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The Relationship Between Computerized Face and Tongue Image Segmentation and Metabolic Parameters in Patients with Type 2 Diabetes Based on Machine Learning

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Objective: We aim to examine and reestablish the correlational and linear regression relationships, as well as the predictive value, between the significant facial and tongue features and the metabolic parameters in type 2 diabetes mellitus (T2DM).

Materials and Methods: From March to May 2024, we studied 269 patients with T2DM in the endocrinology department of Shanghai Pudong Hospital. The patients' facial and tongue characteristics were sampling by a tongue imaging device equipped with artificial intelligence (AI) (XiMaLife, Sinology, China) of automated and advanced machine learning algorithms. Then, the imaging features were examined in relation to the blood examination.

Results: Multiple facial and tongue features, as well as dimensional facial and tongue color parameters, were significantly correlated with glycated hemoglobin A1c (HbA1c) ($r < 0.3$, $p < 0.05$), glycated albumin (GA) ($-0.20 < 0.30$, $p < 0.05$), C-peptide ($-0.20.20$, $p < 0.05$), plasma insulin ($r < 0.30$, $p < 0.05$), fasting plasma glucose (FPG) ($r < 0.3$, $p < 0.05$), significant hepatic and renal function indicators ($-0.30 < r < 0.20$, $p<0.05$), cardiac injury markers ($-0.30 < r < 0.30$, $p < 0.05$), tumor markers ($-0.5 < r < 0.5$, $p < 0.05$), thyroid function ($-0.15 < r < 0.55$, $p < 0.05$), and blood cell count, including white blood cells ($r < 0.2$, $p < 0.05$), and hemoglobin (Hb) ($-0.30 < r < 0.3$, 0.0001. The correlational results demonstrated that the tongue's characteristics and signs may be linked with the dynamic of the metabolic status of T2DM. In order to examine the causal relationships, we performed linear regression analyses, which revealed that various facial and tongue imaging parameters partially determined the metabolic indicators. The predictive value of imaging features was evaluated by receiver operating characteristic curve (ROC) to assess metabolic status in T2DM.

Conclusion: This study demonstrated that metabolic status, renal and hepatic, cardiac, and thyroid function, the proportion of blood cells, and Hb in T2DM were intimately associated with facial and tongue features. The precise analysis of facial and tongue features through AI and advanced machine learning could be used to predict T2DM's conditions and progression.

Keywords: type 2 diabetes, tongue imaging, face imaging, cardiovascular disease, machine learning

Introduction

In ancient Greek medicine and Chinese Traditional Medicine (TCM), physicians examined the tongue and face's surface for various characteristic features, including color, hydration, coating, and texture, to obtain insight into a patient's

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overall health.[1–3] The tongue and face observation are critical components of the numerous tools for diagnosis.[4,5] Tongue and face diagnosis, also referred to as tongue and face inspection, can provide valuable insights into the efficacy of treatment, the progression of the disease, and the overall health status of a patient.[6] The tongue and face's color can vary from colorless to dark red, suggesting a variety of pathologies, including blood deficiency and Qi deficiency. The tongue coating and texture also indicate conditions such as metabolic abnormalities in the internal environment, abnormal proliferation of gut microbiota, serum lipid imbalance, and microvascular damage.[7–9]

A global health concern, type 2 diabetes is a prevalent metabolic disorder that is distinguished by elevated blood glucose levels as a result of insulin resistance and insufficient insulin production.[10] Although blood tests and clinical symptoms are the primary diagnostic tools, recent research and traditional medical practices have underscored the potential of tongue and face observations as non-invasive indicators of this condition.[11–13] In TCM, DM was termed "XiaoKe", or emaciation and thirst syndrome, in which the patient experiences weight loss and thirst secondary to the polyuria and hyperglycemia; XiaoKe could be traced to the TCM pathophysiology of lung dryness causing thirst, stomach heat causing hyperphagia and weight-loss, and renal asthenia causing polyuria and diabetes; therefore, the syndromes could be classified into lung-stomach dry-heat, spleen-stomach Qi asthenia, renal Yin-asthenia, Yin and Yang asthenia syndromes, which were accompanied by the distinct and specific tongue and facial signs. The TCM physicians could diagnose the DM patients with different signs according to the various manifestations of the tongue combined with other clinical symptoms and signs as well as pulse signs, acknowledge the condition or progress or treatment efficacies, and eventually administer respective medications (dialect therapy) and other therapies such as acupuncture. Thus, the facial and tongue signs are critical to diagnosing and treating DM by TCM physicians. For example, some TCM physicians could judge the patients with "spleen" (could be alternated to the modern medicine notion of pancreas) Qi asthenia by observing thick white tongue fur with other characteristics such as expanded tongue volume, slippery tongue, or scalloped tongue, indicating the accumulating of the dampness (a sign may be associated with incompetently handling the fluid transforming and transportation of the spleen caused by Qi asthenia), a classical sign in XiaoKe and obese patients, therefore alerting us if we should measure the pancreatic function and insulin resistance in these spleen Qi asthenia T2DM patients; another example would be the purple tongue or lips or even facial, suggesting stagnant of blood, a sign alert to exclude potential cerebrocardiovascular complications, or to implement respective preventive measures.

To validate and further explore the intimate metabolic relationships between the tongue and facial signs with T2DM via the modern medicine multiparameter assay, in this paper, we investigate the scientific foundation and clinical implications of observing the correlation between T2D and its manifestation through tongue and face characteristics. The incorporation of TCM and modern medicine would not only fill the gap between them, for instance, to promote the mutual understanding between them on the rationale or mechanism distinction of diagnosis and treatment, but also strengthen both of them, such as standardized and precise TCM diagnosis and treatment, or improve individualized therapy for the T2DM patients in modern medicine especially in chronic diabetic complications.

The use of image processing techniques to digitize and analyze tongue and face observation was becoming increasingly prevalent due to technological advancements.[14–17] The precision and reproducibility of tongue and face diagnosis are enhanced by these techniques, which increases its accessibility to all physicians worldwide who are not familiar with Traditional Chinese Medicine (TCM). These technologies can potentially improve the efficacy and reliability of ancient diagnostic methods by integrating precise laboratory metabolic data with the ancient tongue and face diagnosis in T2DM patients. This paper examines the implications of tongue-and-face observation on the metabolic parameters of patients with T2DM.

Materials and Methods

Source of Patient Data

The study includes 269 adult T2DM patients admitted to the Department of Endocrinology at Shanghai Pudong Hospital between March and May 2024. They were selected in a randomized manner and fulfilled the diagnostic criteria for T2DM, as defined by the established World Health Organization (WHO) and American Diabetes Association (ADA) guidelines.[18] Oral anti-diabetic medication, such as metformin, sulfonylurea, glinides, pioglitazone, sodium-glucose co-

transporter inhibitors (SGLT-2i), α-glucosidase inhibitors, and dipeptidyl peptidase-IV inhibitors (DPP-IV inhibitors), as well as injectables, such as glucagon-like peptide-1 receptor agonists (GLP-1RA) and insulin (basal insulin or combined with prandial insulin or premixed insulin), were administered to patients in accordance with disease progression, glycemic control, and complications such as liver or kidney insufficiency. The selection criteria excluded other types of diabetes, such as T1DM, secondary DM, gestational DM, and other specific forms of DM. The study also excluded a few severe conditions, such as diabetic acidosis, hyperosmolar hyperglycemic state, lactic acidosis, shock, hypoperfusion of circulation, severe systemic disorders, stroke, asthma, uremia, intestinal obstruction, and severe sepsis.

