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ORIGINAL RESEARCH

Relationship Between Monocyte-to-High-Density Lipoprotein Cholesterol Ratio and Visceral Obesity in Patients with Type 2 Diabetes Mellitus: A Cross-Sectional Study

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Purpose: The study aimed to explore the relationship between the monocyte-to-high-density lipoprotein cholesterol ratio (MHR) and visceral fat area (VFA) in patients with type 2 diabetes mellitus (T2DM).

Patients and Methods: A total of 2156 patients with T2DM who received medical treatment at Zhejiang Provincial People's Hospital participated in this study. Patients were categorized into two groups based on VFA: the increased VFA group (VFA ≥ 100 cm^2, n = 1091) and the normal VFA group (VFA < 100 cm^2, n = 1065). Biochemical indicators were measured via blood tests, whereas VFA was measured using bioelectrical impedance analysis. Spearman correlation and linear regression analysis were conducted to examine the association between MHR and VFA. Receiver operating characteristic (ROC) curves for predicting the VFA were constructed, and areas under the ROC curves were estimated.

Results: MHR level was significantly higher in the increased VFA group ($p < 0.001$) than in the normal VFA group. Spearman correlation analysis showed a positive association between VFA and MHR (r = 0.366, $p < 0.001$). Multivariate linear regression analysis revealed that elevated MHR is an independent factor for increased VFA (β = 20.64, 95% CI 13.46–27.82, $p < 0.001$). After stratification by hemoglobin A1c levels and diabetes duration, MHR remained independently associated with VFA. ROC analysis indicated that MHR has a predictive effect on VFA, with an area under the curve of 0.708 (specificity = 58%, sensitivity = 73%).

Conclusion: MHR levels are associated with visceral fat area in patients with T2DM, which has a modest predictive value, and it may be useful in detecting visceral obesity.

Keywords: visceral fat area, monocyte-to-high-density lipoprotein cholesterol ratio, type 2 diabetes mellitus, abdominal fat distribution

Introduction

In recent years, the prevalence of type 2 diabetes mellitus (T2DM) has gradually increased, with obesity becoming a significant risk factor. Obesity, particularly visceral obesity, is closely associated with many diseases that pose serious health threats to humans.[1,2] Visceral fat accumulation is a key risk factor contributing to insulin resistance and impaired glucose metabolism, which is often accompanied by increased cytokines and other inflammatory markers.[3,4]

Monocytes are key cells that secrete pro-inflammatory and pro-oxidative factors, and their increase is linked to subclinical inflammation.[5] High-density lipoproteins (HDLs) play an anti-inflammatory role by inhibiting monocyte activity and preventing their differentiation into macrophages.[6] Several studies have shown that monocytes and monocyte-derived markers are associated with inflammatory conditions.[7–9] HDL-based markers have also been linked to various inflammatory conditions, including hypertension, hepatic steatosis, thyroiditis, and metabolic syndrome.[10,11]

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In recent years, the peripheral blood monocyte-to-high-density lipoprotein cholesterol ratio (MHR), a novel inflammatory marker, has garnered significant interest owing to its association with various metabolic diseases, including atherosclerosis.[12] Research has demonstrated that both obesity and T2DM are linked to a high inflammatory burden.[13–15] Particularly, visceral obesity leads to adipose tissue dysfunction and compromised adipocytokine secretion, which triggers oxidative stress and inflammatory response, ultimately inducing insulin resistance and T2DM.[16–18] Additionally, obesity, particularly visceral obesity, places the body in a state of chronic inflammation, which aggravates insulin resistance in patients with T2DM, increases the risk of vascular complications, and elevates the mortality of patients.[19] Therefore, we hypothesize that MHR acts as a predictor of visceral obesity.

Previous studies have established that the MHR is significantly elevated in patients with metabolic syndrome and is closely associated with conditions like obesity and polycystic ovarian syndrome.[20,21] However, the relationship between MHR and visceral obesity in patients with T2DM, as well as its predictive role, have not been explored. This distinction is critical because T2DM confers a disproportionately higher risk of cardiovascular disease, and visceral fat accumulation is a key driver of this risk, independent of general obesity.[22] The prevalence of T2DM and visceral obesity is constantly increasing worldwide, in China alone, the prevalence of diabetes has surpassed 11%.[23] Therefore, identifying a simple, cost-effective biomarker like MHR that can reflect visceral fat area (VFA) in T2DM patients holds significant practical value. It could aid in early risk stratification, allowing for more targeted interventions in resource-limited settings. This study analyzed the correlation between MHR levels and VFA in patients with T2DM and evaluated the predictive value of MHR on visceral obesity.

Methods

Study Design and Participants

This cross-sectional study analyzed the relationship between MHR levels and visceral obesity. Our research team had previously explored the association between thyroid autoimmunity and visceral fat distribution in T2DM patients within a similar but very small sample size population.[24] The present study extends this line of inquiry by focusing on a novel inflammatory marker, MHR, which has not been previously examined in relation to visceral obesity in T2DM patients in our cohort.

