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Development and validation of a predictive model for metabolic syndrome in a large cohort of people living with HIV

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Abstract

Background The global prevalence of metabolic syndrome (MetS) in people living with HIV (PLWH) is on the rise in the post era of antiretroviral therapy (ART). Nevertheless, there are no validated predictive models available for assessing the risk of MetS in this specific population.

Methods This study included PLWH who participated in annual follow-ups at Southern Medical University Nanfang Hospital from September 2022 to November 2023. Participants enrolled in this study were divided into the training set and validation set based on the follow-up duration. We employed both multivariate logistic regression and lasso regression to develop three distinct prediction models. Subsequently, the optimal model was determined through comprehensive analyses, including receiver operating characteristic (ROC) curve analysis, calibration curve, and decision curve analysis (DCA). Ultimately, we generated a nomogram for the optimal model and analyzed the correlation between the model score and the components of MetS.

Results A total of 1017 participants were included in this study, with 814 in the training set and 203 in the validation set. The ultimate prediction model of MetS risk in PLWH incorporated five factors: age, CD8 + T cell counts, controlled attenuation parameter (CAP), gamma-glutamyl transferase (γ-GT) and lactate dehydrogenase (LDH). The area under the ROC curve (AUC) of the model in the training set and validation set was 0.849 and 0.834, respectively. Furthermore, we revealed a significant correlation between the model score and the MetS components. Additionally, the model score revealed significant group differences in MetS and related metabolic disorders.

Conclusions This study established a potential model for predicting MetS in PLWH.

Keywords HIV/AIDS, Metabolic syndrome, Clinical prediction model, Nomogram, Clinical endocrinology

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Introduction

The post antiretroviral therapy (ART) era has witnessed a remarkable increase in the life expectancy of people living with HIV (PLWH) [1, 2]. However, this population is now confronted with age-related and antiretroviral treatment-related complications such as metabolic disorders, renal impairment, osteoporosis, neurocognitive impairment, and cardiovascular disease (CVD) [3–5]. Among these, the adverse prognostic implications associated with metabolic syndrome (MetS) are gradually emerging as a significant threat to the well-being of PLWH [6, 7].

MetS constitutes a complex interplay of components, encompassing abdominal obesity, impaired fasting glucose (IFG), elevated blood pressure, hypertriglyceridemia (HTG), and low levels of high-density lipoprotein cholesterol (HDL-C) [8]. Its primary clinical consequence is the occurrence of cardiovascular events, and it is intrinsically linked to an elevated risk of atherosclerosis and mortality [9, 10]. Immune activation and inflammation persist even with successful viral suppression from ART among PLWH, potentially leading to metabolic disturbances that contribute to MetS [11]. Additionally, the metabolic side effects of ART may exacerbate issues such as insulin resistance, dyslipidemia, and central obesity [12]. Therefore, the combination of sustained low-level immune activation, the metabolic toxicity associated with ART, and intricate interactions involving traditional risk factors may collectively elevate the risk of MetS among PLWH [13, 14].

The identification and management of MetS have become a critical issue for PLWH receiving combination antiretroviral therapy [4]. Nevertheless, despite these challenges, there is still a lack of effective and viable models for predicting MetS in this population. Therefore, the primary objective of this study was to establish an effective MetS prediction model in PLWH through regression analysis of a large cohort. We aim for this model to provide a theoretical basis for clinical decision-making and the implementation of health interventions, ultimately contributing to the reduction of poor prognosis in PLWH.

Methods

Study design

This cross-sectional study was conducted from September 2022 to November 2023 at Nanfang Hospital, affiliated with Southern Medical University. We included PLWH who participated in annual follow-ups during this period. Exclusion criteria encompassed individuals with (1) any history of cancer, (2) systemic infections, (3) pregnancy status, and (4) an absence of essential clinical data. Subsequently, the participant cohort was divided into the training cohort and the validation cohort based on follow-up dates, with the first 80% assigned to the training cohort for model construction and the remaining 20% to the validation cohort for model evaluation.

Data collection

We systematically gathered demographic and clinical information from the study participants. These data encompassed age, gender, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), the duration of ART, ART regimen, CD4+T cell counts, CD8+T cell counts, CD4/CD8 ratio, acquired immunodeficiency syndrome (AIDS) stage, white blood cell count (WBC), lymphocyte count (LYM), neutrophil count (NEU), monocyte count (MONO), eosinophil count (EOS), red blood cell count (RBC), hemoglobin (HGB), platelet count (PLT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin (ALB), globulin (G), total bilirubin (TBIL), direct bilirubin (DBIL), alkaline phosphatase (ALP), gamma-glutamyl transferase (γ-GT), uric acid (UA), creatinine (CR), blood urea nitrogen (BUN), estimated glomerular filtration rate (eGFR), triglycerides (TG), total cholesterol (CHOL), HDL-C, low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), fasting blood glucose (FPG), glycosylated hemoglobin A1c (HbA1c), lactate dehydrogenase (LDH), hydroxybutyrate dehydrogenase (HBDH), creatine kinase (CK), creatine kinase myocardial band (CKMB), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR). Concurrently, we conducted hepatic assessments on the participants utilizing transient elastography. The controlled attenuation parameter (CAP) was to evaluate liver steatosis and liver stiffness measurements (LSM) to assess liver fibrosis. The above data were sourced from medical records or databases.

Diagnosis of metabolic disorders

MetS was defined according to the International Diabetes Federation (IDF) criteria [8], which require the presence of any three of the five following components: (1) TG levels ≥ 1.70 mmol/L or being on treatment for dyslipidemia. (2) Low HDL-C levels were defined as < 1.0 mmol/L for men and < 1.3 mmol/L for women, or if the participant was receiving treatment for dyslipidemia. (3) Elevated blood pressure was defined as ≥ 130 mmHg and/or DBP ≥ 85 mmHg or if the participant was using antihypertensive medication. (4) FBG levels ≥ 5.6 mmol/L, a diagnosis of type 2 diabetes, or treatment with oral hypoglycemic agents. (5) Obesity was defined as waist circumference ≥ 90 cm for men or ≥ 80 cm for women, or BMI > 27.5 kg/m^2, based on the World Health Organization guidelines for the Asian population [15, 16].

