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Familial Hypercholesterolemia: Evaluating CRP/Albumin Ratio and Blood Count Parameters

Ailesel Hiperkolesterolemi: Crp/Albümin Oranı ve Kan Sayımı Parametrelerinin Değerlendirilmesi

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ABSTRACT

Objective: This study aimed to evaluate the CRP-to-albumin ratio (CAR) and complete blood count parameters in patients with familial hypercholesterolemia (FH).

Methods: A retrospective study included 101 patients (61 female) and 35 healthy controls (18 female) who visited our hospital from January 2015 to June 2018. Serum levels of total cholesterol (TC), triglycerides (TG), LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), albumin, and CRP were measured using the Hitachi 917 biochemistry analyzer. Complete blood count was performed with the Abbott CELL-DYN Ruby® hematology analyzer. Statistical analysis was conducted with SPSS 27.

Results: The FH patients had significantly higher median values of TC (328 mg/dL), TG (218 mg/dL), LDL-C (269 mg/dL), CRP (5.6 mg/dL), WBC (8.3×10^3/uL), NEU (4.9×10^3/uL), PLT (286×10^3/uL), and CAR (0.128), compared to the healthy controls. Significant differences were found between the two groups in TC, TG, LDL-C, albumin, CRP, CAR, WBC, NEU, LYM, and PLT ($p<.05$). The area under the curve (AUC) for CAR was 0.715, indicating its potential to distinguish FH patients from healthy controls (95% Confidence Interval: 0.626-0.824).

Conclusion: CAR is a valuable inflammatory marker for diagnosing and monitoring familial hypercholesterolemia, showing significant differences between FH patients and healthy controls.

Keywords: CRP-to-albumin ratio, familial hypercholesterolemia, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio

ÖZ

Amaç: Bu çalışmanın amacı, ailesel hiperkolesterolemili (FH) hastalarda CRP/albümin oranı (CAR) ve tam kan sayımı parametrelerini değerlendirmektir.

Yöntem: Ocak 2015 ile Haziran 2018 arasında hastanemize başvuran 101 hasta (61 kadın) ve 35 sağlıklı kontrol (18 kadın) üzerinde retrospektif bir çalışma yapıldı. Hastaların serumundaki toplam kolesterol (TC), trigliseritler (TG), LDL-kolesterol (LDL-C), HDL-kolesterol (HDL-C), albümin ve CRP düzeyleri Hitachi 917 biyokimya analizörü kullanılarak ölçüldü. Tam kan sayımı Abbott CELL-DYN Ruby® hematoloji analizörü ile gerçekleştirildi. İstatistiksel analiz SPSS 27 programı kullanılarak yapıldı.

Bulgular: FH hastalarında, sağlıklı kontrollere kıyasla TC (328 mg/dL), TG (218 mg/dL), LDL-C (269 mg/dL), CRP (5.6 mg/dL), WBC (8.3×10^3/uL), NEU (4.9×10^3/uL), PLT (286×10^3/uL) ve CAR (0.128) medyan değerleri anlamlı derecede yüksekti. TC, TG, LDL-C, albümin, CRP, CAR, WBC, NEU, LYM ve PLT değerleri açısından iki grup arasında anlamlı farklar bulundu ($p<.05$). CAR' ın eğri altındaki alan (AUC) değeri 0.715 olarak hesaplandı, bu da CAR' ın FH hastalarını sağlıklı kontrollerden ayırt etme potansiyelini gösterdi (Güven Aralığı: %95, 0.626-0.824).

Sonuç: CAR, ailesel hiperkolesterolemi tanı ve takibinde değerli bir inflamatuar belirteç olup, FH hastaları ile sağlıklı kontroller arasında önemli farklılıklar göstermektedir.

