The Study of Key Tongue Features for Prediabetes Risk and Diabetes Risk using Principal Component Analysis and Logistic Regression

Jun Li (✉ ljzy05@126.com)

Shanghai University of Traditional Chinese Medicine <https://orcid.org/0000-0001-5624-2146>

Jiacai Li

Shanghai University of Traditional Chinese Medicine

Xiaojuan Hu

Shanghai University of Traditional Chinese Medicine

Liping Tu

Shanghai University of Traditional Chinese Medicine

Yulin Shi

Shanghai University of Traditional Chinese Medicine

Zijuan Bi

Shanghai University of Traditional Chinese Medicine

Changle Zhou

Shanghai University of Traditional Chinese Medicine

Ji Cui

Shanghai University of Traditional Chinese Medicine

Jiatuo Xu

Shanghai University of Traditional Chinese Medicine

Research

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The study of key tongue features for prediabetes risk and diabetes risk using principal component analysis and logistic regression

Jun Li^{1†}, Jiakai Li¹, Xiaojuan Hu², Liping Tu¹, Yulin Shi¹, Zijuan Bi¹, Changle Zhou³, Ji Cui^{1*}, Jiatuo Xu^{1*}

1 School of Basic Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai, China

2 Shanghai Collaborative Innovation Center of Health Service in Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai, China

3 Cognitive Science Department, Xiamen University, Xiamen, China

*Co-corresponding author:

Dr. Ji Cui

Address: School of Basic Medicine, Shanghai University of Traditional Chinese Medicine, Cailun Road, Shanghai, China

Email: maatcui@163.com

*Corresponding Author:

Prof. Jiatuo Xu

Address: School of Basic Medicine, Shanghai University of Traditional Chinese Medicine, Cailun Road, Shanghai, China

Phone: 86 21 51322432

Email: xjt@fudan.edu.cn

Abstract

Background: Carrying out routine diabetes risk assessment and prediction is conducive to controlling the incidence of diabetes. Previous studies have confirmed that tongue features can reflect changes in glucose metabolism. We want to find the key tongue features related to glucose metabolism for early warning of prediabetes and diabetes. This will benefit the prevention and control of diabetes.

Methods: We investigated 719 subjects in Shuguang Hospital affiliated with Shanghai University of TCM in Shanghai, China, during the August 2018 – December 2019 period. We used PCA to reconstruct 25 new features on the basis of the original features, and used logistic regression to analyze these new features. Based on the factor loading method, we associate the new features with the original features. Finally, we determined the key tongue features and change patterns related to prediabetes risk and diabetes risk.

Results: For the prediabetes, TB-ASM, TC-ASM and TB-Cr are protective factors. TB-CON, TC-CON, TB-MEAN, TC-MEAN, TB-ENT and TC-ENT are risk factors. For the diabetes, TB-a, TB-S, TB-Cr, TB-b and TC-b are protective factors, and Per-all and TB-Cb are risk factors.

Conclusion: The PCA eliminates the redundancy of original features and refines the original features. The PCA combined with logistic regression found the key tongue features reflecting glucose metabolism, and clarified the significance of the changes in these tongue features in the prediabetes and diabetes population. This study provides a research foundation for using tongue features to implement early warning of diabetes risk.

Keywords: Tongue image, Tongue diagnosis, Prediabetes, Diabetes, PCA, Logistic regression.

Introduction

Tongue diagnosis is a rapid, objective, simple, noninvasive and valuable method that provides access to physiology and pathology information for TCM doctor. The doctor observes the color, texture and moisture of the tongue body and tongue coating to identify the health status of an individual. At present, with the development of standardized tongue diagnosis equipment, objective tongue information continues to accumulate. Researchers use tongue diagnosis equipment to collect and analyze the subjects' tongue images, calculate and extract tongue features.

According to WHO, the prediabetes is associated with a high risk for developing diabetes. In addition, prediabetes is related to early atherosclerosis, subclinical inflammation, and cardiovascular disease (CVD). The occurrence of prediabetes is due to the joint action of insulin resistance and β -cell dysfunction^[1, 2]. WHO has set the prevention of T2DM as a priority goal. At the same time, the 2018 Berlin Declaration called on the world to take early measures to prevent T2DM. Individuals at high risk of diabetes should actively implement lifestyle modification^[3]. Many diabetic patients were missed due to hidden onset^[4]. Delay in diagnosis and treatment not only affects the patient's prognosis, but also incurs high medical costs^[5, 6]. Therefore, it is necessary to establish a routine diabetes risk screening mechanism. However, Routine blood glucose monitoring is an invasive examination and will incur a certain cost. Therefore, it is necessary to establish a low-cost, convenient, non-invasive, and accurate diabetes risk screening system. For example, The American Diabetes Association (ADA) recommends a noninvasive assessment tool to assess diabetes risk^[7].

Our previous studies have confirmed that tongue features has a potential role in predicting risks of diabetes^[8]. However, among the many tongue features, which tongue features are more important in the early warning of hyperglycemia and still need to be explored. Using PCA and logistic regression analysis, we hope to reconstruct new features on the basis of the original features to solve the collinear and redundancy of the original features, and to find features that can accurately distinguish between normal and hyperglycemia, especially find the key tongue features for risk warning of prediabetes and diabetes. This will benefit the prevention and treatment of diabetes.

Methods

Subjects

In our study, we investigated 719 subjects in Shuguang Hospital affiliated with Shanghai University of TCM in Shanghai, China during the August 2018 – December 2019 period. Subjects were divided into normal case (3.9mmol/L < fasting blood glucose (FPG) < 6.1mmol/L and HbA1c < 5.7%), and those with prediabetes (FPG 6.1-6.9mmol/L or HbA1c 5.7–6.4%), and

and those with diabetes ($\text{FPG} \geq 7.0\text{mmol/L}$ or $\text{HbA1c} \geq 6.5\%$). We confirm that all experiments were performed in accordance with relevant guidelines and regulations. All subjects signed an informed consent form. The study was approved by the IRB of Shuguang Hospital affiliated with Shanghai University of TCM.

Collection of clinical data

We collected basic information, blood samples and tongue images of subjects on the same day. Basic information included: Gender, Age, Height, Weight, Systolic blood pressure (SBP), Diastolic blood pressure (DBP).

Laboratory results included: 1) blood routine tests including white blood cell (WBC) count, neutrophils (NE#), lymphocytes (LY#), monocytes (MO#), eosinophils (EO#), basophils (BA#), red blood cell (RBC) count, red cell distribution width - coefficient of variation (RDW-CV), hematocrit (HCT), mean corpuscular volume (MCV), hemoglobin (HGB), Mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet (PLT) count, platelet distribution width (PDW), plateletcrit (PCT), mean platelet volume (MPV). 2) blood chemistry tests including: Total cholesterol (TCHO), triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), uric acid (UA), total protein (TP), globulin (GLB), albumin (ALB), blood urea(UREA) nitrogen, creatinine (CREA), estimated glomerular filtration rate (eGFR), total bile acids (TBA), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), alkaline phosphatase (ALP), alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (GGT), aspartate transaminase (AST) (Table 1).