In this study, a total of 2156 patients with T2DM who received medical treatment at Zhejiang Provincial People's Hospital between July 2020 and July 2023 were included. All participants provided complete questionnaire data, underwent physical examinations, and completed laboratory assessments.

The inclusion criteria were as follows: (1) age $\geq$ 18 years; (2) diagnosis of T2DM based on the 2020 American Diabetes Association (ADA) Standards of Medical Care in Diabetes.

The exclusion criteria were as follows: (1) acute diabetic complications, such as ketoacidosis, hyperosmolar hyperglycemia state, and acute infections; (2) history of hematological disorders; (3) history of malignant tumors; (4) having hyperthyroidism or hypothyroidism; (5) currently taking lipid-lowering therapy, GLP-1RA, SGLT2i, thiazolidinediones, systemic steroids, and thyroid medications; (6) severe dysfunction of the heart, liver, or kidneys; (7) pregnancy or lactation. The screening process is shown in Figure 1.

Data Collection

Demographic and clinical data were collected using a standardized questionnaire, including age, sex, T2DM duration, medical history, medication use, and lifestyle factors such as smoking and alcohol consumption. Anthropometric measurements (height, weight, waist circumference, hip circumference) and blood pressure were recorded. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

Laboratory indicators were based on early-morning venous blood after an 8 hours fast, and the detection items included: white blood cell count (WBC), monocyte count (MONO), hemoglobin (Hb), platelet count (PLT), fasting blood glucose (FBG), fasting insulin (FINS), glycated hemoglobin (HbA1c), lipid profile (total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C)), liver and renal function markers (albumin (ALB), aspartate aminotransferase (AST), alanine transaminase (ALT), alkaline phosphatase

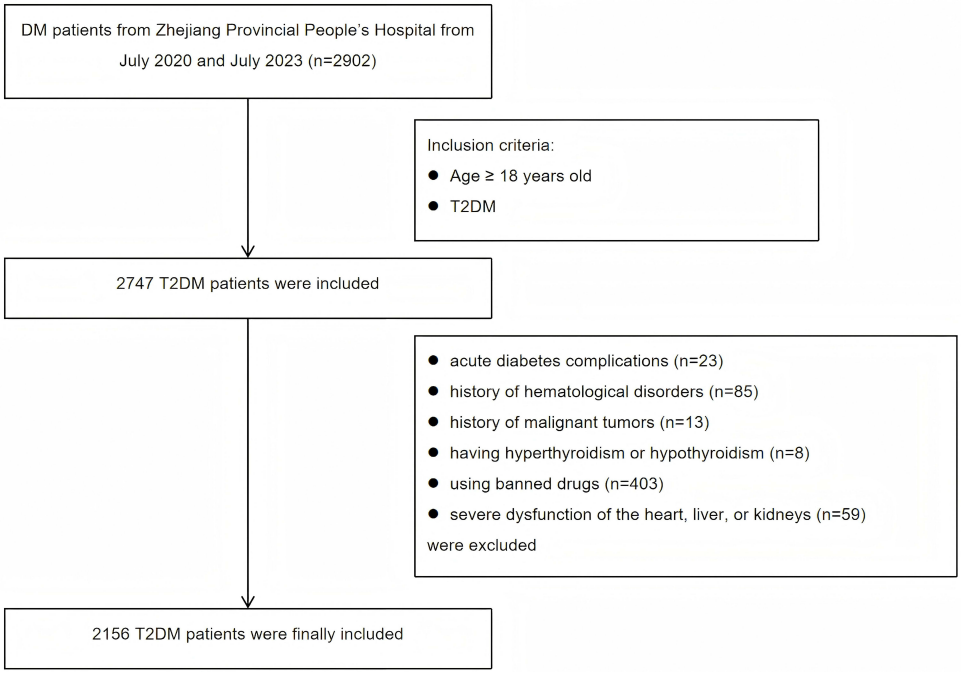

Figure 1 Flow chart of study.

(ALP), blood urea nitrogen (BUN), serum creatinine (Scr)), uric acid (UA), and thyroid function indicators (free thyroxine (FT4), free triiodothyronine (FT3), and thyroid stimulating hormone (TSH)). Insulin resistance was estimated using the homeostasis model assessment (HOMA-IR) formula: FINS (mU/L) × FBG (mmol/L) / 22.5. There was missing data on ALP for 56 participants and missing data on AST for 54 participants. We used the random forest method for imputation. The important research indicators were complete.

VFA and subcutaneous fat area (SFA) were measured using bioelectrical impedance analysis (BIA) with the DUALSCAN HDS-2000. The measurement was conducted in the morning after an overnight fast, with participants in a supine position, having emptied their bladder, and was performed by the same nurse using the same equipment. Based on the VFA, participants were divided into two groups: the increased VFA group (VFA ≥ 100 cm^2, n = 1091) and the normal VFA group (VFA < 100 cm^2, n = 1065).

