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Anthropometric and metabolic parameters associated with visceral fat in non-obese type 2 diabetes individuals



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Abstract

Background and Aim Visceral fat (VF) was proved to be a more precise predictor of atherosclerotic cardiovascular disease (ASCVD) risk in individuals with type 2 diabetes mellitus (T2DM) than body mass index (BMI) itself. Even when the BMI was normal, visceral fat area (VFA) \geq 90 cm² could raise the ten-year risk of developing ASCVD. Therefore, it was worth evaluating the association of influencing factors with high VF in non-obese T2DM individuals.

Methods This study enrolled 1,409 T2DM participants with T2DM, of whom 538 had a normal BMI. Based on VFA, these subjects were divided into two groups: VF (+) (VFA \geq 90cm²) (n = 110) and VF (-) (VFA < 90cm²) (n = 428). The measurement of VFA was conducted using an Omron VF measuring device. Anthropometric and metabolic parameters were detected. Novel insulin resistance indices, such as lipid accumulation product (LAP) was calculated. Factors associated with VF were screened using univariate analysis, multifactorial binary logistic regression models and chi-squared automatic interaction detector decision tree model.

Results The VF (+) OB (-) (BMI \leq 23.9 kg/m²) prevalence were 7.8% in T2DM subjects (n = 1,409) and 20.4% in T2DM subjects with normal BMI (n = 538), respectively. In T2DM subjects with normal BMI, the logistic regression model suggested that neck circumference (NC) had an odds ratio (OR) of 1.891 (95% CI: 1.165–3.069, P = 0.010). The OR for VF gradually increased from the 1st to the 4th in LAP quartile (P < 0.05). LAP emerged as the root node, followed by NC in the decision tree model. Receiver operating characteristic curve (ROC) analysis demonstrated that the area under the curve (AUC) for NC in predicting high VF levels was 0.640 for males and 0.682 for females. Optimal NC cut-off points were 37.75 cm for males and 34.75 cm for females, respectively. Additionally, the AUC values of LAP in predicting high VF levels were 0.745 for males and 0.772 for females, with optimal LAP cut-off points of 22.64 and 26.45 for males and females, respectively.

Conclusion This study identified NC and LAP can be considered predictors of high VF in T2DM subjects with normal BMI.

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Introduction

The global prevalence of obesity and diabetes is increasing, with type 2 diabetes (T2DM) comprising 96.0% of all diabetes cases [1-3]. Cardiovascular disease (CVD) is the main cause of morbidity and mortality in T2DM subjects [4]. Obesity is closely related to the high risk of cardiovascular events in T2DM subjects. Furthermore, the distribution of adiposity in T2DM subjects becomes an important factor in determining CVD risk, in which the visceral fat (VF) accumulation significantly increasing the likelihood of CVD [5]. Asians with T2DM are characterized by central obesity, particularly excessive accumulation of VF [6]. Excessive VF accumulation has been implicated in the pathogenesis of insulin resistance and inflammation [7, 8]. Consequently, it is strongly associated with T2DM and its complications and comorbidities, including coronary artery disease (CAD), stroke, sleep apnea, hypertension, dyslipidemia, and certain types of cancer [9-13].

Traditionally, a high body mass index (BMI) has been identified as a significant risk factor for T2DM and atherosclerotic cardiovascular disease (ASCVD) [2, 14]. However, recent research has challenged this notion, suggesting that the "obesity paradox" may arise when using BMI to define obesity [15]. In 2013, Coutinho et al. found that among patients with coronary heart disease, individuals with normal BMI but central obesity exhibited a higher long-term mortality rate compared to those with other types of obesity (measured by combined BMI and central obesity indicators). Conversely, elevated BMI in the absence of central obesity did not adversely affect survival in patients with coronary artery disease [16]. A growing body of evidence supports the notion that the accumulation of VF poses a heightened risk of cardiovascular and metabolic complications, even in individuals with normal BMI. Moreover, T2DM subjects typically have higher levels of VF compared to non-diabetic individuals with similar BMI, which may increase their risk of CVD. Given that BMI cannot differentiate between body fat distribution, the accumulation of VF can serve as a more reliable indicator for predicting cardiovascular mortality in T2DM subjects [5, 17, 18]. In 2015, Bouchi R et al. confirmed that T2DM subjects with increased VF and normal weight [VF(+) OB (-)] faced similar risks of arterial stiffness progression as those with VF (+) OB (+) in a Japanese population [19]. A more recent study involving 8,839 Chinese T2DM subjects revealed that increased VF emerged as an independent risk factor for arterial stiffness in individuals with normal BMI, thereby elevating their risk of atherosclerosis [20]. Furthermore, a 2023 study conducted on 16,460 adults in China demonstrated that VF is a more accurate predictor of ASCVD risk in T2DM subjects than BMI itself. Even with a normal BMI, high VF can increase the ten-year risk of developing ASCVD [21]. Therefore, it is imperative to pay closer attention to T2DM individuals with VF (+) OB (-) [visceral fat area (VFA) \ge 90cm², BMI \le 23.9 kg/



