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Fibrosis-4 index is related to left atrial volume index in patients with acute coronary syndrome

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ABSTRACT

Objectives: This study aims to evaluate the predictive value of fibrosis-4 (FIB-4) index and left atrial (LA) indices in patients with acute coronary syndrome (ACS).

Patients and methods: Between September 2023 and March 2024, a total of 300 consecutive patients with ACS (244 males, 56 females; mean age: 62.7±11.7 years; range, 49 to 78 years) were included in the study. The study group was divided into two groups according to the LA volume index (LAVI) measurements as those with <34 mL/m^2 (Group 1, n=226) and those with ≥34 mL/m^2 (Group 2, n=74). Demographic, clinical and laboratory data of the patients were recorded.

Results: Among a total of 300 patients, 25.6% (n=77) were diagnosed with ST-elevation myocardial infarction (STEMI), 54% (n=162) with non-STEMI (NSTEMI), and 20.3% (n=61) with unstable angina pectoris (USAP). The FIB-4 index was positively associated with the LAVI (odds ratio [OR]=6.419; 95% confidence interval [CI]: 1.505-27.38; p=0.012). In addition, elevated FIB-4 index could predict a LAVI of ≥34 mL/m^2 (area under the curve [AUC]: 0.705, p<0.001).

Conclusion: An elevated FIB-4 index is correlated with increased LAVI scores, which may serve as a well-established indicator of adverse outcomes and a reliable measure of cardiovascular risk in patients with ACS.

Keywords: Acute coronary syndrome, fibrosis-4 index, left atrial volume index.

Acute coronary syndrome (ACS) significantly contributes to cardiovascular disease (CVD)-related mortality. It encompasses a spectrum of disorders, including acute myocardial infarction (MI) and unstable angina pectoris (USAP) and all of them are marked by significant myocardial damage.[1]

The atrial, particularly the left atrium (LA), size and function have a robust role in the clinical assessment of various cardiac conditions.[2] In daily practice, LA size is typically assessed by measuring the diameter obtained anteroposterior image.[3] Owing to the asymmetrical nature of the LA, volumetric measurements offer a more precise indication of its size compared to evaluations based solely on diameter or area. To evaluate the size of the LA, the preferred method involves calculating the LA volume and normalizing it to the body surface area.[4] Research has shown that, among the various parameters for evaluating cardiac organ damage, the LA volume index (LAVI) stands out for most discriminating measure.[5] Moreover, LAVI has emerged as a robust predictor of increased mortality risk, exhibiting independent significance from left ventricular (LV) geometry in a population with preserved systolic function.[6] Left ventricular diastolic dysfunction, induced by ventricular hypertrophy, arterial hypertension, and other cardiovascular (CV) conditions, results in elevated filling pressures and structural alterations in the atria owing to sustained pressure overload.[7] Researchers have suggested that the LAVI can be used to assess the intensity and longevity of diastolic dysfunction. Additionally, LAVI was identified to be potential

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indicator of adverse clinical outcomes including embolic stroke, atrial fibrillation (AF) development, and heart failure.[8] Various previous trials have shown that LAVI can predict major unfavorable cardiac events during hospitalization and beyond.[9,10]

The increasing prevalence of non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome has led to their recognition as common liver disorders on a global scale. The former affects various organs outside the liver, including the CV system.[11] Clinical studies have demonstrated that NAFLD plays a contributory role for accelerating the atherogenic process and the association between CVD and NAFLD is causative or both diseases result from a common pathogenic origin.[12] Notably, NAFLD patients with an increased risk of progressive fibrosis are particularly at a higher risk for CVD, which significantly contributes to adverse event rates in this group of patients. Fibrosis in the liver not only affects the liver, but also initiates an inflammatory process throughout the body.[13] Additionally, studies indicate that as fibrosis progresses in the liver, there is an increase in the fibrotic process in the heart.[14] Current guidelines strongly advise the utilization of non-invasive markers and scoring systems to determine the prognostic risk associated with liver-related conditions.[15] The diagnostic protocol should incorporate a basic assessment, through the Fibrosis-4 (FIB-4) or NAFLD score, for better predicting of possible advanced fibrosis, as recommended by established guidelines.[16] Aspartate transaminase, alanine transaminase, and platelet levels and patient age are used to calculate the FIB-4 index which is straightforward, non-invasive, and valuable instrument for estimating fibrosis.

