

Predictive Modeling of the Risk of Hyperglycemia in Psoriasis Patients Using Machine Learning: A Multicenter Retrospective Study

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Purpose: This study aims to develop and validate machine learning models for predicting hyperglycemia risk in psoriasis patients.

Methods: Clinical data from 575 psoriasis patients admitted to the Department of Dermatology were collected and randomly split into a training set and an internal test set in a 7:3 ratio. An external test set was derived from 135 psoriasis patients enrolled in the National Health and Nutrition Examination Survey (NHANES) during 2003–2004 and 2011–2012. Eleven machine learning algorithms, including decision trees, random forests, extreme gradient boosting (XGboost), light gradient boosting machine, support vector machines, multilayer perceptron, K-nearest neighbors, logistic regression, lasso regression, ridge regression, and elastic net, were systematically compared. Model performance was evaluated using area under the receiver operating characteristic curve (AUC), calibration curves and clinical decision curve (DCA).

Results: The extreme gradient boosting (XGboost) was selected as the final predictive model due to its robust performance across multiple evaluation metrics. The area under the curve values for the training, internal, and external test sets were 0.821 (95% confidence Interval (CI): 0.775–0.866), 0.820 (95% CI: 0.751–0.888), and 0.788 (95% CI: 0.695–0.881), respectively. Calibration and clinical decision curve analysis confirmed the model's accuracy and clinical utility. Additionally, a web-based calculator was developed to improve the model's accessibility and application.

Conclusion: The XGBoost-based model effectively predicts hyperglycemia risk in psoriasis patients, emphasizing personalized treatment plans for high-risk individuals to manage hyperglycemia progression and psoriasis-related inflammation.

Keywords: psoriasis, hyperglycemia, machine learning

Introduction

Psoriasis is a chronic inflammatory skin condition and a systemic disease. Compared to the general population, individuals with psoriasis are at an increased risk of developing metabolic and cardiovascular diseases.¹ A retrospective cohort study revealed that the risk ratios for diabetes mellitus, hypertension, and hypercholesterolemia increase with increasing psoriasis severity.² Psoriasis and diabetes share a common pathogenesis, including overlapping susceptibility genes, including PTPN22, ST6GAL1, and JAZF1³ and shared inflammatory pathways. In psoriasis, systemic inflammation is characterized by elevated serum pro-inflammatory cytokines (IL-17, IL-23, and TNF- α) and abnormal adipocytokine expression, which contribute to insulin resistance.^{4–7} Patrick et al confirmed a strong causal relationship between type 2 diabetes and psoriasis using Mendelian randomization.⁸ Additionally, a national cohort study in Denmark demonstrated that psoriasis increases the risk of newly diagnosed diabetes,⁹ with severe psoriasis exhibiting the strongest association.¹⁰

Diabetes exacerbates psoriasis and reduces responsiveness to biologic therapies,¹¹ resulting in suboptimal treatment outcomes. Psoriasis patients at risk for diabetes require active glycemic management to mitigate metabolic complications. Early detection of high-risk individuals and integrated therapeutic strategies are essential to improving outcomes, as psoriasis and diabetes synergistically contribute to poor prognoses. Established risk factors for diabetes in psoriasis patients include age, gender, obesity, smoking history, alcohol use, blood pressure, lipid profiles, liver and renal function, and psoriatic arthritis.^{12–16} Additionally, the systemic immune-inflammatory index (SII), a novel inflammatory marker, positively correlates with psoriasis.¹⁷ Each standard deviation (SD) increase in SII is associated with a 4–5% higher risk of type 2 diabetes and insulin resistance.¹⁸ Additionally, the SII aids in identifying impaired glucose tolerance in non-diabetic patients.¹⁹

However, using merely one or a handful of indications to make accurate forecasts is still not feasible. Machine learning algorithms have demonstrated significant practical value in the medical area and are able to learn and generate predictions based on a huge number of data samples. Machine learning is still a useful tool to support clinical decision-making and can aid physicians with disease diagnosis, therapy, and prognosis, despite drawbacks such as poor interpretability, limited generalization ability, and bias risk. As of right now, there is no prediction model for psoriasis patients' risk of hyperglycemia. Therefore, in order to screen out the high-risk group and implement early intervention, as well as to provide guidance for the individualized treatment of psoriasis patients, we propose to build a prediction model for the risk of hyperglycemia in psoriasis patients using clinical data of psoriasis patients and machine learning algorithms.

Materials and Methods

Research Objectives

This was a retrospective study performed on the clinical data from 575 psoriasis patients admitted to the Department of Dermatology at The Affiliated Hospital of Guilin Medical University between December 1, 2018, and December 31, 2022, retrieved through the inpatient electronic medical record system. For patients with multiple hospitalizations, only data from the initial admission were included. Based on the presence or absence of hyperglycemia, patients were categorized into the psoriasis-combined hyperglycemia group and the psoriasis-not-combined hyperglycemia group. The dataset was randomly divided into a training and an internal test set in a 7:3 ratio. Furthermore, data from 135 psoriasis patients were extracted from the National Health and Nutrition Examination Survey (NHANES) databases for 2003–2004 and 2011–2012, serving as an external test set. Among the 8862 respondents to the NHANES psoriasis questionnaire, 202 were identified as having psoriasis. Of these, 135 psoriasis patients met this study's inclusion and exclusion criteria. We confirmed that all methods were carried out following relevant guidelines and regulations. Our study complies with the Declaration of Helsinki.

Inclusion and Exclusion Criteria

Patients were included if they were over 18 years old and satisfied the diagnostic criteria for psoriasis. Exclusion criteria included the absence of hyperglycemia data, severe renal impairment (renal insufficiency progressing to uremia), hepatic impairment (transaminase levels exceeding three times the upper limit of normal, Liver function reference ranges: ALT: 9–50 U/L for males, 7–40 U/L for females; AST: 15–40 U/L for males, 13–35 U/L for females²⁰), pregnancy or lactation, and a history of malignant tumors. The study was approved by the Guilin Medical College Hospital Physical Committee (Approval No. 2024IITLL-31). The patient data were anonymized before analysis to ensure privacy and did not influence patient prognosis or treatment. Therefore, informed consent was not required; however, NHANES participants provided written informed consent. The study protocol was approved by the institutional review board of the National Center for Health Statistics.

Data Extraction

The extracted data included demographic details (age, gender, smoking, and drinking status), medical history (diabetes, hypertension, renal impairment, malignancy, pregnancy, lactation, and psoriatic arthritis), physical examination findings (weight, height, body mass index (BMI), and blood pressure), and laboratory test results. Laboratory assessments included fasting plasma glucose (FPG), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), creatinine (Cr), high-

sensitivity C-reactive protein (hs-CRP), SII (neutrophils multiplied by platelets divided by lymphocytes), and white blood cell (WBC) counts. The primary outcome measure was hyperglycemia.

