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Visceral fat area loss reduces 10-year atherosclerotic cardiovascular disease risk in Chinese population with type 2 diabetes mellitus: a prospective cohort study

Jing Jin¹, Yu Lei^{2*}, Jia Zheng³, Jinjian Xu², Linna Chen^{2,4}, Shuning Liu^{2,5}, Xingyue Cao², Ye Hu², Chenyan Yan², Xiaohong Wu^{2#}

Abstract

Background: Among individuals diagnosed with type 2 diabetes mellitus (T2DM), an abnormal accumulation of visceral fat heightens the risk of cardiovascular problems (CVR), and the major reason for death for these people is atherosclerotic cardiovascular disease (ASCVD). This study set out to gain further details about the longitudinal relationship of CVR with visceral fat area (VFA) among patients having T2DM, and to contrast the predictive performance of additional abdominal obesity measures and VFA for CVR changes.

Methods: This prospective cohort study included 316 patients having T2DM who were followed up for more than one year, and VFA was measured by bioimpedance method. This study determined how a VFA percentage change (Δ VFA, %) was prospectively associated with CVR and evaluated the potential nonlinear relationships between Δ VFA (%) and 10-year ASCVD risk increase. Furthermore, the area under the pooled curve (AUC) was contrasted for both Δ VFA (%) as well as other abdominal obesity indices.

Results: The excessive VFA loss group showed lower low-density lipoprotein cholesterol (LDL-C), non-high-density lipoprotein cholesterol (non-HDL-C), total cholesterol (TC),

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triglyceride–glucose index,²⁸ LDL-C/HDL-C, brachial-ankle pulse wave velocity, 10-year ASCVD risk, atherogenic index of plasma, TC/HDL-C, and apolipoproteins B/apolipoproteins A-1 than the VFA gain group (all $\beta < 0$, HR < 1 , all $P < 0.05$) after covariate controlling. VFA reduction more than 14.82% led to a reduction in the stated risk. Moreover, Δ VFA (%) demonstrated superior¹⁸ predictive value for the change of ASCVD risk, with an AUC of 0.585 (95% CI: 0.513-0.656), compared to other obesity indices.

Conclusions: Excessive VFA reduction improved¹ 10-year ASCVD risk in patients diagnosed with T2DM. VFA was a more effective predictor of 10-year ASCVD risk changes than other abdominal obesity measures.

Introduction

A major health condition across the globe,³⁰ type 2 diabetes mellitus (T2DM), has been tied to increased morbidity and death from atherosclerotic cardiovascular diseases (ASCVD) [1]. Interestingly, ASCVD is the major reason for mortality among persons having T2DM [2]. A T2DM diagnosis dramatically increases the likelihood of acquiring cardiovascular disease (CVD) over 10 years for both men and women and all stages of life, with young individuals being most affected, as reported by Gyldenkerne et al. [3]. Therefore, early prevention of cardiovascular events is a key focus in T2DM management.

Excessive visceral fat is closely linked to heart risks among individuals with T2DM. Visceral obesity is a key contributor of T2DM, atherosclerosis, and CVD [4].²² Data from the Framingham Heart Study indicate that the accumulation of visceral fat intensifies CVR factors, including impaired glucose metabolism, and dyslipidemia, consequently elevating the

occurrence of cardiovascular events within general population [5, 6]. Given that patients with T2DM exhibit more pronounced metabolic abnormalities, additional research is necessary to determine how buildup of visceral fat affects their CVR.

The benchmark to detect visceral obesity is the visceral fat area (VFA), which is assessed using computed tomography (CT) or magnetic resonance imaging (MRI) [7]. However, CT radiation exposure and the time-consuming and expensive nature of MRI limit their routine clinical application. Bioelectrical impedance analysis (BIA) refers to a harmless, inexpensive, and convenient alternative to CT for measuring VFA [8]. Recent studies monitored abdominal fat accumulation using indicators like lipid accumulation product (LAP), Chinese visceral adiposity index (CVAI), body roundness index (BRI), and waist circumference (WC) [9-12], which can indirectly reflect visceral fat buildup levels. Moreover, no research has been conducted on the dynamic correlation between visceral fat accumulation and the 10-year ASCVD risk among patients diagnosed with T2DM. Therefore, the study aimed to screen the body anthropometry and other indices for the determination of CVR in individuals diagnosed with T2DM and to explore the long-term relationship between CVR and visceral fat changes.

Methods

Study design and participants

In the present prospective observational research, 959 people were recruited and followed up for more than 1 year, from March 2020 to May 2024, at Zhejiang Provincial People's Hospital (Zhejiang, China). Excluded participants comprised those who had diabetes types other than T2DM (n = 51), lacked VFA data (n = 530), had a history of ASCVD (n = 40); or

failed to follow up (n = 22), leaving 316 for this analysis (Fig. 1). Zhejiang Provincial People's Hospital's Ethics Committee gave its blessing to the study, which followed all the rules laid down²⁶ in the Helsinki Declaration. All participants submitted a written declaration of informed consent (QT2023298).

Data collection

Data on general characteristics were collected using a standardized questionnaire during patient visits. Laboratory measurements were taken the next morning after an 8-hour nighttime fast (see Supplementary Methods for collection of laboratory indicators).⁶ Height, weight, WC, hip circumference, and blood pressure, were measured uniformly by specialist nurses (see Supplementary Methods for collection of anthropometric indicators). A bioelectrical impedance analyser (DUALSCAN HDS-2000, OMRON, Dalian, China) was used to quantify VFA and subcutaneous fat area [13], and a volume plethysmography device (BP-203RPEIII, OMRON, Dalian, China) was used to determine³¹ the brachial-ankle pulse wave velocity (baPWV). Pressure measurements for posterior tibial and brachial arteries were obtained with four cuffs placed around the arms and ankles. By measuring the distance between the patient's upper arm and ankle, depending on their height, time-phase analysis automatically calculated baPWV. The average of both sides of the body was subsequently used for assessment. Cardiovascular-related risk indices, namely¹² the atherogenic index of plasma (AIP),² low-density lipoprotein cholesterol/high-density lipoprotein cholesterol (LDL-C/HDL-C), triglyceride-glucose (TyG) index,² total cholesterol/high-density lipoprotein cholesterol (TC/HDL-C), and apolipoproteins B/apolipoproteins A1 (apoB/apoA1), were also analysed.

88

89 Definitions

90 Grouping was based on the percentage change in VFA (Δ VFA, %) as follows: VFA gain
91 (Δ VFA $\geq 10\%$, n = 90); VFA stability ($-10\% < \Delta$ VFA $< 10\%$, n = 94); mild VFA loss (-20%
92 $< \Delta$ VFA $\leq -10\%$, n = 41); moderate VFA loss ($-30\% < \Delta$ VFA $\leq -20\%$, n = 34); and excessive
93 VFA loss (Δ VFA $\leq -30\%$, n = 57). The World Health Organization criteria published in 1999
94 was used to identify T2DM [14] (see Supplementary Methods for diagnostic criteria).

95 ASCVD is a clinical condition within the cardiovascular system that results from
96 atherosclerosis [15] (see Supplementary Methods for the conditions).¹⁰ The Prediction for
97 ASCVD Risk in China (China-PAR) model [16], a customized CVR evaluation instrument for
98 Chinese people, was used to evaluate the²⁰ 10-year ASCVD risk. In this analysis, '10-year
99 ASCVD risk increase', which was chosen as the primary cardiovascular outcome, was defined
100 as a situation where⁷ the 10-year risk of ASCVD at the follow-up stage was equal to or exceeded
101 the 1% absolute threshold from baseline. Meanwhile, alterations in lipid markers,
102 cardiovascular - associated parameters, and vascular rigidity were selected as the secondary
103 cardiovascular outcomes.

