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High serum adipocyte fatty acid binding protein concentration linked with increased aortic arterial stiffness in patients with type 2 diabetes

Pei-Wei Tseng[a,1], Jia-Sian Hou[b,1], Du-An Wu[a,c,*], Bang-Gee Hsu[a,b,**]

[a] School of Medicine, Tzu Chi University, Hualien, Taiwan
[b] Division of Nephrology, Buddhist Tzu Chi General Hospital, Hualien, Taiwan
[c] Division of Metabolism and Endocrinology, Buddhist Tzu Chi General Hospital, Hualien, Taiwan

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ABSTRACT

Background: Adipocyte fatty acid binding protein (A-FABP) is a novel adipokine that contributes to the development of metabolic disorder, type 2 diabetes mellitus (T2DM) and atherosclerosis. We determined the correlation between serum A-FABP and aortic stiffness in T2DM patients.
Methods: Fasting blood samples were obtained from 156 patients with T2DM. Serum A-FABP concentration were determined using a commercial enzyme immunoassay. Carotid-femoral pulse wave velocity (cfPWV) was measured using SphygmoCor System, and cfPWV values of > 10 m/s were defined as high aortic stiffness.
Results: Sixty participants (38.4%) fell under the high aortic stiffness group. This group, compared to the control group, showed older age ($P = .004$), higher systolic blood pressure ($P < .001$), diastolic blood pressure ($P = .027$), urine albumin-to-creatinine ratio ($P = .003$), serum A-FABP ($P < .001$) and lower estimated glomerular filtration rate ($P = .001$). After adjusting for factors significantly associated with aortic stiffness using multivariable logistic regression analysis, serum A-FABP [OR = 1.029 (1.002–1.058), $P = .039$] was found to be an independent predictor of aortic stiffness in T2DM patients.
Conclusions: Serum A-FABP is positively correlated with aortic arterial stiffness in patients with T2DM.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of mortality and morbidity in patients with type 2 diabetes mellitus (T2DM) [1]. Distinct characteristics of CVD include stiffness of vessels, thickening of intima media and loss of vascular distensibility [2]. Among the aforementioned parameters that could be measured non-invasively, aortic stiffness expressed in terms of carotid-femoral pulse wave velocity (cfPWV) offers high predictive value for CVD and all-cause mortality [3]. cfPWV is currently regarded as the gold standard in the measurement of aortic stiffness [4].

An increasing number of studies have identified adipocyte fatty acid binding protein (A-FABP) as a novel adipokine that regulates systemic metabolism, and it contributes to the development of metabolic disorder, T2DM and atherosclerosis [5,6]. A-FABP, also known as aP2 or FABP4, belongs to the family of FAPB cytoplasmic proteins which bind reversibly to hydrophobic ligands including both saturated and unsaturated long chain free fatty acids (FFA), thus enhancing their solubility and transportation [7]. A-FABP makes up 6% of total protein in mature adipocytes and is highly produced in macrophages, where it plays a role in inflammatory responses [8,9]. The pro-inflammatory properties of A-FABP are detrimental to vascular function, metabolic function and insulin resistance, all of which are classical risk factors of CVD [10]. A novel biomarker of CVD in diabetic patients such as A-FABP could provide means to predict the risk of future cardiovascular events and allow early interventions to be made.

2. Materials and methods

2.1. Participants

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Protection of the Human Subjects Institutional Review Board of Tzu-Chi University and Hospital.

* Correspondence to: Du-An Wu, Division of Nephrology, Buddhist Tzu Chi General Hospital, 707, Section 3, Chung Yang Road, Hualien, Taiwan.
** Correspondence to: Bang-Gee Hsu, Division of Metabolism and Endocrinology, Buddhist Tzu Chi General Hospital, 707, Section 3, Chung Yang Road, Hualien, Taiwan.
E-mail addresses: despdu@yahoo.com.tw (D.-A. Wu), gee.lily@msa.hinet.net (B.-G. Hsu).
[1] These authors contributed equally to this study.

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Informed written consent was obtained from all patients prior to their enrolment in this study. A total of 156 T2DM patients were enrolled at a medical center in Hualien, Taiwan from November 2014 through March 2015. Blood pressure (BP) were measured in the morning by trained staff using standard mercury sphygmomanometers with appropriate cuff sizes, after sitting for at least 10 min. Systolic BP (SBP) and diastolic BP (DBP) were taken 3 times at 5-min intervals and the data were averaged for analysis. Patients were excluded if they had an acute infection, acute myocardial infarction, heart failure and malignancy at the time of blood sampling, or if they refused to provide informed consent for the study.

