Am J Cancer Res 2025;15(6):2855-2871
www.ajcr.us /ISSN:2156-6976/ajcr0164983

Original Article

Risk factors for postoperative vascular crisis in squamous cell carcinoma reconstruction using supraclavicular artery flaps

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Received April 1, 2025; Accepted June 2, 2025; Epub June 25, 2025; Published June 30, 2025

Abstract: Objectives: To identify risk factors associated with vascular crisis in patients undergoing reconstruction with supraclavicular artery flaps for squamous cell carcinoma (SCC) of the tongue and buccal mucosa. Methods: A retrospective analysis was conducted on 777 patients with tongue or buccal SCC who underwent supraclavicular artery flap reconstruction between January 2019 and December 2023. Patients were divided into two groups based on the occurrence of postoperative vascular crisis: Occurred Group (n = 101) and No Occurred Group (n = 676). Demographic data, clinical history, hematologic and biochemical parameters were collected. Pearson and Spearman correlation analyses, univariate analysis, and multivariate logistic regression were performed to identify independent risk factors. An external validation cohort was used to verify the findings, and a predictive model was developed using ROC curve and nomogram analysis. Results: Independent risk factors for vascular crisis included higher BMI, long-term smoking, long-term alcohol consumption, elevated fasting blood glucose, increased C-reactive protein, higher white blood cell count, and elevated SCC antigen (all $P < 0.05$). Platelet count was inversely associated with risk. Flap survival rate was significantly lower in the vascular crisis group. The predictive model demonstrated strong discriminatory power (AUC = 0.975). Conclusions: Several modifiable clinical and biochemical factors are significantly associated with postoperative vascular crisis. Preoperative optimization of these variables may improve flap survival and surgical outcomes.

Keywords: Squamous cell carcinoma, supraclavicular artery flap, vascular crisis, risk factors, reconstruction surgery, postoperative complications

Introduction

Squamous cell carcinoma (SCC) is the second most common form of skin cancer worldwide, characterized by malignant proliferation of keratinocytes and often associated with considerable morbidity. Its incidence continues to rise, primarily due to increased ultraviolet radiation exposure and an aging population [1, 2]. Surgical excision remains the gold standard for treatment, particularly when the lesion is located in cosmetically and functionally sensitive regions such as the head and neck, where precise reconstructive techniques are essential to restore both form and function [3].

Among the available reconstructive options, the supraclavicular artery flap has gained increasing attention for its reliability, the favorable cosmetic outcomes [4]. This flap has undergone various refinements over time, extending its clinical applications [5, 6]. Itis particularly well-suited for head and neck reconstruction due to its thin, pliable tissue, which closely resembles facial skin, and the low morbidity associated with its donor site. This flap is vascularized by the supraclavicular branch of the transverse cervical artery, providing sufficient reach without compromising perfusion [7, 8].

Despite these advantages, postoperative vascular compromise remains a major concern. Vascular crisis, defined by clinical signs such as color change (pallor or cyanosis), edema, and reduced tissue elasticity, often necessitates urgent surgical re-exploration. These

https://doi.org/10.62347/ZHMS1734

events are predominantly caused by venous congestion, although arterial insufficiency may also contribute [9]. Early recognition and management are crucial, as delayed intervention can result in partial or total flap loss, nullifying reconstructive efforts [10, 11].

Given these risks, identifying preoperative and intraoperative predictors of vascular crisis is critical to optimizing outcomes [12]. While meticulous surgical planning and technique have been shown to improve flap survival [13, 14], studies specifically focusing on risk factors for vascular crisis in supraclavicular artery flap reconstruction for SCC-related defects remain limited.

This knowledge gap underscores the need for further research. Addressing this issue is essential not only for improving clinical outcomes but also for enhancing patients' postoperative quality of life. The present study aims to bridge this gap by systematically identifying risk factors for postoperative vascular crisis and developing a predictive model that integrates systemic biomarkers and lifestyle factors.

The innovative contribution of this study lies in the establishment of a comprehensive predictive model and a corresponding nomogram, which together offer a practical, evidence-based tool for individualized risk stratification. These findings are expected to support personalized surgical planning and improve the precision of clinical decision-making in reconstructive surgery.

Materials and methods

Case selection

Study population: A retrospective study was conducted on 777 patients with SCC of the tongue or buccal mucosa who underwent supraclavicular artery flap reconstruction at Jinan Stomatological Hospital between January 2019 and December 2023. All cases were pathologically confirmed as SCC and underwent appropriate surgical treatment. Patients were stratified into two groups based on the occurrence of postoperative vascular crisis, defined as any significant perfusion compromise of the flap requiring intervention within 7 days postoperatively. The "No Occurred Group" included 676 patients without vascular crisis, while the "Occurred Group" included 101 patients who experienced vascular crisis.

The study was approved by the Institutional Review Board and Ethics Committee of Jinan Stomatological Hospital. Given its retrospective nature and use of anonymized data, the requirement for informed consent was waived, in accordance with institutional and regulatory guidelines.

To ensure model robustness, 10-fold cross-validation was applied for internal validation. Additionally, an external validation cohort comprising 308 patients from the Jinan Health Data Sharing Platform - meeting the same inclusion criteria - was included. Based on vascular crisis occurrence, this cohort was also divided into a "No Occurred Group" (n = 268) and an "Occurred Group" (n = 40).

Inclusion and exclusion criteria: Inclusion criteria: (i) Pathologically confirmed SCC of the tongue or buccal mucosa with surgical defects; (ii) Reconstruction using a supraclavicular artery flap; (iii) Age between 18 and 60 years; (iv) Complete clinical data. Exclusion criteria: (i) Metastatic or recurrent tumors; (ii) Long-term immunosuppressive therapy or active autoimmune disease; (iii) Co-existing malignancies; (iv) Pregnancy during surgery; (v) Documented mental illness or significant cognitive impairment (**Figure 1**).

Data extraction

Data source: Clinical data were collected from electronic medical records and included demographics (age, sex), history of diabetes and hypertension, admission blood glucose and blood pressure, and psychological and inflammatory status. Perioperative variables such as operation time, intraoperative blood loss, and hospital stay were also collected.