Collection and analysis of tongue features

Tongue image acquisition equipment (type TFDA-1 tongue diagnosis instrument) (Fig. 1) and analysis software (Tongue diagnosis analysis system, TDAS) were designed and developed by the intelligent diagnosis technology research team in Shanghai University of TCM^[9]. TFDA-1 is equipped with a high-definition camera and standard light source to ensure a stable shooting environment. The tongue images were recorded as JPEG files (5568 x 3712 pixels).

Based on the color image segmentation method^[10], TDAS first implemented tongue segmentation. According to the difference between the pixel values of the tongue coating and the tongue body, the tongue coating was separated from the tongue body and the color features of both in the RGB, Lab, HIS, YCrCb color space were calculated. According to the difference statistical method^[11], TDAS automatically calculates the texture features of tongue body and tongue coating. The principle of tongue coating ratio feature calculation was: tongue coating area calculated based on pixel value/full tongue area (Per-all), tongue coating area calculated based on pixel value/tongue coating area calculated based on pixel position (Per-part).

(a) Rear view

(b) Front view

(c) Side view

Fig.1 Type TFDA-1 tongue diagnosis instrument

Statistical analysis and machine learning modeling

The measurement data presented as $\bar{X} \pm SD$ and median (interquartile range). For measurement data that conformed to a normal distribution and homogeneity of variance, the independent sample t-test was used, and for measurement data that did not conform to a normal distribution, the Mann-Whitney rank sum test was used. Enumeration data were analyzed by the Chi-square test. Statistical analysis were performed using Python (version 3.7.4).

We used principal component analysis to reduce data dimensionality. In the case of retaining the information of the original data to the greatest extent, new features (principal component, PC) were reconstructed on the basis of the original features to reduce data redundancy and prevent the multicollinearity of the original features from affecting the reliability of logistic regression analysis. PCA calculation involves five steps: 1) The standardization was performed on each feature (Eq.1). 2) The covariance matrix (Eq.5) was calculated based on primary data (Eq.2). 3) Calculating the eigenvalues and eigenvector (Eq.6). Eq.3 means an original feature. Eq.4 means calculating the covariance of two features. 4) Calculating a set of eigenvectors and eigenvalues: $\{(\lambda_1, v_1), (\lambda_2, v_2) \cdots (\lambda_i, v_i)\}$, we sorted the eigenvalues in descending order and selected the top 25. 5) Projecting the primary data matrix to the new feature space (Eq.7). Factor loading method is presented as Eq.8.

$$x' = \frac{x - \bar{x}}{std} \quad (1)$$

$$X = \begin{bmatrix} x_{11} & x_{12} & \cdots & x_{1k} \\ x_{21} & x_{22} & \cdots & x_{2k} \\ \vdots & \vdots & \cdots & \vdots \\ x_{n1} & x_{n2} & \cdots & x_{nk} \end{bmatrix} \quad (2)$$

$$X_k = (x_{1k}, x_{2k} \cdots x_{nk})^T \quad (3)$$

$$Cov(X_{k-1}, X_k) = \frac{1}{n-1} \sum_{i=1}^n (X_{k-1} - \bar{X}_{k-1})(X_k - \bar{X}_k) \quad (4)$$

$$C = \begin{bmatrix} Cov(X_1, X_1) & Cov(X_1, X_2) & \cdots & Cov(X_1, X_k) \\ Cov(X_2, X_1) & Cov(X_2, X_2) & \cdots & Cov(X_2, X_k) \\ \vdots & \vdots & \cdots & \vdots \\ Cov(X_k, X_1) & Cov(X_k, X_2) & \cdots & Cov(X_k, X_k) \end{bmatrix} \quad (5)$$

$$Cv = \lambda v \quad (6)$$

$$X_{pca} = \begin{bmatrix} v_1^T \cdot X^T \\ v_2^T \cdot X^T \\ \vdots \\ v_i^T \cdot X^T \end{bmatrix} \quad (7)$$

$$L = v\sqrt{\lambda} \quad (8)$$

Results

Table.1, Table.2, Table.3 and Table.4 show the basic information, laboratory examinations and tongue features among subjects with diabetes, prediabetes and normal. Using PCA to reduce the dimensions of the original data, the cumulative explained variance reached 91.9% and 91.8%, respectively, and retained the information carried in the original data to the greatest extent (Figure.2 and Figure.8).

For the prediabetes group, PC_0, PC_4, PC_8, PC_15 and PC_20 are risk factors, PC_1 and PC_5 are protection factors (Table.5). The original features were associated with the PCs through factor loading method(Table.6). Figure.3 showed the original features highly related to PC_0. Figure.4 shows the original features highly related to PC_1. Figure.5 shows the original features highly related to PC_4. Combining factor loadings can determine that TB-ASM, TC-ASM and TB-Cr are protective factors. TB-CON, TC-CON, TB-MEAN, TC-MEAN, TB-ENT and TC-ENT are risk factors (Figure.6 and Figure.7).

Table.1 Gender composition

Group	Female	Male	Total	χ^2	P value
Normal	85	182	267	5.749	0.056
Prediabetes	96	191	287		
Diabetes	38	127	165		
Total	219	500	719		

Table.2 Basic information

Item	Normal	Prediabetes	Diabetes
Age (years)	49.985±9.456	50.474±10.596	52.182±10.557
Height (cm)	168.157±8.069	168.707±8.498	169.139±7.798
Weight (kg)	70.0(61.0,78.0)	72.0(63.0,79.0)**	75.0(66.0,82.0)***
BMI (kg/m ²)	24.539(21.933,26.534)	24.802(22.85,27.143)**	25.952(23.939,27.757)***
SBP (mmHg)	128.202±17.383	130.711±16.847***	141.085±19.272***
DBP (mmHg)	80.0(73.0,88.0)	81.0(75.0,88.0)***	87.0(80.0,94.0)***

Note: Compared with normal group: **P<0.01, ***P<0.001.

Table.3 Laboratory test results

Item	Normal	Prediabetes	Diabetes
WBC (10 ⁹ /L)	5.7(5.0,6.7)	6.0(5.2,7.1)***	6.6(5.7,7.9)***
NE# (10 ⁹ /L)	3.3(2.7,4.05)	3.5(2.8,4.1)***	3.8(3.1,4.6)***
LY# (10 ⁹ /L)	1.8(1.5,2.25)	2.0(1.6,2.3)*	2.2(1.7,2.5)***
MO#	0.4(0.3,0.5)	0.4(0.3,0.5)	0.4(0.3,0.5)*
RBC (10 ¹² /L)	4.82(4.515,5.145)	4.83(4.52,5.12)**	4.98(4.67,5.26)**
HCT (%)	0.441(0.412,0.467)	0.438(0.409,0.464)**	0.45(0.423,0.468)*

