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Relation of Plasma Fatty Acid Binding Proteins 4 and 5 With the Metabolic Syndrome, Inflammation and Coronary Calcium in Patients With Type-2 Diabetes Mellitus

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Abstract

Fatty acid–binding proteins (FABPs) 4 and 5 play coordinated roles in rodent models of inflammation, insulin resistance, and atherosclerosis, but little is known of their role in human disease. The aim of this study was to examine the hypothesis that plasma adipocyte and macrophage FABP4 and FABP5 levels would provide additive value in the association with metabolic and inflammatory risk factors for cardiovascular disease as well as subclinical atherosclerosis. Using the Penn Diabetes Heart Study (PDHS; n = 806), cross-sectional analysis of FABP4 and FABP5 levels with metabolic and inflammatory parameters and with coronary artery calcium, a measure of subclinical coronary atherosclerosis, was performed. FABP4 and FABP5 levels had strong independent associations with the metabolic syndrome (for a 1-SD change in FABP levels, odds ratio [OR] 1.85, 95% confidence interval [CI] 1.43 to 2.23, and OR 1.66, 95% CI 1.41 to 1.95, respectively) but had differential associations with metabolic syndrome components. FABP4 and FABP5 were also independently associated with C-reactive protein and interleukin-6 levels. FABP4 (OR 1.26, 95% CI 1.05 to 1.52) but not FABP5 (OR 1.13, 95% CI 0.97 to 1.32) was associated with the presence of coronary artery calcium. An integrated score combining FABP4 and FABP5 quartile data had even stronger associations with the metabolic syndrome, C-reactive protein, interleukin-6, and coronary artery calcium compared to either FABP alone. In conclusion, this study provides evidence for an additive relation of FABP4 and FABP5 with the metabolic syndrome, inflammatory cardiovascular disease risk factors, and coronary atherosclerosis in type 2 diabetes mellitus. These findings suggest that FABP4 and FABP5 may represent mediators of and biomarkers for metabolic and cardiovascular disease in type 2 diabetes mellitus.

Although fatty acid–binding proteins (FABPs) 4 and 5 have been shown to be important in mouse studies of inflammation, insulin resistance, and atherosclerosis, only limited

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information is available for their role in human disease.[1–5] In Chinese population-based studies, circulating FABP4 predicted incident metabolic syndrome[6] and type 2 diabetes mellitus (T2DM),[7] independently of adiposity and insulin resistance. Aside from the Nurses' Health Study and the Health Professionals Follow-Up Study, in which a genetic variant of FABP4 was associated with metabolic dyslipidemia, T2DM, and coronary artery disease,[8] data are lacking for plasma FABP4's relation to clinical atherosclerotic cardiovascular disease (CVD). FABP5's role in human disease remains to be studied. Furthermore, a cooperative role of FABP4 and FABP5 in metabolic perturbation, inflammation, and atherosclerosis in humans has not been studied. In this study, we examined the individual relations of plasma levels of FABP4 and FABP5, and their combined association, with metabolic and inflammatory parameters as well as with coronary artery calcium (CAC), a measure of subclinical coronary atherosclerosis, using the Penn Diabetes Heart Study (PDHS) cohort of adult patients with T2DM.

Methods

Details of the PDHS[9] have been reported previously. In brief, the PDHS is an ongoing single-center, cross-sectional, community-based study of subjects with T2DM without clinical evidence of CVD (defined as myocardial infarction, coronary revascularization, angiographic disease, or positive stress test results) or overt chronic kidney disease recruited at the University of Pennsylvania. Inclusion criteria were age 35 to 75 years, diagnosis of T2DM, and negative pregnancy test result if female. Exclusions were clinical CVD, clinical diagnosis of type 1 diabetes mellitus (insulin use before 35 years of age), serum creatinine >2.5 mg/dl, and weight >300 lb (136 kg). In this report, we studied 806 patients with T2DM in whom FABP4 and FABP5 were measured.

