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ORIGINAL RESEARCH

# Association Between Platelet Parameters and Metabolic Syndrome in Residents of Wuhu, China: A Mediation Analysis of Insulin Resistance

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Video Abstract

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**Objective:** To examine the associations between platelet parameters and metabolic syndrome (MetS) and to explore their relationships with insulin resistance (IR).

**Patients and Methods:** This cross-sectional study included approximately 570,000 adults who underwent health examinations at the Health Management Center of the First Affiliated Hospital of Wannan Medical College between 2017 and 2023. Demographic and behavioral data were collected using questionnaires, and relevant clinical measurements were obtained through physical examinations. Platelet parameters and metabolic indicators were measured using an automated analyzer. Restricted cubic spline (RCS) models and multivariable logistic regression analyses were used to assess the associations between platelet parameters and MetS. Bootstrap-based mediation analysis was applied to explore the statistical associations among platelet parameters, IR, and MetS.

**Results:** The prevalence of MetS was 19.5%. Platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) were all positively associated with MetS (all $P < 0.001$). After multivariable adjustment, PCT and PDW showed relatively stronger associations with MetS (PCT: Q4 vs Q1, aOR = 1.85, 95% CI: 1.81–1.89; PDW: Q4 vs Q1, aOR = 1.73, 95% CI: 1.69–1.76). Multivariable linear regression analysis showed that PDW was positively associated with IR assessed by the triglyceride–glucose index (TyG) ($\beta = 0.150$, 95% CI: 0.146–0.155). Within the analytical models of this study, PDW, IR, and MetS exhibited statistically significant associations.

**Conclusion:** Elevated platelet parameters were positively associated with MetS, with particularly pronounced associations observed for PCT and PDW. PDW was significantly associated with IR, and IR was in turn closely associated with MetS.

**Keywords:** cross-sectional study, triglyceride-glucose index, biomarker, metabolic disorders, platelet activation

## Introduction

Metabolic syndrome (MetS) has become increasingly prevalent worldwide. Recent data show that the weighted prevalence of MetS was approximately 34.7% among US adults during, 2011–2016 [1] about 32.4% in African populations,[2] and approximately 31.1% among Chinese adults based on nationally representative surveillance.[3] This rising burden is largely driven by rapid urbanization, sedentary lifestyles, and shifts in dietary patterns, making MetS a major public health challenge.[4] MetS substantially increases the risk of chronic diseases, including cardiovascular disease and type 2 diabetes.[5,6] Therefore, effective prevention strategies and early screening are essential for timely identification and intervention. Platelet parameters are derived from routine complete blood counts, are low-cost and widely accessible, and thus have the potential to serve as early population-level indicators of MetS risk.[7]

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Previous studies suggest that platelet parameters are associated with various metabolic disorders and may reflect early metabolic abnormalities. Mean platelet volume (MPV) and platelet distribution width (PDW) are often elevated in individuals with diabetes and its complications.[8,9] In addition, platelet count (PLT) and plateletcrit (PCT) have been reported to correlate with obesity, hyperglycemia, and dyslipidemia.[10] Regarding MetS, some studies have reported higher PLT, PDW, and PCT among individuals with MetS.[11] In contrast, a meta-analysis indicates that the most consistent alteration in MetS is an increased PLT, whereas differences in MPV are not significant.[12] Overall, the evidence on the associations between platelet parameters and MetS remains inconsistent, and these relationships warrant further investigation.

Among platelet indices, PDW reflects heterogeneity in platelet volume distribution and is commonly regarded as an indirect indicator related to platelet activation and turnover.[13,14] Insulin resistance (IR), a key pathophysiological basis of MetS,[15] is frequently accompanied by endothelial dysfunction and enhanced oxidative stress.[16] These alterations may promote platelet activation and increase heterogeneity in platelet morphology and volume distribution, thereby resulting in elevated PDW.[17,18] In addition, IR-related adipokine imbalance, such as altered levels of leptin and adiponectin, may further modulate platelet reactivity and exacerbate changes in PDW.[19] Conversely, activated platelets can release various pro-inflammatory mediators and aggravate endothelial inflammatory responses, which may in turn interfere with insulin signaling and contribute to the persistence or progression of IR-related metabolic abnormalities.[20] Based on these considerations, the present study aimed to evaluate the associations between platelet parameters and MetS, and to further explore their relationships with IR–related metabolic status.

# Materials and Methods

## Study Population

This study was based on health examination data collected between 2017 and 2023 at the Health Check-up Center of the First Affiliated Hospital of Wannan Medical College in Wuhu, Anhui Province, China. Adults aged 18 years or older were eligible for inclusion. Participants were identified through encrypted personal identification numbers, and for individuals with multiple examination records, only the earliest record was retained to ensure that each participant was included once.

According to a predefined data-cleaning protocol, records with missing key variables were excluded, including platelet parameters (PLT, PDW, MPV, and PCT), anthropometric measurements (height and weight), blood pressure measurements (SBP and DBP), metabolic indicators (triglycerides, HDL-C, and fasting plasma glucose), as well as demographic and lifestyle information (age, sex, smoking status, alcohol consumption, and marital status). Body mass index (BMI) was subsequently calculated. Records with implausible or extreme values were also excluded to minimize the influence of potential data entry or measurement errors.

After these exclusions, a total of 577,431 participants were included in the final analysis, comprising 317,973 men and 259,458 women.

## Questionnaire

Information on demographic characteristics (age, sex, and marital status) and lifestyle factors (smoking and alcohol consumption) was obtained through a standardized questionnaire.

## Physical Examination

Anthropometric measurements were obtained with participants barefoot and wearing light clothing. Height (±0.1 cm) and weight (±0.1 kg) were measured using calibrated instruments, and body mass index (BMI) was calculated as weight divided by height squared ($kg/m^2$). Blood pressure was measured in the right arm after participants had rested for at least 5 minutes. Two measurements were taken using standardized equipment, and the average values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded.

## Laboratory Measurements

Blood samples were collected in the morning after an overnight fast via venipuncture, and all samples were analyzed within 24 hours of collection. Platelet parameters, including platelet count (PLT), platelet distribution width (PDW), mean platelet volume (MPV), and plateletcrit (PCT), as well as metabolic parameters, including high-density lipoprotein cholesterol, triglycerides, and fasting plasma glucose, were measured using automated analyzers. All laboratory analyses were performed by trained laboratory personnel following standardized procedures.