Diagnostic Criteria and Definitions

Psoriasis diagnosis adhered to the “China Psoriasis Diagnosis and Treatment Guidelines (2023 edition)”.²¹ Hyperglycemia was defined as having a prior confirmed diagnosis of diabetes mellitus or meeting the following criteria: FPG ≥ 6.1 mmol/L or oral glucose tolerance test, 2-h plasma glucose ≥ 7.8 mmol/L. The hypertension was defined as follows: the systolic blood pressure of ≥ 140 mmHg and/or the diastolic blood pressure of ≥ 90 mmHg from three measurements on different days without the use of antihypertensive drugs and/or a previously definitive diagnosis of hypertension managed with antihypertensive treatment. NHANES defined psoriasis: if a participant answered “Yes” to the question, “Have you ever been told by a healthcare provider that you have psoriasis?” they were considered to have the condition. The following categories were used to classify drinking and smoking status: “current smoker”, “current non-smoker”, “current drinker”, and “current non-drinker.”

Statistical Methods

R (version 4.2.1; R Foundation for Statistical Computing) and the Statistical Package for the Social Sciences (IBM SPSS Statistics 26.0) software were used to analyze the data. Multiple interpolation was employed to fill in the missing data (tidyverse package) for less than 10% of the data. In a 7:3 ratio, 575 psoriasis patients were randomly divided into training and internal test sets, while 135 patients from the NHANES database served as an external test set. For continuous data, the Shapiro–Wilk test was used to determine the data normality. Normally distributed data was expressed as mean $\pm$ SD, while non-normally distributed data was expressed as median and interquartile spacing (M (P25 and P75)). Count data are expressed as percentages (%). The model’s features were subjected to Spearman correlation analysis to determine the degree of correlation between them. A correlation index of < 0.4 was considered as low correlation, 0.4–0.7 as medium correlation, and > 0.7 as strongly correlated.

Eleven machine learning algorithms, including decision trees, random forests, extreme gradient boosting (XGboost), light gradient boosting machine, support vector machines, multilayer perceptron, K-nearest neighbors, logistic regression, lasso regression, ridge regression, and elastic net, were applied for model construction and validation using the tidymodel package. Five-fold cross-validation is used to determine the ideal hyperparameters in order to maximize the accuracy of the model. To thoroughly evaluate each model’s predictive power, the receiver operator characteristic curve (ROC) was used for each dataset, and the area under the curve (AUC) was calculated along with the accuracy, F1 score, and Brier score. The model’s accuracy was determined using calibration curves. Its clinical applicability was evaluated using clinical decision curve analysis (DCA), and the best model was selected by creating and launching an online calculator on the shinyapp website. Additionally, the value of each variable’s contribution to the prediction was determined using the SHapley Additive exPlanations (SHAP) approach to rank the variables’ significance and explain the final model’s output.

Results

Data Description and Variable Correlation Test

A total of 575 patients were included in the study and were randomly assigned to the training set (404 patients) and internal test set (171 patients) in a 7:3 ratio. Among these, 92 (22.7%) patients in the training set and 38 (22.2%) in the internal test set had both psoriasis and hyperglycemia. Similarly, 29 (21.4%) of the 135 patients in the external test set, sourced from the NHANES database, exhibited both conditions. Table 1 shows the comparison between the hyperglycemic and non-hyperglycemic populations in the training set. Psoriasis patients with hyperglycemia showed significantly higher prevalence rates of male gender, smoking history, and hypertension compared to normoglycemic psoriasis patients. Furthermore, these patients had elevated mean values for age, TG, BUN, Cr, AST and ALT, coupled with reduced HDL-C level ($P < 0.05$). Spearman correlation analysis was conducted for all variables in the model, with results

Table 1 Comparison of Hyperglycemic versus Non-Hyperglycemic Individuals in the Training Set [n (%), M (P25, P75)]

Characteristic	Non-Hyperglycemia (n=312)	Hyperglycemia (n=92)	Total (n=404)	P Value
Gender				0.007
Female	83 (26.6)	12 (13)	95 (23.5)	
Male	229 (73.4)	80 (87)	309 (76.5)	
Age(y)	51 (37, 60)	58 (53.5, 65)	53 (40.8, 62)	< 0.001
Smoking				0.01
No	239 (76.6)	58 (63)	297 (73.5)	
Yes	73 (23.4)	34 (37)	107 (26.5)	
Drinking				0.058
No	275 (88.1)	74 (80.4)	349 (86.4)	
Yes	37 (11.9)	18 (19.6)	55 (13.6)	
Psoriatic Arthritis				0.944
No	267 (85.6)	79 (85.9)	346 (85.6)	
Yes	45 (14.4)	13 (14.1)	58 (14.4)	
Hypertension				< 0.001
No	240 (76.9)	43 (46.7)	283 (70)	
Yes	72 (23.1)	49 (53.3)	121 (30)	
TG (mmol/L)	1.3 (0.9, 1.7)	1.6 (1.2, 2.2)	1.3 (0.9, 1.9)	< 0.001
HDL-C (mmol/L)	1.1 (0.9, 1.2)	1 (0.8, 1.2)	1.1 (0.9, 1.2)	< 0.001
BUN (mmol/L)	4.3 (3.5, 5.4)	5.5 (4, 6.5)	4.5 (3.6, 5.6)	< 0.001
Cr (μmol/L)	71.3 (60, 82)	80 (66.5, 95.2)	72.7 (61, 84)	< 0.001
AST (U/L)	19 (15.1, 22.5)	20.7 (15.1, 26)	19.1 (15.1, 23.2)	0.046
ALT (U/L)	17.7 (11.5, 24.7)	21.2 (13.3, 31)	18.1 (12, 25.7)	0.019
WBC (10 ⁹ /L)	6.9 (6, 8.5)	7.8 (6.2, 8.9)	7 (6, 8.6)	0.104
BMI (kg/m ²)	23.6 (21.5, 26.2)	23.8 (21.5, 26.5)	23.6 (21.5, 26.3)	0.433
SII	589.6 (414.9, 914.4)	577.1 (410.6, 805.7)	585.4 (414.7, 848)	0.597

visualized in a heat map of correlation coefficients (Figure 1). The analysis confirmed that none of the features demonstrated a strong correlation, ensuring that multicollinearity did not compromise the model.

Model Construction and Selection

Eleven machine learning algorithms were applied to construct predictive models, using a five-fold cross-validation approach to enhance stability and optimize hyperparameters. Model performance was evaluated using accuracy, F1 score, Brier score, and AUC values calculated for the training, internal, and external test datasets. The AUC provided a numerical summary of predictive accuracy, while the ROC curve, which was composed of the true positive rate and false positive rate, served as a visual representation of model performance. An AUC closer to 1 indicates superior performance. Accuracy, ranging from 0 to 1, measures the proportion of accurately predicted samples to the total sample size, with higher values indicating better classification capability. The F1 score, representing the harmonic mean of precision and recall, ranges from 0 to 1, with higher values reflecting a balanced performance between these metrics. The Brier score, inversely related to model performance, quantifies the difference between predicted probabilities and actual outcomes, with lower scores indicating better predictive accuracy. Additionally, the mean and SD of these metrics across the datasets were calculated to determine model stability. Lower SD values indicate minimal variability and suggest robust model generalization, mitigating overfitting risks.

