Original Article

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Predicting non-alcoholic fatty liver disease (NAFLD) using machine learning algorithms: Evidence from a large-scale community cohort in Taiwan

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SUMMARY: Closely associated with metabolic disorders, non-alcoholic fatty liver disease (NAFLD) substantially increases the risk of hepatocellular carcinoma. This study aimed to apply machine learning (ML) algorithms to a community-based cohort in southern Taiwan to identify key risk factors for NAFLD and to develop predictive models with clinical applicability. Data were derived from community health examinations, and eighteen clinical and demographic features were analyzed. Five ML algorithms were evaluated: logistic regression (LR), random forest (RF), K-nearest neighbors (KNN), adaptive boosting (AdaBoost), and extreme gradient boosting (XGBoost). Model performance was assessed using accuracy, precision, recall, F1 score, and area under the receiver operating characteristic curve (AUROC). A total of 7,510 participants were included (38.8% male; mean age 50.9 ± 15.0 years). The dataset was randomly divided into training (80%) and testing (20%) subsets, with no significant differences observed between groups in most independent variables. The Synthetic Minority Over-sampling Technique (SMOTE) was employed to balance NAFLD and non-NAFLD groups in the training dataset. Among all models, XGBoost achieved the highest performance, with an accuracy of 83.48%, precision of 84.31%, recall of 81.21%, F1 score of 82.72%, and AUROC of 92.85%. Feature importance analysis identified low-density lipoprotein cholesterol (LDL-C), body mass index (BMI), waist circumference, fasting plasma glucose (FPG), and triglycerides (TG) as the most influential predictors of NAFLD. ML algorithms, particularly XGBoost, demonstrated high accuracy in predicting NAFLD and effectively identified key clinical predictors. These findings may enhance early diagnosis and facilitate the development of targeted intervention strategies in the management of NAFLD.

Keywords: non-alcoholic fatty liver disease (NAFLD), risk factor, machine learning, prediction

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) represents one of the most prevalent chronic liver conditions globally, with an estimated prevalence of approximately 30.0%, showing an upward trend annually (*1*). Projections indicate that by 2040, the global prevalence of NAFLD will escalate to 55.7%, particularly affecting regions such as Asia and Europe (*2*). In Taiwan, NAFLD affects approximately one-third of the population

(*3*). This condition encompasses a spectrum of liver pathologies, including non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH), which can progress to liver fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). NAFLD is closely linked with obesity, type 2 diabetes, and metabolic syndrome, and it significantly elevates the risk of non-viral HCC (*4-6*). The increasing incidence and associated mortality of NAFLD present substantial health challenges, highlighting the critical importance of early identification and intervention strategies.

The integration of artificial intelligence into medical research has facilitated the extensive application of machine learning (ML) in predicting liver disease risk and treatment outcomes (*7*). ML algorithms, categorized into supervised and unsupervised learning, utilize large datasets to discern complex patterns, thereby enhancing predictive accuracy and classification efficiency. Supervised learning, which relies on training models with labeled datasets, enables precise analysis and prediction. Prominent supervised methods include Logistic Regression (LR), Random Forest (RF), K-Nearest Neighbors (KNN), Adaptive Boosting (AdaBoost), and eXtreme Gradient Boosting (XGBoost). Compared to traditional approaches, ML optimizes predictive capabilities by refining preprocessing models, thereby supporting more effective and precise decision-making.

The present study leveraged a real-world, multi-regional screening database from southern Taiwan to examine risk factors associated with NAFLD using ML algorithms. Advanced artificial intelligence techniques were employed to construct predictive models, identify the most accurate model, and analyze the relative contributions of key influencing factors.

2. Patients and Methods

2.1. Data source and study population

The study population comprised individuals who underwent community health screenings in southern Taiwan between June 1, 2001, and December 31, 2023. Eligibility criteria included the availability of anthropometric and biochemical data, along with abdominal ultrasound records. Major exclusion criteria encompassed duplicate screenings, age below 18 years, hepatitis B or C infection, and excessive alcohol consumption. As illustrated in Figure 1, a total of 7,510 participants met the inclusion criteria. The study was also approved by the Institutional Review Board of Kaohsiung Medical University Hospital (KMUHIRB-E(I)-20220347). Written informed consent was obtained from all participants, and the study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

2.2. Study variables

All participants underwent standardized assessments within a controlled evaluation setting. Data collection encompassed demographic variables (age, sex), medical history (hypertension, diabetes, hyperlipidemia), and lifestyle factors (smoking, alcohol consumption). Anthropometric measurements included height, weight, waist circumference, systolic blood pressure (SBP), and diastolic blood pressure (DBP). Biochemical analyses were conducted using a multichannel automatic analyzer (Hitachi, Tokyo, Japan) to measure aspartate aminotransferase (AST), alanine aminotransferase (ALT), triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). Fasting plasma glucose (FPG) levels were determined *via* radioimmunoassay (Diagnostic Products Co., Los Angeles, CA), and hepatic assessments were performed using ultrasound imaging.