104 The formulas used are shown in Supplementary Methods.

105

106 Statistical analysis

107 ¹ The Shapiro - Wilk method was employed to assess the normality of the data distribution.
108 After conducting the normality test, continuous parameters have been²⁷ presented as either the
109 average $\pm$ standard deviation or the median along with the inter-quartile range. Frequencies

show categorical parameters. Kruskal-Wallis rank sum test evaluated group variations, in addition to analysis of variance. To compare categorical parameters, the chi-squared test was used.

A Cox proportional-hazards regression evaluated potential relationships of VFA groups with the increased 10-year ASCVD risk. Every multivariate model included possible confounding variables. Receiver operating characteristic (ROC) curves were generated for subjects at increased 10-year ASCVD risk, and the areas beneath these ROC curves (AUC) were calculated. Restricted cubic splines (RCS) curve was used in this study in order to analyse the potential non-linear relationship between Δ VFA (%) and the 10-year increased risk of ASCVD, (knot=4, k2 was used as the reference point). Threshold effects was employed to explore the relationship and inflection points between Δ VFA (%) and the increased 10-year ASCVD risk.

Both R v3.6 (R Foundation for Statistical Computing, Vienna, Austria) and SPSS v25.0 (IBM Corp, NY, USA) processed all numerals. A statistically significant value of $P < 0.05$ was determined.

Results

Characteristics at the baseline of the study participant

Table 1 has a list of the general attributes of patients with T2DM grouped by VFA alterations. Of the 316 participants, 236 (74.7%) were male and 80 (25.3%) were female. After a minimum of 1 year and a maximum of 3.5 years of follow-up, 90 (28.5%) participants exhibited VFA gain, 94 (29.7%) exhibited stable VFA, and 132 (41.8%) showed VFA loss, with 41 (13.0%),

34 (9.8%), and 57 (18.0%) showing mild, moderate, and excessive VFA loss. All five VFA groups showed variations in LDL-C, TC, LDL-C/HDL-C, and UA (all $P < 0.05$) (Table 1).

Contrast of Δ VFA (%), Δ LAP (%), Δ BMI (%), Δ WC (%), Δ BRI (%), and Δ CVAI (%) for predicting ASCVD risk increase in patients with T2DM

Δ VFA (%), Δ LAP (%), Δ WC (%), Δ CVAI (%), Δ BRI (%), and Δ BMI (%) have different diagnostic efficacies predicting 10-year ASCVD risk increase. AUCs and ROC curves for these six indicators were shown in Fig. 2. The AUCs for Δ VFA (%), Δ LAP (%), Δ WC (%), Δ CVAI (%), Δ BRI (%), and Δ BMI (%) for predicting the 10-year increased risk of ASCVD in a population with T2DM were 0.585 (95%CI: 0.513-0.656), 0.480 (95%CI: 0.407-0.533), 0.522 (95%CI: 0.452-0.591), 0.535 (95%CI: 0.461-0.609), 0.522 (95%CI: 0.453-0.592), 0.559 (95%CI: 0.488-0.631), and statistically significant only for Δ VFA (%) ($P = 0.020$) (Fig.2).

Association between Δ VFA (%) and the CVR factors

The results indicated that Δ VFA (%) exhibited a robust correlation with lipid profiles in both univariate and multivariable regression analyses ($P < 0.05$) (Table 2). Additionally, throughout the follow-up period, Δ VFA (%) was independently linked to a rise in 10-year ASCVD risk (HR = 1.004, $P = 0.005$) (Table 2).

Associations between the groups of changes in VFA and the secondary cardiovascular outcomes in patients with T2DM

Using the Δ VFA groups, the association between secondary cardiovascular outcomes and VFA in individuals suffering from T2DM was further examined (Table 3). Table 4 displays the variations in patients' CVR indices by Δ VFA groups. Δ LDL-C, Δ TC, Δ HDL-C, Δ TyG, Δ non-HDL-C, Δ TC/HDL-C, Δ LDL/HDL-C, and Δ baPWV, along with Δ apoB/apoA-1, Δ AIP differed among the five Δ VFA groups (all $P < 0.05$) (Table 3). Significant differences were seen between the excessive VFA loss group and the VFA stability and VFA gain groups for Δ HDL-C, Δ TC, Δ LDL-C, Δ TyG, Δ non-HDL-C, Δ LDL/HDL-C, Δ TC/HDL-C, Δ AIP, and Δ apoB/apoA-1. Additionally, the least significant difference (LSD) multiple comparisons showed that the excessive VFA loss group's Δ baPWV was different from the VFA gain group's Δ baPWV (all $P < 0.05$) (Table 3).

β -values of Δ TC, Δ TyG, Δ TC/HDL-C, and Δ AIP in both the excessive and moderate VFA loss groups differed significantly from those in the VFA gain group, and differences in Δ TC and Δ TyG persisted even when hypertension, smoking, sex, age, drinking, Δ weight (%), Δ WC (%), hyperlipemia, antihypertensive drugs, antihyperlipidemic drugs, sodium-glucose cotransporter-2 inhibitor (SGLT2i) or glucagon-like peptide-1 receptor agonist (GLP-1 RA), and diabetes duration were adjusted. Only the excessive VFA loss group's β -values differed substantially from the VFA gain group's values for both Δ AIP and Δ TC/HDL-C (all $P < 0.05$, all $\beta < 0$, Table 4). In the excessive VFA loss group, the β -values for Δ HDL-C, Δ apoB/apoA-1, Δ LDL-C, Δ LDL-C/HDL-C, and Δ non-HDL-C varied from the VFA gain group's values, with $\beta > 0$ for Δ HDL-C and $\beta < 0$ for the other secondary cardiovascular outcomes, regardless of correction (all P for trend < 0.05 , all $P < 0.05$, Table 4). Notably, the β -values of Δ baPWV

for all the VFA loss groups varied from values of the VFA gain group before and after correction for confounders ($P < 0.05$, $\beta < 0$, P for trend < 0.05) (Table 4).

Link of VFA changes with rise in 10-year ASCVD risk

Table 5, Table 6 and Figure 3 demonstrate the correlation between the VFA alterations and the 10-year rise in ASCVD risk. The rise in 10-year risk of ASCVD was substantially linked to the Δ VFA (%) ($P < 0.05$, Table 5).

Of the 316 participants, 50 (62.50%) from the VFA gain group, 45 (52.33%) from the VFA stability group, 21 (60.00%) from the mild VFA loss group, 16 (55.17%) from the moderate VFA loss group, and 17 (34.69%) from the excessive VFA loss group showed a rise in ASCVD risk. The excessive VFA loss group showed lower unadjusted HR than the VFA gain group ($HR = 0.168$, 95% CI: 0.065 – 0.437, $P < 0.001$, Table 5). The HR of rise in ASCVD risk in the excessive VFA loss without correction was lower than that of the mild VFA loss group ($HR = 0.150$, 95% CI: 0.047 – 0.475, $P = 0.001$, Table 5). According to trend analysis, VFA reduction reduced the mentioned risk (all P for trend < 0.05 , Table 5).

Adjusted variables: sex, smoking, drinking, Δ weight, Δ WC, hypertension, hyperlipemia, antihypertensive drugs, antihyperlipidemic drugs, SGLT2i or GLP-1 RA and diabetes duration. In people having T2DM, the RCS curve suggested that the HR was < 1 at $< -14.79\%$ Δ VFA (%) (Fig. 3). In addition, using a two-stage linear regression model, the study found a nonlinear relationship between Δ VFA (%) and increased 10-year ASCVD risk with an insertion point of -14.82% after correcting for the confounders mentioned above (Table 6).

