Int J Cardiovasc Sci. 2023; 36:e20220222

ORIGINAL ARTICLE

The Relationship Between Carcinoembryonic Antigen and Epicardial Adipose Tissue

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Abstract

Background: Inflammation, which is associated with an unhealthy lifestyle, plays a critical role in the development of both cardiometabolic diseases (CMD) and cancer. Carcinoembryonic antigen (CEA) is a tumor marker which also has proinflammatory properties. Recent studies have reported CEA to be associated with atherosclerosis, metabolic syndrome, and visceral adiposity. Epicardial adipose tissue (EAT) can exhibit highly inflammatory and pathogenic properties, and is a known risk factor for CMD. However, its relationship with CEA is still unknown.

Objectives: This study aimed to investigate the possible association of CEA with EAT.

Methods: A total of 134 Caucasian (males = 56, females = 78) individuals, aged (22-83 years), who were admitted for routine health control, were enrolled in this cross-sectional study. CEA was measured with chemiluminescent microparticle immunoassay (CMIA). EAT was measured by transthoracic echocardiography, and the visceral fat rating (VFR) was assessed by a body composition analyzing machine. The *p*-value <0.05 was considered statistically significant.

Results: CEA levels were categorized as tertiles: T1, 0.5-1.04; T2, 1.06–1.69; and T3, ≥1.7 ng/ml. The mean age, weight, VFR, EAT, and fasting glucose, as well as the median of systolic blood pressure (SBP), creatinine, and AST increased with the increasing CEA tertiles. CEA was significantly associated with EAT (r = 0.55, P<0.001) and VFR (r = 0.36, P<0.001). Multivariate linear regression analysis confirmed that gender, age, and EAT were the significant independent variables associated with CEA.

Conclusion: Individuals with increased EAT have higher levels of CEA, suggesting that this biomarker is most likely produced by EAT; however, additional investigations are required to improve the present work.

Keywords: Carcinoembryonic Antigen; Pericardium; Epicardial adipose tissue; Inflammation.

Introduction

Inflammation plays a key role in the development and progression of cardiometabolic disease (CMD) and cancer.[1-3] Numerous inflammatory mediators including C-reactive protein (CRP), adiponectin, monocyte chemoattractant protein 1 (MCP-1), and lipoprotein-associated phospholipase A_2 (Lp-PLA_2), as well as alterations of gut microbiota, have been reported to be associated with an increased risk of CMD.[4,5] CRP is the most extensively studied marker of inflammation and is most widely used in daily clinical practice. Yet the precise role of CRP in the assessment of cardiometabolic risk continues to evolve.[1,6,7] However, recent studies have suggested that EAT and carcinoembryonic antigen (CEA) are novel surrogates of inflammation that contribute to the development of CMD.[8,9] EAT is an accumulation of visceral fat that covers 80% of the heart surface. EAT plays

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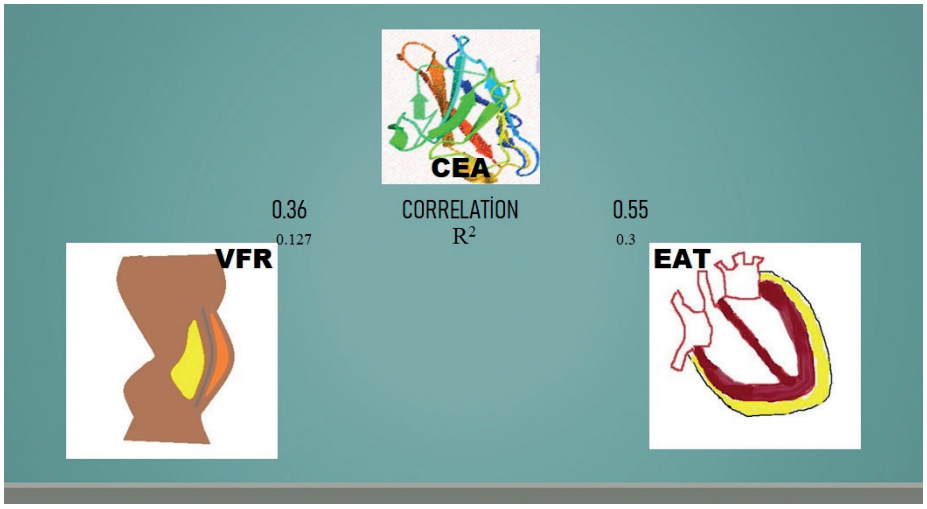
DOI: https://doi.org/10.36660/ijcs.20220222

Manuscript received December 18, 2022; revised manuscript July 27, 2023; accepted September 6, 2023.