NAFLD is diagnosed through imaging or histological confirmation of significant hepatic steatosis, excluding alternative causes such as Wilson's disease, celiac disease, chronic hepatitis C, chronic hepatitis B, and excessive alcohol consumption (>210 g/week in men, >140 g/week in women), in accordance with the American Association for the Study of Liver Diseases (AASLD) guidelines (*8*). Abdominal ultrasound examinations were conducted by licensed hepatology specialists trained at the same institution to ensure diagnostic consistency and minimize

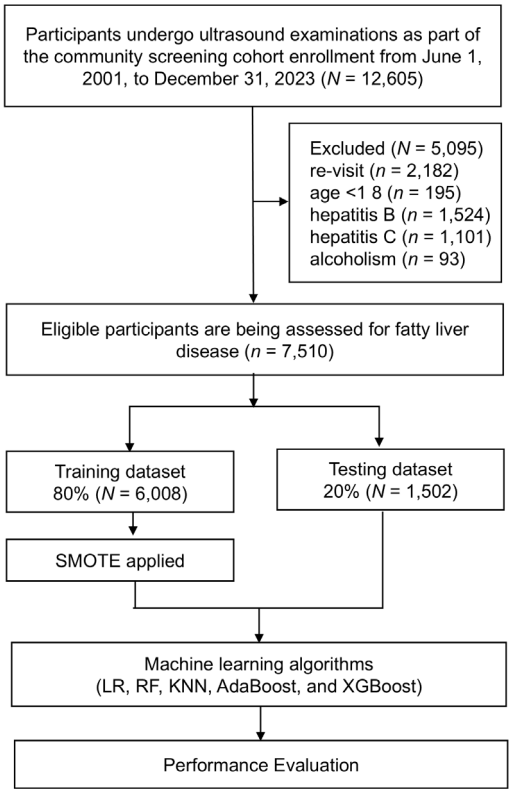

Figure 1. Study flow chart. *Abbreviation*: SMOTE, the synthesized minority oversampling technique. LR, logistic regression; RF, random forest; KNN, k-nearest neighbors; AdaBoost, adaptive boosting; XGBoost, eXtreme Gradient Boosting.

interobserver variability.

2.3. ML algorithms

ML models were constructed using five widely adopted supervised learning algorithms. These included logistic regression (LR), a linear model-based approach, and random forest (RF), an ensemble method utilizing bagging to aggregate multiple decision trees. The k-nearest neighbors (KNN) algorithm predicts outcomes based on feature-space proximity, while adaptive boosting (AdaBoost) iteratively enhances model performance by combining multiple weak learners. Additionally, extreme gradient boosting (XGBoost), an advanced gradient boosting algorithm, integrates bagging and boosting techniques to optimize predictive accuracy and computational efficiency.

2.4. ML algorithms construction and validation

This study included 3,660 individuals in the NAFLD group and 3,850 in the non-NAFLD group, resulting in a data imbalance that could compromise algorithm stability and predictive accuracy. To address this, the synthetic minority oversampling technique (SMOTE) was applied only to the training dataset to balance class distribution during model development (*9*). The dataset was randomly partitioned using the Monte Carlo method into 80% for training and 20% for testing, enabling simultaneous model construction and internal validation. At the same time, the test set retained the original class distribution to provide an unbiased evaluation of model performance. Feature selection was performed through univariate analysis to identify statistically significant predictors for the ML models. Model validation was conducted using 10-fold cross-validation and 1,000 bootstrap resampling iterations.

2.5. Model Interpretability: SHAP Method

When applying ML in medicine, there is often a trade-off between model interpretability and prediction accuracy. Medical decision making relies heavily on understanding the model inference logic to increase the credibility of predictions. To this end, we utilize the Shapley Additive exPlanations (SHAP) method, an additive feature attribution technique based on game-theoretic Shapley values that assesses the relative contribution of each feature to the model output. Through SHAP analysis, we can gain a more transparent understanding of the drivers of model predictions, thereby promoting trust and acceptance in clinical applications (*10,11*).

2.6. Statistical analysis

The unit of analysis was the individual patient who underwent community health screenings in southern Taiwan during the study period. Continuous variables were reported as mean ± standard deviation, while categorical variables were expressed as frequencies and proportions. Comparisons of continuous variables were conducted using Student *t*-test, whereas categorical data were analyzed using the chi-square test. Univariate logistic regression was performed to identify independent risk factors for NAFLD. Mean differences across multiple independent groups were assessed using one-way analysis of variance.