Previous research has shown a convincing association between FIB-4 index and atherosclerotic process, besides AF and CV events.[17] However, its relationship with LAVI, particularly, has not been elucidated yet. In the present study, we hypothesized that the FIB-4 index, a score associated with cardiac preload, could also correlate with the LAVI, a parameter influenced by this preload. We, therefore, aimed to evaluate the predictive value of FIB-4 index and LA indices in ACS patients.

PATIENTS AND METHODS

This single-center, cross-sectional, observational cohort study was conducted at Recep Tayyip Erdoğan University Faculty of Medicine, Department of Cardiology between September 2023 and March 2024. A total of 300 consecutive patients with ACS (244 males, 56 females; mean age: 62.7±11.7 years; range, 49 to 78 years) were included in the study. In accordance with the current guidelines,[18] multiple factors, such as 12-lead electrocardiogram (ECG) results, cardiac-related symptoms, and increased levels of blood markers indicating myocardial necrosis, were used to diagnose ACS. For patients experiencing typical chest discomfort and suspected of having ACS, the diagnosis of ST-elevation MI (STEMI) was established when the ECG revealed ST-segment elevation in two adjacent leads. Non-ST elevation MI (NSTEMI) was identified in cases where the ECG lacked ST elevation, but troponin levels exceeded the 99th percentile. Unstable angina pectoris was characterized by myocardial ischemia occurring during rest or minimal physical activity without evidence of acute cardiomyocyte damage or death. Exclusion criteria were as follows: a substantial decline in renal function (estimated glomerular filtration rate [eGFR] below 30 mL/min/1.73 m^2), moderate-to-severe heart valve disease, chronic alcohol consumption, severe hematological disorders, active inflammatory diseases, malignancy, having a diagnosis or previous history of bile duct obstruction, liver transplantation, acute or chronic viral hepatitis, taking any medication that may affect aspartate transaminase, alanine transaminase and platelet count, and extremely frail elderly patients. A written informed consent was obtained from each patient. The study protocol was approved by the Recep Tayyip Erdoğan University Non-Interventional Clinical Research Ethics Committee (date: 12.09.2023, no: 2023/203). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Demographic and laboratory data

Lipid panel assessments were derived from blood samples acquired after a 12-h fasting period, whereas other laboratory analyses were performed using venous blood samples acquired upon admission to the emergency department. Diabetes mellitus and hypertension were defined according to current guidelines.[19,20] Hyperlipidemia was defined as either a prior diagnosis of hypercholesterolemia or the use of previous or current cholesterol-lowering therapies. Demographic and clinical data, including age, sex, and medication use, was documented. The definition of smoking included individuals who consumed at least one cigarette daily. The FIB-4 index

was calculated using a formula that incorporates commonly measured laboratory values: FIB-4 index: (age [years] × aspartate transaminase [U/L])/(platelet count [×10^9/L] × square root of alanine transaminase [U/L]).[21]

Echocardiographic evaluation

All participants undertook through two-dimensional transthoracic echocardiography conducted with a Philips EPIQ 7 device (Philips Medical Systems, Andover, MA, USA) utilizing an X5-1 transducer operating at a frequency range of 1 to 5 MHz. In accordance with the established guidelines, late diastolic peak flow velocity (A) and early diastolic peak flow velocity (E) were measured at the tips of the mitral leaflets using pulse-wave Doppler echocardiography. Two-dimensional M-mode echocardiographic images were gained to measure the LA and LV diameters. The LV ejection fraction (LVEF) was calculated using the modified Simpson's method.[22] Early (Em) and late (Am) diastolic velocities of the mitral annulus were obtained by tissue Doppler echocardiography. During end-diastole at parasternal long-axis view, the thickness of both the LV posterior wall and the interventricular septum (IVS) was measured.

