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RESEARCH

The association between C-reactive protein/albumin ratio and aortic arch calcification in acute coronary syndrome patients

Akut koroner sendrom hastalarında C-reaktif protein/albümin oranı ile aort ark kalsifikasyonu arasındaki ilişki

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Abstract

Purpose: We evaluated the association between the severity of aortic arch calcification (AAC) and C-reactive protein/albumin ratio (CAR) in acute coronary syndrome (ACS) patients.

Materials and Methods: 288 patients who presented with ACS and underwent coronary angiography were enrolled analysis. CAR was calculated as serum CRP/albumin x 10. The AAC was separated into four groups (0 to 3): Grade 0-1 AAC was defined as the non-severe AAC group, and those with grade 2-3 AAC were defined as the severe AAC group.

Results: CRP and CAR were significantly higher in the severe AAC group than in the non-severe AAC group. Multivariate analysis determined that CAR and age were positively associated in ACS patients as an independent predictor of severe AAC. CAR area under the curve (AUC) and CRP AUC demonstrated parallel curves compared to albumin levels, indicating higher statistical significance. The AUC for albumin was 0.349 (95% CI: 0.286-0.413). The AUC for CAR was 0.695, 95% CI 0.625 to 0.753, for CRP the AUC was 0.684 (95% CI: 0.620-0.748). After stratification into 2 groups according to the CAR cut-off value (1.664), the rate of severe AAC was importantly often in high CAR patients compared to in low CAR patients (56.7% vs 23.7%).

Conclusion: CAR, an easily calculable, repeatable, and valid surrogate marker of inflammation, can be used reliably to indicate severe AAC in ACS patients.

Keywords:. C-reactive protein, aortic arch calcification, acute coronary syndrome

Öz

Amaç: Akut koroner sendrom (AKS) hastalarında aortik ark kalsifikasyonunun ciddiyeti (AAC) ile C-reaktif protein/Albümin oranı (CAR) arasındaki ilişkiyi değerlendirdik.

Gereç ve Yöntem: AKS ile başvuran ve koroner anjiyografi yapılan 288 hasta analize dahil edildi. CAR serum CRP/albümin x 10 olarak hesaplandı. AAC dört gruba ayrıldı (0 ila 3): Grade 0-1 AAC, ciddi olmayan AAC grubu olarak; grade 2-3 AAC olanlar ise ciddi AAC grubu olarak tanımlandı.

Bulgular: CRP ve CAR, ciddi AAC grubunda, ciddi olmayan AAC grubuna göre anlamlı derecede yüksekti. Çok değişkenli analiz, AKS hastalarında ciddi AAC'nin bağımsız bir belirleyicisi olarak CAR ve yaşın pozitif ilişkili olduğunu belirledi. Eğri altındaki CAR alanı (AUC) ve CRP AUC, albümin seviyesine kıyasla paralel eğriler gösterdi ve bu da daha yüksek istatistiksel anlamlılığa işaret ettiğini gösterdi. Albüminin AUC'si 0,349'du (%95 GA: 0,286-0,413). CAR için AUC 0,695, %95 GA 0,625 ila 0,753, CRP için AUC 0,684 (%95 GA: 0,620-0,748) idi. CAR kesme değerine (1,664) göre 2 gruba ayrıldıktan sonra, ciddi AAC oranı, yüksek CAR hastalarında düşük CAR hastalarına kıyasla önemli ölçüde daha sık görüldü (%56,7 vs %23,7).

Sonuç: Kolayca hesaplanabilen, tekrarlanabilir ve geçerli bir inflamasyon belirteci olan CAR, AKS hastalarında ciddi AAC'yi öngörmek için güvenilir bir şekilde kullanılabilir.