Discussion

This study discovered that excessive VFA loss was associated with improvements in the 10-year ASCVD risk, lipid indicators, cardiovascular-related indices, and baPWV in participants with T2DM. Notably, a decrease of over 14.82% in VFA was linked to a decline in the patient's 10-year risk of ASCVD. In addition, Δ VFA (%) was a better indicator of fluctuations in the increased 10-year ASCVD risk than Δ BMI (%), Δ LAP (%), Δ WC (%), Δ BRI (%), and Δ CVAI (%). These findings suggest that excess VFA loss (VFA reduction of more than 30%) significantly improves CVR in the target population.

Abnormal adipose tissue spreading, and not overall fat mass, better determines CVD risk [17]. While cohort studies investigating the link between visceral fat and CVR predominantly focus on the general population [5, 6], patients with T2DM exhibit major differences in body fat distribution compared to the healthy population, which may lead to differences in their CVR [18, 19]. In a former cohort analysis that explored the longitudinal connections between obesity metrics and the chance of cardiovascular complications among persons with T2DM, all of aforementioned obesity markers had been shown to be strongly correlated to a greater chance of cardiac events [20], but none of them could precisely depict the real volume of visceral tissue. Park et al. validated the application of BIA for quantifying visceral fat volume, demonstrating that VFA measured via the DUALSCAN HDS-2000 (bi-abdominal BIA) exhibits greater concordance with CT-derived VFA measurements [21]. Therefore, using VFA as determined by the DUALSCAN HDS-2000 equipment, this study investigated longitudinal estimations of visceral fat and cardiovascular health in patients with T2DM. The China-PAR model quantified the ASCVD risk over 10 years, which is individualised, intuitive, and applicable to the Chinese

217 population[16], whereas traditional lipid indices, TyG index,²¹ LDL-C/HDL-C, apoB/apoA-1,
218 TC/HDL-C, baPWV, and AIP, can predict CVR, but not as advantageously as³⁶ 10-year ASCVD
219 risk in this study. Therefore, the primary cardiovascular outcome was fluctuations in⁴⁰ the 10-
220 year risk of ASCVD, whereas secondary cardiovascular outcomes were fluctuations in
221 traditional lipid indices, TC/⁵HDL-C, apoB/apoA-1, TyG index, LDL-C/HDL-C, baPWV, and
222 AIP. However, the metabolic phenotype of Asian populations with lower BMI but relatively
223 higher intrinsic adiposity [22], and the China-PAR based on the Chinese population in this
224 study, have limitations for the extension of this study to non-Asian populations. The future
225 study plan to collaborate between teams with data from different ethnic cohorts.

226 This study first found that excessive VFA loss was related to improvement among lipid
227 indicators and cardiovascular-related indices. The observed associations maintained their
228 statistical significance even when accounting for drinking, sex, antihypertensive drugs,
229 hyperlipemia, age, smoking, hypertension, antihyperlipidemic drugs, SGLT2i or GLP-1 RA,
230 and diabetes duration. Visceral obesity is commonly linked to raised⁹ LDL-C, TC, and non-
231 HDL-C levels, while reduced HDL-C levels, all of which contribute to a high CVR [23].
232 According to a cohort research, Japanese men's elevated visceral fat may interfere with their
233³⁸ TG and HDL-C levels [24]. According to the research, patients with excessive VFA loss had
234 considerably lesser² LDL-C, non-HDL-C, and TC levels and higher HDL-C levels, which may
235 help avert CVD. Nonetheless, these findings did not indicate a significant connection between
236 TG levels and visceral fat. This lack of correlation might be linked to the patients' dietary
237 makeup [25]. Moreover, this study found that excessive reduction of VFA improved
238 cardiovascular-related indices,³⁴ such as TC/HDL-C together with LDL-C/HDL-C [26, 27],

which is likely attributed to improved LDL-C and TC levels. A prospective study showed that changes in BMI in the general population could mediate CVR by altering the TyG index [28]. This study found that a decrease in VFA levels improved the TyG index in patients with T2DM. Previous cross-sectional studies found that both AIP and apoB/apoA-1 are significantly associated with obesity and CVR [29, 30]. In this study, excess VFA loss was found to increase AIP and apoB/apoA-1 levels in patients with T2DM, which may reduce CVR. Furthermore, even though this study did not detect a relationship between variations in VFA and alterations in the TG/HDL-C among patients with T2DM, certain research has indicated that this parameter was markedly linked to atherosclerosis in individuals with pre-diabetes [31], so this indicator should also be paid attention to.

Atherosclerosis progression can lead to ASCVD, and its severity can be monitored through baPWV [32]. BaPWV is a prognostic indicator of acute coronary syndrome and a risk marker for CVD [33]. VFA is a distinct risk indicator underlying atherosclerosis in persons having T2DM, according to multiple cross-sectional studies [34-36]. Heightened amounts of visceral fat promote insulin insensitivity and increase the levels of free fatty acids in the bloodstream. This, in turn, results in disruptions to lipid metabolism and the development of atherosclerosis [37]. The findings of this research indicated that baPWV was significantly lower in patients with reduced VFA compared to patients with increased VFA, which may be due to the improved mechanisms described above. A research project that gauged atherosclerotic rigidity via baPWV grouped participants according to the ratio of skeletal muscle mass to VFA (SVR) [38]. It discovered that a reduced SVR, meaning an elevated skeletal muscle mass and/or decreased VFA, was independently linked to heightened arterial stiffness among patients

261 diagnosed with ³T2DM, which was consistent with the findings of this study. Thus, patients
262 having T2DM may improve vascular stiffness and thereby reduce CVR by reducing VFA.

263 Lowering ASCVD risk is a primary goal of T2DM clinical management. Abdominal fat
264 buildup and central obesity have been more significantly linked to cardiometabolic risk factors
265 than total obesity, reported by a meta-analysis comprising 72 prospective investigations [39],
266 leading to increased interest in addressing visceral fat deposition in T2DM management. The
267 adverse effects of surplus visceral fat buildup in cardiovascular disease could potentially be
268 linked to abnormal inflammatory activation [40], vascular endothelial dysfunction[17],
269 vascular smooth muscle dysfunction [41], oxidative stress [42], and other visceral tissue-
270 induced mechanisms. Recent research has examined the long-term link between quantified
271 visceral adiposity and CVR, finding a strong correlation between increased visceral adiposity
272 and elevated CVR [43-45]. Furthermore, T2DM contributes to the increased risk of ASCVD
273 through factors such as disorders of glucose and lipid metabolism and genetic predisposition
274 [46]. This study quantified visceral fat in patients suffering from T2DM and individualised the
275 risk of ASCVD over a decade using the China-PAR assessment tool [16]. The outcomes of this
276 study indicated that a decrease in VFA exceeding 14.82% was strongly linked to a decline in
277 the aforementioned risk. A recent multidisciplinary study integrating genetics, lipids, and
278 glucose revealed that familial hypercholesterolemia patients with non-LDL receptor mutations
279 exhibit impaired glucose metabolism, suggesting that multidimensional metabolomics
280 enhances high-risk individual identification [47]. Future research will analyse metabolomics
281 associations with cardiovascular risk variations in patients suffering from T2DM across
282 different VFA changes.

Visceral fat, deposited around internal organs, can be predicted via anthropometric measures and obesity indices. While BMI and WC are common, they do not distinguish visceral from subcutaneous fat [4, 48]. Biomarkers like LAP, CVAI, and BRI, based on WC and lipid metrics [49-51], often overlook fat in metabolically healthy obesity(MUO) ($\text{BMI} \geq 30 \text{ kg/m}^2$, accompanied by abnormal blood pressure, glucose or lipid metabolism [52]) population and still fall short of separating subcutaneous from visceral fat. This study found that longitudinal changes in VFA in patients with T2DM had the highest predictive value for 10-year ASCVD risk variations compared with other obesity indices. However, ASCVD is a complex multi-factor interaction of complex diseases, and a single indicator is very limited in predicting the change of 10-year ASCVD risk. VFA may be included in the prediction model in the future. This may be complementary to CVR assessment in patients with T2DM.