Surgical protocol: All patients underwent preoperative Doppler ultrasound to assess vascular anatomy and rule out abnormalities at the donor site. Reconstruction was performed using a single supraclavicular artery flap. Postoperatively, patients were instructed to maintain strict head immobilization for 7 days. Flap monitoring was performed hourly, assessing

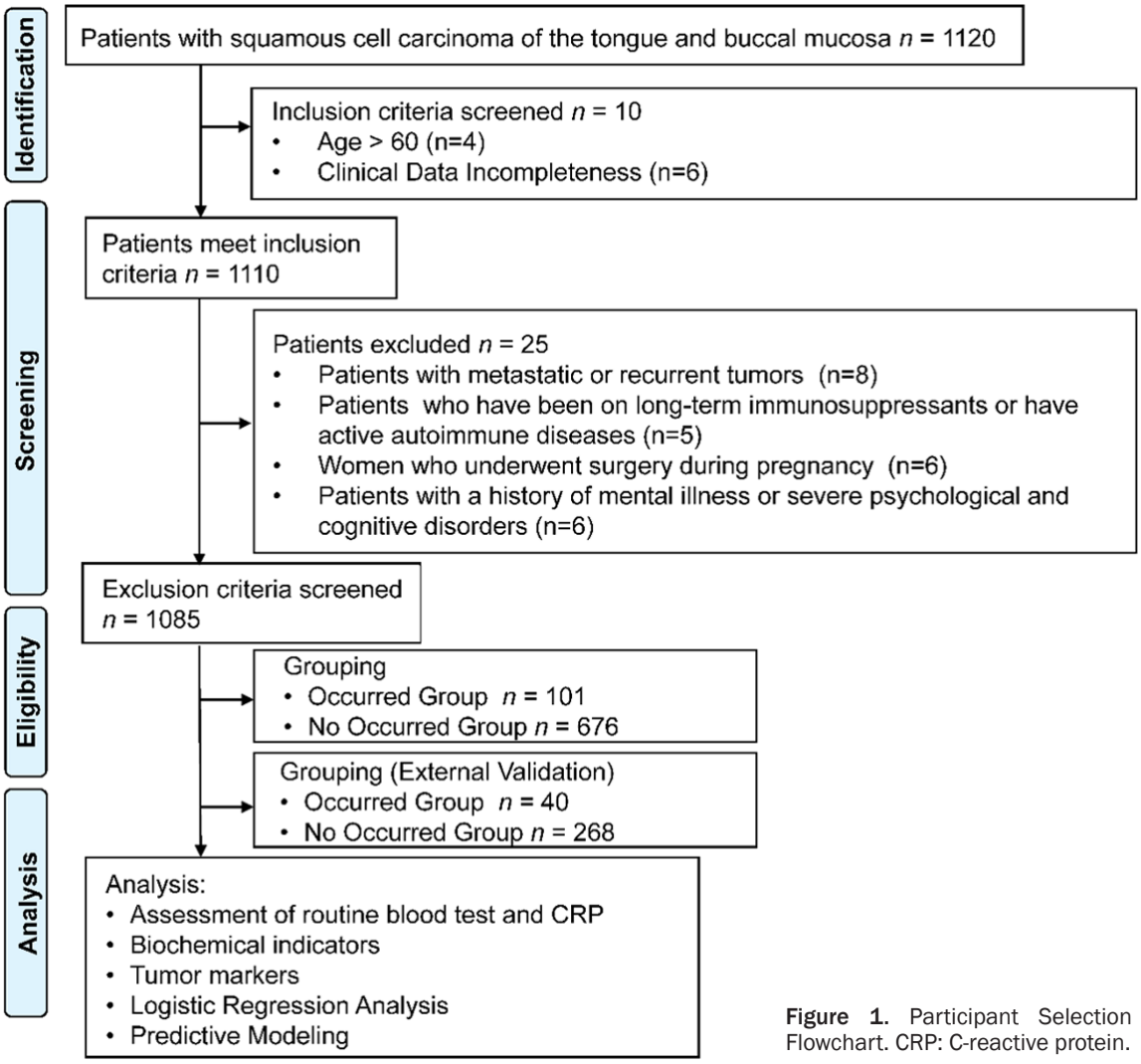

Figure 1. Participant Selection Flowchart. CRP: C-reactive protein.

color and elasticity. If signs of vascular compromise (e.g., color change, swelling, or stiffness) were noted, urgent surgical exploration was conducted. Intraoperative findings of thrombosis were managed via thrombectomy and vascular clearance.

Assessment of psychological status: Medication review: Prescription of anxiolytics (e.g., benzodiazepines) was considered indicative of anxiety. Medical documentation: Clinical notes were reviewed for explicit mentions of "anxiety" or "depression".

Hematological and inflammatory markers: On the day before surgery, fasting venous blood samples (10 mL) were drawn from the antecubital vein. Serum was isolated following centrifugation. A Sysmex CK-21 analyzer (Sysmex Corp., Japan) was used for complete blood count, including white blood cell (WBC), platelet count (PLT), red blood cell count (RBC), absolute neutrophil count (ANC), and absolute lymphocyte count (ALC).

CRP levels were measured using immunoturbidimetric assay based on turbidity changes due to antigen-antibody interactions [15].

Biochemical indicators: Biochemical parameters were assessed using a Beckman AU5800 automatic analyzer (Beckman Coulter, USA). Fasting serum samples were tested fortotal cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), triglycerides (TG), fasting blood

glucose (FBG), apolipoprotein A (APOA), and apolipoprotein B (APOB).

Fasting antecubital venous blood (4 mL), were collected from patients the day before surgery. Tumor markers [SCC antigen (SCC-Ag), carcinoembryonic antigen (CEA), carbohydrate antigen 50 (CA50), and cytokeratin 19 fragment antigen 21-1 (CYFRA21-1)] were measured via electrochemiluminescence using the Roche Cobas e601 system (Roche Diagnostics, Switzerland) [16].

Intraoperative parameters: Operative records were reviewed to assess flap harvest time, flap size, repair site, intraoperative blood loss, and hospital length of stay.

Outcome measures

Primary outcomes: Postoperative vascular crisis was defined as any clinically significant compromise in flap perfusion requiring medical or surgical intervention within 7 days following surgery [17].

Color changes: Pallor or cyanosis (bluish-purple), indicating arterial or venous obstruction.

Texture changes: Increased firmness or softness, suggesting ischemia or edema.

Temperature changes: Decreased local temperature, indicative of Capillary refill time: Delayed return of color (> 2 seconds) after pressing and releasing the flap suggests impaired circulation [18].

Severity classification: Mild (Reversible Crisis): Transient color or temperature changes with mildly prolonged refill time, reversible by repositioning, warming, or Moderate (Partial Dysfunction): Marked reduction in blood flow requiring pharmacologic or surgical intervention; partial necrosis may occur but Severe (Irreversible Necrosis): No detectable perfusion; flap appears black and rigid. Emergency surgical exploration or flap removal is required [19].

Flap monitoring was performed hourly for the first 7 postoperative days to enable early identification and management of vascular compromise.

Secondary outcomes: Hematological markers and inflammation: WBC count, PLT, and CRP were measured preoperatively using a Sysmex CK-21 analyzer and immunoturbidimetric assay.

Biochemical indicators: Serum levels of TC, HDL-c, LDL-c, TG, FBG, APOA, and APOB were assessed using a Beckman AU5800 analyzer.

Tumor markers: SCC-Ag, CEA, CA50, and CYFRA21-1 were quantified using electrochemiluminescence on a Roche Cobas e601 system.

All secondary outcomes were measured one day prior to surgery.