2.2. Anthropometric analysis

Body weight was measured to the nearest 0.5 kg with participants wearing light clothing and no shoes, while body height was measured to the nearest 0.5 cm. Waist circumference was measured using a tape measurement around the waist from the point between the lowest ribs and the hip bones with the participant's hands on the hips. Bioimpedance measurements of body fat mass were performed at the bedside according to the standard tetrapolar whole body (hand-foot) technique, using a single-frequency (50-kHz) analyzer (Biodynamic-450, Biodynamics Corp.). All measurements were carried out by the same operator [11–14].

2.3. Biochemical investigations

Approximately 5 ml blood samples of all participants were obtained after an overnight fasting and immediately centrifuged at 3000*g* for 10 min. Serum concentration of blood urea nitrogen, creatinine, fasting glucose, glycated hemoglobin (HbA1c), total cholesterol (TCH), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) were measured using an autoanalyzer (Siemens Advia 1800, Siemens Healthcare GmbH) [11–14]. Urine albumin-to-creatinine ratio (UACR) using random spot urine testing was also recorded. Serum A-FABP concentration were measured using a commercially available enzyme immunoassay (EIA; SPI- BIO) [11–13]. Serum insulin concentration were measured using the commercially available enzyme-linked immunosorbent assay (ELISA) (Labor Diagnostika Nord) [12,13]. Insulin resistance was evaluated using a homeostasis model assessment of insulin resistance (HOMA-IR) as follows: HOMA-IR = fasting plasma glucose (mg/dl) × fasting serum insulin (μU/ml)/405 [12,13]. The estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation.

2.4. Aortic stiffness by carotid-femoral pulse wave velocity measurements

Aortic stiffness by measurement of cfPWV was performed using a pressure applanation tonomentry (SphygmoCor system, AtCor Medical, Australia) as previously described [11,13,14]. These measurements were performed in the morning with the participants lying in supine position after taking a minimum of 10 min rest in a quiet and temperature-controlled room. Recordings were made simultaneously with an ECG signal, which provided an *R*-timing reference. Pulse wave recordings were performed consecutively at 2 superficial artery sites (carotid-femoral segment). The carotid-femoral distance was obtained by subtracting the carotid measurement site to sternal notch distance from the sternal notch to femoral measurement site distance. An integral software was used to process each set of pulse wave and ECG data to calculate the mean time difference between *R*-wave and pulse wave on a beat-to-beat basis, with an average of 10 consecutive cardiac cycles. The cfPWV was calculated using the distance and mean time difference between the 2 recorded points. Quality indices, included in the software, were set to ensure uniformity of the data. In this study, cfPWV values of > 10 m/s were defined as high aortic stiffness, while values ≤10 m/s were regarded as the control group [11,13,14].

2.5. Statistical analysis

Data were tested for normal distribution using the Kolmogorov–Smirnov test. Normally distributed data were expressed as the mean ± SD, and comparisons between patients were performed using the Student's independent *t*-test (2-tailed). Data that were not normally distributed were expressed as medians and interquartile ranges and comparisons between patients were performed using the Mann-Whitney *U* test (age, TG, fasting glucose, HbA1c, BUN, creatinine, UACR, insulin and HOMA-IR). Data expressed as the number of patients were analyzed by the χ^2 test. Since age, TG, fasting glucose, HbA1c, BUN, creatinine, UACR, insulin and HOMA-IR were not normally distributed, the data underwent base 10 logarithmic transformations to achieve normality. Clinical variables that correlated with serum A-FABP concentration in T2DM patients were evaluated using simple linear regression analysis and variables that were significantly associated with A-FABP concentration in T2DM patients were tested for independency in multivariable forward stepwise regression analysis. Variables that were significantly associated with aortic stiffness were tested for independence by multivariable logistic regression analysis (adapted factors: age, SBP, DBP, eGFR, UACR, and A-FABP). Data were analyzed using SPSS for Windows (ver 19.0). A $P < .05$ was considered to be statistically significant.