Anahtar Kelimeler: Ailesel hiperkolesterolemi, CRP/albümin oranı, nötrofil/lenfosit oranı, trombosit/lenfosit oranı

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Introduction

Familial hypercholesterolemia (FH) represents an autosomal dominant hereditary anomaly related to lipid metabolism. Increased plasma concentrations of low-density lipoprotein cholesterol (LDL-C) disrupt vascularization and subsequently promote the untimely onset of coronary artery disease (CAD). High LDL-C levels also increase the susceptibility to heart disease by 2.5 to 10 times. The factor most likely to cause increased mortality associated with FH is cardiovascular disease (CVD). FH often occurs together with metabolic disorders such as hypercholesterolemia, insulin resistance, diabetes mellitus, and obesity which serve as possible predisposing factors for inflammatory pathologies that underlie atherosclerotic lesions. Atherosclerosis is a chronic immune inflammatory disease, characterized by a protracted and inflammatory process, that impairs vascular physiology and is an important precursor to various CVDs such as myocardial infarction and strokes (Falk, 2006; Hansson, 2005). It is also an important common disease cause of global mortality. Multifaceted interactions of genetic and environmental determinants are recognized to be involved in its etiology. Major risk factors leading to atherosclerosis are hypercholesterolemia, hypertension, diabetes mellitus, smoking, and adiposity [high body mass index (BMI)—measured as weight (in kg) divided by squared height (in m2)] according to the 2021 European Society of Cardiology Guidelines on cardiovascular disease prevention in clinical practice (Ross, 1999). These factors influence the formation of atherosclerosis and pathogenic blood flow through complex interactions. The onset of inflammation is initiated by the infiltration of cholesterol-laden lipoproteins into the vascular intima and the subsequent triggering of the secretion of proinflammatory cytokines by the sustained activation of macrophages. In addition, these cytokines spark the hepatic synthesis of inflammatory proteins such as C-reactive protein (CRP). Consequently, the persistence of chronic vascular inflammation is deemed paramount in this context (Ikonomidis et al., 1999, Hirschfield, 2003).

CRP, one of the proteins called acute phase reactants produced by the liver and fat cells, is an indicator of inflammatory processes, enabling a direct quantification of the magnitude of the inflammatory response. Recently, the high-sensitivity (hs)-CRP test has been used as an inflammation biomarker and gained recognition as a significant cardiovascular risk determinant (Visseren et al., 2021). Albumin, another hepatocyte-synthesized protein, assumes a pivotal role in upholding blood colloidal osmotic pressure, facilitating diverse molecular transport, and exhibiting antioxidant properties. Low albumin concentrations may indicate malnutrition or malabsorption, liver failure or diseases, renal impairment, and some inflammatory and infectious diseases. Many studies have demonstrated a robust inverse correlation between serum albumin levels and CRP concentrations (Sheinenzon et al., 2021, Eckart et al., 2020). The CRP-to-albumin ratio (CAR) is derived by dividing the CRP concentration (mg/L) by the albumin concentration (g/L). High CARs, signify an underlying disequilibrium between inflammatory processes (reflected by CRP levels) and nutritional status (reflected by albumin levels), prominently manifesting in cases characterized by severe or prolonged inflammation. While the magnitude of this ratio may exhibit inter-individual variability, it has been identified as a promising prognostic indicator across a spectrum of serious medical pathologies, encompassing septic conditions (Günes et al., 2021), cardiovascular diseases, neoplastic disorders (Arakawa et al., 2021, Ishizuka et al., 2016, Kinoshita et al., 2015) and acute kidney injury (Yu et al., 2020). For example, according to a retrospective study, significant associations were found between the elevated CAR and mortality rates at presentation to the emergency department, especially in individuals over 65 years of age (Park et al., 2018).

The amount of circulating LDL-C plays a role in the regulation of T and B lymphocytes, which have important roles in the innate immune response. In particular, an increase in the amount of oxidized LDL-C decreases the number of regulatory T lymphocytes, which are key atheroprotective cells. As a result, the numbers of T helper 1 and T helper 2 increase, resulting in increased secretion of proinflammatory cytokines and atherosclerotic inflammation (Ait-Oufella et al., 2006). Under hypercholesterolemic conditions, an increase in the number of circulating neutrophils and constitutively active neutrophils may be observed (Farah et al., 2010). In addition, serum levels of neutrophil chemoattractants are increased by hypercholesterolemia, thus increasing neutrophil mobilization. Neutrophilia in FH is associated with increased degranulation and the release of large amounts of cytotoxic and destructive factors that can cause vascular tissue destruction. For example, neutrophils produce large amounts of reactive oxygen radicals via myeloperoxidase and NADPH oxidase, which are involved in the formation of oxidized LDL-C, impairing the performance of endothelial cells and leading to endothelial dysfunction (Malle et al., 2006).