The statistical analysis in this study was conducted in five distinct steps. Initially, The full dataset of 7,510 cases was randomly divided into a training dataset (6,008 cases) for model development and a testing dataset (1,502 cases) for internal validation. Baseline characteristics between the training and testing datasets were compared using Student *t* test for continuous variables and the chi-square test for categorical variables to ensure representativeness and balance. In the second step, univariate logistic regression analyses were performed to identify variables significantly associated with NAFLD. These variables, together with the NAFLD outcome, were used as inputs for ML model development. The third step involved ML model development and performance evaluation. The models were trained using the training dataset, and predictive outputs were generated from the testing dataset. To assess model stability and estimate 95% confidence intervals, 1,000 bootstrap resamples of the datasets were generated. For each resample, model predictions were obtained, and five key performance metrics: accuracy, precision, recall, F1 score, and the area under the receiver operating characteristic curve (AUROC), were calculated. Differences in performance metrics across the models were evaluated using one-way analysis of variance (ANOVA). Confusion matrices were constructed to summarize true positives, true negatives, false positives, and false negatives for each model (*12,13*). The final step involved feature importance analysis to identify the most influential variables for NAFLD. Feature importance was assessed using SHAP, which quantifies the contribution of each feature to the model predictions based on cooperative game theory (*10,11*) SHAP values provide a consistent, model-agnostic measure of feature impact and allow for detailed interpretation of both global and individual level effects, ensuring a robust identification of key predictors.

Statistical analyses were performed using IBM SPSS Statistics v23.0 (IBM Corp., Armonk, NY, USA) and the Python programming language with Anaconda (Spyder v6.1.0). All tests were two-tailed, with statistical significance set at $p < 0.05$.

3. Results

3.1. Distribution of the study variables

This study encompassed a total of 7,510 individuals,

Table 1. Comparisons between the NAFLD and non-NAFLD groups in the screening population were performed

Variables	Total (N = 7,510)	No NAFLD group (n = 3,850, 51.3%)	NAFLD group (n = 3,660, 48.7%)	p-value
Sex, male	2,912 (38.8)	1,388 (36.1)	1,524 (41.6)	< 0.001
Age, years	50.9 ± 15.0	49.1 ± 16.2	52.8 ± 13.4	< 0.001
BMI, kg/m^2	24.9 ± 4.2	23.2 ± 3.5	26.3 ± 4.1	< 0.001
Waist circumference, cm	82.9 ± 10.7	78.5 ± 9.5	87.4 ± 10.0	< 0.001
Smoking	495 (6.6)	221 (5.7)	274 (7.5)	0.002
Alcohol	416 (5.5)	165 (4.3)	251 (6.7)	< 0.001
Hypertension	1,242 (16.5)	461 (12.0)	781 (21.3)	< 0.001
Diabetes	481 (6.4)	150 (3.9)	331 (9.0)	< 0.001
Hyperlipidemia	690 (9.2)	238 (6.2)	452 (12.4)	< 0.001
SBP, mmHg	129.4 ± 19.2	125.6 ± 19.2	133.4 ± 18.5	< 0.001
DBP, mmHg	79.9 ± 11.6	77.7 ± 11.3	82.1 ± 11.6	< 0.001
AST, U/L	26.0 ± 18.9	24.2 ± 16.6	28.0 ± 20.9	< 0.001
ALT, U/L	23.6 ± 17.6	19.7 ± 14.1	27.8 ± 19.7	< 0.001
Triglyceride, mg/dL	133.8 ± 104.5	108.8 ± 86.7	160.1 ± 114.7	< 0.001
Total cholesterol, mg/dL	203.7 ± 36.9	200.8 ± 37.0	206.8 ± 36.5	< 0.001
HDL-C, mg/dL	56.9 ± 13.5	60.5 ± 14.0	53.2 ± 12.0	< 0.001
LDL-C, mg/dL	121.6 ± 28.4	118.0 ± 28.0	125.4 ± 28.3	< 0.001
FPG, mg/dL	94.0 ± 29.3	88.9 ± 24.2	99.4 ± 33.1	< 0.001

Values are presented as mean ± standard deviation or n (%). *Abbreviations*: NAFLD, non-alcoholic fatty liver disease; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose.

including 2,912 males (38.8%) and 4,598 females (61.2%), with a mean age of 50.9 ± 15.0 years (Table 1). The non-NAFLD and NAFLD groups included 3,850 and 3,660 individuals, respectively, accounting for 51.3% and 48.7% of the total population. The distributions of independent variables are presented in Table 1. Univariate statistical analysis identified significant independent variables, which were subsequently included as predictors in the ML models (Table 2).

Table 2. Univariate analysis of NAFLD associated variables in the training dataset (N = 6,008)

Variables	OR (95% CI)	p-value
Sex, male *vs*. female	1.30 (1.17-1.44)	< 0.001
Age, years	1.02 (1.01-1.02)	< 0.001
BMI, kg/m^2	1.30 (1.27-1.32)	< 0.001
Waist circumference, cm	1.10 (1.09-1.11)	< 0.001
Smoking, yes *vs*. no	1.27 (1.04-1.56)	0.020
Alcohol, yes *vs*. no	1.58 (1.26-1.98)	< 0.001
Hypertension, yes *vs*. no	1.96 (1.71-2.26)	< 0.001
Diabetes, yes *vs*. no	2.36 (1.89-2.96)	< 0.001
Hyperlipidemia, yes *vs*. no	2.05 (1.71-2.46)	< 0.001
SBP, mmHg	1.02 (1.02-1.03)	< 0.001
DBP, mmHg	1.03 (1.03-1.04)	< 0.001
AST, U/L	1.02 (1.01-1.02)	< 0.001
ALT, U/L	1.04 (1.03-1.04)	< 0.001
Triglyceride, mg/dL	1.01 (1.01-1.01)	< 0.001
Total cholesterol, mg/dL	1.00 (1.00-1.01)	<0.001
HDL-C, mg/dL	0.96 (0.95-0.96)	<0.001
LDL-C, mg/dL	1.01 (1.01-1.01)	< 0.001
FPG, mg/dL	1.02 (1.02-1.02)	< 0.001