Fig. 1 Graphical Depiction of Research Workflow

m²] as they may be at increased risk for cardiovascular complications.

Given the strong correlation between VF accumulation and ASCVD risk, VFA \ge 90 cm² was used as a high VF threshold [21]. Traditional methods for measuring VF, such as computed tomography (CT) scans and dual bioelectrical impedance analysis (BIA) measurements [22], were often costly, radiation exposure involved, and other limitations included. Some studies have demonstrated an association between indicators of VF replacement and VF in individuals without diabetes [23, 24]. This study aimed to develop a rapid and accessible supplementary method for evaluating VF in T2DM subjects with limited access to specialized facilities.

Materials and methods

Study population

A total of 2,235 subjects enrolled in the National Metabolic Management Center (MMC) at the Affiliated Hospital of Yunnan University between January 2020 and December 2023 were included in this study. The diagnosis of diabetes mellitus was based on the 2020 American Diabetes Association (ADA) guidelines [25]. Subjects were excluded if they met the criteria outlined in Fig. 1. Ultimately, this study enrolled 1,409 T2DM participants with T2DM, of whom 538 had a normal BMI. Based on VFA, these subjects were divided into two groups: VF (+) (VFA \ge 90cm²) (*n* = 110) and VF (-) (VFA < 90cm²) (n = 428). The subjects were unrelated individuals residing in Yunnan Province, China. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki for clinical research and was approved by the Ethics Committee of the Affiliated Hospital of Yunnan University (No.2020038). Written informed consent was obtained from all subjects.

Research methods

Data collection

A dedicated nurse from MMC collects the subject's general characteristics data on the day of the visit using the same questionnaire, which covers the subject's general information, anthropometric parameters (such as neck circumference, waist circumference, hip circumference, etc.), as well as past medical history. VFA was obtained using an Omron visceral fat measuring device (DUALS-CAN HDS-2000) [22, 26]. Venous blood samples were collected in the morning after an 8-hour fasting period. All laboratory parameters (biochemical and diabetesrelated indicators) were measured using standard methods used by the hospital.

Definitions

Previous studies [27, 28] have reported that the optimal NC cut-off points for diagnosing metabolic syndrome

and obesity are 38 cm in men and 35 cm in women. In China, according to the guidelines [29] recommends the following diagnostic criteria for adults: overweight (24.0 kg/m² \leq BMI < 28.0 kg/m²) and obesity $(BMI \ge 28.0 \text{ kg/m}^2)$. To evaluate the centrality of obesity, the waist-to-hip ratio (WHR) is used, with thresholds of \geq 0.90 for obese males and \geq 0.85 for obese females. Adult central obesity is diagnosed using a WC \geq 90.0 cm for men and ≥ 85.0 cm for women [30]. According to current European and global guidelines [31–33], hypertension is defined as an SBP \geq 140mmHg and/or a DBP \geq 90mmHg based on three non-simultaneous in-office blood pressure measurements taken without antihypertensive medication. According to previous studies [34-37], subjects were divided into groups based on their carotid intimamedia thickness (CIMT) and ankle-brachial index (ABI). The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula [38]. The DKD staging system [39], which utilizes the GA staging approach. G represents the estimated eGFR level (G1-G5), and A represents the albuminuria level (A1-3). According to previous guidelines [40-42], the participants were classified based on their dyslipidemia, hyperuricemia, fasting plasma glucose, postprandial 2-hour plasma glucose, and glycated hemoglobin levels. See Additional file 2.