Blood Sampling and Methods of Laboratory Assessment

The metabolic parameters were collected from patients on the day following their admission. These laboratory parameters include serum blood glucose, pancreatic islet function, hemoglobin A1C (HbA1C), thyroid function, hepatic and renal function, and whole blood cells. All biochemical indicators, including fasting blood glucose, hepatic function, and kidney function indicators, were analyzed using a full-automatic biochemical analyzer (ADVIA Chemistry XPT, SIEMENS, USA). The TOSOH G8 analyzer was used to determine the glycemic control level over the past three months. C-peptide and thyroid function indicators were processed using chemiluminescence methods in a full-automatic chemiluminescence immunoassay analyzer (ADIVA Centaur XPT, SIEMENS, USA).

Data Collection of Face and Tongue Color

Upon admission to the ward, the patients were arranged to receive the facial and tongue information sampling in an exclusive room with sufficient light and quietness. A prior request was made to the patient to clean their face and mouth. Subsequently, the tongue device was equipped with advanced AI ((XiMaLife, Sinology, China) and automatic machine learning to analyze the segmented features of the tongue and face by incorporating the fundamental information of each patient, and the based rationale of AI has been previously established.[19–21] This analysis includes color correction (RGB value retraction, CIELab space analyzing based on machine learning, segmentation algorithm optimization utilizing ASPP module analyzing multiple alternative parameters), DetNet algorithm, a real-time Anchor-free model detection utilizing ATSS target-sampling and Generalized Focal Loss function to classification and boundary regression, the SegNet to improve the tongue segmentation analyses.

The face and tongue images of T2DM patients were subsequently acquired by the device equipped with a high-definition camera. Patients volunteered to receive the facial and tongue image sampling by the device at the standardized light source aligned to the CIELAB standards. The data were subsequently transferred to the private database of Shanghai Traditional Medicine University for backup. The technician subsequently retracted the backend information and privately transmitted it to the investigators of this study. Numerous previous studies have found this machine's operating system information and detailed calculations and processes.

The categorical features for facial color are defined by machine calculation and include pale, normal, redness or yellow, and black. Lip color: red or dark red. Facial gloss: glossy or Dull. Tongue characteristics include pale white, light red, red, deep red, or dark red. Color of fur: yellow and white. Fur greasy: normal fur, oily fur, or lacking fur. Fur thickness: Thick or thin; Tongue lesion: normal or fission. Tongue volume: average or fat.

The face, lip, gloss, tongue, or fur color data were calculated using the Lab Color Space, also known as the CIELAB color space. This color-opponent space is based on the coordinates of the nonlinearly compressed CIE XYZ color space. It consists of three dimensions: L, a, and b, representing brightness, and two color-opponent dimensions, respectively. L (Lightness) refers to the pixel's luminance, which ranges from pure black to pure white: 0–255. a (Red-Green): Indicates the range from red to green, with values ranging from approximately 0 (green) to 255 (red). b (Yellow-Blue): Indicates the spectrum from yellow to blue, with values ranging from approximately 0 (blue) to 255 (yellow). The discrete dimensional color parameter allows the machine to analyse the tongue and facial condition of individual T2DM patients. The sampling procedure is illustrated in Figure 1.

Statistical Analyses

The statistical analyses were conducted using Prism (GraphPad, version 10.0) and SPSS (IBM, version 26.0). We utilized Spearman correlational analysis, a nonparametric analysis, to establish correlational relationships between facial and tongue

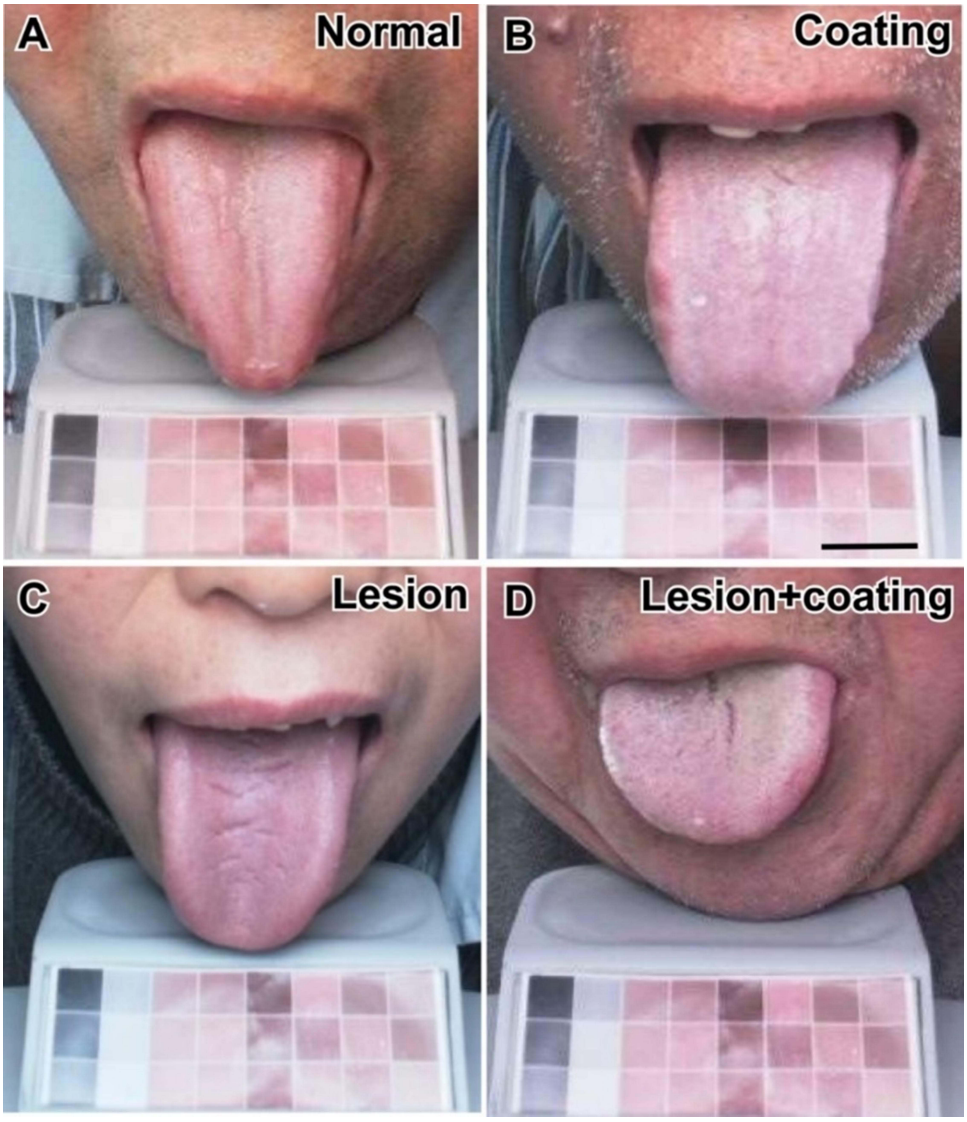

Figure 1 The tongue imaging device discern the different pathological features of tongue displayed as normal color (**A**), coating (**B**) tongue lesion (**C**), and both (**D**).

imaging features and dimensional parameters with glucose metabolic, hepatic, renal function, cardiac injury, tumor, thyroid function, and blood cell indicators. We screened the p-coefficient with values below 0.05 as two parameters significantly correlated. A multilinear regression analysis was employed to determine the independent facial and tongue imaging features associated with significant indicators. Multiple receiver operating characteristic curves (ROCs) were drawn to assess the predictive value of significant facial and tongue imaging parameters for metabolic parameters. $p < 0.05$ was established as the significance threshold for all statistical analyses. Data were presented as the mean ± standard error of the mean (SEM).

Results

The Characteristics of Patients with T2DM

Our study included T2DM patients for facial and tongue feature analyses. Table 1 displays the demographic characteristics, glucose metabolic status, lipid profile, and serum uric acid level.