Statistical analysis

All statistical analyses were conducted using SPSS version 29.0 (SPSS Inc., Chicago, IL, USA). To ensure sufficient power to detect meaningful associations between risk factors and vascular crisis, a sample size calculation was performed using G*Power 3.1.9.7. Assuming an odds ratio (OR) of 1.8 for a primary risk factor (e.g., long-term smoking), with $\alpha = 0.05$ and power = 80%, a minimum of 768 patients was required. To accommodate potential dropouts and missing data, 777 patients were enrolled. An estimated incidence of 15% for vascular crisis was assumed.

Categorical variables were expressed as frequencies and percentages [n (%)]. The chi-square test (χ^2) was used for comparisons, and Fisher's exact test was applied when expected cell counts were < 5.

Continuous variables were assessed for normality using the Shapiro-Wilk test. Normally distributed variables were expressed as mean ± standard deviation (X ± sd) and compared using the t-test. Non-normally distributed data were presented as median [IQR] and analyzed with the Wilcoxon rank-sum test.

Univariate logistic regression was used to screen potential risk factors. Correlation between variables and vascular crisis was further examined using Spearman correlation analysis. Significant variables from the univariate analysis were then included in a multivariate logistic regression to identify independent predictors.

Receiver operating characteristic (ROC) curve analysis was used to evaluate diagnostic performance. The Youden Index was applied to determine optimal cutoff values. A nomogram incorporating independent predictors was constructed for clinical risk estimation. All tests were two-sided, with $P < 0.05$ considered statistically significant.

Results

Comparison of general characteristics

This study evaluated demographic and clinical variables to identify potential risk factors for postoperative vascular crisis in patients undergoing supraclavicular artery flap reconstruction following surgery for SCC of the tongue or buccal mucosa. No significant differences were observed between the vascular crisis group (n = 101) and the non-crisis group (n = 676) in terms of age, disease duration, sex, Han ethnicity, comorbidities, or complication history (all $P > 0.05$).

However, a higher proportion of patients in the vascular crisis group had a body mass index (BMI) ≥ 24 kg/m^2 (37.62%) compared to the non-crisis group (25.74%), which was statistically significant ($P = 0.012$). Similarly, long-term smoking, long-term alcohol consumption, and a history of diabetes were more prevalent in the vascular crisis group (all $P < 0.05$). Admission blood glucose levels were also significantly higher in the vascular crisis group (5.62 ± 2.24 mmol/L) than in the non-crisis group (5.07 ± 1.16 mmol/L, $P = 0.016$).

No significant associations were found for hypertension history, normal blood pressure at admission, use of anxiolytics, presence of anxiety or depression in medical records, tumor site, histological differentiation, or TNM staging (all $P > 0.05$). See **Table 1**.

Comparison of routine blood parameters and CRP

PLT levels were significantly lower in the vascular crisis group (259.36 ± 22.45 × 10^9/L) compared to the non-crisis group (265.34 ± 23.18 × 10^9/L, $P = 0.015$), while WBC counts were significantly higher (7.89 ± 1.55 vs. 7.33 ± 1.67 × 10^9/L, $P = 0.002$). Additionally, CRP levels were elevated in the crisis group (7.21 ± 1.02 mg/L) compared to the non-crisis group (6.89 ± 1.02 mg/L, $P = 0.003$) (**Figure 2**).

No significant differences were found for RBC, ANC, or ALC (all $P > 0.05$). These results indicate that lower preoperative PLT levels, elevated WBC, and higher CRP may serve as potential predictors of vascular crisis.

Comparison of intraoperative conditions

Flap survival was significantly lower in the vascular crisis group (84.16%) compared to the non-crisis group (95.56%) ($P < 0.001$) (**Table 2**). However, no significant differences were observed in flap preparation time (80.56 ± 12.02 vs. 79.47 ± 11.78 minutes, $P = 0.385$), flap size (36.67 ± 4.12 vs. 37.45 ± 3.87 cm^2, $P = 0.061$), postoperative hospital stay (29.12 ± 5.87 vs. 28.36 ± 6.55 days, $P = 0.288$), or intraoperative blood loss (219.49 ± 20.12 vs. 223.48 ± 19.73 mL, $P = 0.059$).

Comparison of biochemical indicators

SCC-Ag levels were significantly higher in the vascular crisis group (102.34 ± 36.24 ng/mL) than in the non-crisis group (93.45 ± 33.12 ng/mL, $P = 0.013$), indicating a potential association with postoperative vascular complications (**Table 3**).

No statistically significant differences were observed for TC, TG, HDL-c, LDL-c, APOA, APOB, FBG, CEA, CA50, and CYFRA21-1, with *P*-values ranging from 0.097 to 0.983.

Correlation analysis

A higher BMI (≥ 24 kg/m^2) showed a weak but significant positive correlation with the occurrence of postoperative vascular crisis (rho = 0.090, $P = 0.012$) (**Figure 3**). Long-term smoking and drinking were also positively correlated with crisis occurrence, with rho values of 0.109 ($P = 0.002$) and 0.101 ($P = 0.005$), respectively. Similarly, both a history of diabetes (rho = 0.107, $P = 0.003$) and elevated blood glucose on admission (rho = 0.077, $P = 0.033$) showed positive correlations.

Among inflammatory markers, WBC (rho = 0.122, $P < 0.001$) and CRP (rho = 0.100, P =

Table 1. Comparison of general information

Parameter		No occurred (n = 676)	Occurred (n = 101)	t/χ^2	P
Age (years)		41.25 ± 12.16	42.13 ± 11.65	0.684	0.494
Disease duration (months)		10.13 ± 4.29	10.55 ± 4.18	0.906	0.365
Gender (Male: 1/Female: 0) [n (%)]		208 (30.77)/468 (69.23)	33 (32.67)/68 (67.33)	0.149	0.7
Han ethnicity (Yes: 1/No: 0) [n (%)]		621 (91.86)	94 (93.07)	0.174	0.677
Other medical history (Yes: 1/No: 0) [n (%)]		40 (5.92)	6 (5.94)	0	0.993
Complications (Yes: 1/No: 0) [n (%)]		104 (15.38)	14 (13.86)	0.158	0.691
BMI ≥ 24 (Yes: 1/No: 0) (kg/m^2)		174 (25.74)	38 (37.62)	6.255	0.012
Long-term smoking (Yes: 1/No: 0) [n (%)]		267 (39.50)	56 (55.45)	9.202	0.002
Long term drinking [n (Yes: 1/No: 0) (%)]		294 (43.49)	59 (58.42)	7.895	0.005
History of diabetes (Yes: 1/No: 0) [n (%)]		57 (8.43)	18 (17.82)	8.884	0.003
Blood glucose level upon admission		5.07 ± 1.16	5.62 ± 2.24	2.44	0.016
History of hypertension (Yes: 1/No: 0) [n (%)]		73 (10.80)	17 (16.83)	3.123	0.077
Normal blood pressure level upon admission		572 (84.61)	82 (81.18)	0.775	0.379
Use of anxiolytics (Yes: 1/No: 0) [n (%)]		115 (17.01)	20 (19.80)	0.477	0.490
Anxiety/Depression in medical notes (Yes: 1/No: 0) [n (%)]		164 (24.26)	25 (24.75)	0.012	0.914
Cancer position (ATC: 0/BTC: 1/MBM: 2/LBM: 3/other: 4) [n (%)]	ATC	154 (22.78)	20 (19.80)	1.524	0.822
	BTC	144 (21.30)	26 (25.74)		
	MBM	174 (25.74)	23 (22.77)		
	LBM	164 (24.26)	26 (25.74)		
	other	40 (5.92)	6 (5.95)		
Degree of differentiation (WDS: 0/MDS: 1/PDS: 2/UC: 3) [n (%)]	WDS	105 (15.53)	15 (14.85)	0.455	0.929
	MDS	193 (28.55)	27 (26.73)		
	PDS	179 (26.48)	26 (25.74)		
	UC	199 (29.44)	33 (32.67)		
TNM staging system (Early stage (I, II): 1/Late stage (III, IV): 0) [n (%)]	Early stage (I, II)	418 (61.83)	63 (62.38)	0.011	0.917
	Late stage (III, IV)	258 (38.17)	38 (37.62)		

