

The Relationship between Recurrent Hospitalization and Inflammation in Heart Failure Patients

Yasemin Kaya¹(ID), Ahmet Kaya²(ID), Fatih Akkaya²(ID), Mehmet Filiz²(ID)

¹Department of Internal Medicine, Faculty of Medicine, Ordu University, Ordu, Turkey.

²Department of Cardiology, Faculty of Medicine, Ordu University, Ordu, Turkey.

Received: 29 March 2023, Accepted: 29 April 2023, Published online: 30 April 2023

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Abstract

Objective: In this study, we aimed to show whether there is a relationship between inflammatory markers and recurrent hospitalizations within 1 year in patients with heart failure.

Methods: All patients over the age of 18 who were followed up with a diagnosis of heart failure in the cardiology outpatient clinic between 2020-2021 were included in the study. The files of the patients were scanned and their sociodemographic characteristics, hemogram and biochemical parameters were recorded. Platelet lymphocyte ratio (P/L), neutrophil lymphocyte ratio (N/L), monocyte HDL (monocyte/HDL) ratios were calculated from inflammatory markers. It was screened how many times the patients were hospitalized and followed up in the hospital in the last year. The correlation between the number of hospitalizations and inflammatory markers were evaluated.

Results: 483 patients were included in the study. The mean age of the patients was 65.65±11.75 years. The mean ejection fraction of the patients was found to be 29.53±6.102% (minimum 15 and maximum 45). CRP=8.01±9.29, monocyte HDL ratio=0.0172±0.010, platelet-lymphocyte ratio=149.24±88.80, neutrophil-lymphocyte ratio=4.54±4.88. It was determined that 73 (15.1%) of the patients had recurrent hospitalizations within one year. A significant positive correlation was found between recurrent hospitalizations and monocyte HDL ratio ($r=0.123$, $p=0.007$), but no significant correlation was found with other parameters.

Conclusion: A significant positive correlation was found between recurrent hospitalizations and only monocyte HDL ratio. No significant correlation was found between other inflammatory markers. Larger studies with a large number of cases are needed to evaluate the relationship between recurrent hospitalization and inflammation.

Key Words: Heart failure, recurrent hospitalization, inflammatory markers.

Kalp Yetmezliği Hastalarında Mükerrer Yatış ile İnflamasyon arasındaki İlişki

Özet

Amaç: Bu çalışmada kalp yetmezliği olan hastalarda inflamatuvar belirteçler ile bir yıl içinde tekrarlayan hastaneye yatışlar arasında ilişki olup olmadığını göstermeyi amaçladık.

Metod: 2020-2021 tarihleri arasında kardiyoloji polikliniğinde kalp yetmezliği tanısı ile takip edilen 18 yaş üstü tüm hastalar çalışmaya dahil edildi. Hastaların dosyaları taranarak sosyodemografik özellikleri, hemogram ve biyokimyasal parametreleri kaydedildi. İnflamatuvar belirteçlerden platelet lenfosit oranı (P/L), nötrofil lenfosit oranı (N/L), monosit HDL (monosit/HDL) oranları hesaplandı. Hastaların son bir yıl içinde kaç defa yatırılarak hastanede takip edildikleri tarandı. Hastaneye yatış sayısı ile inflamatuvar belirteçler arasındaki korelasyon değerlendirildi.

Bulgular: Çalışmaya 483 hasta dahil edilmiştir. Hastaların yaş ortalaması 65.65±11.75 yıl idi. Hastaların ejeksiyon fraksiyonu ortalama % 29.53±6.102 (minimum 15 maksimum 45) olarak bulundu. CRP=8.01±9.29, monosit HDL oranı=0.0172±0.010, platelet lenfosit oranı=149.24±88.80, nötrofil lenfosit oranı=4.54±4.88 olarak bulundu. Hastaların 73 (%15,1) nün bir yıl içinde hastaneye tekrarlayan yatışları olduğu tespit edildi. tekrarlayan hastaneye yatışlar ile monosit HDL oranı arasında anlamlı pozitif korelasyon bulundu ($r=0.123$, $p=0.007$), diğer parametreler ile anlamlı bir korelasyon bulunamadı.