Abbreviations: NAFLD, non-alcoholic fatty liver disease; OR, odds ratio; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose.

3.2. Comparison of the ML models

The dataset was stratified into training and testing subsets, with a division ratio of 80:20. The training subset comprised 6,008 individuals, while the testing subset included 1,502 individuals (Supplementary Table S1, *https://www.biosciencetrends.com/action/getSupplementalData.php?ID=289*). Statistical analyses revealed no significant differences in most independent variables between the two datasets, indicating that both were derived from a relatively homogeneous population. Moreover, optimal hyperparameters and model architectures for the ML models were determined through grid search during the hyperparameter tuning process. The number of training epochs was fine-tuned through the procedure detailed in Supplementary Table S2 (*https://www.biosciencetrends.com/action/getSupplementalData.php?ID=289*).

Supplementary Figure S1 (*https://www.biosciencetrends.com/action/getSupplementalData.php?ID=289*) presents the confusion matrices for all ML models applied to the SMOTE resampled training (80%) and testing (20%) datasets. The performance metrics for LR, RF, KNN, AdaBoost, and XGBoost on the testing dataset were as follows: accuracy (0.72, 0.80, 0.66, 0.81, 0.84), precision (0.71, 0.82, 0.74, 0.81, 0.84), recall (0.72, 0.76, 0.47, 0.80, 0.83), F1 score (0.72, 0.79, 0.57, 0.80, 0.83), and AUROC (0.80, 0.88, 0.72, 0.90, 0.93) (Supplementary Table S3, *https://www.biosciencetrends.com/action/getSupplementalData.php?ID=289*). To enhance model robustness and mitigate overfitting, 10-fold cross-validation was conducted on both datasets (*data*

Table 3. Comparison of the machine learning (ML) model performance metrics following bootstrapping (*N* = 7,510)

Training dataset (*n* = 6,008)					
Model	Accuracy (95% CI)	Precision (95% CI)	Recall (95% CI)	F1 score (95% CI)	AUROC (95% CI)
LR	72.55% (71.39-73.81%)	72.25% (70.50-74.01%)	70.89% (69.12-72.67%)	71.56% (70.12-73.04%)	79.09% (77.89-80.36%)
RF	80.59% (79.55-81.65%)	81.75% (80.21-83.26%)	77.47% (75.87-79.09%)	79.55% (78.30-80.77%)	88.59% (87.71-89.47%)
KNN	82.85% (81.78-83.84%)	100.00% (100.00-100.00%)	64.81% (62.89-66.57%)	78.64% (77.22-79.93%)	93.89% (93.40-94.32%)
AdaBoost	82.18% (81.14-83.13%)	81.93% (80.40-83.37%)	81.36% (79.85-82.84%)	81.64% (80.49-82.77%)	90.70% (89.95-91.40%)
XGBoost	89.03% (88.16-89.88%)	89.21% (87.96-90.38%)	88.17% (86.94-89.50%)	88.68% (87.75-89.59%)	96.51% (96.13-96.88%)
p-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Testing dataset (*n* = 1,502)					
Model	Accuracy (95% CI)	Precision (95% CI)	Recall (95% CI)	F1 score (95% CI)	AUROC (95% CI)
LR	73.41% (71.21-75.80%)	73.68% (70.44-76.98%)	70.72% (67.07-74.14%)	72.15% (69.46-74.89%)	79.79% (77.55-82.04%)
RF	79.22% (76.91-81.42%)	81.36% (78.09-84.38%)	74.44% (70.95-77.60%)	77.73% (74.98-80.13%)	88.04% (86.13-89.71%)
KNN	65.38% (62.92-67.80%)	73.51% (68.95-77.75%)	45.29% (41.38-49.08%)	56.02% (52.33-59.28%)	71.29% (68.61-73.83%)
AdaBoost	81.74% (79.50-83.79%)	83.03% (79.94-85.83%)	78.64% (75.27-81.71%)	80.76% (78.24-83.13%)	91.02% (89.49-92.36%)
XGBoost	83.48% (81.50-85.42%)	84.31% (81.48-87.18%)	81.21% (78.24-84.17%)	82.72% (80.46-85.00%)	92.85% (91.55-94.13%)
p-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