Table 1 The Demographic Characteristics of Included T2DM Patients

Variables	Value	CV	Reference Range
Numbers	269	/	/
Age	62.45±13.21	0.211	/
Bw (kg)	69.48±11.83	0.170	/
BMI (kg/m^2)	25.74±3.59	0.140	18–24
Gender (m/f)	136/133	/	/
Diabetes Duration (y)	8.96±7.90	0.882	/
HbA1c (%)	9.34±2.31	0.247	4.0–6.0
Hb (g/L)	130.06±19.08	0.147	130–175
GA (%)	24.78±8.59	0.347	11–17
FPG (mmol/L)	8.18±3.24	0.396	4.1–5.9
2hPPG (mmol/L)	12.58±4.37	0.347	<7.8
FPCP (nmo/L)	0.69±0.56	0.804	0.27–1.28
2hPPCP (nmo/L)	1.26±0.97	0.773	1.35–2.50
FINS (pmol/L)	109.10±103.45	0.948	20.90–174.10
2hPPINS (pmol/L)	329.50±250.66	0.76	/
UACR (mg/gCr)	67.50±43.59	0.646	<30
eGFR (mL/min*1.73m^2)	83.85±26.45	0.315	/
BUN (mmol/L)	6.73±2.86	0.43	3.1–8.0
SCr (μmol/L)	82.16±54.96	0.67	59.0–104
UA (μmol/L)	333.96±102.68	0.307	200–415
TPOAb (U/mL)	65.89±119.02	1.806	<30
TgAb (IU/mL)	203.74±386.86	1.898	<75
Tg (ng/mL)	19.72±20.71	1.050	1–39
TRAb (IU/L)	1.74±3.18	1.829	0–2.0
FT3 (pmol/L)	4.97±1.47	0.295	3.5–7.0
FT4 (pmol/L)	15.78±3.93	0.249	10–22
TSH (mIU/L)	2.73±2.03	0.745	0.35–4.75
TC (mmol/L)	4.51±1.40	0.310	3.10–5.20
TG (mmol/L)	2.28±2.77	1.216	0.40–1.82
HDL (mmol/L)	1.05±0.30	0.281	≥0.90
LDL (mmol/L)	2.56±0.92	0.359	0–3.1
ALB (g/L)	38.60±3.65	0.09	40.0–55.0
Globin (g/L)	25.51±4.09	0.16	20.0–35.0

(*Continued*)

Table 1 (Continued).

Variables	Value	CV	Reference Range
ALT (U/L)	27.61±22.62	0.82	7.0–40.0
AST (U/L)	22.48±14.37	0.64	13.0–35.0
γ-GGT (U/L)	47.92±122.96	2.57	10.0–60.0
TBil (μmol/L)	11.07±5.47	0.49	<21.0
DBil (μmol/L)	3.73±2.20	0.59	<8.0
SBil (μmol/L)	7.08±3.37	0.48	0–13.0
CK (U/L)	75.59±46.37	0.61	50.0–310.0
CKMB (U/L)	15.50±6.30	0.41	0–24.0
BNP (pg/mL)	43.69±60.08	1.38	<100.0
MYO (ng/mL)	24.19±30.28	1.25	0–100.0
cTNI (ng/mL)	0.32±0.12	0.39	0–0.10
AFP (ng/mL)	2.71±1.36	0.50	0–10.0
CA125 (U/mL)	11.59±10.42	0.90	0–35.0
CA153 (U/mL)	10.68±4.96	0.46	0–28.5
CA199 (U/mL)	38.46±254.16	6.61	0–35.0
CEA (ng/mL)	2.70±1.72	0.64	0–5.0
SCC (ng/mL)	0.47±0.29	0.62	0–1.50
CYFRA211 (ng/mL)	3.06±1.29	0.42	0–3.30
NSE (ng/mL)	11.60±6.99	0.60	0–20.0
ProGRP (pg/mL)	49.57±25.01	0.50	0–65.0
fPSA (ng/mL)	0.35±0.59	1.70	0–0.944
cPSA (ng/mL)	1.28±1.86	1.45	0–3.60
WBC (10^9/L)	6.36±2.00	0.31	3.50–9.50

Abbreviations: CV, coefficient of variance; Bw, bodyweight; BMI, body mass index; HbA1c, glycated hemoglobin A1c; Hb, hemoglobin; GA, glycated albumin; FPG, fasting plasma glucose; 2hPPG, 2 hours postprandial plasma glucose; FPCP, fasting plasma C-peptide; 2hPPCP, 2 hours postprandial plasma C-peptide; FINS, fasting plasma insulin; 2hPPINS, 2 hours postprandial plasma insulin; UACR, urinary albumin to creatinine ratio; eGFR, estimated glomerular filtration rate; BUN, blood urea nitrogen; SCr, serum creatinine; UA, uric acid; TPOAb, thyroid peroxidase antibody; TgAb, thyroid anti-globin antibody; Tg, thyroid globin; TRAb, thyroid stimulating hormone receptor antibody; FT3, free triiodothyronine; FT4, free thyroxine; TSH, Thyroid stimulating hormone; TC, total cholesterol; TG, triglyceride; HDL, high density lipoprotein; LDL, low density lipoprotein; ALB, serum albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; γ-GGT, γ-glutamyl transpeptidase; TBil, total bilirubin; DBil, direct bilirubin; SBil, indirect bilirubin; CK, creatine kinase; CKMB, creatine kinas type-MB; BNP, brain natriuretic peptide; MYO, myoglobin; cTNI, cardiac troponin I; AFP, α-fetoprotein; CA125, carbohydrate antigen-125; CA153, carbohydrate antigen-153; CA199, carbohydrate antigen-199; CEA, carcinoembryonic antigen; SCC, squamous cell carcinoma antigen; CYFRA211, cytokeratin antigen-19 fragment 211; NSE, neuron specific enolase; ProGRP, pro-gastrin-releasing peptide; fPSA, free prostate-specific antigen; cPSA, complexed prostate-specific antigen; WBC, white blood cell.

Table 2 The Correlational Relationship Between Significant Facial and Tongue Feature with the Glucose Metabolic Status

		Facial color	Tongue Color	Lip color	Fur thickness	Tongue Volume
HbA1c	**r**	/	0.226	/		
	p		0.002			
GA	**r**	/	0.229	−0.153	/	
	p		0.003	0.049		
FPCP	**r**	/			0.142	/
	p				0.042	
PPCP	**r**	0.155	/		0.183	/
	p	0.030			0.010	
FINS	**r**	/				0.220
	p					0.017

Abbreviations: PPG, 2 hours postprandial glucose; FPCP, fasting plasma C-peptide; PPCP, 2 hours postprandial plasma C-peptide; FINS, fasting insulin concentration; PINS, 2 hours postprandial insulin concentration; UACR, urinary albumin creatinine ratio.

Table 3 The Correlational Relationship Between the Significant Dimensional Parameters of Facial and Tongue Colors and Glucose Metabolic Status

		Face L	Face a	Gloss L	Gloss M	Tongue a	Tongue b	Fur L	Fur a
HbA1c	**r**	/	0.150	/	/	0.164	/	/	0.157
	p		0.046			0.029			0.036
GA	**r**			/	/			−0.160	
	p							0.039	
FPG	**r**	0.209	/	/	/	/			
	p	0.038							
PPCP	**r**	−0.147	/	/	−0.170	/			
	p	0.040			0.017				

Abbreviations: HbA1c, glycated hemoglobin A1c; GA, glycated albumin; PPCP, 2 hours postprandial C-peptide; FaceL, facial color L; Face a, facial color a; Gloss L, facial gloss color M; Tongue a, tongue color a; Tongue b, tongue color b; Fur L, tongue fur color L; Fur a, tongue fur color a.

The Relationship Between the Facial and Tongue Features and Parameter of Glucose Metabolic State

We analyzed the correlational relationships between the facial and tongue features with dimensional color parameters and glucose metabolic status represented by HbA1c, GA, C-peptide, and insulin levels. The significant results are shown in Tables 2 and 3.

