Association Study Between Metabolic-Associated Fatty Liver Disease and Hyperglycemia and Construction of a Joint Prediction Model Based on a Physical Examination Cohort (Postprint)

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Abstract

Background The global prevalence and incidence of metabolic-associated fatty liver disease (MAFLD) coexisting with type 2 diabetes mellitus (T2DM) continue to rise, and this coexistence increases the risk of liver-related adverse outcomes. In clinical practice, screening and early diagnosis of high-risk patients with MAFLD combined with hyperglycemia are needed to delay its progression.

Objective Based on the relationship between T2DM and MAFLD, this study utilized existing large-scale physical examination data to explore the impact of systemic hyperglycemia on hepatic steatosis and liver fibrosis in MAFLD, and to analyze the key factors influencing the occurrence of MAFLD combined with hyperglycemia.

Methods Data were collected from 18,286 healthy examinees at the First Affiliated Hospital of Soochow University between March and July 2024, including basic information, medical history, abdominal ultrasound examinations, biochemical indicators, and complete blood count parameters. Based on abdominal ultrasound findings and MAFLD diagnostic criteria, 5,258 MAFLD patients were screened. These patients were divided into three groups according to the Fibrosis-4 Index (FIB-4) levels: Group T1 (FIB-4<1.3, n=4,275), Group T2 (1.3≤FIB-4$ 2.67, n = 924), andGroupT3(FIB − 4 > 2.67, n = 59), anddifferencesinclinicalindicatorsamongthethreegroupswerecompared.Furthermore, basedonthepres (meeting any one criterion), MAFLD patients were divided into a MAFLD with hyperglycemia group (n=752) and a MAFLD without hyperglycemia group (n=4,506), and differences in hepatic steatosis and liver fibrosis-related indicators between the two groups were compared. Univariate and multivariate logistic regression analyses were employed to explore the key factors influencing the occurrence of MAFLD combined with hyperglycemia. Receiver operating characteristic (ROC) curves were used to evaluate the predictive value of the combined prediction model for the occurrence of MAFLD with hyperglycemia.

Results Comparisons among the three groups revealed statistically significant differences in smoking, hypertension, diabetes, hyperlipidemia, hyperuricemia, coronary heart disease, age, BMI, FBG, HbA1c, platelet count (PLT), white blood cell count (WBC), red blood cell count (RBC), hemoglobin (Hb), red cell distribution width (RDW), neutrophil count (NEUT), lymphocyte count (LYM), monocyte count (MONO), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), albumin (ALB), gamma-glutamyl transpeptidase (GGT), uric acid (UA), creatinine (Cr), blood urea nitrogen (BUN), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), alkaline phosphatase (ALP), and estimated glucose disposal rate (eGDR) ($P<0.05$). The MAFLD with hyperglycemia group exhibited higher fatty liver index (FLI), hepatic steatosis index (HSI), and ZJU index compared to the MAFLD without hyperglycemia group ($P<0.05$). The MAFLD with hyperglycemia group also showed higher FIB-4, AST/PLT ratio (APRI), non-alcoholic fatty liver disease fibrosis score (NFS), body mass index, aspartate aminotransferase/alanine aminotransferase ratio, and BARD score compared to the MAFLD without hyperglycemia group ($P<0.05$). The MAFLD with hyperglycemia group and MAFLD without hyperglycemia group were randomly assigned to training and test sets at a 1:1 ratio. Univariate and multivariate logistic regression analyses of all indicators in the training set revealed that age, waist circumference (WC), hypertension, hyperlipidemia, TG, GGT, UA, and BUN were influencing factors for the occurrence of MAFLD combined with hyperglycemia ($P<0.05$). Subsequent ROC analysis of these indicators demonstrated that age, WC, hypertension, hyperlipidemia, TG, GGT, UA, and BUN, as independent predictors, possessed certain predictive accuracy for identifying the occurrence of MAFLD with hyperglycemia (0.53≤AUC$ $0.75). A prediction model was constructed by combining these eight key predictors and ROC curves were plotted. The results showed that the combined model achieved a predictive accuracy of 0.805 (95%CI=0.781~0.828), with a sensitivity of 75.8% and specificity of 72.6%. Validation of this combined model in the test set yielded a positive predictive accuracy of 0.705, negative predictive accuracy of 0.731, and overall predictive accuracy of 0.727.