Anahtar kelimeler: C-reaktif protein, aortik ark kalsifikasyonu, akut koroner sendrom

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INTRODUCTION

Although vascular calcification (VC) has been considered a degenerative process and part of aging, recent studies have shown that VC in patients with cardiovascular disease involves different pathophysiological mechanisms[1,2]. Although it has been shown that VC can occur in almost any part of the aorta, from the aortic arch to the abdominal aorta, the underlying mechanism between aortic VC and the associated deterioration in cardiovascular function is unclear. Studies show that vascular calcification, particularly aortic arch calcification (AAC), is a risk factor for adverse cardiovascular events and mortality[3-5]. As there are no treatments available to prevent or regress AAC, new markers have recently become important to diagnose the onset of the VC process or to prevent the development of VC[6]. Therefore, there is a need to identify reproducible, easily calculable, cost-effective, and clinically applicable markers that can serve as early warnings in the prediction of AAC.

Inflammation is important in the development of atherosclerosis and VC. Inflammatory biomarkers, such as interleukin, fibrinogen, and C-reactive protein (CRP) are related to subclinical cardiovascular diseases and coronary artery disease[7-10]. Albumin has been described as a negative acute phase reactant. Epidemiological research has demonstrated an association between hypoalbuminemia and the development of cardiovascular disease[11].

Some research suggests that the CRP/albumin ratio (CAR) is more valuable in predicting inflammation[12,13]. Early warning markers are needed to predict severe AAC in ACS patients and may contribute to the development of treatment strategies to prevent adverse cardiac events. However, no studies have shown whether there is a relationship between the severity of AAC and CAR in ACS patients. In this study, we investigated the relationship between the severity of AAC and CAR in ACS patients.

MATERIALS AND METHODS

Sample

The minimum number of patients who needed to be included for an effect size of 0.2 and 90% power was calculated and 288 ACS patients were included in this retrospective study. Inclusion criteria were patients diagnosed with ACS who underwent coronary angiography at Karabük University Training and Research Hospital between November 2021 and December 2022, regardless of whether they received medical treatment, coronary artery bypass surgery, or percutaneous coronary intervention were retrospectively included in the study.

Patient records and data were carefully reviewed by 2 expert cardiologists. Patients with incomplete clinical data and insufficient angiographic or chest radiographic images and reports were excluded from the analysis. ACS was defined as ST-segment elevation myocardial infarction (STEMI), unstable angina pectoris (USAP), non-ST-segment elevation myocardial infarction (NSTEMI) for which coronary angiography was performed and was diagnosed according to the European Society of Cardiology guidelines[14]. This research adhered to the Declaration of Helsinki. Informed consent was obtained from all patients. The research was approved by the Ethics Committee of Karabuk University (Date: 2023/02/27, No: 2023/1276).

Data collection

Patient demographics, medical history, laboratory test results, echocardiography, angiography, procedural characteristics, and chest radiography were obtained from hospital records. After diagnosis of ACS, blood samples were taken from peripheral veins before the coronary angiography. Complete blood count and conventional biochemical parameters were checked. Serum albumin and CRP levels were calculated with a Cobas 8000 c502 automated biochemistry analyzer (Roche Diagnostics, Indianapolis, Indiana). CAR was calculated as serum CRP/albumin x 10.

Angiographic analysis

The percutaneous transfemoral or transradial technique was used in all patients who underwent selective coronary angiography. All patients without contraindications received oral chewable acetylsalicylic acid (300 mg) and a loading dose of ticagrelor (180 mg) or clopidogrel (600 mg). In STEMI patients, stenting and balloon angioplasty were used to treat the culprit lesions, if necessary. For NSTEMI and USAP patients, the decision to PCI or medical management was made by the operator, and for patients considered for bypass, by the Heart Council, consisting of cardiology and cardiovascular surgery specialists.

Evaluation of aortic arch calcification

Patients participating in the research had a chest x-ray (AXIOM Aristos MX, SIEMENS, Germany) or a removable chest x-ray (MUX-200D, SHIMADZU, Japan) during their hospitalization. AAC was evaluated in a blinded manner by two independent, experienced cardiologists. The extent of AAC is separated into four groups (0 to 3): grade 0, no calcification; grade 1, small patches of calcification in the aortic knob or a single thin area of calcification; grade 2, one or more thick zones of calcification; grade 3, circumferential calcification of the aortic knob[15]. Fifty randomly selected chest X-rays were assessed for intra- and interobserver variability by two cardiologists blinded to the study results. There was a reasonably close agreement consistency between assessments (intraobserver kappa value = 0.916, interobserver kappa value = 0.832, $p < 0.001$ for both assessments).