The Relationship Between the Tongue Color and Parameters of Hepatic and Renal Function

We analyzed the correlational relationships between the facial and tongue features with dimensional color parameters and hepatic and renal function. The significant results are shown in Tables 4 and 5.

Table 4 The Correlational Relationship Between the Significant Facial and Tongue Feature and Critical Hepatic and Renal Function Indicators

		Gloss Color	Tongue Color	Tongue Volume
Alb	**r**	/	−0.175	/
	p		0.022	
ALT	**r**	−0.191	/	/
	p	0.012		
yGGT	**r**	−0.240	/	/
	p	0.002		
SCr	**r**	/	−0.154	/
	p		0.033	
eGFR	**r**	−0.166		−0.158
	p	0.030		0.040
UA	**r**	/	−0.153	/
	p		0.046	

Abbreviation: Alb, albumin; ALT, alanine aminotransferase; γGGT; γ-glutamyl transpeptidase; SCr, serum creatinine; eGFR, estimated glomerular filtration rate; UA, uric acid.

Table 5 The Correlational Relationship Between the Significant Dimensional Facial and Tongue Colors and the Critical Hepatic and Renal Function Indicators

		Face L	Face a	Lip L	Lip a	Lip b	Gloss L	Gloss M	Tongue L	Fur L
Globin	**r**	/	/	/					−0.154	/
	p								0.044	
γGGT	**r**	/			/	/	0.173	/		
	p						0.024			
TBil	**r**	/	−0.156	/	/	/				
	p		0.041							
BUN	**r**	/		−0.154	−0.163	/	/	/	−0.171	/
	p			0.045	0.034				0.026	
SCr	**r**	−0.176	/	−0.173	/			−0.162	`/	/
	p	0.014		0.016				0.024		
UA	**r**	/			/	0.153	0.178	/		0.158
	p					0.047	0.020			0.039

Note: Alb, albumin; γGGT, γ-glutamyl transpeptidase; TBil, total bilirubin; BUN, blood urea nitrogen; SCr, serum creatinine; UA, uric acid; Face L, facial color L; face a, facial color a; Lip L, lip color L; lip a, lip color a; lip b, lip color b; Gloss L, facial gloss L; Gloss M, facial gloss M; Tongue L, tongue color L; Fur L, tongue fur L.

Table 6 The Correlational Relationship Between the Significant Facial and Tongue Imaging Feature and Dimensional Color with the Cardiac Injury Markers

		Tongue Color	Face a	Face b	Lip a	Lip b	Gloss L	Gloss N	Tongue a	Tongue b	Fur a
CK	**r**	−0.167	/								
	p	0.042									
CKMB	**r**	/	0.243	0.184	0.194	0.265	0.299	0.171	0.260	0.189	0.238
	p		0.003	0.025	0.018	0.001	<0.0001	0.037	0.001	0.021	0.003
MYO	**r**	/			−0.209	/					
	p				0.001						

Abbreviations: CK, creatine kinase; CKMB, creatine kinase MB type; MYO, myoglobin; Face a, facial color a; face b, facial color b; Lip a, lip color a; lip b, lip color b; Gloss L, facial gloss L; Gloss N, facial gloss N; Tongue a, tongue color a; Tongue b, tongue color b; Fur a, tongue fur a.

Table 7 The Correlational Relationship Between the Significant Facial and Tongue Imaging Feature with the Tumor Markers in T2DM

		Facial Color	Gloss Color	Tongue Color	Fur Greasy	Tongue Fission	Tongue Volume
CYFRA211	**r**	/	/	−0.359	/		
	p			0.019			
NSE	**r**	0.286	/	//			
	p	0.028					
cPSA	**r**	/	−0.197	/			
	p	/	0.048				

Abbreviations: CA153, carbohydrate antigen 153; CYFRA211, NSE, Neuron-specific Enolase; cPSA, complexed prostate specific antigen.

Table 8 The Correlational Relationship Between the Significant Facial and Tongue Imaging Dimensional Color with the Tumor Marker in T2DM

		Face a	Face b	Lip a	Lip b	Gloss L	Gloss M	Tongue a	Tongue b	Fur a
CA125	**r**	/			0.160	/			0.144	/
	p				0.021				0.038	
CEA	**r**	/	0.156	/			−0.210	/	0.159	/
	p		0.048				0.007		0.044	
SCC	**r**	0.422	0.334	0.366	/	0.399	/	0.417	0.323	0.309
	p	0.001	0.011	0.005		0.002		0.001	0.014	0.019

Abbreviations: CA125, carbohydrate antigen 125; CEA, carcinoembryonic antigen; SCC, squamous cell carcinoma antigen; cPSA, complexed prostate specific antigen; Face a, facial color a; face b, facial color b; Lip a, lip color a; lip b, lip color b; Gloss L, facial gloss L; Gloss M, facial gloss M; Tongue a, tongue color a; Tongue b, tongue color b; Fur a, tongue fur a.

Table 9 The Correlational Relationship Between the Significant Facial and Tongue Feature and Dimensional Color with the Thyroid Function, Hb, WBC, and Plt

		Facial Color	Lip Color	Gloss Color	Fur Color	Fur Thickness	Tongue Volume
FT3	**r**	/		−0.144	/		
	p			0.033			
TSH	**r**	/		0.185	/		
	p			0.006			
TPOAb	**r**	/			0.241	/	
	p				0.018		
TgAb	**r**	/				0.444	/
	p					0.023	
Tg	**r**	/		0.311	/	0.256	/
	p			0.003		0.015	
Hb	**r**	/		−0.299	/		
	p			<0.0001			
WBC	**r**	/	0.160	/			
	p		0.020				

Abbreviations: FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid stimulating hormone; TPOAb, anti-thyroid peroxidase antibody; TgAb, anti-thyroid globin antibody; Tg, thyroid globin; Hb, hemoglobin; WBC, white blood cell; Plt, platelet.

Table 10 The Correlational Relationship Between the Dimensional Color of Facial and Tongue Imaging and Thyroid Function, Hb, WBC, and Plt

		Face L	Face a	Face b	Lip L	Lip a	Lip b	Gloss L	Gloss M	Gloss N
FT3	**r**	−0.146	/			0.135	/	0.160	/	
	p	0.030				0.046		0.017		
TRAb	**r**	/		0.268	/		0.259	/		0.211
	p			0.010			0.013			0.044
TgAb	**r**	/	0.463	0.389	/	0.514	0.439	0.480	//	
	p		0.020	0.05		0.009	0.028	0.015		
Tg	**r**	0.271	/		0.232				0.270	/
	p	0.010			0.028				0.011	
Hb	**r**	−0.181	0.160			0.157	0.164	0.304	//	
	p	0.009	0.020			0.023	0.018	<0.0001		
		Tongue L	**Tongue a**			**Tongue b**	**Fur L**	**Fur a**	**Fur b**	
TRAb	**r**	/				0.234	//			
	p					0.020				

(*Continued*)

Table 10 (Continued).

		Face L	Face a	Face b	Lip L	Lip a	Lip b	Gloss L	Gloss M	Gloss N
TgAb	**r**	−0.414	0.597					0.555	/	
	p	0.040	0.002					0.004		
Tg	**r**	/						0.224	/	
	p							0.031		
Hb	**r**	/	0.179			/		0.233	/	
	p		0.009					0.001		

Abbreviations: FT3, free triiodothyronine; TRAb, Anti-thyroid stimulating hormone receptor antibody; TSH, thyroid stimulating hormone; TPOAb, anti-thyroid peroxidase antibody; TgAb, anti-thyroid globin antibody; Tg, thyroid globin; Hb, hemoglobin. Face L, facial color L; Face a, facial color a; face b, facial color b; Lip L, lip color L; Lip a, lip color a; lip b, lip color b; Gloss L, facial gloss L; Gloss M, facial gloss M; Gloss N, facial gloss N.

