis, nonfatal myocardial infarction, major adverse cardiovascular events, and mortality were seen frequently. Kanbay et al. [9] showed that MHR was increased with decreasing glomerular filtration rate (eGFR) in predialytic chronic kidney disease (CKD) patients. Increased MHR was arising as independent predictors of major cardiovascular events and associated with a worse cardiovascular profile. In this study, a total of 340 subjects with stage 1-5 CKD were assessed for fatal and nonfatal CV events. MHR was negatively correlated with estimated eGFR ($p<0.001$). Aydin et al. [23] showed that in patients with primary hypertension (PHT), there was a relationship between the MHR and asymptomatic organ damage. A total of 366 participants (275 cases with a diagnosis of PHT and 91 healthy volunteers) were enrolled. MHR was found to be an independent risk factor associated with these indicators of asymptomatic organ damage in PHT. In a study, Cagli et al. estimated the association of MHR, a recently emerged inflammatory marker, with abdominal aortic aneurysm (AAA) size. A total of 120 patients with asymptomatic AAA were enrolled. All data were compared between patients with low and high admission MHR. Cagli et al. [24] showed that MHR is independently associated with AAA diameter.

Our study is the first study conducted between AP and MHR. Our study showed that MHR was significantly positively correlated with both Ranson score and hs-CRP. MHR has been found to be an independent parameter for the occurrence of AP (odds ratio: 1.136, 95% confidence interval: 1.065-1.212, $p<0.001$). ROC analysis for MHR at the cutoff level of 17 has 75% sensitivity, 72% specificity, 0.682 under curve area, and $p<0.001$ (Tables 4, 5 and Fig. 1). On the basis of the means of these parameters, we have shown that MHR is a prognostic marker for severity in AP.

In general, neutrophil shows a response to systemic inflammation, while lymphopenia reflects the weakness of cellular immunity. DNLR may be interpreted as demonstrating the adequacy of the cellular immune response against the magnitude of systemic inflammation. The prognostic role of DNLR in some malignancies is discussed. The reason for the poor effect on the prognosis of DNLR increase in cancer patients is that neutrophil predominance can suppress cytotoxic T cells. It has been reported in systematic meta-analyses and in many studies that it can be used as a poor prognosis predictor in malignancies and chemotherapy resistance [14]. Song et al. [10] evaluated the prognostic value of the biomarkers including the DNLR in predicting overall survival in patients with gastric cancer. A total of 1990 consecutive gastric cancer patients who underwent gastrectomy were enrolled. In univariate analyses, DNLR was closely associated with both overall survival. In patients with peripheral arterial disease, Belaj et al. [25] investigated a possible association of DNLR with critical limb ischemia. A total of 1995 patients with peripheral arterial disease were enrolled. This study has shown that a high DNLR is associated with an increased rate of critical limb ischemia in patients with peripheral arterial disease.

Our study is the first study to highlight the association between AP and DNLR. In this study, DNLR was significantly positively correlated with both Ranson score and hs-CRP. DNLR has been found to be an independent parameter for the severity of AP (odds ratio: 1.107, 95% confidence interval: 1.103-1.115,

p=0.010). ROC analysis for DNLR has shown cutoff 6.30, sensitivity 41%, specificity 34%, under curve area 0.552, and p=0.007 (Tables 4, 5 and Fig. 1). On the basis of the means of these parameters, we found that DNLR is a prognostic marker for the severity of AP.

Our study has some limitations. One of the main limitations of the study is that it is observational, single center, and retrospective. In addition, other limitations are the calculation of neutrophil, monocyte, lymphocyte, and PLT counts from peripheral blood by automated method, not comparing Ranson criteria with the parameters checked after 48 h, and not looking into the relationship with other methods used to evaluate the severity of AP.

## Conclusion

In patients with severe AP, MHR and DNLR levels are independent predictors of the severity of the disease. The levels of MHR and DNLR evaluated during the follow-up of patients with AP are low-cost and easily accessible parameters to help the clinician in determining the severity of the disease.

**Conflict of Interest:** The authors declare that there is no conflict of interest.

**Ethics Committee Approval:** The study was approved by The Cukurova University Faculty of Medicine Non-interventional Clinical Research Ethics Committee (No: 44, Date: 05/10/2018).

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