Central Illustration: The Relationship Between Carcinoembryonic Antigen and Epicardial Adipose Tissue

INTERNATIONAL JOURNAL OF Cardiovascular SCIENCES



Int J Cardiovasc Sci. 2023; 36:e20220222

Correlation of CEA with EAT and VFR. CEA: carcinoembryonic antigen; VFR: visceral fat rating; EAT: epicardial adipose tissue.

a particularly important role in cardiovascular physiology and pathophysiology. Ordinarily, it has cardioprotective mechanical, metabolic, thermogenic, and endocrine/paracrine functions. However, structural and functional changes in EAT have proven to be associated with several CMDs, including insulin resistance and coronary artery disease.[10-13] In pathologic conditions thickened EAT acts as a source of inflammatory mediators and secretes a higher amount of proinflammatory mediators and neuro-hormones so that increased EAT can pathologically influence the cardiovascular system and cause worse outcomes.[10-13]

CEA is a serological marker overexpressed in adenocarcinoma of the colon and other organs.[6] However, serum CEA levels may increase mildly with age and could appear to be high in many nonneoplastic conditions, including smoking, chronic renal failure, hypothyroidism, and chronic hepatitis.[8,11-13] Although its exact function has not been elucidated, the stimulation of monocytes and macrophages by CEA may result in an increased production of proinflammatory cytokines[11-12] and endothelial adhesion molecules,[14] which may subsequently lead to atherosclerotic cardiovascular disorders and the metastasis of malignant cells.[9,14] Other possible underlying mechanisms may include imbalanced oxidative damage and endoplasmic reticulum stress production, which triggers redox imbalance and increasing oxidative damage to proteins, lipids, and DNA.[2,11-14] Furthermore, recent studies have reported CEA to be related to metabolic syndrome and visceral adiposity.[8] Moreover, Chang et al. has suggested a CEA level of ≥ 3 ng/mL for the early detection and prevention of CMDs through individualized lifestyle modifications.[2] As mentioned earlier, EAT and CEA both have inflammatory characteristics.[2,10] However, reports linking CEA concentration to the EAT do not exist. Therefore, the present study aimed to investigate the possible association between EAT and CEA.

Methods

The study sample consists of Caucasian men and women who visited our hospital for routine health checkups from November 2021 to May 2022. This is a cross-sectional study conducted with 134 individuals (male = 56, female = 78), aged 22 to 83 years. Individuals who were over 18 years of age, and who were willing to participate, were included in the study. Subjects who had a history of cancer, hypothyroidism, active infection, diabetes, coronary/peripheral artery disease, heart failure, chronic renal disease, chronic liver disease, history of current or past smokers, pregnant women, and individuals with evident contraindication to VFR assessment, such as an acute medical condition, patients with an implanted cardioverter defibrillator or pacemaker, unstable weight, inability to assume

required positions, and age changes were not included in the study. Demographic, clinical, and laboratory data were obtained from the hospital's electronic database. EAT thickness was assessed by transthoracic echocardiography. Visceral fat rating (VFR) was measured by a bioelectrical impedance analysis (BIA) machine. The present study was conducted in accordance with the guidelines proposed in the Declaration of Helsinki and has been approved by a local clinical research ethics committee. Written informed consent was obtained from all participants included in the study.

VFR measurement

VFR as an index of visceral adiposity was measured with a BIA device (TANITA MC-780MA). This analyzer uses a single frequency BIA at 50 kHz, which mainly evaluates extracellular water and about 25% of intracellular water. Measurements were made while the participants were dressed in light clothing, barefoot, and standing on metal foot pads. A very low and safe electrical signal was sent from metal electrodes to the legs and abdomen during bio-impedance measurement. Information regarding the age, gender, weight, and height of the participants was recorded in the system for the computing of the BIA algorithms. The body composition analyzer provided a VFR range of 1 to 59. According to the manufacturer's information, a grade between 1 and 12 indicates a healthy level of visceral adiposity, whereas a grade between 13 and 59 indicates excess visceral adiposity. As mentioned in the Methods section, contraindications to the BIA method were taken into consideration.