In addition, metabolic disorders associated with MetS were defined as follows: HTG was defined as TG ≥ 1.7mmol/L [17]. Low level of high-density

lipoprotein, also known as hypoalphalipoproteinemia (HA), was defined as HDL-C≤1.03 mmol/L in men and ≤1.29 mmol/L in women [18]. Hypertension was defined as ≥140 mmHg, and/or DBP≥90 mmHg or if the participant was using antihypertensive medication [19]. Elevated fasting glucose includes diagnostic criteria for IFG and diabetes, defined as FPG≥5.6mmol/L [20, 21].

Construction and evaluation of the prediction model

In our study, we performed univariate and multivariate binary logistic regression analyses in the training set to identify factors associated with MetS in PLWH. Variables directly related to the definition of MetS were excluded, while all other variables were included in the univariate analysis. Variables demonstrating a p-value<0.05 in the univariate analysis were subsequently incorporated into the multivariate model. The independent predictors identified through this process served as the foundation for Model 1. Subsequently, we applied Least Absolute Shrinkage and Selection Operator (LASSO) regression analysis, using the same set of variables as in the logistic regression model. While cross-validation initially identified an optimal λ that selected a larger number of variables, we opted for a λ value that yielded the same number of variables as Model 1 to maintain model simplicity and interpretability. This selection allowed us to construct Model 2 with a comparable level of complexity. Drawing from the insights of these two models, we developed a simplified prediction model, denoted as Model 3.

To evaluate and compare the predictive performance of these models, we generated receiver operating characteristic (ROC) curves and calculated the area under the ROC curve (AUC). Furthermore, we employed calibration curves to assess the concordance between actual risk and predicted risk, and decision curve analysis (DCA) curves to ascertain the clinical net benefit. With the refinement of our optimal model, we created a nomogram, which serves as a visual tool to enhance the representation of its clinical utility.

Statistical analysis

In our analysis, variables with a normal distribution were presented as mean±standard deviation, with comparisons between two groups conducted using Student's t-test. For non-normally distributed variables, the median (interquartile range) was used, and comparisons were made with the Mann-Whitney U test. Categorical data were expressed as percentages and subjected to comparison through the Chi-square test or Fisher's exact test. The relationship between model scores and clinical variables was explored using Pearson correlation analysis. It is noteworthy that all data analysis and graphical representations were performed using R version 4.2.1.

Results

Characteristics of participants enrolled

According to the flowchart in Fig. 1, a total of 1017 participants were ultimately included in the cohort, with 814 in the training set and 203 in the validation set. The demographic and clinical characteristics of our cohort were presented in Table 1. Notably, no statistically significant differences in clinical data were observed between the validation and training sets. Subsequently, when we grouped participants according to their MetS diagnosis as listed in Supplementary Table 1, several differences were observed between the Non-MetS and MetS groups, including, but not limited to, age ($P<0.001$), BMI ($P<0.001$), and CD8+T cell counts ($P<0.001$).

Regression analysis and model construction

We conducted both univariate and multivariate logistic regression analyses on the training set (Supplementary Table 2). The outcomes of these analyses revealed that age (OR=1.062, $P<0.001$), CAP (OR=1.017, $P<0.001$), and γ-GT (OR=1.007, $P=0.002$) were independent risk factors for MetS in PLWH, while CD4/CD8 ratio (OR=0.431, $P=0.024$) and CKMB (OR=0.985, $P=0.021$) were identified as protective factors. Based on these independent factors, we constructed Model 1 for MetS prediction.

Additionally, we employed LASSO regression analysis on the training set (Supplementary Fig. 1). Since Model 1 comprised five variables, we selected the LASSO Model including five variables to build Model 2, which included age (OR=1.065, $P<0.001$), CD8+T counts (OR=1.001, $P<0.001$), CAP (OR=1.020, $P<0.001$), γ-GT (OR=1.008, $P<0.001$), and LDH (OR=1.008, $P=0.007$). To streamline the model, common variables from both Model 1 and Model 2 were extracted to form Model 3, which included age (OR=1.059, $P<0.001$), CAP (OR=1.021, $P<0.001$) and γ-GT (OR=1.008, $P<0.001$). Ultimately, we proposed three distinct models for predicting MetS in PLWH and provided their model score calculation formulas separately (Table 2).

Model evaluation and nomogram of optimal model

To assess and compare the predictive performance of the three models in both the training and validation sets, we initiated our analysis with the construction of ROC curves (Fig. 2A-B) and calculated the corresponding AUC values. In the training set, Model 1 achieved an AUC of 0.843, Model 2 achieved 0.849, and Model 3 achieved 0.831. In the validation set, the AUC values were 0.829 for Model 1, 0.834 for Model 2, and 0.824 for Model 3. These results indicated robust predictive capabilities for all three models, with Model 2 displaying the highest AUC in both sets. Additionally, we generated calibration curves (Fig. 2C-D), which demonstrated