Conclusion In MAFLD patients grouped by FIB-4, hypertension, FBG, HbA1c, PLT, WBC, RBC, LYM, AST, and eGDR levels showed significant differences among the three groups. Systemic hyperglycemia can exacerbate the degree of hepatic steatosis and liver fibrosis in MAFLD. Furthermore, age, WC, hypertension, hyperlipidemia, TG, GGT, UA, and BUN are influencing factors contributing to the progression from MAFLD to MAFLD combined with hyperglycemia. The prediction model constructed by combining these eight indicators can enhance the predictive accuracy for assessing the occurrence of hyperglycemia in MAFLD populations and may provide a reference basis for early identification

of hyperglycemia in MAFLD patients in clinical practice.

Full Text

Correlation Analysis and Model Construction of Metabolic Associated Fatty Liver Disease and Hyperglycemia Based on a Health Examination Cohort

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Abstract

Background The global prevalence and incidence of Metabolic Associated Fatty Liver Disease (MAFLD) co-occurring with Type 2 Diabetes Mellitus (T2DM) are increasing, significantly elevating the risk of liver-related adverse outcomes. In clinical practice, early screening and diagnosis of high-risk MAFLD patients with hyperglycemia are crucial to slowing disease progression.

Objective Based on the relationship between T2DM and MAFLD, this study evaluates the impact of hyperglycemia on hepatic steatosis and liver fibrosis in MAFLD using large-scale health examination data and aims to identify key factors influencing the development of MAFLD with hyperglycemia.

Methods Data from 18,286 individuals who underwent health examinations at the First Affiliated Hospital of Soochow University between March and July 2024 were analyzed. The dataset included demographic information, medical history, abdominal ultrasound results, biochemical markers, and routine blood tests. Individuals meeting the MAFLD diagnostic criteria were classified into the MAFLD group, which was further stratified into three subgroups according to the Fibrosis-4 index (FIB-4) scores: T1 (FIB-4<1.3), T2 ($1.3 \leq$ FIB-4 ≤ 2.67), and T3 (FIB-4>2.67). Clinical indicators among these subgroups were compared. Additionally, the MAFLD group was divided into two subgroups: MAFLD with hyperglycemia and MAFLD without hyperglycemia, based on a history of diabetes, fasting blood glucose (FBG) $\geq$ 7.0 mmol/L, or glycated hemoglobin A1c (HbA1c) $\geq$ 6.5% (meeting any one criterion). Differences in hepatic steatosis and liver fibrosis-related indicators between these subgroups were analyzed. Univariate and multivariate Logistic regression analyses were performed to identify key factors associated with MAFLD with hyperglycemia. The predictive performance of a combined model for MAFLD with hyperglycemia was evaluated using receiver operating characteristic (ROC) curve analysis.

Results Among the T1, T2, and T3 subgroups, significant differences ($P<0.05$) were observed in clinical indicators, including smoking, hypertension, diabetes, hyperlipidemia, hyperuricemia, coronary heart disease, age, BMI, FBG, HbA1c, platelet count (PLT), white blood cell count (WBC), red blood cell count (RBC), hemoglobin (Hb), red blood cell distribution width (RDW), neutrophil count (NEUT), lymphocyte count (LYM), monocyte count (MONO), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), albumin (ALB), glutamyl transferase (GGT), uric acid (UA), creatinine (Cr), blood urea nitrogen (BUN), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), alkaline phosphatase (ALP), and estimated glucose processing rate (eGDR). Moreover, the fatty liver index (FLI), hepatic steatosis index (HSI), and ZJU index were significantly higher in the MAFLD with hyperglycemia group compared to the MAFLD without hyperglycemia group ($P<0.05$). Additionally, the FIB-4, AST/PLT ratio index (APRI), non-alcoholic fatty liver disease fibrosis score (NFS), BMI, AST/ALT ratio, and diabetes score (BARD) were also higher in the MAFLD with hyperglycemia group ($P<0.05$). The samples of MAFLD with hyperglycemia and MAFLD without hyperglycemia groups were randomly divided into training and validation sets at a 1:1 ratio respectively. In the training set, univariate and multivariate logistic regression analyses identified age, waist circumference (WC), hypertension, hyperlipidemia, TG, GGT, UA and BUN as key influencing factors associated with MAFLD with hyperglycemia ($P<0.05$). Further ROC analysis of these factors demonstrated moderate predictive accuracy for MAFLD with hyperglycemia ($0.53 \leq \text{AUC} \leq 0.75$). A predictive model incorporating these eight key factors achieved an area under the curve (AUC) of 0.805 (95%CI=0.781-0.828), with a sensitivity of 75.8% and specificity of 72.6%. Validation of this combined model in the validation set yielded a positive predictive value of 0.705, a negative predictive value of 0.731, and an overall predictive accuracy of 0.727.

