RETROSPECTIVE EVALUATION OF PATIENTS DIAGNOSED WITH ACUTE CORONARY SYNDROME

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Abstract

Introduction. Early diagnosis and treatment of acute coronary syndromes as a life threatening disease group is crucial in emergency departments. Acute coronary syndrome (ACS) term is used to define a disease spectrum including unstable angina pectoris, ST-segment elevation myocardial infarction (STEMI), and non-ST-segment elevation myocardial infarction (NSTEMI).

The objective of this study was to compare unstable angina pectoris (USAP), ST-segment elevation myocardial infarction (STEMI), and non-ST-segment elevation myocardial infarction (NSTEMI) groups in terms of the blood parameters such as mean platelet volume (MPV), red cell distribution width (RDW), C-reactive protein (CRP), neutrophil-to-lymphocyte and platelet-to lymphocyte ratios; and data such as patients' sociodemographic and clinical characteristics, time and day of the admission, diagnosis of the admission to coronary intensive care unit, ECG findings, and comorbidity, and to investigate the relationship between them.

Materials and methods: A total of 659 patients included in the study. Patients were divided into 3 groups according to the diagnosis of admission as STEMI, NSTEMI, and USAP groups. Patients' age, gender, complaints of presentation to emergency department (ED), presumed diagnosis, hemogram, MPV, RDW, CRP, troponin, neutrophil-to-lymphocyte, and platelet-to-lymphocyte ratios were evaluated.

Results: The patients were mostly male (71.8%), the most common age range was 45-59 years (40.2%). Troponin value was significantly lower in USAP group compared to STEMI and NSTEMI group (p<0.05). The median RDW value was lower in the STEMI group than NSTEMI and USAP groups (p<0.05). Neutrophil-to lymphocyte ratio was significantly lower in USAP compared to STEMI and NSTEMI groups (p<0.05). No significant difference was found between the three groups in terms of platelet-to-lymphocyte ratio (p>0.05).

Conclusion: In this study, we evaluated data of ACS patients who presented to the emergency department. We believe that such data will be guiding diagnosis and treatment of patients with ACS.

Keywords: Emergency, Acute Coronary Syndromes, NLR, PLR.

Резюме

РЕТРОСПЕКТИВНАЯ ОЦЕНКА ПАЦИЕНТОВ С ДИАГНОЗОМ ОСТРЫЙ КОРОНАРНЫЙ СИНДРОМ

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Актуальность. Ранняя диагностика и лечение острого коронарного синдрома как группы заболеваний, угрожающих жизни, что имеет решающее значение в отделениях неотложной помощи. Термин «острый коронарный синдром» (ОКС) используется для определения спектра заболеваний, включая нестабильную стенокардию, инфаркт миокарда с подъемом сегмента ST (STEMI) и инфаркт миокарда без подъема сегмента ST (NSTEMI).

Целью данного исследования было сравнение групп пациентов с нестабильной стенокардией (USAP), инфарктом миокарда с подъемом сегмента ST (STEMI) и инфарктом миокарда без подъема сегмента ST (NSTEMI) с точки зрения таких параметров крови, как средний объем тромбоцитов (MPV), ширина распределения эритроцитов (RDW), С-реактивный белок (CRP), отношение нейтрофилов к лимфоцитам и тромбоцитов к лимфоцитам. Также сравнивались такие данные, как социально-демографические и клинические характеристики пациентов, время и день поступления, диагноз при поступлении в отделение интенсивной терапии, результаты ЭКГ и сопутствующие заболевания, а также взаимосвязи между ними.

Материалы и методы: в исследование включено 659 пациентов. Пациенты были разделены на 3 группы в зависимости от диагноза госпитализации: STEMI, NSTEMI и USAP. Были оценены возраст пациентов, пол, жалобы на поступление в отделение неотложной помощи (ED), предполагаемый диагноз, гемограмма, MPV, RDW, CRP, тропонин, соотношение нейтрофил-лимфоцит и соотношение тромбоцитов к лимфоцитам.