Statistical analysis

Statistical analysis was reported using the IBM SPSS program (IBM SPSS Statistics for Windows, Version 21.0, IBM Corp., Armonk, New York, USA). Normally distributed continuous variables were reported as means (±SD). Categorical variables were reported as numbers and percentages. Continuous variables with normal distribution between the two groups were evaluated with the Student's *t*-test. Categorical data was evaluated with the Chi-square or Fisher's exact test. The Cohen's kappa value was utilized to calculate intra and interobserver variability. To establish the independent predictors of severe AAC, univariate and multivariate logistic regression analyses were applied. Since the calculation of CAR included CRP and albumin, these risk factors were excluded from univariate and multivariate analyses. The diagnostic value of CAR for predicting the severity of AAC was analyzed by receiver operating characteristic (ROC) curve analysis. Then, patients were classified by the best CAR cut-off value.

RESULTS

Between November 2021 and December 2022, 314 patients who were diagnosed with ACS and underwent coronary angiography were screened. After 26 patients (10 STEMI, 12 NSTEMI, 4 USAP) were excluded from the research missing information, the remaining 288 patients were divided into 2 groups according to AAC status. Those with grade 0-1 AAC were defined as the non-severe AAC group, and those with grade 2-3 AAC were defined as the severe AAC group.

Baseline clinical, and laboratory characteristics between the groups are displayed in Table 1. The severe AAC group was older than the non-severe AAC group ($p<0.001$). However, EF was significantly lower in the severe AAC group ($p=0.002$). History of hypertension, diabetes, hyperlipidemia, and MI were more common in the severe AAC group compared to the non-severe AAC group (all $p<0.05$). Although GFR and triglyceride were significantly lower in the severe AAC group compared to the non-severe AAC group, CRP and CAR were significantly higher (all $p<0.05$).

Angiographic characteristics and in-hospital adverse events between the groups are shown in Table 2. Multivessel disease was observed remarkably more in the severe AAC group than in the non-severe AAC group ($p<0.001$). In-hospital mortality and inotropic agent use were significantly more frequent in the severe AAC group compared with the non-severe AAC group (all $p<0.05$).

The univariate and multivariate analysis and independent predictors of severe AAC were presented in Table 3. Univariate analysis revealed that gender, age, myocardial infarction, hypertension, diabetes mellitus, hyperlipidemia, EF, GFR, and CAR were risk factors for severe AAC (all $p<0.05$). Multivariate analysis found that age and CAR were positively associated as independent predictors of severe AAC in ACS patients.

CRP, albumin, and CAR were compared by ROC curve analysis. CRP area under the curve (AUC) and CAR AUC demonstrated parallel curves compared to albumin levels, indicating higher statistical significance (Figure 1). The AUC of CAR was 0.695 (95% CI 0.625 to 0.753) ($p<0.001$). The cut-off value of CAR to predict severe AAC was 1.664, with a sensitivity of 73.1% and specificity of 60.6%.

The frequency of severe AAC in the classification made according to the cut-off value of the CAR was shown in Figure 2. After stratification into 2 groups according to the cut-off value of CAR, there were 154 (53.4%) patients with a high CAR (≥1.664) and 134 (46.6%) patients with a low CAR (<1.664). Severe AAC was found significantly more often in patients with a high CAR than in those with a low CAR (56.7% vs 23.7% $p<0.001$)