3. Results

3.1. The relationships between baseline demographics, clinical characteristics, and drugs used with aortic stiffness

The demographic, biochemical and clinical characteristics of the 156 T2DM patients with high aortic stiffness or control group were summarized in Table 1. A total of 60 participants (38.4%) fell under the high aortic stiffness group. Compared to the control group, high aortic stiffness group showed older age ($P = .004$), higher cfPWV values ($P < .001$), SBP ($P < .001$), DBP ($P = .027$), UACR ($P = .003$), serum A-FABP ($P < .001$), and lower eGFR ($P < .001$) in T2DM patients. There was no statistically significant difference in sex and the use of anti-hypertensive, anti-hyperlipidemic or anti-diabetic drugs, namely: angiotensin-converting enzyme inhibitor (ACEi), angiotensin II receptor blocker (ARB), β-blocker, calcium channel blocker (CCB), statin, fibrate, metformin, sulfonylurea, dipeptidyl peptidase 4 inhibitor and insulin between the two groups.

3.2. Subgroup comparisons of serum A-FABP concentration and drugs used in T2DM patients

Clinical characteristics of drugs used and serum A-FABP concentration for these patients were presented in Table 2. The A-FABP concentration were significantly higher in female than in male T2DM patients ($P = .002$). No statistically significant differences in the A-FABP concentration were found as a result of the use of ACEi, ARB, β-blockers, CCB, statins, fibrate, metformin, sulfonylureas, DDP-4 inhibitor, or insulin.

3.3. Correlation between A-FABP concentration and clinical and biochemical parameters in T2DM patients

The simple and multivariable regression analyses of the correlation between serum A-FABP concentration and clinical variables among the T2DM patients were presented in Table 3. Simple regression analysis showed A-FABP to be positively correlated with female T2DM patient (r: 0.252, $P = .002$), waist circumference (r: 0.211, $P = .008$), BMI (r: 0.199, $P = .013$), body fat mass (r: 0.395, $P < .001$), cfPWV (r: 0.355, $P < .001$), SBP (r: 0.283, $P < .001$), DBP (r: 0.162, $P = .043$),

Table 1
Clinical variables of the 156 diabetic patients with high or low aortic stiffness.

Characteristics	All patients (*N* = 156)	Control group (*N* = 96)	High aortic stiffness group (*N* = 60)	*P* value
Age (years)	65.00 (57.00–70.00)	65.00 (56.00–68.00)	66.00 (59.25–74.75)	0.004*
Height (cm)	161.69 ± 8.35	162.70 ± 8.36	160.08 ± 8.15	0.057
Body weight (kg)	70.77 ± 13.52	71.37 ± 14.42	69.81 ± 11.98	0.484
Waist circumference (cm)	90.77 ± 9.44	90.19 ± 10.13	91.68 ± 8.21	0.339
Body mass index (kg/m^2)	26.95 ± 3.96	26.84 ± 4.18	27.13 ± 3.62	0.657
Body fat mass (%)	31.48 ± 7.54	30.88 ± 7.61	32.44 ± 7.40	0.210
cfPWV (m/s)	9.77 ± 2.77	8.10 ± 1.39	12.45 ± 2.27	< 0.001*
SBP (mmHg)	142.49 ± 20.19	137.93 ± 18.13	149.78 ± 21.29	< 0.001*
DBP (mmHg)	82.80 ± 11.29	81.23 ± 10.95	85.32 ± 11.47	0.027*
Pulse pressure (mmHg)	59.69 ± 14.47	56.70 ± 13.85	64.47 ± 14.26	0.001*
Total cholesterol (mg/dl)	161.95 ± 31.12	162.66 ± 28.46	160.82 ± 35.19	0.721
Triglyceride (mg/dl)	114.50 (85.00–172.00)	110.50 (78.50–155.75)	117.00 (89.00–152.00)	0.068
HDL-C(mg/dl)	46.76 ± 12.69	47.56 ± 11.94	45.47 ± 13.80	0.317
LDL-C(mg/dl)	99.58 ± 27.07	100.79 ± 25.55	97.63 ± 29.45	0.480
Fasting glucose (mg/dl)	138.00 (121.00–174.50)	131.00 (118.25–167.75)	144.00 (121.50–184.50)	0.156
Glycated hemoglobin (%)	7.50 (6.60–8.98)	7.25 (6.53–8.80)	8.10 (6.73–9.35)	0.125
Blood urea nitrogen (mg/dl)	16.00 (12.00–19.00)	16.00 (12.00–18.00)	17.00 (13.25–20.75)	0.141
Creatinine (mg/dl)	0.8 (0.70–1.00)	0.80 (0.70–1.00)	0.90 (0.80–1.20)	0.055
eGFR (ml/min)	68.44 ± 19.50	93.02 ± 26.50	78.44 ± 26.89	0.001*
UACR (mg/g)	16.28 (7.57–88.37)	12.41 (7.13–36.44)	25.71 (9.84–248.39)	0.003*
Insulin (uIU/ml)	6.79 (3.62–13.90)	6.79 (3.06–13.13)	6.85 (4.28–14.54)	0.543
HOMA-IR	2.51 (1.23–4.95)	2.45 (1.04–4.63)	2.58 (1.52–5.48)	0.304
A-FABP (ng/ml)	27.45 ± 14.15	24.36 ± 10.68	32.40 ± 17.37	< 0.001*
Male, n (%)	88 (56.4)	59 (61.5)	29 (48.3)	0.108
ACE inhibitor use, n (%)	11 (7.1)	7 (7.3)	4 (6.7)	0.882
ARB use, n (%)	64 (41.0)	36 (37.5)	28 (46.7)	0.257
β-blocker use, n (%)	20 (12.8)	9 (9.4)	11 (18.3)	0.103
CCB use, n (%)	46 (29.5)	30 (31.3)	16 (26.7)	0.541
Statin use, n (%)	77 (49.4)	46 (47.9)	31 (51.7)	0.649
Fibrate use, n (%)	9 (5.8)	6 (6.3)	3 (5.0)	0.745
Metformin use, n (%)	85 (54.5)	53 (55.2)	32 (53.3)	0.819
Sulfonylureas use, n (%)	84 (53.8)	52 (54.2)	32 (53.3)	0.919
DDP-4 inhibitor use, n (%)	95 (60.9)	59 (61.5)	36 (60.0)	0.856
Insulin use, n (%)	41 (26.3)	26 (27.1)	15 (25.0)	0.774