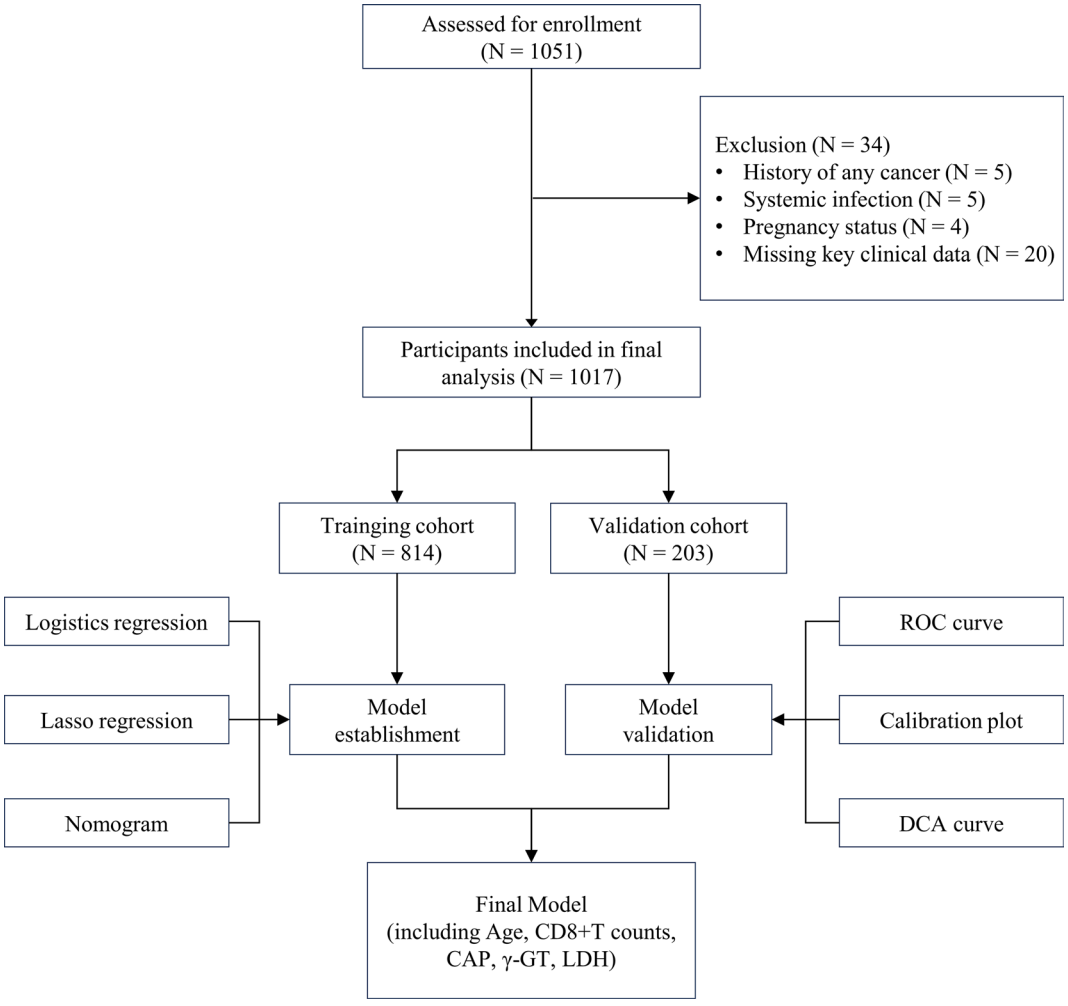

Fig. 1 Study flow diagram. Abbreviations ROC, receiver operating characteristic; DCA, decision curve analysis; CAP, controlled attenuation parameter; γ-GT, gamma-glutamyl transferase; LDH, lactate dehydrogenase

a close alignment between predicted probabilities and actual probabilities, affirming the well-calibrated nature of the models. Furthermore, the DCA curves (Fig. 2E-F) provided evidence of substantial clinical benefit associated with the predictive models. Importantly, Model 2 consistently outperformed the other models, exhibiting superior predictive performance in both the training and validation sets.

For the sake of enhanced clinical applicability and more intuitive representation, we formulated a nomogram for the optimal model (Fig. 3). The nomogram provided a practical tool for healthcare professionals, facilitating the estimation of the risk of developing MetS in PLWH.

Correlation between model score with components of MetS among PLWH

According to the formulation of the optimal model, we calculated the model score for the validation set. Subsequently, we carried out correlation analysis between the model score and each component of MetS (Fig. 4), which encompassed BMI (r=0.661, P<0.001), TG (r=0.512, P<0.001), HDL-C (r = -0.163, P=0.020), SBP (r=0.344, P<0.001), DBP (r=0.166, P=0.018) and FPG (r=0.237, P<0.001). The results revealed a significant and noteworthy correlation between the model score and each component of MetS, which underscored the utility of the model in effectively predicting and assessing the risk factors associated with MetS in PLWH.

The relationship between model score with metabolic disorders

Our analysis extended to the exploration of the relationship between model score and MetS as well as associated metabolic disorders (Fig. 5). The results indicated significant differences in the model score when comparing the training set and the validation set across groups with or without MetS (P<0.001), obesity (P<0.001), HTG (P<0.001), HA (P<0.05), IFG (P<0.001), and