Table 1. Baseline demographics, clinical and laboratory characteristics

Parameters	Total (n = 288)	Non-Severe AAC (n = 170)	Severe AAC (n = 118)	p
Age, years	63 (±13.1)	57.6 (±12.1)	71.9 (±9.3)	<0.001
Gender (Male)	224 (77.6%)	142 (83.5%)	82 (69.4%)	<0.001
Killip Classification				0.113
1	251 (86.9%)	154 (90.6%)	97 (81.7%)	
2	17 (6.2%)	9 (5.3%)	8 (7.5%)	
3	13 (4.5%)	5 (2.9%)	8 (6.7%)	
4	7 (2.4%)	2 (1.2%)	5 (4.2%)	
EF (%)	46.2 (±8.5)	47.5 (±8.7)	44.3 (±7.8)	0.002
Medical history				
Hypertension	124 (42.8%)	49 (28.8%)	75 (62.5%)	<0.001
Diabetes mellitus	99 (34.2%)	50 (29.4%)	52 (44.0%)	0.031
Hyperlipidemia	28 (9.7%)	10 (5.9%)	18 (15.0%)	0.010
MI	78 (26.8%)	38 (22.4%)	40 (33.3%)	0.038
PCI	62 (21.5%)	33 (19.4%)	29 (24.2%)	0.331
CABG	17 (5.9%)	7 (4.1%)	10 (8.3%)	0.132
Laboratory findings				
LDL-c (mg/dl)	97 (±35.1)	98.9 (±35.8)	95.4 (±35)	0.422
HDL-c (mg/dl)	44 (±10)	43.5 (±10.5)	43.5 (±10.2)	0.973
Total cholesterol (mg/dl)	170 (±46)	173.2 (±46.9)	164.7 (±44.6)	0.12
Triglycerid (mg/dl)	123 (±106)	130 (±120)	113 (±88)	0.022
GFR (mL/min)	85,5 (±30.7)	93 (±29.7)	74.1 (±29.1)	<0.001
FPG (mg/dl)	106 (±44)	104.5 (±43)	109 (±47)	0.598
WBC (10^9/L)	10.2 (4.9)	10.3 (4.5)	9.85 (5.6)	0.759
CRP (mg/L)	7.6 (14)	6.1 (7.4)	12.5 (32.3)	<0.001
Albumin (g/dL)	4.3 (0.6)	4.3 (0.4)	4.3 (0.4)	0.069
CRP/Albumin	4.47 (±8.47)	2.65 (±4.48)	7.1 (±11.6)	<0.001

Continuous variables presented as mean (±standard deviation) or median (interquartile range). Other data is presented as numbers (percentages). P values indicate the difference between Non-severe AAC and Severe AAC. EF, ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; GFR, glomerular filtration rate; FPG, fasting plasma glucose; WBC, white blood cells; CRP, C-reactive protein.

Table 2. Comparison of angiographic, procedural characteristics, and in-hospital outcomes

Parameters	Total (n = 288)	Non-Severe AAC (n = 170)	Severe AAC (n =118)	p
MI type				
STEMI	145 (50.7%)	83 (48.8%)	62 (53.3%)	0.735
NSTEMI	140 (28.3%)	85 (50.0%)	55 (45.8%)	
USAP	3 (1%)	2 (1.2%)	1 (0.8%)	
Vessel count				
0	6 (2%)	5 (3.1%)	1 (0.8%)	<0.001
1	122 (42%)	86 (52.8%)	36 (30.5%)	
2	60 (20.7%)	33 (20.2%)	27 (22.9%)	
3	93 (32%)	39 (23.9%)	54 (45.8%)	
Results				
PTCA/PCI	213 (74.1%)	133 (78.2%)	80 (68.3%)	0.164
Medical	29 (10.0%)	14 (8.2%)	15 (12.5%)	
CABG	46 (15.9%)	23 (13.5%)	23 (19.2%)	
In hospital outcomes				
Death	12 (4.1%)	3 (1.8%)	9 (7.5%)	0.016
CPR	18 (6.2%)	7 (4.1%)	11 (9.2%)	0.079
VT/VF	24 (8.3%)	11 (6.5%)	13 (10.8%)	0.184
Hemodialysis	6 (2.1%)	3 (1.8%)	3 (2.5%)	0.665
Inotropic Agent	25 (8.6%)	10 (5.9%)	15 (12.5%)	0.048
Transient Pacemaker	5 (1.7%)	2 (1.2%)	3 (2.5%)	0.394
AF during Hospitalization	1 (0.3%)	0 (0.0%)	1 (0.8%)	0.233

Data is presented as numbers (percentage%). P values indicate the difference between Non-severe AAC and Severe AAC. MI, myocardial infarction; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction; USAP, unstable anjına pectoris; PTCA, percutaneous transluminal coronary angioplasty; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CPR, cardiopulmonary resuscitation; VT, ventricular tachycardia; VF, ventricular fibrillation; AF, atrial fibrillation.