The comparative results of these metrics (Table 2) indicated XGBoost as the top-performing model, followed by logistic regression. XGBoost achieved AUC values of 0.821 (95% CI: 0.775–0.866) for the training set, 0.820 (95% CI: 0.751–0.888) for the internal test set, and 0.788 (95% CI: 0.695–0.881) for the external test set (Figure 2A). Calibration curves and clinical decision curves (DCA) further validated the model’s accuracy and clinical applicability (Figure 2B and C). We created a web-based free calculator to help the reader see the model and comprehend the machine learning

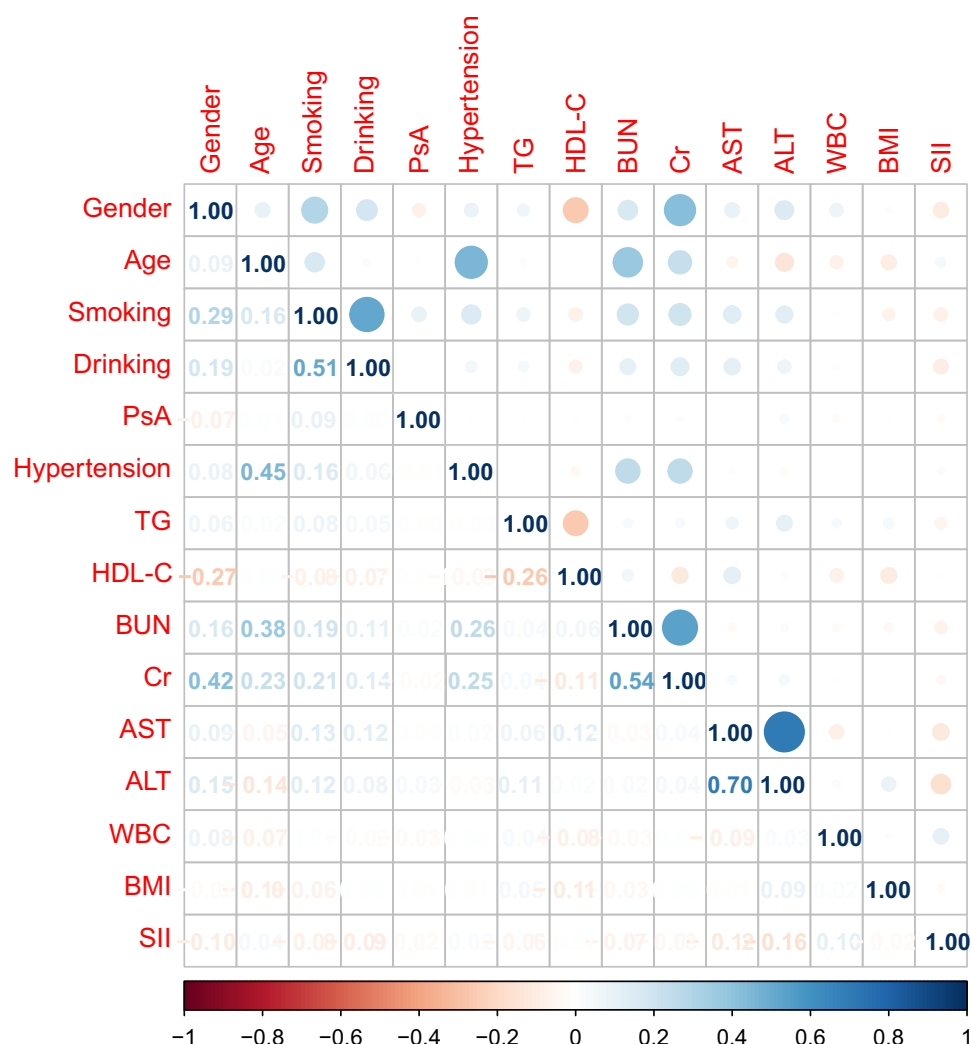


Figure 1 Correlation analysis based on Spearman analysis. The brighter the colors, the higher the relevance among variables.

method (URL: <https://nemn.shinyapps.io/xgbdudu/>). Users can input relevant values (Age 61, TG 13.92 mmol/L, and HDL-C 2.53 mmol/L) into the calculator to predict hyperglycemia risk. The output categorizes patients as “No” for low-risk or provides explicit risk predictions (Figure 3).

Importance Ranking of Model Features

The SHAP method was used to interpret the final model, quantifying the contribution of each variable to predictions. The top five features influencing the model were age, BUN, ALT, HDL-C, and TG. A summary bar chart (Figure 4A) ranked these features by average SHAP values. Conversely, a dot plot (Figure 4B) visualized the distribution of SHAP values across individual predictions, elucidating each variable’s role. Figure 4C represents the waterfall plot of a representative patient’s data, illustrating the individual contributions of each feature to the predicted outcome. Comparisons of actual and SHAP values for all 15 features (Figure 4D) further clarified their impact on the model.

Optimal cutoff values for the top five features were derived using the maximum Youden index method: Age (54 years), BUN (5.35 mmol/L), ALT (21.4 U/L), HDL-C (0.825 mmol/L), and TG (1.235 mmol/L). These thresholds divided patients into high- and low-risk groups for hyperglycemia. To ensure reliability, confounding variables were addressed using propensity score matching (1:1 matching with a caliper of 0.02). This analysis yielded 103 matched cases for age, 95 for BUN, 67 for ALT, 60 for HDL-C, and 144 for TG. Chi-square tests indicated statistically significant differences in hyperglycemia incidence between high- and low-risk groups for all features except ALT (Figure 5). This

Table 2 Predictive Algorithms Performance in Training, Internal and External Test Sets

		Decision Tree	Random Forest	XGBoost	Light gbm	SVM	MLP	KNN	Logistic Regression	Lasso	Ridge	ENet
AUC	Training	0.953	0.91	0.821	0.823	0.785	0.756	1	0.789	0.773	0.781	0.775
	Internal test	0.695	0.773	0.82	0.798	0.801	0.75	0.628	0.8	0.801	0.785	0.799
	External test	0.578	0.748	0.788	0.768	0.745	0.753	0.747	0.782	0.762	0.76	0.76
	Mean	0.742	0.81*	0.81*	0.796*	0.777	0.753	0.792	0.79	0.779	0.775	0.778
	Sd	0.192	0.087	0.019	0.028	0.029	0.003*	0.190	0.009*	0.020	0.013*	0.020
Accuracy	Training	0.879	0.804	0.733	0.678	0.614	0.7	0.998	0.735	0.668	0.671	0.584
	Internal test	0.678	0.673	0.719	0.667	0.614	0.69	0.725	0.719	0.649	0.661	0.573
	External test	0.704	0.659	0.726	0.711	0.452	0.644	0.763	0.719	0.637	0.63	0.548
	Mean	0.754*	0.712	0.726*	0.685	0.56	0.678	0.829*	0.724	0.651	0.654	0.568
	Sd	0.109	0.08	0.007*	0.023	0.094	0.03	0.148	0.009*	0.016*	0.021	0.018
F1 Score	Training	0.772	0.678	0.578	0.545	0.524	0.522	0.995	0.556	0.531	0.537	0.512
	Internal test	0.421	0.472	0.529	0.513	0.507	0.465	0.319	0.538	0.508	0.517	0.49
	External test	0.355	0.452	0.532	0.519	0.413	0.478	0.448	0.548	0.484	0.49	0.45
	Mean	0.516	0.534	0.546*	0.526	0.481	0.488	0.587*	0.547*	0.508	0.515	0.484
	Sd	0.224	0.125	0.027	0.017*	0.060	0.030	0.359	0.009*	0.024*	0.024	0.031
Brier Score	Training	0.069	0.115	0.156	0.153	0.149	0.183	0.033	0.143	0.154	0.161	0.164
	Internal test	0.201	0.146	0.154	0.153	0.139	0.181	0.069	0.14	0.147	0.157	0.16
	External test	0.215	0.147	0.157	0.153	0.162	0.181	0.163	0.14	0.145	0.155	0.162
	Mean	0.162	0.136*	0.156	0.153	0.15	0.182	0.088*	0.141*	0.149	0.158	0.162
	Sd	0.08	0.018	0.002*	0*	0.012	0.001*	0.067	0.002	0.005	0.003	0.002

Note: * Indicates models that rank among the top three in the corresponding metrics.

rigorous analysis confirms the clinical relevance and predictive reliability of the XGBoost model, offering a robust tool for determining hyperglycemia risk in psoriasis patients.