Table 1 Characteristics of participants or the training and validation cohorts

Characteristics	Training, *N* = 814	Validation, *N* = 203	*P* value
Age, years	33 [27, 43]	34 [28, 44]	0.398
Gender, male	748 (91.89%)	188 (92.61%)	0.735
MetS	211 (25.92%)	50 (24.63%)	0.706
BMI, kg/m^2	22.30 [20.02, 24.56]	22.23 [19.54, 24.28]	0.385
SBP, mmHg	125.00 [117.00, 133.00]	125.00 [117.00, 134.00]	0.833
DBP, mmHg	86.00 [80.00, 92.00]	86.00 [80.00, 91.00]	0.719
CD8 + T counts, cells/μl	729.50 [555.00, 942.00]	746.00 [539.50, 987.00]	0.505
CD4 + T counts, cells/μl	464.00 [329.00, 629.00]	465.00 [327.00, 631.00]	0.753
CD4/CD8 ratio	0.66 [0.44, 0.90]	0.64 [0.41, 0.91]	0.623
HAART Regimen			0.814
DTG group	112 (13.76%)	27 (13.30%)	
B/T/F group	199 (24.45%)	52 (25.62%)	
EFV group	477 (58.60%)	115 (56.65%)	
LPV/r group	26 (3.19%)	9 (4.43%)	
HAART duration, months	24 [12, 48]	24 [12, 48]	0.616
AIDS stage	398 (48.89%)	93 (45.81%)	0.432
CAP, dB/m	213.00 [191.00, 249.75]	211.00 [187.50, 241.00]	0.403
LSM, kPa	5.10 [4.40, 5.80]	5.10 [4.40, 5.90]	0.987
WBC, 10^9/L	6.08 [5.10, 7.03]	6.06 [5.17, 7.05]	0.706
LYM, 10^9/L	1.99 [1.60, 2.46]	1.99 [1.65, 2.48]	0.634
NEU, 10^9/L	3.37 [2.69, 4.21]	3.30 [2.81, 4.08]	0.964
MONO, 10^9/L	0.40 [0.32, 0.49]	0.40 [0.34, 0.50]	0.227
EOS, 10^9/L	0.10 [0.06, 0.17]	0.10 [0.06, 0.18]	0.909
RBC, 10^{12}/L	4.85 [4.52, 5.14]	4.81 [4.52, 5.14]	0.595
HGB, g/L	151.00 [142.00, 159.00]	151.00 [141.00, 159.50]	0.979
PLT, 10^9/L	239.50 [202.00, 276.75]	238.00 [205.00, 274.50]	0.977
ALT, U/L	23.00 [16.00, 34.75]	20.00 [15.50, 32.00]	0.108
AST, U/L	21.00 [18.00, 27.00]	20.00 [17.00, 25.50]	0.24
ALB, g/L	47.00 [44.90, 48.90]	46.90 [44.95, 48.50]	0.351
G, g/L	27.70 [25.00, 30.90]	27.30 [24.50, 30.60]	0.234
TBIL, μmol/L	7.70 [5.20, 11.10]	7.20 [5.35, 10.95]	0.671
DBIL, μmol/L	3.10 [2.40, 4.10]	3.10 [2.40, 4.05]	0.801
ALP, U/L	88.00 [70.25, 111.00]	87.00 [71.00, 109.50]	0.689
γ-GT, U/L	32.00 [21.25, 50.00]	30.00 [20.50, 47.00]	0.382
UA, μmol/L	370.50 [316.00, 437.00]	368.00 [308.50, 430.50]	0.841
CR, μmol/L	81.00 [70.00, 90.75]	78.00 [69.50, 90.00]	0.365
BUN, mmol/L	4.40 [3.70, 5.20]	4.30 [3.70, 5.30]	0.964
eGFR, $mL/min/1.73m^2$	105.88 [92.66, 117.03]	106.06 [91.26, 117.68]	0.715
TG, mmol/L	1.28 [0.90, 2.07]	1.23 [0.85, 1.88]	0.277
CHOL, mmol/L	4.34 [3.78, 4.96]	4.41 [3.74, 4.98]	0.551
HDL-C, mmol/L	1.10 [0.97, 1.28]	1.13 [0.95, 1.30]	0.777
LDL-C, mmol/L	2.70 [2.27, 3.18]	2.72 [2.18, 3.16]	0.639
VLDL-C, mmol/L	0.45 [0.28, 0.67]	0.48 [0.33, 0.66]	0.476
FPG, mmol/L	5.14 [4.82, 5.53]	5.21 [4.84, 5.58]	0.248
HbA1c, %	5.40 [5.10, 5.70]	5.40 [5.10, 5.70]	0.406
LDH, U/L	162.00 [146.00, 180.00]	163.00 [146.00, 179.00]	0.853
HBDH, U/L	122.00 [109.00, 136.00]	118.00 [106.00, 135.00]	0.072
CK, U/L	107.00 [82.00, 144.00]	112.00 [84.00, 147.50]	0.279
CKMB, U/L	23.50 [14.00, 41.00]	25.00 [14.00, 45.50]	0.357

Table 1 (continued)

Characteristics	Training, *N* = 814	Validation, *N* = 203	*P* value
CRP, mg/L	1.02 [0.50, 2.34]	1.03 [0.56, 2.86]	0.319
ESR, mm/1 h	5.00 [3.00, 10.00]	5.00 [4.00, 10.00]	0.397

Continuous variables are presented as Median [Interquartile Range] (IQR), and categorical variables are presented as N (%)

Abbreviations: MetS, metabolic syndrome; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HAART, highly active antiretroviral therapy; DTG, dolutegravir group; B/F/T, Bictegravir group; EFV, Efavirenz group; LPV/r, lopinavir/ritonavir group; AIDS, acquired immunodeficiency syndrome; CAP, controlled attenuation parameter; LSM, liver stiffness measurement; WBC, white blood cell count; LYM, lymphocyte count; NEU, neutrophil count; MONO, monocyte count; EOS, eosinophils count; RBC, red blood cell count; HGB, hemoglobin; PLT, platelets count; ALT, alanine aminotransferase; AST, aspartic aminotransferase; ALB, albumin; G, globulin; TBIL, total bilirubin; DBIL, direct bilirubin; ALP, alkaline phosphatase; γ-GT, gamma-glutamyl transferase; UA, uric acid; CR, creatinine; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; TG, total triglycerides; CHOL, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VLDL-C, very low-density lipoprotein cholesterol; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin A1c; LDH, lactate dehydrogenase; HBDH, hydroxybutyrate dehydrogenase; CK, creatine kinase; CKMB, creatine kinase myocardial band; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate

Table 2 The models for predicting MetS in PLWH

Models	Variables	B	SE	Wald	OR (95% CI)	*P* value
Model 1	(Intercept)	-7.379	0.668	11.050		
	Age	0.060	0.008	7.253	1.062 (1.045–1.079)	< 0.001
	CD4/CD8 ratio	-0.945	0.302	-3.133	0.389 (0.212–0.691)	0.002
	CAP	0.020	0.002	9.322	1.020 (1.016–1.024)	< 0.001
	γ-GT	0.009	0.002	4.902	1.009 (1.006–1.013)	< 0.001
	CKMB	-0.014	0.006	-2.502	0.986 (0.975–0.997)	0.012
	Model score = -7.379 + 0.060*Age − 0.945*CD4/CD8 ratio + 0.020*CAP + 0.009*γ-GT − 0.014*CKMB					
Model 2	(Intercept)	-10.781	0.856	12.598		
	Age	0.063	0.009	7.351	1.065 (1.048–1.083)	< 0.001
	CD8 + T counts	0.001	0.000	4.126	1.001 (1.001–1.002)	< 0.001
	CAP	0.019	0.002	9.064	1.020 (1.015–1.024)	< 0.001
	γ-GT	0.008	0.002	4.254	1.008 (1.004–1.012)	< 0.001
	LDH	0.008	0.003	2.712	1.008 (1.002–1.014)	0.007
	Model score = -10.781 + 0.063*Age + 0.001*CD8 + T counts + 0.019*CAP + 0.008*γ-GT + 0.008*LDH					
Model 3	(Intercept)	-8.510	0.622	13.678		
	Age	0.058	0.008	7.185	1.059 (1.043–1.076)	< 0.001
	CAP	0.021	0.002	10.046	1.021 (1.017–1.025)	< 0.001
	γ-GT	0.008	0.002	4.343	1.008 (1.004–1.012)	< 0.001
	Model score = -8.510 + 0.058*Age + 0.021*CAP + 0.008*γ-GT					