EAT assessment

All subjects underwent a 2D transthoracic echocardiographic assessment using a 1 to 55 MHz S4-2 broadband transducer (iE33, Philips Healthcare, İnc, Andover, MA). Subjects were examined in the left lateral decubitus position, and measurements were averaged over five consecutive heart beats. All standard 2D transthoracic echocardiography images from the parasternal long axis, and short and apical four-chamber-view were recorded on videotapes. EAT thickness was measured perpendicularly on the free wall of the right ventricle at end-diastole from the parasternal long- and short-axis views. Echocardiography records were read by two experienced cardiologists who were blinded to the participants' anthropometric features.

Physical examination

Participants' blood pressure was measured manually in the sitting position after a 10 min rest. Anthropometric parameters were measured by a single, trained examiner while individuals wore light clothing without shoes. Body mass index (BMI) was calculated by dividing weight in kilograms by the square of height in metres, and waist circumference (WC) was measured at the upper iliac crest level while the subject was in the standing position.

Biochemical analysis

Blood samples were obtained from the participants in the morning after an overnight fast, and the assays for variables analyzed in the present study were performed on the same day of drawing blood without freezing the samples. Serum CEA was measured with a chemiluminescent microparticle immunoassay kit (CMIA-Architec, Abbottt cİ4200). Hematological parameters, such as hemoglobin (Hgb), white blood cells (WBC), neutrophil and lymphocyte counts, and red cell distribution width (RDW) were measured as part of the automated complete blood count (CBC) using a Sysmex XT-1800i (Roche Diagnostic, Istanbul, Turkey). Low-density lipoprotein cholesterol (LDL-C) was measured directly by a colorimetric method using Abbott Architect Plus ci8200 integrated analysis system (Abbott Labs, Chicago, IL, USA). Other blood tests, including lipid parameters, were performed using standard methods. The Cockcroft-Gault formula was employed to estimate the glomerular filtration rate (GFR).

Statistical analysis

Statistical analyses of this work were performed using SPSS, versions 17.0 and 26 (SPSS Inc., Chicago, IL, USA). A p-value <0.05 was considered statistically significant. Histogram with a bell curve and one-sample Kolmogorov-Smirnov test were used to assess the data distribution. Continuous variables with normal distribution were described through mean and standard deviation and continuous variables that do not present a normal distribution were described in the median format (Q1 - Q3), where Q1 is the first quartile and Q3 is the third quartile. CEA data were transferred to the natural logarithm scale before statistical analysis. One-Way ANOVA and Kruskal-Wallis tests were used to compare continuous variables and the Chi-Square test was used to compare categorical variables. Additionally, for pairwise

comparisons of parametric and nonparametric variables that differed significantly between tertiles, Bonferroni and Kruskal-Wallis1-way ANOVA (k samples) post hoc tests were used, respectively. In addition, to know if the CEA can be predicted by EAT, univariate and multivariate linear regression analyses were performed. All assumptions necessary for the use of linear regression analysis have been validated. The interclass correlation coefficient measurement was used to determine whether there was agreement between operators in terms of echocardiographic measurements.

Results

Table 1 shows the basal characteristics of the sample-134 subjects (mean age 46.24±11.93 y, 78 female, 56 males) according to serum CEA tertiles. CEA tertiles were categorized separately as follows: T1, 0.5-1.04; T2, 1.06–1.69; and T3, ≥1.7 ng/ml. The mean age, weight, VFR, EAT, and fasting glucose, as well as the median of systolic blood pressure (SBP), creatinine, and aspartate aminotransferase (AST) increased with the increasing CEA tertiles. By contrast, height, BMI, WC, diastolic blood pressure (DBP), heart rate (HR), total cholesterol (TC), LDL-C, high density lipoprotein cholesterol (HDL-C), triglyceride (TG), hemogloin-A1c (HbA1c), GFR, WBC, CRP, RDW, neutrophil to lymphocyte ratio (NLR), alanine aminotransferase (ALT), and thyroid stimulating hormone (TSH) values were not significantly different between CEA categories.