Participants were evaluated at the Clinical and Translational Research Center at the University of Pennsylvania Medical Center after we obtained informed consent from patients and approval from our institutional review board. After a 12-hour overnight fast, clinical parameters, including blood pressure, waist circumference, and laboratory values, were assessed as previously reported.[9] Plasma lipids were measured enzymatically (Hitachi 912 AutoAnalyzer; Roche Diagnostics GmbH, Basel, Switzerland) in lipoprotein fractions after ultracentrifugation (β-quantification technique) at the University of Pennsylvania's Centers for Disease Control and Prevention–certified lipid laboratory. Framingham risk scores, using total cholesterol, were calculated as described by Wilson et al.[10] Subjects were classified as having the metabolic syndrome using the definition of the National Cholesterol Education Program.[11] All subjects were classified as having National Cholesterol Education Program metabolic syndrome glucose criteria. Global CAC scores were quantified as described[9] according to the method of Agatston et al[12] using electron-beam tomography.

Plasma levels of FABP4 and FABP5 were measured by enzyme-linked immunosorbent assay according to the manufacturer's instructions (Biovendor Laboratory Medicine, Prague, Czech Republic). All samples were assayed in duplicate, and pooled human plasma samples were included to assess variability; intra- and interassay coefficients of variation were 5.6% and 14% for FABP4 and 8.8% and 17% for FABP5. Plasma levels of adiponectin and leptin (Linco, St. Charles, Missouri), as well as interleukin-6 (IL-6; ultrasensitive; R&D Systems, Minneapolis, Minnesota), were measured by enzyme-linked immunosorbent assay, and high-sensitivity C-reactive protein (CRP) was measured by immunoturbidimetric assay (Wako, Ltd., Osaka, Japan).[9] The intra- and interassay coefficients of variation for pooled human plasma were 5.65% and 9.9% for adiponectin, 5.5% and 12.4% for leptin, 8.7% and 10.9% for IL-6, and 8.0% and 8.3% for CRP. Laboratory test results were generated by personnel blinded to the clinical characteristics and CAC scores of research subjects.

Data are reported as median (interquartile range) or as mean ± SD for continuous variables and as proportions for categorical variables. The crude association of FABP data with quantitative lipid, metabolic, and inflammatory parameters was examined using Spearman's correlation analysis, and the Kruskal-Wallis test was used to test for associations of the FABPs with the metabolic syndrome and its binary components. To assess the combined effect of FABP4 and FABP5, we generated gender-specific quartiles of FABP4 (coded from 0 to 3) and FABP5 (coded from 0 to 3), and combined these quartile data in an additive fashion into an ordinal 7-level score (0 to 6) termed the FABP score. Multivariate associations of FABP data (effect of 1 SD of the log of FABP4, FABP5, or the FABP score) with the metabolic syndrome and log-transformed CRP data were examined in logistic and linear regression models, respectively, with incremental adjustment for confounding risk factors. For CAC scores, we performed logistic regression of the presence of CAC (score >0), because this cut point has been shown to predict CVD events, as well as exploratory analysis using tobit conditional regression of natural log (CAC + 1), which is suited to analysis of the many zero scores but marked right skew of CAC data.[13] Data are presented as a combined sample of men and women because there was no interaction by gender on each of the outcomes studied. Statistical analyses were performed using Stata version 10.0 (StataCorp LP, College Station, Texas).

Results

Table 1 summarizes study sample characteristics. As expected, obesity was seen in about 1/3 of men and women, and the National Cholesterol Education Program–defined metabolic syndrome was present in >2/3. Plasma FABP levels were higher in women than in men. As expected, men had higher CAC scores than women, and CAC prevalence was consistent with greater subclinical atherosclerosis in asymptomatic T2DM[14,15]: >1/3 of men and almost 30% of women had CAC scores >75th percentile of age and gender adjusted in the general population.