Abbreviations: CAP, controlled attenuation parameter; γ-GT, gamma-glutamyl transferase; CKMB, creatine kinase myocardial band; LDH, lactate dehydrogenase

hypertension ($P<0.05$). These findings collectively underscored the efficacy of the model in effectively predicting and discerning metabolic-related conditions in PLWH.

Discussion

In this study, we divided the cohort of 1017 participants into training and validation cohorts. Employing both multivariate logistic regression and Lasso regression, we systematically constructed predictive models. These models were rigorously evaluated for sensitivity, specificity, and calibration to determine the best model for further development into a nomogram scoring system. Furthermore, we delved into the correlation analysis between model score and the components of MetS. Our investigation also extended to the relationship between model score and related metabolic disorders. The final risk score model incorporated five robust risk predictors: age, CD8 + T counts, CAP, γ-GT, and LDH. Notably, our model differed from those predicting MetS in the general population by incorporating the CD8 + T cell counts, which accounted for the complex interplay between inflammation and immunosuppression and their potential role in metabolic disease in PLWH.

Researchers suggest that age-related diseases are primarily driven by chronic inflammation and immune system activation, which are commonly observed in older adults [22]. These factors play a significant role in the development of cardiovascular diseases and MetS [23–25]. The increased life expectancy has exposed PLWH to the effects of aging itself, which was defined as "inflammatory AIDS" towards the later stage of HIV infection [26]. In parallel, our findings emphasized the potential of age as a predictor of MetS in PLWH, aligning with the conclusions of other researchers.

It has been reported that the CD4/CD8 ratio has emerged as a potential indicator for predicting MetS in individuals with HIV/AIDS [27–29]. Additionally, some researchers have suggested that elevated CD8 + T cell

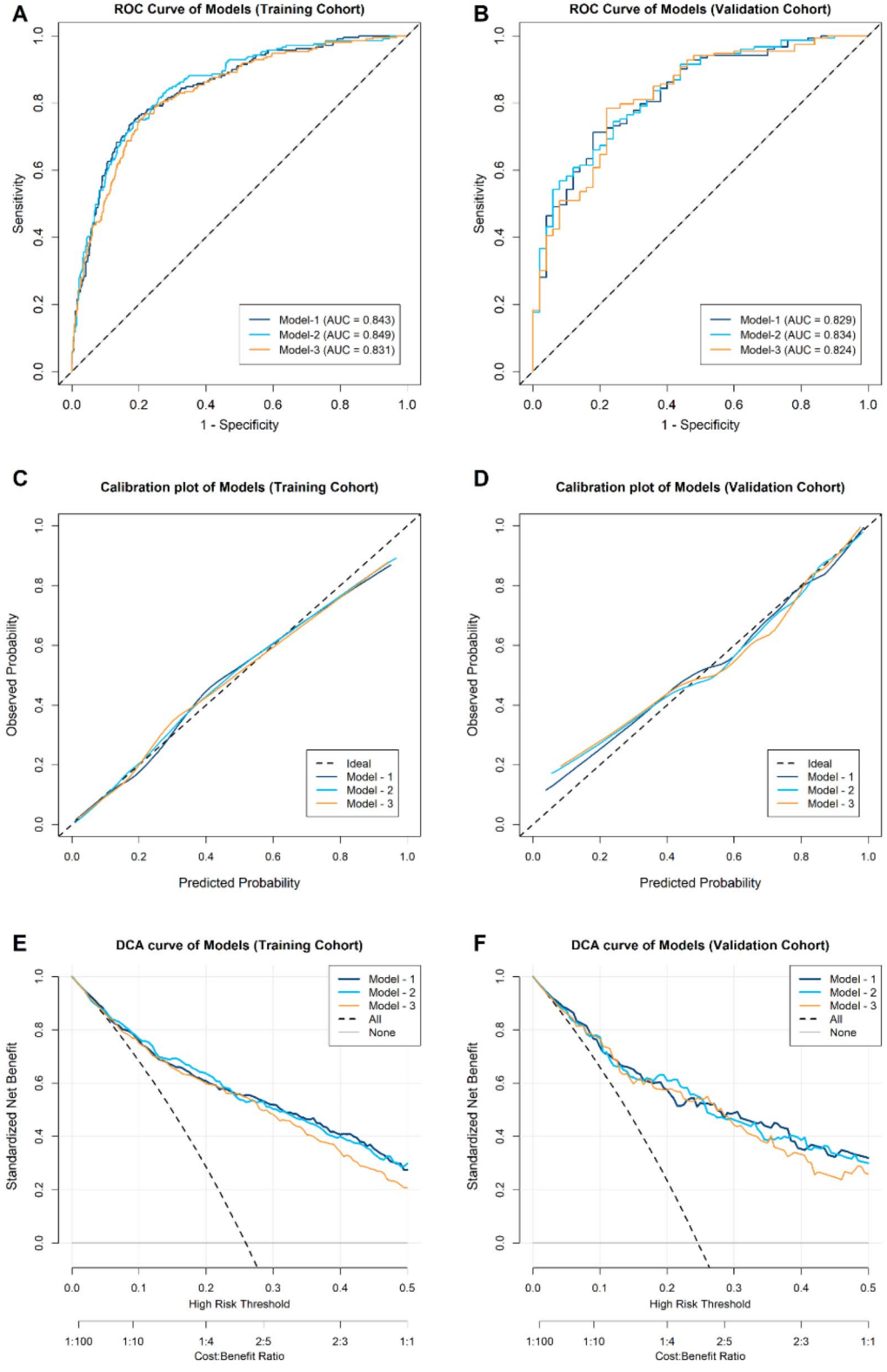

Fig. 2 Performance evaluation of the models. (**A**) ROC curve for predictive models in the training cohort. (**B**) ROC curve for predictive models in the validation cohort. (**C**) Calibration plot of models in the training cohort. (**D**) Calibration plot of models in the validation cohort. (**E**) DCA curve of models in the training cohort. (**F**) DCA curve of models in the validation cohort