MCV (fL)	90.9(88.6,93.45)	90.8(88.4,92.9)	90.5(87.7,93.5)
RDW-CV (%)	13.1(12.7,13.5)	13.1(12.8,13.6)	13.0(12.6,13.4)
HGB (g/L)	149.0(138.0,159.0)	149.0(138.0,157.0)**	152.0(144.0,159.0)*
MCH (pg)	30.7(29.9,31.65)	30.8(29.85,31.5)	30.8(29.5,31.6)
MCHC (10 ⁹ /L)	338.0(335.0,341.0)	338.0(335.0,341.0)	338.0(335.0,342.0)
PLT (10 ⁹ /L)	216.0(186.5,249.0)	220.0(189.5,260.0)	221.0(186.0,250.0)
PCT (%)	0.19(0.17,0.21)	0.19(0.17,0.23)	0.19(0.17,0.22)
MPV (fL)	8.8(8.1,9.5)	8.8(8.2,9.6)	8.5(8.2,9.4)
PDW (%)	16.5(16.2,16.9)	16.6(16.3,17.0)	16.6(16.3,17.1)
TCHO (mmol/L)	5.31(4.77,5.98)	5.56(4.8,6.105)	5.38(4.69,6.07)
TG (mmol/L)	1.36(0.97,2.06)	1.55(1.085,2.235)***	2.01(1.35,2.72)***☆
LDL (mmol/L)	3.143±0.796	3.29±0.783	3.116±0.907
HDL (mmol/L)	1.31(1.12,1.56)	1.28(1.1,1.5)***	1.15(1.01,1.33)***
UA (umol/L)	368.0(305.0,442.0)	379.0(323.5,440.0)	376.0(309.0,439.0)
ALT (U/L)	21.0(15.0,30.0)	22.0(16.5,35.0)*	26.0(17.0,41.0)***☆
GGT (U/L)	25.0(18.0,40.0)	30.0(19.0,43.0)***	35.0(24.0,56.0)***☆
AST (U/L)	23.0(19.0,27.0)	23.0(19.0,28.0)	23.0(19.0,32.0)
ALP (U/L)	78.0(67.0,92.5)	76.0(62.5,89.0)	79.0(68.0,95.0)
TBA (umol/L)	2.65(1.8,3.99)	2.8(1.8,4.12)*	3.2(2.2,4.8)**
TBIL (umol/L)	14.4(11.95,18.75)	13.5(10.7,16.6)	14.1(11.1,18.0)**
DBIL (umol/L)	2.6(2.1,3.3)	2.4(1.9,3.1)	2.6(2.0,3.2)**
IBIL (umol/L)	11.7(9.65,15.45)	10.9(8.85,13.6)	11.6(9.2,14.9)**
CREA (umol/L)	74.0(63.0,85.0)	76.0(64.0,85.0)	74.0(60.0,83.0)
BUN (mmol/L)	5.01(4.295,5.995)	5.23(4.405,6.14)	5.29(4.6,6.3)*
eGFR (ml/min*1.73m ²)	97.7(88.45,108.45)	96.45(86.4,107.3)**	101.51(90.2,116.03)
TP (g/L)	75.7(73.45,78.05)	76.1(73.7,78.95)	76.4(74.0,79.7)
GLB (g/L)	30.3(27.9,32.25)	31.0(28.5,32.95)	31.0(29.2,33.4)***
ALB (g/L)	45.4(43.8,47.2)	45.3(43.85,46.8)	45.4(43.9,47.0)

Note: Compared with normal group: * $P<0.05$, ** $P<0.01$, *** $P<0.001$; Compared with prediabetes group: * $P<0.05$, ** $P<0.01$.

Table.4 Tongue features

Item	Normal	Prediabetes	Diabetes
Per-All	0.334(0.277,0.398)	0.355(0.285,0.413)	0.378(0.295,0.437)**
Per-Part	1.172(1.084,1.315)	1.16(1.091,1.325)	1.133(1.071,1.276)
TB-CON	68.675(55.111,86.709)	72.534(56.031,90.586)*	65.487(49.502,83.002)
TB-ENT	1.2(1.152,1.256)	1.215(1.155,1.266)*	1.19(1.127,1.247)
TB-ASM	0.079(0.07,0.09)	0.077(0.068,0.089)*	0.082(0.071,0.095)
TB-MEAN	0.025(0.023,0.028)	0.026(0.023,0.029)*	0.024(0.021,0.028)
TC-CON	76.007(54.91,102.513)	84.678(60.534,113.175)*	74.908(54.693,98.32)*
TC-ENT	1.227(1.153,1.298)	1.253(1.177,1.314)*	1.222(1.155,1.291)*
TC-ASM	0.073(0.061,0.087)	0.069(0.059,0.082)*	0.074(0.062,0.087)*
TC-MEAN	0.027(0.023,0.031)	0.028(0.024,0.032)*	0.027(0.023,0.031)*
TB-R	160.0(156.0,164.0)	159.0(155.0,163.0)	159.0(156.0,163.0)
TB-G	95.513±6.985	96.143±7.723	96.733±7.315
TB-B	99.0(94.0,105.0)	100.0(95.0,105.0)	100.0(96.0,107.0)
TC-R	151.0(142.0,158.0)	152.0(144.0,158.0)	151.0(145.0,157.0)
TC-G	105.0(96.0,113.0)	107.0(98.0,114.0)	106.0(99.0,113.0)
TC-B	107.0(97.0,116.0)	109.0(101.0,117.0)	109.0(101.0,115.0)
TB-H	356.274(354.699,358.551)	356.114(354.525,357.843)	355.767(354.084,358.26)

TB-I	118.0(114.0,122.0)	118.0(114.0,122.0)	119.0(115.0,122.0)
TB-S	0.194±0.022	0.191±0.023	0.187±0.024**
TC-H	358.25±4.285	357.494±4.033	357.291±4.412
TC-I	121.0(111.0,128.0)	122.0(114.0,129.0)	121.0(115.0,128.0)
TC-S	0.134(0.12,0.146)	0.13(0.118,0.145)	0.129(0.114,0.145)
TB-L	103.771(102.245,105.191)	103.725(102.107,105.355)	104.187(102.376,105.433)
TB-a	23.028±2.375	22.702±2.503	22.198±2.529**
TB-b	5.735(4.756,7.415)	5.516(4.538,6.705)	5.293(4.065,6.618)**
TC-L	105.679(102.422,108.271)	106.219(103.312,108.49)	106.019(103.322,108.121)
TC-a	15.518±2.148	15.583±2.241	15.302±2.286
TC-b	4.591±1.965	4.21±1.748	4.095±1.999**
TB-Y	115.204(111.43,118.37)	114.839(111.325,118.412)	115.815(111.441,118.745)
TB-Cr	156.11(154.583,157.367)	155.61(153.996,157.177)*	155.171(152.964,156.845)***
TB-Cb	120.457(119.09,121.303)	120.699(119.675,121.448)	120.874(119.842,122.022)***
TC-Y	118.133(110.166,124.507)	119.408(112.381,124.985)	118.814(112.779,124.355)
TC-Cr	147.468(145.967,148.832)	147.479(146.12,148.797)	147.254(145.14,148.857)
TC-Cb	122.087±1.599	122.337±1.475	122.478±1.711

Note: Compared with normal group: * $P<0.05$, ** $P<0.01$, *** $P<0.001$; Compared with prediabetes group: * $P<0.05$.