Conclusion Among MAFLD patients stratified by FIB-4, significant differences in hypertension, FBG, HbA1c, PLT, WBC, RBC, LYM, AST, and eGDR were observed across the three subgroups. Hyperglycemia exacerbates hepatic steatosis and liver fibrosis in MAFLD. Furthermore, age, WC, hypertension, hyperlipidemia, TG, GGT, UA and BUN were identified as significant risk factors for the progression of MAFLD to MAFLD with hyperglycemia. The predictive model incorporating these eight indicators enhances the accuracy of assessing hyperglycemia risk in MAFLD, potentially providing a reference for the early

differential diagnosis in clinical practice.

Keywords: Metabolic associated fatty liver disease; Hyperglycemia; Hepatic steatosis; Liver fibrosis; Predictive model

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Introduction

Metabolic Associated Fatty Liver Disease (MAFLD) is a chronic progressive liver disease caused by nutritional excess and insulin resistance in genetically susceptible individuals. The global prevalence and incidence of this disease continue to rise, particularly in China, where the situation is especially severe. MAFLD patients often present with metabolic syndrome components, including obesity, Type 2 Diabetes Mellitus (T2DM), hyperlipidemia, and hypertension. Research indicates that T2DM is the most closely related risk factor for MAFLD development, with approximately 70% of T2DM patients concurrently suffering from MAFLD, demonstrating a significant overlap between the two conditions. Pathophysiologically, T2DM can accelerate MAFLD progression, thereby hastening the development of hepatic and extrahepatic adverse outcomes. Conversely, MAFLD also increases the risk of developing T2DM and adversely affects glucose metabolism in patients with existing diabetes. The coexistence of these two diseases significantly elevates the risk of liver-related complications and imposes a more severe burden on extrahepatic prognosis, constituting a major public health challenge.

Consequently, in clinical practice, MAFLD patients require screening and early diagnosis for diabetes, while T2DM patients need timely assessment of liver disease progression. Fasting blood glucose (FBG) and glycated hemoglobin (HbA1c), as essential components of T2DM diagnostic criteria, are also closely associated with MAFLD disease progression. However, beyond glycemic indicators, other key factors influencing the liver disease course in MAFLD patients remain to be fully investigated. More importantly, the impact of hyperglycemia on liver disease progression and the risk factors for MAFLD combined with hyperglycemia are not yet clearly understood.

This study aims to investigate the effects of hyperglycemia on hepatic steatosis and liver fibrosis in MAFLD and analyze the risk factors influencing the development of MAFLD with hyperglycemia by leveraging existing large-scale health examination data based on the relationship between T2DM and MAFLD. Additionally, we sought to construct a comprehensive prediction model to assess the risk of MAFLD with hyperglycemia, providing a more effective tool for MAFLD risk assessment and management in clinical practice.

Methods

1.1 Study Population We selected individuals who underwent health examinations at the Health Management Center of the First Affiliated Hospital of Soochow University between March and July 2024. After excluding samples with incomplete clinical data, 18,286 subjects were included. Based on liver B-ultrasound examination results, the complete dataset was divided into fatty liver patients (6,727 cases) and non-fatty liver patients (11,559 cases). Subsequently, according to MAFLD diagnostic criteria, non-MAFLD cases were excluded from the fatty liver patients, resulting in a final cohort of 5,258 MAFLD patients.