Spearman's correlations revealed modest associations of FABP4 and FABP5 with each other in men and women and with metabolic and inflammatory parameters but not with total or low-density lipoprotein cholesterol (Table 2). The 2 FABPs were strongly correlated with waist circumference and body mass index. Overall, FABP4 tended to have stronger associations with measures of adiposity than FABP5, but the 2 were equally related to the inflammatory markers CRP and IL-6.

In unadjusted analysis, plasma levels of FABP4 and FABP5 were higher in participants with the metabolic syndrome (Table 3), but they had a distinct pattern of association with metabolic syndrome components; FABP4 had stronger associations with waist criteria, whereas FABP5 had greater relations with high-density lipoprotein cholesterol, triglycerides, and blood pressure (Table 3). Notably, levels of FABP4 (median 34.4 ng/ml [interquartile range 22.9 to 55.0] vs 22.7 ng/ml [interquartile range 15.0 to 35.9], $p < 0.001$), but not FABP5 ($p = 0.88$), were higher in patients receiving thiazolidinedione therapy.

In multivariate analysis, the association of 1 SD of plasma FABP4 data (Table 4) and FABP5 (Table 4) with the metabolic syndrome remained significant even after adjusting for individual metabolic syndrome components (except for FABP4 adjusted for waist circumference). Remarkably, relative to either FABP, 1 SD of the combined FABP score had a stronger association with the metabolic syndrome even after adjusting for each individual metabolic syndrome component and individual FABP levels (Table 4). Likelihood ratio testing revealed that the addition of FABP score added value to the association with the metabolic syndrome beyond each individual FABP (e.g., chi-square = 22.1, $p < 0.001$, for score added to FABP4 and chi-square = 22.6, $p < 0.001$ for score added to

FABP5 in an age-, gender-, and race-adjusted model). These findings suggest an additive relation of FABP4 and FABP5 levels with atherogenic metabolic disturbance in T2DM.

In unadjusted analysis, FABP4 and FABP5 levels were correlated with the 2 major inflammatory markers CRP and IL-6 (Table 5). In adjusted analysis, the association of 1 SD of plasma FABP4 and FABP5 (Table 5) with plasma CRP levels was significant after adjusting for multiple CVD risk factors. Again, relative to either FABP, 1 SD of the combined FABP score had a stronger association with plasma CRP, even after adjusting for Framingham risk score, the metabolic syndrome, additional risk factors, and levels of each individual FABP (Table 5). Findings were almost identical for associations with plasma IL-6. These results further support an additive relation of the 2 FABPs with inflammatory atherogenic risk in T2DM.

Next we determined individual FABP and combined FABP score associations with CAC, a strong independent predictor of clinical CVD. In adjusted analysis, a 1-SD change in FABP4 level (Table 6) had a modest association with the presence of any CAC, while a weak trend for FABP5 association with CAC was not statistically significant (Table 6). The FABP score had a stronger association with the presence of CAC, independent of individual risk factors (Table 6). However, the association of individual FABPs and the FABP score was attenuated in fully adjusted models that included all CVD risk factors. Tobit modeling of CAC provided broadly similar findings (data not shown).

Discussion

FABP4 and FABP5 signal at the interface of adipocyte and macrophage biology and play a coordinated role in adipose inflammation, insulin resistance, and atherosclerosis in experimental models.[1,2,5,16] However, limited data are available addressing their integration in cardiometabolic disease in humans, particularly in T2DM, a setting of increased CVD risk. This is the first report characterizing the relation of FABP5 with metabolic and inflammatory CVD risk factors in humans and also showing that FABP4 and FABP5 relate in an additive manner to CVD risk factors and to the burden of subclinical coronary atherosclerosis in T2DM. Hence, in combination, FABP4 and FABP5 may represent mediators and biomarkers of metabolic and CVD disease in T2DM.