Table 3. Multivariate Regression Analysis for Potential Predictors of Severe AAC

Parameters	Univariate analysis		Multivariate analysis		Odds Ratio (95% CI)
	β	p	β	p	
Age, years	0.112	<0.001	0.086	<0.001	1.09 (1.052-1.13)
Gender (Male)	0.93	0.001	0.658	0.110	1.93 (0.861-4.325)
Myocardial infarction	0.552	0.039	0.34	0.352	1.404 (0.687-2.87)
Hypertension	1.415	<0.001	0.05	0.889	1.052 (0.517-2.141)
Diabetes mellitus	0.539	0.031	-0.144	0.694	0.866 (0.422-1.777)
Hyperlipidemia	1.038	0.012	0.339	0.519	1.403 (0.501-3.931)
EF (%)	-0.044	0.003	-0.024	0.262	0.977 (0.937-1.018)
GFR (mL/min)	-0.023	<0.001	-0.002	0.748	0.998 (0.986-1.01)
CRP/Albumin	0.125	<0.001	0.136	0.001	1.146 (1.057-1.243)

CI, confidence interval; EF, ejection fraction; GFR, glomerular filtration rate; CRP, C-reactive protein.

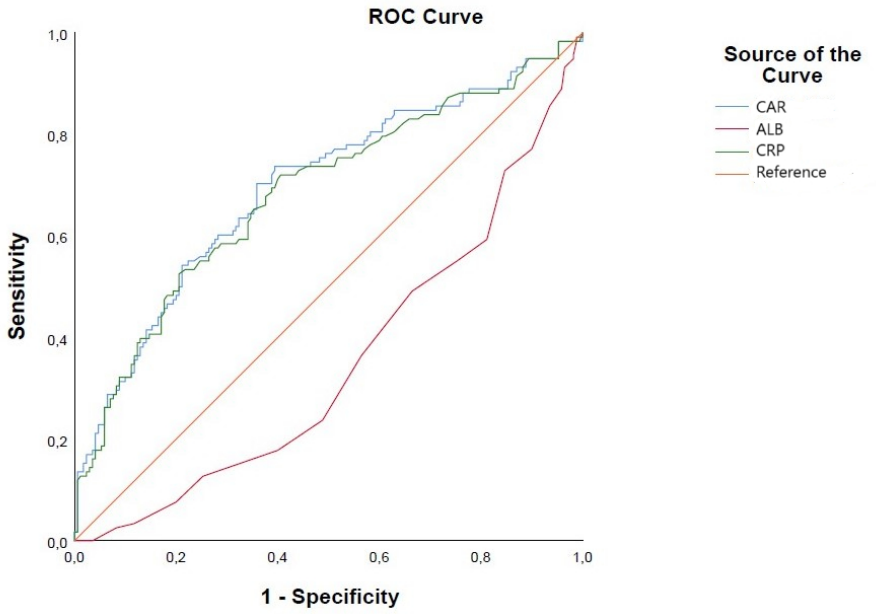

Figure 1. Receiver operating characteristic (ROC) curves of C-reactive protein (CRP), albumin, and CRP/albumin ratio (CAR) (Area Under the Curve (AUC) for CRP 0.684 (95% CI: 0.620-0.748). AUC for albumin, 0.349 (95% CI: 0.286-0.413). AUC for CAR, 0.695 (95% CI 0.625-0.753, p<0.001).