The triglyceride–glucose (TyG) index, a surrogate marker of insulin resistance, was calculated as ln [fasting triglycerides (mg/dL) × fasting plasma glucose (mg/dL)/2].[21] The reference ranges for platelet parameters were as follows: PLT, 150–450 × 10□/L; MPV, 6.7–9.6 fL; PCT, 0.14–0.28% for males and 0.15–0.31% for females;[22] and PDW, 15.0–17.6%.[23]

## Diagnostic Criteria

MetS was defined according to the modified Adult Treatment Panel III (ATP III) criteria.[24] Participants who met three or more of the following five components were classified as having metabolic syndrome: (1) abdominal obesity, for which the definition was modified based on the Asia-Pacific World Health Organization guidelines[25] and defined as a body mass index (BMI) ≥25 kg/m$^2$ due to the unavailability of waist circumference data; (2) elevated triglycerides, defined as serum triglyceride levels ≥150 mg/dL (1.7 mmol/L); (3) reduced high-density lipoprotein cholesterol, defined as <40 mg/dL (1.0 mmol/L) in men and <50 mg/dL (1.3 mmol/L) in women; (4) elevated blood pressure, defined as blood pressure ≥130/85 mmHg or current use of antihypertensive medication; and (5) diabetes mellitus, defined as a fasting plasma glucose level ≥7.0 mmol/L or a previous physician-diagnosed history of diabetes mellitus.

## Statistical Analysis

Continuous variables are presented as means ± standard deviations, and categorical variables as frequencies (percentages). Group comparisons were performed using independent-samples *t* tests for continuous variables and chi-square tests for categorical variables. Participants were categorized into quartiles according to platelet parameter levels. Multivariable logistic regression models were used to assess the associations between platelet parameters and MetS, with results reported as adjusted odds ratios (aORs) and 95% confidence intervals (CIs). Covariates included age, sex, marital status, smoking status, alcohol consumption, and examination year.

Restricted cubic spline (RCS) models, with knots placed at the 5th, 35th, 65th, and 95th percentiles, were applied to examine potential nonlinear associations between platelet parameters and MetS. Stratified analyses were further conducted to evaluate the associations between PDW and MetS according to sex, age (≤65 and >65 years), smoking status, and alcohol consumption, with results presented using forest plots.

Multivariable linear regression models were used to examine the associations between platelet parameters and the TyG index, and logistic regression models were applied to assess the association between the TyG index and MetS. The TyG index was calculated using fasting triglyceride and fasting plasma glucose levels. Prior to analysis, the TyG index and PCT were standardized using Z-score transformation to improve the comparability of regression coefficients and model stability. Mediation analysis was performed using the Bootstrap method with 1000 resamples to evaluate the statistical associations among the TyG index, PDW, and MetS.

In analyses of MetS severity, participants were categorized according to the number of diagnostic components (three, four, or five). Multivariable logistic regression models were applied, with the lowest quartile (Q1) of platelet parameters and participants with mild MetS (three components) serving as the reference groups.

This study was a cross-sectional analysis based on a health examination database, and no a priori sample size calculation was performed. All eligible participants during the study period (n = 577,431) were included in the analyses.

All statistical analyses were conducted using R software (version 4.3; R Foundation for Statistical Computing), and a two-sided $P$ value < 0.05 was considered statistically significant.

# Results

## Baseline Characteristics

A total of 577,431 participants were included in this study, with an overall prevalence of MetS of 19.5%. As shown in Table 1, participants with MetS were significantly older and were more likely to be male, smokers, and alcohol drinkers compared with those without MetS (all $P < 0.0001$). In addition, statistically significant differences were observed in platelet parameters between the two groups. Participants with MetS showed higher levels of PLT, MPV, PCT, and PDW than those without MetS (all $P < 0.0001$).

## Association Between Platelet Parameters and Metabolic Syndrome

As shown in Table 2, higher quartiles of platelet parameters were generally associated with increased odds of MetS in both unadjusted and fully adjusted models. In the fully adjusted model, PCT showed the strongest association with MetS (Q4 vs Q1: aOR = 1.85, 95% CI: 1.81–1.89; P < 0.0001). PDW was also strongly associated with MetS (Q4 vs Q1: aOR = 1.73, 95% CI: 1.69–1.76; P < 0.0001). PLT demonstrated a moderate association (Q4 vs Q1: aOR = 1.58, 95% CI: 1.55–1.61; P < 0.0001), whereas MPV showed a weaker but still statistically significant association (Q4 vs Q1: aOR = 1.08, 95% CI: 1.05–1.10; P < 0.0001).

## Platelet Parameters and MetS in Relation to IR

As shown in Table 3, multivariable linear regression analyses demonstrated statistically significant positive associations between platelet parameters and the TyG index, with PDW exhibiting the most pronounced association ($\beta = 0.150$, 95% CI: 0.146–0.155; $P < 0.0001$). In multivariable logistic regression models, the TyG index was significantly associated with MetS. Each 1-SD increase in the TyG index was associated with higher odds of MetS (aOR = 7.10, 95% CI: 7.01–7.19; $P < 0.0001$).

**Table 1** Baseline Characteristics of the Study Participants Stratified by MetS Status

| Characteristic | Overall | Metabolic Syndrome | | *P* value |
|---|---|---|---|---|
| | | No | Yes | |
| All persons (n) | n=577431 | n=464635 | n=112796 | |
| Age (years), mean ± SD | 45.60±13.45 | 44.71±13.44 | 49.30±12.88 | <0.0001 |
| Sex, n (%) | | | | <0.0001 |
| Male | 317,973(55.1) | 236,061(50.8) | 81,912(72.6) | |
| Female | 259,458(44.9) | 228,574(49.2) | 30,884(27.4) | |
| Smoking status, n (%) | | | | <0.0001 |
| Yes | 119,555(20.7) | 85,162(18.3) | 34,393(30.5) | |
| No | 457,876(79.3) | 379,473(81.7) | 78,403(69.5) | |
| Alcohol consumption, n (%) | | | | <0.0001 |
| Yes | 145,681(25.2) | 103,272(22.2) | 42,409(37.6) | |
| No | 431,750(74.8) | 361,363(77.8) | 70,387(62.4) | |
| Platelet parameters, mean ± SD | | | | |
| Platelet count,($10^9$/L) | 209.10±56.50 | 208.60±56.00 | 211.30±58.30 | <0.0001 |
| Mean platelet volume (fL) | 10.80±1.50 | 10.88±1.49 | 10.96±1.51 | <0.0001 |
| Plateletcrit (%) | 0.22±0.05 | 0.22±0.05 | 0.23±0.05 | <0.0001 |
| Platelet distribution width (%) | 16.28±0.54 | 16.26±0.55 | 16.37±0.52 | <0.0001 |

**Notes**: Continuous variables are presented as mean ± SD, and categorical variables as number (percentage).
**Abbreviation**: SD, standard deviation.

