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Original Article

Development of a predictive model for the relationship between serum pan-immunoinflammatory index levels and scar formation in facial burn patients

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Abstract: Objectives: This study aims to develop a predictive model for scar risk in patients with facial burns using the Pan-Immune Inflammation Value (PIV) and other serological markers. Methods: A retrospective cohort study was conducted on 367 patients with facial burns treated at a single institution between June 2021 and June 2023. Patients were categorized based on the presence of the scar 7 days post-treatment. Serum markers, including PIV, TNF-α, IL-10, EPO, TGF-β1, and ICAM-1, were measured. Multivariate logistic regression was employed to identify independent predictors of scar formation. A predictive model was developed and validated using a test set of 144 patients. Results: Scar formation was associated with elevated levels of TNF-α and ICAM-1, and reduced levels of IL-10, EPO, and TGF-β1, indicating a pro-inflammatory profile. Patients with scars showed higher symptom severity, emotional distress, and functional impairment. The predictive model, incorporating these markers, achieved an AUC of 0.815 in the training set and 0.845 in the test set, demonstrating good predictive performance. Conclusion: Elevated pro-inflammatory markers and altered PIV levels were significant predictors of scar formation in patients with facial burns.

Keywords: Facial burns, scar formation, pan-immunoinflammatory index

Introduction

Facial burns represent a significant clinical challenge due to their complex nature and profound physiological and psychological impacts. Facial scarring, a common sequelae of burn injuries, substantially contributes to long-term morbidity, including disfigurement, functional impairments, and psychological distress [1, 2]. Understanding the mechanisms underlying scar formation remains a fundamental objective in burn treatment and recovery.

The skin's response to burns involves dynamic processes characterized by inflammation, proliferation, and remodeling [3, 4]. The degree and duration of these responses dictate the quality of healing and scar formation. While acute inflammatory response is essential for wound healing, dysregulated inflammation can exacerbate tissue damage and lead to hypertrophic scars [5, 6]. Therefore, insights into this response and its modulators are crucial for developing effective intervention strategies.

Among the indices utilized to evaluate systemic inflammation, the Pan-Immunoinflammatory Index (PIV) emerges as a potentially valuable marker. PIV is a composite indicator calculated using peripheral blood neutrophil, lymphocyte, monocyte, and platelet counts [7-9]. Its application in predicting inflammation-related outcomes in various diseases has gained substantial interest, yet its relevance in burn injury and subsequent scar development remains to be fully elucidated [10, 11].

Several cytokines and growth factors are implicated in the regulation of scarring, whether through pro-inflammatory or reparative path-

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ways [12-14]. Understanding the interplay between these markers is crucial for devising strategies to mitigate hypertrophic scarring.

Despite advances in understanding scar biology, predicting patients at risk for significant scarring remains a challenge [15]. Current predictive assessments largely rely on clinical judgement and subjective evaluations. However, emerging evidence underscores the potential of biomarkers in enhancing predictive accuracy. This highlights the necessity for developing objective predictive tools that incorporate both clinical and molecular data to refine risk stratification and optimize therapeutic interventions [16, 17].

This study aims to bridge this gap by establishing a predictive model that evaluates the relationship between serum PIV levels and scar formation in patients with facial burns. By integrating key serological markers, the model seeks to offer a more comprehensive insight into the inflammatory milieu associated with burn injuries.

Materials and methods

Subjects

This retrospective cohort study was conducted on 367 patients admitted to Friendship Plastic Surgery Hospital of Nanjing Medical University between June 2021 and June 2023. Demographic data, general information, relevant hematological parameters, and Skindex-16 scores were collected via the hospital's medical record system. The study was approved by the Ethics Review Committee of Friendship Plastic Surgery Hospital of Nanjing Medical University and adhered to the relevant guidelines set forth in the Declaration of Helsinki. Given the retrospective nature of the study, informed consent was waived.

Inclusion Criteria: (1) aged 18 years or older with normal cognitive function and able to cooperate with various examinations and treatments; (2) diagnosed with second-degree facial burns according to established diagnostic criteria [18] and were treated conservatively; (3) had burns covering an area of 2% to 15% of their body surface; and (4) availability of complete clinical data.