P values were calculated using one-way analysis of variance (ANOVA) to assess whether differences in performance metrics were statistically significant across ML models. *Abbreviations*: AUROC, area under the receiver operating characteristic curve; LR, logistic regression; RF, random forest; KNN, K-nearest neighbors; AdaBoost, adaptive boosting; XGBoost, eXtreme gradient boosting.

not shown). Furthermore, model stability was assessed through 1,000 bootstrap resampling iterations, followed by ANOVA, which demonstrated statistically significant differences among the models ($p < 0.05$) (Table 3). Among the models evaluated, XGBoost exhibited the highest predictive performance for NAFLD in both the training and testing datasets, with a test set accuracy of 83.48% (95% CI 81.50-85.42%), precision of 84.31% (95% CI 81.48-87.18%), recall of 81.21% (95% CI 78.24-84.17%), F1 score of 82.72% (95% CI 80.46-85.00%), and AUROC of 92.85% (95% CI 91.55-94.13%).

3.3. Results of feature importance analysis

The analysis demonstrated that among the five ML models evaluated, XGBoost achieved the highest classification performance across all key metrics, establishing it as the most effective model for predicting NAFLD. To further elucidate the relative contribution of individual predictors, a feature importance analysis was performed using the SHAP framework. SHAP values quantify the impact of each independent variable on model predictions, with higher absolute values indicating a stronger contribution to NAFLD risk. As illustrated in Figure 2, the five most influential variables of NAFLD were LDL-C, BMI, waist circumference, FPG, and TG. While XGBoost internal feature importance provided similar trends (Figure 3), SHAP analysis was used as the primary interpretability tool due to its model agnostic transparency and stability against correlated variables.

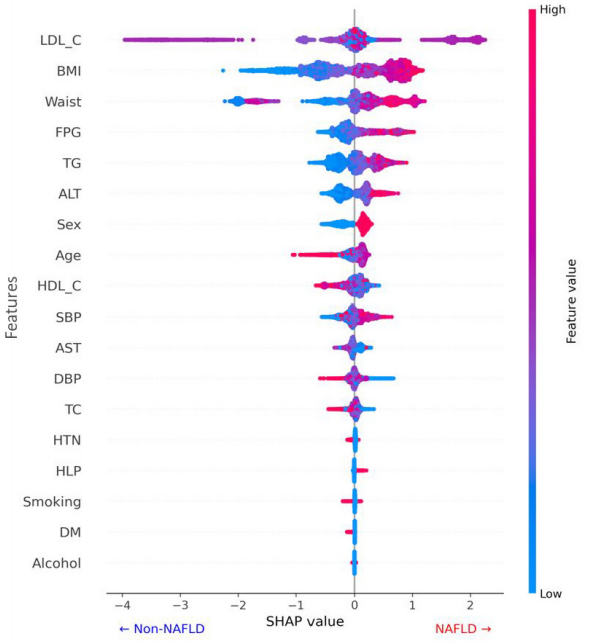

Figure 2. SHAP summary plot. The SHAP summary plot combined the feature importance and effects on non-alcoholic fatty liver. *Abbreviation*: SHAP, Shapley additive explanations; LDL-C, low-density lipoprotein cholesterol; BMI, body mass index; FPG, fasting plasma glucose; TG, triglyceride; ALT, alanine aminotransferase; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; AST, aspartate aminotransferase; DBP, diastolic blood pressure; TC, Total Cholesterol; HTN, hypertension; HLP, hyperlipidemia; DM, diabetes mellitus.

4. Discussion

4.1. Major findings

Given the absence of effective pharmacological interventions for NAFLD, early detection and prevention are paramount in improving patient outcomes. The increasing integration of AI and ML in healthcare has enhanced clinicians' ability to analyze the epidemiology,