**Table 2** Study on the Association Between Platelet Parameters and Metabolic Syndrome

| Platelet Parameters | Unadjusted Model | | Multiple Adjusted Model | |
|---|---|---|---|---|
| | *OR* (95% *CI*) | *P* value | *aOR* (95% *CI*) | *P* value |
| Platelet count (×$10^9$/L) | | | | |
| Q1 | Reference | | Reference | |
| Q2 | 0.96(0.94,0.98) | <0.0001 | 1.09(1.07,1.12) | <0.0001 |
| Q3 | 0.99(0.98,1.01) | 0.5151 | 1.26(1.23,1.28) | <0.0001 |
| Q4 | 1.11(1.09,1.13) | <0.0001 | 1.58(1.55,1.61) | <0.0001 |
| Mean platelet volume (fL) | | | | |
| Q1 | Reference | | Reference | |
| Q2 | 1.06(1.04,1.08) | <0.0001 | 1.03(1.01,1.05) | 0.0028 |
| Q3 | 1.09(1.07,1.11) | <0.0001 | 1.04(1.02,1.06) | <0.0001 |
| Q4 | 1.16(1.14,1.18) | <0.0001 | 1.08(1.05,1.10) | <0.0001 |
| Plateletcrit (%) | | | | |
| Q1 | Reference | | Reference | |
| Q2 | 0.99(0.97,1.00) | 0.1738 | 1.16(1.14,1.19) | <0.0001 |
| Q3 | 1.07(1.05,1.09) | <0.0001 | 1.39(1.37,1.42) | <0.0001 |
| Q4 | 1.25(1.23,1.28) | <0.0001 | 1.85(1.81,1.89) | <0.0001 |
| Platelet distribution width (%) | | | | |
| Q1 | Reference | | Reference | |
| Q2 | 1.22(1.20,1.24) | <0.0001 | 1.09(1.07,1.12) | <0.0001 |
| Q3 | 1.55(1.51,1.58) | <0.0001 | 1.31(1.29,1.34) | <0.0001 |
| Q4 | 2.11(2.07,2.15) | <0.0001 | 1.73(1.69,1.76) | <0.0001 |

**Notes**: The unadjusted model provides crude estimates without covariate adjustment. The multivariable-adjusted model was adjusted for age, sex, marital status, smoking status, alcohol consumption, and examination year. Platelet parameters were analyzed in quartiles, with the lowest quartile (Q1) serving as the reference group. Quartiles of platelet parameters were defined as follows: platelet count (PLT, ×10□/L): Q1 ≤171, Q2 172–206, Q3 207–243, and Q4 >243; mean platelet volume (MPV, fL): Q1 ≤9.8, Q2 9.9–10.7, Q3 10.8–11.8, and Q4 >11.8; plateletcrit (PCT, %): Q1 ≤0.190, Q2 0.200–0.220, Q3 0.230–0.252, and Q4 >0.252; platelet distribution width (PDW, %): Q1 ≤16.1, Q2 16.2–16.3, Q3 16.4–16.6, and Q4 >16.6.
**Abbreviations**: OR, odds ratio; CI, confidence interval; aOR, adjusted odds ratio.

**Table 3** Associations Among Platelet Parameters, TyG Index, and Metabolic Syndrome

| **Panel A. Associations between platelet parameters and TyG index (linear regression)** | | | |
|---|---|---|---|
| **Platelet parameter** | **β (95% CI)** | | ***P* value** |
| Platelet distribution width (%) | 0.150 (0.146, 0.155) | | <0.0001 |
| Mean platelet volume (fL) | 0.015 (0.014, 0.017) | | <0.0001 |
| Platelet count (10^9/L) | 0.0015 (0.0014, 0.0016) | | <0.001 |
| Plateletcrit (%, standardized) | 0.123 (0.121, 0.126) | | <0.0001 |
| **Panel B. Association between TyG index and metabolic syndrome (logistic regression)** | | | |
| **Predictor** | **Outcome** | **Adjusted OR (95% CI)** | ***P* value** |
| TyG index (per 1 SD increase) | Metabolic syndrome | 7.099(7.008,7.192) | <0.0001 |

**Notes**: In Panel A, β coefficients were derived from multivariable linear regression models with the TyG index as a continuous outcome; PCT was standardized using Z-score transformation, whereas other platelet parameters were entered on their original scales. In Panel B, ORs were derived from multivariable logistic regression models with MetS as the outcome, with the TyG index entered per 1 SD increase. All models were adjusted for age (continuous), sex, marital status, smoking status, alcohol consumption, and examination year.
**Abbreviations**: TyG, triglyceride–glucose; OR, odds ratio; CI, confidence interval; SD, standard deviation.


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## Restricted Cubic Spline Analysis of Platelet Parameters and MetS

Restricted cubic spline analyses (Figure 1) showed distinct patterns in the associations between platelet parameters and MetS. MPV was associated with MetS in an approximately linear manner. For both PLT and PCT, the odds of MetS increased gradually across most of their distributions, with a steeper increase observed at higher levels. PDW showed a non-linear association with MetS, with an evident change in the slope of the curve around 16.3%.