Lifestyle changes (e.g., dietary control and exercise interventions) [53-55], pharmacological treatments (e.g., SGLT2i and GLP-1 RA) [56, 57] and surgical procedures (e.g., bariatric surgery) [58] have demonstrated their efficacy in decreasing visceral fat and improving CVR factors. Although these confounders, such as smoking, alcohol consumption, SGLT2i, and GLP-1RA, were corrected for in the present study, it is indeed possible that there are other lifestyle or interventional information that were not collected and incorporated into the confounders, such as dietary habits, exercise intensity, and medication adherence. In the future, the impact of confounding factors may be reduced if the uniform management of patients can be enhanced. For instance, combined nutrition and rehabilitation units can offer guidance on patients' dietary choices and physical activities. Moreover, the application of more advanced medications can be employed to boost patients' compliance with their prescribed medication

regimens. Recent studies have shown that Inclisiran [59], a pioneering siRNA therapy targeting hepatic PCSK9 synthesis, Inclisiran administered subcutaneously every two years consistently lowers LDL-C, significantly improving adherence compared to daily oral administration or fortnightly injections. As this study is an observational cohort study and could not investigate the link between artificially controlled changes in visceral adiposity and CVR in patients suffering from T2DM. The enduring effects of lifestyle interventions, pharmacological treatments, combination interventions, and individual differences in visceral fat accumulation on the CVR in patients with T2DM remain to be further explored.

3 Strengths and Limitations

The research being conducted has several strengths. First, this prospective cohort study can effectively explain the longitudinal association of quantified visceral adiposity with CVR in patients with T2DM. Second, to make sure these findings were reliable, the study corrected the results for possible confounders. This study does have certain drawbacks, though. First, it used neither CT nor MRI to quantify visceral fat, resulting in an inaccurate reflection of its quantity and quality. Therefore, the VFA in this study may be subject to measurement bias. Second, because of the limited follow-up period, this study could not analyse the relationship between VFA changes and cardiovascular endpoint events. However, the follow-up study will further extend the follow-up time to explore the relationship between the two mentioned above, as well as the prospective validation of the optimal thresholds and cardiovascular endpoint events in this study. Third, the investigation of causal relationships between VFA and CVR in people having T2DM is constrained by this research's observational character. Fourth, residual

327 confounding as well as selection bias could persist even after multivariate models account for
328 possible risk factors. Last but not least, further verification is required to determine if these
329 results are applicable to other populations. This is because the China - PAR assessment tool is
330 specific to the Chinese population.

331 **Conclusion**

332 To conclude, this prospective cohort study suggested that excessive VFA reduction in
333 patients with T2DM could result in cardiovascular benefits. In addition, quantified VFA may
334 better predict CVR changes in patients with T2DM than abdominal obesity markers. Therefore,
335 dynamic follow-up of VFA in patients with T2DM is needed for early detection of trends in
336 CVR in this population and early initiation of protective interventions. Future studies should
337 validate the benefit of cardiovascular endpoint events in patients suffering from and the
338 consistency of the benefit of VFA reduction in this study population with other populations.

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Table 1 The baseline characteristics of the study participants (N=316) according to the change groups of visceral fat area

Characteristic	VFA gain (N=90)	VFA stability (N=94)	VFA loss (N=132)			P-value
			Mild VFA loss (N=41)	Moderate VFA loss (N=34)	Excessive VFA loss (N=57)	
Demographic variables						
Age, year	50.00 (42.00, 60.00)	52.00 (43.50, 61.00)	52.00 (38.00, 58.00)	48.00 (40.25, 52.50)	48.00 (38.00, 57.00)	0.204
Males	65 (72.22)	70 (74.47)	29 (70.73)	26 (76.47)	46 (80.70)	0.776
Diabetes duration, month	34.50 (3.25,122.75)	60.00 (2.00,133.50)	54.50 (13.75,122.00)	53.00 (2.50,94.50)	1.00 (0.00,65.00)	0.011
Hypertension	31 (34.44)	38 (40.43)	20 (48.78)	13 (38.24)	13 (22.81)	0.634
Hyperlipemia	28 (31.11)	40 (42.55)	16 (39.02)	15 (44.12)	19 (33.33)	0.449
Antihypertensive drugs	25 (27.78)	28 (29.79)	13 (31.71)	9 (26.47)	11 (19.30)	0.634
Antihyperlipidemic drugs	12 (13.33)	17 (18.09)	6 (14.63)	3 (8.82)	5 (8.77)	0.487
SGLT2i or GLP-1 RA	26 (28.89)	35 (37.23)	20 (48.78)	15 (44.12)	18 (31.58)	0.172
Smoking						0.672
Never	47 (52.22)	48 (51.06)	24 (58.54)	13 (38.24)	33 (57.89)	
Ever	9 (10.00)	14 (14.89)	6 (14.63)	6 (17.65)	6 (10.53)	
Current	34 (37.78)	32 (34.04)	11 (26.83)	15 (44.12)	18 (31.58)	
Drinking						0.925
Never	49 (54.44)	42 (44.68)	21 (51.22)	17 (50.00)	29 (50.88)	
Ever	29 (32.22)	39 (41.49)	13 (31.71)	12 (35.29)	22 (38.60)	
Current	12 (13.33)	13 (13.83)	7 (17.07)	5 (14.71)	6 (10.53)	
Weight, kg	68.53 (59.14,75.72)	69.12 (62.38,80.72)	66.70 (61.65,79.00)	73.97 (66.15,79.68)	68.70 (60.00,74.00)	0.250
BMI, kg/m ²	24.24 (21.80,26.07)	24.87 (22.35,27.61)	23.88 (22.05,28.40)	25.55 (23.36,27.58)	23.64 (22.16,25.86)	0.193
WC, cm	90.00 (84.00, 98.00)	91.60 (86.25, 100.00)	92.00 (85.00, 101.00)	91.00 (87.25, 97.75)	90.60 (83.00, 98.00)	0.549
HC, cm	95.00 (91.00, 100.75)	98.00 (93.00, 103.00)	97.00 (93.00, 102.00)	96.00 (94.00, 100.00)	95.40 (92.00, 100.00)	0.313
SFA, cm ²	164.00 (123.00, 201.75)	178.90 (144.85, 217.75)	161.00 (137.00, 218.00)	181.10 (144.35, 222.00)	149.80 (121.00, 202.00)	0.076

Table 1 (continued)