Statistical Analysis

Data distribution was assessed using the Kolmogorov–Smirnov test. Normally distributed continuous variables were expressed as mean ± standard deviation, while non-normally distributed variables were reported as median (interquartile range). Group comparisons were performed using Student's *t*-test or Mann–Whitney *U*-test, as appropriate. Categorical variables were compared using chi-square tests. The relationship between MHR and VFA was analyzed using Spearman correlation analysis. Univariate and multivariate linear regression models were constructed to identify factors associated with VFA. Meanwhile, two linear regression models were performed to adjust for confounding factors. Model 1 adjusted for age and sex. Model 2 further adjusted for drinking habits, and levels of waist circumference, SFA, ALT, Scr, TG, FT3. Subgroup analyses were conducted based on the duration of diabetes (< 10 vs ≥10 years) and HbA1c levels (< 7% vs ≥ 7%) to assess the consistency of the MHR-VFA association. Receiver operating characteristic (ROC) curves for predicting the VFA were constructed, and areas under the ROC curves were estimated.

Statistical analyses were conducted using SPSS software (version 26.0; IBM Corp., Armonk, NY, USA) and R software (version 4.1.0; R Foundation for Statistical Computing, Auckland, New Zealand). R packages, including ggplot2, mice, survival, missForest, VIM, Hmisc, rms, regplot, tableone, and glmnet, were used for data analysis and visualization. Statistical significance was set at $P<0.05$ for all tests.

Results

Participant Clinical Characteristics

An overview of the study characteristics of the two groups was presented in Table 1. In contrast to the T2DM without visceral obesity group, smoking and drinking habit incidences were significantly higher in the T2DM with visceral obesity group (39.32% vs 26.29% [$p < 0.001$] and 44.55% vs 30.80% [$p < 0.001$], respectively). The indices of blood pressure, BMI, waist circumference, SFA, HOMA-IR, FBG, HbA1c, ALT, AST, ALP, ALB, Scr, UA, TG, FT3, TSH and MHR were significantly higher in the T2DM with visceral obesity group than those in the T2DM without visceral obesity group ($p < 0.05$); conversely, HDL-C, age and duration were significantly lower ($p < 0.05$). No significant differences were observed in the levels of BUN, TC, LDL-C, FT4 and PLT between the two groups.

Table 1 Clinical Characteristics of T2DM Patients with and without Visceral Obesity

	Total (n = 2156)	Normal (n = 1065)	Visceral Obesity (n = 1091)	*P* Value
Age (years)	53.00 (42.75, 61.25)	55.00 (45.00, 62.00)	52.00 (40.00, 61.00)	<0.001
Female, n (%)	679 (31.49)	455 (42.72)	224 (20.53)	<0.001
Smoking, n (%)	709 (32.88)	280 (26.29)	429 (39.32)	<0.001
Alcohol, n (%)	814 (37.76)	328 (30.80)	486 (44.55)	<0.001
Duration of T2DM, month	37.00 (0.00, 122.00)	49.00 (1.00, 126.00)	27.00 (0.00, 101.50)	<0.001
Duration ≥ 10years, n(%)	581 (26.95)	328 (30.80)	253 (23.19)	<0.001
SBP, mmHg	129.00 (119.00, 140.00)	127.00 (117.00, 138.00)	131.00 (121.00, 142.00)	<0.001
DBP, mmHg	79.00 (72.00, 86.00)	77.00 (70.00, 84.00)	80.00 (73.00, 87.00)	<0.001
BMI, kg/m^2	25.06 (22.89, 27.48)	23.26 (21.60, 24.93)	26.99 (25.10, 29.40)	<0.001
Waist circumference, cm	92.00 (86.00, 99.00)	87.00 (82.00, 92.00)	98.00 (92.00, 105.00)	<0.001
SFA, cm^2	173.00 (138.00, 218.00)	143.60 (118.00, 172.00)	211.00 (172.25, 252.00)	<0.001
Hb, g/L	145.00 (134.00, 156.00)	141.00 (131.00, 152.00)	149.00 (138.00, 159.00)	<0.001
WBC, x10^9/L	6.35 (5.40, 7.50)	5.99 (5.17, 7.08)	6.69 (5.67, 7.89)	<0.001
MONO, x10^9/L	0.38 (0.30, 0.45)	0.34 (0.29, 0.41)	0.40 (0.32, 0.50)	<0.001
PLT, x10^9/L	212.00 (177.00, 249.25)	212.00 (177.00, 249.00)	212.00 (177.00, 250.50)	0.679
FBG, mmol/L	6.54 (5.51, 8.08)	6.41 (5.46, 7.87)	6.69 (5.59, 8.28)	0.022
HOMA-IR	1.79 (0.82, 3.44)	1.43 (0.61, 2.75)	2.24 (1.11, 4.26)	<0.001
HbA1c, %	9.00 (7.20, 10.70)	8.80 (6.90, 10.70)	9.10 (7.60, 10.70)	<0.001
HbA1c ≥ 7%, n(%)	1714 (79.50)	796 (74.74)	918 (84.14)	<0.001
ALT, U/L	24.00 (17.00, 39.00)	20.00 (15.00, 30.00)	29.00 (20.00, 49.00)	<0.001
AST, U/L	22.00 (18.00, 30.00)	21.00 (17.00, 26.00)	25.00 (19.00, 35.00)	<0.001
ALP, U/L	78.00 (64.00, 95.00)	76.00 (63.00, 93.00)	80.00 (66.00, 97.00)	0.001
ALB, g/L	41.00 (38.00, 44.00)	40.50 (37.60, 43.60)	41.30 (38.30, 44.20)	0.002
BUN, mmol/L	5.16 (4.27, 6.18)	5.16 (4.31, 6.21)	5.17 (4.25, 6.16)	0.754
Scr, μmol/L	71.60 (61.00, 82.60)	68.70 (58.80, 80.00)	74.30 (63.40, 84.90)	<0.001
UA, μmol/L	333.00 (274.00, 398.00)	311.00 (257.00, 367.00)	352.00 (299.50, 419.00)	<0.001
TG, mmol/L	1.43 (1.01, 2.19)	1.22 (0.88, 1.82)	1.68 (1.18, 2.52)	<0.001
TC, mmol/L	4.69 (3.94, 5.40)	4.69 (3.99, 5.34)	4.68 (3.91, 5.48)	0.551
HDL-C, mmol/L	1.01 (0.87, 1.18)	1.06 (0.92, 1.26)	0.95 (0.83, 1.08)	<0.001
LDL-C, mmol/L	2.75 (2.17, 3.33)	2.73 (2.19, 3.31)	2.76 (2.13, 3.36)	0.949
FT3, ng/L	3.21 (2.94, 3.51)	3.13 (2.88, 3.43)	3.29 (3.01, 3.58)	<0.001
FT4, ng/L	9.34 (8.42, 10.39)	9.32 (8.39, 10.41)	9.36 (8.44, 10.36)	0.802
TSH, mIU/L	1.60 (1.11, 2.31)	1.54 (1.06, 2.23)	1.65 (1.13, 2.39)	0.008
MHR	0.37 (0.28, 0.48)	0.32 (0.25, 0.40)	0.43 (0.32, 0.54)	<0.001