## Correlation of Platelet Parameters with MetS Components

Table 4 reveals distinct associations of platelet parameters with MetS components: (1) PDW showed the strongest associations, particularly with elevated triglycerides (OR = 1.556, 95% CI: 1.531–1.581) and fasting plasma glucose (OR = 1.367, 95% CI: 1.334–1.401). (2) PCT was associated with hypertension (OR = 1.133, 95% CI: 1.098–1.168) and hyperglycemia (OR = 1.144, 95% CI: 1.092–1.199). (3) MPV exhibited weaker, though positive, associations with overweight/obesity (OR = 1.052, 95% CI: 1.039–1.065) and hypertriglyceridemia (OR = 1.064, 95% CI: 1.051–1.077). (4) PLT demonstrated minimal associations across components (OR range: 1.000–1.005).

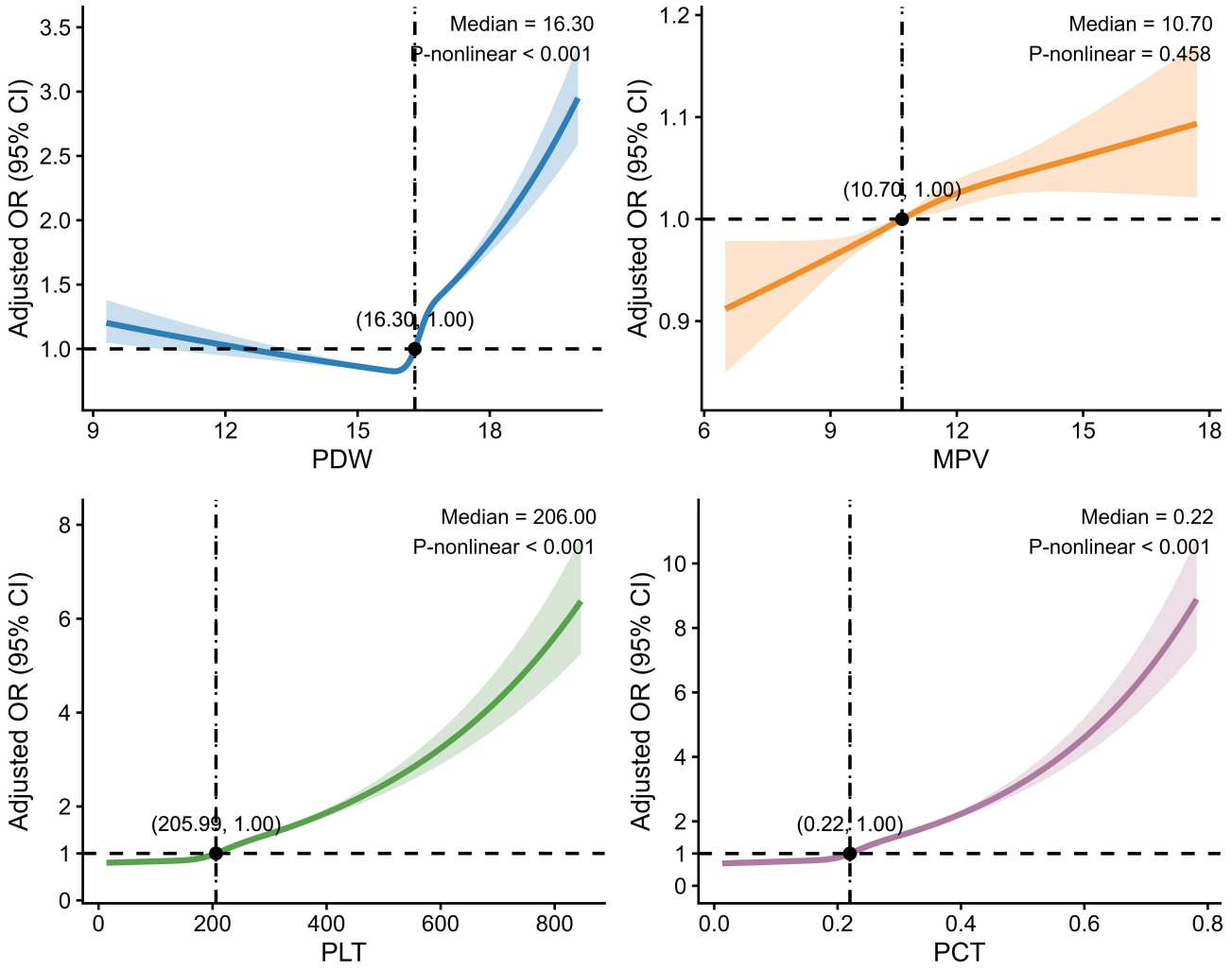


**Figure 1** Restricted cubic spline analyses of platelet parameters and the odds of metabolic syndrome. Solid lines represent adjusted odds ratios, and shaded areas indicate 95% confidence intervals. The horizontal dashed line denotes an odds ratio of 1.0, and the vertical dashed line represents the median value of each platelet parameter used as the reference. Models were adjusted for age, sex, marital status, smoking status, alcohol consumption, and examination year.
**Abbreviations**: PLT, platelet count; MPV, mean platelet volume; PDW, platelet distribution width; PCT, plateletcrit; OR, odds ratio; CI, confidence interval.


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**Table 4** Relationship Between Platelet Parameters and MetS Components

| | Overweight/Obesity | Elevated BP | Elevated TG | Reduced HDL-C | Elevated FPG |
|---|---|---|---|---|---|
| | *OR (95% CI)* | *OR (95% CI)* | *OR (95% CI)* | *OR (95% CI)* | *OR (95% CI)* |
| **Mean platelet volume (fL)** | 1.052(1.039,1.065) *P*<0.0001 | 1.050(1.037,1.062) *P*<0.0001 | 1.064(1.051,1.077) *P*<0.0001 | 1.040(1.020,1.221) *P*=0.322 | 1.061(1.061,1.062) *P*=0.0802 |
| **Platelet count (10^9/L)** | 1.003(1.003,1.004) *P*<0.0001 | 1.001(1.000,1.002) *P*<0.0001 | 1.005(1.004,1.006) *P*<0.0001 | 1.005(1.004,1.006) *P*<0.0001 | 1.000(0.999,1.001) *P*=0.6205 |
| **Plateletcrit (%)** | 1.095(1.062,1.129) *P*<0.0001 | 1.133(1.098,1.168) *P*<0.0001 | 1.044(1.011,1.077) *P*=0.0077 | 0.864(0.823,0.906) *P*=0.973 | 1.144(1.092,1.199) *P*<0.0001 |
| **Platelet distribution width (%)** | 1.197(1.181,1.213) *P*<0.0001 | 1.098(1.085,1.112) *P*<0.0001 | 1.556(1.531,1.581) *P*<0.0001 | 1.194(1.168,1.221) *P*<0.0001 | 1.367(1.334,1.401) *P*<0.0001 |

**Notes**: Values are odds ratios derived from multivariable logistic regression models, with corresponding 95% confidence intervals. All models were adjusted for age, sex, marital status, smoking status, alcohol consumption, and examination year.
**Abbreviations**: BP, blood pressure; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose; OR, odds ratio; CI, confidence interval.