Exclusion Criteria: (1) local or systemic infections; (2) coexisting diabetes or hypertension; (3) acute cardiovascular or cerebrovascular diseases; (4) hematological disorders; or (5) coagulation dysfunction.

Grouping criteria and treatment methods

Treatment method: The wound area was initially cleaned with physiological saline, followed by irrigation with a 0.1% benzalkonium bromide solution (Shanghai Yunjia Huangpu Pharmaceutical Co., Ltd., approval number H31021811). Severely contaminated or shriveled and curled eschars were excised, while blisters were punctured for drainage, and any remaining intact eschars were perforated. The wound was then treated with a thin layer of recombinant bovine basic fibroblast growth factor gel (Guilin HuanoWeGene Pharmaceutical Co., Ltd., approval number S20020112). Subsequently, gauze impregnated with sulfadiazine zinc ointment (Henan Quanyu Pharmaceutical Co., Ltd., approval number H41022525) was applied, and the wound was securely covered with sterile gauze bandages. Dressings were replaced every other day.

For patients with deep second-degree burns, negative pressure closed drainage was additionally used. The skin within 5 cm of the wound margin was sterilized using 75% alcohol. Polyvinyl alcohol medical sponge dressings (Jiangsu Keyu Medical Instrument Co., Ltd.) were trimmed to fit the wounds and applied directly to its surface. The wound was sealed using a transparent breathable adhesive film, and the drainage tube was secured using the mesenteric method. The ZN100 intelligent negative pressure comprehensive therapy device (Shandong Chuangkang Biotechnology Co., Ltd.) was employed, set to a negative pressure of -16.6 kPa, for continuous application over 14 days. To prevent hardening of the dressing, 20 ml of physiological saline per 200 m^2 was injected daily into the drainage tubes and dressings.

Grouping criteria: Participants were divided into two groups based on the presence of scar formation seven days following conservative treatment: the scar formation group (n = 106) and the no scar formation group (n = 117). Additionally, an external validation test set comprising 134 patients, adhering to the same

inclusion, exclusion, and grouping criteria, was similarly categorized into a scar formation group (n = 66) and a no scar formation group (n = 78).

Blood testing

To prepare for biochemical analyses, a 5 ml sample of venous blood was collected from patients who had fasted before 8 a.m. The DxH800 blood analyzer (Beckman Coulter, Inc., Brea, CA, USA) was employed to measure neutrophils, lymphocytes, platelets, and monocytes. The PIV was calculated using the following formula: PIV = (Neutrophil Count × Monocyte Count × Platelet Count)/Lymphocyte Count. C-reactive protein (CRP) levels were determined using the BECKMAN Synchronx20 fully automatic biochemical analyzer (Beckman Coulter, Inc., Brea, CA, USA) with a rate scattering turbidimetry method.

The blood sample was centrifuged at 3,000 revolutions per minute for 5 minutes to isolate the supernatant, which was subsequently analyzed for tumor necrosis factor (TNF-α) and interleukin-10 (IL-10). Additionally, levels of erythropoietin (EPO), transforming growth factor Beta-1 (TGF-β1), and intercellular adhesion molecule-1 (ICAM-1) were measured using enzyme-linked immunosorbent assays (ELISA). Reagent kits specific for TNF-α (ab181421, Abcam, USA), IL-10 (ab185986, Abcam, USA), EPO (ab100757, Abcam, USA), TGF-β1 (DB100, R&D Systems, Minneapolis, MN, USA), and ICAM-1 (DY297B, R&D Systems, Minneapolis, MN, USA) were used in these assays.

Skindex-16 subscale

The Skindex-16 is a tool used to evaluate skin health, comprising 16 questions that cover various aspects of skin-related quality of life. The assessment is structured into three main dimensions: symptoms, emotions, and function. Higher scores on this scale suggest a greater impact of skin issues of the individual. The instrument's reliability was confirmed by Cronbach's alpha values of 0.867 for symptoms, 0.930 for emotions, and 0.888 for function, indicating strong internal consistency across these domains [19].