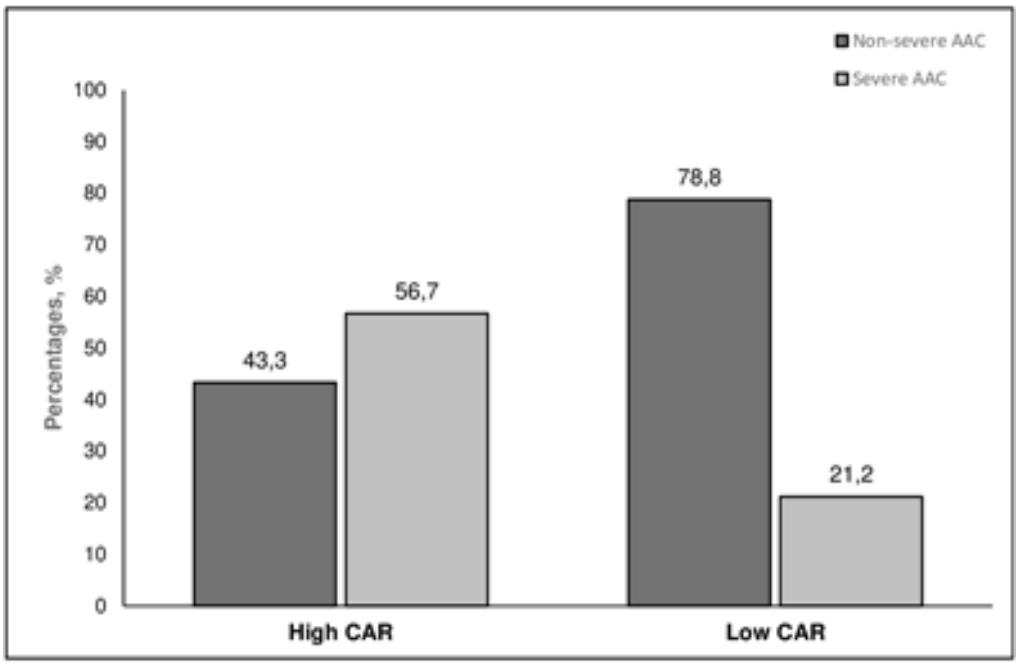

Figure 2: Severe AAC according to CRP/albumin ratio groups (56.7% vs 23.7%, p<0.001).

DISCUSSION

Key findings from this research: First, CAR levels were significantly higher in patients with severe AAC compared to patients with non-severe AAC. CAR was observed to be an independent predictor of AAC severity in ACS patients. Second, when patients were divided according to the CAR cut-off value, a significantly higher proportion of severe AAC was observed in high CAR patients than in low CAR patients (56.7% vs. 23.7% $p<0.001$).

VC comprises a result of calcium deposition in the intima and media laminas of the vessel wall and can be easily identified using non-invasive radiographic imaging techniques[16]. AAC shows calcification of the aortic arch on standard chest x-ray and also reflects calcification of other parts of the aorta and other vascular structures[17]. AAC is a significant predictor of subclinical atherosclerosis and adverse cardiovascular events[18-19]. In addition, AAC is associated with atherosclerosis-associated diseases, including stroke, heart failure, diabetes mellitus, coronary artery disease, and chronic renal failure[20,21].

Similar risk factors are associated with both calcifications in the thoracic aorta and coronary artery disease. The underlying mechanism of thoracic aortic calcification and coronary atherosclerosis is similar[20-22]. However, not every AAC grade may have high predictive power in predicting cardiovascular events[23]. One study found that the degree of severe AAC (grade 2-3) had a stronger predictive value in predicting adverse adverse cardiovascular events. However, when each AAC grade was analyzed separately, AAC grade 1 had no statistically significant predictive value compared with grade 0[24]. It was suggested that negligible aortic arch calcification may not be a detectable cardiovascular risk. There may be differences between non-severe and severe AAC patients. In our study, since there was no statistical difference between AAC grade 0 and grade 1, we divided them into two groups: non-severe AAC and severe AAC. Therefore, there is a particular need for early warning markers that indicate the severity of AAC degree.

Inflammation is present at all stages of atherosclerotic lesions. Elevation of inflammatory markers is an important finding indicating the activation of vascular damage[25]. In addition, inflammation resulting from atherosclerosis may also ultimately contribute to VC. Inflammatory biomarkers, particularly CRP, are important in determining the severity and prognosis of coronary artery disease[7,26]. However, since serum albumin levels are inversely proportional to the inflammatory response, albumin is considered a negative acute phase reactant. It is known that albumin synthesis decreases and catabolism increases during inflammation. The relationship between hypoalbuminemia and ACS has been shown[27]. The neutrophil-to-lymphocyte ratio has been accepted as a valuable index related to atherosclerotic diseases. It is a better predictor of the severity of aortic arch calcification than neutrophil or lymphocyte counts, especially in patients with ischaemic stroke[28,29]. We used CAR, assuming that the indices created by combining two parameters would have a better predictive value than a single parameter.