## Subgroup Analysis by Hypertension and Diabetes Status

The subgroup analyses, stratified by hypertension and diabetes status, revealed heterogeneity in the strength of associations between platelet parameters and MetS (Tables 5 and 6). Among hypertensive individuals, higher quartiles of PLT, PDW, and PCT were associated with increased odds of MetS. PDW showed the strongest association (Q4 OR = 1.64, 95% CI: 1.60–1.69), while the association for MPV was weak (Q4 OR = 1.08, 95% CI: 1.05–1.10). In the non-hypertensive subgroup, PCT exhibited the strongest association (Q4 OR = 1.86, 95% CI: 1.79–1.92).

In participants with diabetes, PLT, PDW, and PCT were associated with MetS, with PCT showing the strongest association (Q4 OR = 1.55, 95% CI: 1.45–1.65). Among non-diabetic participants, positive associations were observed for all platelet parameters, with the strongest association again seen for PCT (Q4 OR = 1.88, 95% CI: 1.84–1.93).

## Forest Plot of PDW and MetS

Forest plot analysis (Figure 2) revealed differences in the association between PDW and MetS across population subgroups, with statistically significant interaction effects (all P for interaction < 0.001). The association was more pronounced in men (OR = 1.460, 95% CI: 1.434–1.488) than in women (OR = 1.183, 95% CI: 1.153–1.214). Similarly, stronger associations were observed among smokers (OR = 1.539, 95% CI: 1.494–1.586) compared to non-smokers (OR = 1.319, 95% CI: 1.296–1.342), and among alcohol drinkers (OR = 1.499, 95% CI: 1.459–1.539) compared to non-drinkers (OR = 1.318, 95% CI: 1.295–1.342). Although a statistically significant interaction by age was present (P <

**Table 5** Associations of Platelet Parameters with Metabolic Syndrome by Hypertension

| PLT,% | *OR (95% CI)* | *P* value | MPV,fL | *OR (95% CI)* | *P* value | PDW,% | *OR (95% CI)* | *P* value | PCT,% | *OR (95% CI)* | *P* value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Hypertension | | | | | | | | | | | |
| Q1 | Reference | | Q1 | Reference | | Q1 | Reference | | Q1 | Reference | |
| Q2 | 1.05(1.02,1.08) | <0.0001 | Q2 | 1.03(1.00,1.06) | 0.0151 | Q2 | 1.11(1.08,1.14) | <0.0001 | Q2 | 1.08(1.05,1.11) | <0.0001 |
| Q3 | 1.14(1.10,1.17) | <0.0001 | Q3 | 1.06(1.03,1.09) | 0.0001 | Q3 | 1.29(1.26,1.33) | <0.0001 | Q3 | 1.19(1.16,1.23) | <0.0001 |
| Q4 | 1.28(1.24,1.31) | <0.0001 | Q4 | 1.08(1.05,1.10) | <0.0001 | Q4 | 1.64(1.60,1.69) | <0.0001 | Q4 | 1.43(1.39,1.47) | <0.0001 |
| Non-Hypertension | | | | | | | | | | | |
| Q1 | Reference | | Q1 | Reference | | Q1 | Reference | | Q1 | Reference | |
| Q2 | 1.06(1.02,1.10) | 0.0011 | Q2 | 1.01(0.98,1.05) | 0.4875 | Q2 | 1.07(1.04,1.11) | 0.0001 | Q2 | 1.14(1.10,1.18) | <0.0001 |
| Q3 | 1.23(1.18,1.27) | <0.0001 | Q3 | 1.00(0.97,1.03) | 0.9781 | Q3 | 1.26(1.21,1.30) | <0.0001 | Q3 | 1.39(1.34,1.44) | <0.0001 |
| Q4 | 1.61(1.56,1.67) | <0.0001 | Q4 | 1.03(1.00,1.06) | 0.9781 | Q4 | 1.59(1.53,1.64) | <0.0001 | Q4 | 1.86(1.79,1.92) | <0.0001 |


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**Table 6** Associations of Platelet Parameters with Metabolic Syndrome by Diabetes

| PLT,% | *OR (95% CI)* | P value | MPV,fL | *OR (95% CI)* | P value | PDW,% | *OR (95% CI)* | P value | PCT,% | *OR (95% CI)* | *P value* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Diabetes | | | | | | | | | | | |
| Q1 | Reference | | Q1 | Reference | | Q1 | Reference | | Q1 | Reference | |
| Q2 | 1.10(1.04,1.17) | 0.0012 | Q2 | 1.03(0.96,1.09) | 0.3646 | Q2 | 1.10(1.02,1.18) | 0.0134 | Q2 | 1.11(1.05,1.18) | <0.0001 |
| Q3 | 1.24(1.16,1.32) | <0.0001 | Q3 | 1.02(0.95,1.09) | 0.5713 | Q3 | 1.26(1.17,1.35) | <0.0001 | Q3 | 1.34(1.26,1.43) | <0.0001 |
| Q4 | 1.44(1.34,1.54) | <0.0001 | Q4 | 1.07(1.01,1.15) | 0.0371 | Q4 | 1.57(1.46,1.69) | <0.0001 | Q4 | 1.55(1.45,1.65) | <0.0001 |
| Non-Diabetes | | | | | | | | | | | |
| Q1 | Reference | | Q1 | Reference | | Q1 | Reference | | Q1 | Reference | |
| Q2 | 1.11(1.09,1.14) | <0.0001 | Q2 | 1.01(0.99,1.03) | 0.5530 | Q2 | 1.07(1.05,1.10) | <0.0001 | Q2 | 1.19(1.16,1.22) | <0.0001 |
| Q3 | 1.28(1.26,1.31) | <0.0001 | Q3 | 1.01(0.98,1.03) | 0.6257 | Q3 | 1.25(1.22,1.28) | <0.0001 | Q3 | 1.42(1.39,1.45) | <0.0001 |
| Q4 | 1.64(1.60,1.67) | <0.0001 | Q4 | 1.03(1.00,1.05) | 0.0193 | Q4 | 1.55(1.51,1.58) | <0.0001 | Q4 | 1.88(1.84,1.93) | <0.0001 |