Statistical methods

All statistical analyses were performed using SPSS software version 19 (SPSS Inc., Chicago, IL, USA) and the R software package version 3.0.2 (Free Software Foundation, Inc., Boston, MA, USA). Measurement data following a normal distribution were expressed as mean ± standard deviation, and unpaired t-tests were used to compare continuous variables between two groups. Categorical data were presented as frequencies and percentages. Chi-square tests or Fisher's exact tests were employed to compare categorical variables between the scar formation group and the no scar formation group, depending on the expected cell counts. Mann-Whitney U tests were applied for non-normally distributed continuous variables.

Multivariate logistic regression analyses were conducted to calculate the odds ratio (OR) and 95% confidence interval (CI) for each parameter when treated as a continuous variable. Spearman's rank correlation coefficient was employed to evaluate the correlations between variables. Receiver Operating Characteristic (ROC) curve analysis was conducted using SPSS software to assess the predictive performance of the combined model. The area under the curve (AUC) was calculated with corresponding 95% confidence intervals to evaluate the discriminative ability of the model. A *P* value of less than 0.05 was considered statistically significant.

Results

General information in the training set

In the study population comprising 223 patients with facial burns, various demographic and baseline characteristics were evaluated for their association with scar formation post-burn injury (**Table 1**). Among the evaluated parameters, a history of aging signs demonstrated a significant correlation with scar formation, observed in 31.13% of patients in scar group compared to 47.86% in no scar group (P = 0.011). There were no significant differences between the two groups in terms of age, BMI, education level, gender distribution, employment status, or residential status (P > 0.05). Additionally, smoking history, alcohol consumption history, marital status, the degree of burn, total burn area, and burn cause were not significantly different between the two groups (P > 0.05). These findings suggest that among the factors evaluated, aging signs may be the most

Table 1. Comparison of demographic and baseline characteristics between two patient groups in the training set

Parameters	Scar Formation (n = 106)	No Scar Formation (n = 117)	t/χ^2	P
Age (years)	42.23 ± 11.45	44.67 ± 12.89	1.492	0.137
BMI (kg/m^2)	25.12 ± 3.64	24.98 ± 3.52	0.291	0.772
Education level (years)	12.45 ± 3.21	12.78 ± 3.15	0.773	0.440
Gender [n (%)]			0.016	0.900
Male	58 (54.72%)	65 (55.56%)		
Female	48 (45.28%)	52 (44.44%)		
Employment, work for pay [n (%)]	83 (78.30%)	96 (82.05%)	0.494	0.482
Residential status [n (%)]			0.259	0.611
Urban	70 (%)	81 (69.23%)		
Rural	36 (%)	36 (30.77%)		
Smoking history [n (%)]	35 (33.02%)	42 (35.90%)	0.204	0.652
Alcohol consumption history [n (%)]	28 (26.42%)	35 (29.91%)	0.336	0.562
Marital status [n (%)]			0.754	0.686
Married	69 (65.09%)	78 (66.67%)		
Single	27 (25.47%)	25 (21.37%)		
Divorced	10 (9.43%)	14 (12.0%)		
Aging signs [n (%)]	33 (31.13%)	56 (47.86%)	6.492	0.011
Degree of burn [n (%)]			0.942	0.332
Superficial second-degree burn	54 (50.94%)	52 (44.44%)		
Deep second-degree burn	52 (49.06%)	65 (55.56%)		
Total burn area (%)	8.75 ± 2.43	8.91 ± 2.51	0.458	0.648
Burn cause [n (%)]			0.064	0.996
Flame burn	45 (42.45%)	50 (42.74%)		
Scald burn	38 (35.85%)	42 (35.89%)		
Electric burn	13 (12.26%)	15 (12.82%)		
Chemical burn	10 (9.43%)	10 (8.55%)		

Note: BMI: body mass index.

relevant predictor for scar formation following facial burns.

Hematologic parameters in the training set

Patients with scar formation exhibited significantly lower IL-10 levels (P = 0.03), higher TNF-α levels (P = 0.003), and significantly elevated EPO and TGF-β1 levels (P < 0.001 for both). ICAM-1 and PIV were also higher in the scar group (P = 0.001 and P < 0.001). There was no significant difference in CRP levels (P = 0.406) (**Table 2**). These results suggest a significant association between increased pro-inflammatory markers and reduced anti-inflammatory mediators with scar formation in facial burn patients.