We calculated traditional insulin resistance indices, such as the homeostasis model assessment for insulin resistance (HOMA-IR) [43], and novel insulin resistance indices, such as lipid accumulation product (LAP) [44], visceral fat index (VAI) [45], and triglyceride glucose index (TyG) [46]. LAP was calculated from waist circumference (WC) in cm and triglyceride (TG) in mmol/L using the following formulae: LAP for female=(WC-58) ×TG; LAP for male=(WC-65) ×TG. Moreover, the homeostasis model assessment β cell function (HOMA- β) was also assessed [47].

Statistical analyses

Statistical analysis of data was conducted using SPSS 25.0 software and Prism (GraphPad, version 9.0). Initially, normality and homogeneity of variance tests were performed. Measurement data that conformed to normal distribution were expressed as mean \pm standard deviation. For comparisons between the two groups, a *t*-test was used. For comparisons between three groups, a one-way ANOVA was employed, followed by multiple LSD comparisons. Measurement data that did not follow a normal distribution were represented by median (M) and interquartile range (P₂₅, P₇₅). Non-parametric tests were used for comparisons between groups: the Mann-Whitney U test for two groups and the Kruskal-Wallis H test with Bonferroni multiple comparisons for multiple groups. Categorical data were expressed as percentages (%) and

compared between groups using the chi-squared test. For quantitative data that met the normal distribution, Pearson correlation analysis was used. Spearman correlation analysis was employed for skewed quantitative data. Factors related to VF in T2DM were selected using a single-factor analysis (P < 0.05), and a multivariable logistic regression model was applied using the forward method. Additionally, a Chi-square automatic interaction detection decision tree model was utilized. The cross-validation significance level, split node significance level,

value of high VF occurrence. This study employed a cross-sectional design, and the sample size was calculated using PASS15 software. Based on previous studies, the prevalence of abdominal obesity in the Chinese region was 29.1% [48]. A specified tolerance error of 2.91%, a confidence level of $1-\alpha = 0.95$, and PASS15 software calculations resulted in a required sample size of N=975 cases. Considering a non-response rate of 10%, the sample size was adjusted to N=975/0.9=1,083 cases. Assuming a 90% pass rate for the questionnaire, the total required sample size was N=1,083/0.9=1,203 cases. Given these calculations, a sample size of 1,203 cases was deemed necessary. Therefore, including 1,409 subjects in this study was reasonable.

and combined category significance level were all set to

0.05. The tree growth depth was limited to 3 layers, and

the minimum number of cases for parent and child nodes

was set to 100 and 50, respectively. Finally, receiver oper-

ating characteristic (ROC) curves were generated based

on the risk factors identified through decision tree and

logistic regression analysis to evaluate the predictive

Results

Clinical characteristics of our study population

A total of 1,409 subjects with T2DM (males n=868, females n=541) aged 56 (49,64) years were included in the study. Table 1 shows the clinical characteristics of the participants according to VFA quartile. TG and TyG were higher in participants in quartiles 3 and 4 than in quartiles 1 and 2 (P<0.001). BMI, Waist and Hip increased with increasing VFA quartile (P<0.001). There were no significant differences in age, fasting glucose (Glu0), 2-hour postprandial glucose (Glu120), glycated hemoglobin (HbA1c), low-density lipoprotein (LDL-C) or urinary albumin to creatinine ratio (UACR) among the four quartiles (Table 1). Our analysis revealed that LAP increased with increasing VFA quartiles in both males and females (P<0.001). Additionally, NC increased with increasing VFA quartiles in females (P<0.001).