Figure.2 Proportion of variance explained by PCs in prediabetes group

Table.5 Logistic regression analysis for PCs in prediabetes group

Item	Coef	Std err	Z	OR	P value	Lower limit	Upper limit
PC_0	0.058	0.023	2.513	1.059	0.012	0.013	0.102
PC_1	-0.073	0.028	-2.589	0.93	0.010	-0.128	-0.018
PC_2	0.055	0.038	1.438	1.057	0.150	-0.020	0.131
PC_3	0.066	0.043	1.533	1.068	0.125	-0.018	0.150
PC_4	0.171	0.050	3.441	1.187	0.001	0.074	0.269
PC_5	-0.202	0.058	-3.511	0.817	0.000	-0.315	-0.089
PC_6	-0.014	0.060	-0.227	0.987	0.821	-0.130	0.103
PC_7	-0.065	0.062	-1.049	0.937	0.294	-0.186	0.056

PC_8	0.174	0.067	2.597	1.189	0.009	0.043	0.304
PC_9	0.056	0.069	0.815	1.058	0.415	-0.079	0.191
PC_10	0.012	0.070	0.173	1.012	0.863	-0.124	0.148
PC_11	0.013	0.073	0.182	1.013	0.855	-0.129	0.156
PC_12	0.118	0.078	1.521	1.125	0.128	-0.034	0.270
PC_13	0.040	0.080	0.499	1.041	0.618	-0.117	0.197
PC_14	-0.065	0.082	-0.782	0.938	0.434	-0.226	0.097
PC_15	0.199	0.089	2.228	1.22	0.026	0.024	0.373
PC_16	-0.027	0.088	-0.308	0.973	0.758	-0.200	0.146
PC_17	-0.129	0.092	-1.400	0.879	0.161	-0.310	0.052
PC_18	0.080	0.093	0.857	1.083	0.391	-0.103	0.263
PC_19	-0.043	0.098	-0.435	0.958	0.664	-0.234	0.149
PC_20	0.323	0.102	3.175	1.381	0.001	0.123	0.522
PC_21	-0.004	0.105	-0.035	0.996	0.972	-0.209	0.202
PC_22	0.059	0.105	0.558	1.06	0.577	-0.147	0.264
PC_23	0.007	0.108	0.062	1.007	0.950	-0.205	0.218
PC_24	-0.214	0.114	-1.887	0.807	0.059	-0.437	0.008
const	0.082	0.091	0.899	1.085	0.369	-0.096	0.260

Table.6 Factor loadings for PCs in prediabetes group

Item	PC_0	PC_1	PC_4	PC_5	PC_8	PC_15	PC_20
Gender	0.476	0.121	-0.025	0.155	0.096	0.129	0.025
Age	-0.334	0.009	-0.172	-0.467	-0.046	0.099	-0.179
BMI	0.127	0.038	0.063	-0.31	-0.042	-0.023	-0.142
SBP	-0.183	0.098	0.111	-0.471	-0.028	0.003	-0.009
DBP	-0.022	0.112	0.188	-0.337	-0.003	-0.006	0.074
WBC	0.133	0.179	0.737	0.194	-0.039	-0.087	0.037
NE#	0.052	0.186	0.626	0.226	-0.113	-0.147	0.093
LY#	0.195	0.021	0.491	0.004	0.103	0.076	-0.188
MO#	0.14	0.127	0.554	0.098	-0.025	0.046	-0.054
EO#	0.163	0.14	0.194	-0.022	0.21	0.057	0.312
BA#	0.07	0.06	0.359	0.077	0.145	-0.112	0.154
RBC	0.056	0.297	0.297	0.292	0.228	0.12	-0.116
HCT	0.111	0.314	0.222	0.124	-0.024	0.072	-0.119
MCV	-0.517	0.258	-0.078	-0.213	-0.342	-0.012	-0.004
RDW-CV	-0.595	0.207	0.066	0.033	0.177	0.15	0.026
HGB	0.146	0.295	0.18	0.08	-0.069	0.059	-0.086
MCH	-0.428	0.235	-0.113	-0.248	-0.375	-0.024	0.029
MCHC	-0.832	0.335	-0.047	-0.106	-0.146	0.053	0.058
PLT	0.076	0.072	0.449	0.326	-0.111	0.254	-0.081
PCT	0.004	0.108	0.48	0.339	-0.036	0.187	-0.237
MPV	-0.413	0.136	-0.055	-0.093	0.106	-0.14	-0.226
PDW	-0.641	0.246	-0.061	-0.161	-0.022	0.006	0.109
TCHO	-0.094	0.07	0.245	-0.247	0.513	-0.13	0.015
TG	0.317	-0.02	0.184	-0.33	-0.047	-0.113	0.211
LDL	0.039	0.033	0.241	-0.186	0.542	-0.103	-0.124
HDL	-0.55	0.102	-0.058	0.196	0.101	0.068	0.099
UA	0.885	0.009	-0.253	-0.036	0.104	-0.167	0.013
ALT	0.327	-0.005	0.147	-0.17	0.016	0.216	-0.075

GGT	0.382	0.101	0.202	-0.201	-0.075	0.012	0.312
AST	0.171	-0.004	0.083	-0.235	-0.021	0.231	-0.089
ALP	-0.069	0.072	0.214	-0.252	-0.121	-0.31	-0.31
TBA	-0.013	0.057	-0.001	-0.128	0.029	0.31	0.064
TBIL	0.095	0.041	-0.38	0.506	0.04	-0.059	-0.005
DBIL	0.014	0.037	-0.442	0.551	-0.055	-0.001	-0.022
IBIL	0.109	0.041	-0.36	0.487	0.058	-0.07	-0.002
CREA	0.292	0.155	-0.185	0.011	0.457	0.159	-0.024
BUN	-0.115	0.101	-0.146	-0.252	0.391	0.216	0.184
eGFR	-0.367	0.087	0.261	0.264	-0.458	-0.112	0.12
TP	-0.586	0.256	0.247	-0.004	0.071	-0.218	0.145
GLB	-0.372	0.119	0.204	-0.17	0.1	-0.214	0.043
ALB	-0.499	0.275	0.147	0.217	-0.011	-0.087	0.187
Per-All	0.001	-0.463	0.068	-0.086	-0.229	0.105	0.091
Per-Part	-0.231	0.355	-0.075	0.191	0.054	-0.155	0.074
TB-CON	-0.032	-0.538	0.089	-0.017	-0.123	-0.105	-0.067
TB-ENT	-0.462	-0.355	0.086	-0.003	-0.11	-0.067	-0.04
TB-ASM	-0.272	0.601	-0.061	-0.016	0.061	0.133	0.029
TB-MEAN	-0.144	-0.508	0.085	-0.01	-0.122	-0.107	-0.05
TC-CON	-0.048	-0.664	0.094	0.028	-0.022	0.107	0.053
TC-ENT	-0.435	-0.558	0.114	0.033	-0.011	0.131	0.083
TC-ASM	-0.183	0.736	-0.096	-0.059	-0.043	-0.057	-0.091
TC-MEAN	-0.15	-0.661	0.101	0.04	-0.005	0.111	0.078
TB-R	-0.876	-0.032	-0.072	0.077	0.174	-0.1	-0.106
TB-G	-0.664	-0.471	-0.116	0.026	0.082	-0.069	-0.031
TB-B	-0.56	-0.552	-0.022	0.039	0.138	-0.131	-0.036
TC-R	-0.583	-0.624	0.084	0.099	0.125	0.017	0.035
TC-G	-0.46	-0.8	0.081	0.027	0.029	0.066	-0.004
TC-B	-0.393	-0.821	0.113	0.046	0.083	0.016	0.009
TB-H	-0.908	0.348	-0.014	-0.014	-0.053	0.096	0.007
TB-I	-0.773	-0.365	-0.079	0.05	0.144	-0.108	-0.064
TB-S	-0.196	0.693	0.107	0.032	0.032	0.042	-0.074
TC-H	-0.885	0.36	-0.009	-0.027	-0.08	0.112	-0.003
TC-I	-0.491	-0.767	0.093	0.06	0.082	0.031	0.014
TC-S	-0.189	0.793	-0.077	0.083	0.084	-0.069	0.055
TB-L	-0.96	-0.023	-0.046	0.016	0.042	-0.0	-0.026
TB-a	-0.222	0.625	0.123	0.051	0.091	-0.02	-0.066
TB-b	-0.411	0.455	-0.163	-0.003	-0.065	0.113	-0.032
TC-L	-0.841	-0.44	0.086	0.031	0.021	0.082	0.013
TC-a	-0.186	0.643	-0.003	0.133	0.208	-0.14	0.086
TC-b	-0.268	0.485	-0.132	-0.015	-0.112	0.116	-0.015
TB-Y	-0.824	-0.304	-0.09	0.043	0.115	-0.078	-0.056
TB-Cr	-0.851	0.458	0.026	0.018	0.02	0.045	-0.035
TB-Cb	-0.877	0.244	0.083	-0.021	-0.036	0.064	0.027
TC-Y	-0.555	-0.732	0.088	0.051	0.063	0.051	0.01
TC-Cr	-0.881	0.397	0.02	0.046	0.04	0.036	0.037
TC-Cb	-0.88	0.264	0.058	-0.02	-0.019	0.054	0.008