The Relationship Between the Facial and Tongue Imaging Feature and the Cardiac Injury Markers

We analyzed the correlational relationships between the facial and tongue features with dimensional color parameters and cardiac injury markers. The significant results are shown in Table 6.

Table 11 The Multilinear Regression Models of Variables to the Significant Metabolic Parameters' Changes

Multilinear Regress								
HbA1c	**Glucose Metabolism R**	**0.210**	**R^2**	**0.044**	**Adjusted R^2**	**0.037**		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	6.643	0.601		8.268	<0.001		
	Fur a	0.104	0.043	0.145	2.411	0.017	0.996	1.004
	Tongue color	0.575	0.243	0.142	2.366	0.019	0.996	1.004
FPCP	**R**	0.249	**R^2**	0.062	**Adjusted R^2**	0.051		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	1.476	0.356		4.144	<0.001		
	Tongue color	−0.148	0.065	−0.142	−2.280	0.023	0.913	1.095
	Gloss M	−0.013	0.004	−0.257	−3.413	0.001	0.624	1.601
	Fur L	0.009	0.004	0.170	2.197	0.029	0.592	1.690
PPCP	**R**	0.210	**R^2**	0.044	**Adjusted R^2**	0.037		
	Variables	**B**	**SE**	**β**	**T**	**Sig**	**Tolerance**	**VIF**
	Constant	2.926	0.478		6.125	<0.0001		
	Face L	−0.009	0.003	−0.163	−2.693	0.008	0.982	1.019
	Tongue color	−0.280	0.108	−0.157	−2.595	0.010	0.982	1.019
	Hepatic function							
Globin	**R**	0.155	**R^2**	0.024	**Adjusted R^2**	0.020		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	28.691	1.256		22.841	<0.0001		
	Fur greasy	−1.102	0.430	−0.155	−2.566	0.011	1.000	1.000
ALT	**R**	0.189	**R^2**	0.036	**Adjusted R^2**	0.029		

(*Continued*)

Table 11 (Continued).

Multilinear Regress								
HbA1c	**Glucose Metabolism R**	**0.210**	**R^2**	**0.044**	**Adjusted R^2**	**0.037**		
	Variables	**B**	**SE**	**β**	**T**	**Sig**	**Tolerance**	**VIF**
	Constant	41.155	4.433		9.274	<0.0001		
	Facial color	−2.651	1.196	−0.133	−2.216	0.028	0.999	1.001
	Gloss color	−5.391	2.483	−0.131	−2.171	0.031	0.999	1.001
γGGT	**R**	0.182	**R^2**	0.033	**Adjusted R^2**	0.030		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	−13.902	21.226		−0.655	0.513		
	Tongue fission	55.245	18.222	0.182	3.032	0.003	1.000	1.000
TBil	**R**	0.157	**R^2**	0.025	**Adjusted R^2**	0.021		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	8.707	0.948		9.185	<0.0001		
	Tongue fission	2.110	0.814	0.157	2.593	0.010	1.000	1.000
eGFR	**Renal function R**	0.204	**R^2**	0.042	**Adjusted R^2**	0.035		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	53.582	56.200		0.610	0.341		
	Lip a	1.215	0.364	0.231	3.333	0.001	0.752	1.329
	Face b	−1.031	0.458	−0.156	−2.254	0.025	0.752	1.329
UA	**R**	0.193	**R^2**	0.037	**Adjusted R^2**	0.030		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	354.187	34.884		10.153	< 0.0001		
	Gloss L	5.394	2.158	0.151	2.499	0.013	0.988	1.012
	Tongue color	−24.202	10.613	−0.138	−2.280	0.023	0.988	1.012
CKMB	**Cardiac injury R**	0.248	**R^2**	0.061	**Adjusted R^2**	0.054		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	8.887	1.623		5.475	<0.0001		
	Gloss L	0.460	0.124	0.225	3.718	<0.0001	0.965	1.036
	Fur b	0.596	0.234	0.154	2.547	0.011	0.965	1.036
CK	**R**	0.251	**R^2**	0.063	**Adjusted R^2**	0.060		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	47.455	6.944		6.834	<0.0001		
	Fur b	7.161	1.690	0.251	4.238	<0.0001	1.000	1.000
MYO	**R**	0.301	**R^2**	0.090	**Adjusted R^2**	0.077		
	Variables	**B**	**SE**	**β**	**T**	**Sig**	**Tolerance**	**VIF**

(*Continued*)

Table 11 (Continued).

Multilinear Regress								
HbA1c	**Glucose Metabolism R**	**0.210**	**R^2**	**0.044**	**Adjusted R^2**	**0.037**		
	Constant	47.154	15.347		3.072	0.002		
	Lip L	−0.437	0.112	−0.235	−3.898	<0.0001	0.950	1.053
	Fur b	3.593	1.457	0.148	2.466	0.014	0.955	1.047
	Gloss color	8.714	3.983	0.131	2.188	0.030	0.965	1.036
	Tongue color	−7.460	3.785	−0.118	−1.971	0.050	0.956	1.046
CA125	**Tumor markers R**	0.233	**R^2**	0.054	**Adjusted R^2**	0.047		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	−37.443	17.016		−2.200	0.029		
	Fur b	1.546	0.460	0.204	3.359	0.001	0.965	1.037
	Tongue b	0.336	0.130	0.157	2.592	0.010	0.965	1.037
CEA	**R**	0.142	**R^2**	0.020	**Adjusted R^2**	0.017		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	4.184	0.637		6.568	<0.0001		
	Gloss M	−0.020	0.009	−0.142	−2.350	0.020	1.000	1.000
SCC	**R**	0.226	**R^2**	0.051	**Adjusted R^2**	0.044		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	0.296	0.046		6.440	<0.0001		
	Gloss L	0.011	0.004	0.197	3.233	0.001	0.965	1.036
	Fur b	0.017	0.007	0.153	2.517	0.012	0.965	1.036
FT3	**Thyroid function R**	0.208	**R^2**	0.043	**Adjusted R^2**	0.036		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	5.780	0.570		10.134	<0.0001		
	Fur greasy	−0.471	0.173	−0.163	−2.721	0.007	1.000	1.000
	Fur b	0.139	0.066	0.127	2.114	0.035	1.000	1.000
TgAb	**R**	0.196	**R^2**	0.038	**Adjusted R^2**	0.035		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	111.728	29.041		3.847	<0.0001		
	Gloss L	9.917	3.040	0.196	3.263	0.001	1.000	1.000
TPOAb	**R**	0.241	**R^2**	0.058	**Adjusted R^2**	0.047		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	−426.035	181.452		−2.348	0.020		
	Face L	0.995	0.299	0.199	3.192	0.002	0.919	1.089
	Face b	3.317	1.346	0.149	2.465	0.014	0.977	1.023
	Lip color	−22.013	9.548	0.144	−2.306	0.022	0.914	1.094

(*Continued*)

Table 11 (Continued).

Multilinear Regress								
HbA1c	**Glucose Metabolism R**	**0.210**	**R^2**	**0.044**	**Adjusted R^2**	**0.037**		
Hb	**Blood cell R**	0.397	**R^2**	0.157	**Adjusted R^2**	0.148		
	Variables	**B**	**SE**	**β**	**t**	**Sig**	**Tolerance**	**VIF**
	Constant	289.080	68.388		4.171	<0.0001		
	Gloss L	3.681	0.837	0.499	4.395	<0.0001	0.246	4.059
	Gloss color	−6.800	2.296	−0.177	−2.962	0.003	0.886	1.128
	Face a	−1.335	0.554	−0.269	−2.409	0.017	0.256	3.912

Abbreviations: Face L, facial color L; Face b, facial color b; Gloss L, facial gloss color L; Lip L, lip color L; Lip a, lip color a; lip b, lip color b; Gloss L, facial gloss L; Gloss M: facial gloss color M; Gloss N, facial gloss N; Fur L, tongue fur L; Fur a, tongue fur color a; Fur b, tongue fur color b; Tongue L, tongue color L; Tongue a, tongue color a; Tongue b, Tongue color b.