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; SFA, subcutaneous fat area; Hb, hemoglobin; WBC, white blood cells; MONO, monocyte count; PLT, platelet; FBG, fasting blood glucose; HOMA-IR, homeostasis model assessment of insulin resistance; HbA1c, glycosylated hemoglobin; ALT, alanine transaminase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; ALB, albumin; BUN, blood urea nitrogen; Scr, serum creatinine; UA, uric acid; TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid stimulating hormone; MHR, monocyte to high-density lipoprotein cholesterol ratio.

Correlations Between MHR and VFA

To further assess the relationship between MHR and visceral obesity, we analyzed the correlation between VFA and MHR. The Spearman correlation analysis indicated that an increased MHR was significantly positively correlated with VFA (r = 0.366, $p < 0.001$) (Figure 2).

Association Between the MHR and VFA in Patients with T2DM

We conducted a univariate linear regression analysis to assess the variables influencing visceral obesity in patients with T2DM. Using VFA as the dependent variable, the independent variables were sequentially screened (Table 2). Variables with $p < 0.05$, including age, sex, smoking and drinking habits, duration of T2DM, and levels of HbA1c, MHR, SBP, DBP, BMI, waist circumference, SFA, FBG, ALT, AST, ALB, Scr, UA, TG, FT3, and TSH, were included in the multivariate linear regression analysis. The multiple linear regression model revealed that elevated MHR was an independent factor for increased VFA (β = 20.64, 95% confidence interval [CI] 13.46–27.82, $p < 0.001$) (Table 3).

Subgroup Analysis

Univariate linear regression analysis showed that MHR was associated with VFA (β = 92.04, 95% CI 82.15–101.94, $p < 0.001$). After adjusting for age and sex, MHR was still associated with the VFA (β = 80.09, 95% CI 69.76–90.42, $p < 0.001$). We further adjusted for the drinking habits, and levels of waist circumference, SFA, ALT, Scr, TG and FT3, MHR remained independently associated with the VFA (β = 22.10, 95% CI 14.97–29.23, $p < 0.001$). Moreover, we performed a subgroup linear regression according to HbA1c levels (< 7% vs ≥ 7%) and T2DM duration (< 10 vs ≥ 10 years). After adjusting for age and sex, MHR remained associated with the VFA in all subgroups. After further adjusting for the other variables, MHR was still independently associated with VFA ($p < 0.05$) (Table 4).