Some studies suggest that the CAR may be better at predicting infection and inflammatory responses[12,13]. However, there are studies investigating the relationship between serum CAR and inflammatory diseases (such as ulcerative colitis, acute pancreatitis, cancer, sepsis, and coronary artery disease)[11]. In our research, we investigated the role of CAR in predicting severe AAC in patients with ACS. We demonstrated that CAR was an independent predictor of severe AAC in ACS patients. However, the CRP AUC and CAR AUC demonstrated parallel curves compared to the albumin levels, indicating higher statistical significance. Although CAR AUC and CRP AUC were similar, CAR AUC performed better than CRP AUC. In addition, the rate of severe AAC was significantly higher in patients with high CAR than in those with low CAR (56.7% vs. 23.7% $p<0.001$). A causal relationship cannot be established with these results and randomized controlled studies are needed to prove this.

Our study has several limitations. 1) Our study is relatively underpowered because it is single-centre and retrospective. 2) The number of patients is relatively small. 3) CRP and albumin levels were only measured during hospitalization and no repeated measurements were made.

In conclusion; CAR, an easily calculable, cost-effective, reproducible, and valid marker of inflammation, can be reliably used as an indicator of severe AAC in ACS patients. CAR can be used as an early warning marker in predicting severe AAC in ACS patients and may improve risk stratification and contribute to prognosis by providing therapeutic

applications in the clinical evaluation of ACS patients. It may contribute to the development of treatment strategies to prevent adverse cardiac events. At the same time, it may have economic, social, and psychological benefits by shortening the duration of hospital stay.