The area-length method was utilized to measure LA volume using the apical two- and four-chamber

Table 1
Baseline demographic and clinical data of patients

Variables	LAVI <34 mL/m^2 (n=226)					LAVI ≥34 mL/m^2 (n=74)					*p*
	n	%	Mean±SD	Median	25th-75th percentiles	n	%	Mean±SD	Median	25th-75th percentiles	
Demographic data											
Sex											
Male	196	86.7				48	64.9				<0.001
Age (year)			60.8±10.9					68.6±11.6			<0.001
BMI (kg/m^2)			29.1±4.7					29.6±4.9			0.356
SBP (mmHg)			131.9±22.4					134.6±22.3			0.379
DBP (mmHg)			77.6±13.2					76.7±14.5			0.645
HT	122	54				57	77				<0.001
DM	83	36.7				35	47.3				0.030
HPL	96	42.5				26	35.1				0.059
Current smoking	109	48.2				17	23.0				<0.001
PAD	9	4.0				5	6.8				0.144
CVA	10	4.4				6	8.1				0.106
STEMI	95	42.0				31	41.9				0.108
Previous CABG	9	4.0				10	13.5				0.005
Previous PCI	43	19.0				14	18.9				0.135
Killip class >I	8	3.6				7	9.5				0.035
FIB-4 index				1.6	1.16-2.40				2.2	1.5-3.3	<0.001
Medication usage data (prehospital)											
ASA	52	23.6				17	23.0				0.073
Beta blocker	41	18.1				9	12.2				0.154
ACE-i	28	12.4				13	17.6				0.175
ARB	30	13.3				10	13.5				0.958
P2Y12 inhibitor	10	4.4				3	4.1				0.258

LAVI: Left atrium volume index; SD: Standard deviation; BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HT: Hypertension; DM: Diabetes mellitus; HPL: Hyperlipidemia; PAD: Peripheral arterial disease; CVA: Cerebrovascular accident; STEMI: ST-elevation myocardial infarction; CABG: Coronary artery bypass graft; PCI: Percutaneous coronary intervention; FIB-4: Fibrosis-4; ASA: Aspirin salicylic acid; ACE-i: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker.

views with dismissing of LA appendage and pulmonary veins from the measurements. To obtain the LAVI in mL/m^2, the LA volume was divided by the body surface area. Body mass index was calculated by dividing weight in kg by the square of height in cm. A LAVI above 34 mL/m^2 was considered to indicate an abnormally enlarged LAVI.[4] The study group was divided into two groups according to the LAVI measurements as those with <34 mL/m^2 (Group 1, n=226) and those with ≥34 mL/m^2 (Group 2, n=74).

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 23.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed in mean ± standard deviation (SD) or median (25th-75th percentiles), while categorical variables were expressed in number and frequency. Normality of distribution of the variables was checked using the Shapiro-Wilk or Kolmogorov-Smirnov test. A univariate logistic regression analysis was used to identify parameters

Table 2

Comparison of echocardiographic, angiographic, and laboratory data

Variable	LAVI <34 mL/m^2 (n=226)			LAVI ≥34 mL/m^2 (n=74)			*p*
	Mean±SD	Median	25th-75th percentiles	Mean±SD	Median	25th-75th percentiles	
Echocardiographic data							
LVEF (%)	53.6±9.7			49.2±12.5			0.002
IVS (mm)	11.6±1.6			12.5±1.9			0.001
PW (mm)	10.8±1.5			11.6±1.5			<0.001
E (cm/s)	67.5±17.2			85.4±27.2			<0.001
A (cm/s)	85.1±20.6			74.7±44.1			<0.001
Em (cm/s)	6.4±2.1			6.7±2.1			0.497
Am (cm/s)	8.8±2.2			6.4±3.6			<0.001
E/Em ratio	11.1±3.6			13.6±5.1			<0.001
E/A ratio	0.80±0.30			0.96±0.46			0.005
Angiographic data							
Stent count (n)	1.2±0.5			1.3±0.7			0.136
Stent length (n)	25.7±11.3			27.8±13.7			0.178
Lesion count (n)	1.2±0.5			1.2±0.6			0.710
Prevalence of CAD (n)	1.3±0.6			1.6±0.8			0.004
Laboratory data							
Glucose (mg/dL)	148.3±72.9			166.1±83.9			0.081
Serum creatinine (mg/dL)	0.90±0.29			1.03±0.36			0.180
Total cholesterol (mg/dL)	157.7±11.4			192.8±41.5			0.444
HbA1c (%)	6.5±1.5			6.9±1.8			0.153
Peak troponin (Ng/dL)	23.1±21.1			25.5±20.7			0.456
e-GFR (mL/min/1.73 m^2)	80.9±20.1			70.9±23.1			<0.001
WBC (10^3/µl)	10.1±3.3			10.1±3.4			0.969
Hemoglobin (gr/L)	14.5±1.7			13.1±2.1			<0.001
CRP (mg/dL)		0.63	0.35-1.30		0.99	0.52-2.20	<0.001