Skindex-16 subscale score in the training set

Patients with scar formation reported significantly higher scores for symptoms (P = 0.002), emotional subscale (P = 0.005), and functioning subscale (P = 0.027) (**Figure 1**). These results indicate that patients with facial burn scars experience significantly higher symptom severity, emotional distress, and functional impairment as measured by the Skindex-16.

Univariate correlation analysis in the training set

Significant factors associated with scar formation included aging signs (P = 0.011), symptoms (P = 0.006), emotional scores (P = 0.005), functioning scores (P = 0.038), TNF-α levels (P

Table 2. Comparison of hematologic parameters between two patient groups in the training set

Parameters	Scar Formation (n = 106)	No Scar Formation (n = 117)	t/χ^2	P
IL-10 (μg/L)	4.13 ± 1.42	4.56 ± 1.48	2.186	0.03
TNF-α (pg/ml)	12.45 ± 3.21	10.98 ± 3.15	2.99	0.003
CRP (mg/L)	10.53 ± 3.45	10.17 ± 3.12	0.832	0.406
EPO (U/L)	18.45 ± 4.21	20.48 ± 4.15	3.622	< 0.001
TGF-β1 (pg/ml)	25.12 ± 5.45	27.98 ± 5.12	4.039	< 0.001
ICAM-1 (KU)	0.86 ± 0.21	0.78 ± 0.19	3.23	0.001
PIV	1.35 ± 0.34	1.17 ± 0.31	4.247	< 0.001

Note: IL, interleukin; TNF, tumor necrosis factor; CRP, C-reactive protein; EPO, Erythropoietin; TGF-β1, Transforming Growth Factor beta-1; ICAM-1, Intercellular Adhesion Molecule-1; PIV, Pan-immune-inflammation value.

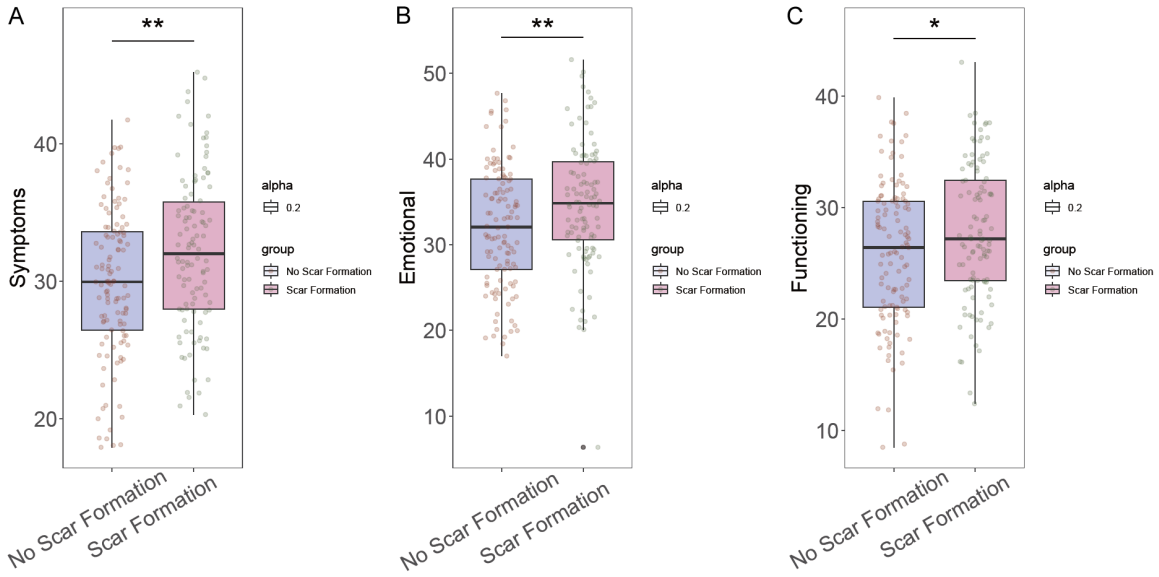

Figure 1. Comparison of Skindex-16 subscale scores between two groups of patients in the Training Set. A: Symptoms; B: Emotional; C: Functioning. *: P < 0.05; **: P < 0.01.