Characteristic	VFA gain (N=90)	VFA stability (N=94)	VFA loss (N=132)			P-value
			Mild VFA loss (N=41)	Moderate VFA loss (N=34)	Excessive VFA loss (N=57)	
SBP, mmHg	124.00 (117.25, 135.75)	130.00 (118.50, 144.00)	128.00 (121.00, 137.00)	125.50 (120.50, 139.25)	126.00 (115.00, 139.00)	0.266
DBP, mmHg	79.00 (71.00, 85.00)	80.00 (73.00, 86.00)	80.00 (73.00, 87.00)	79.00 (75.00, 86.75)	76.00 (70.00, 86.00)	0.515
Laboratory variables						
HbA _{1c} , %	8.75 (6.70, 11.52)	8.70 (7.00, 10.50)	8.40 (7.30, 10.80)	7.75 (6.60, 10.33)	8.50 (7.00, 10.70)	0.703
FBG, mmol/L	6.02 (5.12, 7.44)	6.60 (5.53, 7.84)	6.75 (5.17, 7.81)	6.57 (4.95, 8.31)	6.48 (5.30, 7.76)	0.425
2h-PBG, mmol/L	14.12 (9.30, 17.70)	14.80 (10.71, 17.53)	14.59 (11.89, 18.10)	15.40 (11.11, 17.91)	15.58 (10.93, 18.90)	0.790
F-INS, μ IU/mL	3.66 (1.64, 8.23)	6.10 (2.37, 11.62)	6.35 (2.04, 10.07)	6.27 (3.14, 10.50)	5.36 (2.38, 9.83)	0.332
2h-PINS, μ IU/mL	22.99 (10.25, 46.76)	30.94 (15.76, 54.44)	29.63 (21.61, 44.25)	28.70 (16.03, 59.37)	24.95 (19.40, 44.12)	0.323
FCP, ng/mL	1.38 (0.77, 2.00)	1.71 (0.94, 2.67)	1.74 (0.88, 2.29)	2.00 (1.21, 2.64)	1.56 (0.99, 2.36)	0.117
2h-PCP, ng/mL	4.83 (3.15, 6.99)	5.38 (3.13, 7.48)	5.63 (4.16, 7.32)	4.96 (3.14, 8.04)	5.21 (3.83, 7.04)	0.636
TG, mmol/L	1.33 (0.96, 1.95)	1.51 (1.03, 2.51)	1.82 (1.26, 2.47)	1.60 (0.87, 2.66)	1.61 (0.91, 2.03)	0.177
TC, mmol/L	4.32 (3.84, 5.07) ^{de}	4.64 (3.95, 5.57) ^d	4.91 (3.90, 5.43) ^d	5.00 (4.51, 5.90) ^{abc}	5.20 (4.41, 5.79) ^a	0.001
HDL-C, mmol/L	1.02 (0.87, 1.21)	1.03 (0.90, 1.21)	1.03 (0.88, 1.16)	1.06 (0.87, 1.25)	1.02 (0.89, 1.25)	0.907
LDL-C, mg/dL	2.50 (1.95, 3.02) ^{de}	2.68 (2.18, 3.33) ^e	2.76 (2.07, 3.37) ^e	2.81 (2.40, 3.52) ^a	3.26 (2.67, 3.60) ^{abc}	<0.001
non-HDL-C, mmol/L	3.26 (2.73, 3.98)	3.39 (2.77, 4.22)	3.59 (3.03, 4.27)	3.65 (3.06, 4.23)	4.01 (2.92, 4.54)	0.114
apoA-1, g/L	1.19 (1.06, 1.38)	1.21 (1.11, 1.41)	1.22 (1.14, 1.36)	1.20 (1.08, 1.40)	1.24 (1.15, 1.44)	0.865
apoB, g/L	0.81 $\pm$ 0.22	0.84 $\pm$ 0.21	0.87 $\pm$ 0.26	0.86 $\pm$ 0.29	0.94 $\pm$ 0.28	0.060
eGFR, ml/min/1.73m ²	97.47 (89.18, 112.74)	99.45 (88.92, 108.43)	105.03 (87.51, 117.17)	98.02 (90.26, 111.84)	96.20 (83.59, 107.05)	0.477
Scr, μ mol/L	76.70 (63.83, 88.70)	79.00 (66.30, 86.00)	71.70 (55.90, 85.70)	78.45 (69.80, 86.65)	80.30 (71.70, 86.00)	0.506
UA, μ mol/L	322.50 (258.25, 362.25) ^{bc}	353.00 (304.00, 407.00) ^a	330.00 (300.00, 405.00) ^a	350.00 (304.25, 396.00)	314.00 (285.00, 399.00)	0.029
ALT, IU/L	23.00 (17.00, 33.00)	25.00 (16.00, 37.00)	29.00 (16.00, 37.50)	35.00 (22.00, 48.25)	24.50 (16.75, 36.50)	0.105
AST, IU/L	21.00 (17.75, 29.25)	22.00 (18.00, 30.50)	23.00 (18.00, 27.00)	27.00 (20.00, 32.00)	21.00 (17.00, 29.00)	0.452

Table 1 (continued)

Characteristic	VFA gain (N=90)	VFA stability (N=94)	VFA loss (N=132)			P-value
			Mild VFA loss (N=41)	Moderate VFA loss (N=34)	Excessive VFA loss (N=57)	
Comparison of CVR						
TyG	4.81 (4.51, 4.95)	4.83 (4.59, 5.14)	4.93 (4.72, 5.12)	4.87 (4.55, 5.22)	4.90 (4.57, 5.00)	0.167
TG/HDL-C	1.40 (0.85, 2.06)	1.60 (0.87, 2.62)	1.93 (1.04, 2.86)	1.52 (0.90, 2.88)	1.53 (0.89, 2.21)	0.330
TC/HDL-C	4.15 (3.28, 5.30)	4.57 (3.67, 5.37)	4.49 (3.70, 5.46)	4.58 (3.85, 6.09)	4.92 (3.96, 5.89)	0.124
LDL-C/HDL-C	2.47 (1.79, 3.23) ^e	2.59 (2.02, 3.13) ^e	2.64 (2.05, 3.21) ^e	2.73 (2.14, 3.50)	3.12 (2.58, 3.62) ^{abc}	0.013
apoB/apoA-1	0.65 (0.49, 0.83)	0.66 (0.55, 0.78)	0.68 (0.54, 0.87)	0.63 (0.50, 0.94)	0.78 (0.64, 0.93)	0.198
AIP	0.34 (0.12, 0.50)	0.39 (0.12, 0.61)	0.47 (0.21, 0.65)	0.37 (0.14, 0.65)	0.37 (0.14, 0.53)	0.339
baPWV, cm/s	1469.75 (1316.50, 1648.00)	1480.00 (1349.75, 1716.25)	1487.00 (1361.50, 1723.50)	1543.50 (1357.38, 1642.50)	1450.50 (1271.50, 1570.50)	0.384
10-year ASCVD risk, %	4.70 (2.15, 8.70)	5.95 (2.80, 9.32)	5.30 (1.95, 8.10)	4.10 (2.30, 5.00)	3.90 (1.60, 6.40)	0.061

Abbreviations: VFA, visceral fat area; SGLT2i, sodium-glucose cotransporter-2 inhibitor; GLP-1 RA, glucagon-like peptide-1 receptor agonist; BMI, body mass index; WC, waist circumference; HC, hip circumference; SFA, subcutaneous fat area; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA_{1c}, glycosylated hemoglobin A_{1c}; FBG, fasting blood glucose; 2h-PBG, 2h postprandial blood-glucose; F-INS, fasting serum insulin; 2h-PINS, 2h postprandial serum insulin; FCP, fasting C-peptide; 2h-PCP, 2h postprandial C-peptide; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; non-HDL-C, non-high-density lipoprotein cholesterol; apoA-1, apolipoproteins A-1; apoB, apolipoproteins B; eGFR, estimated glomerular filtration rate; Scr, serum creatinine; UA, uric acid; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TyG, triglyceride-glucose index; AIP, atherogenic index of plasma; baPWV, brachial-ankle pulse wave velocity; ASCVD, atherosclerotic cardiovascular diseases.

After intergroup comparisons, ^a $P < 0.05$ was considered significantly different from VFA gain; ^b $P < 0.05$ was considered significantly different from VFA stability; ^c $P < 0.05$ was considered significantly different from mild VFA loss; ^d $P < 0.05$ was considered significantly different from moderate VFA loss; ^e $P < 0.05$ was considered significantly different from excessive VFA loss.