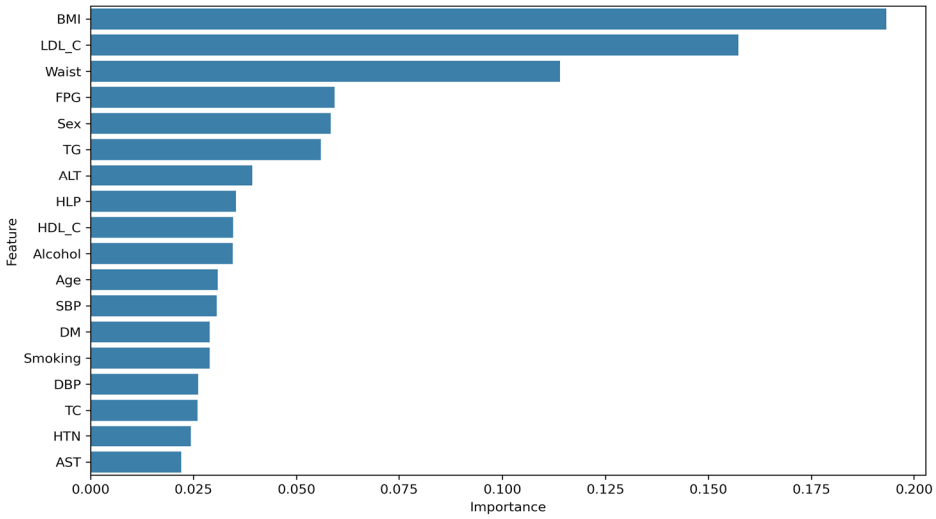

Figure 3. Analysis of feature importance for the occurrence of non-alcoholic fatty liver disease using the XGBoost model. *Abbreviation*: XGBoost, eXtreme Gradient Boosting; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose; TG, triglyceride; ALT, alanine aminotransferase; HLP, hyperlipidemia; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DM, diabetes mellitus; DBP, diastolic blood pressure; TC, Total Cholesterol; HTN, hypertension; AST, aspartate aminotransferase.

etiology, and management of diseases. Leveraging AI-driven analysis of healthcare big data enables the precise identification of at-risk individuals, facilitating targeted interventions and optimizing patient care strategies (*14-16*).

4.2. Comparison of ML-based NAFLD prediction with previous literatures

This study assessed five ML models for predicting fatty liver disease in a Taiwanese community cohort. Using data from 7,510 individuals and 18 anthropometric and biochemical variables, XGBoost demonstrated superior predictive performance (AUROC: 96.51% training, 92.85% validation). By integrating gradient boosting and regularization, XGBoost effectively addresses multicollinearity and overfitting, enhancing classification performance (*17*). A review of global studies highlights XGBoost superior accuracy in liver disease prediction, particularly in early NAFLD detection (*18-27*). Table 4 summarizes related studies on ML-based NAFLD prediction (*18-27*). Its robustness is enhanced by optimizing max depth and colsample bytree, while the application of multiple imputation by chained equations (MICE) for missing data and SMOTE for class balancing mitigates bias and overfitting. XGBoost has demonstrated excellence in diagnosing and staging MASLD. In our previous study, we have compared five ML models for predicting direct-acting antiviral drugs treatment failure in hepatitis C, with XGBoost outperforming others through iterative gradient boosting (*20*). Similarly, in a liver cancer risk model using epigenomic data, XGBoost achieved the highest accuracy (99.67%) and AUROC (100%) (*24*). This study assessed LR, RF, KNN, AdaBoost, and XGBoost using accuracy, precision, recall, F1 score, and AUROC. XGBoost consistently outperformed other models, underscoring its potential for precise NAFLD prediction and its clinical utility in personalized medicine.

4.3. Comparison of risk factors of NAFLD with previous literatures

Feature contributions assessed *via* SHAP values in the XGBoost model identified LDL-C, BMI, waist circumference, FPG, and TG as the five most significant predictors of NAFLD. NAFLD, defined by hepatic lipid accumulation exceeding 5%, is strongly associated with metabolic dysfunction, including obesity, insulin resistance, and hypertension (*28*). Hepatic lipid accumulation arises from dysregulated lipid metabolism, characterized by excessive hepatic de novo lipogenesis (DNL), impaired fatty acid oxidation, and altered lipid export *via* very low-density lipoproteins (VLDL-C) (*29*). These metabolic disturbances contribute to atherogenic dyslipidemia, marked by elevated TG, small dense LDL-C (sdLDL-C), and decreased high-density lipoprotein cholesterol (HDL-C) (*30,31*). The accumulation of LDL-C promotes vascular plaque formation, thereby increasing the risk of cardiovascular disease (CVD) and potentially exacerbating hepatic steatosis and progression to steatohepatitis, underscoring its significant association with NAFLD.

Notably, the SHAP summary plot demonstrated that the contribution of LDL-C to NAFLD prediction was not strictly monotonic, as both positive and negative SHAP values were observed across comparable LDL-C levels. This distribution indicates that the influence of LDL-C on NAFLD risk is dependent and likely modified by coexisting metabolic characteristics, including BMI,

Table 4. Summary of related studies on machine learning (ML) algorithms in individuals with non-alcoholic fatty liver disease (NAFLD)