The Relationship Between the Facial and Tongue Imaging and the Tumor Markers in T2DM

We analyzed the correlational relationships between the facial and tongue features with dimensional color parameters and tumor markers. The significant results are shown in Tables 7 and 8.

The Relationship Between the Facial and Tongue Imaging with the Thyroid Function, Hemoglobin, White Blood Cell, and Palate in T2D

We analyzed the correlational relationships between the facial and tongue features with dimensional color parameters and thyroid function, blood cells. The significant results are shown in Tables 9 and 10.

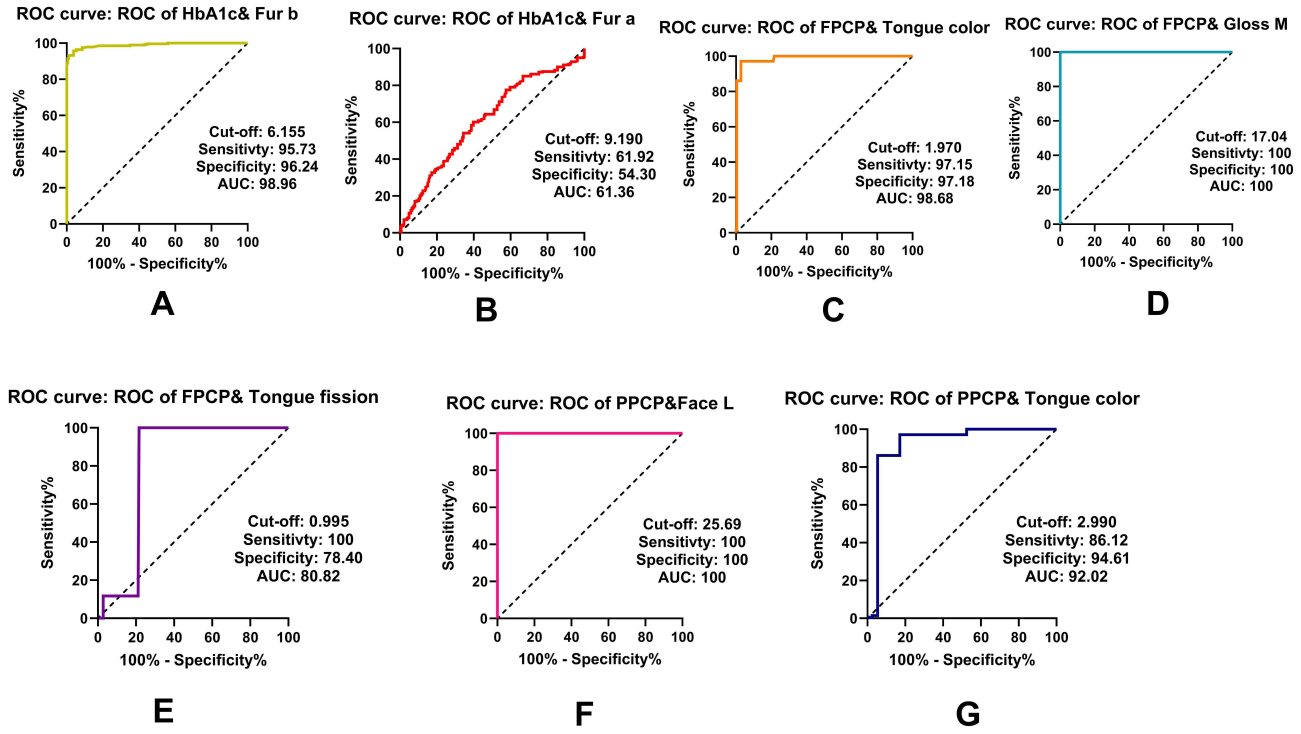

Figure 2 The ROC curve of facial and tongue imaging feature and dimensional color for glucose metabolic parameters including HbA1c (**A** and **B**), FPCP (**C**–**E**), and PPCP (**F** and **G**).
Abbreviations: HbA1c, glycated hemoglobin A1c; FPCP, fasting plasma C-peptide; PPCP: 2 hours postprandial plasma C-peptide.

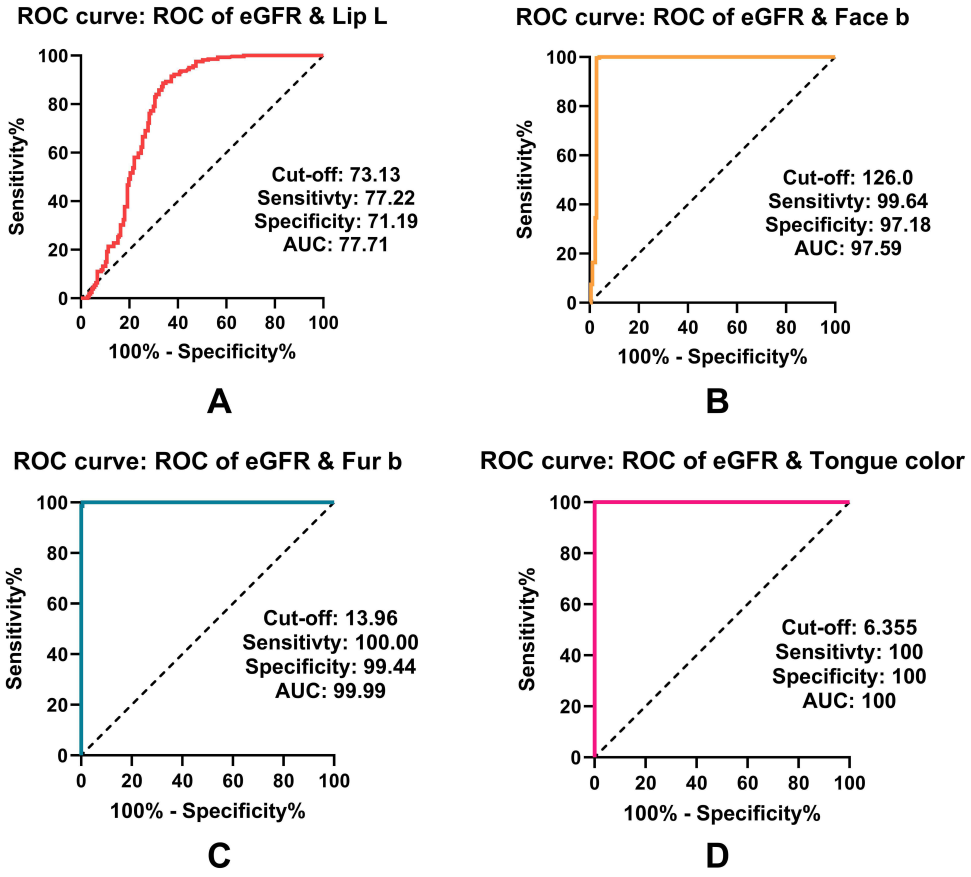

Figure 3 The ROC curve of facial and tongue imaging feature and dimensional color for renal function parameters represented by eGFR: Lip L (**A**); Face b (**B**); Fur (**C**); Tongue color (**D**).
Abbreviation: eGFR: estimated glomerular filtration rate.

The Multilinear Regression Analyses Use Parameters of Facial and Tongue Imaging as the Independent Determinators for the Significant Metabolic Indicators

We performed the regression analyses to determine the facial and tongue features with dimensional color parameters to the aforementioned significant metabolic parameters. The significant determinants are displayed in Table 11.

The Predictive Value of the Significant Facial and Tongue Imaging Parameters in Glucose Metabolism, Renal Function, Cardiac Injury, Tumor Markers, Thyroid Function and Blood Cells via ROC

Finally, we created the receiver operating characteristic curve (ROC) to assess the predictive value of significant facial and tongue imaging parameters for glucose metabolism (Figure 2), eGFR (Figure 3), cardiac injury (Figure 4), tumor markers (Figure 5), thyroid function and blood cells (Figure 6).