**Notes**: Analyses were stratified by hypertension status (Table 5) and diabetes status (Table 6). Odds ratios were estimated using multivariable logistic regression models adjusted for age, sex, marital status, smoking status, alcohol consumption, and examination year.
**Abbreviations**: PLT, platelet count; MPV, mean platelet volume; PDW, platelet distribution width; PCT, plateletcrit; OR, odds ratio; CI, confidence interval.

0.001), the odds ratios were similar between participants aged ≤65 years (OR = 1.358, 95% CI: 1.337–1.380) and those >65 years (OR = 1.374, 95% CI: 1.308–1.443).

## Mediation Analysis of PDW and MetS

The TyG index was selected as an indicator of IR for mediation analysis. The total effect of PDW on MetS was 0.00165 (95% CI: 0.00136–0.00198). The indirect effect was 0.00168 (95% CI: 0.00133–0.00213). After inclusion of the TyG index, the direct effect of PDW on MetS was no longer statistically significant (direct effect = −0.0000365, 95% CI: −0.000152–0.0000424). The proportion mediated was 102.2% (95% CI: 97.1–107.8%) (Figure 3).

Additional mediation and severity analyses are presented in Supplementary Figure S1 and Supplementary Table S1.

# Discussion

In this large population-based study, all platelet parameters (PLT, MPV, PDW, and PCT) were significantly and positively associated with MetS after multivariable adjustment, with relatively stronger associations observed for PCT and PDW. Notably, PDW showed a robust association with MetS and was also positively correlated with triglycerides, fasting glucose, and the insulin resistance surrogate TyG. Further mediation analyses suggested that the association between PDW and MetS may, to some extent, be related to its correlation with IR.

The biological mechanisms linking MetS with platelet parameters are not yet fully elucidated; however, previous studies provide a biological basis for the present findings. MetS is characterized by a state of chronic low-grade inflammation,[26] which may enhance megakaryocyte activity and platelet production, leading to increased PLT.[27] Inflammatory factors and metabolic disturbances, such as hyperglycemia and dyslipidemia, may also be associated with platelet activation and increased size heterogeneity, manifested as elevated PDW,[28] whereas increased PCT may reflect combined changes in platelet number and volume.[29] In contrast, although the association between MPV and MetS was statistically significant, the effect size was small, suggesting potentially limited clinical relevance, which may be attributable to the influence of multiple physiological and pathological factors on MPV.[30]

Nevertheless, the overall effect sizes of platelet parameters were modest, with adjusted odds ratios mainly ranging from approximately 1.1 to 1.9 (Table 2). Compared with traditional metabolic risk factors, platelet parameters are not strong clinical predictors, but may serve as readily accessible supplementary markers reflecting underlying inflammatory and metabolic dysregulation associated with MetS.

PDW was closely associated with individual components of MetS, showing particularly strong positive correlations with triglyceride levels and fasting plasma glucose. Previous studies have suggested that hypertriglyceridemia may induce lipotoxicity, chronic low-grade inflammation, and oxidative stress, thereby affecting megakaryopoiesis and platelet membrane properties, which can increase platelet size heterogeneity and result in elevated PDW.[31,32] In addition,