Author (Country)	No. of subjects	Major findings
Lin *et al*., 2026 (Taiwan)	A total of 7,510 subjects participated in community health and abdominal ultrasound examinations	In predicting NAFLD using logistic regression (LR), random forest (RF), k-nearest neighbors (KNN), adaptive boosting (AdaBoost), and extreme gradient boosting (XGBoost), XGBoost exhibited the highest accuracy, emerging as the superior predictive model.
Cao *et al*., 2024 (China) (*18*)	22,140 health checkup participants	XGBoost outperformed LR, naive bayes (NB), and decision tree (DT) models in the early prediction of NAFLD.
McTeer *et al*., 2024 (UK) (*19*)	European non-alcoholic fatty liver disease (NAFLD) database	Using XGBoost to diagnose and stage patients with metabolic dysfunction-associated steatotic liver disease (MASLD), the AUROC reached 99%.
Lu *et al*., 2024 (Taiwan) (*20*)	34,301 hepatitis patients received direct-acting antiviral (DAA) therapy	Among five machine learning models: LR, DT, RF, XGBoost, and artificial neural network (ANN), used to predict factors leading to treatment failure in hepatitis C patients receiving direct-acting antiviral (DAA) therapy, XGBoost exhibited the highest predictive capability.
Peng *et al*., 2023 (China) (*21*)	578 physical examination subjects	Using machine learning algorithms such as LR, RF, XGBoost, gradient boosting machine (GBM), and support vector machine (SVM), the development and validation of models for NAFLD were performed, with XGBoost showing the best performance.
Zeng *et al.*, 2023 (China) (*22*)	6,648 patients with decompensated cirrhosis (DC)	The overall performance of the XGBoost model surpasses that of the traditional LR model and accurately predicts the risk of developing decompensated cirrhosis.
Suárez *et al*., 2023 (Mexico) (*23*)	215 patients with non-alcoholic steatohepatitis (NASH)	XGBoost outperformed SVM, DT, GBM, and KNN in predicting liver fibrosis progression in NASH patients.
Vekariya *et al*., 2022 (Canada) (*24*)	The Cancer Genome Atlas (TCGA)	Using epigenomic data, a predictive model for hepatocellular carcinoma risk was developed by applying XGBoost, RF, NB, KNN, multilayer perceptron (MLP), DT, and SVM. XGBoost emerged as the best model.
Ghandian *et al*., 2022 (U.S.A) (*25*)	141,293 patients with NAFLD	XGBoost outperformed LR and MLP models in assessing the risk of progression from NAFLD to NASH or fibrosis in patients.
Liu e*t al*., 2021 (China) (*26*)	15,315 adults underwent health check-ups	Compared to LR, SVM, stochastic gradient descent (SGD), MLP, convolutional neural network (CNN), and long short-term memory (LSTM) models, XGBoost exhibits superior predictive capability for NAFLD.
Agarwal *et al*., 2021 (India) (*27*)	828 patients with chronic liver disease	The application of XGBoost models has enhanced the accuracy of predicting esophageal variceal bleeding in patients with compensated advanced chronic liver disease.

waist circumference, triglyceride concentrations, and glycaemic status, all of which ranked highly in feature importance. Such non-linear and interaction patterns are intrinsic to tree-based ML algorithms and reflect complex multivariable dependencies rather than independent linear associations. However, formal interaction analyses, such as SHAP interaction values or stratified modeling approaches, were not undertaken in the present study. Further research incorporating explicit interaction modeling is warranted to elucidate these metabolic interrelationships and to enhance interpretability of model risk estimates. Previous research has demonstrated that elevated LDL-C levels, even within the normal range, constitute a significant risk factor for NAFLD (*32*). A retrospective study conducted in Japan by Tomizawa *et al*. identified a strong correlation between triglyceride levels and NAFLD within the context of dyslipidemia (*33*). Furthermore, a meta-analysis confirmed obesity as an independent risk factor, indicating that obese individuals have a 3.5-fold increased risk of developing NAFLD (*34*). The same analysis revealed a dose-dependent association between BMI and NAFLD risk, with each unit increase in BMI corresponding to a 1.20-fold elevation in risk. Additionally, a meta-analysis of 20 studies demonstrated that abdominal obesity, as measured by waist circumference, poses a greater risk for NAFLD than general obesity, as assessed by BMI (*35*). Elevated FPG levels may indicate an increased risk

Table 5. Selected studies on risk factors influencing non-alcoholic fatty liver disease (NAFLD)