Variable	Q1(≤71.00) (<i>n</i> =359)	Q2(71.10–92.00) (n=358)	Q3(92.10-114.50) (n=340)	Q4(>114.50) (n=352)	Н	Р
Age (years)	55(49,63)	57(50,64)	56(49,64)	55(46,64)	3.197	0.362
BMI (kg/m ²)	22.30(20.50,23.80)	24.10(22.80,25.50) ^a	25.50(24.23,27.10) ^{ab}	27.80(26.00,30.18) ^{abc}	645.919	< 0.001
Waist (cm)	80.00(76.00,84.00)	87.00(83.00,90.00) ^a	91.00(87.00,95.00) ^{ab}	97.00(92.25,102.00) ^{abc}	690.231	< 0.001
Hip (cm)	88.50(85,92)	92(89,96) ^a	95(91,100) ^{ab}	100(95,103) ^{abc}	446.093	< 0.001
Glu0 (mmol/L)	7.02(5.53,9.70)	7.51(6.08,9.70)	7.76(6.25,9.99)	7.49(6.26,9.60)	6.085	0.108
Glu120 (mmol/L)	13.60(10.30,17.85)	13.69(11.20,17.68)	13.89(11.30,17.80)	13.60(10.40,17.80)	1.847	0.605
HbA1c (%)	9.90(7.24,12.10)	9.50(7.70,11.40)	9.40(7.70,11.20)	9.30(7.60,11.00)	4.183	0.242
TG (mmol/L)	1.21(0.87,1.89)	1.73(1.21,2.49) ^a	1.97(1.39,3.39) ^{ab}	2.15(1.46,3.14) ^{ab}	166.312	< 0.001
TC (mmol/L)	4.64(4.00,5.34)	4.68(4.02,5.39)	4.88(4.23,5.66) ^a	4.81(4.08,5.58)	11.512	0.009
HDL-C (mmol/L)	1.13(0.94,1.37)	0.98(0.85,1.15) ^a	0.97(0.83,1.13) ^a	0.92(0.81,1.08) ^{ab}	114.791	< 0.001
LDL-C (mmol/L)	2.69(2.16,3.25)	2.67(2.11,3.29)	2.77(2.11,3.37)	2.71(2.14,3.37)	1.157	0.763
eGFR (mL/min/ 1.73 m ²)	105.69(89.69,128.79)	103.66(87.09,122.47)	102.49(86.28,117.80) ^a	102.99(85.28,119.00) ^a	11.756	0.008
UACR (mg/g)	21.48(12.82,44.49)	20.55(12.89,43.77)	20.53(12.76,39.61)	21.46(13.23,49.52)	1.423	0.763
TyG	8.87(8.43,9.36)	9.24(8.80,9.77) ^a	9.45(8.93,10.09) ^{ab}	9.50(9.01,9.99) ^{ab}	124.544	< 0.001
HOMA-IR	2.41(1.28,4.54)	2.83(1.69,5.15) ^a	3.25(1.82,6.05) ^a	3.96(2.21,6.10) ^{ab}	51.193	< 0.001
ΗΟΜΑ-β	26.35(11.54,61.30)	39.51(20.49,78.80) ^a	38.81(19.69,77.10) ^a	51.99(28.83,95.60) ^{abc}	64.551	< 0.001
Male (<i>n</i> = 868)	Q1(≤73.15) (n=217)	Q2(73.25-95.00) (n=224)	Q3(95.10–118.00) (n=215)	Q4(>118.00) (n=212)		
LAP	20.40(11.66,34.32)	42.76(26.99,65.31) ^a	53.12(36.72,94.36) ^{ab}	75.03(45.20,118.66) ^{abc}	255.915	< 0.001
Neck circumference (cm)	37(36,38.55)	39(38,40) ^a	39(38,41) ^{ab}	41(40,43) ^{abc}	264.916	< 0.001
VAI	1.47(0.86,2.49)	2.44(1.58,4.01) ^a	2.82(1.94,5.29) ^a	3.30(1.93,5.43) ^{ab}	119.467	< 0.001
Female	Q1(≤69.00)	Q2(69.10-86.00)	Q3(86.10-108.80)	Q4(>108.80)		
(n=541)	(n = 139)	(n = 135)	(n = 132)	(n = 135)		
LAP	23.75(14.85,38.64)	39.99(24.96,63.68) ^a	61.91(38.56,81.86) ^{ab}	80.96(52.50,105.84) ^{abc}	178.154	< 0.001
Neck circumference (cm)	33(32,35)	34(33.50,36) ^a	36(35,37) ^{ab}	37(35,38.60) ^{abc}	138.257	< 0.001
VAI	1.96(1.36,3.42)	2.73(1.83,4.77) ^a	3.58(2.22,5.82) ^a	4.27(2.96,6.08) ^{ab}	75.048	< 0.001