LAVI: Left atrium volume index; SD: Standard deviation; LVEF: Left ventricular ejection fraction; IVS: Interventricular septum wall thickness; PW: Posterior wall thickness; E: Early diastolic peak flow velocity; A: Late diastolic peak flow velocity; Em: Early mitral annular diastolic velocity; Am: Late mitral annular diastolic velocity; CAD: Coronary artery disease; HbA1c: Hemoglobin A1c; eGFR: Estimated glomerular filtration rate; WBC: White blood count; CRP: C-reactive protein.

which significantly differed. A multivariate logistic regression analysis incorporating statistically significant *p* values into the model was conducted. Receiver operating characteristic (ROC) analysis was carried out to calculate the sensitivity and specificity of the FIB-4 index in predicting high LAVI patients. The Spearman or Pearson correlation tests were also employed to evaluate the association of the FIB-4 index and LAVI. A *p* value of <0.05 was considered statistically significant.

RESULTS

Among a total of 300 patients, 25.6% (n=77) were diagnosed with STEMI, 54% (n=162) with NSTEMI, and 20.3% (n=61) with USAP. Group 1 had a LAVI of <34 mL/m^2 and Group 2 had a LAVI of ≥34 mL/m^2. Baseline demographic and clinical data of the patients are summarized in Table 1. The mean prevalence of coronary artery disease (CAD) was significantly higher in Group 2 (p=0.004) (Table 2). Paradoxically, individuals with normal LAVI measurements were found to have a higher incidence of smoking (p<0.001). The median FIB-4 index levels were higher in Group 2 (2.2 [1.5-3.3] *vs.* 1.6 [1.16-2.40], p<0.001). Figure 1 demonstrates the strong relationship between the FIB-4-index and LAVI (p<0.001). Correlation analysis revealed a significant positive correlation between the FIB-4 index and LAVI (r=0.238, p<0.001), indicating that elevated FIB-4 index score was associated with enlarged LAVI (Figure 2).

Table 3
Univariate and multivariate logistic regression analysis results

	Univariate			Multivariate		
Variables	OR	95% CI	*p*	OR	95% CI	*p*
Age	1.063	1.037-1.090	<0.001			
Sex						
Male	0.283	0.153-0.521	<0.001			
Hypertension	2.858	1.566-5.216	<0.001			
Diabetes mellitus	1.546	0.910-2.682	0.107			
Current smoking	0.320	0.175-0.584	<0.001	0.292	0.117-0.732	0.009
Previous CABG	3.767	1.468-9.671	0.006			
Killip class >I	2.834	0.991-8.104	0.052			
Prevalence of CAD	1.668	1.172-2.432	0.005	1.819	1.112-2.975	0.002
FIB-4 index (log)	4.552	1.81-11.5	0.001	6.419	1.505-27.38	0.012
LVEF	0.966	0.943-0.989	0.003	0.956	0.927-0.987	0.005
IVS	1.339	1.150-1.558	<0.001	1.549	1.255-1.913	<0.001
PW	1.457	1.211-1.753	<0.001			
E	1.040	1.025-1.055	<0.001			
A	0.998	0.979-0.007	0.009			
Am	0.742	0.668-0.825	<0.001			
E/Em	1.142	1.072-1.216	<0.001			
E/A	2.809	1.318-5.984	0.004	4.283	1.691-10.849	0.002
GFR	0.979	0.967-0.991	<0.001			
Hemoglobin	0.686	0.591-0.797	<0.001	0.689	0.559-0.834	<0.001
CRP	2.313	1.287-4.157	0.005			

OR: Odds ratio; CI: Confidence interval; CABG: Coronary artery bypass graft; CAD: Coronary artery disease; FIB-4: Fibrosis-4; LVEF: Left ventricular rejection fraction; IVS: Interventricular septum wall thickness; PW: Posterior wall thickness; E: Early diastolic peak flow velocity; A: Late diastolic peak flow velocity; Am: Late mitral annular diastolic velocity; Em: Early mitral annular diastolic velocity; eGFR: Estimated glomerular filtration rate; CRP: C-reactive protein.