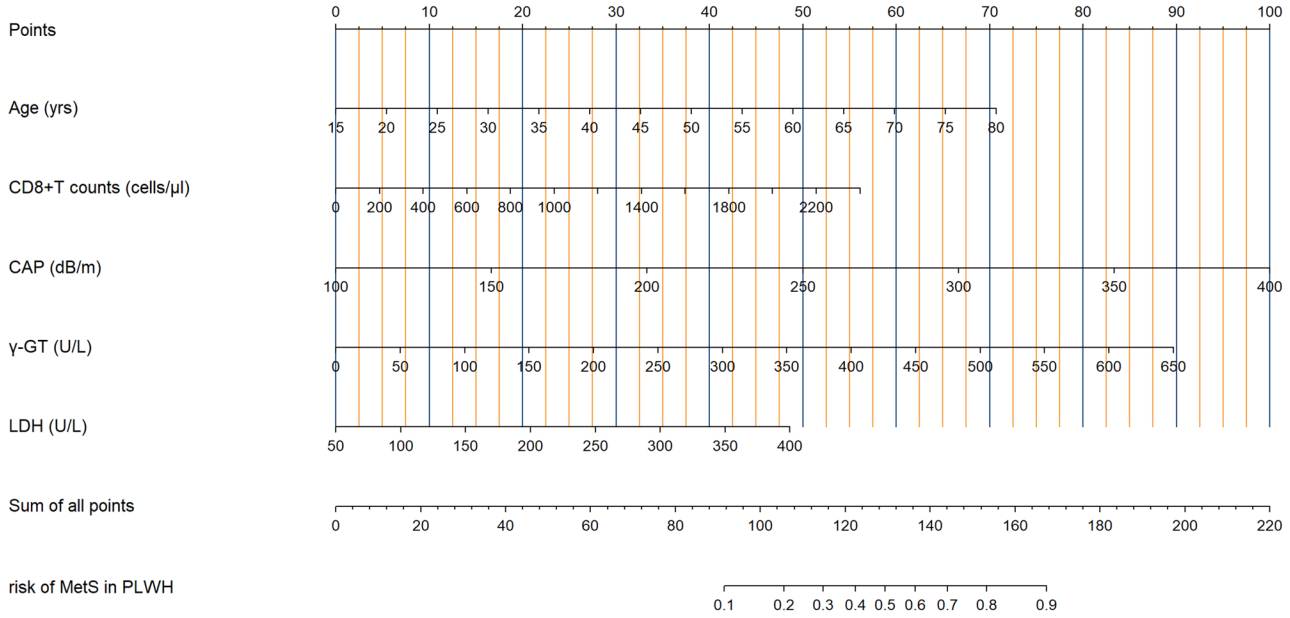

Fig. 3 Nomogram of the optimal model. This nomogram illustrates the predictive model for MetS in PLWH. To use the nomogram, find each variable's value (e.g., age, CD8 + T cell count, CAP, γ-GT, and LDH) on its respective axis and draw a line upward to get the corresponding points. Sum all points and locate the total score on the "Sum of all points" axis. This total score maps to a predicted risk of MetS on the bottom scale, with higher scores indicating a greater risk. Abbreviations: CAP, controlled attenuation parameter; γ-GT, gamma-glutamyl transferase; LDH, lactate dehydrogenase; MetS, metabolic syndrome; PWLH, people living with HIV