Author (Country)	No of subjects	Major findings
Lin *et al.*, 2026 (Taiwan)	7,510 subjects participated in community health examinations and abdominal ultrasound screenings	The primary risk factor for NAFLD is low-density lipoprotein cholesterol (LDL-C), followed by body mass index (BMI), waist circumference (WC), fasting plasma glucose (FPG), and triglycerides (TG).
Alnimer & Alnimer, 2023 (U.S.A) (*37*)	2017-2018 national health and nutrition examination survey (NHANES) dataset	TG, age, BMI, and glycated hemoglobin (HbA1c) are the primary factors influencing the prediction of hepatic steatosis.
Wang *et al*., 2023 (China) (*38*)	31,718 adults undergoing medical examinations	The prevalence of NAFLD is 53.5%. key risk factors include age, BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), FPG, total bilirubin, TG, and LDL-C.
Noureddin *et al.*, 2022 (U.S.A) (*39*)	2017-2018 NHANES dataset	Risk factors influencing NAFLD include gender, HbA1c, BMI, WC, and AST.
Huang *et al*., 2022 (Taiwan) (*40*)	2,483 subjects who underwent community health examinations	The prevalence of NAFLD and metabolic syndrome was 44.5% and 15.8%, respectively. Increasing age, higher BMI (obesity), and elevated insulin resistance (IR) were identified as major risk factors for NAFLD, with high IR serving as a significant independent predictor in both obese and non-obese individuals.
Chen *et al*., 2022 (Taiwan) (*41*)	31,930 adults aged 20 and older underwent health screenings and ultrasounds.	ALT, BMI, WC, and TG are important risk factors influencing NAFLD.
Long *et al*., 2018 (U.S.A) (*42*)	685 participants in the Framingham Heart Study	Significant associated factors include age, female sex, BMI, alcohol consumption, and TG.
Sun *et al*., 2016 (Korea) (*32*)	20,433 subjects who underwent liver ultrasound	Elevated LDL-C levels are a risk factor for NAFLD.
Li *et al*., 2016 (China) (*43*)	21 studies were selected for this study (381,655 participants)	Obesity increases the risk of NAFLD by 3.5 times, demonstrating a clear dose-response relationship between BMI and NAFLD.
Pang *et al*., 2015 (China) (*35*)	20 studies were selected from PubMed, EMBASE, and the ISI Web of Science for this analysis	Abdominal obesity, measured by WC, is associated with a higher risk of developing NAFLD compared to general obesity assessed by BMI.
Tomizawa *et al*., 2014 (Japan) (*33*)	293 subjects underwent abdominal ultrasound	Among lipid abnormalities, TG are closely correlated with NAFLD, and elevated TG levels serve as an important marker for the condition.
Eguchi *et al*., 2012 (Japan) (*44*)	5,075 subjects who underwent health examinations	The prevalence of NAFLD is 29.7%, with males (41.0%) showing a three-fold higher rate than females (17.7%). Significant relationship exists between NAFLD prevalence and metabolic indices, including BMI, TG, and LDL-C ($p < 0.001$).

of NAFLD, and this association is more pronounced in shorter individuals (*36*). The important influencing factors related to NAFLD are summarized in Table 5 (*32,33,35,37-44*). Collectively, these findings highlight LDL-C, BMI, waist circumference, FPG, and TG as major contributors to metabolic dysfunction underlying NAFLD. Given that NAFLD is now encompassed under the concept of metabolic dysfunction–associated steatotic liver disease (MASLD) (*45*), these factors reflect underlying metabolic derangements, including dyslipidemia, insulin resistance, and central obesity, that contribute to both hepatic steatosis and cardiometabolic risk. Consequently, monitoring and managing these variables may provide critical opportunities for early identification and intervention in individuals at risk of MASLD.

4.4. Strengths and limitations

This study has several notable strengths. First, unlike prior research primarily based on single-institution datasets or interdisciplinary studies, this study utilizes community health check-up data from multiple counties and cities in southern Taiwan, thereby enhancing its generalizability and applicability to the broader Taiwanese population. Second, rather than incorporating all variables into the ML model without distinction, this study employed univariate analysis to identify

significant predictors of NAFLD, thereby mitigating the risk of confounding effects and improving model interpretability. Furthermore, the application of SMOTE to balance the sample sizes of NAFLD and non-NAFLD groups effectively addresses class imbalance, minimizing selection bias across variables. In contrast to previous studies that relied solely on absolute performance metrics for model comparison, this study adopted a more rigorous approach by implementing the bootstrap method with Monte Carlo simulations, conducting 1,000 resampling iterations. ANOVA testing was subsequently performed to assess the statistical significance of performance differences among models. Finally, feature importance analysis of the optimal model identified key predictors of NAFLD risk, ensuring that the predictive accuracy is robust and reflective of the relative contribution of each variable.

This study has several limitations. First, the absence of diagnostic evaluations for drug-induced, acquired metabolic, and genetic liver diseases, including autoimmune hepatitis, primary biliary cholangitis, and hemochromatosis, precludes the precise exclusion of these conditions, thereby limiting the accuracy of NAFLD classification. Second, key clinical variables, such as lifestyle and dietary factors, were not incorporated into the analysis, potentially introducing unaccounted confounding effects and affecting the performance metrics of the models. Third, the study was restricted to five commonly used ML algorithms. Future research should explore a broader spectrum of predictive models to enhance the methodological rigor, predictive accuracy, and generalizability of the findings. Fourth, although SHAP analysis enhances model interpretability, the present study did not conduct formal interaction or non-linear effect modeling to quantify dependencies among metabolic predictors. The observed SHAP patterns should be interpreted as reflecting complex multivariable relationships rather than isolated independent effects. Future investigations incorporating explicit interaction terms or causal models may further elucidate these underlying mechanisms. Finally, the lack of external validation represents an important limitation, as the models were evaluated only within the internal dataset. This may limit their applicability in real-world settings, where population characteristics and clinical practices may differ, underscoring the need for external validation before clinical implementation.

In conclusion, ML algorithms facilitate the development of highly accurate predictive models and the identification of key determinants of disease risk, providing critical insights for diagnosis and intervention. Among the five models analyzed, XGBoost exhibited the highest predictive performance for NAFLD, identifying LDL-C, BMI, waist circumference, FPG, and TG as significant risk factors. This model enhances the understanding of NAFLD pathophysiology and supports early detection and targeted prevention strategies, thereby contributing to improved public health outcomes and healthcare quality.

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