Figure.3 Factor loadings of PC_0 in prediabetes group

Note: TB-Cr, TB-ENT, TC-ENT are negatively correlated with the risk factor PC_0, and the correlations are -0.851, -0.462, and -0.435, respectively.

Figure.4 Factor loadings of PC_1 in prediabetes group

Note: PC_1 is a protective factor, TC-ASM, TB-ASM, TB-Cr and PC_1 are positively correlated, and the correlation coefficients are 0.736, 0.601 and 0.458, respectively. TC-CON, TC-MEAN, TC-ENT, TB-CON, TB-MEAN, TB-ENT are negatively correlated with PC_1, the correlation coefficients are -0.664, -0.661, -0.558, -0.538, -0.508, -0.355, respectively.

Figure.5 Factor loadings of PC_4 in prediabetes group

Note: PC_4 is a risk factor, WBC, NE#, LY# are positively correlated with PC_4, and the correlation coefficients are 0.737, 0.626, 0.491, respectively.

Figure.6 Biplot of PC_0 and PC_1 in prediabetes group

Note: A biplot shows how strongly each feature influences a principal component. The position coordinates of the feature are determined by the weight of feature of the corresponding PC. The angle between features indicates the correlation between features. An acute angle ($< 90^\circ$) indicates a positive correlation between two features. Right angles (90°) indicate irrelevance. Obtuse angles ($> 90^\circ$) indicate negative correlation. PC_0 is a risk factor, TB-Cr mainly acts on PC_0 (The vector that is sub-parallel to the x-axis), and TB-Cr has a reverse effect on PC_0 and is a protective factor. PC_1 is a protective factor, TB-ASM, TC-ASM, TB-CON, TC-CON, TB-MEAN, TC-MEAN, TC-ENT mainly act on PC_1 (The vectors that are sub-parallel to the y-axis). TB-ASM and TC-ASM play a positive role on PC_1 and are protective factors; TB-CON, TC-CON,

TB-MEAN, TC-MEAN and TC-ENT play a negative role on PC_1 and are risk factors.

Figure.7 Biplot of PC_1 and PC_4 in prediabetes group

Note: PC_1 is a protective factor, TB-ENT mainly act on PC_1 (The vector that is sub-parallel to the x-axis). TB-ENT plays a negative role on PC_1 and is risk factor.

For the diabetes group, PC_0, PC_3, PC_4, PC_5, PC_9, PC_11, PC_19 were risk factors. PC_2, PC_18, PC_21 and PC_24 are protective factors (Table.7). The original features were associated with the PCs through the factor loading method (Table.8). Figure.9 shows the original features highly related to PC_0, Figure.10 shows the original features highly related to PC_2, and Figure.11 shows the original features highly related to PC_3. Figure.12, Figure.13, and Figure.14 respectively calculated the position and orientation of key tongue features in the coordinate system composed of PC_0 and PC_2, PC_0 and PC_3, PC_2 and PC_3. Combined with factor loading analysis, it can be determined that TB-a, TB-S, TB-Cr, TB-b and TC-b are protective factors, and Per-all and TB-Cb are risk factors.

Figure.8 Proportion of variance explained by PCs in diabetes group

Table.7 Logistic regression analysis for PCs in diabetes group

Item	Coef	Std err	Z	OR	P value	Lower limit	Upper limit
PC_0	0.139	0.035	3.982	1.149	0.000	0.071	0.208
PC_1	-0.052	0.038	-1.370	0.95	0.171	-0.125	0.022
PC_2	-0.188	0.057	-3.298	0.829	0.001	-0.299	-0.076
PC_3	0.294	0.059	5.004	1.342	0.000	0.179	0.410
PC_4	0.214	0.062	3.451	1.238	0.001	0.092	0.335
PC_5	0.453	0.081	5.559	1.572	0.000	0.293	0.612
PC_6	-0.027	0.087	-0.305	0.974	0.760	-0.198	0.145
PC_7	0.005	0.084	0.059	1.005	0.953	-0.159	0.169
PC_8	0.083	0.088	0.940	1.086	0.347	-0.090	0.256
PC_9	0.182	0.089	2.048	1.199	0.041	0.008	0.355
PC_10	-0.062	0.092	-0.665	0.94	0.506	-0.242	0.120
PC_11	0.310	0.099	3.127	1.364	0.002	0.116	0.505
PC_12	-0.130	0.105	-1.244	0.878	0.214	-0.336	0.075
PC_13	-0.049	0.111	-0.439	0.953	0.661	-0.265	0.168
PC_14	-0.196	0.116	-1.688	0.822	0.091	-0.424	0.032
PC_15	0.064	0.118	0.542	1.066	0.588	-0.167	0.295
PC_16	-0.146	0.118	-1.232	0.864	0.218	-0.378	0.086
PC_17	0.054	0.121	0.441	1.055	0.659	-0.184	0.291
PC_18	-0.368	0.128	-2.873	0.692	0.004	-0.618	-0.117
PC_19	0.388	0.142	2.725	1.474	0.006	0.109	0.667
PC_20	0.227	0.135	1.680	1.254	0.093	-0.038	0.491
PC_21	-0.375	0.136	-2.762	0.688	0.006	-0.640	-0.109
PC_22	-0.069	0.137	-0.506	0.933	0.613	-0.337	0.199
PC_23	0.197	0.139	1.415	1.217	0.157	-0.076	0.469
PC_24	-0.417	0.147	-2.840	0.659	0.005	-0.705	-0.129
const	-0.687	0.126	-5.463	0.503	0.000	-0.933	-0.440