Table 2 demonstrates the pairwise comparison of significantly different variables among the tertiles of Table 1. Participants of tertiles 2 and 3 were significantly older in comparison to the tertile 1 participants. The mean weight, VFR, glucose, SBP, creatinine, and AST were significantly different only between tertiles 1 and 3. The mean EAT and CEA were significantly different among all pairs; as tertile 3>tertile 2>tertile 1.

First, univariate analysis was performed, which identified age, gender, BMI, WC, SBD, DBS, AST, LDL-C, TG, FG, HBA1C, VFR, and EAT as possible predictors of CEA. As seen in Table 2 and Figure 1, EAT has a stronger correlation with CEA than other variables. All of these variables were then included in a multivariate linear regression analysis for a truly adjusted result. Multivariate linear regression analysis confirmed that gender, age, and EAT were the significant independent variables associated with CEA, accounting for a combined 42.9% of the variance in serum CEA. However, the contribution of BMI, WC, SBD, DBS, AST, LDL-C, TG, FG, HBA1C, and VFR to the model proved to be insignificant, as shown in Tables 3 and 4.

An excellent interobserver agreement regarding EAT measurement was observed; the intraclass correlation coefficient was (İCC; 0.966 %Cİ; 0.824-0.987).

Discussion

Our analysis revealed a significant relationship between EATs and serum CEA levels (Central illustration). Moreover, the multivariate linear regression analysis confirmed that EAT was among the significant explanatory variables for CEA. This clearly indicates that EAT thickness is closely related to, as well as a good predictor of, CEA.

CEA, is an oncofetal glycoprotein (180- to 200-kDa), expressed in normal mucosal cells, and is overexpressed in adenocarcinoma, particularly in colorectal malignancies. In addition, elevated CEA levels are also associated with several non-cancerous conditions, including cigarette smoking, older age, chronic renal and hepatic failure, and metabolic disorders.[11-14] Furthermore, recent studies have reported a positive relationship between CEA and carotid atherosclerosis, arterial stiffness, metabolic syndrome, and low-grade chronic inflammation.[8,15,16] Similar to the oxidized LDL-C,[9,14] CEA stimulates monocytes and macrophages and may cause an increase in the production of proinflammatory cytokines,[14] which may subsequently induce endothelial cell expression of adhesion molecules, such as vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule 1 (ICAM-1), and E-selectin that bind monocytes and T lymphocytes, allowing them to penetrate the intima. These processes play a key role in facilitating the metastasis of cancer cells as well as in the early stage of atherosclerosis, which involves the recruitment of inflammatory cells and their trans-intimal migration.

Low-grade chronic inflammation is also promoted by EAT, a very active secreting visceral adipose tissue.[9] Structurally and functionally altered EAT is associated with a greater inflammatory response, which appears to be one of its mechanisms of developing cardiovascular diseases, including coronary artery disease, aortic stenosis, and heart failure. As previously mentioned, CEA levels are associated with various chronic inflammatory diseases. Therefore, increased inflammatory cytokines and adipokines secreting from EAT may stimulate

Tabel 1 – The baseline characteristics of the entire study sample and the differences in the variables according to the CEA tertiles.