1.2 Inclusion and Exclusion Criteria **Inclusion criteria:** (1) Complete clinical data; (2) Laboratory tests and auxiliary examinations such as abdominal B-ultrasound completed as required, with B-ultrasound diagnosis of fatty liver; (3) At least one component of metabolic syndrome (MetS): BMI $\geq$ 24.0 kg/m^2, or waist circumference (WC) $\geq$ 90 cm (males) and 85 cm (females), or excess body fat and body fat percentage; FBG $\geq$ 6.1 mmol/L, or 2-hour post-load blood glucose $\geq$ 7.8 mmol/L or HbA1c $\geq$ 5.7%, or history of type 2 diabetes, or homeostasis model assessment of insulin resistance $\geq$ 2.5; Fasting serum triglycerides (TG) $\geq$ 1.70 mmol/L, or receiving lipid-lowering medication; Serum high-density lipoprotein cholesterol (HDL-C) $\leq$ 1.0 mmol/L (males) and 1.3 mmol/L (females), or receiving lipid-lowering medication; Blood pressure $\geq$ 130/85 mmHg (1 mmHg = 0.133 kPa), or receiving antihypertensive medication.

Exclusion criteria: (1) Incomplete clinical data; (2) B-ultrasound diagnosis of non-fatty liver; (3) B-ultrasound diagnosis of fatty liver with any of the following conditions: Diseases that can cause fatty liver such as genotype 3 HCV infection, drug-induced fatty liver, Wilson’ s disease, and malnutrition; Malignant tumors and history of tumor surgery; Excessive alcohol consumption (weekly ethanol intake $\geq$ 210 g for males, $\geq$ 140 g for females).

1.3 Research Methods We collected general patient information and relevant clinical examination indicators, including gender, smoking history (smoking $\geq$ 1 cigarette/day for 6 months or more continuously or cumulatively), drinking history [including no drinking (never drank), occasional drinking (small amount and irregular frequency), moderate drinking (regular frequency but not reaching excessive drinking standards), and excessive drinking (ethanol intake $\geq$ 210 g/week for males, $\geq$ 140 g/week for females)], history of hypertension, diabetes, hyperlipidemia, hyperuricemia, coronary heart disease, tumor history, age, BMI, WC, FBG, HbA1c, platelet count (PLT), white blood cell count (WBC), red blood cell count (RBC), hemoglobin (Hb), red blood cell distribution width (RDW), neutrophil count (NEUT), lymphocyte count (LYM), monocyte count (MONO), neutrophil percentage (NEUT%), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol (TC), TG, HDL-C, low-density lipoprotein cholesterol (LDL-C), albumin (ALB), globulin (GLB), γ-glutamyl transpeptidase (GGT), uric acid (UA), creatinine (Cr), blood urea nitrogen (BUN), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), alkaline phosphatase (ALP), and ultrasound examinations.

Additional combined indices were calculated using the following formulas: (1) Hepatic steatosis-related indices: Fatty Liver Index (FLI) = $100/[1+e^{-}]$, where z = 0.953×ln(TG) + 0.139×BMI + 0.718×ln(GGT) + 0.053×WC - 15.745; Hepatic Steatosis Index (HSI) = 8×ALT/AST + BMI + 2 (if DM) + 2 (if female); ZJU index = BMI + FPG + TG + 3×ALT/AST + 2 (if female). (2) Liver fibrosis-related indices: AST/PLT ratio (APRI) = [(AST/40)/PLT]$\times 100; Fibrosis-4index(FIB-4) = age\times AST/[PLT\times(ALT)^{\{1\}/}\{2\}]; Non-alcoholicfattyliverdiseasefibrosisscore(NFS) = -1.675+0.037\times age+0.094\times BMI+1.13\times(abnormalFBG/DM, yes=1, no=0) + 0.99\times AST/ALT - 0.013\times PLT - 0.66\times$ALB; BMI, AST/ALT ratio, and diabetes score (BARD score) = AST/ALT (if $ $0.8=2) + BMI (if $ $28 = 1) + 1(ifDM).(3) Insulinresistance-relatedindices: Triglyceride-glucoseindex(TyG) = ln(TG\times FBG/2); Triglyceride-glucose-BMI(TyG-BMI) = TyG\times BMI; Estimatedglucosedisposalrate(eGDR) = 19.02 - 0.22\times BMI - 3.26\times HTN - 0.61\times$HbA1c, where HTN is hypertension (yes=1, no=0).