Table 8 Factor loadings for original features in diabetes group

Item	PC_0	PC_2	PC_3	PC_4	PC_5	PC_9	PC_11	PC_18	PC_19	PC_21	PC_24
Gender	0.427	0.301	0.508	-0.241	-0.096	0.016	-0.036	-0.003	0.039	0.208	0.052
Age	-0.299	0.163	-0.155	-0.021	0.308	0.226	-0.042	-0.106	0.084	0.211	-0.148
BMI	0.073	-0.01	0.325	0.105	0.295	0.161	0.224	-0.169	-0.033	-0.239	-0.129
SBP	-0.086	0.042	0.145	0.24	0.55	0.268	0.371	0.139	-0.027	0.036	-0.01
DBP	0.059	0.034	0.241	0.222	0.485	0.202	0.423	0.179	-0.013	-0.035	0.198
WBC	0.135	-0.203	0.538	0.536	-0.269	0.158	0.04	-0.108	-0.129	-0.027	0.012
NE#	0.059	-0.147	0.482	0.428	-0.3	0.098	0.002	-0.023	-0.074	0.003	-0.004
LY#	0.18	-0.18	0.267	0.425	-0.031	0.13	0.123	-0.296	-0.284	-0.066	0.029
MO#	0.159	-0.187	0.408	0.351	-0.178	0.227	0.057	-0.091	-0.083	0.081	0.016
EO#	0.125	-0.088	0.219	0.158	-0.001	0.194	-0.096	0.24	0.491	-0.148	-0.01
BA#	0.034	-0.136	0.359	0.247	-0.082	0.126	-0.005	0.44	0.023	0.059	0.088
RBC	-0.046	0.283	0.576	0.144	-0.178	-0.075	0.014	0.083	0.148	-0.011	-0.055
HCT	-0.0	0.445	0.679	0.099	-0.053	-0.194	-0.14	0.087	0.018	-0.012	-0.053
MCV	-0.564	0.257	0.186	-0.036	0.165	-0.188	-0.193	-0.033	-0.141	-0.02	0.027
RDW-CV	-0.587	-0.26	-0.111	0.049	-0.076	0.271	0.125	-0.065	0.164	0.29	0.133
HGB	0.025	0.475	0.68	0.063	-0.01	-0.227	-0.135	0.072	0.021	-0.034	-0.063
MCH	-0.494	0.306	0.214	-0.073	0.204	-0.235	-0.189	-0.046	-0.13	-0.053	0.01
MCHC	-0.879	0.156	0.126	-0.046	0.094	-0.131	-0.006	-0.086	0.021	-0.067	0.007
PLT	0.03	-0.466	-0.108	0.44	-0.469	-0.036	0.186	-0.024	0.079	-0.042	-0.003
PCT	-0.059	-0.465	-0.106	0.46	-0.423	-0.007	0.094	0.093	-0.159	-0.026	-0.113
MPV	-0.432	0.099	0.042	-0.062	0.193	0.053	-0.179	0.154	-0.347	0.034	-0.153
PDW	-0.738	0.076	0.142	-0.056	0.121	-0.013	0.034	-0.065	0.033	0.025	0.029
TCHO	-0.048	-0.02	-0.052	0.473	0.152	-0.1	-0.301	-0.116	0.053	0.17	0.043
TG	0.311	-0.024	0.142	0.176	0.25	-0.199	0.252	-0.317	0.143	0.042	0.138
LDL	-0.006	0.009	-0.001	0.388	0.049	-0.025	-0.439	-0.05	-0.013	0.141	-0.091
HDL	-0.525	-0.029	-0.247	0.055	-0.106	0.079	-0.096	0.373	-0.055	0.013	0.116
UA	0.744	0.141	0.014	-0.235	-0.021	0.011	-0.082	0.022	-0.138	0.0	0.031
ALT	0.489	-0.099	0.044	0.116	0.35	0.116	-0.118	-0.015	0.009	-0.1	0.043
GGT	0.467	-0.103	0.089	0.119	0.283	-0.077	-0.126	-0.11	0.247	0.004	-0.052
AST	0.305	-0.084	0.035	0.165	0.426	0.169	-0.168	-0.022	-0.042	-0.065	0.117
ALP	0.013	-0.025	0.162	0.026	0.276	0.095	0.059	0.057	-0.098	0.123	-0.056
TBA	0.03	-0.114	0.095	0.01	0.351	0.092	0.19	0.158	-0.151	0.323	-0.24
TBIL	0.053	0.564	0.216	-0.237	-0.322	0.308	0.142	-0.083	-0.002	0.006	-0.051
DBIL	-0.022	0.519	0.184	-0.335	-0.336	0.338	0.118	-0.008	-0.01	-0.008	-0.055
IBIL	0.067	0.561	0.218	-0.213	-0.313	0.296	0.144	-0.096	0.0	0.009	-0.049
CREA	0.212	0.329	0.189	-0.324	-0.008	0.375	-0.114	-0.07	-0.042	0.076	0.277
BUN	-0.048	0.2	0.017	-0.146	0.165	0.26	-0.08	0.025	0.049	-0.425	-0.297
eGFR	-0.362	-0.243	0.15	0.241	-0.084	-0.429	0.163	0.081	0.021	0.044	-0.11
TP	-0.572	0.005	0.035	0.362	0.072	0.031	0.019	0.05	0.073	-0.085	-0.043
GLB	-0.333	-0.205	-0.137	0.403	0.149	0.213	-0.012	-0.052	0.098	-0.085	-0.154
ALB	-0.532	0.259	0.224	0.101	-0.064	-0.21	0.046	0.146	-0.0	-0.036	0.119
Per-All	0.067	-0.068	0.505	-0.085	0.066	-0.22	0.074	-0.102	0.085	-0.025	0.127
Per-Part	-0.245	0.214	-0.245	0.021	-0.108	0.191	-0.01	-0.068	0.207	0.212	-0.124
TB-CON	0.083	0.545	-0.264	0.208	-0.021	-0.141	0.191	0.0	0.015	0.1	-0.158
TB-ENT	-0.458	0.598	-0.198	0.253	-0.015	-0.123	0.183	-0.033	0.028	0.008	-0.067
TB-ASM	-0.31	-0.537	0.206	-0.206	0.028	0.101	-0.165	-0.024	-0.015	0.027	0.097