Table 2 The association between Δ VFA (%) and CVR factors in patients with T2DM

	unadjusted		adjusted	
	β or HR (95% CI)	P-value	β or HR (95% CI)	P-value
Δ SBP	0.411 (-0.262, 1.083)	0.231		
Δ DBP	0.248 (-0.187, 0.683)	0.263		
Δ FBG	0.730 (-1.321, 2.780)	0.484		
Δ 2h-PBG	1.179 (-0.044, 2.402)	0.059		
Δ HbA _{1c}	-1.422 (-3.988, 1.144)	0.276		
Δ TC	7.311 (2.475, 12.148)	0.003	7.486 (2.636, 12.335)	0.003
Δ TG	0.619 (-1.652, 2.890)	0.592		
Δ HDL-C	-51.657 (-86.846, -16.468)	0.004	-55.386 (-91.484, -19.287)	0.003
Δ LDL-C	12.470 (5.679, 19.262)	<0.001	12.220 (5.303, 19.138)	<0.001
Δ non-HDL-C	6.974 (1.956, 11.993)	0.007	6.207 (1.033, 11.381)	0.019
Δ eGFR	-0.445 (-0.936, -0.045)	0.076		
Δ TyG	16.960 (0.506, 33.414)	0.044	17.054 (0.438, 33.670)	0.045
Δ TG/HDL-C	0.346 (-1.183, 1.875)	0.658		
Δ TC/HDL-C	6.345 (2.452, 10.237)	0.002	6.948 (3.006, 10.890)	<0.001
Δ LDL-C/HDL-C	13.941 (7.313, 20.570)	<0.001	13.958 (7.208, 20.708)	<0.001
Δ apoB/apoA-1	29.284 (4.184, 54.384)	0.023	27.803 (2.417, 53.190)	0.033
Δ AIP	32.383 (9.420, 55.346)	0.006	34.053 (10.974, 57.131)	0.004
Δ baPWV	0.043 (0.007, 0.078)	0.020	0.041 (0.006, 0.077)	0.024
10-year ASCVD risk increase	1.003 (1.001, 1.006)	0.003	1.004 (1.001, 1.006)	0.005

HR: hazard ratio; CI: confidence interval.

Adjusted for age, sex, smoking, drinking, UA, antihypertensive drugs, antihyperlipidemic drugs, SGLT2i or GLP-1 RA and diabetes duration.

Table 3 The association between the different changes of VFA and CVR factors in patients with T2DM

	VFA gain (N=90)	VFA stability (N=94)	VFA loss (N=132)			P-value
			Mild VFA loss (N=41)	Moderate VFA loss (N=34)	Excessive VFA loss (N=57)	
Primary cardiovascular outcome						
percent of 10-year ASCVD risk increase	31 (38.75) ^e	24 (27.91) ^e	12 (34.29) ^e	10 (34.38) ^e	5 (10.20) ^{abcd}	0.012
Secondary cardiovascular outcomes						
ΔTC	-0.26 (-1.00, 0.33) ^{de}	-0.25 (-1.14, 0.36) ^{de}	-0.41 (-1.09, 0.24) ^{de}	-0.59 (-1.99, -0.14) ^{abc}	-0.88 (-1.65, -0.23) ^{abc}	0.009
ΔHDL-C	0.02 (-0.06, 0.16) ^e	0.06 (-0.06, 0.13) ^e	0.06 (-0.04, 0.09) ^e	0.10 (-0.06, 0.18) ^e	0.15 (0.05, 0.32) ^{abcd}	<0.001
ΔLDL-C	-0.21 (-0.67, 0.30) ^e	-0.31 (-1.00, 0.22) ^e	-0.08 (-0.92, 0.38) ^e	-0.48 (-1.17, 0.31)	-0.94 (-1.60, -0.36) ^{abc}	0.002
Δnon-HDL-C	-0.18 (-0.92, 0.47) ^e	-0.10 (-1.03, 0.34) ^e	-0.35 (-1.12, 0.56) ^e	-0.33 (-1.21, 0.46)	-0.94 (-1.88, -0.18) ^{abc}	0.008
ΔTyG	0.03 (-0.25, 0.26) ^{de}	0.02 (-0.20, 0.20) ^{de}	-0.14 (-0.29, 0.12)	-0.06 (-0.34, 0.05) ^{ab}	-0.15 (-0.40, 0.03) ^{ab}	0.016
ΔTC/HDL-C	-0.39 (-1.29, 0.30) ^{de}	-0.44 (-1.19, 0.17) ^{de}	-0.44 (-1.45, 0.04) ^e	-0.78 (-1.91, -0.06) ^{ab}	-1.52 (-2.40, -0.78) ^{abc}	<0.001
ΔLDL-C/HDL-C	-0.35 ± 0.95 ^e	-0.46 ± 0.92 ^e	-0.39 ± 0.90 ^e	-0.56 ± 1.12 ^e	-1.22 ± 0.93 ^{abcd}	<0.001
ΔapoB/apoA-1	-0.02 ± 0.24 ^e	-0.07 ± 0.25 ^e	-0.02 ± 0.19 ^e	-0.05 ± 0.32 ^e	-0.25 ± 0.27 ^{abcd}	<0.001
ΔAIP	-0.05 ± 0.31 ^{de}	-0.04 ± 0.24 ^{de}	-0.12 ± 0.28	-0.17 ± 0.34 ^{ab}	-0.21 ± 0.25 ^{ab}	0.002
ΔbaPWV	36.25 (-58.50, 164.50) ^{cde}	38.50 (-106.50, 125.50)	-65.00 (-216.88, 28.12) ^a	-73.00 (-172.00, 70.50) ^a	-64.00 (-151.50, 60.00) ^a	<0.001

Data are presented as median (IQR), n (%), or mean ± SD.

After intergroup comparisons, ^a $P < 0.05$ was considered significantly different from VFA gain; ^b $P < 0.05$ was considered significantly different from VFA stability; ^c $P < 0.05$ was considered significantly different from mild VFA loss; ^d $P < 0.05$ was considered significantly different from moderate VFA loss; ^e $P < 0.05$ was considered significantly different from excessive VFA loss.

Table 4 The prospective associations between the changes of VFA and secondary cardiovascular outcomes in patients with T2DM

	Model 1		Model 2		Model 3	
	β (95% CI)	P-value	β (95% CI)	P-value	β (95% CI)	P-value
ΔTC						
VFA gain	Ref.		Ref.		Ref.	
VFA stability	0.04 (-0.36, 0.43)	0.861	0.07 (-0.36, 0.50)	0.742	0.05 (-0.39, 0.49)	0.823
Mild VFA loss	-0.06 (-0.56, 0.45)	0.822	-0.08 (-0.64, 0.47)	0.766	-0.11 (-0.68, 0.46)	0.699
Moderate VFA loss	-0.62 (-1.16, -0.09)	0.024	-0.71 (-1.30, -0.13)	0.017	-0.69 (-1.29, -0.10)	0.022
Excessive VFA loss	-0.56 (-1.01, -0.10)	0.017	-0.59 (-1.11, -0.06)	0.028	-0.56 (-1.09, -0.03)	0.040
P for trend	0.002		0.002		0.005	
ΔHDL-C						
VFA gain	Ref.		Ref.		Ref.	
VFA stability	0.00 (-0.05, 0.06)	0.895	0.00 (-0.06, 0.06)	0.915	0.01 (-0.05, 0.07)	0.781
Mild VFA loss	0.00 (-0.06, 0.07)	0.896	0.00 (-0.08, 0.07)	0.911	0.01 (-0.06, 0.09)	0.741
Moderate VFA loss	0.03 (-0.05, 0.10)	0.483	0.02 (-0.06, 0.10)	0.602	0.02 (-0.06, 0.10)	0.574
Excessive VFA loss	0.13 (0.07, 0.19)	<0.001	0.13 (0.06, 0.21)	<0.001	0.12 (0.05, 0.19)	<0.001
P for trend	<0.001		<0.001		0.002	
ΔLDL-C						
VFA gain	Ref.		Ref.		Ref.	
VFA stability	-0.15 (-0.44, 0.13)	0.293	-0.15 (-0.46, 0.15)	0.323	-0.15 (-0.46, 0.15)	0.328
Mild VFA loss	-0.03 (-0.39, 0.34)	0.887	-0.09 (-0.48, 0.31)	0.671	-0.07 (-0.47, 0.33)	0.731
Moderate VFA loss	-0.32 (-0.71, 0.07)	0.105	-0.37 (-0.78, 0.05)	0.084	-0.31 (-0.73, 0.11)	0.151
Excessive VFA loss	-0.65 (-0.98, -0.33)	<0.001	-0.73 (-1.10, -0.36)	<0.001	-0.68 (-1.06, -0.31)	<0.001
P for trend	<0.001		<0.001		<0.001	