Discussion

TCM is a comprehensive system of diagnosis and treatment that is predicated on an understanding of the internal equilibrium and harmony of the human body.[22] The four diagnostic procedures in Traditional Chinese Medicine are inspection, inquiry, sensing and listening, and palpation. Inspection diagnosis, particularly tongue observation, is considered the most fundamental and initial stage of these, as it provides an insight into the patient's internal state. The tongue is regarded as the external entrance of the heart in Traditional Chinese Medicine (TCM), and it

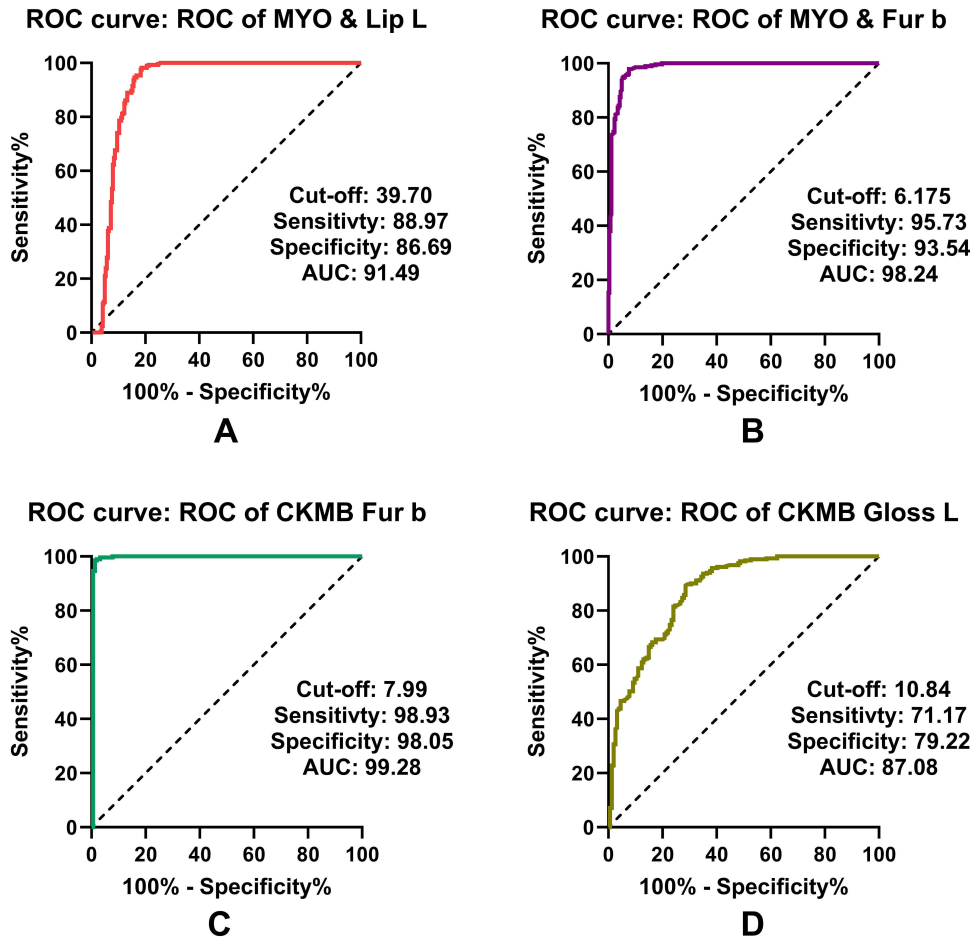

Figure 4 The ROC curve of facial and tongue imaging feature and dimensional color for cardiac injury markers represented by MYO (**A** and **B**) and CKMB (**C** and **D**): Lip L (**A**); Fur b (**B**); Fub (**C**); Gloss L (**D**).
Abbreviations: MYO: myoglobin; CKMB: creatine kinase MB type.

is responsible for the cardiovascular system's condition. In recent decades, emerging consensus on the tongue pattern as the diagnostic tool in multiple diseases has provoked scientists and clinicians to develop instruments for observing the condition of the tongue in order to assist therapy of both local and systemic diseases,[23,24] and even advanced the predictive or diagnostic tools in diabetes with minimal or non-invasive paradigms.[11,25]

In the present research, we discovered that the metabolic status and related organic laboratory parameters, including hepatic and renal function, cardiac injury markers, tumor markers, thyroid function, and blood cell count, were correlated with the facial, tongue, lip, fur, and other features, as well as dimensional color parameters. This suggests that there is a close correlation between the facial, tongue, and color characteristics and the metabolic status of T2DM patients, as evidenced by the precise analysis. The predictive value of these indicators was evaluated for the laboratory markers that were evaluated in the present study using the ROC assay. Consequently, we could combine these features with other clinical parameters to create a more comprehensive model for predicting the condition and progression of T2DM in patients. This model would be particularly useful for assisting physicians in evaluating the risks of microvascular and macrovascular complications and the therapeutic effects of these patients in future clinical practices.

Additionally, there is an increasing practice of incorporating tongue and facial diagnosis from Traditional Chinese Medicine (TCM) into Western medical practices. Numerous medical professionals, such as physicians, nurses, and therapists, realize the importance of integrating traditional Chinese diagnostic methods into their clinical practices.[26,27] This integration enables a more comprehensive approach to patient care by integrating the strengths of