Neutrophil to lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) are considered to be predictive parameters of systemic inflammation and are also some of the routine tests used to predict cardiovascular and peripheral vascular diseases (Condado et al., 2016). PLR is predicted as a new predictor of in-hospital mortality in patients in the cardiac intensive care unit. Patients with higher PLR levels have been observed to be associated with cardiac diseases such as congestive heart failure, arrhythmias, atrial fibrillation, and valvular disease (Zhai et al., 2021). When people with angiographically confirmed coronary occlusion were compared with healthy young individuals, a significant association between decreased HDL-cholesterol (HDL-C) levels

and increased PLR levels was reported (Tok et al., 2014). The principal objective of this investigation was to evaluate the CAR and complete blood count parameters in patients diagnosed with FH.

Methods

This retrospective study included a total of 136 participants, 101 patients with FH aged ≥18 years (61 female) and 35 healthy controls with LDL-C<160 mg/dL (18 female) using an electronic database of individuals admitted to Erzurum Regional Training and Research Hospital between January 2015 and July 2018. All procedures involving participants and data were in accordance with the revised Helsinki Declaration of 2000 and the study was approved by Erzurum Regional Training and Research Hospital, Medical Ethics Committee (approval date: 08.11.2018 and number: 2018/17-160). The patients were diagnosed with FH according to recommendations of the Dutch Lipid Clinic Network after a comprehensive physical examination and an extensive evaluation of their family medical history and laboratory results. Then, the patients with FH were divided into three subgroups according to LDL-C levels: mildly increased LDL-C (G3, [N=30]: LDL-C 190–249 mg/dL); moderately increased LDL-C (G2, [N=37]: LDL-C 250–329 mg/dL); and severely increased LDL-C (G1, [N=34]: LDL-C >330 mg/dL) and, each group compared with healthy ([N=35]: LDL-C 48-129 mg/dL). The patients with secondary hyperlipidemia due to diabetes, hypothyroidism, hyperthyroidism, acute or chronic renal failure, adrenal disorders, chronic liver disorders, malignancies, inflammatory diseases, and acute or chronic infection diseases were excluded from the study.

Venous blood samples were taken from patients in the morning, after 8-12 hours of fasting, into gel vacuum tubes (Vacusera, Turkey) for biochemistry and hematology testing. Total cholesterol (TC), triglyceride (TG), LDL-C, HDL-C, and albumin levels in the serum of the patients were measured using the enzymatic photometric method and hs CRP was measured using the immunonephelometric method on the Hitachi 917 biochemistry analyzer (Boehringer Mannheim, USA). Complete blood count was measured by the CELL-DYN Ruby® hematology analyzer (Abbott Diagnostics, USA). Then, the CAR, NLR, and PLR were calculated based on these count measurements. NLR is calculated by dividing the absolute neutrophil count by the absolute lymphocyte count and PLR is calculated by dividing the absolute platelet count by the absolute lymphocyte count. The two-level (normal and pathologic) internal quality control materials provided by kit manufacturers (Bio-Rad, Hercules, CA, USA) were routinely analyzed once a day, and the one-level external quality control program materials (Bio-Rad, Hercules, CA, USA) were analyzed monthly. All the results were acceptable during the study.

Statistical Analysis

All data were analyzed using the IBM SPSS© Statistics (version 27.0) program (SPSS, Chicago, USA). The normal distribution of continuous variables was assessed through the Kolmogorov-Smirnov test. For comparing control and patients' independent groups, the independent samples t-test was employed under conditions of normal distribution, while the Mann–Whitney U test was applied when normal distribution assumptions were not met. Where the parametric test assumptions were met, the one-way ANOVA test was used; otherwise, the Kruskal–Wallis test was used to compare differences in clinical-biochemical parameters between the subgroups. Comparative analyses concerning categorical variables were performed using the chi-square test and, where applicable, Fisher's exact test. Continuous variables were expressed as mean ± standard deviation (SD) or medians and the 1st and 3rd quartiles (Q1–Q3), and categorical variables as frequencies and percentages. The correlations between two continuous variables were assessed using the Pearson correlation test when normal distribution criteria were satisfied, and the Spearman correlation test was utilized when such conditions were not met. Linear regression analysis was employed to investigate the association between numerical variables. The Receiver Operating Characteristic (ROC) curve analysis was implemented to ascertain the diagnostic utility of continuous variables. The Area Under the Curve (AUC) value shows the overall discriminatory ability of the CAR. The AUC value of 1 indicates perfect discrimination, while the AUC value of 0.5 suggests no discrimination (equivalent to random guessing). The results (except age) are shown as mean ± standard deviation for parameters with normal distribution, and as median and 1st–3rd quartiles for parameters not showing normal distribution. Ages are shown as median and minimum–maximum. The differences between groups were considered significant if the p-value was less than .05 (two-tailed).