Table 3. Univariate correlation analysis of factors influencing scar formation in the training set

Risk Factors	Rho	P
Aging signs [n (%)]	0.171	0.011
Symptoms	0.183	0.006
Emotional	0.187	0.005
Functioning	0.139	0.038
IL-10 (μg/L)	-0.136	0.043
TNF-α (pg/ml)	0.203	0.002
EPO (U/L)	-0.226	p < 0.001
TGF-β1 (pg/ml)	-0.260	p < 0.001
ICAM-1 (KU)	0.209	0.002
PIV	0.252	p < 0.001

Note: IL, interleukin; TNF, tumor necrosis factor; CRP, C-reactive protein; EPO, Erythropoietin; TGF-β1, Transforming Growth Factor beta-1; ICAM-1, Intercellular Adhesion Molecule-1; PIV, Pan-immune-inflammation value.

= 0.002), ICAM-1 levels (P = 0.002), and PIV (P < 0.001). Negative correlations were found between scar formation and IL-10 (P = 0.043), EPO (P < 0.001), and TGF-β1 (P < 0.001) (**Table 3**). These findings highlight the role of both pro-inflammatory mediators and psychosocial factors in the development of scars in this patient cohort.

Multivariate logistic regression in the training set

Elevated TNF-α levels (P = 0.003) and ICAM-1 levels (P = 0.003), as well as increased PIV (P < 0.001) were strongly associated with an increased risk of scarring. In contrast, lower IL-10 levels (P = 0.003), and decreased EPO and TGF-β1 levels were inversely associated with the risk of scar formation (P = 0.001 for

Table 4. Multivariate logistic regression analysis of scar formation and related serum inflammatory markers

Risk Factors	β	SE	Wald	OR (95% CI)	P
IL-10 (μg/L)	-0.352	0.117	-2.997	0.704 (0.559-0.885)	0.003
TNF-α (pg/ml)	0.154	0.052	2.946	1.167 (1.053-1.293)	0.003
EPO (U/L)	-0.129	0.040	-3.230	0.879 (0.812-0.950)	0.001
TGF-β1 (pg/ml)	-0.110	0.032	-3.468	0.896 (0.842-0.953)	< 0.001
ICAM-1 (KU)	2.416	0.809	2.987	11.196 (2.294-54.634)	0.003
PIV	2.287	0.528	4.335	9.848 (3.501-27.703)	< 0.001

Note: IL, interleukin; TNF, tumor necrosis factor; EPO, Erythropoietin; TGF-β1, Transforming Growth Factor beta-1; ICAM-1, Intercellular Adhesion Molecule-1; PIV, Pan-immune-inflammation value.

both) (**Table 4**). These findings indicate that serum pan-immune inflammation markers, including PIV, TNF-α, ICAM-1, IL-10, EPO, and TGF-β1, are independent risk factors for scar formation in patients with facial burns.

Establishment of combined predictive model in the training set

This study integrated these identified independent risk factors and constructed a combined predictive model for scar formation in patients with facial burns. The model demonstrated good predictive value, evidenced by an area under the curve (AUC) of 0.815 (**Figure 2**).

General information in the test set

In examining the demographic and baseline characteristics of patients in the test set (N = 144), no statistically significant differences were observed between the groups with and without scar formation in relation to age, BMI, education level, gender, employment status, residential status, smoking history, alcohol consumption history, marital status, degree of burn, total burn area, and burn cause (P > 0.05) (**Table 5**). However, a significant difference was identified in the occurrence of aging signs between the two groups (P = 0.033), suggesting a potential link between aging signs and scar formation in patients with facial burns.

Serum inflammatory factors in the test set

IL-10 levels were lower while TNF-α levels were higher in the scar formation group (P = 0.02, P = 0.006). CRP levels showed no significant difference (P = 0.224) between the two groups. EPO levels (P = 0.002) and TGF-β1 levels (P < 0.001) were significantly decreased in the scar formation group. ICAM-1 levels (P = 0.002) and PIV were markedly elevated in the scar formation group (P < 0.001) (**Table 6**). These findings indicate a strong association between elevated serum inflammatory factors and the presence of scar formation in patients with facial burns.

Skindex-16 subscale score in the test set

The scar formation group reported higher Symptoms scores (P = 0.005), Emotional scores (P = 0.004), and Functioning scores (P = 0.006) (**Figure 3**). These results indicate that scar formation was associated with a greater impact on symptoms, emotional wellbeing, and functioning as measured by the Skindex-16, suggesting a broader psychosocial effect of scar formation in patients with facial burns.