TB-MEAN	-0.107	0.627	-0.255	0.256	-0.018	-0.14	0.211	-0.015	0.017	0.035	-0.095
TC-CON	-0.006	0.488	-0.26	0.322	-0.007	0.008	-0.001	0.037	-0.055	-0.02	0.146
TC-ENT	-0.429	0.464	-0.169	0.327	0.013	0.034	-0.041	0.011	-0.029	-0.059	0.154
TC-ASM	-0.227	-0.398	0.177	-0.292	-0.006	-0.081	0.07	-0.066	0.03	0.066	-0.109
TC-MEAN	-0.131	0.482	-0.234	0.334	0.003	0.039	-0.028	0.035	-0.047	-0.05	0.167
TB-R	-0.864	-0.118	-0.083	-0.143	-0.035	0.043	0.083	0.046	-0.037	-0.003	-0.02
TB-G	-0.599	-0.299	0.144	-0.289	-0.004	-0.05	0.146	0.018	-0.014	-0.037	0.015
TB-B	-0.469	-0.164	0.309	-0.243	0.048	-0.073	0.14	0.048	-0.001	0.032	-0.026
TC-R	-0.525	-0.11	0.064	0.044	-0.039	0.228	-0.216	-0.024	-0.001	-0.023	-0.028
TC-G	-0.359	-0.147	0.153	0.011	-0.017	0.131	-0.154	-0.027	0.012	0.027	-0.052
TC-B	-0.29	-0.091	0.227	0.038	0.009	0.131	-0.171	-0.013	0.019	0.031	-0.041
TB-H	-0.935	-0.01	-0.012	0.005	-0.01	-0.012	0.014	-0.071	0.018	-0.027	0.051
TB-I	-0.728	-0.209	0.121	-0.243	0.004	-0.024	0.133	0.04	-0.019	0.0	-0.013
TB-S	-0.322	0.291	-0.166	0.241	0.008	0.071	-0.073	-0.018	0.007	0.072	-0.024
TC-H	-0.915	-0.001	-0.023	-0.004	-0.011	-0.027	0.036	-0.07	0.018	-0.008	0.028
TC-I	-0.403	-0.119	0.151	0.031	-0.017	0.167	-0.187	-0.021	0.009	0.011	-0.041
TC-S	-0.33	0.101	-0.202	0.022	-0.012	0.062	0.05	0.017	-0.01	-0.096	0.095
TB-L	-0.952	-0.119	0.091	-0.133	0.001	-0.031	0.085	-0.023	0.003	-0.016	0.025
TB-a	-0.345	0.308	-0.171	0.225	-0.005	0.09	-0.086	0.022	-0.006	0.072	-0.049
TB-b	-0.437	-0.14	-0.435	0.009	-0.111	0.095	-0.023	-0.046	-0.034	-0.109	0.059
TC-L	-0.795	-0.083	0.139	0.035	-0.011	0.11	-0.136	-0.055	0.021	0.009	-0.017
TC-a	-0.316	0.165	-0.119	0.072	-0.012	0.133	-0.064	0.014	-0.015	-0.083	0.073
TC-b	-0.31	-0.102	-0.351	-0.067	-0.092	0.031	0.075	-0.034	-0.033	-0.059	0.004
TB-Y	-0.79	-0.223	0.092	-0.236	-0.008	-0.024	0.128	0.024	-0.018	-0.019	0.003
TB-Cr	-0.897	0.085	-0.071	0.061	-0.011	0.026	-0.007	-0.035	0.005	0.007	0.015
TB-Cb	-0.905	0.099	0.227	0.029	0.055	-0.066	0.024	-0.064	0.045	0.034	0.026
TC-Y	-0.472	-0.128	0.14	0.026	-0.02	0.161	-0.176	-0.029	0.011	0.011	-0.041
TC-Cr	-0.923	0.048	-0.027	0.04	-0.012	0.061	-0.04	-0.053	0.01	-0.041	0.047
TC-Cb	-0.904	0.081	0.175	0.04	0.047	-0.057	0.016	-0.057	0.04	0.02	0.043

Figure.9 Factor loadings of PC_0 in diabetes group

Note: PC_0 is a risk factor, TB-Cb, TB-Cr, TB-b, TB-a, TB-S, TC-b are negatively correlated with PC_0, and the correlation coefficients are -0.905, -0.897, -0.437, -0.345, -0.322, -0.31, respectively.

Figure.10 Factor loadings of PC_2 in diabetes group

Note: PC_2 is a protective factor, TB-a is positively correlated with PC_2, and the correlation coefficient is 0.308.

Figure.11 Factor loadings of PC_3 in diabetes group

Note: PC_3 is a risk factor, TB-b and TC-b are negatively correlated with PC_3, and the correlation coefficients are -0.435 and -0.351, respectively.

Figure.12 Biplot of PC_0 and PC_2 in diabetes group

Note: PC_0 is a risk factor, TB-Cr, TB-b, TC-b mainly act on PC_0 (The vectors that are sub-parallel to the x-axis), TB-Cr, TB-b and TC-b play a negative role on PC_0 and are protective factors. PC_2 is a protective factor, TB-a and TB-S mainly act on PC_2 (The vectors that are sub-parallel to the y-axis), TB-a and TB-S positively act on PC_2 as a protective factor.

Figure.13 Biplot of PC_0 and PC_3 in diabetes group

Note: PC_3 is a risk factor, Per-all mainly acts on PC_3 (The vector that is sub-parallel to the y-axis), Per-all has a positive effect on PC_3 and is a risk factor.

Figure.14 Biplot of PC_2 and PC_3 in diabetes group

Note: PC_3 is a risk factor, TB-Cb mainly acts on PC_3 (The vector that is sub-parallel to the y-axis), TB-Cb has a positive effect on PC_3 and is a risk factor.

Discussion

Through PCA combined with logistic regression, the key tongue features and changing laws during the onset of diabetes were analyzed. In the prediabetic group, TB-ASM, TC-ASM and TB-Cr are protective factors. As these indicators increase, the risk of prediabetes decreases. TB-CON, TC-CON, TB-MEAN, TC-MEAN, TB-ENT and TC-ENT are risk factors. As these indicators increase, the risk of prediabetes increases. At the same time, this also suggests that in the early stage of the disorder of glucose metabolism, the texture features are the first to change, and these texture features reflect the tenderness of the tongue and the moisturizing of the tongue coating. When prediabetes occurs, the texture of the tongue will become rough, and the tongue coating will be dry, which manifests as TB-CON, TC-CON, TB-MEAN, TC-MEAN, TB-ENT and TC-ENT increase, and TB-ASM And TC-ASM decreased. In the diabetes group, TB-Cb and Per-all are risk factors. As these indicators increase, the risk of diabetes increases. TB-Cr, TB-a, TB-S, TB-b and TC-b are protective factors. As these indicators increase, the risk of diabetes decreases. Entering the diabetes stage, the color features begin to change, manifested as the red component of the tongue decreases, the blue component increases, and the blue component of the tongue coating increases. In addition, the increase of Per-all indicates that the tongue coating increases and thickens. Tongue features include both protective factors and risk factors, and they have a bidirectional predictive effect on prediabetes and diabetes. In the prediabetic population, the texture feature was found to have an early warning effect; in the diabetic population, the color feature and the tongue coating

ratio feature were found to have an early warning effect.