Table 1	Clinical	characteristics	of the	participants	according to	VFA quartile

Note: Data from skewed distributions are expressed as median (upper quartile, lower quartile). Comparisons between multiple groups were made by nonparametric tests, by Kruskal-Wallis H-test, and between groups by Bonferroni multiple comparisons. Quartiles were taken and grouped according to Q1 ($\leq P_{25}$), Q2(> P_{25} , $\leq P_{50}$), Q3 (> P_{50} , $\leq P_{75}$), Q4 (> P_{75})

Abbreviations: UACR, urinary albumin to creatinine ratio; BMI, body mass index; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, lowdensity lipoprotein; TC, total cholesterol; TG, triglycerides; Glu0, fasting glucose, Glu120, 2-hour postprandial glucose; HbA1c, glycated hemoglobin. Units: VFA (cm²)

^a Significant difference from Q1 group (P < 0.05)

^b Significant difference from Q2 group (P < 0.05)

^c Significant difference from Q3 group (P<0.05)

Analysis of results for different VFA in T2DM with normal BMI

Analysis of decision tree model in T2DM with normal BMI

In the univariate analysis of 1,409 T2DM subjects, 21 variables were screened with VFA as the dependent variable (Additional file 1) and each variable was assigned a value (Additional file 2). A Chi-square automatic interaction detector decision tree model with a tree growth of 3 levels and 11 terminal node counts was employed. The decision tree model (Fig. 2) revealed a high VF rate of 52.8% (n = 744) in the 1,409 T2DM subjects. Additionally, the prevalence of VF (+) OB (-) was 7.8% (n = 110) in T2DM subjects (n = 1,409). Each decision rule and decision result (Fig. 2) showed that BMI was the root node leading to the branch line, normal BMI (BMI ≤ 23.9 kg/m²) was a non-leaf node, LAPQ3 or LAPQ2, LAPQ1 was a non-leaf node, and LAPQ4, gender, NC were leaf nodes.

The normal BMI T2DM subjects (males n = 317, females n = 221) aged 58(50,66) years were further analyzed. In a univariate analysis of 538 T2DM subjects with normal BMI, the 11 variables listed above were screened using VFA as the dependent variable (Additional file 3). These variables were supplemented with assigned values (Additional file 4). The decision tree model with a tree growth of 3 levels and 5 terminal nodes was employed. As depicted in Fig. 3, the decision tree model revealed a prevalence of VF (+) OB (-) of 20.4% (n = 110) among T2DM subjects with normal BMI (n = 538). Figure 3 presents the decision rules and outcomes of the decision tree. In this tree, one of the rules demonstrated LAP as the root node variable, while LAPQ4 or LAPQ3 served as non-leaf nodes, and an increase in NC represented a leaf node. A high VF rate of 42.6% was observed across all rules.



Fig. 2 Decision tree model of different VFAs in 1,409 subjects with T2DM

Multifactorial binary logistic regression analysis of different VFAs with normal BMI

A univariate analysis of 538 T2DM subjects with normal BMI, including 11 variables, was conducted. A multivariable binary logistic regression analysis was conducted using the forward method. The analysis identified NC, BMI, and LAP as relevant factors for high VF in T2DM with normal BMI (Fig. 4). NC had an odds ratio (OR) of 1.891 (95% CI: 1.165–3.069, P=0.01). In T2DM subjects with normal BMI, the OR for VF gradually increased from the 1st to the 4th quartile of LAP. Subjects with normal BMI who exhibited an increase in NC, higher LAP, and higher BMI were identified as relevant factors for high VF (P<0.05).

Spearman's correlation analysis of LAP and NC with VFA in different genders in T2DM with normal BMI.

Spearman's correlation analysis was conducted on 538 T2DM subjects with normal BMI to assess the correlation between LAP, NC, and VFA. The results demonstrated a positive correlation between LAP and VFA in both males (r = 0.552) and females (r = 0.525). Similarly, a positive correlation was observed between NC and VFA

in males (r = 0.356) and females (r = 0.347). These correlations were statistically significant ($P \le 0.001$), as illustrated in Fig. 5.