Experimental data provide strong evidence for the individual roles of FABP4 and, to a lesser extent, FABP5 in insulin resistance and atherosclerosis. Rodents deficient in FABP4, which is expressed almost exclusively in adipocytes and monocyte-macrophages, have a striking resistance to the development of insulin resistance and multiple features of the metabolic syndrome.[4] FABP4 deficiency attenuates inflammatory transcription factor signaling and multiple proinflammatory responses in macrophages.[17] These inflammatory-metabolic actions are known to promote adipose inflammation and insulin resistance as well as drive atherosclerosis and CVD.[18] Indeed, FABP4 regulates macrophage cholesterol metabolism and foam cell formation.[17,19] It is not surprising, therefore, that FABP4 deficiency attenuated atherosclerosis in the apolipoprotein E–deficient model.[17,20] A small-molecule inhibitor of FABP4 was recently reported to reduce macrophage-related inflammation while attenuating insulin resistance and atherosclerosis in rodents, suggesting therapeutic potential for targeting FABP4 in human disease.[3] Our clinical findings are consistent with these experimental data in demonstrating an association of FABP4 with the metabolic syndrome, inflammation, and coronary calcification in humans.

As with FABP4, FABP5 deficiency protects against insulin resistance, with enhanced insulin-stimulated glucose transport in isolated adipocytes, while mice overexpressing FABP5 in adipose have reduced insulin sensitivity.[21] However, this metabolic protection is

more modest than that observed with FABP4 deficiency,[5,21] and it is not clear that FABP5 deficiency alone protects against the development of atherosclerosis. We present the first data in humans demonstrating a robust relation, independent of FABP4, between plasma FABP5 levels and metabolic and markers of inflammation. Consistent with rodent studies to date, we did not find a significant association of FABP5 with coronary calcification, although our sample size may have lacked power to detect a modest relation.

The combined deficiency of FABP4 and FABP5 in experimental models suggests that FABP4 and FABP5 may act synergistically to promote inflammatory, metabolic, and atherogenic pathology.[5] The FABP4-FABP5 double-knockout mouse has a striking resistance to the development of insulin resistance and the metabolic syndrome.[5,22] Furuhashi et al[16] found that the deletion of FABP4 and FABP5 selectively in either adipocytes or macrophages revealed nonredundant roles for FABPs in crosstalk between these 2 cell types in promoting inflammation and insulin resistance in rodents. Furthermore, Boord et al[1] demonstrated a striking attenuation of early and late atherosclerosis as well as improvement in survival in apolipoprotein E–deficient mice that lack both FABPs. Our data support this model of additive effects of FABP4 and FABP5 on the metabolic syndrome, inflammation, and atherosclerosis in humans.

Emerging data suggest a role for FABP4 in human disease. In the Nurses' Health Study and the Health Professionals Follow-Up Study, a functional variant in the FABP4 gene that results in reduced adipose FABP4 messenger ribonucleic acid expression was associated with reduced risk for metabolic dyslipidemia, T2DM, and coronary atherosclerosis.[8] In approximately 500 Chinese subjects without diabetes, those with higher baseline FABP4 levels had increased risk for developing the metabolic syndrome and T2DM in long-term follow-up, independent of all existing metabolic risk factors, including abdominal obesity, insulin resistance, atherogenic dyslipidemia, and hypertension.[6,7] Plasma FABP4 levels were associated also with carotid atherosclerosis in Asians,[23] but not all studies have confirmed relations with human atherosclerosis.[24] Our findings extend previous work by demonstrating an association of circulating FABP4 with inflammatory and metabolic CVD risk in T2DM and by establishing a link between FABP4 and coronary atherosclerosis in this high-risk setting.