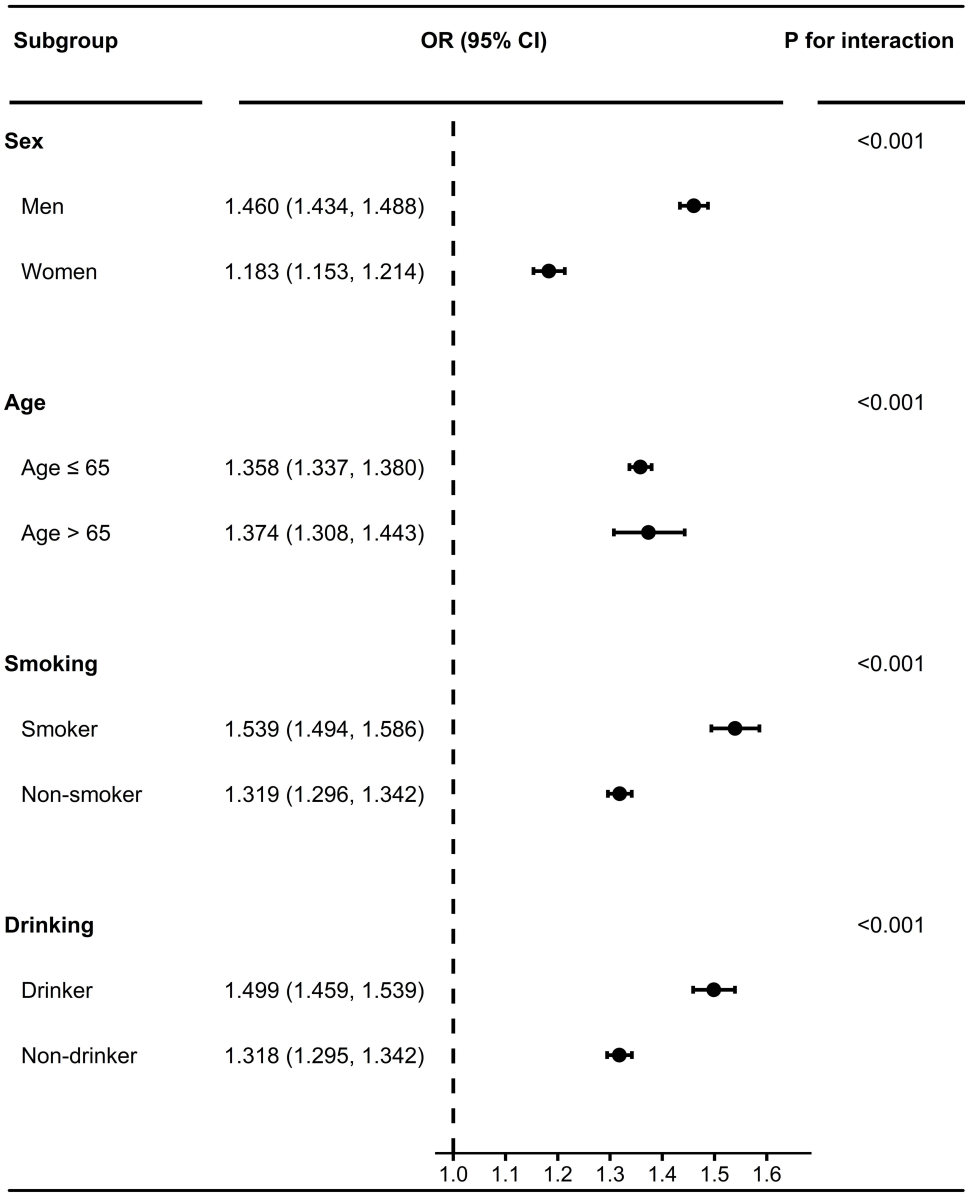


**Figure 2** Subgroup analyses of the association between PDW and MetS. ORs and 95% CIs were estimated using multivariable logistic regression models, adjusted for age, sex, marital status, smoking status, drinking status, and examination year, except for the stratification variable. The dashed vertical line indicates the null value (OR = 1.0). *P* for interaction was calculated by including an interaction term between PDW and each subgroup variable.
**Abbreviations**: PDW, platelet distribution width; MetS, metabolic syndrome; OR, odds ratio; CI, confidence interval.

hyperglycemia has been shown to promote non-enzymatic glycation of platelet membrane proteins and enhance platelet activation, leading to structural and functional alterations of platelets that may also contribute to increased PDW.[33]

The TyG index, derived from triglycerides and fasting plasma glucose, is a commonly used surrogate marker of IR.[34] PDW was also significantly positively correlated with the TyG index, indicating an association between PDW and IR-related metabolic status. Therefore, results from analyses of individual metabolic components (Table 4) and the composite metabolic indicator (Table 3) were consistent in the direction of association.

Previous studies have reported that the reference range of PDW in healthy adults is approximately 15.0%–17.6%.[23] In the RCS analysis of the present study, the odds of MetS changed only modestly at lower PDW levels, whereas a more pronounced upward trend in the association was observed when PDW exceeded the median value (16.3%), indicating a non-linear association. This pattern may reflect a transition of platelet status from a relatively compensatory state to persistent activation in the context of progressively worsening metabolic disturbance and chronic low-grade


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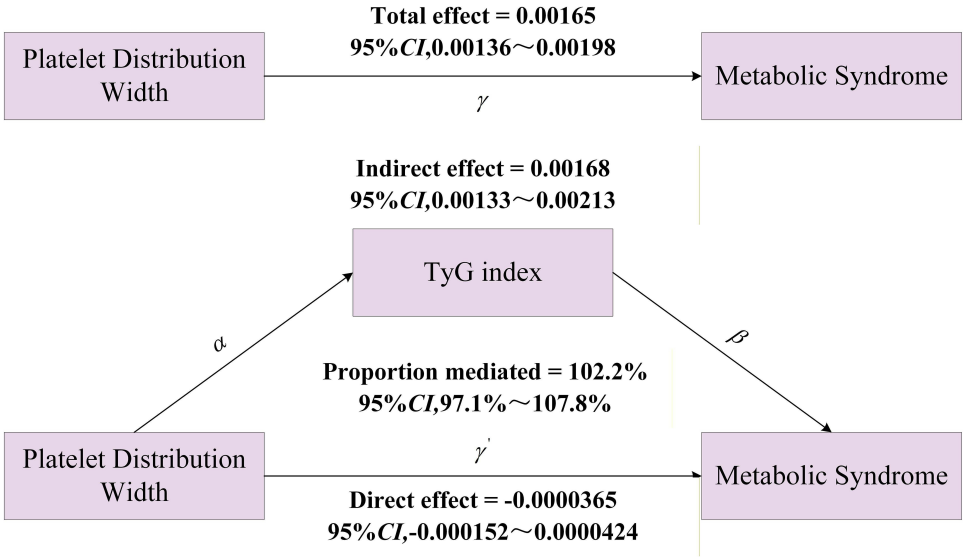


**Figure 3** Mediation model for the association between PDW and MetS with TyG as the mediator. Path α denotes the regression coefficient for the association between PDW and TyG estimated using linear regression. Path β denotes the regression coefficient for the association between TyG and MetS estimated using logistic regression. Path γ′ denotes the direct effect of PDW on MetS after adjustment for TyG, and path γ denotes the total effect of PDW on MetS without adjustment for TyG.
**Abbreviations**: TyG, triglyceride–glucose index; CI, confidence interval.

inflammation.[35] It should be emphasized that the PDW values indicated by the RCS analysis are intended solely to describe the shape of the risk association and should not be interpreted as clinical diagnostic thresholds; their generalizability requires further validation in prospective studies.

After stratification by hypertension and diabetes status, the strength of the association between platelet parameters and MetS showed some variation, which may be related to differences in platelet functional status under distinct metabolic backgrounds. Hypertension and diabetes are both closely associated with chronic low-grade inflammation, endothelial dysfunction, and sustained platelet activation.[17,36,37] Under these conditions, the baseline levels of certain platelet parameters may be altered, thereby reducing their discriminatory ability for MetS risk. PDW reflects heterogeneity in platelet volume distribution and is better able to capture the pathological state in which platelet production and consumption coexist;[13] therefore, it maintains a relatively stable association with MetS across different metabolic states.[13,38] Pharmacological treatments that modulate inflammatory responses and platelet function may, to some extent, influence the observed associations.[39]

Forest plot analyses showed that PDW was significantly associated with MetS across multiple population subgroups, although the magnitude of the association varied. Overall, the association appeared to be more pronounced in men and in individuals older than 65 years. These differences may be related to variations in baseline metabolic status, inflammatory burden, and lifestyle exposures across subgroups. In China, the prevalence of smoking and alcohol consumption is substantially higher in men than in women.[40] Smoking has been shown to increase platelet activation and aggregation, thereby influencing platelet morphology and size distribution.[41,42] Alcohol consumption may also interfere with platelet function and lipid metabolism, further enhancing platelet reactivity in the context of metabolic disturbance.[43] It should be noted that the above analyses were exploratory in nature and should not be interpreted as evidence of fundamental biological differences.