Discussion

The primary pathophysiological mechanisms of type 2 diabetes include insulin resistance and impaired pancreatic β -cell function. Extensive research, including epidemiological, genetic, and inflammatory pathway studies, has demonstrated a significant association between psoriasis and diabetes.^{3–7,22} In addition to the three primary pathogenic genes—PTPN22, ST6GAL1, and JAZF1⁴—a widely accepted mechanism involves the activation of dendritic cells in psoriasis patients, which release IL-12 and IL-23. These cytokines activate Th1, Th22, and T-cells, producing IL-17. These T-cells stimulate the release of pro-inflammatory cytokines, including IL-1, IL-6, and TNF- α , resulting in increased insulin resistance and β -cell dysfunction, which increases blood glucose levels.²³ Moreover, dysregulated adipokine production, including leptin, lipocalin, and reticulon, contributes to the secretion of TNF- α and IL-6. These factors not only exacerbate inflammation in psoriasis but also enhance insulin resistance.²⁴

However, in clinical practice, obtaining these specific indicators for diagnosing and treating patients remains challenging. In this study, we used eleven machine learning algorithms to develop a predictive model for hyperglycemia risk in psoriasis patients, using clinically available and research-validated variables and initial proof of a possible link between hyperglycemia and psoriasis. The XGBoost algorithm was the most effective after screening, exhibiting high discrimination across the training, internal, and external test sets (AUC values of 0.821, 0.820, and 0.788, respectively). Clinical decision curves further highlighted the model's clinical utility. However, models created by machine learning algorithms are typically perceived as “black boxes”, and in order to portray the models visually, we constructed a web-based online calculator that may be better understood and used by physicians.

This study used the SHAP method to rank variables by their impact on predictive outcomes, identifying AGE, BUN, ALT, HDL-C, and TG as the top five influential features. Age was the most significant, highlighting its key role in model prediction. Aging is linked to the decline of bodily systems, especially immune and metabolic.

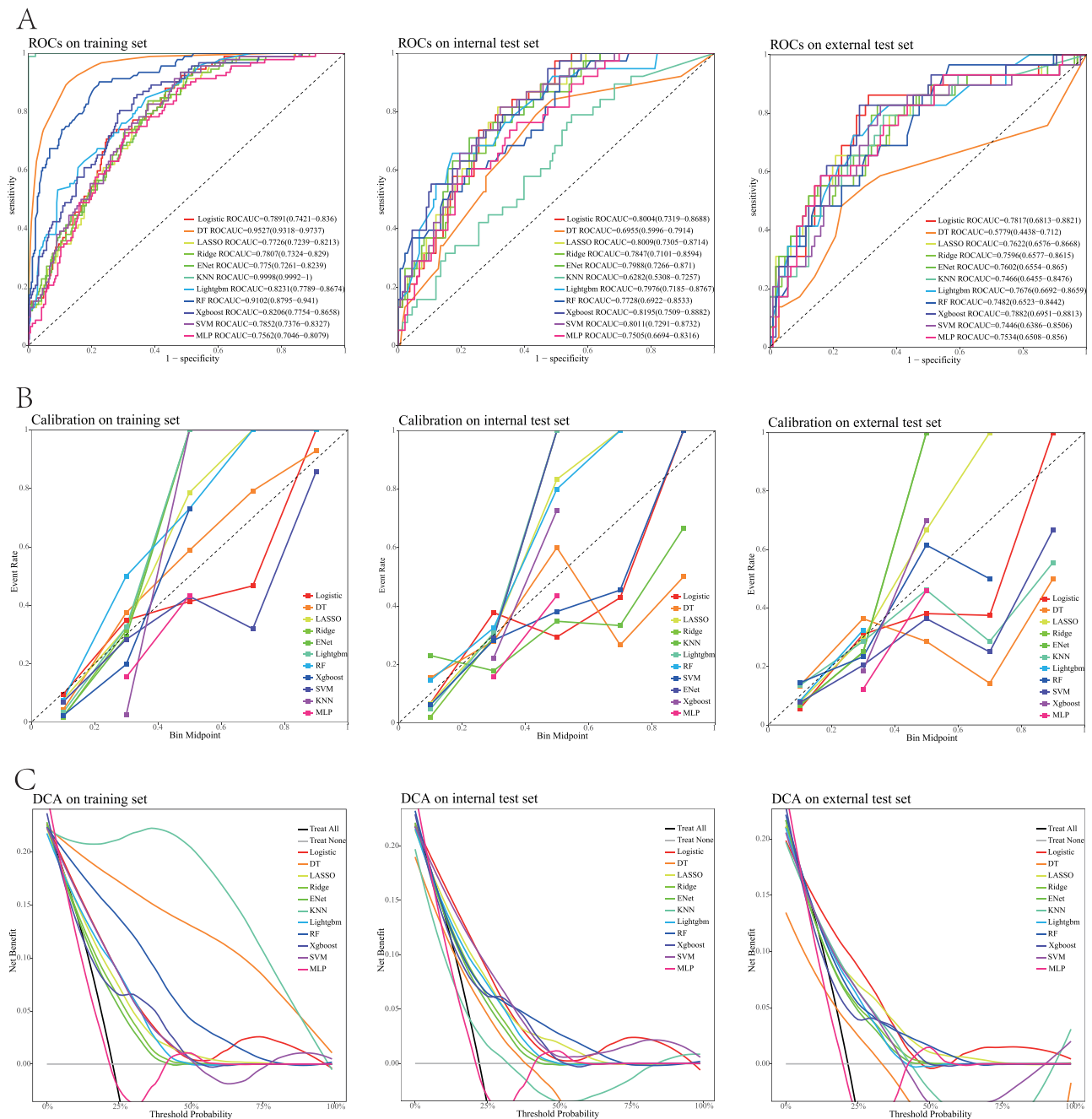


Figure 2 ROC, calibration, and DCA curves of all algorithms. **(A)** Receiver operating characteristic curve of all algorithms. **(B)** Calibration of all algorithms. **(C)** Decision curve analysis curves of all algorithms.