Few data exist on FABP5 in humans. We report, for the first time, a significant association of plasma FABP5 with inflammatory biomarkers and the metabolic syndrome. Notably, this relation was as strong as that for FABP4, but FABP5 had a different pattern of association with components of the metabolic syndrome: greater with dyslipidemia and hypertension but less with central adiposity. This may be due to differential tissue expression patterns, particularly with restriction of FABP4 largely to adipose, which leads to different metabolic and physiologic effects. Unlike FABP4, FABP5 levels were not significantly related to CAC scores. The combination of FABP4 and FABP5 in the FABP score, however, provided incremental value in association with metabolic syndrome and inflammation independent of other CVD risk factors and even beyond FABP4 and FABP5 data individually. Furthermore, the FABP score also predicted CAC to a greater extent than either FABP individually. Overall, these data suggest an additive effect of FABP4 and FABP5 on metabolic-inflammatory CVD risk and atherosclerosis in humans.

Our study had several limitations. Analyses were cross-sectional, so causal and longitudinal relations were not addressed. For example, we are not able to tell whether elevated FABP levels are partially the cause of rather the effect of the increased inflammatory state of T2DM. However the few previous genetic and longitudinal studies in humans to date suggest that FABP has a more causative role. Our sample size was modest and may have lacked power to detect weak associations between FABP5 and CAC. However, this sample

demonstrated robust correlations between FABPs, individually and in combination, with metabolic and inflammatory risk factors and provides support for CAC associations for the combined FABP score. We also did not examine clinical outcomes, although our data are consistent with prospective studies of FABP4. CAC is an estimate, not a direct measure of coronary atherosclerosis, so it may fail to detect some coronary atherosclerotic plaques. Despite this limitation, we chose CAC scores as our measure of subclinical atherosclerosis, because they are strong, independent predictors of CVD,[25] including in patients with diabetes.[26] Risk factor associations with CAC in T2DM can be confounded by the presence of chronic kidney disease,[27] but this was not the case in our analysis, likely because >95% of the PDHS sample have estimated glomerular filtration rates >60 ml/min.

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Table 1

Characteristics of study sample

Variable	Women (n = 313)	Men (n = 493)
Age (years)	58 (52–65)	60 (54–68)
White	50.5%	70.2%
Black	46.3%	24.1%
Other	3.2%	5.7%
Blood pressure (mm Hg)		
Systolic	129.5 (120.5–140)	130.5 (121.5–140)
Diastolic	74 (70–79)	76.5 (71–82)
Body mass index (kg/m^2)	33.5 (29.0–37.8)	31.1 (28.0–34.2)
Total cholesterol (mg/dl)	180 (158–207)	171 (148–196)
LDL cholesterol (mg/dl)	102 (82–122)	94 (78–116)
HDL cholesterol (mg/dl)	53 (45–64)	44 (38–51)
Triglycerides (mg/dl)	104 (75–147)	123 (83–186)
Metabolic syndrome	78.9%	69.6%
Estimated GFR (ml/min)	110 (85–140)	104 (85–132)
Duration of diabetes (years)	5 (2–10)	5 (2–10)
Glycosylated hemoglobin (%)	6.9 (6.3–7.7)	6.8 (6.2–7.8)
Current smokers	7.6%	11.5%
Medications		
Statins	43.9%	61.0%
Fibrates	2.0%	9.2%
Aspirin	40.7%	47.3%
ACE inhibitors	56.9%	63.7%
Metformin	63.0%	64.2%
Sulfonylureas	31.0%	44.4%
Thiazolidinediones	23.6%	31.0%
Insulin	22.0%	16.2%
FABP4 (ng/ml)	37.1 (23.0–55.2)	20.9 (14.0–30.9)
FABP5 (ng/ml)	1.5 (1.2–1.93)	1.4 (1.1–1.8)
Adiponectin (μg/ml)	10.4 (7.0–16.2)	7.9 (5.3–12.3)
Leptin (ng/ml)	27.1 (17.5–36.5)	8.5 (5.3–13.7)
CRP (mg/l)	2.9 (1.5–7.0)	1.5 (0.7–3.0)
IL-6 (pg/ml)	1.6 (0.9–2.5)	1.3 (0.8–2.0)
CAC score		
Mean ± SD	109 ± 289	448 ± 801
Median (IQR)	0 (0–74)	108 (4–538)
>75th percentile	29.6%	33.3%

Data are expressed as median (IQR) or as percentages, except as indicated.