Although multiple platelet parameters were statistically associated with MetS, this study focused on PDW in the Discussion. Unlike PCT, which primarily reflects platelet mass and count burden, PDW better characterizes heterogeneity in platelet size and morphology.[13,18,44] In mediation analyses, PDW showed a closer statistical association with the IR surrogate index TyG, and its association with MetS remained relatively stable across different analytical models.

IR is a core pathophysiological feature of MetS.[15] We found that PDW was significantly associated with MetS and was positively correlated with IR-related metabolic indices (Table 3), suggesting close statistical coupling among PDW, IR, and MetS. Mediation analyses further showed that after adding IR-related indices to the model, the effect estimate for

the PDW–MetS association was markedly attenuated. This finding indicates substantial overlap, at the statistical level, between the PDW–MetS association and IR-related metabolic status.

From a mechanistic perspective, elevated PDW reflects increased heterogeneity in platelet size and morphology and is generally indicative of enhanced platelet activation and accelerated turnover. Activated platelets can release a variety of inflammatory mediators and interact with monocytes and endothelial cells, thereby promoting low-grade inflammation and oxidative stress,[45] which may contribute to impairment of insulin signaling and the development and aggravation of IR.[36]

Given the cross-sectional design of the present study, the temporal sequence and directionality of the observed associations cannot be determined. A reverse influence of IR on platelet function and turnover cannot be excluded, and both may also change in parallel under the influence of upstream metabolic disturbances.

Prior evidence provides mechanistic support for IR-related abnormalities in platelet parameters. Under physiological conditions, insulin inhibits platelet aggregation and activation by stimulating platelet constitutive nitric oxide synthase (cNOS), thereby promoting nitric oxide production and increasing intracellular levels of cyclic guanosine monophosphate (cGMP) and cyclic adenosine monophosphate (cAMP).[18,46,47] In states of IR, this protective pathway may be impaired, rendering platelets more prone to a hyperreactive state.[48]

In sensitivity analyses (Supplementary Figure 1), when IR (as assessed by TyG) was specified as the exposure and PDW as the mediator, no significant mediation effect of PDW was observed, suggesting that PDW is unlikely to serve as an independent mediator in the IR–MetS relationship. Taken together, the findings across analyses indicate that the association between PDW and MetS more likely reflects its statistical correlation with insulin resistance. Given the overlap between TyG and components of MetS, the observed mediation effect should be interpreted as a statistical association rather than a causal pathway; a proportion mediated exceeding 100% may indicate suppression effects or inconsistent mediation, and causal inference should therefore be made with caution.

This study has several limitations: (1) the cross-sectional design precludes determination of the temporal sequence and causal relationships among PDW, IR, and MetS; (2) TyG was used as a surrogate marker of IR and is derived from triglyceride and glucose levels, which overlap with components of MetS and may have inflated the estimated proportion of mediation; (3) although multiple demographic and clinical confounders were adjusted for, the influence of unmeasured factors, such as inflammatory biomarkers or past and current medication use, cannot be fully excluded; (4) participants were recruited from a single-center health examination population in Wuhu, China, which may introduce selection bias and limit the generalizability of the findings; (5) given the large sample size, statistically significant associations with small effect sizes should be interpreted cautiously; and (6) future multi-center prospective cohort studies are warranted to further validate these findings.

## Conclusion

This cross-sectional study demonstrates consistent associations between elevated platelet parameters—particularly PCT and PDW—and increased odds of MetS, with PDW showing the most stable associations across analyses. PDW was significantly associated with IR, and IR was in turn strongly associated with MetS. These findings support PDW as a candidate hematological marker associated with MetS, while the potential predictive value of platelet parameters warrants confirmation in prospective longitudinal studies.

## Abbreviations

MetS, Metabolic Syndrome; PLT, Platelet Count; MPV, Mean Platelet Volume; PCT, Plateletcrit; PDW, Platelet Distribution Width; BMI, Body Mass Index; HDL-C, High-Density Lipoprotein Cholesterol; TG, Triglycerides; FPG, Fasting Plasma Glucose; ATP III, Adult Treatment Panel III; IR, Insulin Resistance; OR, Odds Ratio; CI, Confidence Interval; RCS, Restricted Cubic Spline; aOR, Adjusted Odds Ratio.

## Data Sharing Statement

The authors collected participant data and uploaded it to a database. This system conveniently shields irrelevant data and effectively protects participant privacy. The data supporting this study's findings are available from the Health Management Center at the First Affiliated Hospital of Wannan Medical College, Wuhu, China. However, access to

these data is restricted as they were used under license for this study and are not publicly available. Data can be provided upon reasonable request and with the Health Management Center's permission. For data requests, please contact Yufeng Wen, the corresponding author.

## Ethics Approval and Informed Consent

The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Committee of Wannan Medical College (Approval No. (2024) 7). A formal waiver of informed consent was granted for the use of pre-existing anonymized health records. All personally identifiable information (including names, identification numbers, and contact details) was permanently removed by the Medical Examination Center prior to data analysis, ensuring complete anonymization. Strict data protection protocols were maintained throughout the research.

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## Author Contributions

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Catherine Adaeze Ezeokafor: Writing – Review & Editing, Validation.
Yue Wu: Supervision, Validation, Writing – Review & Editing.
Xinyu Ma: Conceptualization, Supervision, Resources, Writing–Review & Editing.
Tong Wang: Methodology, Supervision, Resources, Writing–Review & Editing.
Yufeng Wen: Conceptualization, Supervision, Project Administration, Methodology, Writing – Review & Editing.
All authors 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 that they do not have any competing interests in this work.

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