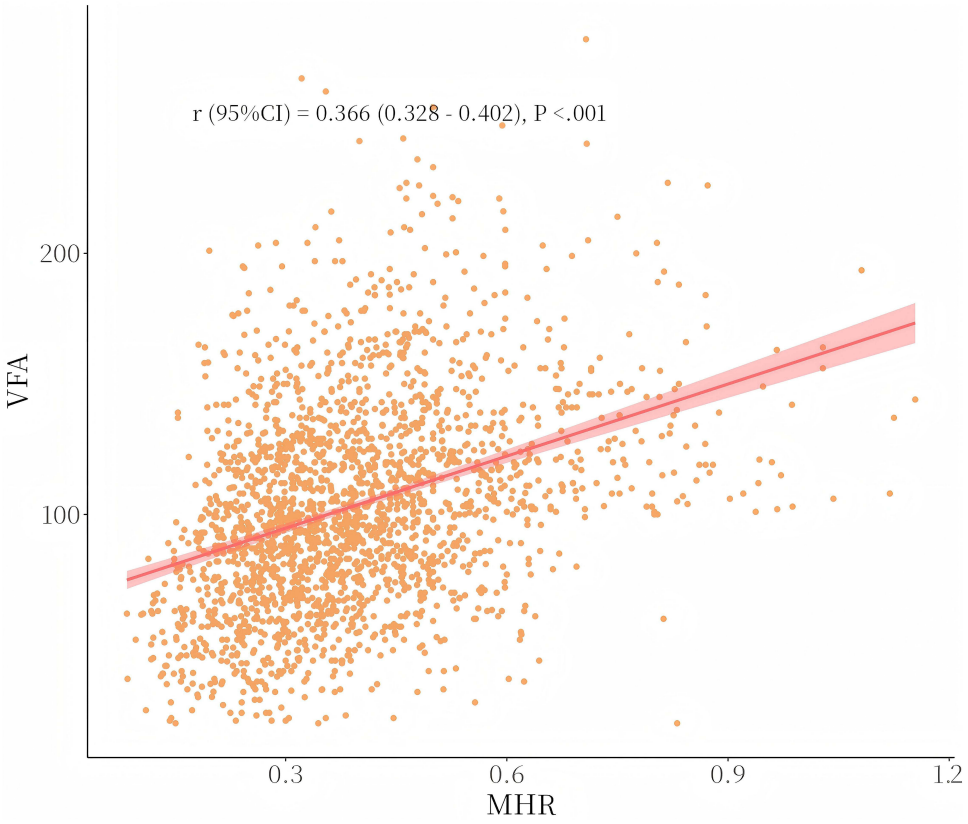

Figure 2 The correlations between MHR and VFA: an increased MHR was significantly positively correlated with VFA (r = 0.366, $p < 0.001$).

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Table 2 Univariate Linear Regression Analysis for Factors Associated with VFA in T2DM Patients

Variables	β	S.E	t	*P* Value	β (95% CI)
Female	−20.14	1.79	−11.25	<0.001	−20.14 (−23.65 ~ −16.63)
Smoking	10.03	1.81	5.55	<0.001	10.03 (6.48 ~ 13.57)
Alcohol	11.31	1.75	6.47	<0.001	11.31 (7.88 ~ 14.74)
Duration of T2DM < 10 years	9.26	1.92	4.83	<0.001	9.26 (5.50 ~ 13.02)
HbA1c < 7%	−12.51	2.10	−5.95	<0.001	−12.51 (−16.63 ~ −8.39)
MHR	92.04	5.05	18.23	<0.001	92.04 (82.15 ~ 101.94)
Age	−0.41	0.07	−6.20	<0.001	−0.41 (−0.55 ~ −0.28)
SBP	0.78	0.08	9.86	<0.001	0.78 (0.63 ~ 0.94)
DBP	0.50	0.05	9.44	<0.001	0.50 (0.40 ~ 0.61)
BMI	7.98	0.16	49.82	<0.001	7.98 (7.66 ~ 8.29)
Waist circumference	2.79	0.06	49.79	<0.001	2.79 (2.68 ~ 2.90)
SFA	0.44	0.01	48.32	<0.001	0.44 (0.43 ~ 0.46)
FBG	1.07	0.35	3.10	0.002	1.07 (0.40 ~ 1.75)
HOMA-IR	0.14	0.07	1.86	0.063	0.14 (−0.01 ~ 0.28)
ALT	0.59	0.03	18.31	<0.001	0.59 (0.53 ~ 0.66)
AST	0.78	0.05	16.38	<0.001	0.78 (0.68 ~ 0.87)
ALB	0.91	0.20	4.55	<0.001	0.91 (0.52 ~ 1.31)
Scr	0.35	0.05	7.59	<0.001	0.35 (0.26 ~ 0.44)
UA	0.13	0.01	15.04	<0.001	0.13 (0.11 ~ 0.15)
TG	6.55	0.54	12.21	<0.001	6.55 (5.50 ~ 7.60)
FT3	17.74	2.01	8.80	<0.001	17.74 (13.79 ~ 21.68)
TSH	3.35	0.87	3.87	<0.001	3.35 (1.65 ~ 5.05)

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; SFA, subcutaneous fat area; FBG, fasting blood glucose; HOMA-IR, homeostasis model assessment of insulin resistance; HbA1c, glycosylated hemoglobin; ALT, alanine transaminase; AST, aspartate aminotransferase; ALB, albumin; Scr, serum creatinine; UA, uric acid; TG, triglycerides; FT3, free triiodothyronine; TSH, thyroid stimulating hormone; MHR, monocyte to high-density lipoprotein cholesterol ratio.