Table 4
Significant predictors of LAVI ≥34 mL/m² in multivariate logistic regression analysis

Predictor	OR	95% CI	*p*
Smoking	0.292	0.117-0.732	0.009
Prevalence of CAD	1.819	1.112-2.975	0.002
FIB-4 index (log)	6.419	1.505-27.38	0.012
LVEF	0.956	0.927-0.987	0.005
IVS	1.549	1.255-1.913	<0.001
E/A ratio	4.283	1.691-10.849	0.002
Hemoglobin	0.689	0.559-0.834	<0.001

OR: Odds ratio; CI: Confidence interval; CAD: Coronary artery disease; FIB-4: Fibrosis-4; LVEF: Left ventricular ejection fraction; IVS: Interventricular septum wall thickness; E: Early diastolic peak flow velocity; A: Late diastolic peak flow velocity.

Comparing echocardiographic data between the groups, significant differences were observed in terms of LV wall thicknesses (Table 2). Comparing laboratory values, the mean eGFR and hemoglobin levels were lower in Group 2 (p<0.001 for both). However, there was an elevation in C-reactive protein (CRP) levels in Group 2, indicating a statistically significant difference (p<0.001). On the other hand, the mean peak troponin levels were comparable between the groups (p=0.437).

The univariate analysis was carried out to identify parameters which significantly differed between the groups (Table 3). In the multivariate analysis, smoking status (odds ratio [OR]= 0.292, 95% confidence interval [CI]: 0.117-0.732; p=0.009), CAD history (OR= 1.819, 95% CI: 1.112-2.975; p=0.002), FIB-4 index (OR=6.419, 95% CI: 1.505-27.38; p=0.012), LVEF (OR=0.956, 95% CI: 0.927-0.987; p=0.005), IVS thickness (OR=1.549, 95% CI: 1.255-1.913; p<0.001), E/A ratio (OR=4.283, 95% CI: 1.691-10.849; p=0.002), and hemoglobin levels (OR=0.689, 95% CI: 0.559-0.834; p<0.001) were independent predictors of increased LAVI (Table 4). The ROC analysis showed that the area under the curve (AUC) for the FIB-4 index was 0.705 (p<0.001) (Figure 3).

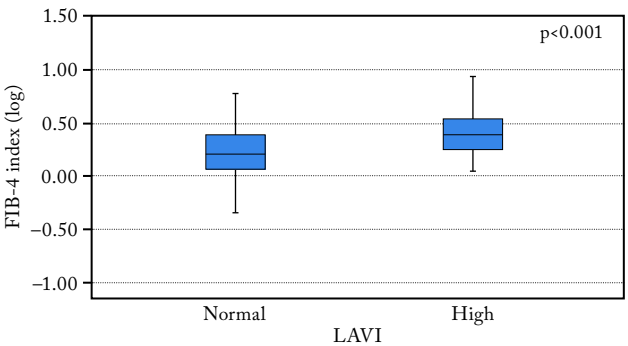

Figure 1. Graph showing the strong relationship between LAVI and FIB-4-index.
LAVI: Left atrium volume index; FIB-4: Fibrosis-4.

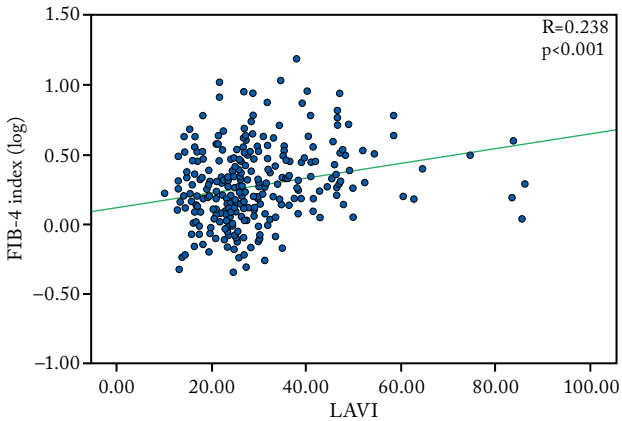

Figure 2. Correlation analysis of LAVI and FIB-4-index.
LAVI: Left atrium volume index; FIB-4: Fibrosis-4.