The research revealed that age is associated with an increased risk of type 2 diabetes.²⁵ As individuals age, the immune system exhibits characteristics of “immunosenescence”,²⁶ characterized by diminished T-cell functionality and the persistent release of inflammatory mediators such as IL-6 and TNF- α . These inflammatory mediators not only directly contribute to the development of psoriatic lesions but also impede the insulin signaling pathway, thereby exacerbating insulin resistance. Additionally, aging leads to changes in gut microbiota, including decreased diversity and fewer short-chain fatty acids.²⁷ A deficiency in SCFAs may compromise intestinal barrier integrity, facilitate the translocation of endotoxins (eg, lipopolysaccharides), and activate immune components such as the NLRP3 inflammasome, thereby exacerbating systemic inflammation and insulin resistance. Given that age is an immutable factor, vigilant monitoring of

New Sample

age: 61 TG: 13.92

HDLC: 2.53 BUN: 17.1

Cr: 2.35 AST: 120.3

ALT: 120.3 WBC: 15.6T

BME: 39.6449701142012 SR: 3713.24101141144

gender: 1 smoking: 0

dialysis: 0 psoriasis: 1

hypertension: 1

Model

Prediction

Prob(status=Yes) is 0.4546

status is No

NewObservations

age	TG	HDLC	BUN	Cr	AST
61	13.92	2.53	17.1	2.35	120.3

Previous 1 Next

Figure 3 Web-based calculator using the XGBoost algorithm.

blood glucose levels is particularly crucial for middle-aged and elderly psoriasis patients. Treatment plans should account for age-related declines in health and avoid drugs that might worsen blood sugar issues.

The XGBoost model ranked BUN as the second most important variable, suggesting that renal function is crucial in hyperglycemia development. BUN, a byproduct of protein metabolism primarily produced in the liver and excreted by the kidneys, is a key indicator of glomerular filtration function. Elevated BUN levels typically reflect impaired kidney function. A meta-analysis has demonstrated that psoriasis patients exhibit an elevated risk of developing chronic kidney disease (CKD) and end-stage renal disease (ESRD) in comparison to non-psoriatic controls, with these risks being positively associated with the severity of psoriasis.²⁸ Psoriasis can induce renal dysfunction through various mechanisms, including dysregulation of the Th17/Tregs balance,²⁹ immune complex deposition,³⁰ and alterations in renal vasculature.³¹ Renal dysfunction can result in insulin resistance through various factors, including chronic inflammation, oxidative stress, metabolic acidosis, anemia, adipokine disorders, and lack of exercise. These factors contribute to insulin resistance or β -cell apoptosis by acting on the insulin signaling pathway or damaging β -cells, thereby promoting the development of type 2 diabetes.³² Monitoring BUN levels allows clinicians to detect renal function changes early and adjust treatments to prevent hyperglycemia and further kidney damage.

Furthermore, we identified ALT as a predictive variable for hyperglycemia. Psoriasis is frequently associated with liver dysfunction.³³ The hyperactivation of Th17 cells, in conjunction with pro-inflammatory cytokines such as IL-17 and IL-23, exerts effects on the liver by activating hepatic Kupffer cells. This activation induces oxidative stress injury in hepatocytes, thereby initiating liver fibrosis.³⁴ Concurrently, TNF- α , released during cutaneous inflammation, can upregulate the hepatic NF- κ B signaling pathway, consequently promoting hepatocyte apoptosis.³⁵ Furthermore, drugs commonly prescribed for psoriasis, such as methotrexate³⁶ and cyclosporin,³⁷ are known to possess significant hepatotoxic effects. The liver is integral to glucose metabolism, engaging in processes including glycogen synthesis, glycolysis, and gluconeogenesis. Serum ALT and AST levels have long been used as markers of hepatic injury. Notably, every 1 SD increase in ALT has been associated with an increased risk of hypertension, metabolic syndrome, diabetes mellitus, impaired fasting glucose, and insulin resistance (OR 1.29–1.85, all $P \leq 0.002$)³⁸. Elevated ALT levels, even within the normal range, are associated with a dose-response relationship with type 2 diabetes, independent of BMI.³⁹ Therefore, for psoriasis patients with elevated ALT levels, it is essential to further evaluate liver function, adjust therapeutic medications, and implement measures to protect hepatic function, thereby reducing the risk of hyperglycemia development.

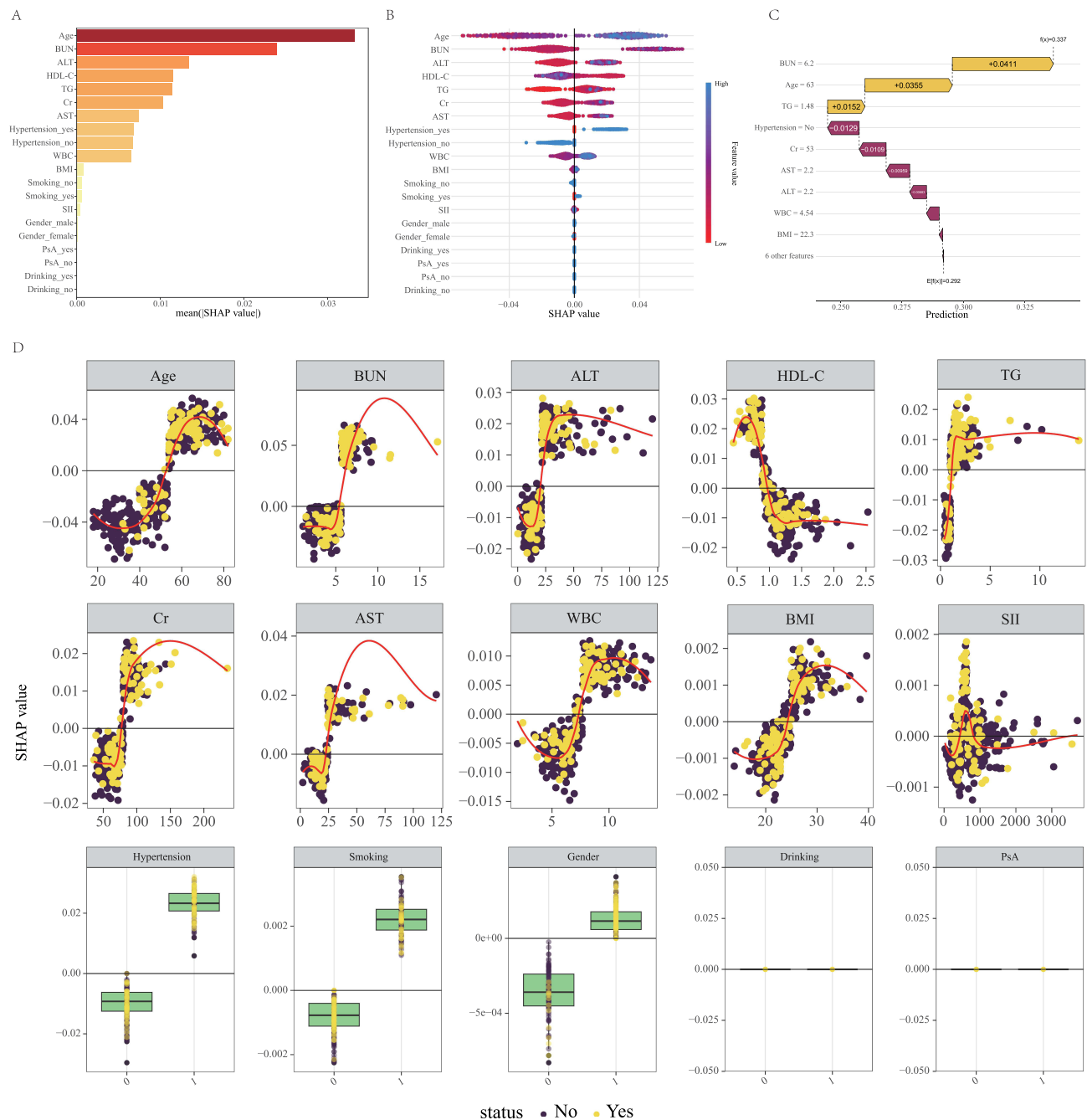


Figure 4 SHAP value. (A) The mean SHAP value of all features. (B) Distribution of SHAP values for each feature. (C) Contribution of patient 1's characteristics in the training set to hyperglycemic outcome. (D) Comparison of actual and SHAP values for each feature.