Establishment of combined predictive model in the test set

The constructed predictive model was further validated in the test set, and it also yielded a good predictive value, evidenced by an AUC of 0.845 (**Figure 4**).

Discussion

In this study, we developed a predictive model to understand the relationship between serum PIV levels and scar formation in patients with facial burns. One of the most significant findings from our analysis was the association between increased pro-inflammatory markers and the risk of scar formation. Elevated levels of TNF-α and ICAM-1 were strongly correlated with scar formation. TNF-α is a potent pro-inflammatory cytokine involved in systemic inflammation and it plays a key role in the acute phase reaction [20]. Consistent with our find-

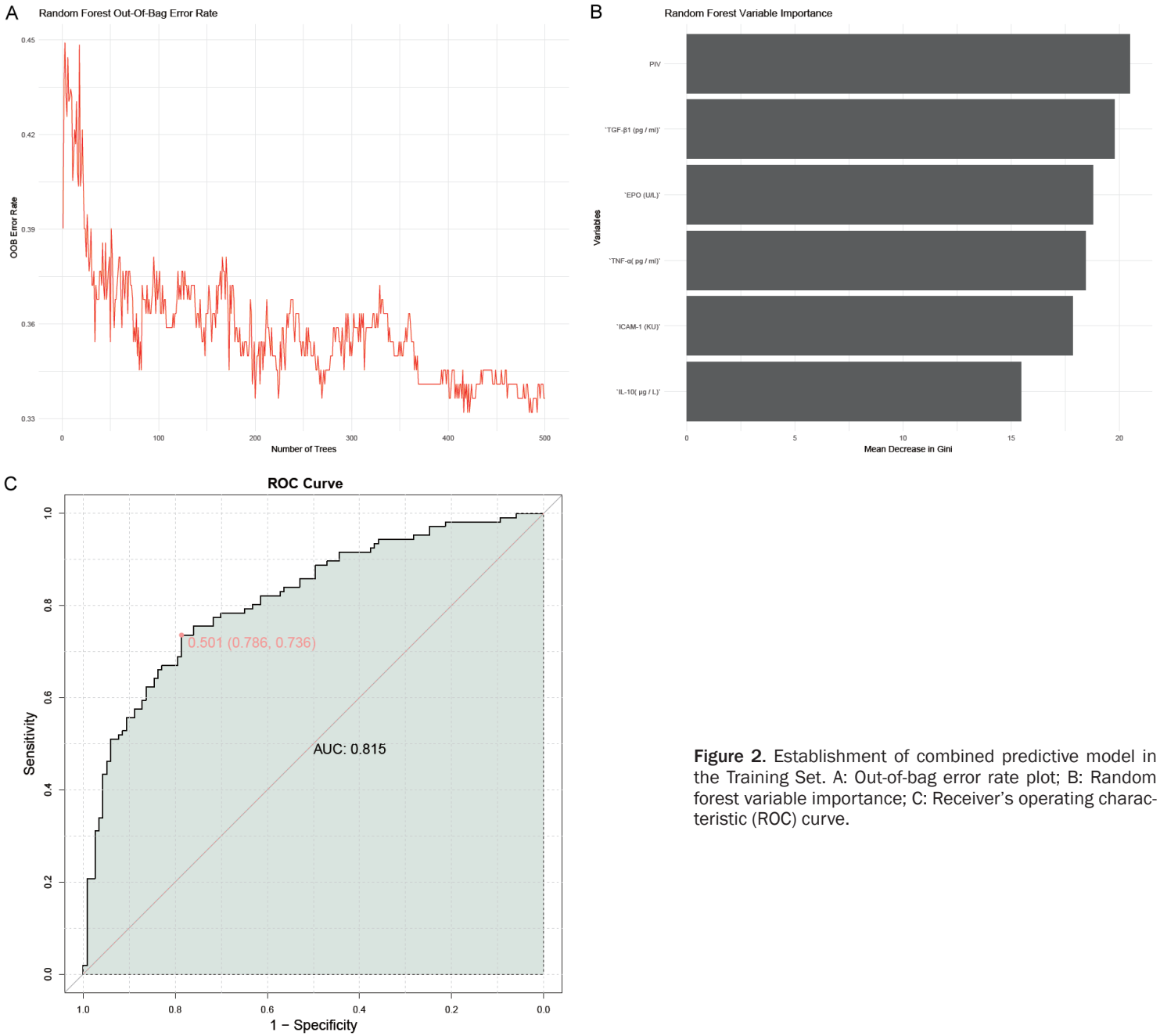

Figure 2. Establishment of combined predictive model in the Training Set. A: Out-of-bag error rate plot; B: Random forest variable importance; C: Receiver's operating characteristic (ROC) curve.