ACE = angiotensin-converting enzyme; GFR = glomerular filtration rate; HDL = high-density lipoprotein; IQR = interquartile range; LDL = low-density lipoprotein.

Table 2

Spearman's correlations of lipid, metabolic, and inflammatory variables with plasma levels of fatty acid–binding proteins

Risk Factor	FABP4		FABP5	
	Women	Men	Women	Men
Age	0.13*	0.02	0.05	0.1*
Body mass index	0.46‡	0.38‡	0.34‡	0.16‡
Waist circumference	0.46‡	0.41‡	0.38‡	0.20‡
Leptin	0.48‡	0.51‡	0.40‡	0.30‡
Adiponectin	0.08	0.22‡	–0.17†	–0.08
Blood pressure				
Systolic	0.4	0.08	0.06	0.13†
Diastolic	–0.01	0.02	0.03	0.01
Total cholesterol	–0.04	–0.06	–0.04	–0.01
LDL cholesterol	–0.03	–0.09	–0.04	–0.03
HDL cholesterol	–0.23‡	–0.11*	–0.30‡	–0.17‡
Triglycerides	0.25‡	0.14†	0.25‡	0.12†
Estimated GFR	0.13*	0.08	0.06	–0.07
CRP	0.18†	0.08	0.18†	0.14†
IL-6	0.18†	0.26‡	0.15†	0.27‡
FABP 4	—	—	0.45‡	0.38‡

Abbreviations as in Table 1.

* p <0.05

† p <0.01

‡ p <0.001.

Table 3

Association of plasma levels of fatty acid–binding proteins with metabolic syndrome components

Metabolic Syndrome Component	Plasma FABP4	Plasma FABP5
HDL cholesterol		
Absent (n = 527)	23.9 (15.3–38.1)	1.3 (1.1–1.7)
Present (n = 274)	29.0 (18.5–44.2)	1.6 (1.3–2.0)
Chi-square	13.5 (p <0.001)	31.9 (p <0.001)
Triglycerides		
Absent (n = 550)	24.7 (15.6–40.1)	1.4(1.1–1.8)
Present (n = 251)	26.7 (17.2–43.0)	1.5 (1.2–2.0)
Chi-square	2.7 (p = 0.10)	13.9 (p <0.001)
Blood pressure		
Absent (n = 407)	26.2 (15.8–41.5)	1.4 (1.1–1.8)
Present (n = 399)	25.0 (16.5–40.6)	1.5 (1.2–1.9)
Chi-square	0.08 (p = 0.78)	7.1 (p <0.01)
Waist circumference		
Absent (n = 240)	17.3 (12.1–26.0)	1.3 (1.0–1.6)
Present (n = 566)	29.2 (20.0–46.3)	1.5 (1.2–1.9)
Chi-square	115.9 (p <0.001)	43.0 (p <0.001)
All		
Absent (n = 323)	22.3 (14.1–32.6)	1.3 (1.0–1.7)
Present (n = 480)	28.0 (18.1–44.9)	1.5 (1.2–1.9)
Chi-square	29.8 (p <0.001)	36.2 (p <0.001)

Data are expressed as median (IQR).

Abbreviations as in Table 1.

Table 4

Association of the metabolic syndrome with fatty acid–binding protein levels and the fatty acid–binding protein score

Model	FABP4	FABP5	FABP Score
Basic model (age, gender, race)	1.85 (1.53–2.23)	1.66 (1.41–1.95)	2.01 (1.68–2.41)
Basic model + HDL cholesterol	1.66 (1.35–2.02)	1.46 (1.23–1.72)	1.76 (1.45–2.13)
Basic model + triglycerides	1.65 (1.35–2.02)	1.56 (1.32–1.86)	1.84 (1.52–2.23)
Basic model + blood pressure	1.85 (1.53–2.25)	1.61 (1.36–1.89)	1.97 (1.64–2.37)
Basic model + waist circumference	1.17 (0.95–1.45)	1.39 (1.17–1.65)	1.35 (1.10–1.65)
Basic model + FABP4	—	1.46 (1.23–1.72)	1.85 (1.43–2.39)
Basic model + FABP5	1.58 (1.30–1.93)	—	1.85 (1.43–2.38)

Odds ratios and 95% confidence intervals for the metabolic syndrome are presented for 1-SD changes in the log values of FABP4, FABP5, and the FABP score.