Table 4 (continued)

	Model 1		Model 2		Model 3	
	$\beta(95\% CI)$	<i>P</i> -value	$\beta(95\% CI)$	<i>P</i> -value	$\beta(95\% CI)$	<i>P</i> -value
$\Delta LDL-C/HDL-C$						
VFA gain	Ref.		Ref.		Ref.	
VFA stability	-0.10 (-0.39, 0.18)	0.472	-0.10 (-0.40 ~ 0.21)	0.537	-0.11 (-0.41, 0.20)	0.492
Mild VFA loss	-0.04 (-0.40, 0.33)	0.846	-0.06 (-0.45 ~ 0.33)	0.764	-0.07 (-0.47, 0.33)	0.723
Moderate VFA loss	-0.21 (-0.60, 0.17)	0.284	-0.19 (-0.61 ~ 0.22)	0.359	-0.15 (-0.56, 0.27)	0.492
Excessive VFA loss	-0.86 (-1.19, -0.54)	<0.001	-0.92 (-1.28 ~ -0.55)	<0.001	-0.86 (-1.23, -0.49)	<0.001
<i>P</i> for trend	<0.001		<0.001		<0.001	
$\Delta apoB/apoA-1$						
VFA gain	Ref.		Ref.		Ref.	
VFA stability	-0.05 (-0.13, 0.04)	0.275	-0.05 (-0.14 ~ 0.05)	0.325	-0.04 (-0.13, 0.06)	0.450
Mild VFA loss	0.00 (-0.11, 0.11)	0.999	-0.02 (-0.14 ~ 0.10)	0.736	-0.02 (-0.14, 0.10)	0.758
Moderate VFA loss	-0.02 (-0.14, 0.09)	0.691	-0.05 (-0.18 ~ 0.07)	0.408	-0.01 (-0.14, 0.11)	0.825
Excessive VFA loss	-0.23 (-0.33, -0.13)	<0.001	-0.27 (-0.38 ~ -0.16)	<0.001	-0.24 (-0.36, -0.13)	<0.001
<i>P</i> for trend	<0.001		<0.001		<0.001	
ΔAIP						
VFA gain	Ref.		Ref.		Ref.	
VFA stability	0.02 (-0.07, 0.10)	0.699	0.04 (-0.05 ~ 0.13)	0.420	0.03 (-0.06, 0.12)	0.518
Mild VFA loss	-0.06 (-0.17, 0.04)	0.242	-0.03 (-0.15 ~ 0.09)	0.622	-0.05 (-0.17, 0.07)	0.441
Moderate VFA loss	-0.12 (-0.23, -0.01)	0.038	-0.11 (-0.23 ~ 0.01)	0.079	-0.12 (-0.24, 0.01)	0.064
Excessive VFA loss	-0.16 (-0.25, -0.06)	0.001	-0.15 (-0.26 ~ -0.04)	0.008	-0.15 (-0.26, -0.03)	0.010
<i>P</i> for trend	<0.001		<0.001		0.001	

Table 4 (continued)

	Model 1		Model 2		Model 3	
	$\beta(95\% CI)$	<i>P</i> -value	$\beta(95\% CI)$	<i>P</i> -value	$\beta(95\% CI)$	<i>P</i> -value
$\Delta non-HDL-C$						
VFA gain	Ref.		Ref.		Ref.	
VFA stability	-0.15 (-0.57, 0.27)	0.485	-0.14 (-0.59, 0.30)	0.525	-0.10 (-0.55, 0.34)	0.649
Mild VFA loss	-0.17 (-0.70, 0.36)	0.541	-0.29 (-0.86, 0.28)	0.325	-0.19 (-0.78, 0.40)	0.523
Moderate VFA loss	-0.40 (-0.97, 0.17)	0.171	-0.58 (-1.19, 0.02)	0.061	-0.48 (-1.09, 0.13)	0.127
Excessive VFA loss	-0.83 (-1.32, -0.35)	<0.001	-0.96 (-1.50, -0.41)	<0.001	-0.87 (-1.43, -0.32)	0.002
<i>P</i> for trend	<0.001		<0.001		0.001	
ΔTyG						
VFA gain	Ref.		Ref.		Ref.	
VFA stability	0.00 (-0.12, 0.12)	0.990	0.03 (-0.09, 0.16)	0.611	0.02 (-0.11, 0.15)	0.764
Mild VFA loss	-0.06 (-0.21, 0.08)	0.392	-0.01 (-0.18, 0.15)	0.864	-0.02 (-0.19, 0.14)	0.785
Moderate VFA loss	-0.17 (-0.33, -0.01)	0.037	-0.15 (-0.32, 0.02)	0.087	-0.16 (-0.34, 0.01)	0.067
Excessive VFA loss	-0.17 (-0.31, -0.04)	0.012	-0.15 (-0.30, 0.01)	0.062	-0.14 (-0.30, 0.01)	0.077
<i>P</i> for trend	0.002		0.011		0.015	
$\Delta TC/HDL-C$						
VFA gain	Ref.		Ref.		Ref.	
VFA stability	0.13 (-0.36, 0.61)	0.614	0.17 (-0.36, 0.71)	0.521	0.12 (-0.42, 0.66)	0.663
Mild VFA loss	-0.06 (-0.69, 0.56)	0.844	-0.02 (-0.72, 0.67)	0.944	-0.14 (-0.85, 0.57)	0.706
Moderate VFA loss	-0.69 (-1.35, -0.03)	0.042	-0.71 (-1.43, 0.02)	0.057	-0.72 (-1.45, 0.01)	0.054
Excessive VFA loss	-0.88 (-1.44, -0.32)	0.002	-0.85 (-1.50, -0.20)	0.010	-0.79 (-1.45, -0.14)	0.018
<i>P</i> for trend	<0.001		0.001		0.002	

Table 4 (continued)

	Model 1		Model 2		Model 3	
	β(95% CI)	P-value	β(95% CI)	P-value	β(95% CI)	P-value
ΔbaPWV						
VFA gain	Ref.		Ref.		Ref.	
VFA stability	-63.19 (-127.02, 0.64)	0.053	-76.12 (-144.38, -7.86)	0.030	-74.67 (-143.47, -5.87)	0.034
Mild VFA loss	-162.09 (-239.67, -84.51)	<0.001	-170.14 (-255.34, -84.95)	<0.001	-182.64 (-270.06, -95.21)	<0.001
Moderate VFA loss	-124.62 (-207.73, -41.51)	0.004	-128.34 (-217.10, -39.58)	0.005	-131.52 (-221.77, -41.28)	0.005
Excessive VFA loss	-127.37 (-197.39, -57.35)	<0.001	-146.14 (-228.00, -64.28)	<0.001	-147.93 (-231.24, -64.62)	<0.001
P for trend	<0.001		<0.001		<0.001	

Model 1: unadjusted.

Model 2: adjusted for age, sex, smoking, drinking, Δ weight, Δ WC.

Model 3: model 2 plus adjustment for hypertension, hyperlipemia, antihypertensive drugs, antihyperlipidemic drugs, SGLT2i or GLP-1 RA and diabetes duration.