TG and TG/HDL-C ratios have been suggested as markers of insulin resistance.⁴⁰ High TG levels are correlated with insulin resistance, even in individuals with normal glucose tolerance.⁴¹ Elevated TG levels and reduced HDL-C were observed in psoriasis patients compared to healthy controls.⁴² The chronic inflammatory state associated with psoriasis is posited to disrupt lipid metabolism, resulting in increased serum TG levels, decreased HDL-C concentrations, and compromised HDL functionality.⁴³ These alterations in lipid metabolism may contribute to insulin resistance, impair pancreatic β -cell secretion, and exacerbate the inflammatory response. Consequently, clinical management of psoriasis should incorporate patient education focused on weight management, dietary modifications, and the administration of lipid-lowering agents to ameliorate dyslipidemia, enhance insulin sensitivity, and mitigate the risk of hyperglycemia.

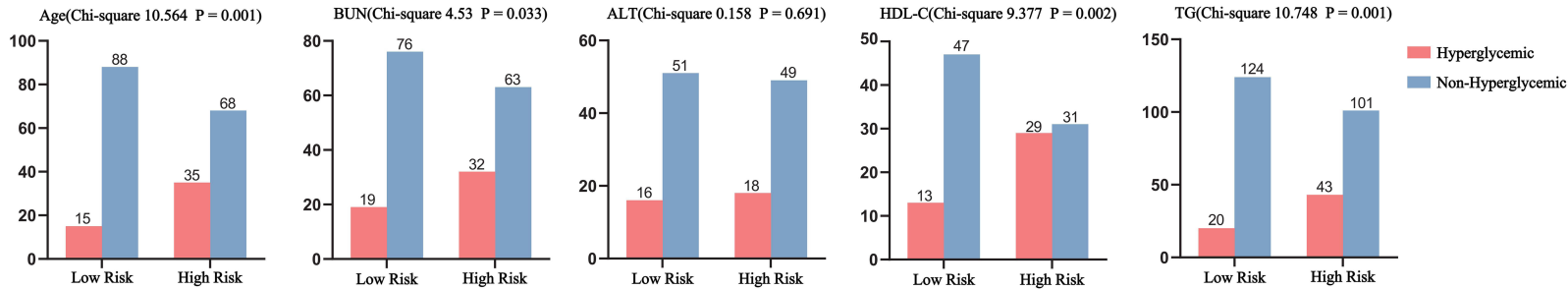


Figure 5 Comparison of the incidence of hyperglycemia in high-risk and low-risk groups.

We established optimal cutoff values for each of the five continuous variables—age, BUN, ALT, HDL-C, and TG—and used these to categorize high- and low-risk groups, facilitating clinical decision-making. Besides, no significant difference in hyperglycemia incidence was observed between high- and low-risk groups for ALT after propensity score matching (likely due to the small sample size); however, significant differences were found for AGE, BUN, HDL-C, and TG. Furthermore, BUN > 5.35 mmol/L and TG > 1.235 mmol/L were identified as risk factors for hyperglycemia. However, these values were lower than the upper limits of normal for adults (7.1 mmol/L for BUN and 1.7 mmol/L for TG). This suggests that psoriasis patients can require more stringent renal and lipid management to reduce hyperglycemia risk.

The inflammatory injury associated with diabetes and psoriasis comorbidity can be mitigated by treatments that reduce systemic inflammation in psoriasis. Retinoids can treat psoriasis while reducing blood glucose levels.⁴⁴ In addition to being a standard treatment for type 2 diabetes, metformin can reduce diabetes risk in individuals with pre-diabetes. A randomized controlled trial demonstrated that metformin treatment significantly improved obesity, FPG, TG, total cholesterol, and low-density lipoprotein cholesterol levels in psoriasis patients while improving erythema, scaling, and induration (ESI).⁴⁵ In autoimmune diseases, including psoriasis and spondyloarthritis, where IL-17A is over-expressed, anti-IL-17A monoclonal antibodies can block IL-17A binding to IL-17RA, inhibiting inflammation. A study by IKUMI et al⁴⁶ suggested that blocking IL-17A prevents β -cell dysfunction and the progression of type 2 diabetes while improving hyperglycemic symptoms in psoriasis patients. Consequently, intensive glycemic management and repair of metabolic abnormalities should be integral to treating psoriasis patients with diabetes or those at high risk for hyperglycemia.

This work offers a viable method to predict the presence of hyperglycemia in psoriasis patients and investigates the probable correlation between psoriasis and hyperglycemia. Even with the model's predictive power, our research still has additional drawbacks: First, the study's generalizability was impacted because the training and internal test sets' data originated from the same hospital. Additionally, the training set, internal validation set, and external validation set sample populations come from various continents, and bias may result from environmental and ethnic variations. Furthermore, the cross-sectional retrospective design of this study made it impossible to record several important blood glucose-related indicators (such as PASI scores, inflammatory markers, therapy type, etc.), which further diminishes the study's therapeutic value. Therefore, new multicenter prospective studies with large samples are required to control for the aforementioned bias in order to further corroborate the conclusion, as the current findings are insufficient to inform therapeutic decision-making.

Conclusion

Since hyperglycemia and psoriasis are linked, we developed a prediction model for the incidence of hyperglycemia in psoriasis patients using their clinical examination indexes and general data. We also investigated the relationship between the two in a preliminary manner, which gave guidance for the next study. Five of these indicators—age, BUN, ALT, HDL-C, and TG—may have a rather strong correlation with blood glucose. A customized treatment plan is required for psoriasis patients who are also hyperglycemic or at risk for hyperglycemia in order to coordinate the management of psoriasis inflammation and glycemic development.

Abbreviations

IL-17, Interleukin 17; IL-23, Interleukin 23; TNF- α , Tumor necrosis factor α ; SII, Systemic immune inflammatory index; IGT, Impaired glucose tolerance; NHANES, National Health and Nutrition Examination Survey; NCHS, National Center for Health Statistics; PsA, Psoriasis arthropathica; BMI, Body mass index; BUN, Blood urea nitrogen; Cr, Creatinine; hs-CRP, High sensitive C-reactive protein; TG, Triglycerides; HDL-C, High-density lipoprotein cholesterol; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; FPG, Fasting plasma glucose; WBC, White blood cell; OGTT, Oral glucose tolerance test; HbA1c, Glycosylated hemoglobin; DT, Decision Trees; RF, Random Forests; XGboost, Extreme Gradient Boosting; LightGBM, Light Gradient Boosting Machine; SVM, Support Vector Machines; MLP, Multilayer Perceptron; KNN, K-Nearest Neighbors; LR, Logistic Regression; ENET, Elastic Net; ROC, Receiver operator characteristic curve; AUC, Area Under Curve; DCA, clinical decision curve analysis; SHAP, SHapley Additive exPlanations; TPR, True Positive Rate; FPR, False Positive Rate; IL-6, Interleukin 6; MetS, metabolic syndrome.