Results

A total of 136 individuals over 18 years old participated in our study, the control group consisted of 35 [39±14 (18–68) years] individuals, and the patient group consisted of 101 [40±14 (18–77) years] individuals diagnosed with FH. Of these, 50% of the participants were female (n= 18) in the control group, whereas 61% of FH patients were female (n= 61). There were no statistically significant differences between both groups in gender and age (p>.05). The median and Q1–Q3 or mean ± standard deviation values of TC (mg/dL), TG (mg/dL), LDL-C (mg/dL), HDL-C (mg/dL), Albumin (mg/dL), CRP (mg/dL), WBC, neutrophil (NEU), lymphocyte (LYM), platelet (PLT), CAR, NLR, PLR were 328 (274–398), 218 (171–368), 269 (229–340), 48 (41–58), 43 (38–45), 5.6 (1.6–10), 8.3 ± 1.94.9 ± 1.7, 2.57 ± 0.9, 286 (236–331), 0.128 (0.043–0.244), 1.87 (1.21–2.62), 113 (87–148) for FH patients and161±23, 84±37, 95±20, 47 (42–58), 45±2.6, 2 (1–3), 6.5 ± 1.2, 3.7±1, 2.21±0.49, 223±50, 0.044 (0.042–0.051), 1.58 (1.21–2.12), 104±28for healthy controls, respectively. There were significant differences between two groups in TC, TG, LDL-C, AL, CRP, CAR, WBC, NEU, LYM, and PLT (p<.05). The characteristics, biochemical and hematological results for the patients with FH and controls are seen in Table 1, and for subgroups in Table 2. CAR was the only parameter among all the investigated that showed significant differences in pair wise comparisons between all groups (p<.05). The medians of the CAR in the control and patients subgroups (G1, G2, or G3) are seen in Figure 1.

Table 1. The characteristics, biochemical, and hematological results of the patients with familial hypercholesterolemia and healthy controls

	Control (N=35)	FH (N=101)	P-value
Age (years)	39±14 (18–68)	40±14(18–77)	NS
Gender (Female: N, % /Male: N, %)	18.51 / 17.49	61.60 / 40.40	NS
TC (mg/dL)	161±23	328 (274–398)	.001*
TG (mg/dL)	84±37	218 (171–368)	.001*
LDL-C(mg/dL)	95±20	269 (229–340)	.001*
HDL-C(mg/dL)	47 (42–58)	48 (41–58)	NS
ALB (g/dL)	45±2.6	43 (38–45)	.001*
CRP (mg/L)	2 (1–3)	5.6 (1.6–10)	.002*
WBC (K/µL)	6.5 ± 1.2	8.3 ± 1.9	.001*
NEU (K/µL)	3.7±1	4.9 ± 1.7	.001*
LYM (K/µL)	2.21±0.49	2.57 ± 0.9	.03*
PLT (K/µL)	223±50	286 (236–331)	.001*
CAR	0.044 (0.042–0.051)	0.128 (0.043–0.244)	.001*
NLR	1.58 (1.21–2.12)	1.87 (1.21–2.62)	NS
PLR	104±28	113 (87–148)	NS

Note: FH, familial hypercholesterolemia; CRP, c-reactive protein; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride; WBC, white blood cells; NEU, neutrophil; LYM, lymphocyte; PLT, platelet; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CAR, CRP-to-albumin ratio; NS, non-significant. The results (except age) are shown as mean ± standard deviation for parameters with normal distribution or as median and 1st–3rd quartiles for parameters not showing normal distribution. Ages are shown as median and minimum–maximum.*The differences between groups were considered significant if the p-value was less than .05 (two-tailed).