1.4 Study Grouping The MAFLD group was divided into T1 group (FIB-4<1.3), T2 group (1.3 ≤ FIB-4 ≤ 2.67), and T3 group (FIB-4>2.67) based on FIB-4 levels. The MAFLD group was also divided into MAFLD with hyperglycemia group and MAFLD without hyperglycemia group based on the presence of diabetes history, FBG ≥ 7.0 mmol/L, or HbA1c ≥ 6.5% (meeting any one criterion).

1.5 Statistical Analysis Data analysis was performed using SPSS 27.0 and GraphPad 9.0 software. Normality tests were conducted on measurement data; all measurement data in this study did not conform to normal distribution and were expressed as M(P25,P75). Comparisons between two groups were performed using Mann-Whitney U test, and comparisons among multiple groups were performed using Kruskal-Wallis H test. Count data were expressed as relative numbers, and inter-group comparisons were performed using ^{2} test. Univariate and multivariate Logistic regression analyses were used to explore key factors influencing the development of MAFLD with hyperglycemia. Receiver operating characteristic (ROC) curves were plotted to evaluate the predictive value of the combined prediction model for MAFLD with hyperglycemia, and the area under the ROC curve (AUC) was used to assess predictive performance. P<0.05 was considered statistically significant.

Results

2.1 Comparison of General Data Among MAFLD Patients Grouped by FIB-4 Levels No statistically significant differences were observed among the T1, T2, and T3 groups in gender, WC, NEUT%, GLB, TyG, and TyG-BMI ($P>0.05$). However, significant differences were found among the three groups in smoking, hypertension, diabetes, hyperlipidemia, hyperuricemia, coronary heart disease, age, BMI, FBG, HbA1c, PLT, WBC, RBC, Hb, RDW, NEUT, LYM, MONO, ALT, AST, TC, TG, HDL-C, LDL-C, ALB, GGT, UA, Cr, BUN, TBIL, DBIL, IBIL, ALP, and eGDR ($P<0.05$) .

2.2 Comparison of Hepatic Steatosis and Fibrosis Indices Between MAFLD with Hyperglycemia and MAFLD without Hyperglycemia Groups The FLI, HSI, and ZJU indices were significantly higher in the MAFLD with hyperglycemia group compared to the MAFLD without hyperglycemia group (Z=-5.550, P=2.86E-08; Z=-3.505, P=4.57E-04; Z=-14.442, P=2.81E-47) [Figure 1: see original paper]. Additionally, the FIB-4, APRI, NFS, and BARD scores were significantly higher in the MAFLD with hyperglycemia group compared to the MAFLD without hyperglycemia group (Z=-15.518, P=2.61E-54; Z=-3.261, P=1.11E-03; Z=-31.115, P=1.51E-212; Z=-15.286, P=9.43E-53) [Figure 2: see original paper].

2.3 Comparison of General Data Between MAFLD with Hyperglycemia and MAFLD without Hyperglycemia Groups No statistically significant differences were observed between the MAFLD with hyperglycemia and MAFLD without hyperglycemia groups in BMI, RBC, Hb, LYM, AST, TBIL, DBIL, and IBIL ($P>0.05$). However, significant differences were found between the two groups in gender, smoking, hypertension, hyperlipidemia, hyperuricemia, coronary heart disease, age, WC, PLT, WBC, RDW, NEUT, MONO, NEUT%, ALT, TC, TG, HDL-C, LDL-C, ALB, GLB, GGT, UA, Cr, BUN, and ALP ($P<0.05$) .