Data Sharing Statement

The data supporting the results of this study are available from the corresponding author upon reasonable request. The NHANES data used in this study are publicly available at the NCHS of the Centers for Disease Control and Prevention (<https://www.cdc.gov/nchs/nhanes/index.htm>). The protocols and statistical analysis methods used in this study can be obtained directly from the corresponding author after study approval.

Ethical Statement

We confirm that this study was approved by the Ethics Committee of the Affiliated Hospital of Guilin Medical University (Approval No. 2024IITLL-31) with a waiver of informed consent. The waiver was granted based on the following justifications:

1. The research involved only de-identified retrospective data;
2. Strict anonymization protocols ensured no risk of privacy breaches, and the study had no impact on patient prognosis or treatment.

All procedures complied with:

- The 《Declaration of Helsinki》.
- Relevant regulations, including the “Management Measures for Clinician-Initiated Clinical Research in Healthcare Institutions (Trial)” (2021 issued by the National Health Commission of the People’s Republic of China (NHC).

NHANES participants provided written informed consent, and the Institutional Review Board of the National Center for Health Statistics approved the study protocol.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no conflicts of interest to declare.

References

1. Gao N, Kong M, Li X. et al. The association between psoriasis and risk of cardiovascular disease: a Mendelian randomization analysis. *Front Immunol.* 2022;13:918224. doi:10.3389/fimmu.2022.918224
2. Hajiebrahimi M, Song C, Hägg D, Andersson TM, Villacorta R, Linder M. The occurrence of metabolic risk factors stratified by psoriasis severity: a swedish population-based matched cohort study. *Clin Epidemiol.* 2020;12:737–744. doi:10.2147/CLEP.S252410
3. Wang H, Wang Z, Rani PL, et al. Identification of PTPN22, ST6GAL1 and JAZF1 as psoriasis risk genes demonstrates shared pathogenesis between psoriasis and diabetes. *Exp Dermatol.* 2017;26(11):1112–1117. doi:10.1111/exd.13393
4. Dowlatabadi EA, van der Voort EA, Arends LR, Nijsten T. Markers of systemic inflammation in psoriasis: a systematic review and meta-analysis. *Br J Dermatol.* 2013;169(2):266–282. doi:10.1111/bjd.12355

5. Rajappa M, Rathika S, Munisamy M, Chandrashekar L, Thappa DM. Effect of treatment with methotrexate and coal tar on adipokine levels and indices of insulin resistance and sensitivity in patients with psoriasis vulgaris. *J Eur Acad Dermatol Venereol*. 2015;29(1):69–76. doi:10.1111/jdv.12451
6. Dal Bello G, Gisondi P, Idolazzi L, Girolomoni G. Psoriatic arthritis and diabetes mellitus: a narrative review. *Rheumatol Ther*. 2020;7(2):271–285. doi:10.1007/s40744-020-00206-7
7. Karadag AS, Ertugrul DT, Kalkan G, et al. The effect of Acitretin treatment on insulin resistance, retinol-binding protein-4, leptin, and adiponectin in psoriasis vulgaris: a noncontrolled study. *Dermatology*. 2013;227(2):103–108. doi:10.1159/000351769
8. Patrick MT, Stuart PE, Zhang H, et al. Causal relationship and shared genetic loci between psoriasis and type 2 diabetes through trans-disease meta-analysis. *J Invest Dermatol*. 2021;141(6):1493–1502. doi:10.1016/j.jid.2020.11.025
9. Khalid U, Hansen PR, Gislason GH, et al. Psoriasis and new-onset diabetes: a Danish nationwide cohort study. *Diabetes Care*. 2013;36(8):2402–2407. doi:10.2337/dc12-2330
10. Armstrong AW, Harskamp CT, Armstrong EJ. Psoriasis and the risk of diabetes mellitus: a systematic review and meta-analysis. *JAMA Dermatol*. 2013;149(1):84–91. doi:10.1001/2013.jamadermatol.406
11. Enos CW, Ramos VL, McLean RR, et al. Comorbid obesity and history of diabetes are independently associated with poorer treatment response to biologics at 6 months: a prospective analysis in Corrona Psoriasis Registry. *J Am Acad Dermatol*. 2022;86(1):68–76. doi:10.1016/j.jaad.2021.06.883
12. Chen X, Zhou S, Yang L, et al. Risk prediction of diabetes progression using big data mining with multifarious physical examination indicators. *Diabetes Metab Syndr Obes*. 2024;17:1249–1265. doi:10.2147/DMSO.S449955
13. Gisondi P, Tessari G, Conti A, et al. Prevalence of metabolic syndrome in patients with psoriasis: a hospital-based case-control study. *Br J Dermatol*. 2007;157(1):68–73. doi:10.1111/j.1365-2133.2007.07986.x
14. Tas B, Kabeloglu V. Prevalence of metabolic syndrome and its parameters and their correlations with psoriasis duration, severity, and sleep quality in psoriasis patients: a cross-sectional study. *Dermatol Pract Concept*. 2021;11(3):e2021049. doi:10.5826/dpc.1103a49
15. Yoo SA, Sayo MIA, Lee JH. Association between chronic renal disease and psoriasis risk in diabetes patients: a Korean population-based study. *Indian J Dermatol Venereol Leprol*. 2024;91(2):152–157. doi:10.25259/IJDVL_669_2023
16. Yuan Z, Guo Y. Risk of incident type 2 diabetes in patients with psoriatic arthritis: a systematic review and meta-analysis of cohort studies. *Int J Rheum Dis*. 2022;25(9):1029–1037. doi:10.1111/1756-185X.14375
17. Ma R, Cui L, Cai J, et al. Association between systemic immune inflammation index, systemic inflammation response index and adult psoriasis: evidence from NHANES. *Front Immunol*. 2024;15:1323174. doi:10.3389/fimmu.2024.1323174
18. Zhao Q, Liu X, Xu J, Rao X, Liu M. Association of systemic immunity-inflammation index with type 2 diabetes and insulin resistance in NHANES 2005–2018. *Sci Rep*. 2024;14(1):30133. doi:10.1038/s41598-024-79763-8
19. Qing W, Qian Y. Association between systemic immunity-inflammation index and glucose regulation in non-diabetic population: a population-based study from the NHANES (2005–2016). *PLoS One*. 2024;19(11):e0313488. doi:10.1371/journal.pone.0313488
20. Wan X, Lu X, editors. *Diagnostics*. 10th ed. Beijing: People's Medical Publishing House; 2024:346.
21. Committee on Psoriasis, Chinese Society of Dermatology. Guideline for the diagnosis and treatment of psoriasis in China (2023 edition). *Chin J Dermatol*. 2023;56:573–625. doi:10.35541/cjd.20220839
22. Pereira RR, Amladi ST, Varthakavi PK. A study of the prevalence of diabetes, insulin resistance, lipid abnormalities, and cardiovascular risk factors in patients with chronic plaque psoriasis. *Indian J Dermatol*. 2011;56(5):520–526. doi:10.4103/0019-5154.87144
23. Bai F, Zheng W, Dong Y, et al. Serum levels of adipokines and cytokines in psoriasis patients: a systematic review and meta-analysis. *Oncotarget*. 2017;9(1):1266–1278. doi:10.18632/oncotarget.22260
24. Gelfand JM, Wan MT. Psoriasis: a novel risk factor for type 2 diabetes. *Lancet Diabetes Endocrinol*. 2018;6(12):919–921. doi:10.1016/S2213-8587(18)30127-X
25. Yeung RO, Zhang Y, Luk A, et al. Metabolic profiles and treatment gaps in young-onset type 2 diabetes in Asia (the JADE programme): a cross-sectional study of a prospective cohort [published correction appears in *Lancet Diabetes Endocrinol*. 2014;2(12):e17]. *Lancet Diabetes Endocrinol*. 2014;2(12):935–943. doi:10.1016/S2213-8587(14)70137-8
26. Borgoni S, Kudryashova KS, Burka K, de Magalhães JP. Targeting immune dysfunction in aging. *Ageing Res Rev*. 2021;70:101410. doi:10.1016/j.arr.2021.101410
27. Rashidah NH, Lim SM, Neoh CF, et al. Differential gut microbiota and intestinal permeability between frail and healthy older adults: a systematic review. *Ageing Res Rev*. 2022;82:101744. doi:10.1016/j.arr.2022.101744
28. Jing X, Zhuyuan W, Aijun C, Jianxia X, Kun H, Ping W. Association of psoriasis with chronic kidney disease and end-stage renal disease: a systematic review and meta-analysis. *Front Med*. 2023;10:1175477. doi:10.3389/fmed.2023.1175477
29. Dellepiane S, Leventhal JS, Cravedi P. T cells and acute kidney injury: a two-way relationship. *Front Immunol*. 2020;11:1546. doi:10.3389/fimmu.2020.01546
30. Thomas J, Küpper M, Batra R, et al. Is the humoral immunity dispensable for the pathogenesis of psoriasis? [published correction appears in *J Eur Acad Dermatol Venereol*. 2019;33(12):2380. doi:10.1111/jdv.16019]. *J Eur Acad Dermatol Venereol*. 2019;33(1):115–122. doi:10.1111/jdv.15101
31. Alba BK, Greaney JL, Ferguson SB, Alexander LM. Endothelial function is impaired in the cutaneous microcirculation of adults with psoriasis through reductions in nitric oxide-dependent vasodilation. *Am J Physiol Heart Circ Physiol*. 2018;314(2):H343–H349. doi:10.1152/ajpheart.00446.2017
32. Marassi M, Fadini GP. The cardio-renal-metabolic connection: a review of the evidence. *Cardiovasc Diabetol*. 2023;22(1):195. doi:10.1186/s12933-023-01937-x
33. Kozłowska D, Harasim-Symbor E, Myśliwiec H, Milewska AJ, Chabowski A, Flisiak I. Lipid profile disturbances may predispose psoriatic patients to liver dysfunction. *Postepy Dermatol Alergol*. 2021;38(2):310–318. doi:10.5114/ada.2021.106209
34. Meng F, Wang K, Aoyama T, et al. Interleukin-17 signaling in inflammatory, Kupffer cells, and hepatic stellate cells exacerbates liver fibrosis in mice. *Gastroenterology*. 2012;143(3):765–776.e3. doi:10.1053/j.gastro.2012.05.049
35. Faletti L, Peintner L, Neumann S, et al. TNF α sensitizes hepatocytes to FasL-induced apoptosis by NF κ B-mediated Fas upregulation. *Cell Death Dis*. 2018;9(9):909. doi:10.1038/s41419-018-0935-9