ATC: Anterior tongue cancer; BTC: Base of tongue cancer; MBM: Medial buccal mucosa cancer; LBM: Medial buccal mucosa cancer; WDS: Well-differentiated squamous cell carcinoma; MDS: Moderately differentiated squamous cell carcinoma; PDS: Poorly differentiated squamous cell carcinoma; UC: Undifferentiated carcinoma.

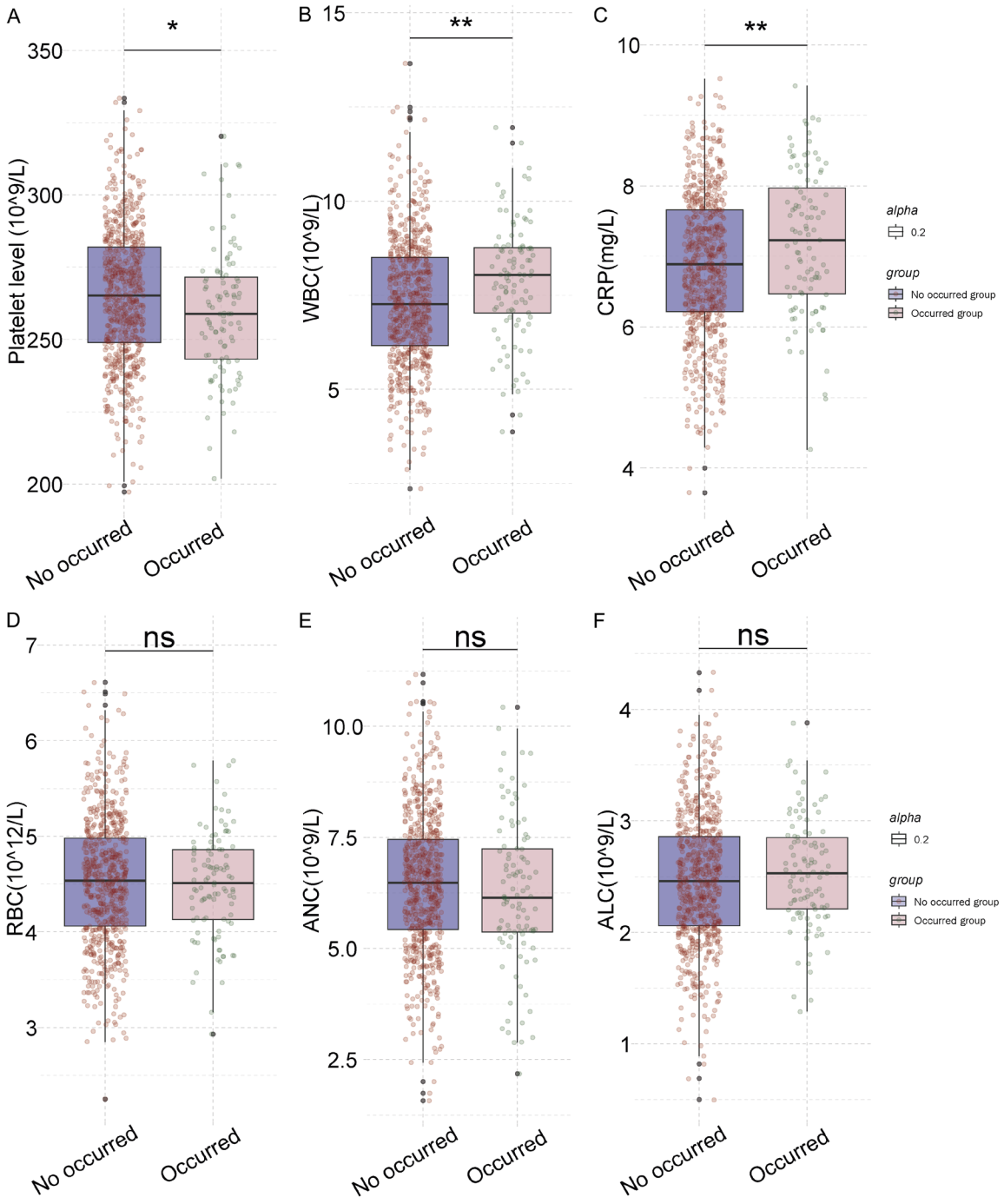

Figure 2. Routine blood test and CRP before surgery. A: Platelet level (10^9/L); B: WBC (10^9/L); C: CRP (mg/L); D: RBC (10^{12}/L); E: ANC (10^9/L); F: ALC (10^9/L). WBC: White Blood Cell Count; CRP: C-reactive protein; RBC: Red Blood Cell Count; ANC: Absolute Neutrophil Count; ALC: Absolute Lymphocyte Count. Ns: No significant difference; *: $P < 0.05$; **: $P < 0.01$.

0.005) were significantly positively correlated with vascular crisis. Platelet levels showed a weak negative correlation (rho = -0.095, P = 0.008), while flap survival rate exhibited a stronger negative association (rho = -0.162, P < 0.001). Scc-Ag was marginally correlated (rho = 0.089, P = 0.013). These findings reflect the multifactorial nature of vascular complica-

Table 2. Comparison of intraoperative conditions

Parameter	No occurred (n = 676)	Occurred (n = 101)	t/χ^2	P
Time of flap preparation (min)	79.47 ± 11.78	80.56 ± 12.02	0.868	0.385
Survival (Yes: 1/No: 0) [n (%)]	646 (95.56)	85 (84.16)	20.517	< 0.001
Flap size (cm^2)	37.45 ± 3.87	36.67 ± 4.12	1.878	0.061
Postoperative time (d)	28.36 ± 6.55	29.12 ± 5.87	1.107	0.268
Bleeding volume	223.48 ± 19.73	219.49 ± 20.12	1.889	0.059