2.4 Logistic Regression Analysis of Factors Influencing MAFLD with Hyperglycemia Using random grouping methods, samples from the MAFLD with hyperglycemia and MAFLD without hyperglycemia groups were divided into training and testing sets at a 1:1 ratio. Among the 752 cases in the MAFLD with hyperglycemia group, 376 were allocated to the training set and 376 to the testing set. Similarly, the MAFLD without hyperglycemia group was divided accordingly. General data for the MAFLD with hyperglycemia and MAFLD without hyperglycemia groups in the training set are presented in . Univariate Logistic regression analysis of all indicators in the training set revealed that smoking, hypertension, hyperlipidemia, hyperuricemia, coronary heart disease, age, WC, PLT, WBC, NEUT, GGT, UA, BUN, and ALP were influencing factors for MAFLD with hyperglycemia ($P<0.05$). Subsequent multivariate Logistic regression analysis of these indicators showed that hypertension, hyperlipidemia, age, WC, TG, GGT, UA, and BUN were independent influencing factors for MAFLD with hyperglycemia ($P<0.05$) .

2.5 Construction and Validation of a Combined Prediction Model for MAFLD with Hyperglycemia ROC curve analysis was performed on the factors identified as influencing MAFLD with hyperglycemia through multivariate Logistic regression analysis in section 2.4. The results demonstrated that age, WC, hypertension, hyperlipidemia, TG, GGT, UA, and BUN, as independent predictors, had moderate predictive accuracy for MAFLD with hyperglycemia ($0.53 \leq \text{AUC} \leq 0.75$). Based on the Logistic regression analysis results, a predictive model for MAFLD with hyperglycemia was constructed using these eight key predictive factors in the training set. The prediction formula was: logit(P) = -7.446 + 0.046×age + 0.036×WC + 0.766×hypertension (yes=1, no=0) + 0.494×hyperlipidemia (yes=1, no=0) + 0.162×TG + 0.005×GGT - 0.007×UA + 0.279×BUN. The combined model achieved a predictive accuracy of 0.805 (95%CI=0.781~0.828), with a sensitivity of 75.8%, specificity of 72.6%, and a cutoff value of -1.842 [Figure 3: see original paper]. The predictive performance of this combined model was validated in the testing set, yielding a positive predictive accuracy of 0.705, negative predictive accuracy of 0.731, and overall predictive accuracy of 0.727 .

Discussion

This study conducted a retrospective data analysis based on large-scale health examination data to explore factors influencing liver fibrosis in MAFLD, primarily including hypertension, FBG, HbA1c, PLT, WBC, RBC, LYM, AST, and eGDR. Through comparison between the MAFLD with hyperglycemia and MAFLD without hyperglycemia groups, this study confirmed that T2DM is an important risk factor for MAFLD, consistent with previous research findings. Our data demonstrated that hepatic steatosis and fibrosis indices (such as FLI and FIB-4) were higher in the MAFLD with hyperglycemia group than in the MAFLD without hyperglycemia group, further supporting the close association between hyperglycemic status and MAFLD progression. This suggests that glycemic control is crucial for slowing MAFLD progression. Hyperglycemia may accelerate liver disease progression not only by promoting hepatic fat deposition but also by exacerbating systemic inflammation and oxidative stress, thereby facilitating hepatic fibrosis development.

This study further identified key influencing factors for MAFLD with hyperglycemia through Logistic regression analysis and ROC curve evaluation, among which age, WC, hypertension, hyperlipidemia, TG, GGT, UA, and BUN were important independent predictors. These indicators are all closely related to metabolic syndrome, particularly hyperlipidemia and abdominal obesity, which are typical features of insulin resistance. Elevated TG levels are closely associated with the development of fatty liver, while increased GGT, UA, and BUN levels can exacerbate the risk of MAFLD. These results suggest that improving metabolic status, especially controlling dyslipidemia and reducing abdominal fat accumulation, may be important for preventing and managing MAFLD with hyperglycemia.