Values for continuous variables are given as mean ± standard deviation and tested by Student's *t*-test; variables not normally distributed are given as median and interquartile range and tested by Mann–Whitney *U* test; values are presented as number (%) and analysis was done using the chi-square test.
cfPWV, carotid–femoral pulse wave velocity; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio; HOMA-IR, homeostasis model assessment of insulin resistance; A-FABP, adipocyte fatty acid binding protein; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; DDP-4, dipeptidyl peptidase 4.
* $P < .05$ was considered statistically significant.

logarithmically transformed HbA1c (log-HbA1c, r: 0.221, $P = .005$), log-UACR (r: 0.304, $P < .001$), log-insulin (r: 0.173, $P = .030$) and log-HOMA-IR (r: 0.200, $P = .012$), while eGFR (r: -0.279, $P < .001$) was negatively correlated. In multivariable forward stepwise linear regression analysis, body fat mass (β = 0.344, adjusted R^2 change: 0.151, $P < .001$), cfPWV value (β = 0.210, adjusted R^2 change: 0.090, $P = .007$), and log-UACR (β = 0.156, adjusted R^2 change: 0.017, $P = .036$) was positively associated, while eGFR (β = −0.177, adjusted R^2 change: 0.033, $P = .020$) was negatively associated with serum A-FABP level in T2DM patients.

3.4. A-FABP level is independently associated with aortic stiffness in T2DM patients

Multivariable logistic regression analysis of the factors significantly associated with aortic stiffness showed that only serum A-FABP level (odds ratio: 1.029, 95% confidence interval (CI): 1.002–1.058, $P = .039$) was an independent predictor of aortic stiffness in patients with T2DM (Table 4).

4. Discussion

Our study showed that T2DM patients with older age, SBP, DBP, UACR, serum A-FABP level, and lower eGFR had high aortic stiffness. Serum A-FABP level was an independent predictor of aortic stiffness in T2DM patients. Body fat mass, cfPWV values and UACR were positively associated, while eGFR was negatively associated with serum A-FABP level in T2DM patients.

Arterial stiffness is an aged-linked process which is a shared consequence of chronic illnesses such as DM, metabolic syndrome and chronic kidney disease [15]. It is a well-established fact that arterial stiffness is closely related to atherosclerosis and the progression of CVD, and it is widely regarded as the surrogate end point of CVD [3]. It has been understood that arterial stiffness leads to a reduction in lumen diameter for a given BP and muscle tone, resulting in premature return of reflected waves during late systole, causing SBP and central pulse pressure to elevate and DBP to decline [11]. The Framingham Study revealed a linear increase in SBP and a simultaneous early rise in DBP in 30–84 years of age [16]. A proposed hypothesis to explain such predominance of systolic hypertension in elderly is that arterial stiffness affects SBP more than DBP [17]. In this study, we found that participants with T2DM in the high aortic stiffness were of older age, higher SBP and DBP than those in the low aortic stiffness group.