Table 3. Comparison of Biochemical indicators before surgery

Parameter	No occurred (n = 676)	Occurred (n = 101)	t	P
TC (mmol/L)	4.91 ± 1.31	4.88 ± 1.22	0.213	0.832
TG (mmol/L)	1.78 ± 0.33	1.73 ± 0.28	1.669	0.097
HDL-C (mmol/L)	1.19 ± 0.28	1.22 ± 0.33	0.747	0.455
LDL-C (mmol/L)	3.11 ± 0.95	3.12 ± 0.92	0.072	0.943
APOA (g/L)	1.44 ± 0.42	1.42 ± 0.38	0.429	0.668
APOB (g/L)	0.98 ± 0.31	0.98 ± 0.29	0.021	0.983
FBG (mmol/L)	6.78 ± 2.89	6.56 ± 2.87	0.715	0.475
CEA/(ng/mL)	158.66 ± 45.73	163.25 ± 46.32	0.939	0.348
CA50/(U/mL)	218.35 ± 74.87	216.87 ± 75.23	0.186	0.852
CYFRA21-1/(ng/mL)	175.12 ± 57.32	178.69 ± 56.91	0.584	0.559
Scc-Ag/(ng/mL)	93.45 ± 33.12	102.34 ± 36.24	2.486	0.013

TC: Total cholesterol; TG: Triglyceride; HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; APOA: Apoliprotein A; APOB: Apoliprotein B; FBG: Fasting blood glucose; CEA: Carcino Embryonic Antigen; CA50: Carbohydrate Antigen 50; CYFRA21-1: Cytokeratin 19 Fragment Antigen 21-1; Scc-Ag: Squamous Cell Carcinoma Antigen.

tions and underscore the influence of metabolic, inflammatory, and lifestyle-related parameters.

Univariate logistic regression results

Univariate logistic regression identified multiple variables significantly associated with postoperative vascular crisis (**Table 4**). Patients with BMI ≥ 24 kg/m^2 had 74% higher odds of crisis (OR = 1.740, 95% CI: 1.116-2.685, P = 0.013). Long-term smoking (OR = 1.906, 95% CI: 1.252-2.916, P = 0.003) and long-term drinking (OR = 1.825, 95% CI: 1.198-2.803, P = 0.005) were also significant risk factors.

Diabetes history was associated with more than double the risk (OR = 2.355, 95% CI: 1.292-4.126, P = 0.004), while elevated admission blood glucose had an OR of 1.331 (95% CI: 1.147-1.545, P < 0.001). WBC and CRP levels were also risk factors (WBC: OR = 1.224, 95% CI: 1.080-1.391, P = 0.002; CRP: OR = 1.376, 95% CI: 1.116-1.706, P = 0.003). PLT count showed a protective effect (OR = 0.989, 95% CI: 0.980-0.998, P = 0.016). Flap survival rate showed strong inverse association (OR = 0.247, 95% CI: 0.131-0.481, P < 0.001). Elevated Scc-Ag was modestly but significantly associated with increased risk (OR = 1.008, 95% CI: 1.002-1.014, P = 0.014).

Multivariate logistic regression results

Multivariate logistic regression revealed several independent risk factors (**Table 5**). Long-term smoking (OR = 1.895, 95% CI: 1.201-2.988, P = 0.006) and drinking (OR = 1.661, 95% CI: 1.059-2.605, P = 0.027) remained significant. Elevated blood glucose (OR = 1.260, 95% CI: 1.082-1.468, P = 0.003), CRP (OR = 1.405,95% CI: 1.120-1.763, P = 0.003), and WBC (OR = 1.242, 95% CI: 1.083-1.425, P = 0.002) also independently predicted vascular crisis.

PLT was inversely associated (OR = 0.989, 95% CI: 0.979-0.998, P = 0.023), while Scc-Ag was positively associated (OR = 1.008, 95% CI: 1.001-1.015, P = 0.022). Flap survival remained a strong protective factor (OR = 0.187, 95%

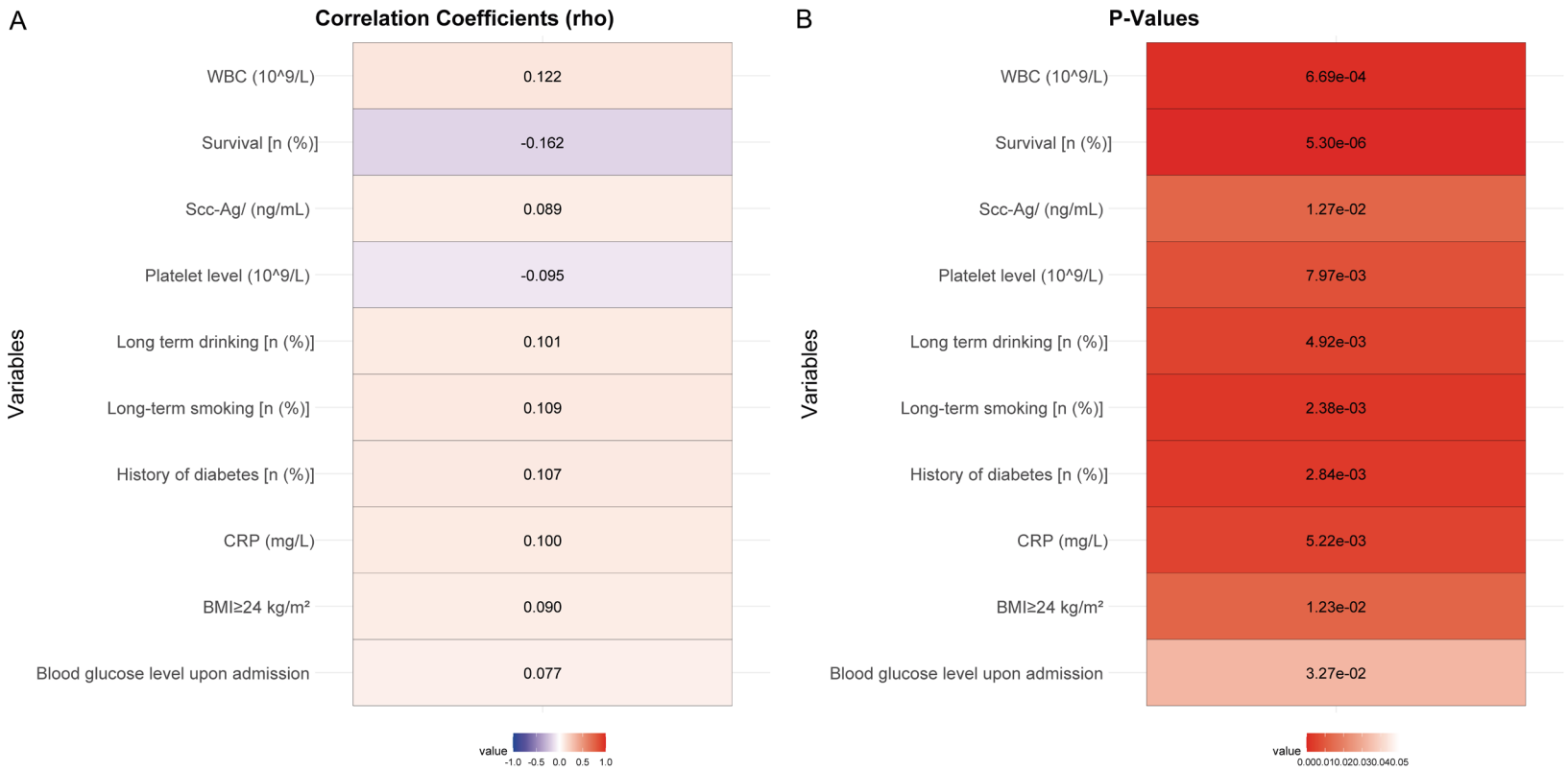

Figure 3. Correlation analysis of factors for postoperative vascular crisis. A: Correlation Coefficients (rho); B: *P*-Values.