Результаты: пациенты были в основном мужчины (71,8%), наиболее распространенный возрастной диапазон составлял 45-59 лет (40,2%). Значение тропонина было значительно ниже в группе USAP по сравнению с группами STEMI и NSTEMI (p <0,05). Среднее значение RDW было ниже в группе STEMI, чем в группах NSTEMI и USAP (p <0,05). Отношение нейтрофилов к лимфоцитам было значительно ниже в USAP по сравнению с группами STEMI и NSTEMI (p <0,05). Не было обнаружено существенного различия между тремя группами в отношении соотношения тромбоцитов к лимфоцитам (p> 0,05).

Заключение: в этом исследовании мы оценили данные пациентов с ОКС, которые были представлены в отделение неотложной помощи. Мы считаем, что такими данными будут руководствоваться при проведении диагностики и лечения пациентов с ОКС.

Ключевые слова: чрезвычайная ситуация, острые коронарные синдромы, NLR, PLR.

Түйіндеме

ЖЕДЕЛ КОРОНАРЛЫҚ СИНДРОМ ДИАГНОЗЫ БАР ПАЦИЕНТТЕРДІ РЕТРОСПЕКТИВТІ БАҒАЛАУ

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Өзектілігі. Жедел коронарлық синдромды өмірге қауіпті аурулар тобы ретінде ерте диагностикалау және емдеу, бұл жедел медициналық көмек бөлімшесінде шешуші маңызға ие. «Жедел коронарлық синдром» (ЖКС) термині аурулардың спектрін, соның ішінде тұрақсыз стенокардияны, инфаркт миокардасын ST сегментінің жоғарылауымен (STEMI және ST сегментінің жоғарылауынсыз (NSTEMI) инфаркт миокардасын анықтау үшін қолданылады.

Осы зерттеудің мақсаты тұрақты емес стенокардиямен (USAP) науқастар тобын, ST сегментінің жоғарылауымен (STEMI) инфаркт миокардасын және ST сегментінің жоғарылауынсыз (NSTEMI) инфаркт миокардасы тромбоциттердің орташа мөлшері (MPV), эритроциттер (RDW таралу ені, С-реактивті ақуыз (CRP), нейтрофилдердің лимфоциттерге және тромбоциттерге лимфоциттерге қатынасы сияқты қан параметрлері бойынша салыстыру болды. Сондай-ақ пациенттердің әлеуметтік-демографиялық және клиникалық сипаттамалары, қабылдау уақыты мен күні, шұғыл терапия бөліміне түскен кездегі диагнозы, ЭКГ нәтижелері және онымен байланысты аурулар, сондай-ақ олардың арасындағы байланыс сияқты мәліметтерді салыстырды.

Материалдар мен әдістері: Зерттеуге 659 науқас енгізілген. Емдеуге жатқызу диагнозына байланысты пациенттер 3 топқа бөлінді: STEMI, NSTEMI және USAP. Пациенттің жасы, жынысы, Шұғыл көмек бөлімшесіне түсу кезіндегі (ED), болжам диагнозы, гемограмма, MPV, RDW, CRP, тропонин, нейтрофил-лимфоциттердің арақатынасы және тромбоциттерден лимфоциттерге қатынасы туралы шағымдар бағаланды.

Нәтижелері: пациенттер негізінен ер адамдар (71,8%), ең көп кездесетін жас ауқымы 45-59 жас (40,2%). STEMI және NSTEMI топтарымен салыстырғанда USAP тобында тропонин мөлшері айтарлықтай төмен болды (p <0.05). NSTEMI және USAP топтарына қарағанда STEMI тобында RDW орташа көрсеткіші төмен болды (p <0.05). Нейтрофилдердің лимфоциттерге қатынасы USAP-та STEMI және NSTEMI топтарына қарағанда айтарлықтай төмен болды (p <0.05). Үш топ арасында тромбоциттердің лимфоциттерге қатынасына қатысты айтарлықтай айырмашылық табылған жоқ (p> 0,05).

Қорытынды: Осы зерттеуде біз шұғыл көмек бөлімшесіне ұсынылған ЖКС-ы бар науқастардың деректерін бағаладық. ЖКС-ы бар науқастарды диагностикалау және емдеу осындай деректерді басшылыққа алады деп ойлаймыз.

Түйінді сөздер: төтенше жағдай, жедел коронарлық синдромдар, NLR, PLR.