Sonuç: Tekrarlayan hastaneye yatışlar ile sadece monosit HDL oranı arasında anlamlı pozitif korelasyon bulundu. Diğer inflamatuvar belirteçler arasında anlamlı bir korelasyon bulunamadı. Tekrarlayan yatış ile inflamasyon arasındaki ilişkiyi değerlendirmek için vaka sayısının fazla olduğu daha büyük çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Kalp yetmezliği, tekrarlayan hastaneye yatış, inflamatuvar belirteçler

Suggested Citation: Kaya Y, Kaya A, Akkaya F, Filiz M. The relationship between recurrent hospitalization and inflammation in heart failure patients. ODU Med J, 2023;10(1): 1-7

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Address for correspondence/reprints:

Yasemin Kaya

Telephone number: +90 533 387 48 85

E-mail: ysmnkcmmz@gmail.com

INTRODUCTION

Heart failure (HF) is defined as a disease associated with heart tissue damage caused by systemic inflammation, arrhythmia, and conduction defects (1). In recent years, survival has increased in patients with acute myocardial infarction due to the improvement of early coronary reperfusion strategies and coronary care. However, the increased survival rate in heart attack patients resulted in an increased rate of heart failure (2). Despite advances in medical and interventional treatments, the risk of heart failure following myocardial infarction is still high (3). Heart failure is among the important causes of morbidity and mortality. With the successful treatment of myocardial infarction and the increasing elderly population, the incidence of chronic diseases such as HF is increasing rapidly. The increase in heart failure causes increased health costs (4).

In the literature, it is stated that chronic activation of the immune system plays a central

role in the occurrence and progression of HF with reduced ejection fraction and HF with preserved ejection fraction (5). It has been shown that there is a correlation between inflammation and adverse cardiovascular events in patients with HF, and inflammation plays a prominent role in both acute and chronic heart failure (1). It has been reported in publications that neutrophil-lymphocyte ratio (NLR) is associated with prognosis in many cardiac diseases such as heart failure, arrhythmia, and valve disease, especially ischemic heart disease (6). It has also been shown in studies that the platelet lymphocyte ratio (PLR), which is also an inflammatory marker, predicts mortality in patients with acute heart failure (7). An association between high monocyte count and low HDL-C levels has been reported in inflammatory disorders. (8)

In this study, we aimed to show whether there is a relationship between inflammatory markers and recurrent hospitalizations within one year in patients with HF.

METHODS

Heart failure is a complex clinical syndrome caused by structural or functional changes affecting the filling and/or ejection capacity of the ventricle. All patients over the age of 18 who were followed up with a diagnosis of heart

failure, with low ejection fraction ($EF \leq 45$) in the cardiology outpatient clinic between 2020-2021 will be included in the study. The files of the patients were scanned and their sociodemographic characteristics, ECG rhythms, New York Heart Association (NYHA) classifications, hemogram and biochemical parameters were recorded. Platelet lymphocyte ratio = Platelet/lymphocyte, neutrophil lymphocyte ratio = neutrophil/ lymphocyte, monocyte HDL ratio = monocyte / HDL were used as inflammatory markers. The number of hospitalizations of the patients in the last year was screened. The endpoint variable for this study was the number of hospitalizations per year. Data were obtained from hospital records. The correlation between the number of hospitalizations and inflammatory markers was evaluated.

Statistical analysis

All statistical analyzes required in the study were performed using the SPSS v25 (IBM Inc., Chicago, IL, USA) statistical program. Data were evaluated for normality with the Kolmogorov-Smirnov test. Pearson correlation test was used for normally distributed data and Spearman correlation test was used for non-normally distributed data to evaluate whether there was a correlation between inflammatory markers and the number of hospitalizations in 1 year. The mean \pm standard deviation, minimum and maximum values were used for numerical data in

the evaluation of the data of the patients. It was evaluated as % in categorical data.