Table 4. Univariate logistic regression analysis of factors for postoperative vascular crisis

	Coefficient	Std Error	Wald	P	OR	95% CI
BMI ≥ 24 (Yes: 1/No: 0) (kg/m^2)	0.554	0.223	2.479	0.013	1.740	1.116-2.685
Long-term smoking (Yes: 1/No: 0) [n (%)]	0.645	0.215	2.999	0.003	1.906	1.252-2.916
Long term drinking (Yes: 1/No: 0) [n (%)]	0.602	0.216	2.782	0.005	1.825	1.198-2.803
History of diabetes (Yes: 1/No: 0) [n (%)]	0.857	0.295	2.908	0.004	2.355	1.292-4.126
Blood glucose level upon admission	0.286	0.076	3.767	< 0.001	1.331	1.147-1.545
Platelet level (10^9/L)	-0.011	0.005	2.411	0.016	0.989	0.980-0.998
WBC (10^9/L)	0.202	0.065	3.139	0.002	1.224	1.080-1.391
CRP (mg/L)	0.319	0.108	2.950	0.003	1.376	1.116-1.706
Survival rate (Yes: 1/No: 0) (%)	-1.400	0.33	4.236	< 0.001	0.247	0.131-0.481
Scc-Ag/(ng/mL)	0.008	0.003	2.468	0.014	1.008	1.002-1.014

Table 5. Multivariate logistic regression analysis of factors for postoperative vascular crisis

	Coefficient	Std Error	Wald Stat	P	OR	OR CI Lower	OR CI Upper
BMI ≥ 24 (Yes: 1/No: 0) (kg/m^2)	0.457	0.241	1.898	0.058	1.580	0.985	2.534
Long-term smoking (Yes: 1/No: 0) [n (%)]	0.639	0.232	2.750	0.006	1.895	1.201	2.988
Long term drinking (Yes: 1/No: 0) [n (%)]	0.507	0.230	2.209	0.027	1.661	1.059	2.605
History of diabetes (Yes: 1/No: 0) [n (%)]	0.540	0.323	1.668	0.095	1.715	0.910	3.233
Blood glucose level upon admission	0.231	0.078	2.967	0.003	1.260	1.082	1.468
Platelet level (10^9/L)	-0.012	0.005	-2.269	0.023	0.989	0.979	0.998
WBC (10^9/L)	0.217	0.070	3.090	0.002	1.242	1.083	1.425
CRP (mg/L)	0.340	0.116	2.942	0.003	1.405	1.120	1.763
Survival rate (Yes: 1/No: 0) (%)	-1.676	0.358	-4.682	< 0.001	0.187	0.093	0.377
Scc-Ag/(ng/mL)	0.008	0.003	2.282	0.022	1.008	1.001	1.015

CI: 0.093-0.377, P < 0.001). Although BMI ≥ 24 kg/m^2 (OR = 1.580, 95% CI: 0.985-2.534, P = 0.058) and diabetes history (OR = 1.715, 95% CI: 0.910-3.233, P = 0.095) did not reach significance in this model, their marginal effects suggest they may still contribute to risk in some patients.

Evaluation of the comprehensive predictive model

Figure 4 illustrates the predictive model through a ROC curve and a nomogram. Cut-off thresholds were determined as follows: BMI ≥ 24 kg/m^2; Long-term smoking: > 5 years, ≥ 10 cigarettes/day; Long-term drinking: > 5 years, ≥ 3 times/week; Blood glucose ≥ 7.12 mmol/L; PLT < 273.84 × 10^9/L; WBC > 7.575 × 10^9/L; CRP > 7.545 mg/L; Scc-Ag > 112.88 ng/mL; Flap survival < 93%.

The ROC curve demonstrated excellent discriminative power with an AUC of 0.975, indicating high accuracy in distinguishing patients with or without vascular crisis. The nomogram incorporated independent risk variables (e.g., smoking history, alcohol consumption, preoperative blood glucose, platelet count, WBC, CRP, and SCC-Ag) and enabled clinicians to calculate a total risk score (range: 0.1-0.7) to predict the probability of vascular crisis. Supported by internal (10-fold cross-validation) and external validation, this model provides a reliable tool for personalized surgical planning and risk stratification in clinical practice.

Comparison of external validation results

Table 6 presents validation results using an independent cohort. No significant differences were found in most baseline variables, including age, gender, disease duration, blood pressure, anxiety status, tumor characteristics, or common biochemical markers (all P > 0.05).

However, BMI ≥ 24 kg/m^2 was significantly more common in the occurred group (40.00%