Variables	Entire sample n: 134	Tertile 1 n: 43	Tertile 2 n: 46	Tertile 3 n: 45	P
Gender (female/male)	78/56	33/10	26/20	19/26	0.004
Age	46.24±11.93	40.53±9.73	46.37±12.23	51.56±11.22	<0.001
Height	166.98±10.57	165.44±9.57	166.21±10.65	169.22±11.24	0.205
Weight	77.98±15.18	73.44±13.87	78.45±15.75	81.85±14.95	0.032
BMI	27.99±5	26.84±4.72	28.48±5.67	28.58±4.39	0.189
WC	95.05±11.61	91.72±11.51	95.63±12.62	97.64±9.99	0.051
SBP	125 (115-135)	120 (110-130)	125 (114-132)	130 (120-143)	0.023
DBP	78.89±10.08	76.49±9.65	79.78±10.28	80.27±10.07	0.162
HR	72.87±10.24	74.86±9.16	73.91±10.41	69.91±10.59	0.052
VFR	8.09±3.77	6.42±2.94	8.22±4.21	9.56±3.43	<0.001
EAT	3.03±1.72	1.89±1.21	3.04±1.57	4.1±1.62	<0.001
CEA	1.34 (0.87-2.01)	0.72 (0.60-0.85)	1.33 (1.16-1.53)	2.31 (1.99-3.25)	<0.001
Total-C	206.06±38.23	198.86±39.24	207.11±38.89	211.87±36.28	0.275
LDL-C	130.87±30.72	122.12±31.44	133.87±31.53	136.16±27.93	0.071
HDL-C	57.63±15.13	59.26±15.08	57.61±17.48	56.09±12.56	0.621
TG	109 (79-162)	93 (69-153)	110.5 (81-166)	124 (89-169)	0.070
Glucose	96.46±10.06	93.40±7.79	96.93±11.3	98.89±10.09	0.034
HbA1c	5.67±0.5	5.56±0.37	5.65±0.66	5.80±0.39	0.079
Cr	0.79 (0.7-0.9)	0.72 (0.67-0.81)	0.76 (0.69-0.88)	0.85 (0.78-0.97)	0.002
GFR	117.12±30.40	119.91±28.38	118.48±30.43	113.08±32.43	0.539
WBC	6.67±1.75	6.59±1.72	6.90±1.95	6.52±1.57	0.557
CRP	1.85 (1.4-3.73)	1.6 (1.3-3.7)	2 (1.49-4.80)	1.9 (1.35-2.90)	0.221
RDW	13.2 (12.80-13.73)	13.1 (12.7-13.8)	13.2 (12.8-13.4)	13.3 (12.9-13.9)	0.235
NLR	1.7 (1.41-2.26)	1.65 (1.46-2.12)	1.63 (1.26-2.01)	1.77 (1.41-2.44)	0.433
ALT	17 (14.0-23.25)	15 (11-22)	17 (14-23)	20 (15.5-28.0)	0.067
AST	17 (15-20)	16 (13-18)	17 (15-19)	19 (15.5-23.5)	0.013
TSH	1.59 (1.14-2.31)	1.43 (1.08-2.28)	1.60 (1.16-2.42)	1.61 (1.24-2.29)	0.812

Note: Data for CEA was logarithmically transformed to normalize its distribution before statistical analyses. Continuous variables that do not present a normal distribution described in the median format (Q1 - Q3), where Q1 is the first quartile and Q3 is the third quartile.
BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; VFR: visceral fat rating; EAT: epicardial adipose tissue; CEA: carcinoembryonic antigen; Total-C: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TG: triglyceride; Cr: creatinine; GFR: glomerular filtration rate; CRP: C-reactive protein; RDW: red cell distribution width; NLR: neutrophil to lymphocyte ratio; ALT: alanine aminotransferase; AST: aspartate aminotransferase; TSH: thyroid stimulating hormone; HbA1c: hemogloin-A1c; WBC: white blood cells.

Table 2 – Pairwise comparison of the variables that were found to be significantly different among the tertiles of Table 1

Variables	Groups	Groups	P
Age	Tertile 1	Tertile 2	0.044
	Tertile 1	Tertile 3	<0.001
	Tertile 2	Tertile 3	0.084
Weight	Tertile 1	Tertile 2	0.347
	Tertile 1	Tertile 3	0.027
	Tertile 2	Tertile 3	0.834
VFR	Tertile 1	Tertile 2	0.058
	Tertile 1	Tertile 3	<0.001
	Tertile 2	Tertile 3	0.230
EAT	Tertile 1	Tertile 2	0.001
	Tertile 1	Tertile 3	<0.001
	Tertile 2	Tertile 3	0.003
Glucose	Tertile 1	Tertile 2	0.280
	Tertile 1	Tertile 3	0.030
	Tertile 2	Tertile 3	1.000
SBP	Tertile 1	Tertile 2-	1.000
	Tertile 1	Tertile 3	0.022
	Tertile 2	Tertile 3	0.202
CEA	Tertile 1	Tertile 2	<0.001
	Tertile 1	Tertile 3	<0.001
	Tertile 2	Tertile 3	<0.001
Cr	Tertile 1	Tertile 2	0.421
	Tertile 1	Tertile 3	0.001
	Tertile 2	Tertile 3	0.121
AST	Tertile 1	Tertile 2	0.483
	Tertile 1	Tertile 3	0.010
	Tertile 2	Tertile 3	0.346