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REFERENCES

1. Lee SJ, Lee IK, Jeon JH. Vascular calcification-new insights into its mechanism. Int J Mol Sci. 2020;21:2685.
2. Singh A, Tandon S, Tandon C. An update on vascular calcification and potential therapeutics. Mol Biol Rep. 2021;48:887-96.
3. Demer LL, Tintut Y. Vascular calcification: Pathobiology of a multifaceted disease. Circulation. 2008;117:2938-48.
4. Greenland P, Bonow RO, Brundage BH, Budoff MJ, Eisenberg MJ, Grundy SM et al. Accf/aha 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: A report of the american college of cardiology foundation clinical expert consensus task force (accf/aha writing committee to update the 2000 expert consensus document on electron beam computed tomography) developed in collaboration with the society of atherosclerosis imaging and prevention and the society of cardiovascular computed tomography. J Am Coll Cardiol. 2007;49:378-402.
5. Guzman RJ. Clinical, cellular, and molecular aspects of arterial calcification. J Vasc Surg. 2007;45:A57-63.
6. Rajamannan NM, Evans FJ, Aikawa E, Grande-Allen KJ, Demer LL, Heistad DD et al. Calcific aortic valve disease: Not simply a degenerative process: A review and agenda for research from the national heart and lung and blood institute aortic stenosis working group. Executive summary: Calcific aortic valve disease-2011 update. Circulation. 2011;124:1783-91.
7. Danesh J, Wheeler JG, Hirschfield GM, Eda S, Eiriksdottir G, Rumley A et al. C-reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. N Engl J Med. 2004;350:1387-97.
8. Li JJ, Zhu CG, Yu B, Liu YX, Yu MY. The role of inflammation in coronary artery calcification. Ageing Res Rev. 2007;6:263-70.
9. Ross R. Atherosclerosis--an inflammatory disease. N Engl J Med. 1999;340:115-26.
10. Sung JH, Lee JE, Samdarshi TE, Nagarajarao HS, Taylor JK, Agrawal KK et al. C-reactive protein and subclinical cardiovascular disease among african-americans: (the jackson heart study). J Cardiovasc Med (Hagerstown). 2014;15:371-6.
11. Arques S. Human serum albumin in cardiovascular diseases. Eur J Intern Med. 2018;52:8-12.
12. Li L, Dai L, Wang X, Wang Y, Zhou L, Chen M et al. Predictive value of the c-reactive protein-to-prealbumin ratio in medical icu patients. Biomark Med. 2017;11:329-37.
13. Qin G, Tu J, Liu L, Luo L, Wu J, Tao L et al. Serum albumin and c-reactive protein/albumin ratio are useful biomarkers of crohn's disease activity. Med Sci Monit. 2016;22:4393-400.
14. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A et al. 2023 esc guidelines for the management of acute coronary syndromes. Eur Heart J. 2023;44:3720-826.
15. Symeonidis G, Papanas N, Giannakis I, Mavridis G, Lakasas G, Kyriakidis G et al. Gravity of aortic arch calcification as evaluated in adult greek patients. Int Angiol. 2002;21:233-6.
16. Chen NX, Moe SM. Vascular calcification: Pathophysiology and risk factors. Curr Hypertens Rep. 2012;14:228-37.
17. Adar A, Erkan H, Gokdeniz T, Karadeniz A, Cavusoglu IG, Onalan O. Aortic arch calcification is strongly associated with coronary artery calcification. Vasa. 2015;44:106-14.
18. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with framingham score for risk prediction in asymptomatic individuals. Jama. 2004;291:210-5.
19. Adar A, Onalan O, Cakan F, Akbay E, Colluoglu T, Dasar U et al. A strong and reliable indicator for early postoperative major cardiac events after elective orthopedic surgery: Aortic arch calcification. Heart Lung. 2019;48:446-51.
20. Iribarren C, Sidney S, Sternfeld B, Browner WS. Calcification of the aortic arch: Risk factors and association with coronary heart disease, stroke, and peripheral vascular disease. Jama. 2000;283:2810-5.
21. Li LC, Lee YT, Lee YW, Chou CA, Lee CT. Aortic arch calcification predicts the renal function progression in patients with stage 3 to 5 chronic kidney disease. Biomed Res Int. 2015;2015:131263.
22. Takasu J, Katz R, Nasir K, Carr JJ, Wong N, Detrano R et al. Relationships of thoracic aortic wall calcification to cardiovascular risk factors: The multi-ethnic study of atherosclerosis (mesa). Am Heart J. 2008;155:765-71.

23. Hashimoto H, Iijima K, Hashimoto M, Son BK, Ota H, Ogawa S et al. Validity and usefulness of aortic arch calcification in chest x-ray. J Atheroscler Thromb. 2009;16:256-64.
24. Iijima K, Hashimoto H, Hashimoto M, Son BK, Ota H, Ogawa S et al. Aortic arch calcification detectable on chest x-ray is a strong independent predictor of cardiovascular events beyond traditional risk factors. Atherosclerosis. 2010;210:137-44.
25. Weissberg PL, Bennett MR. Atherosclerosis--an inflammatory disease. N Engl J Med. 1999;340:1928-9.
26. Wang J, Tan GJ, Han LN, Bai YY, He M, Liu HB. Novel biomarkers for cardiovascular risk prediction. J Geriatr Cardiol. 2017;14:135-50.
27. Murat SN, Kurtul A, Yarlioglues M. Impact of serum albumin levels on contrast-induced acute kidney injury in patients with acute coronary syndromes treated with percutaneous coronary intervention. Angiology. 2015;66:732-7.
28. Wang X, Zhang G, Jiang X, Zhu H, Lu Z, Xu L. Neutrophil to lymphocyte ratio in relation to risk of all-cause mortality and cardiovascular events among patients undergoing angiography or cardiac revascularization: A meta-analysis of observational studies. Atherosclerosis. 2014;234:206-13.
29. Zhou S, Cai B, Zhang Y, Wang L, Liu X, Xu G. The relationship between neutrophil-to-lymphocyte ratio and aortic arch calcification in ischemic stroke patients. J Stroke Cerebrovasc Dis. 2017;26:1228-32.