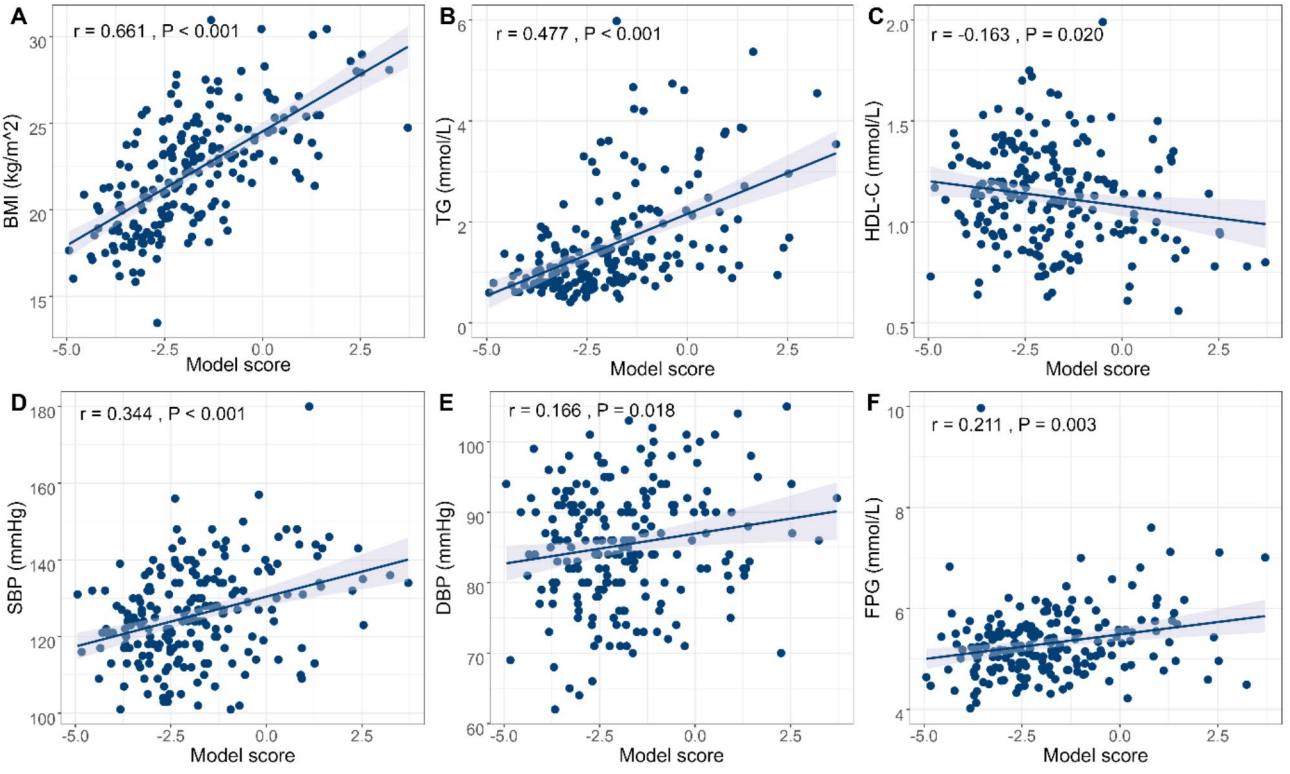

Fig. 4 Correlation between model score with MetS components among PLWH in the validation cohort. The Scatter plots of model score and BMI (**A**), TG level (**B**), HDL-C level (**C**), SBP level (**D**), DBP level (**E**), and FPG level (**F**). Abbreviations: BMI, body mass index; TG, total triglycerides; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose

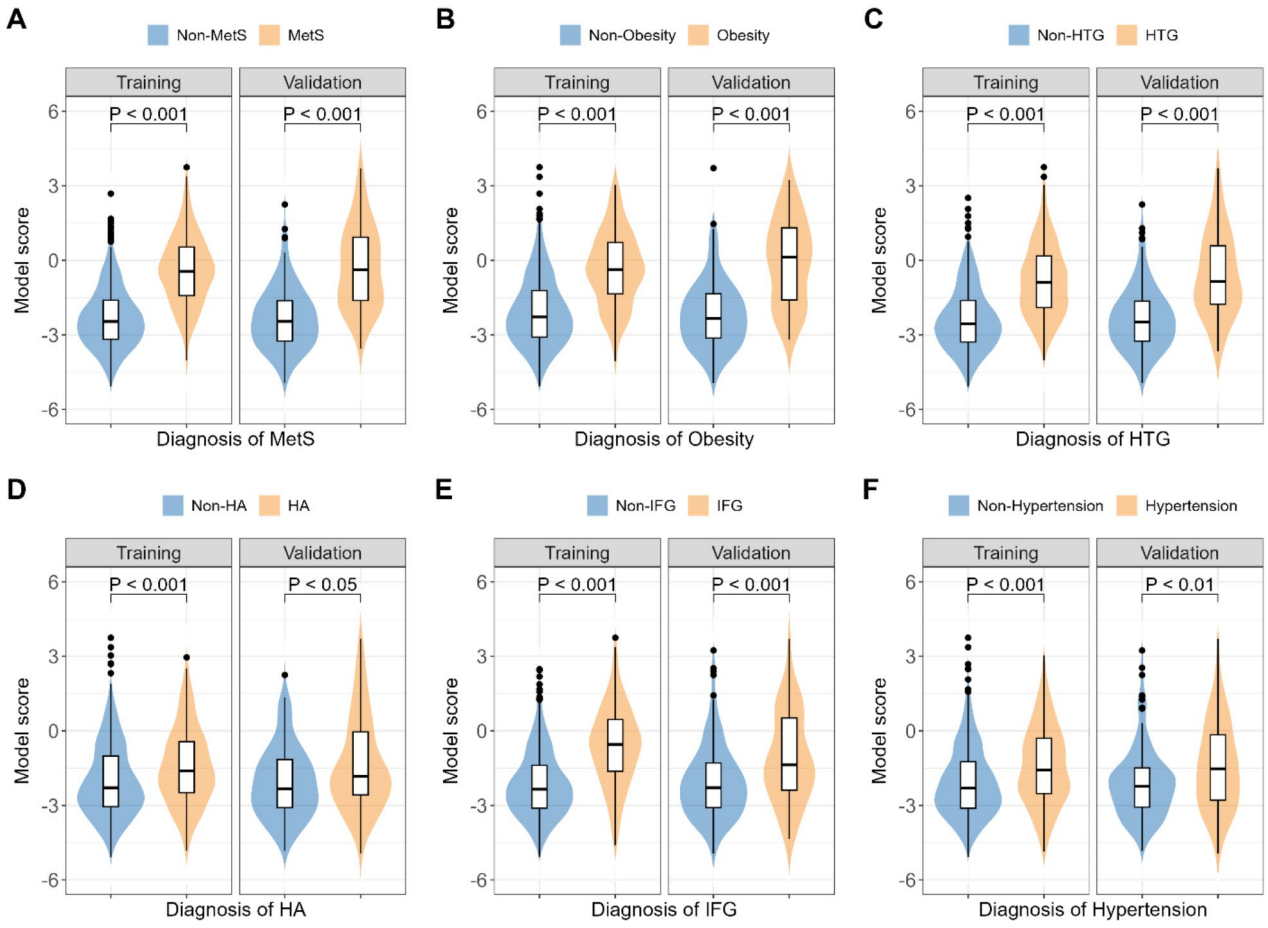

Fig. 5 The model score between metabolic disorders among PWLH. (**A**) The model score in PLWH between Non-MetS group and MetS group. (**B**) The model score in PLWH between Non-Obesity group and Obesity group. (**C**) The model score in PLWH between Non-HTG group and HTG group. (**D**) The model score in PLWH between Non-HA group and HA group. (**E**) The model score in PLWH between Non-IFG group and IFG group. (**F**) The model score in PLWH between Non-Hypertension group and Hypertension group. Abbreviations: MetS, metabolic syndrome; HTG, hypertriglyceridemia; HA, hypoalphalipoproteinemia; IFG, impaired fasting glucose

counts may constitute a moderate risk factor for stroke in PLWH [27, 30]. In addition, elevated CD8+T cell counts have been closely associated with immunosenescence in PLWH, suggesting that CD8+T cells may play a pivotal role in linking immunosenescence with metabolic disorders [31]. Notably, in our study, we observed a significant difference in CD8+T cell counts between the non-MetS and MetS groups in PLWH, and CD8+T cell counts were also identified as independent predictors in our predictive model. This finding supports the potential of CD8+T cells as a risk marker for MetS in PLWH and provides a direction for future research to explore the role of CD8+T cells in predicting and managing MetS in this population.