36. Gau SY. Methotrexate use and liver outcomes in psoriasis and rheumatoid arthritis patients: a commentary on “Risk of liver disease in psoriasis patients, psoriatic arthritis and rheumatoid arthritis receiving methotrexate: a population-based study”. *J Am Acad Dermatol.* **2021**;85(6):e399–e400. doi:10.1016/j.jaad.2021.07.069
37. Rosmarin DM, Lebwohl M, Elewski BE, Gottlieb AB; National Psoriasis Foundation. Cyclosporine and psoriasis: 2008 National Psoriasis Foundation Consensus Conference. *J Am Acad Dermatol.* **2010**;62(5):838–853. doi:10.1016/j.jaad.2009.05.017
38. Porter SA, Pedley A, Massaro JM, Vasan RS, Hoffmann U, Fox CS. Aminotransferase levels are associated with cardiometabolic risk above and beyond visceral fat and insulin resistance: the Framingham Heart Study. *Arterioscler Thromb Vasc Biol.* **2013**;33(1):139–146. doi:10.1161/ATVBAHA.112.300075
39. Wang CS, Chang TT, Yao WJ, Wang ST, Chou P. Impact of increasing alanine aminotransferase levels within normal range on incident diabetes. *J Formos Med Assoc.* **2012**;111(4):201–208. doi:10.1016/j.jfma.2011.04.004
40. Hannon TS, Bacha F, Lee SJ, Janosky J, Arslanian SA. Use of markers of dyslipidemia to identify overweight youth with insulin resistance. *Pediatr Diabetes.* **2006**;7(5):260–266. doi:10.1111/j.1399-5448.2006.00199.x
41. Moro E, Gallina P, Pais M, Cazzolato G, Alessandrini P, Bittolo-Bon G. Hypertriglyceridemia is associated with increased insulin resistance in subjects with normal glucose tolerance: evaluation in a large cohort of subjects assessed with the 1999 World Health Organization criteria for the classification of diabetes. *Metabolism.* **2003**;52(5):616–619. doi:10.1053/meta.2003.50102
42. Fernández-Armenteros JM, Gómez-Arbonés X, Buti-Soler M, et al. Psoriasis, metabolic syndrome and cardiovascular risk factors. A population-based study. *J Eur Acad Dermatol Venereol.* **2019**;33(1):128–135. doi:10.1111/jdv.15159
43. Holzer M, Wolf P, Curcic S, et al. Psoriasis alters HDL composition and cholesterol efflux capacity. *J Lipid Res.* **2012**;53(8):1618–1624. doi:10.1194/jlr.M027367
44. Qian H, Kuang Y, Su J, et al. Reductive effect of acitretin on blood glucose levels in Chinese patients with psoriasis. *Front Med.* **2021**;8:764216. doi:10.3389/fmed.2021.764216
45. Liang Y, Wang Y, Peng A, et al. Molecular mechanisms and drug therapy of metabolism disorders in psoriasis [J]. *J Dermatolog Treat.* **2024**;35(1):2375580.
46. Ikumi K, Odanaka M, Shime H, et al. Hyperglycemia is associated with psoriatic inflammation in both humans and mice. *J Invest Dermatol.* **2019**;139(6):1329–1338.e7. doi:10.1016/j.jid.2019.01.029

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