Comparison of MHR, HDL-C, and MONO for Predicting the VFA in Patients with T2DM

The ROC curves and AUCs for MHR, HDL-C, and MONO were shown in Figure 3 and Table 5. The AUC of MHR, HDL-C, and MONO was respectively 0.708 (95% CI: 0.687–0.730), 0.653 (95% CI: 0.630–0.676), and 0.658 (95% CI: 0.635–0.681). In addition, the difference in AUC between MHR and HDL-C was 0.0552 ($Z = 5.380$, $p < 0.001$), between MHR and MONO was 0.0504 ($Z = 6.645$, $p < 0.001$), between MONO and HDL-C was 0.00472 ($Z = 0.289$, $p = 0.772$). The predictive effect of MHR on VFA was superior to that of HDL-C or MONO alone, and the difference was significant.

Discussion

Obesity and T2DM are main public health concerns worldwide. Obesity is closely related to a variety of chronic diseases, including T2DM, hypertension, hyperlipidemia, and cardiovascular disease (CVD).[25] The prevalence of obesity among adults has nearly tripled in the past decade, and abdominal obesity has risen by nearly half.[26] Previous studies have shown an increase in cardiovascular health markers and a decrease in abnormal glucose metabolism. Conversely, an elevation in cardiovascular risk factors such as obesity is associated with an increase in T2DM.[27] Notably, visceral obesity is considered a major risk factor for various metabolic diseases, especially T2DM and CVD, and may play a role through a series of adipose-specific cytokines (such as leptin), inflammatory cytokines, and immune cytokines.[28,29] Circulating monocytes can independently predict CVD risk. HDLs play an anti-inflammatory role by inhibiting the activity of mononuclear cells and their differentiation into macrophages.[6,27] Therefore, MHR, as the ratio of two conventional test indicators, is regarded as a contemporary marker of de novo inflammation. In this study, we selected patients with T2DM as study participants and analyzed for the first time the correlation between the novel inflammatory

Table 3 Multivariate Linear Regression Analysis for Independent Factors Associated with VFA in T2DM Patients

Variables	R	0.657	R^2	0.432	Adjusted R^2	0.426
	β	S.E	t	*P* value	β (95% CI)	VIF
Female	−5.42	1.52	−3.57	<0.001	−5.42 (−8.40 ~ −2.44)	2.029
Smoking	−0.05	1.26	−0.04	0.970	−0.05 (−2.51 ~ 2.41)	1.416
Alcohol	3.35	1.16	2.89	0.004	3.35 (1.08 ~ 5.62)	1.280
Duration of T2DM < 10 years	2.60	1.24	2.09	0.037	2.60 (0.16 ~ 5.03)	1.236
HbA1c < 7%	−4.03	1.35	−2.99	0.003	−4.03 (−6.67 ~ −1.38)	1.207
MHR	20.64	3.66	5.64	<0.001	20.64 (13.46 ~ 27.82)	1.357
Age	0.48	0.05	9.31	<0.001	0.48 (0.38 ~ 0.58)	1.737
SBP	0.07	0.06	1.09	0.276	0.07 (−0.06 ~ 0.19)	1.798
DBP	0.03	0.04	0.62	0.533	0.03 (−0.06 ~ 0.11)	1.758
BMI	2.97	0.28	10.57	<0.001	2.97 (2.42 ~ 3.52)	4.249
Waist circumference	0.88	0.09	10.10	<0.001	0.88 (0.71 ~ 1.05)	3.310
SFA	0.16	0.02	10.63	<0.001	0.16 (0.13 ~ 0.19)	3.892
FBG	0.22	0.22	1.00	0.317	0.22 (−0.21 ~ 0.64)	1.148
ALT	0.09	0.04	2.51	0.012	0.09 (0.02 ~ 0.16)	3.239
AST	0.09	0.05	1.79	0.074	0.09 (−0.01 ~ 0.19)	2.938
ALB	0.17	0.14	1.20	0.231	0.17 (−0.11 ~ 0.44)	1.396
Scr	0.10	0.03	3.18	0.001	0.10 (0.04 ~ 0.17)	1.474
UA	0.01	0.01	1.53	0.127	0.01 (−0.00 ~ 0.02)	1.418
TG	1.08	0.36	3.01	0.003	1.08 (0.38 ~ 1.77)	1.230
FT3	2.68	1.32	2.03	0.043	2.68 (0.09 ~ 5.28)	1.242
TSH	0.21	0.52	0.40	0.689	0.21 (−0.81 ~ 1.23)	1.064

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; SFA, subcutaneous fat area; FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; ALT, alanine transaminase; AST, aspartate aminotransferase; ALB, albumin; Scr, serum creatinine; UA, uric acid; TG, triglycerides; FT3, free triiodothyronine; TSH, thyroid stimulating hormone; MHR, monocyte to high-density lipoprotein cholesterol ratio.