Table 5 The prospective associations between the changes of VFA and 10-year ASCVD risk increase in patients with T2DM

	Model 1		Model 2		Model 3	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
ΔVFA (%)	1.003 (1.001, 1.006)	0.003	1.003 (1.001, 1.006)	0.012	1.003 (1.001, 1.006)	0.011
VFA gain	Ref.		Ref.		Ref.	
VFA stability	0.645 (0.375, 1.109)	0.112	0.592 (0.332, 1.056)	0.076	0.592 (0.326, 1.075)	0.085
Mild VFA loss	0.979 (0.500, 1.914)	0.950	1.178 (0.568, 2.444)	0.660	1.003 (0.468, 2.147)	0.995
Moderate VFA loss	0.566 (0.274, 1.170)	0.125	0.687 (0.320, 1.474)	0.335	0.666 (0.305, 1.454)	0.308
Excessive VFA loss	0.168 (0.065, 0.437)	<0.001	0.154 (0.056, 0.425)	<0.001	0.142 (0.050, 0.405)	<0.001
P for trend	<0.001		0.003		0.001	
Mild VFA loss	Ref.		Ref.		Ref.	
Moderate VFA loss	0.535 (0.226, 1.264)	0.154	0.582 (0.222, 1.523)	0.270	0.400 (0.127, 1.263)	0.118
Excessive VFA loss	0.150 (0.047, 0.475)	0.001	0.089 (0.021, 0.374)	<0.001	0.133 (0.031, 0.576)	0.007
P for trend	<0.001		<0.001		0.004	

HR: hazard ratio; CI: confidence interval.

Model 1: unadjusted.

Model 2: adjusted for age, sex, smoking, drinking, Δ weight, Δ WC.

Model 3: model 2 plus adjustment for hypertension, hyperlipemia, antihypertensive drugs, antihyperlipidemic drugs, SGLT2i or GLP-1 RA and diabetes duration.

Table 6 Threshold effect analysis of the changes of VFA on 10-year ASCVD risk increase in patients with T2DM

	Adjusted HR (95% CI)	P-value
Inflection point	-14.82%	
Δ VFA (%) < -14.82%	1.067 (1.004, 1.133)	0.036
Δ VFA (%) $\geq$ -14.82%	1.002 (0.999, 1.006)	0.204
P for likelihood test		0.003

HR: hazard ratio; CI: confidence interval.

Age, sex, smoking, drinking, Δ weight, Δ WC, hypertension, hyperlipemia, antihypertensive drugs, antihyperlipidemic drugs, SGLT2i or GLP-1 RA and diabetes duration were adjusted.

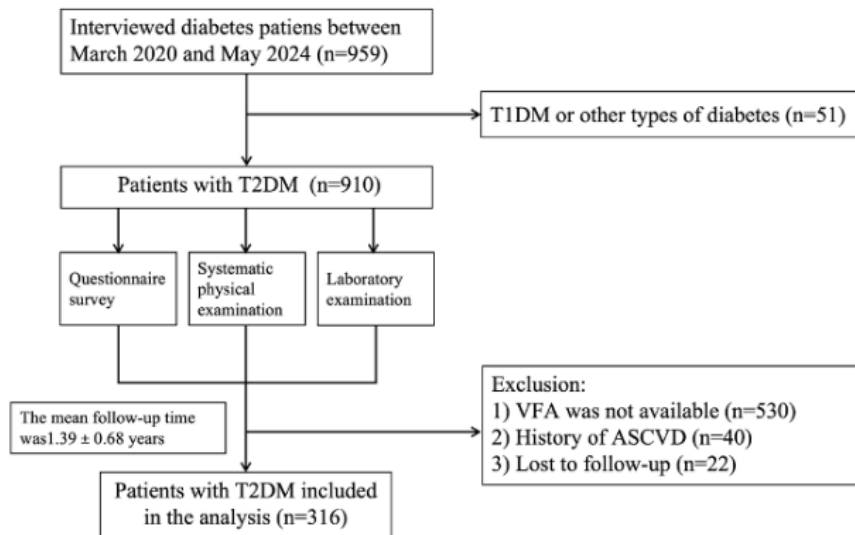
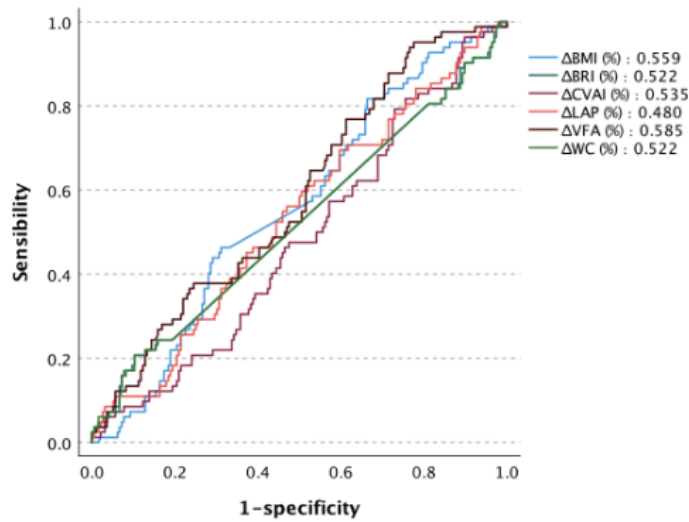


Fig. 1 Flow chart of patient recruitment. T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; VFA: visceral fat area; ASCVD, atherosclerotic cardiovascular diseases.



	AUC	95%CI	Youden Index	Sensibility	Specificity	P-value
ΔVFA (%)	0.585	0.513-0.656	0.176	0.951	0.224	0.020
ΔBMI (%)	0.559	0.488-0.631	0.154	0.817	0.337	0.103
ΔWC (%)	0.522	0.452-0.591	0.105	0.207	0.900	0.537
ΔBRI (%)	0.522	0.453-0.592	0.105	0.207	0.900	0.534
ΔCVAI (%)	0.535	0.461-0.609	0.098	0.695	0.403	0.352
ΔLAP (%)	0.480	0.407-0.553	0.065	0.963	0.102	0.587

Fig. 2 The calculation of AUCs for diagnosing 10-year ASCVD risk increase in patients with T2DM.

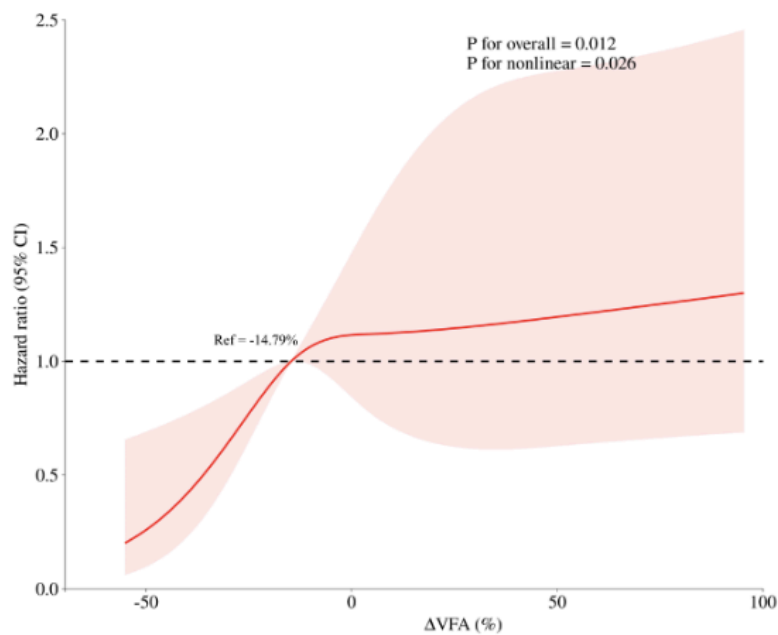


Fig. 3 The association between Δ VFA (%) and 10-year ASCVD risk increase in patients with T2DM. The result was adjusted by age, sex, smoking, drinking, Δ weight, Δ WC, hypertension, hyperlipemia, antihypertensive drugs, antihyperlipidemic drugs, SGLT2i or GLP-1 RA and diabetes duration.