Table 2. The characteristics, biochemical, and hematological results of the subgroups of the patients with familial hypercholesterolemia and healthy controls

Parameters		Control (N=35)	G1 (N=34)	G2 (N=37)	G3 (N=30)	P value
Age (years)		39±14 (18–68)	47±15 (18–77)	52±10 (24–59)[ab]	25±4 (20–44)[abc]	.001[a]
Gender	Male (n,%)	17 (% 49)	14 (% 42)	11 (% 30)	15 (% 50)	NS
	Female (n,%)	18 (% 51)	20 (% 58)	26 (% 70)	15 (% 50)	
TC (mg/dL)		161±23	417 (392–481)[a]	325 (307–346)[b]	258 (254–275)[ab]	.001[a]
TG (mg/dL)		84±37	468 (260–683)[a]	206 (160–284)[ab]	218±81[ab]	.001[a]
LDL-C (mg/dL)		95±20	362 (339–390)[a]	268 (258–278)[b]	212±15[b]	.001[a]
HDL-C (mg/dL)		47 (42–58)	56±23[a]	47±10[b]	46 (42–58)	NS
ALB (g/dL)		45±2.6	40 (33–44)[a]	44 (41–46)[ab]	43±5[ab]	.001[a]
CRP (mg/L)		2 (1–3)	7.2 (1.8–12.6)[a]	5.9 (2.5–9.1)[a]	3.1 (1.3–7.2)[ac]	.003[a]
WBC (K/µL)		6.5 ± 1.2	8.7 ± 2.3[a]	7.8 ± 1.6	8.48 ± 1.1.7	.001[a]
NEU (K/µL)		3.7±1	5.4±2.1[a]	4.4±1.3	5±1.6[a]	.001[a]
LYM (K/µL)		2.2±0.5	2.4±0.9[a]	2.6±0.9[a]	2.7±0.8[a]	.03[a]
PLT (K/µL)		223±50	278 (233–353)[a]	289±81[ab]	288±57[c]	.001[a]
CAR		0.044 (0.042–0.051)	0.189 (0.054–0.339)[a]	0.134 (0.059–0.220)[ab]	0.068 (0.031–0.172)[ac]	.001[a]
NLR		1.5 (1.2–2.1)	2 (1.3–3.6)[a]	1.7 (1.2–2.3)	1.5 (1.1–2.6)[a]	NS
PLR		104±28	127 (96–183)[a]	110 (83–146)[ab]	105 (90–126)	NS

Note: FH, familial hypercholesterolemia; CRP, c-reactive protein; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride; WBC, white blood cells; NEU, neutrophil; LYM, lymphocyte; PLT, platelet; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CAR, CRP-to-albumin ratio; NS, non-significant. The results (except age) are shown as mean ± standard deviation for parameters with normal distribution or as median and 1st–3rd quartiles for parameters not showing normal distribution. Ages are shown as median and minimum–maximum. p<.050 was considered statistically significant. [a]p<.050, vs. the control group. [b]p<.050, vs. the G1 group. [c]p<.050, vs. the G2 group

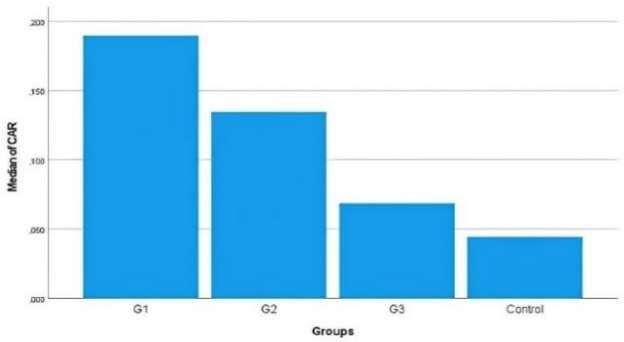

Figure 1. The median values of CRP-to-albumin ratio for the subgroups of patients with familial hypercholesterolemia (G1, G2, G3) and the controls.