Analysis of LAP, neck circumference ROC curves in T2DM subjects with normal BMI

ROC curve analysis revealed that the area under the curve (AUC) for NC in predicting high VF in T2DM subjects with normal BMI was 0.640 in males and 0.682 in females. The optimal cut-off points for NC were 37.75 cm for males and 34.75 cm for females. Similarly, the AUC for LAP in predicting high VF in males and females was 0.745 and 0.772, respectively. The optimal cut-off point for LAP was 22.64 cm for males and 26.45 cm for females. In conclusion, both NC and LAP might be used as an assessing value for high VF in T2DM subjects with normal BMI. However, compared with NC, LAP had a more relevant factor with VF, as illustrated in Table 2; Fig. 6.



Fig. 3 Decision tree model of different VFAs in 538 T2DM subjects with normal BMI

Discussion

This study found that among subjects with T2DM (n=1,409), the prevalence of VF (+) OB (-) was 7.8% (n = 110). In T2DM subjects with normal BMI (n = 538), the prevalence of VF (+) OB (-) was 20.4% (n = 110). Previous studies have reported varying prevalence rates of VF (+) OB (-) in different populations. In 2007, a study of the Japanese general male population (n = 2,336)found a prevalence of 26.8% (n = 401) among 1,497 nonobese subjects (BMI < 25 kg/m²) with VF accumulation $(VFA \ge 100 \text{ cm}^2)$ [49]. In 2022, a study of 1,813 general Chinese adults, categorized by BMI and VF using Chinese standards, identified a prevalence of 28.1% (n = 171) for VF (+) OB (-) among subjects with normal BMI(n = 609) [50]. According to the above two reports, the prevalence of VF (+) OB (-) were 17.2% in the Japanese general male population [49] and 9.4% in general Chinese adults [50], separately. In 2015, a cross-sectional study of 414 T2DM subjects in Japan reported a prevalence of approximately 7.2% (n = 30) for VF (+) OB (-). Among normal BMI subjects (n = 187), the prevalence was 16.0% [19]. A more recent 2023 study of 8,839 T2DM subjects in China found a prevalence of 3.7% (n=327) for VF (+) OB (-), and among normal BMI subjects (n = 2,498), the prevalence was 13.1% [20]. In 2023, a study of 6,997 Chinese T2DM subjects categorized individuals based on BMI and visceral obesity (VFA \ge 100 cm²). Of the 2,860 subjects with normal weight (BMI < 24 kg/m²), 329 were identified as having visceral obesity. The prevalence VF (+) OB (-) were 5.0% in T2DM subjects and 11.5% in the normal BMI subjects [21]. The prevalence of VF (+) OB (-) in T2DM populations ranged from 3.7 to 7.2%, which was lower than that observed in general population. Notably, within T2DM subjects with normal BMI, the prevalence of VF (+) OB (-) reached 11.5–16.0%. When comparing the results of



Fig. 4 Multifactorial binary logistic regression analysis of different VFAs with normal BMI

this study to previous research, it is essential to consider the potential impact of various factors, including differences in ethnicity, sample size, BMI and VFA cut-offs, and measurement methods. In our study, dual bioelectrical impedance analysis (BIA) was employed in measuring visceral fat area. The previous study has also confirmed that BIA was highly correlated with computed tomography [22]. Therefore, the radiation-free tool could provide a reliable result for evaluating VF. Despite these variations, the consistent findings across multiple studies highlight the significant proportion of VF (+) OB (-) individuals in T2DM populations and their associated risk. The slightly higher prevalence observed in our study might be attributed to the lower VFA cutoff ($\geq 90 \text{ cm}^2$) we selected by comparing to previous studies ($\geq 100 \text{ cm}^2$). However, this selected cut-point is relevant to the risk of VF accumulation and ASCVD in T2DM individuals with normal BMI [21]. Based on the prevalence findings, it is imperative to strengthen screening efforts for high VF in non-obese T2DM individuals.