Introduction

Acute coronary syndromes (ACSs) are the leading cause of mortality and morbidity all over the world. ACSs include Unstable Angina Pectoris (USAP), ST-segment elevation myocardial infarction (STEMI), and non-ST-segment elevation myocardial infarction (NSTEMI). In the life-limiting illness list by WHO for 2020, it is stated that ischemic heart disease (IHD) will rank first, and stroke fourth among these diseases (10). According to the results of Coronary Artery Disease Risk Factors in Turkish Adults (TEKHARF) study, there are approximately 2,000,000 patients with coronary artery disease in our country as of 2000 (18). In our country, 65,000 persons die yearly due to sudden death from coronary artery disease. The most common cause of IHD is atherosclerosis which is a chronic, progressive and multifocal intimal disease (10,18).

Currently, the commonly used tests in order to determine myocardial damage include echocardiography which shows left ventricular wall motion disorders and creatine kinase myoglobin (CK MB) isoform which define myocardial necrosis, myoglobin, troponin I and serum levels of troponin T (3). The use of sensitive and specific serum biochemical markers such as cardiac troponins in ACS is helpful in establishment of the diagnosis, and also it is an indicator of increased mortality risk, revascularization need in future, and myocardial infarction (3,7,910,29). Since there is not myocardial necrosis in many of ACP patients at high risk, it is impossible to identify these patients with serum troponins. Therefore, newer cardiac biomarkers are needed for risk assessment, that will help a rapid and definitive diagnosis in ACS patients to be used before the traditional markers showing myocardial cellular damage or in cases of these markers are not elevated. For this purpose, biomarkers of hemostasis, thrombosis, oxidative stress, energy homeostasis, inflammation, and plaque instability are being studied.

At the point of theories developed and studies conducted for the pathogenesis of atherosclerosis for more than a century, it is now well known that inflammation plays a critical role at every step of atherosclerosis (10). Today, inflammation theory is the most accepted. The rupture of thrombus materials or thrombus materials occurring with erosion of the overlying endothelium that are developed at the end of this complex process which involves many cells, adhesion molecules, proinflammatory cytokines, and further numerous molecules are the main feature of ACSs (9).

In this study we aimed to compare MPV, C reactive protein (CRP), red cell distribution width (RDW), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) among ACS forms. In addition, considering it would be helpful for emergency physicians, we examined data such as sosciodemographics, clinical features, admission complaints, and time of admission in patients diagnosed with ACS.

Material and Methods

A total of 659 patients who presented to the emergency department of Sisli Hamidiye Etfal Training and Research Hospital with chest pain, who were diagnosed with ACS and admitted to the coronary intensive care unit between 01/05/2015 and 30/04/2016 were retrospectively included in the study. Patients were divided into 3 groups according to the diagnosis of admission as STEMI, NSTEMI, and USAP groups. Patient's sociodemographics such as age and gender, hemogram, MPV, RDW, CRP, troponin, NLR and PLR were obtained from the patient files and evaluated.

Statistical Analysis: Descriptive statistics of the data are expressed as frequency (n), ratio (%), median and interquartile range (IQR). Distribution of the variables was measured with Kolmogorov-Smirnov test. Continues data were analyzed with Kruskal-Wallis tests. Categorical variables were analyzed with Chi-square test, and with Fischer test when Chi-square conditions were not met. Statistical analysis was performed using SPSS 22.0 software. $p < 0.05$ values were considered statistically significant.

Results

Mean age of patients was 60.01±13.7 and 71.8% of patients were male (n=473). Age and gender distributions of the patients are given in Table 1.

Table 1.
Distribution of patients according age groups.

		n	%
Age groups	18-44	79	12
	45-59	265	40.2
	60-74	206	31.3
	>75	109	16.5
Gender	Male	473	71.8
	Female	186	28.2

Troponin value was significantly lower in USAP group compared to STEMI and NSTEMI groups ($p < 0.05$) (Table 2). Hematologic features of the patients are given in Table 2.

No significant difference was found between STEMI, NSTEMI, and USAP groups in terms of the admission MPV values ($p > 0.05$). There was significant difference found

between STEMI, NSTEMI, and USAP groups in terms of the admission hemoglobin value (p<0.05) The median RDW value was lower in the STEMI group than NSTEMI and USAP groups (p<0.05).