Note; Age, weight, VFR, EAT, and glucose were analyzed using the Bonferroni Post Hoc Test, while SBP, CEA, Cr, and AST were analyzed using an Kruskal-Wallis1-way ANOVA (k samples). AST: aspartate aminotransferase; CEA: carcinoembryonic antigen; Cr: creatinine; EAT: epicardial adipose tissue; SBP: systolic blood pressure; VFR: visceral fat rating

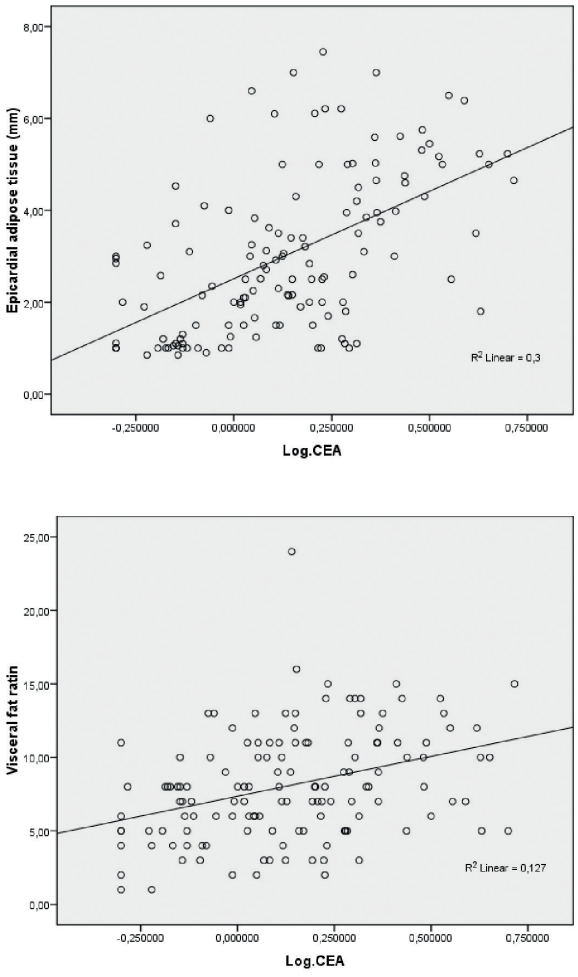


Figure 1 – Scatter plots showing the correlation of CEA concentrations with EAT (upper) and VFR (lower).
CEA: carcinoembryonic antigen.

CEA expression. In addition, it is also conceivable that pathologically thickened EAT can directly express and release CEA.

CEA and EAT are closely associated with aging. In this regard, our findings were in excellent agreement with the literature.[8,9,15] Our results demonstrated a positive correlation between the subject's age and EAT (r = 0.59 P<0.001), as well as age and CEA (r = 0.42, P<0.001). These findings support the concept of increasing inflammatory burden with increasing age. Similarly, our findings were consistent with previously published papers in the context of mean weight, adiposity index, SBP, and fasting glucose, which were gradually increased with a rising CEA concentration.[15,17] These data suggest the possible association of CEA with CMDs. However, findings from

Table 3 – Univariate analysis identifying possible predictors of CEA

Variables	Beta	P
Gender	-0.256	0.003
EAT	0.548	<0.001
VFR	0.356	<0.001
Age	0.418	<0.001
BMI	0.182	0.035
WC	0.217	0.012
TC	0.161	0.064
LDL-C	0.188	0.030
HDL-C	-0.094	0.282
TG*	0.175	0.043
ALT*	0.131	0.130
AST*	0.263	0.002
Glucose	0.235	0.006
HbA1c	0.182	0.035
WBC	-0.023	0.794
NLR*	0.017	0.848
RDW*	0.028	0.748
CRP*	-0.010	0.907
Cr*	0.141	0.104
GFR	-0.112	0.196
SBP*	0.241	0.005
DBP	0.186	0.031
TSH*	-0.009	0.916

Note: Data for CEA was logarithmically transformed to normalize its distribution prior to the statistical analyses.
BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; VFR: visceral fat rating; EAT: epicardial adipose tissue; CEA: carcinoembryonic antigen; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TG: triglyceride; Cr: creatinine; GFR: glomerular filtration rate; CRP: C-reactive protein; RDW: red cell distribution width; NLR: neutrophil to lymphocyte ratio; ALT: alanine aminotransferase; AST: aspartate aminotransferase; TSH: thyroid stimulating hormone; HbA1c: hemogloin-A1c; WBC: white blood cells.

the present study regarding the relationship between CEA and simple markers of inflammation are not consistent with those of other recently published studies.[15,17] In the current study, leucocyte count, NLR, RDW, and CRP values did not significantly differ among CEA tertiles. An explanation for this paradox may be the absence of certain inflammation-promoting confounders, such as smoking, diabetes, and cardiovascular disease in our sample.