NC, as a simple anthropometric measure for assessing subcutaneous fat accumulation in the upper body, is minimally affected by breathing and diet, and has clear anatomical landmarks, high reproducibility, and low variability [24]. NC has been associated with VF [23, 24, 51, 52], insulin resistance [51], metabolic syndrome [53–55], non-alcoholic fatty liver disease [56, 57], diabetes mellitus [58], cardiovascular disease, and all-cause mortality [59, 60]. In 2010, a US study suggested that NC might be a unique, pathogenic fat depot. The influence of NC and VF on cardiometabolic risk factor levels was demonstrated, with a stepwise increase in risk factor levels by tertile of NC for each tertile of VF [61]. In 2018, Zhao L et al. identified that NC could be a supplemental indicator for visceral obesity in general Chinese population [62]. In 2017, Yu qi Luo et al. found that VF was independently correlated with NC in a cross-sectional study involving 1,943 general Chinese individuals. Furthermore, ROC analysis showed that NC predicted VF with an AUC of 0.781 (sensitivity 56.1%, specificity 83.5%) in males and 0.777 (sensitivity 58.1%, specificity 82.5%) in females. The optimal cut-off points for NC were determined to be 38.5 cm in males and 34.5 cm in females, respectively [63]. In combination with these studies, NC has been shown to predict VF in Chinese non-T2DM subjects. In our study, the AUC for NC prediction of high VF in male and female T2DM subjects with normal BMI was 0.640 (sensitivity 68.1%, specificity 52.7%) and 0.682 (sensitivity 60.5%, specificity 76.0%), respectively, with optimal cutoff points of 37.75 cm and 34.75 cm, respectively. Considering that the population in this study consisted both T2DM subjects and the complex pathogenesis of T2DM, the AUC and specificity values in this study were slightly low. While few studies have specifically examined the



Fig. 5 Spearman correlation analysis of VFA with neck circumference and LAP by gender Note: 538 subjects with T2DM had VFA analyzed by spearman correlation with neck circumference (**a**) in male, neck circumference (**b**) in female, LAP (**c**) in male, and (d) in female in subjects with a normal BMI

 Table 2
 LAP, neck circumference ROC curve analysis for different VFAs in T2DM with normal BMI

Characteristic	Gender	AUC	Р	95% CI		Best cutoff point	Sensitivity	Specificity	Youden index
				Lower limit	Upper limit				
Neck circumference	Male	0.640	< 0.001	0.571	0.709	37.75	68.10%	52.70%	0.208
	Female	0.682	< 0.001	0.594	0.770	34.75	60.50%	76.00%	0.365
LAP	Male	0.745	< 0.001	0.688	0.803	22.64	86.10%	54.30%	0.404
	Female	0.772	< 0.001	0.705	0.839	26.45	97.40%	50.30%	0.477

correlation between NC and high VF in T2DM subjects, emphasis has been predominantly placed on that NC was determined to be the best cutoff value for predicting central obesity, defined by waist circumference [28, 64]. In summary, NC can be used as a simple and reliable parameter to assess VF.

In our study, LAP was identified as a positive correlate of VFA in T2DM with normal BMI. LAP, an inexpensive combination of fasting triglyceride and waist circumference, was first described by Henry S Kahn et al. in 2005 as a predictor of cardiovascular outcomes and mortality in an American adult population [44]. In 2006, the same researchers suggested that LAP might be associated with the development of diabetes due to its strong correlation with insulin resistance [65]. LAP represents excessive VF accumulation, which is considered pathological fat deposits. It is a cost-effective and simple indicator of VF replacement [66] and has been associated with the development of VF [67], oxidative stress [68], hyperuricemia [69], Insulin resistance [70, 71], T2DM [65, 72–74], metabolic syndrome [75–77], cardiovascular disease and mortality [78–80], and the development of atherosclerosis [81]. A prospective study of 4,281 nondiabetic adults without systemic or abdominal obesity in South Korea found that a high LAP index was independently associated with T2DM and could be used as



Fig. 6 ROC curve analysis of LAP (A) and neck circumference (B) in T2DM subjects with normal BMI.

a predictive indicator [72]. LAP has been shown to have high accuracy and sensitivity in diagnosing insulin resistance [70]. A study of non-obese Asian Indian men with normal blood glucose demonstrated that the LAP index predicted the risk of insulin resistance with greater accuracy than traditional insulin resistance indicators like HOMA-IR [71]. While there are limited studies on LAP predicting the occurrence of high VF, especially in T2DM subjects with normal BMI, therefore we chose to focused on this specific population in the current study. Given that insulin resistance is a key factor in the pathogenesis of T2DM, we evaluated various insulin indicators to assess high VF in T2DM subjects. Our findings suggest that LAP exhibits a strong discriminative ability in predicting high VF in non-obese T2DM individuals.