No significant difference was found between the three groups in terms of platelet-to-lymphocyte ratio (p>0.05). Neutrophil-to lymphocyte ratio was significantly lower in

USAP compared to STEMI and NSTEMI groups (p<0.05). There was significant difference found between STEMI, NSTEMI, and USAP groups in terms of the admission CRP and Troponin I value (p<0.05) The median CRP and Troponin values were lower in the USAP group than NSTEMI and STEMI groups (p<0.05).

Table 2.

Hematologic an demographic features of the patients.

Variable	USAP	NSTEMI	STEMI	p
Gender (M/F)	62/25	214/105	197/56	**0.017**
Age	56 (16)	61(23)	57(18)	**0.003**
MPV	10(1.10)	10.5(1.10)	10.5 (1.10)	0.068
RDW	13.6(1)	13.8(1.8)	13(1.1)	**0.000**
PLR	104.31(59.44)	103.4 (75.01)	98.61(76.18)	0.481
NLR	2.19(1.52)	2.74(2.75)	2.71(3.64)	**0.014**
CRP	3.9(6)	5.9 (12.4)	5(11.2)	**0.008**
Troponin I	0.10(0.05)	1.08(2.68)	0.55(5.06)	**0.000**

MPV: Mean platelet voume,
RDW: red cell distribution width,
CRP: C reactive protein,
NLR: neutrophil-to-lymphocyte ratio,
PLR: platelet-to-lymphocyte ratio

Discussion

In our study, we investigated and compared demographic, hematologic parameters among the patients who presented to the ED, were diagnosed with ACS and admitted to the coronary intensive care unit.

According to the Turkey data, yearly rate of deaths from IHD is 6.5 per thousand in men, and 2.5 per thousand in women (18). This difference is disappeared with ageing, and F/M ratio becomes equal after 75 years of life (18). *Serinken et al.* showed that the rate of experiencing IHD is higher in men (22). Women develop ACS in earlier ages than men, and the symptoms manifest later in women (4, 27). Consistently with the literature, we also found a higher population of male patients by 71.8% (n=473). The rate of female patients was significantly higher in NSTEMI group than in STEMI group.

The incidence and prevalence of coronary artery disease increase by ageing, and thus age can be considered as the most important risk factor (10). Being aged >45 years in men and >55 in women is a strong risk factor for coronary artery disease. It is reported in the literature that CAD is the most commonly seen after 40 years of life (26). In their study conducted in Turkey in 1998, Onat et al. found the prevalence of CAD by age group as 14.4% in 40-49 years age group, 13.3% in 50-59 years age group, and 21.6% in 60-69 years group (18). In our study, the most common age of experiencing ACS was between 45 and 59 years by 40.2% (n=265). According to our results similar to the literature the chance of developing ACS increases after 40 years of life. Again in parallel with the literature, the risk of ACS was shown to increase by aging.

Clinical trials have shown that serum cardiac troponins is a biomarker that can be determined in the earliest period in the diagnosis of acute coronary disease in humans [5]. *Elmalı et al.* showed that both tests have no superiority on each other in the diagnosis of acute coronary syndrome. At the end of the study, although sensitivity of c-Tn-I was high

enough to compared with the previous study, high rate of false negativity was remarkable. It is understood from our results that regardless the test, outcomes should be evaluated along with the clinical parameters of the patient. It has been underlined that considering only laboratory values in both tests could lead to incorrect clinical procedures (6). The authors compared TnI, TnT and CK-MB, and stated that cTnI is the most sensitive indicator of minor myocardial damage at a cut-off value of 0.1 µg/L. Although elevated cTn is an important marker of coronary ischemia, one should be considered that this parameter can be raised also in other conditions, and it should not be interpreted in favour of coronary ischemia. The rate of elevated cTn-T level (≥0.1 µg/L) has been found as 0.7% in general population. Among the reason for this are left ventricular dysfunction, diabetes mellitus, left ventricular hypertrophy, and moderate renal failure (25). It is known that cTn levels may be read high in the patients who presented to hospital due to any reason or hospitalized patients, rather than healthy persons. In another study, cTn-T levels were measured in 635 patients who presented to hospital due to any reason within a 10-month period. Acute coronary syndrome was diagnosed with >0.1 µg/L cTn-T value in 53% of the patients, while elevated cTn-T was found to not have thrombotic reasons in 41%, and no any reason was detected in 6% of the patients. The results of the mentioned study indicated that although a considerable portion of the patients had elevated cTn, this may be not caused by coronary artery disease [2]. In our study, troponin level was significantly lower in USAP group compared to STEMI and NSTEMI groups. Our results accordances with literature.