The ROC curve analysis of the CAR for distinguishing FH from the controls is presented in Figure 2, showing the relationship between sensitivity and 1-specificity for different threshold values of the CAR. The AUC value was 0.715 (95% confidence interval [CI]: 0.626–0.824, P=0.0001) for CAR. The point of 0.075 on the curve for the CAR exhibited a sensitivity of 62% and a specificity of 94% for distinguishing FH from the controls.

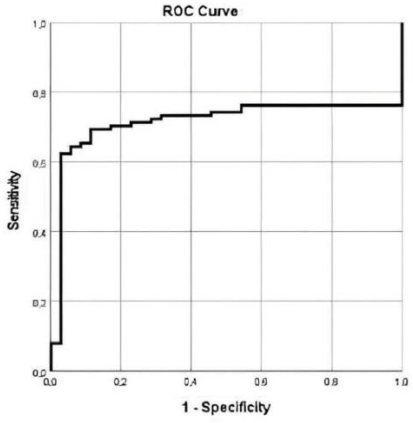

Figure 2. The ROC curve analysis for CRP-to-albumin ratio for distinguishing familial hypercholesterolemia from the controls

Discussion

FH is an inherited disorder of lipid metabolism, and the risk of CAD is high in patients with FM (Falk et al., 2006, Hansson, 2005). Therefore, timely detection of FH before the complications of it begin is very important. Unfortunately, the widespread lack of awareness regarding FH tends to hinder accurate diagnosis of it. Implementation of systematic screening programs for high-risk populations, such as those with a family history of FH or heart disease at an early age, will be useful in early diagnosis of the disease. FH can be diagnosed according to clinical criteria such as the Simon Broome or Dutch Lipid Clinic Criteria. These criteria include high LDL-C levels, family history, and tendon xanthomas (cholesterol deposits under the skin). Nevertheless, the diagnosis and management of FH also require collaboration between primary care physicians, cardiologists, laboratory specialists, and genetic counselors (WHO, 1999). We performed this study considering that the albumin and CRP may provide information about the disease in addition to classical lipid tests in FH. To our knowledge, this study is the first to evaluate the CARin patients with FH.

CAR, which has recently been used in the diagnosis and follow-up of many diseases, is an important parameter that deserves more comprehensive research, considering the severity of FH and the potential to prevent its complications through early diagnosis (Visseren et al., 2021, Eckart et al., 2020). The AUC value of 0.715 calculated for CAR shows good diagnostic ability in familial hypercholesterolemia in the study. Moreover, the p-value of 0.0001 confirms the statistical significance of this discriminatory capacity and increases the robustness of the diagnostic efficiency of this ratio. Current literature predominantly suggests that CAR can be used as a predictor of various medical conditions, including malignancies, sepsis, and septic shock. For example, Kinoshita et al. (2015) investigated the association between survival of patients with hepatocellular carcinoma using a cut-off value of 0.037 for CAR. The findings conclusively demonstrate a significant association between the elevated CAR (The optimal cutoff level ≥0.037) and both tumor progression and decline in liver functional reserve. In addition, the study highlights the plausible role of CAR as a potential prognostic indicator in patients with hepatocellular carcinoma. A comprehensive cohort study of 205 patients was conducted by Yamagata et al. (2021) between 2015 and 2018 to elucidate the prognostic utility of inflammatory markers in oral squamous cell carcinoma (OSCC). The rigorous review revealed CAR exhibiting 59.3% sensitivity and 75.3% specificity when set to a cutoff threshold of 0.032. As a result, CAR has been considered an important prognostic marker for OSCC. This study also validates the potential integration of CAR into routine medical evaluations, coupled with its convenient and rapid acquisition, thus establishing its reputation as a valuable tool in predicting outcomes for patients with OSCC.

The point of 0.075 on the curve for the CAR exhibited a sensitivity of 62% and a specificity of 94% for distinguishing FH from the controls, and it provided significant diagnostic ability. So, a sensitivity rate of 62% showed that the test was suitable for accurately identifying true positives, and a specificity rate of 94% showed that it was quite good at identifying true negatives. The specificity obtained with our findings is higher than that of CARs in studies involving various cancer patients, which is very promising for new studies. This high specificity rate serves as a positive confirmation of the diagnostic robustness and discriminatory potential of our approach and contributes to the overall significance of the results of our study.