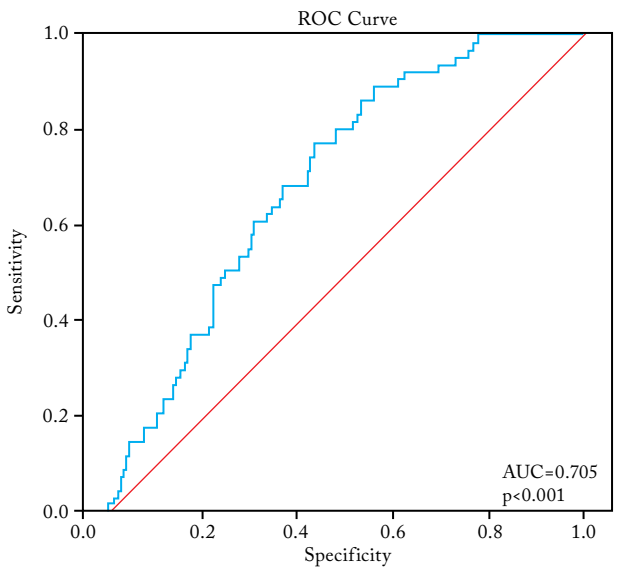

Figure 3. ROC analysis showing that a higher FIB-4 index could predict LAVI ≥34 mL/m², with an AUC of 0.705 (p<0.001).
ROC: Receiver operating characteristic; FIB-4: Fibrosis-4; LAVI: Left atrium volume index.

DISCUSSION

In the present study, we investigated the relationship concerning FIB-4 index and LAVI in ACS patient cohort. Our study results showed that the FIB-4 index was independently correlated with the increased LAVI. This novel relationship indicates that the FIB-4 index may function as a precious instrument in evaluating the risk and predicting outcomes in ACS. Although a considerable improvement has been made in ACS diagnosis and treatment in recent years, the incidence of major adverse cardiac events continues to be substantial.[23] The prognosis varies largely based on the extent of LV damage. Therefore, timely risk evaluation of these patients is essential. Moreover, in our study, prevalence of CAD, lower LVEF, IVS thickness, E/A ratio, and lower hemoglobin levels were significant predictors of high LAVI. More intriguingly, there was a significantly higher smoking rate in the low LAVI group.

As the configuration, utility, and function of the LA deteriorate, the LA pressure increases, which is reflected in the pulmonary capillaries, and the impact of the LA to the LV reduces.[24] Therefore, LAVI is of utmost importance for the early recognition of impaired LA function. In our study, LAVI, which indicates an increase in LA pressure, and the FIB-4 index, which is indirectly related to this condition, were positively correlated.

It has been demonstrated that NAFLD is not only a hepatic disorder, but also a systemic disease and is considered a significant risk factor for diabetes mellitus, metabolic syndrome, and CVD.[11] A study showed significant alterations in the LV function and structure due to NAFLD, despite the lack of overt CVD.[25] In addition, multiple studies and meta-analyses have consistently revealed a link between NAFLD and various CV issues such as increased carotid intima-media thickness, cardiomyopathy, diminished endothelial function, arrhythmias, and heightened arterial stiffness.[26] These results emphasize the significance of recognizing and addressing CV consequences of NAFLD to enhance patient management and outcomes. This can be attributed to various processes such as chronic mild inflammation, oxidative damage, inflammatory proteins, and reduced insulin sensitivity, all of which promote atherosclerosis.[14,27] Moreover, patients with NAFLD have a likelihood of CV complications, including heart failure and acute MI, as evaluated using the FIB-4 index.[28] The presence of proven non-invasive markers makes quick diagnosis more practicable and, if they provide additional predictive value, can also aid in the prevention of CVD. The FIB-4 index is useful in the CV area for predicting unfavorable outcomes, such as readmission to the hospital and death from all causes among heart failure patients.[29] Moreover, an elevated FIB-4 index has been associated with an increased incidence of all-cause mortality in patients with acute MI.[30] Additionally, a recent study demonstrated a substantial correlation between the FIB-4 index and LAVI, LV diastolic and end-systolic diameters, E/Em ratio, deceleration time, and maximal inferior vena cava diameter in patients with significant tricuspid regurgitation without other valve involvement.[31]