Nishizaki et al shown that MPV rather increases during an inflammatory process such as acute coronary syndrome, but basal blood investigations of the IHD patients with angina pectoris (AP) revealed that platelet in these persons were larger than those of normal persons, and platelet aggregation is more compared to normal persons especially

after *in vitro* induction with adrenalin [17]. There are reports showing an association between MPV, ACS occurrence and acute cerebral stroke. In these studies, an increase have been observed platelet volumes, and decrease in platelet count in acute ischemic events, and increased MPV has been proposed to be an independent risk factor in repeating vascular events [23]. *Kilicli-Camur et al.* reported that MPV values were higher in acute MI group compared to USAP group, although the results were not statistically significant [12]. In general, there is an opposite correlation between platelet count and MPV, and this association usually provide a constant platelet mass in the circulation [24]. In our study, admission MPV values were not statistically different among USAP, STEMI, and NSTEMI groups.

There is a strong association between coronary artery diseases and high RDW level, the underlying mechanism is yet to be fully clarified. Studies have shown that neurohumoral system is activated and erythropoiesis process is accelerated because of the increased circulatory levels of neurohumoral mediators, which in turn raises RDW levels in patients with coronary artery diseases and heart failure [14, 20]. Moreover, two large studies have shown that high RDW is a prognostic factor independent from anemia in coronary artery diseases and it may be related to the increased rate of mortality. Mediators that are resulted from the elevated neurohumoral activity during ACS stimulate erythropoiesis, increasing RDW levels. In a large-population study on patients with heart failure, high RDW was found to be an independent risk factor for mortality [17]. Studies have suggested that oxidative stress, inflammation and hemodynamically overload occurring during heart failure increase RDW. Nishizaki et al. found very high RDW values in fatal heart failure and stated that this may be associated with inflammation [17,20]. In our study, the median RDW value was lower in the STEMI group than NSTEMI and USAP groups ($p < 0.05$).

It is known that neutrophilia follows myocardial damage, there is an intense neutrophil infiltration in the infarction area at the first and third days, followed by healing of infarction and finally fibrous tissue takes place. Elevated leukocyte level and neutrophil-to-lymphocyte ratio (NLR) have been associated with short- and long-term mortality in patients with AMI (12,13,16). *Kyne et al.* found a significant correlation between the development of heart failure and elevated NLR at admission during 4-month follow-up of 185 AMI patients (14). However, some studies could not find a significant association such as the known other risk factors (14). In our study, NLR was significantly lower in USAP group than in the other two groups.

In previous studies reported that Platelet to lymphocyte ratio (PLR) was related severity and prognosis of CAD (1,21,28). İpek et al reported any relationship between PLR and CAD (11). In our study, there was no statistically significant difference in the median PLR value according to groups ($p > 0.05$). Our results support İpek et al.

The generally accepted opinion is that plaques with high lipid content, high inflammation and weak fibrous roof tend to rupture. CRP is a good indicator of inflammation (19). Elevated levels of high-sensitivity C-reactive protein (hs-CRP) which is among the inflammatory markers of atherosclerosis have been associated with decreased

coronary collateral circulation in patient populations both with ACS and stable AP (15). These data suggest that increased inflammation induces coronary collateral circulation via unknown mechanisms. In their study, *Habib et al.* found high levels of CRP in patients with ACS (89). In our study, median CRP value was lover in the USAP groups than STEMI and NSTEMI group. We think that CRP levels increase meanwhile vascular occlusion increases.

Conclusion

In this study, we examined sociodemographics and laboratory outcomes of 659 patients diagnosed with ACS, and compared these parameters among USAP, STEMI and NSTEMI groups.

In conclusion, we believe that the levels of RDW, NLR, and CRP which can be studied as a part of full blood count without requiring additional cost, can be used along the other conventional cardiac parameters in order to determine mortality and morbidity from coronary artery diseases in patients presenting to emergency departments.

Conflict Interest

The authors declerated that no conflict interest.

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