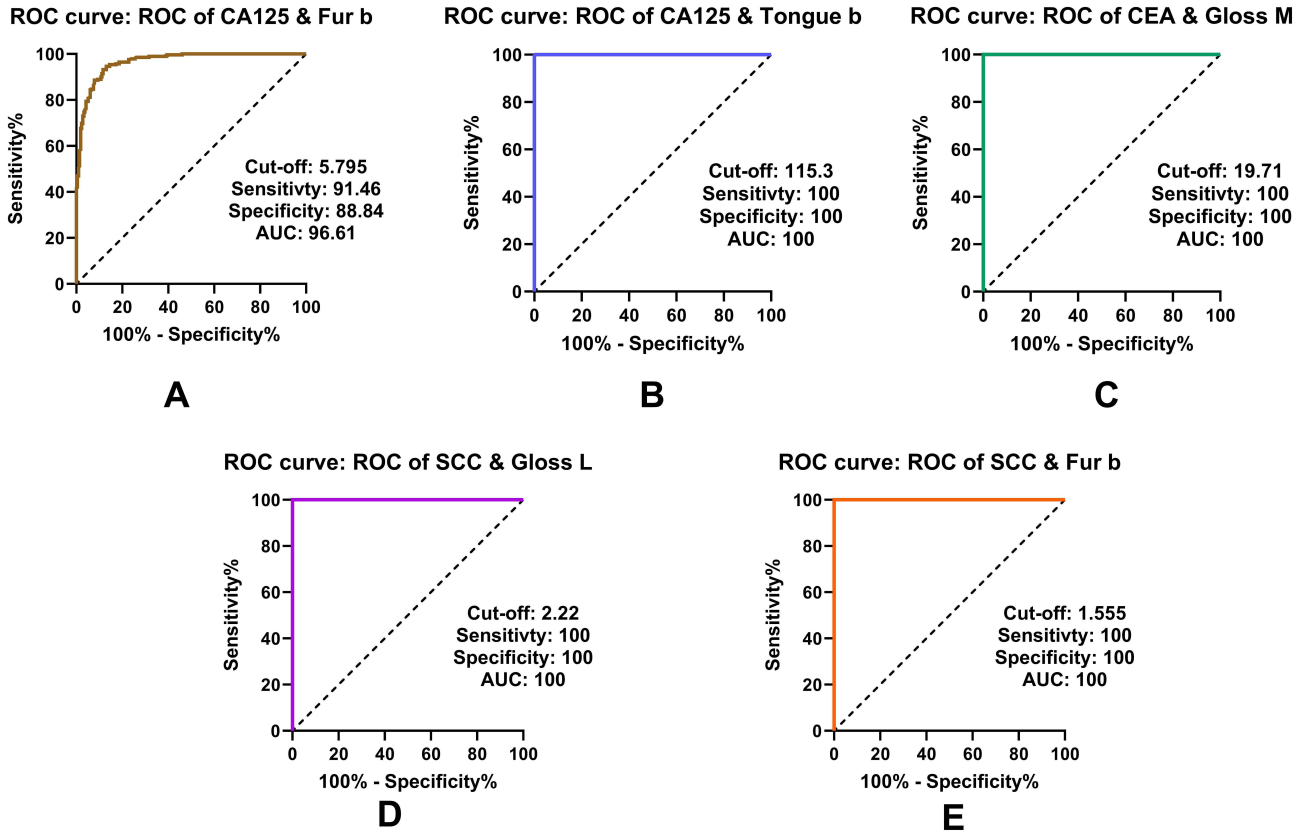

Figure 5 The ROC curve of facial and tongue imaging feature and dimensional color for Tumor markers represented by CA125 (**A** and **B**), CEA (**C**), and SCC (**D** and **E**): Fur b (**A**); Tongue b (**B**); Gloss M (**C**); Gloss L (**D**); Fur b (**E**).
Abbreviations: CA125, carbohydrate antigen 125; CEA, carcinoembryonic antigen; SCC, Squamous cell carcinoma antigen.

both traditional and modern medical systems.[28,29] It is imperative to conduct ongoing research on tongue diagnosis in order to enhance its scientific foundation and clinical application. In order to improve the scientific foundation and clinical application of tongue and face diagnosis, it is essential to conduct supplementary research, such as the current study. The efficacy of this diagnostic instrument could be enhanced by conducting research and AI deep learning on the correlations between tongue manifestations and specific biomarkers, pathological changes, and genetic factors.[30–32] Furthermore, it is imperative that the next generation of healthcare professionals be provided with a thorough comprehension of this valuable diagnostic technique through educational programs and initiatives that are designed to enhance TCM knowledge and skills, such as tongue observation.

In resource-limited environments where advanced diagnostic instruments are not readily accessible, the integration of tongue and face observations into routine assessments can offer valuable insights into a patient's overall health status. This is particularly true in clinical settings. Nevertheless, it is imperative to underscore that these observations should be employed as supplementary tools rather than as independent diagnostic criteria.

Limitations

We did not conduct risk comparisons between individuals with T2DM and those who are not. Additionally, future predictive models must incorporate additional tongue and facial features, laboratory data, and imaging data, including CT, coronary arterial imaging, cranial MRI, and MRA, to evaluate the severity and risks of macrovascular complications. It is also necessary to quantitatively evaluate the TCM syndromes in order to identify and reconstruct the relationships with the condition of T2DM in modern medicine practice. This will enable us to provide more precise and personalized treatment.

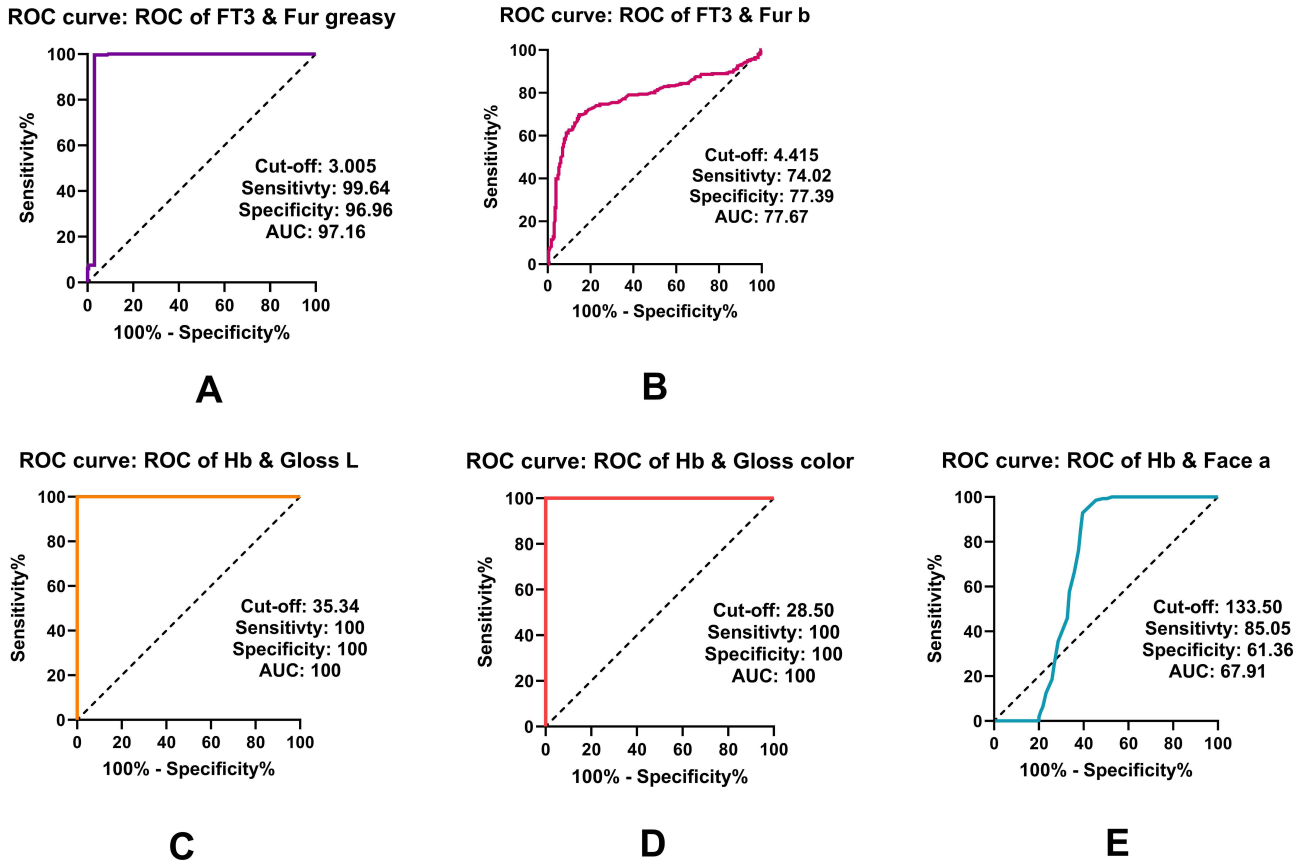

Figure 6 The ROC curve of facial and tongue imaging feature and dimensional color for thyroid function represented by FT3 (**A** and **B**), and Hb (**C**–**E**).
Abbreviations: FT3, free triiodothyronine; Hb, hemoglobin.

Conclusion

In conclusion, tongue and face observation is a critical element of clinical diagnosis in TCM, as it assists to inform treatment decisions, prognosis, and diagnosis by providing a glimpse into the patient's internal state. The integration of modern technologies, such as AI deep learning and digitization, has enhanced its accuracy, reproducibility, and accessibility. Tongue and face diagnosis remain a valuable instrument for the promotion of comprehensive wellness. Although these observations offer a non-invasive, cost-effective approach to obtaining insight into a patient's health status, they require further scientific investigation to verify their diagnostic accuracy. Modern medical research and traditional wisdom can be combined to create a more comprehensive diagnostic and management strategy, thereby improving our understanding of T2DM.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article.

Ethical Statement

The study, including sampling, examinations, and access or utilization of the raw data for this study, obtained ethical approval from the Shanghai Pudong Hospital (WZ-010.). Study participants provided informed consent before the study. The guidelines and procedures were outlined in accordance with the Declaration of Helsinki. All data utilized in this investigation were anonymized prior to their utilization.

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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 declare that there is no potential conflict of interest.

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