At present, both decision tree models [82–86] and logistic regression models are used to construct prediction models of influencing factors. The logistic regression model was employed to analyze the risk factors associated with the occurrence of VF. Meanwhile the logistic regression model may overlook meaningful variables due to collinearity between independent variables [87], the decision tree model can complement it in this regard. Decision tree models can reveal the degree and percentage of influence of various factors on VF in T2DM, mitigating the issue of collinearity. By combining the logistic regression model and the decision tree model, our study provided a better interpretability and visualization analysis for the associated factors leading to high VF. This study included 2,235 individuals, and 1,409 subjects with T2DM were evaluated for inclusion. However, the study is subject to certain limitations. Due to its cross-sectional observational design, causality cannot be established from the results. Additionally, the study did not consider potential influences of medication and treatment regimens, environmental factors, diet, or other variables on the findings. Future follow-up studies of the enrolled subjects will be conducted to address these limitations.

Conclusion

Our study demonstrates that neck circumference and LAP may predict high VF in T2DM subjects with normal BMI.

Abbreviations

ABI	Ankle-Brachial Index
ASCVD	Atherosclerotic Cardiovascular Disease
AUC	Area Under the Curve
ADA	American Diabetes Association
BMI	Body Mass Index
BIA	Dual Bioelectrical Impedance Analysis
CI	Confidence Interval
CT	Computed Tomography
CVD	Cardiovascular Disease
CAD	Coronary Artery Disease
CIMT	Cervical Intima-Media Thickness
DM	Diabetes Mellitus
DBP	Diastolic Blood Pressure
eGFR	Estimated Glomerular Filtration Rate
FPG	Fasting Plasma Glucose
FINS	Fasting Serum Insulin

FCP Glu0 Glu120 HOMA-β	Fasting Serum C-Peptide 0-Hour Blood Glucose 2-Hour Postprandial Blood Glucose Homeostasis Model Assessment β Cell Function
HOMA-IR	Homeostasis Model Assessment of Insulin Resistance
HbA1c	Hemoglobin A1c
HDL-C	High-Density Lipoprotein Cholesterol
MMC	Metabolic Management Center
MDRD	Modification of Diet in Renal Disease
LDL-C	Low-Density Lipoprotein Cholesterol
LAP	Lipid accumulation product
OR	Odds Ratio
OGII	Oral Glucose Tolerance Teste
Scr	Serum Creatinine
SBP	Systolic Blood Pressure
SFA	Subcutaneous Fat Area
T2DM	Type 2 Diabetes Mellitus
TIDM	Type T Diabetes Mellitus
TyG	Triglyceride Glucose Index
IG	Iriglycerides
IC	Iotal Cholesterol
UACR	Urinary Albumin Creatinine Ratio
UA	
ULN	Viscoral Eat
	Visceral Fat
VFA	Visceral Fat Index
VAI	World Lealth Organization
	Waist to Llip Datia
	Waist Circumforon co
VVC	waist circumference

Supplementary Information

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Supplementary Material 1	
Supplementary Material 2	
Supplementary Material 3	
Supplementary Material 4	

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Author contributions

Y.L. and Y.Y. designed the project. X.W., W.T. and J.C. worked out the technical details. H.Y., H.Y., S.Z. and Y.F. collected the data. H.Y., H.Y., S.Z., J.C. and M.J. analysed the results. M.J. wrote the manuscript. Y.Y. and Y.L. took part in drafting the article and revising it critically for important intellectual content. All authors read and approved the final manuscript. M.J. and J.C. contributed equally to this paper. All authors agree to be accountable for all aspects of the work.

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Data availability

No datasets were generated or analysed during the current study.

Ethics approval and consent to participate

The subjects were unrelated individuals residing in Yunnan Province, China. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki for clinical research and was approved by the Ethics Committee of the Affiliated Hospital of Yunnan University (No. 2020038). Written informed consent was obtained from all subjects.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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