RESULTS

483 patients were included in the study. The mean age of the patients was 65.65 ± 11.75 years. The mean ejection fraction of the patients was 29.53 ± 6.102 (minimum 15, maximum 45) (table 1). 35.2% of the patients were female, 64.8% were male, 30.4% had DM, 50.5% had HT, 17% had hyperlipidemia, and 13.3% had chronic kidney disease. In the ECG of the patients, 47% of the patients had atrial fibrillation and 53% of them sinus rhythm. NYHA-1 was found in 138 (28.6%), NYHA-2 in 186 (38.5%), NYHA in 140 (29%) 3.19 (4%) NYHA 4 (table 2).

CRP = 8.01 ± 9.29 , monocyte HDL ratio = 0.0172 ± 0.010 , platelet-lymphocyte ratio = 149.24 ± 88.80 , neutrophil-lymphocyte ratio = 4.54 ± 4.88 (table 1). It was determined that 73 (15.1%) of the patients had recurrent hospitalizations in the last year (table 2). As a result of the correlation between recurrent hospitalizations and monocyte HDL ratio, platelet lymphocyte ratio, neutrophil lymphocyte ratio and CRP, a significant positive correlation was found between recurrent hospitalizations and monocyte HDL ratio ($r = 0.123$, $p = 0.007$), no significant correlation was found with other parameters (table 3).

Table 1 Age, ejection fraction, biochemical and hemogram parameters of the patients

	Minimum	Maximum	Mean	Standard. Deviation
Age, years	26	95	65.65	11.751
C reactive protein, mg/L	.06	73.00	8.0133	9.29417
Fasting blood sugar, mg/dl	41.00	536.00	115.0508	47.95302
URE, mg/dl	6	236	42.14	27.783
Creatinine, mg/dl	0.42	34.00	1.2257	1.76741
Aspartate Aminotransferase, U/L	3	756	33.08	52.821
Alanine Aminotransferase, U/L	5	453	30.48	41.393
Total Cholesterol, mg/dl	87	407	187.95	45.739
HDL Cholesterol, mg/dl	16	79	40.27	11.947
LDL Cholesterol, mg/dl	11	2584	131.44	147.480
Triglyceride, mg/dl	17	1181	146.17	101.612
Uric acid, mg/dl	2.00	72.00	7.2817	8.96299
Ejection fraction, %	15	45	29.53	6.102
Brain natriuretic peptide, pg/ml	32.26	25800.00	3335.6631	3386.96229
Troponin, ng/mL	0.0010	38.7000	.209439	1.8909479
White blood cell, 10 ³ /μL	3.40	46.40	10.4899	5.36377
Thrombocyte, 10 ⁹ /L	10.40	781.00	216.4219	84.25364
Lymphocyte, 10 ⁹ /L	0.32	9.22	1.7449	0.96354
Monocytes, 10 ⁹ /L	0.10	2.80	.6419	0.34704
Neutrophil, 10 ⁹ /L	1.00	34.40	6.0529	4.71955
Monocyte HDL ratio	0.00	0.08	.0172	0.01049
Platelet lymphocyte ratio	4.95	752.50	149.2483	88.80542
Neutrophil lymphocyte ratio	0.22	30.00	4.5478	4.88772
Hemoglobin, g/dl	7.40	152.00	13.8590	6.74415

Table 2. Chronic diseases, ECG rhythms, NYHA classifications of patients

Gender, n(%)	
Female	170 (35.2)
Male	313 (64.8)
Diabetes Mellitus. n(%)	147 (30.4)
Hypertension. n(%)	244 (50.5)
Hyperlipidemia. n(%)	82 (17)
Chronic Kidney Disease. n(%)	64 (13.3)
Ecg Rhythm. n(%)	
Inüs	256 (53)
Atrial fibrillation	227(47)
NYHA Classification. n(%)	
1	138 (28.6)
2	186 (38.5)
3	140 (29)
4	19 (4)
Recurrent hospitalization. n(%)	73 (15.1)

Table 3 Correlation between repeated hospitalizations and inflammatory markers

	Repeated Hospitalizations	
	r	p
C reactive protein. mg/L	0.079	0.083
Monocyte HDL ratio	0.123	0.007
Platelet lymphocyte ratio	0.055	0.231
Neutrophil lymphocyte ratio	0.076	0.093

DISCUSSION

It was determined that 73 (15.1%) of the patients had recurrent hospitalizations in the last year. A significant positive correlation was found between recurrent hospitalizations and monocyte HDL ratio ($r=0.123$, $p=0.007$), but no significant correlation was found with other parameters.