Distortion of the cardiac fiber structure across each stratum indicates enhanced myocardial stress under the conditions of hyperdynamic circulation attributed to splenic arterial vasodilatation and a decrease in systemic vascular resistance in patients with cirrhosis.[32] Diastolic dysfunction has been identified as a prompt marker of cirrhotic cardiomyopathy and may be characterized by four variables: E/Em ratio, mitral annular velocities, tricuspid regurgitation velocity, and LAVI.[33]

The high LAVI group in our study exhibited impacts on both the LV systolic and diastolic parameters. Strong predictors of high LAVI included a reduction in LVEF and an elevation in the E/A ratio. Also, LA enlargement determined by echocardiography may be regarded as a reliable prognosticator of LV systolic and diastolic dysfunction, as LA represents the filling pressure of LV. Similarly, an increase in LA size compared to controls has been previously demonstrated in patients with NAFLD, suggesting a relationship with the disease severity of the disease.[34] It has been also proposed that LA remodeling serves as a proxy for diastolic load and a predictor of CV events, such as heart failure, new-onset AF, or CV death.[35] The possible mechanisms include an elevated inflammatory burden and a proatherogenic environment. Furthermore, a connection between NAFLD and LV diastolic dysfunction has been proposed, potentially leading to LA enlargement through diverse pathways.[36]

In the current study, smokers had a significantly lower LAVI compared to non-smokers. This paradoxical finding can be explained by several

mechanisms. Chronic sympathetic activation due to smoking can induce atrial fibrosis, reduce atrial compliance, and limit the volume expansion. Additionally, smoking-related endothelial dysfunction and reduced nitric oxide bioavailability may contribute to increased atrial stiffness. Furthermore, elevated pulmonary vascular resistance and altered LV filling dynamics can impair the LA preload, leading to a lower LAVI.[37] These findings suggest that smoking may influence atrial remodeling through mechanisms distinct from conventional risk factors which warrants further investigation.

In previous studies, LAVI has been established as a prognostic indicator of ACS. It redirects the cumulative overload of high filling pressures over time and, therefore, does not necessarily reflect sudden drops in cardiac function.[38] Since LAVI reflects subacute or chronic alterations in diastolic function, it is less responsive to abrupt fluctuations.[39] Our study results suggest that a high FIB-4 index is associated with an elevated LAVI in patients with ACS. Additionally, the relationship between the FIB-4 index and AF has been demonstrated in different studies.[40] This may be due to the onset and progression of the fibrotic process in the LA along with the progression of the fibrotic process in the liver and the simultaneous progression of LA pressure in a chronic process.

Nonetheless, this study has several limitations. First, this study was conducted at a single center, and the sample size was relatively small. Further multi-center, large-scale studies are needed to confirm these findings. Second, we did not use any imaging or biopsy procedures to confirm the presence of NAFLD. Further studies utilizing imaging techniques may yield additional outcomes on this subject. Third, echocardiography was the sole method used for cardiac imaging in this study. Future research may involve various imaging techniques such as computed tomography or cardiac magnetic resonance imaging. Furthermore, it would be reasonable to conduct a non-invasive risk estimation study on ACS patients with a larger sample size. Another important limitation is the lack of data on the relationship between the FIB-4 index and clinical outcomes. Finally, since our study is a cross-sectional study, we were unable to follow the patients in the long term. Collecting data by following these patients in the long term may reveal different data regarding the relationship between the FIB-4 index and LAVI.

In conclusion, FIB-4 index has emerged as a basic and non-invasive scoring tool capable of predicting elevated LAVI, a well-established indicator of adverse outcomes and risk quantification, in patients with ACS. However, further well-designed studies are warranted to draw more reliable conclusions on this subject.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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