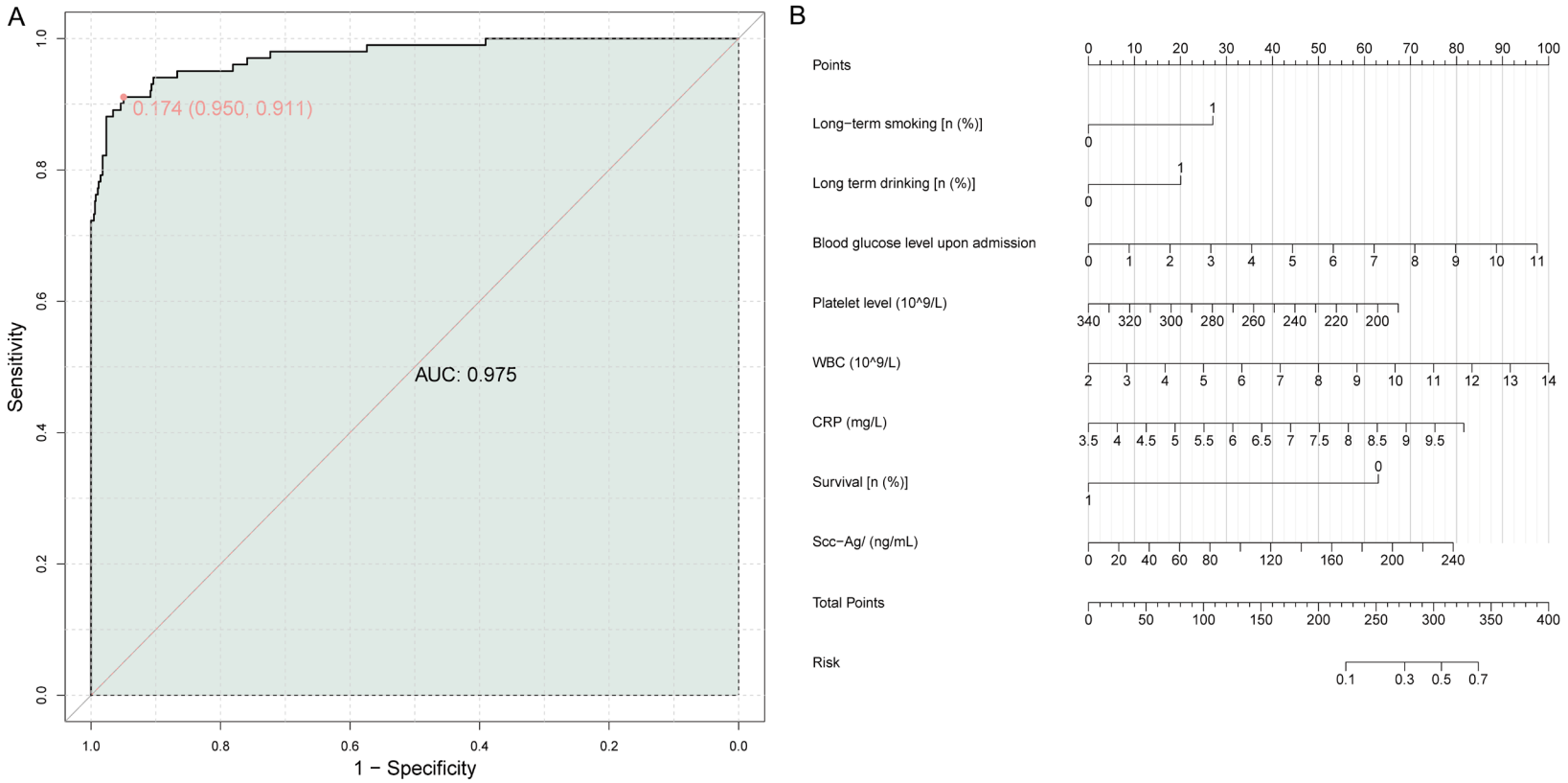

Figure 4. Establishment of predictive model. A: ROC Curve; B: Nomogram.

Table 6. Comparison of parameters between no occurred and occurred groups in the external validation set

Parameter		No occurred (n = 268)	Occurred (n = 40)	t/χ^2	P
Age (years)		40.25 ± 12.06	41.13 ± 11.55	0.43	0.667
Disease duration (months)		10.03 ± 4.19	10.45 ± 4.08	0.596	0.552
Gender (Male: 1/Female: 0) [n (%)]		82 (30.60)/186 (69.40)	13 (32.50)/27 (67.50)	0.059	0.808
Han ethnicity (Yes: 1/No: 0) [n (%)]		246 (91.79)	37 (92.50)	0	1
Other medical history (Yes: 1/No: 0) [n (%)]		14 (5.22)	2 (5.00)	0	1
Complications (Yes: 1/No: 0) [n (%)]		39 (14.55)	5 (12.50)	0.12	0.729
BMI ≥ 24 (Yes: 1/No: 0) (kg/m^2)		67 (25.00)	16 (40.00)	3.978	0.046
Long-term smoking (Yes: 1/No: 0) [n (%)]		104 (38.81)	23 (57.50)	5.02	0.025
Long term drinking (Yes: 1/No: 0) [n (%)]		111 (41.42)	24 (60.00)	4.882	0.027
History of diabetes (Yes: 1/No: 0) [n (%)]		19	8	5.729	0.017
Blood glucose level upon admission		5.05 ± 1.06	5.78 ± 2.04	2.237	0.031
History of hypertension (Yes: 1/No: 0) [n (%)]		30 (11.19)	7 (17.50)	0.781	0.377
Normal blood pressure level upon admission		225 (83.58)	32 (80.00)	0.394	0.53
Use of anxiolytics (Yes: 1/No: 0) [n (%)]		47 (17.54)	8 (20.00)	0.144	0.704
Anxiety/Depression in medical notes (Yes: 1/No: 0) [n (%)]		66 (24.63)	10 (25.00)	0.003	0.959
Cancer position (ATC: 0/BTC: 1/MBM: 2/LBM: 3/other: 4) [n (%)]	ATC	61 (22.76)	8 (20.00)	0.503	0.973
	BTC	58 (21.64)	10 (25.00)		
	MBM	66 (24.63)	9 (22.50)		
	LBM	67 (25.00)	11 (27.50)		
	other	16 (5.97)	2 (5.00)		
Degree of differentiation (WDS: 0/MDS: 1/PDS: 2/UC: 3) [n (%)]	WDS	42 (15.67)	6 (15.00)	0.155	0.984
	MDS	78 (29.10)	11 (27.50)		
	PDS	69 (25.75)	10 (25.00)		
	UC	79 (29.48)	13 (32.50)		
TNM staging system (Early stage (I, II): 1/Late stage (III, IV): 0) [n (%)]	Early stage (I, II)	166 (61.94)	25 (62.50)	0.005	0.946
	Late stage (III, IV)	102 (38.06)	15 (37.50)		
Platelet level ($10^9/L$)		268.33 ± 22.17	258.35 ± 21.44	2.664	0.008
WBC ($10^9/L$)		7.25 ± 1.66	7.88 ± 1.54	2.252	0.025
CRP (mg/L)		6.88 ± 1.01	7.30 ± 1.01	2.503	0.013
RBC ($10^{12}/L$)		4.51 ± 0.65	4.49 ± 0.54	0.256	0.798
ANC ($10^9/L$)		6.44 ± 1.54	6.22 ± 1.67	0.808	0.42
ALC ($10^9/L$)		2.46 ± 0.57	2.52 ± 0.48	0.681	0.496
Time of flap preparation (min)		79.57 ± 11.88	80.66 ± 12.12	0.538	0.591

Survival (Yes: 1/No: 0) [n (%)]	257 (95.90)	34 (85.00)	5.972	0.015
Flap size (cm^2)	37.55 ± 3.97	36.77 ± 4.22	1.146	0.253
Postoperative time (d)	28.46 ± 6.65	29.22 ± 5.97	0.687	0.492
Bleeding volume	223.58 ± 19.83	219.59 ± 20.22	1.186	0.237
TC (mmol/L)	5.01 ± 1.41	4.98 ± 1.32	0.105	0.916
TG (mmol/L)	1.88 ± 0.43	1.83 ± 0.38	0.674	0.501
HDL-C (mmol/L)	1.20 ± 0.38	1.32 ± 0.43	1.72	0.086
LDL-C (mmol/L)	3.20 ± 1.00	3.21 ± 0.99	0.07	0.944
APOA (g/L)	1.5 ± 0.41	1.46 ± 0.35	0.606	0.545
APOB (g/L)	0.99 ± 0.30	0.99 ± 0.28	0.012	0.99
FBG (mmol/L)	6.70 ± 2.80	6.48 ± 2.79	0.468	0.64
CEA/(ng/mL)	158.50 ± 45.60	163.10 ± 46.20	0.594	0.553
CA50/(U/mL)	218.41 ± 74.85	216.94 ± 75.21	0.116	0.908
CYFRA21-1/(ng/mL)	175.20 ± 57.30	178.77 ± 56.90	0.368	0.713
Scc-Ag/(ng/mL)	92.22 ± 33.10	104.24 ± 36.22	2.116	0.035