Inflammation is the body's physiological response to infections, injuries, and toxins. Inflammation is a beneficial response in the short term, but it is hypothesized that when the duration of inflammation is prolonged (due to diseases such as diabetes or obesity), it can have harmful effects (5). Both chronic low-grade inflammation and acute severe inflammation are involved in the pathogenesis of cardiovascular diseases (coronary artery disease and heart failure). Since chronic low-grade inflammation is usually caused by chronic diseases such as diabetes mellitus, hypertension, and obesity, it cannot be corrected (9). In acute inflammation in cardiovascular diseases, an inflammatory response occurs when spleen leukocytes move to the damaged heart as the first defense after myocardial infarction (10). Cardiac inflammation and subsequent tissue damage are regulated by the infiltration and activation of various immune cells into the myocardium, including neutrophils, monocytes, macrophages, eosinophils, mast cells, natural killer cells, and T and B cells. After tissue injury, monocytes and tissue-resident macrophages undergo significant

phenotypic and functional changes and act as key regulators of tissue repair, regeneration, and fibrosis (1). At the same time, besides the activation of inflammatory cells and endothelial cells, the production of reactive oxygen species (ROS), eicosanoids and cytokine/chemokines increase (11). Physiological acute inflammation is essential for cardiac repair after injury. However, if inflammation is suboptimal, this leads to chronic inflammation and subsequently to advanced HF (10). It has been reported in publications that chronic systemic inflammation in the body is associated with an increased risk of heart failure (12).

Studies show that inflammatory mediators are important in cardiac remodeling and in the pathogenesis of chronic heart failure. Studies have reported that inflammatory cytokines such as tumor necrosis factor (TNF) α , interleukin (IL)-1 β and IL-6 are elevated in the plasma and myocardial tissue of HF patients. There is strong evidence that these mediators are involved in processes that lead to cardiac remodeling, such as hypertrophy, fibrosis, and apoptosis. It is said that some of these cytokines can also provide useful prognostic information as reliable biomarkers in this disease (13). As a result of the study by Albar et al., it was concluded that inflammatory biomarkers IL-6, TNF- α and CRP are associated with HF that occurs independently (12).

High-density lipoprotein-cholesterol (HDL-C) has an antiatherosclerotic effect by inhibiting the migration of macrophages and LDL oxidation, neutralizing the proinflammatory and prooxidant effects of monocytes. In addition, HDL plays a role in suppressing the activation of monocytes and the proliferation-differentiation of monocyte progenitor cells (14). Recent studies show that the monocyte HDL-C ratio (MHR), which is an easily calculated measure, may be a new indicator of inflammation (15).

CONCLUSION

As a result of this study, it was found that MHR, which was stated to be one of the inflammatory markers, showed a positive correlation with recurrent hospitalization in heart failure patients with acute and chronic inflammation in the physiopathology. No relationship was demonstrated with other inflammatory markers. Larger studies are needed to examine the relationship between recurrent hospitalization and inflammatory markers.

LIMITATIONS

Inadequate number of cases, being a single-center study, and inability to examine all inflammatory markers can be counted among the limitations.

Ethics Committee Approval: Approval was obtained from Ordu University clinical research ethics committee (12.08.2021 /16/189).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept: YK. AK. Design: YK. AK. FK. MF. Literature search: YK. AK. FK. MF. Data Collection and Processing: YK. AK. FK. MF. Analysis or Interpretation: YK. AK. FK. MF. Written by: YK. AK. FK. MF.

Conflict of Interest: The authors declared no conflict of interest.

Financial Disclosure: The authors declared that this study has not received no financial support.

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