Finally, this study successfully constructed and validated a combined prediction model for MAFLD with hyperglycemia. The model demonstrated high predictive accuracy (AUC=0.805), indicating that indicators such as age, WC, hypertension, hyperlipidemia, TG, GGT, UA, and BUN can be effectively used for early clinical screening and risk assessment. Notably, the model utilizes multiple metabolic factors beyond glycemic indicators to comprehensively evaluate the risk of MAFLD with hyperglycemia. In the testing set, the model achieved a positive predictive accuracy of 0.705 and negative predictive accuracy of 0.731, further proving its clinical application value. Early monitoring and intervention of these key indicators may help delay liver disease progression in MAFLD patients and reduce the risk of hyperglycemia-related complications. This combined prediction model provides clinicians with an effective assessment method for early identification of high-risk patients, facilitating timely targeted prevention and intervention measures, and providing a scientific basis for individualized treatment plans and optimized patient management.

Compared with previous studies, the strengths of this research lie in its large sample size and retrospective design, enhancing the generalizability and reliability of the findings. However, this study has several limitations. First, as a cross-sectional study, it cannot establish causal relationships between hyperglycemia and MAFLD progression. Second, this study did not incorporate broader genetic and environmental factors. Future longitudinal and multicenter studies are needed to further validate the generalizability and reliability of these influencing factors. Additionally, since this study was based on a health examination population, sample selection may have introduced certain biases, and the generalizability of the results requires further validation. Future multicenter, longitudinal cohort studies are planned to comprehensively explore important regulatory factors affecting MAFLD development and progression, providing reference for reducing MAFLD incidence and disease progression.

In summary, this study revealed key risk factors for MAFLD with hyperglycemia and constructed an effective combined prediction model using large-scale population data. Future research will further focus on exploring the underlying mechanisms of key influencing factors and validating and optimizing the prediction model in clinical practice, providing more precise clinical guidance and theoretical reference for early prevention and individualized management of MAFLD with hyperglycemia.

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Author Contributions: Wu Sha was responsible for data analysis, manuscript writing, and revision; Zhang Daiyi was responsible for data collation and analysis; Xuan Qinkao and Qian Xiaodong were responsible for data collection; Li Jin was responsible for data analysis and manuscript revision; Zhu Chuanwu and Pu Jianhong provided research guidance; Zhu Li was responsible for study design, overall research guidance, comprehensive data analysis, and manuscript revision guidance.

Conflict of Interest: The authors declare no conflict of interest.

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References

[1] Chinese Society of Hepatology, Chinese Medical Association. Guidelines for the prevention and treatment of metabolic associated (non-alcoholic) fatty liver disease (2024 edition)[J]. Chinese Journal of Hepatology, 2024, 32(5): 418-434. DOI:10.3760/cma.j.cn501113-20240327-00163.

[2] NIE K X, GAO Y, CHEN S, et al. Diosgenin attenuates non-alcoholic fatty liver disease in type 2 diabetes through regulating SIRT6-related fatty acid uptake[J]. Phytomedicine, 2023, 111: 154661. DOI:10.1016/j.phymed.2023.154661.

[3] QI X L, LI J, CAUSSY C, et al. Epidemiology, screening, and co-management of type 2 diabetes mellitus and metabolic dysfunction-associated steatotic liver disease[J]. Hepatology, 2024. DOI:10.1097/HEP.0000000000000913.

[4] YOUNOSSI Z M, GOLABI P, DE AVILA L, et al. The global epidemiology of NAFLD and NASH in patients with type 2 diabetes: a systematic review and meta-analysis[J]. J Hepatol, 2019, 71(4): 793-801. DOI:10.1016/j.jhep.2019.06.021.

[5] EN LI CHO E, ANG C Z, QUEK J, et al. Global prevalence of non-alcoholic fatty liver disease in type 2 diabetes mellitus: an updated systematic review and meta-analysis[J]. Gut, 2023, 72(11): 2138-2148. DOI:10.1136/gutjnl-2023-330110.

[6] Chinese Diabetes Society. Guidelines for the prevention and treatment of type 2 diabetes in China (2020 edition) (Part 1)[J]. Chinese Journal of Practical Internal Medicine, 2021, 41(8): 668-695. DOI:10.19538/j.nk2021080106.