ATC: Anterior tongue cancer; BTC: Base of tongue cancer; MBM: Medial buccal mucosa cancer; LBM: Medial buccal mucosa cancer; WDS: Well-differentiated squamous cell carcinoma; MDS: Moderately differentiated squamous cell carcinoma; PDS: Poorly differentiated squamous cell carcinoma; UC: Undifferentiated carcinoma; WBC: White Blood Cell Count; CRP: C-reactive protein; NC: Absolute Neutrophil Count; ALC: Absolute Lymphocyte Count; TC: Total cholesterol; TG: Triglyceride; HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; APOA: Apoliprotein A; APOB: Apoliprotein B; FBG: Fasting blood glucose; CEA: Carcino Embryonic Antigen; CA50: Carbohydrate Antigen 50; CYFRA21-1: Cytokeratin 19 Fragment Antigen 21-1; Scc-Ag: Squamous Cell Carcinoma Antigen.

vs. 25.00%, P = 0.046). Likewise, long-term smoking (57.50% vs. 38.81%, P = 0.025), long-term drinking (60.00% vs. 41.42%, P = 0.027), and diabetes history (20.00% vs. 5.22%, P = 0.017) were all significantly associated with vascular crisis. Blood glucose, WBC, CRP, and Scc-Ag were significantly higher in the occurred group, while PLT levels and flap survival rates were significantly lower (all P < 0.05).

These findings confirm the predictive model's applicability in external settings and underscore the clinical relevance of modifiable and measurable risk factors in improving patient prognosis.

Discussion

In this study, we identified several key risk factors associated with postoperative vascular crisis in patients undergoing supraclavicular artery flap reconstruction for tongue and buccal SCC. These factors include hyperglycemia at admission, long-term smoking and alcohol consumption, elevated WBC count, increased CRP levels, elevated SCC-Ag, and lower flap survival rates.

Our findings regarding hyperglycemia are consistent with previous studies demonstrating its adverse effects on vascular health [20, 21]. Elevated blood glucose levels impair endothelial function and promote systemic inflammation, both of which hinder postoperative neovascularization and flap integration. Hyperglycemia contributes to metabolic disturbances such as the accumulation of advanced glycation end products, enhanced oxidative stress, and increased secretion of proinflammatory cytokines (e.g., IL-6, TNF-α), all of which exacerbate endothelial dysfunction. Moreover, hyperglycemia suppresses nitric oxide synthesis, thereby impairing vasodilation and microvascular perfusion [22-24].

Long-term smoking and alcohol consumption were also significant risk factors, aligning with existing literature on their vascular toxicity [25, 26]. Smoking induces oxidative stress and systemic inflammation, damages endothelial cells, and accelerates atherosclerosis. Chronic alcohol consumption further disrupts lipid metabolism, exacerbates oxidative stress, and contributes to vascular instability [27, 28]. These effects collectively increase the risk of thrombosis and compromise microcirculatory perfusion of the flap.

Importantly, SCC-Ag emerged as a notable biochemical risk factor. Elevated SCC-Ag levels are associated with systemic inflammatory activation and endothelial injury [29, 30]. Mechanistically, high SCC-Ag concentrations may stimulate the release of inflammatory mediators, promote oxidative damage, and interfere with endothelial cell integrity. These effects can impair wound healing and increase the risk of thrombotic events at the flap site, ultimately compromising flap survival and integration [31].

Elevated levels of WBC, CRP, and PLT levels serve as markers of systemic inflammation that may predispose patients to vascular complications following surgery. An increased WBC count reflects heightened immune activation, which can disrupt the controlled inflammatory responses essential for tissue repair and angiogenesis. Similarly, CRP, an acute-phase reactant induced by inflammatory stimuli, has been shown to impair arterial wall function and contribute to thrombus formation. High PLT levels suggest a hypercoagulable state, further elevating the risk of vascular occlusion [32]. Elevated preoperative levels of these inflammatory markers may indicate an ongoing inflammatory state that compromises vascular patency, thereby jeopardizing flap viability [33-35].

Flap survival rate, which was negatively associated with vascular crisis, represents both a predictor and a consequence of graft-related complications. A lower survival rate reflects underlying challenges in achieving adequate arterial inflow and venous outflow - processes that are often hindered by microthrombosis or insufficient vascularization, particularly in the presence of systemic inflammation and metabolic derangements [36, 37]. Therefore, improving flap survival necessitates a comprehensive strategy involving preoperative control of inflammation and vascular risk factors, along with meticulous surgical technique to ensure optimal revascularization [38, 39].

Despite the strength of these findings, our study has several limitations. As a retrospective single-center study, it is subject to inherent selection bias and limited external gen-

eralizability. While the sample size was adequate for detecting significant associations, it may not have been sufficiently powered to capture smaller effect sizes or interaction effects among risk factors. Additionally, lifestyle data such as smoking and alcohol consumption were self-reported and thus vulnerable to recall bias. The assessment of psychological factors was based on indirect indicators - such as anxiolytic prescriptions and medical record documentation - which may not fully reflect patients' actual psychological states.

Furthermore, although we identified several risk factors for vascular crisis, the underlying mechanisms linking these variables to vascular events were not explored in detail. Future prospective studies and experimental models are needed to elucidate the molecular and cellular pathways involved. Such research may clarify the role of hyperglycemia, systemic inflammation, and endothelial dysfunction in compromising flap outcomes. Multicenter studies with diverse populations and longitudinal follow-up are also warranted to validate these findings and assess dynamic changes in risk over time.

In conclusion, the development of postoperative vascular crisis following supraclavicular artery flap reconstruction for SCC is driven by a multifactorial interplay of systemic and local factors. Modifiable risk factors such as hyperglycemia, smoking, alcohol use, inflammation, and impaired vascular function significantly influence flap survival. These findings highlight the importance of comprehensive preoperative evaluation that includes metabolic, inflammatory, and behavioral assessments to optimize patient outcomes.

A multidisciplinary and individualized approach to risk stratification and management is critical in minimizing complications. Future research should aim to validate predictive models in diverse populations, investigate biological mechanisms in greater depth, and explore targeted interventions to reduce the incidence of vascular crisis. Through such efforts, the efficacy and safety of reconstructive surgery in patients with head and neck cancer can be substantially improved.

Disclosure of conflict of interest

None.

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