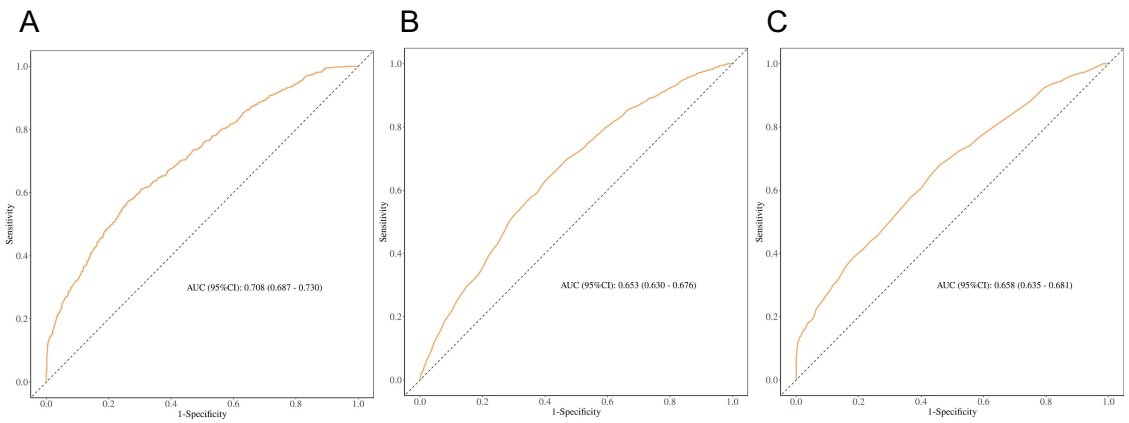
Table 4 Linear Regression Analysis Assessing the Association of the MHR with VFA

Variables	Crude Model			Model 1*		Model 2#	
	n (%)	β (95% CI)	*P* Value	β (95% CI)	*P* Value	β (95% CI)	*P* Value
MHR							
Overall	2156 (100.00)	92.04 (82.15 ~ 101.94)	<0.001	80.09 (69.76 ~ 90.42)	<0.001	22.10 (14.97 ~ 29.23)	<0.001
Stratified by HbA1c							
<7%	442 (20.50)	131.84 (107.92 ~ 155.75)	<0.001	113.37 (88.40 ~ 138.34)	<0.001	23.94 (6.23 ~ 41.66)	0.008
≥7%	1714 (79.50)	80.55 (69.57 ~ 91.53)	<0.001	69.61 (58.15 ~ 81.07)	<0.001	19.90 (12.03 ~ 27.77)	<0.001
Stratified by duration of T2DM							
<10 years	1575 (73.05)	95.67 (84.09 ~ 107.25)	<0.001	84.21 (72.02 ~ 96.39)	<0.001	22.40 (14.03 ~ 30.76)	<0.001
≥10 years	581 (26.95)	75.95 (57.03 ~ 94.88)	<0.001	64.53 (45.14 ~ 83.92)	<0.001	21.79 (8.16 ~ 35.42)	0.002

Notes: *Model 1: adjusted for age and sex. #Model 2: Model 1 + adjusted for drinking habits, and levels of waist circumference, SFA, ALT, Scr, TG, FT3.
Abbreviations: HbA1c, glycosylated hemoglobin; MHR, monocyte to high-density lipoprotein cholesterol ratio; T2DM, Type 2 Diabetes Mellitus.

index MHR and VFA and its predictive role in this population. This study is the first to evaluate the direct relationship between visceral obesity and MHR in a Chinese population with T2DM.

Studies have revealed that MHR can safely and effectively predict disease progression and prognosis, and previous studies have confirmed that MHR is associated with CVD, ischemic stroke, and kidney disease.[30–32] For example, a study by Karatas et al demonstrated that, compared with patients with T2DM exhibiting normoalbuminuria and healthy controls, MHR was significantly higher in individuals with diabetic nephropathy, and independently associated with urinary ALB to creatinine ratio.[33] Vahit et al found that the MHR of patients with metabolic syndrome was significantly



	The difference between AUC	95% CI	Z	*P*
MHR vs HDL-C	0.0552	0.0351 ~ 0.0753	5.380	<.001
MHR vs MONO	0.0504	0.0356 ~ 0.0653	6.645	<.001
MONO vs HDL-C	0.00472	-0.0272 ~ 0.0366	0.289	0.772

Figure 3 (**A**) ROC curve of MHR for predicting the VFA; (**B**) ROC curve of HDL-C for predicting the VFA; (**C**) ROC curve of MONO for predicting the VFA.

higher than that of healthy individuals, and it is well-established that obesity, especially central (visceral) obesity, is a key contributor to metabolic syndrome.[21] Additionally, a study of patients with polycystic ovary syndrome (PCOS) revealed that the MHR levels in the PCOS group were significantly higher than those in the control group. Furthermore, patients with both obesity and PCOS exhibited significantly higher MHR levels than lean patients with PCOS.[34] Therefore, we hypothesized that MHR, as a novel inflammatory indicator, may be associated with visceral obesity. This study found that MHR in patients with T2DM and visceral obesity was significantly higher than in those without visceral obesity, and that MHR was positively correlated and independent associated with VFA. The main risk factors for the occurrence of diabetic complications are poor blood sugar control and a long disease course.[35–37] After we stratified participants based on HbA1c level and disease course, MHR remained independently associated with VFA. Our discovery was in the same direction as previous researches.