Individuals with prediabetes, especially those with Impaired Glucose Tolerance (IGT) or abnormal HbA1c (6.0% - 6.4%), not only are at increased risk of developing diabetes, but also have an increased risk of cardiovascular Diseases^[12]. For individuals with prediabetes, those later diagnosed with diabetes had medical expenditures nearly 1/3 higher than those who were not later diagnosed^[13]. The best way to reverse the epidemic of diabetes is to intervene in prediabetes as early as possible^[14]. For patients with undiagnosed potential diabetes, the insidious onset and lack of awareness of diabetes will lead to missed diagnosis and poor prognosis^[15, 16]. Therefore, it is very important to develop reliable diabetes risk warning tools. Tongue features contain rich physiological and pathological information, which can be obtained non-invasively, and are closely related to glucose metabolism, showing potential advantages^[17]. Therefore, finding the key tongue features related to diabetes risk and clarifying the clinical significance of the changes in these tongue features will provide a basis for the application of tongue features to diabetes risk prediction.

Logistic regression analysis requires that the sample size should be more than 15 times the size of independent variables, and there is no multicollinearity between the independent variables. By introducing PCA, we reduced the data dimension to 25 features (PCs) to eliminate the collinearity of the original features. PCA makes full use of original data and ensures the reliability of analysis conclusions. We used the PCA combined with logistic regression analysis method to find the key tongue features reflecting glucose metabolism, and clarified the significance of the changes in these tongue features. However, tongue features are continuous measurement data, and classification standards need to be established in the future to facilitate future clinical practice. This study did not consider the simultaneous increase of fasting blood glucose and HbA1c. This may mean that the patient's glucose metabolism is more disordered.

Conclusion

In this study, PCA was first used to reduce the dimensionality of the original data and retain more than 90% of the original data information. 25 new features were reconstructed on the basis of 76 original features. Then use logistic regression to calculate the OR value of the new feature. Next, the factor loading method is used to associate the original feature with the new feature. Through this study, the tongue features that are highly related to the risk of diabetes have been determined, and the clinical significance of these changes in tongue features have been clarified. This will lay the foundation for the study of constructing an early warning model of diabetes risk based on the tongue features.

Declarations

Ethics approval and consent to participate We confirm that all experiments were performed in accordance with relevant guidelines and regulations. All subjects signed an informed consent form. The study was approved by the IRB of Shuguang Hospital affiliated with Shanghai University of TCM.

Consent for publication Not applicable.

Availability of data and materials The datasets used and/or analysed during the current study available from the

corresponding author on reasonable request.

Competing interests The authors declare that they have no competing interests.

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Authors' contributions Jun Li wrote the whole manuscript text, analyzing the data, coding the program and plotting the results. These drafts were revised for important scientific content by Jiakai Li, Ji Cui, Changle Zhou and Jiatuo Xu. Xiaojuan Hu and Liping Tu helped in the ideas of study. Yulin Shi, Jiakai Li and Zijuan Bi provided assistance in data collection and analysis. All authors gave final approval of the version to be published. Jiatuo Xu is the guarantor of this work.

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Figures

Figure 1

Type TFDA-1 tongue diagnosis instrument

Figure 2

Proportion of variance explained by PCs in prediabetes group

Figure 3

Factor loadings of PC_0 in prediabetes group Note: TB-Cr, TB-ENT, TC-ENT are negatively correlated with the risk factor PC_0, and the correlations are -0.851, -0.462, and -0.435, respectively.

Figure 4

Factor loadings of PC_1 in prediabetes group Note: PC_1 is a protective factor, TC-ASM, TB-ASM, TB-Cr and PC_1 are positively correlated, and the correlation coefficients are 0.736, 0.601 and 0.458,

respectively. TC-CON, TC-MEAN, TC-ENT, TB-CON, TB-MEAN, TB-ENT are negatively correlated with PC_1, the correlation coefficients are -0.664, -0.661, -0.558, -0.538, -0.508, -0.355, respectively.

Figure 5

Factor loadings of PC_4 in prediabetes group Note: PC_4 is a risk factor, WBC, NE#, LY# are positively correlated with PC_4, and the correlation coefficients are 0.737, 0.626, 0.491, respectively.

Figure 6

Biplot of PC_0 and PC_1 in prediabetes group Note: A biplot shows how strongly each feature influences a principal component. The position coordinates of the feature are determined by the weight of feature of the corresponding PC. The angle between features indicates the correlation between features. An acute angle ($< 90^\circ$) indicates a positive correlation between two features. Right angles (90°) indicate irrelevance. Obtuse angles ($> 90^\circ$) indicate negative correlation. PC_0 is a risk factor, TB-Cr mainly acts on PC_0 (The vector that is sub-parallel to the x-axis), and TB-Cr has a reverse effect on PC_0 and is a protective factor. PC_1 is a protective factor, TB-ASM, TC-ASM, TB-CON, TC-CON, TB-MEAN, TC-MEAN, TC-ENT mainly act on PC_1 (The vectors that are sub-parallel to the y-axis). TB-ASM and TC-ASM play a positive role on PC_1 and are protective factors; TB-CON, TC-CON, TB-MEAN, TC-MEAN and TC-ENT play a negative role on PC_1 and are risk factors.

Figure 7

Biplot of PC_1 and PC_4 in prediabetes group Note: PC_1 is a protective factor, TB-ENT mainly act on PC_1 (The vector that is sub-parallel to the x-axis). TB-ENT plays a negative role on PC_1 and is risk factor.

Figure 8

Proportion of variance explained by PCs in diabetes group

Figure 9

Factor loadings of PC_0 in diabetes group Note: PC_0 is a risk factor, TB-Cb, TB-Cr, TB-b, TB-a, TB-S, TC-b are negatively correlated with PC_0, and the correlation coefficients are -0.905, -0.897, -0.437, -0.345,

-0.322, -0.31, respectively.

Figure 10

Factor loadings of PC_2 in diabetes group Note: PC_2 is a protective factor, TB-a is positively correlated with PC_2, and the correlation coefficient is 0.308.

Figure 11

Factor loadings of PC_3 in diabetes group Note: PC_3 is a risk factor, TB-b and TC-b are negatively correlated with PC_3, and the correlation coefficients are -0.435 and -0.351, respectively.

Figure 12

Biplot of PC_0 and PC_2 in diabetes group Note: PC_0 is a risk factor, TB-Cr, TB-b, TC-b mainly act on PC_0 (The vectors that are sub-parallel to the x-axis), TB-Cr, TB-b and TC-b play a negative role on PC_0 and are protective factors. PC_2 is a protective factor, TB-a and TB-S mainly act on PC_2 (The vectors that are sub-parallel to the y-axis), TB-a and TB-S positively act on PC_2 as a protective factor.

Figure 13

Biplot of PC_0 and PC_3 in diabetes group Note: PC_3 is a risk factor, Per-all mainly acts on PC_3 (The vector that is sub-parallel to the y-axis), Per-all has a positive effect on PC_3 and is a risk factor.

Figure 14

14 Biplot of PC_2 and PC_3 in diabetes group Note: PC_3 is a risk factor, TB-Cb mainly acts on PC_3 (The vector that is sub-parallel to the y-axis), TB-Cb has a positive effect on PC_3 and is a risk factor.