Several studies produced the same results showing higher A-FABP concentration in female subjects, because females have comparatively higher percentages of body fat than males [12,13,18]. A-FABP is regulated by fatty acids, insulin and peroxisome-proliferator- activated receptor-c agonists [19]. Numerous animal research involving knock-out mice have concluded that A-FABP induces metabolic syndrome and insulin resistance [5]. Moreover, A-FABP deficiency decreases lypolysis-

Table 2
Clinical characteristics and serum adipocyte fatty acid binding protein levels of the 156 diabetic patients.

Characteristic		Number (%)	A-FABP (ng/ml)	P value
Sex	Male	88 (56.4)	24.33 ± 12.59	0.002*
	Female	68 (45.6)	31.50 ± 15.09	
ACE inhibitor	No	145 (92.9)	27.03 ± 13.43	0.172
	Yes	11 (7.1)	33.08 ± 21.60	
ARB	No	92 (59.0)	27.15 ± 14.28	0.750
	Yes	64 (41.0)	27.89 ± 14.05	
β-blocker	No	136 (87.2)	26.97 ± 14.35	0.266
	Yes	20 (12.8)	30.74 ± 12.53	
CCB	No	110 (70.5)	26.44 ± 13.70	0.167
	Yes	46 (29.5)	29.87 ± 15.05	
Statin	No	79 (50.6)	25.92 ± 11.42	0.171
	Yes	77 (49.4)	29.03 ± 16.41	
Fibrate	No	147 (94.2)	27.02 ± 14.24	0.120
	Yes	9 (5.8)	34.57 ± 10.78	
Metformin	No	71 (45.5)	26.39 ± 14.22	0.393
	Yes	85 (54.5)	28.34 ± 14.11	
Sulfonylureas	No	72 (46.2)	26.41 ± 13.78	0.394
	Yes	84 (53.8)	28.35 ± 14.48	
DDP-4 inhibitor	No	61 (39.1)	26.69 ± 14.85	0.589
	Yes	95 (60.9)	27.95 ± 13.73	
Insulin	No	115 (73.7)	27.36 ± 14.23	0.896
	Yes	41 (26.3)	27.70 ± 14.09	

Data are expressed as mean ± standard deviation and tested by Student's t-test. A-FABP, adipocyte fatty acid binding protein; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; DDP-4, dipeptidyl peptidase 4.

* $P < .05$ was considered statistically significant after Student's *t*-test.

induced insulin secretion, and increases glucose-stimulated insulin secretion from β-cells [5]. A 10-y follow up study performed on the Chinese cohort showed that high baseline concentration of A-FABP had high predictive value in the development of T2DM, independent of insulin resistance, glycemic indexes and obesity [20]. On the other hand, several studies have found serum A-FABP to be upregulated in subjects with metabolic syndrome [12,13,18]. Our study revealed a positive association between serum A-FABP concentration and the indicators of adiposity and metabolic syndrome in patients with T2DM. Moreover, serum A-FABP level has significant correlation with high serum creatinine and lowers GFR, and independently related to diabetic nephropathy staging [21]. A-FABP protein and mRNA were expressed not only in peritubular capillaries, but also in endothelial cells and macrophages in the glomerulus and the ratio of A-FABP-positive area to total area within glomeruli was positively correlated with urinary protein level at a total of 112 renal biopsy patients [22]. Our results also noted that serum A-FABP level was positively correlated with UACR and negatively correlated eGFR in T2DM patients. After multivariable forward stepwise linear regression analysis, body fat mass, UACR and eGFR were associated with serum A-FABP level in T2DM patients.

A-FABP is known to be upregulated in macrophages and foam cells in human atherosclerostic plagues [23]. Serum A-FABP promotes the formation of atherosclerosis through the accumulation of TG and cholesterol in macrophages while inhibiting cholesterol efflux, and it also induces both proatherogenic and proinflammaotry cytokines in macrophages [5]. A Korean study which utilized 18F-flurodexoyglucose positron emission tomography, confirmed that vascular inflammation is indeed associated with circulating adipokines and serum A-FABP [24]. On the other hand, diabetic patients who have macrovascular complications exhibited significantly elevated concentration of serum A-FABP [25]. The relationship between atherosclerosis and A-FABP was first described in 2007 by Yeung et al., when they found markedly elevated concentration of serum A-FABP in female individuals with carotid atherosclerosis than those who do not [25]. It has also been revealed that A-FABP was positively correlated with coronary atherosclerosis and the number of stenotic coronary vessels [26]. A-FABP has been

Table 3
Correlation between serum adipocyte fatty acid binding protein levels and clinical variables among the 156 diabetic patients.