γ-GT is widely used as a diagnostic marker for liver diseases [32], but increasing evidence suggests that it also plays an important role in cardiometabolic diseases such as obesity, hypertension, and diabetes [33]. Elevated γ-GT levels have been identified as predictive of the occurrence of MetS, CVD events and mortality [34–36]. Independent studies by Nguyen and Fourie have concurred that γ-GT is also linked to CVD risk in PLWH populations [37, 38]. In this study, γ-GT emerged not only as an independent risk factor for MetS in PLWH but also as one of the key elements in the predictive model, further highlighting its significance in predicting MetS occurrence in this population. Nevertheless, we acknowledge that elevated γ-GT may be a result of metabolic syndrome rather than a cause.

Elevated LDH indicates a pathological condition of acute tissue or cell injury [39, 40]. Previous studies have shown an association between elevated LDH and MetS, with LDH levels being closely related to frailty and all-cause mortality [39, 41]. Some researchers have also proposed that LDH tests can be utilized to monitor HIV disease progression and treatment response [42]. Although elevated LDH levels may be a consequence rather than a cause of metabolic syndrome, LDH

emerged as a predictor of MetS in the PLWH population in this study, suggesting its potential as a biomarker for MetS in this group. However, further longitudinal studies are needed to clarify the causal relationship between LDH and MetS in PLWH.

In recent years, Fibroscan has emerged as a widely adopted diagnostic tool, primarily employed for the prediction of fatty liver and liver fibrosis in diverse populations. Notably, previous studies have reported the use of a combination of CAP and LSM for the prediction of nonalcoholic steatohepatitis or liver fibrosis, particularly in PLWH or those coinfected with HCV [43–45]. However, the role of CAP and LSM in predicting MetS has been relatively underexplored. Our findings suggest that CAP may serve as a valuable predictive marker for MetS in PLWH, which could have important implications for the management and prognosis of this population. Nonetheless, we acknowledge that elevated CAP might also reflect the presence of fatty liver as a consequence of MetS, rather than serving as a causal factor. Further longitudinal studies are needed to clarify the directionality of this association.

Our study possesses several strengths. Firstly, it proposes a model that may assist in identifying MetS in PLWH, offering clinicians a possible tool to help assess MetS risk and inform early intervention strategies. Secondly, this study uniquely integrates a multivariate prediction model that considers patient-host characteristics specific to PLWH, revealing potential associations between new variables and MetS in this population. Nonetheless, we acknowledge certain limitations in our study. Firstly, as this is an exploratory analysis, we did not adjust for multiple comparisons across the variables examined, which may increase the likelihood of false positives. Additionally, its retrospective nature may be subject to inherent limitations associated with this study design, as some observed associations may represent consequences rather than contributing factors to metabolic syndrome. Future research should focus on conducting longitudinal studies to assess the model's predictive effectiveness over time. Finally, our model lacks external validation using data from independent sources, underscoring the need for further research to confirm its robustness across diverse cohorts.

Conclusions

In conclusion, our study provides a potential model for assessing the risk of MetS in PLWH, further research is needed to validate its predictive capacity and explore the causal relationships underlying these associations.

Abbreviations

AIDS	Acquired immunodeficiency syndrome
ALB	Albumin
ALP	alkaline phosphatase
ALT	Alanine aminotransferase
ART	Antiretroviral therapy
AST	Aspartic aminotransferase
AUC	Area under the ROC curve
B/F/T	Bictegravir group
BMI	Body mass index
BUN	Blood urea nitrogen
CAP	Controlled attenuation parameter
CHOL	Total cholesterol
CK	Creatine kinase
CKMB	Creatine kinase myocardial band
CR	Creatinine
CRP	C-reactive protein
DBIL	Direct bilirubin
DBP	Diastolic blood pressure
DCA	Decision curve analysis
DTG	Dolutegravir group
EOS	Eosinophils count
EFV	Efavirenz group
eGFR	Estimated glomerular filtration rate
ESR	Erythrocyte sedimentation rate
FPG	Fasting plasma glucose
G	Globulin
HA	Hypoalphalipoproteinemia
HBDH	Hydroxybutyrate dehydrogenase
HDL-C	High-density lipoprotein cholesterol
HGB	Hemoglobin
HTG	Hypertriglyceridemia
IFG	Impaired fasting glucose
LDH	Lactate dehydrogenase
LDL-C	Low-density lipoprotein cholesterol
LPV/r	Lopinavir/ritonavir group
LSM	Liver stiffness measurement
LYM	Lymphocyte count
MetS	Metabolic syndrome
MONO	Monocyte count
PLT	Platelets count
ROC	Receiver operating characteristic
RBC	Red blood cell count
SBP	Systolic blood pressure
TBIL	Total bilirubin
TG	Total triglycerides
UA	Uric acid
VLDL-C	Very low-density lipoprotein cholesterol
WBC	White blood cell count

Supplementary Information

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Supplementary Material 1

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Author contributions

HQZ, JP and SHC contributed to the study conception and design. SLC, YYX and YHJ analyzed and interpreted the data, as well as drafted and finalized the manuscript. SLC, HJC, XXW, ZQ, and XWX participated in data collection and methodology. All the authors critically reviewed and approved the final version of the manuscript.

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Data availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Institutional Ethics Committee of Nanfang Hospital (study identifier: NFEC-2021-448) and the study protocol was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. Informed consent was obtained from all individuals.

Competing interests
The authors declare no competing interests.

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