Jee-Yon Lee et al. reported CEA to be associated with abdominal visceral fat accumulation assessed by computed tomography in the female gender, and they suggested CEA as a mediator of metabolic disturbance.[8] In addition to the visceral adiposity index, in our analysis, CEA recorded a better association both with the VFR as well as with EAT. Thus, this analysis not only complements the aforementioned report, but it also linked CEA with EAT – a more pathological visceral adipose tissue.

Understanding the role of inflammation in atherosclerosis and CMDs has resulted in the prevention of CV events through the development of anti-inflammatory therapies.[3] In this context, CEA's inflammatory characteristics and its association with EAT may enhance the knowledge of the role of different inflammatory actions in the pathophysiology of CMD. Therefore, agents targeting CEA, such as the "CEA-related cell adhesion molecule", may provide additional advantages in CV prevention.

In general terms, our results were consistent with previous studies. In addition, our study counted on the participation of both genders, simultaneously analyzed EAT and VFR, and did not use any ionizing method in the evaluation of visceral adiposity. Moreover, to achieve a purer relationship between CEA and EAT, our study excluded individuals with diabetes and smokers in whom EAT and CEA could be increased. However, the current study does have some limitations. Our sample was small, included only the Caucasian ethnicity, and performed a cross-sectional study that was unable to confirm casualty between CEA and EAT. Furthermore, the method used for EAT assessment has many limitations and is not currently the gold-standard. The use of bioelectrical impedance to assess visceral fat is also an indirect measurement.

Conclusion

The present study showed that EAT is independently associated with CEAs. Our results propose that CEA could be a metabolic marker. Supplemental

Table 4 – Independent variables associated with CEA.

Entire model; r^2 :0.429 P<0.001*	Un-stand Coeff.		Stand. Coeff.	T	p
	Beta	Std. error	Beta		
(Constant)	-0.221	0.361		-0.613	0.541
Age	0.005	0.002	0.231	2.134	0.035
Gender	-0.150	0.047	-0.300	-3.162	0.002
BMI	0.009	0.007	0.190	1.312	0.192
WC	-0.003	0.003	-0.130	-0.883	0.379
SBP	-0.003	0.002	-0.177	-1.466	0.145
DBP	0.004	0.003	0.157	1.376	0.171
AST	0.005	0.003	0.129	1.661	0.099
LDL-C	0.001	0.001	0.066	0.856	0.394
TG	0.000	0.000	0.064	0.771	0.442
FG	-0.001	0.002	-0.054	-0.666	0.507
HbA1c	0.021	0.037	0.043	0.574	0.567
VFR	-0.011	0.011	-0.170	-0.988	0.325
EAT	0.071	0.014	0.494	5.242	<0.001

Note: Data for CEA was logarithmically transformed to normalize its distribution prior to the statistical analyses
BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; VFR: visceral fat rating; EAT: epicardial adipose tissue; AST: aspartate aminotransferase; LDL-C: low-density lipoprotein cholesterol; TG: triglyceride; FG: fasting glucose; HbA1c: hemoglobin A1c.

investigations are required to improve the present work and comprehend the clinical and pathophysiological importance of our results.

Author Contributions

Conception and design of the research: Naser A, Güvenç TS, Demir I, Kirişci M, Ekmekçi A; acquisition of data: Naser A, Isgandarov K; analysis and interpretation of the data: Naser A, Demir I, Kirişci M, Şahin M; statistical analysis: Naser A, Güvenç TS, Demir I, Kirişci M; writing of the manuscript and critical revision of the manuscript for intellectual content: Naser A, Isgandarov K, Güvenç TS, Ekmekçi A, Şahin M.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Istinye University Clinical Research Ethic Commitee under the protocol number 3/2022.K-42.

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