[7] SHI X Y, FU S H, FU Y Y. Construction and efficacy evaluation of a risk prediction model for liver fibrosis in NAFLD patients[J]. Modern Practical Medicine, 2024, 36(3): [page numbers]. DOI: [reference number].

[8] GUO T, HU B, YI W M, et al. Research progress in serological diagnosis of non-alcoholic fatty liver disease[J]. Journal of Clinical Hepatology, 2020, 36(11): 2579-2583. DOI:10.3969/j.issn.1001-5256.2020.11.041.

[9] CHEN Q, HU P, HOU X, et al. Association between triglyceride-glucose related indices and mortality among individuals with non-alcoholic fatty liver disease or metabolic dysfunction-associated steatotic liver disease[J]. Cardiovasc Diabetol, 2024, 23(1): 232. DOI:10.1186/s12933-024-02343-7.

[10] KONG D X, XING Y L, SUN W W, et al. Study on the correlation between estimated glucose disposal rate and type 2 diabetes mellitus combined with metabolic associated fatty liver disease[J]. Chinese General Practice, 2023, 26(26): 3252-3258. DOI:10.12114/j.issn.1007-9572.2023.0103.

[11] KIM K S, HONG S M, HAN K, et al. Association of non-alcoholic fatty liver disease with cardiovascular disease and all cause death in patients with type 2 diabetes mellitus: nationwide population based study[J]. BMJ, 2024, 384: e076388. DOI:10.1136/bmj-2023-076388.

[12] BOCCATONDA A, ANDREETTO L, D' ARDES D, et al. From NAFLD to MAFLD: definition, pathophysiological basis and cardiovascular implications[J]. Biomedicines, 2023, 11(3): 883. DOI:10.3390/biomedicines11030883.

[13] ZHANG D, SUN K, LIU Y, et al. Application value of fatty liver index in the diagnosis of non-alcoholic fatty liver disease[J]. Journal of Internal Medicine Concepts & Practice, 2012, 7(3): 201-204. DOI:10.3969/j.issn.1673-6087.2012.03.013.

[14] LONARDO A, NASCIMBENI F, MAURANTONIO M, et al. Nonalcoholic fatty liver disease: Evolving paradigms[J]. World J Gastroenterol, 2017, 23(36): 6571-6592. DOI:10.3748/wjg.v23.i36.6571.

[15] RUZE R, LIU T T, ZOU X, et al. Obesity and type 2 diabetes mellitus: Connections in epidemiology, pathogenesis, and treatments[J]. Front Endocrinol, 2023, 14: 1161521. DOI:10.3389/fendo.2023.1161521.

[16] SHU J R, LI J Q, LIU Q. Epidemiology and risk factor analysis of non-alcoholic fatty liver disease[J]. Journal of Clinical Hepatology, 2019, 35(9): 2085-2090. DOI:10.3969/j.issn.1001-5256.2019.09.045.

[17] QIAN F F, DAI M Q, ZHAO L, et al. Correlation analysis between serum alkaline phosphatase and type 2 diabetes mellitus combined with non-alcoholic fatty liver disease[J]. Journal of Clinical Hepatology, 2023, 39(1): 83-88. DOI:10.3969/j.issn.1001-5256.2023.01.013.

[18] HOU M M, GU Q, CUI J W, et al. Proportion and clinical characteristics of metabolic-associated fatty liver disease and associated liver fibrosis in an urban Chinese population[J]. Chin Med J, 2024. DOI:10.1097/CM9.0000000000003141.

[19] GAO Y T, ZHAO T Y, SONG S N, et al. Lean nonalcoholic fatty

liver disease and risk of incident type 2 diabetes mellitus: a literature review and meta-analysis[J]. Diabetes Res Clin Pract, 2023, 200: 110699. DOI:10.1016/j.diabres.2023.110699.

[20] MANTOVANI A, TAVERNA A, CAPPELLI D, et al. Long-term adverse effect of liver stiffness on glycaemic control in type 2 diabetic patients with nonalcoholic fatty liver disease: a pilot study[J]. Int J Mol Sci, 2022, 23(20): 12481. DOI:10.3390/ijms232012481.

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