Abbreviation as in Table 1.

Table 5

Association of with fatty acid–binding protein levels and fatty acid–binding protein score with the inflammatory markers C-reactive protein and interleukin-6

Model	FABP4	FABP5	FABP Score
CRP			
Basic model (age, gender, race)	1.17 (1.08–1.28)	1.15 (1.07–1.23)	1.25 (1.16–1.35)
Basic model + FRS	1.17 (1.07–1.27)	1.13 (1.05–1.21)	1.24(1.14–1.34)
Basic model + MS	1.11 (1.02–1.21)	1.10 (1.02–1.18)	1.18 (1.09–1.28)
Basic model + FRS and MS	1.11 (1.02–1.21)	1.09 (1.02–1.17)	1.18 (1.09–1.28)
Full model*	1.11 (1.02–1.21)	1.10 (1.03–1.18)	1.19 (1.09–1.29)
Full model and FABP4	—	1.08 (1.00–1.17)	1.24 (1.10–1.40)
Full model and FABP5	1.08 (0.98–1.18)	—	1.20 (1.07–1.35)
IL-6			
Basic model (age, gender, race)	1.16 (1.10–1.23)	1.17 (1.11–1.22)	1.21 (1.15–1.27)
Basic model + FRS	1.16 (1.10–1.22)	1.16 (1.11–1.21)	1.20 (1.14–1.27)
Basic model + MS	1.13 (1.07–1.20)	1.15 (1.09–1.20)	1.18 (1.12–1.25)
Basic model + FRS and MS	1.13 (1.07–1.20)	1.04 (1.09–1.20)	1.18 (1.12–1.25)
Full model*	1.14 (1.07–1.21)	1.15 (1.10–1.20)	1.19 (1.13–1.26)
Full model and FABP4	—	1.03 (1.07–1.18)	1.21 (1.11–1.31)
Full model and FABP5	1.08 (1.02–1.15)	—	1.12 (1.04–1.22)

Data are expressed as odds ratio (95% confidence interval). The changes in CRP and IL-6 levels are presented for a 1-SD of the log of FABP4, FABP5, or a 1-SD in FABP score.

FRS = Framingham risk score; MS = metabolic syndrome. Other abbreviation as in Table 1.

*The full model included age, gender, race, FRS, the MS, exercise, aspirin, statin or ACE inhibitor use, and alcohol use.

Table 6

Association of coronary artery calcium with fatty acid–binding protein levels and fatty acid–binding protein score

Model	FABP4	FABP5	FABP Score
Basic model (age, gender, race)	1.26 (1.05–1.52)	1.13 (0.97–1.32)	1.28 (1.08–1.53)
Basic model + HDL	1.23 (1.02–1.49)	1.09 (0.93–1.28)	1.25 (1.04–1.50)
Basic model + triglycerides	1.21 (1.00–1.46)	1.09 (0.93–1.27)	1.24 (1.03–1.48)
Basic model + blood pressure	1.26 (1.04–1.51)	1.13 (0.97–1.32)	1.27 (1.06–1.51)
Basic model + waist circumference	1.20 (0.98–1.47)	1.09 (0.92–1.28)	1.23 (1.01–1.49)

Odds ratios and 95% confidence intervals for CAC score >0 are presented for 1-SD changes in the log values of FABP4, FABP5, and the FABP score.

Abbreviation as in Table 1.