CRP testing is widely used in patients with acute pancreatitis both at hospital admission and during treatment follow-up (Staubli et al., 2015). For instance, Piñerúa-Gonsálvezet al. (2023) investigated the correlation between CAR and the severity of acute pancreatitis. In particular, the results showed that an AUC value of 0.68for CAR exceeded the discriminatory capacity of the

Ranson criteria, which had an AUC value of 0.62. Regarding the prognosis of severe acute pancreatitis, a reasonably chosen cut-off value of 7.51 was determined to be optimal, providing a sensitivity of 63.4% and a specificity of 65.6%. These findings demonstrate the potential of CAR to predict the severity of acute pancreatitis. In addition, a study by Wang et al. (2010) showed that decreased albumin levels and elevated CRP levels were predictive of a poor prognosis in patients with acute pancreatitis. These findings also support the concept that the measurement of CRP and albumin levels can be used as predictive markers to assess the risk of death in individuals with acute pancreatitis.

The study performed by Aksu et al. (2019) investigated the association between CAR and stent restenosis with demographics of patients suffering from ST-segment elevation myocardial infarction (STEMI). As a result of the study, a high CAR emerged as a predictive factor for SR in STEMI cases, with a defined cutoff value of 1.25. Its predictive capacity has been highlighted with 84% sensitivity and 70% specificity. Similar to any other research, the cohort study involving 344 patients suffering from acute coronary syndrome revealed a significant result. It has been confirmed that high CAR shows remarkable efficacy in predicting the prognosis of moderate to high SYNTAX scores, thus exceeding the predictive capacity of CRP and albumin alone (Çağdaş et al., 2019). Considering that acute coronary diseases represent the primary cause of death among individuals suffering from FH, and in light of the rather high sensitivity values obtained in our study, our thesis proposes the usage of CAR as a powerful tool to measure the diagnosis and severity of FH.

In our study, as a result of the comparison between the group with the highest LDL-C levels and the control group, WBC, NEU and LYM counts were also significantly higher, which may lead to a judgment in line with studies (Taghizadeh et al., 2020) on the presence of endothelial dysfunction and atherosclerotic inflammation with increased oxidized LDL-C levels. In addition, the significant difference in PLR level between the control group, group 1 and group 2 is consistent with the fact that it is a routine test used in the prediction of cardiovascular diseases (Condado et al., 2016). The significant difference in the NLR ratio between the control group and group 1 in our study, which has a strong correlation with atherosclerotic cardiovascular disease and is considered as an inflammatory biomarker, confirms the possibility of cardiovascular disease with a higher rate in FH patients (Hu et al., 2020).

Conclusion

The findings of our study emphasize the importance of CAR as a diagnostic indicator for FH. Its significance is further amplified by its suitability for assessment through routine clinical tests, its rapid and simple result generation, and its exceptional sensitivity in comparison to numerous alternative diagnostic markers. Thanks to its potential as a valuable prognostic marker, our study will contribute to the literature on the use of CAR in the diagnosis and follow-up of many diseases such as FM. We would like to add that additional prospective studies involving larger and more diverse populations, conducted in multiple research centers, are mandatory to rigorously assess the utility of the CAR as a reliable diagnostic for FH and predictor of mortality. The limitations of our study were as follows: First, there isn't any reliable gold standard method for selecting patients with FH. Moreover, there were more females than males in each group. The sample sizes of each subgroup were too small and. Additionally, our patient groups may differ in the usage of some medications, and we did not have detailed information about whether these drugs affected any test results.

Ethics Committee Approval: Ethical approval was obtained from the "Erzurum Regional Training and Research Hospital, Medical Ethics Committee" (Approval date 08.11.2018 and number: 2018/17-160).
Informed Consent: Due to the retrospective design of the study, informed consent was not taken.
Peer-review: Externally peer-reviewed.
Author Contributions: Concept – A.L.O., K.A.; Design – A.L.O., K.A., K.A.; Supervision – A.L.O., K.A., O.S., M.H.A.; Resources – A.L.O.; Data Collection and/or Processing – A.L.O., K.A., K.A., O.S.; Analysis and/or Interpretation - A.L.O., K.A.; Literature Search - A.L.O., K.A.; Writing - A.L.O.; Critical Review – K.A., K.A., M.H.A.
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