However, the mechanisms underlying the interaction between MHR and visceral obesity remain unclear. Previous studies have found that monocytes and macrophages play an important role in the synthesis and release of pro-inflammatory and pro-oxidative cytokines.[38] In the context of obesity, hypertrophic adipocytes and hypoxia within expanding visceral adipose tissue (VAT) secrete chemokines which recruit circulating classical monocytes into VAT. Upon infiltration, these monocytes differentiate into macrophages and can polarize towards a pro-inflammatory M1 phenotype, amplifying local inflammation through cytokine signaling (eg, TNF-α, IL-6) and contributing to systemic insulin resistance.[39,40] Moreover, the migration of peripheral blood mononuclear cells contributes not only to the

Table 5 The AUC of MHR, HDL-C, and MONO for Predicting the VFA in Patients with T2DM

	AUC	95% CI	Sensitivity	Specificity
MHR	0.708	0.687–0.730	0.73	0.58
HDL-C	0.653	0.630–0.676	0.40	0.37
MONO	0.658	0.635–0.681	0.54	0.68

Abbreviations: MONO, monocyte count; HDL-C, high-density lipoprotein cholesterol; MHR, monocyte to high-density lipoprotein cholesterol ratio.

accumulation of macrophages in adipose tissue but also to their proliferation in adipose tissue.[41–43] HDL-C has been shown to protect endothelial cells from the harmful effects of LDL-C and prevent the oxidation of LDL-C, acting as an anti-inflammatory and antioxidant agent.[44–46] However, a low HDL-C level, as often seen in visceral obesity, may thus fail to adequately counterbalance these pro-inflammatory processes. Therefore, studies suggest that MHR, as the ratio of MONO and HDL-C, can more objectively reflect the level of inflammatory response, and the body's chronic inflammatory response is closely related to obesity and insulin resistance.

Our findings align with this pathophysiological model. The positive correlation and the independent association of MHR with VFA we observed suggest that this circulating inflammatory indicator is robustly linked to visceral fat accumulation. MHR integrates both pro-inflammatory (monocyte) and anti-inflammatory (HDL-C) signals from the systemic circulation, the strength of this association likely reflects the interplay between systemic inflammation and adipose-tissue-specific inflammatory pathways. In our ROC analysis, MHR had superior predictive value for VFA compared to MONO or HDL-C alone (AUC: 0.708 vs 0.658 and 0.653, respectively), implying that the ratio captures synergistic pathophysiological information. Furthermore, we also compared the contributions of HDL-C and MONO. If HDL-C were the predominant driver, we might expect a stronger inverse correlation and a larger AUC difference compared to MONO, which was not the case (MONO vs HDL-C AUC difference: 0.00472, p=0.772). Therefore, it is more appropriate to use MHR which is a circulating proxy to explore the correlation with VFA.

Our study has several limitations. First, magnetic resonance imaging (MRI) and computerized tomography (CT) are internationally recognized as more precise methods, but previous researches have demonstrated that BIA correlated highly with CT measurements, and even believed that BIA could be an alternative to CT to evaluate VFA in patients with T2DM.[47,48] Second, the participants included in this study were recruited from Zhejiang Province in China, which may limit the generalizability of our findings owing to potential differences in race, lifestyle, and regional characteristics. Third, given the cross-sectional design of this study, causality between MHR and visceral obesity could not be established. Further longitudinal studies are warranted to clarify these relationships and explore their underlying mechanisms.

Conclusion

Elevated MHR was positively associated with VFA in T2DM patients, which has a modest predictive value. This index is simple, cost-effective, and extensively used in clinical settings, making it a practical indicator for screening and predicting visceral obesity. Therefore, routine screening of this index in patients with T2DM may help detect and intervene in visceral obesity at an early stage, thereby reducing the risk of associated cardiovascular events.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics Clearance

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Zhejiang Provincial People's Hospital (Ethics Approval Number: QT2024208). As this study was retrospective in nature, the ethical review granted an exemption from informed consent based on the initial patient consent form. Therefore, the study was conducted without obtaining informed consent from the survey participants.

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Author Contributions

Conceptualization: Ye Hu, Xiaohong Wu. Data curation: Ye Hu, Yubo Xing, Yingxiang Song. Formal analysis: Ye Hu, Jia Zheng. Funding acquisition: Ye Hu, Xiaohong Wu. Investigation: Ye Hu, Yubo Xing. Methodology: Ye Hu, Jia

Zheng. Project administration: Ye Hu, Xiaohong Wu. Resources: Xiaohong Wu. Writing-original draft: Ye Hu. Writing-review & editing: Ye Hu, Jia Zheng, Xiaohong Wu. All authors took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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