Variables	A-FABP (ng/ml)				
	Simple regression		Multivariable regression		
	r	P value	Beta	Adjusted R^2 change	P value
Female	0.252	0.002*	–	–	–
Log-age (years)	0.138	0.086	–	–	–
Height (cm)	−0.163	0.200	–	–	–
Body weight (kg)	0.100	0.215	–	–	–
Waist circumference (cm)	0.211	0.008*	–	–	–
Body mass index (kg/m^2)	0.199	0.013*	–	–	–
Body fat mass (%)	0.395	< 0.001*	0.344	0.151	< 0.001*
cfPWV (m/s)	0.355	< 0.001*	0.210	0.090	0.007*
SBP (mmHg)	0.283	< 0.001*	–	–	–
DBP (mmHg)	0.162	0.043*	–	–	–
Total cholesterol (mg/dl)	0.035	0.667	–	–	–
Log-Triglyceride (mg/dl)	0.191	0.057	–	–	–
HDL-C (mg/dl)	−0.092	0.252	–	–	–
LDL-C (mg/dl)	0.002	0.977	–	–	–
Log-Glucose (mg/dl)	0.138	0.087	–	–	–
Log-HbA1c (%)	0.221	0.005*	–	–	–
eGFR (ml/min)	−0.279	< 0.001*	−0.177	0.033	0.020*
Log-UACR (mg/g)	0.304	< 0.001*	0.156	0.017	0.036*
Log-Insulin (uIU/ml)	0.173	0.030*	–	–	–
Log-HOMA-IR	0.200	0.012*	–	–	–

Data of age, triglyceride, glucose, HbA1c, UACR, insulin and HOMA-IR levels showed skewed distribution and therefore were log-transformed before analysis.

Analysis of data was done using the simple regression or multivariable stepwise linear regression analysis (adapted factors were gender, waist circumference, body mass index, body fat mass, cfPWV, SBP, DBP, log-HbA1c, eGFR, log-UACR, log-Insulin and log-HOMA-IR).

A-FABP, adipocyte fatty acid binding protein; cfPWV, carotid–femoral pulse wave velocity; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio; HOMA-IR, homeostasis model assessment of insulin resistance.

* P < .05 was considered statistically significant.

Table 4
Multivariable logistic regression analysis of the factors correlated with aortic stiffness among the 156 diabetic patients.

Variables	Odds ratio	95% confidence interval	P value
Adipocyte fatty acid binding protein (ng/ml)	1.029	1.002–1.058	0.039*

Analysis of data was done using the multivariable logistic regression analysis (adapted factors were age, systolic blood pressure, diastolic blood pressure, estimated glomerular filtration rate, urine albumin-to-creatinine ratio and adipocyte fatty acid binding protein).

* P < .05 was considered statistically significant.

reported to show a positive correlation with augmentation index in patients with T2DM [27]. Our previous studies also noted that serum A-FABP level was positively correlated with aortic stiffness in geriatric subjects and hypertensive patients [11,13]. After adjusting the confounding factors, the multivariable logistic regression analysis revealed that an increased serum A-FABP level was an independent predictor of aortic stiffness in patients with T2DM.

Our study had some limitations. Firstly, such cross-sectional studies led to difficulties in determining the direction of causality between

serum A-FABP and T2DM. Secondly, the sample size of 156 T2DM patients from a single medical center may not be representative of the entire Taiwanese population, and thus the study results may not apply to patients of different ethnicities. Another limitation is that ARBs drug can significantly decrease plasma A-FABP level in hypertensive patients [28,29]. In our study, there were no significant differences in serum A-FABP in terms of the medications used, including ACEi, ARB, β-blockers, CCB, statins, fibrate, metformin, sulfonylureas, DDP-4 inhibitor, or insulin. Further studies are needed to investigate the relationship between these medications and A-FABP concentration in patients with T2DM.

In conclusion, our study found serum A-FABP level to be positively correlated with aortic stiffness in patients with T2DM. Body fat mass, cfPWV values and UACR were positively associated, while eGFR was negatively associated with serum A-FABP level in T2DM patients.

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