Table 5. Comparison of demographic and baseline characteristics between two patient groups in the test set

Parameters	Scar Formation (n = 66)	No Scar Formation (n = 78)	t/χ^2	P
Age (years)	43.12 ± 11.23	45.54 ± 12.45	1.217	0.226
BMI (kg/m^2)	25.34 ± 3.56	25.12 ± 3.45	0.375	0.708
Education level (years)	12.56 ± 3.12	12.67 ± 3.21	0.213	0.831
Gender [n (%)]			0.003	0.955
Male	35 (53.03%)	41 (52.56%)		
Female	31 (46.97%)	37 (47.44%)		
Employment, work for pay [n (%)]	48 (72.73%)	58 (74.36%)	0.049	0.825
Residential status [n (%)]			0.09	0.765
Urban	39 (59.09%)	48 (61.54%)		
Rural	27 (40.91%)	30 (38.46%)		
Smoking history [n (%)]	21 (31.18%)	22 (28.21%)	0.223	0.637
Alcohol consumption history [n (%)]	18 (27.27%)	19(24.36%)	0.159	0.69
Marital status [n (%)]			0.145	0.93
Married	39 (59.09%)	47 (60.26%)		
Single	18 (27.27%)	22 (28.21%)		
Divorced	9 (13.64%)	9 (11.54%)		
Aging signs [n (%)]	29 (43.94%)	21 (26.92%)	4.567	0.033
Degree of burn [n (%)]			0.266	0.606
Superficial second-degree burn	31 (46.97%)	40 (51.28%)		
Deep second-degree burn	35 (53.03%)	38 (48.72%)		
Total burn area (%)	8.74 ± 2.34	8.42 ± 2.45	0.79	0.431
Burn cause [n (%)]			0.137	0.987
Flame Burn	26 (39.39%)	32 (41.03%)		
Scald Burn	22 (33.33%)	26 (33.33%)		
Electric Burn	10 (15.15%)	12 (15.38%)		
Chemical Burn	8 (12.12%)	8 (10.26%)		

Note: BMI: body mass index.

Table 6. Comparison of serum inflammatory factors between two patient groups in the test set

Parameters	Scar Formation (n = 66)	No Scar Formation (n = 78)	t	P
IL-10 (μg/L)	4.02 ± 1.35	4.56 ± 1.42	2.343	0.02
TNF-α (pg/ml)	12.64 ± 3.12	11.01 ± 3.14	2.765	0.006
CRP (mg/L)	10.22 ± 3.34	9.56 ± 3.15	1.221	0.224
EPO (U/L)	18.21 ± 4.12	20.36 ± 4.05	3.149	0.002
TGF-β1 (pg/ml)	25.17 ± 5.21	28.21 ± 5.12	3.526	< 0.001
ICAM-1 (KU)	0.84 ± 0.21	0.74 ± 0.19	3.172	0.002
PIV	1.38 ± 0.32	1.17 ± 0.30	4.1	< 0.001

Note: IL, interleukin; TNF, tumor necrosis factor; CRP, C-reactive protein; EPO, Erythropoietin; TGF-β1, Transforming Growth Factor beta-1; ICAM-1, Intercellular Adhesion Molecule-1; PIV, Pan-immune-inflammation value.

ings, Zhou et al. [21] found that elevated TNF-α levels are associated with prolonged inflammatory responses, leading to excessive fibroblast activity and collagen deposition, which contribute to hypertrophic scars. ICAM-1, an adhesion molecule, is crucial in leukocyte endothelial transmigration [22, 23], and its elevation may suggest enhanced inflammatory cell infiltration into the burn wound area, thereby sustaining the inflammatory response and exacerbating

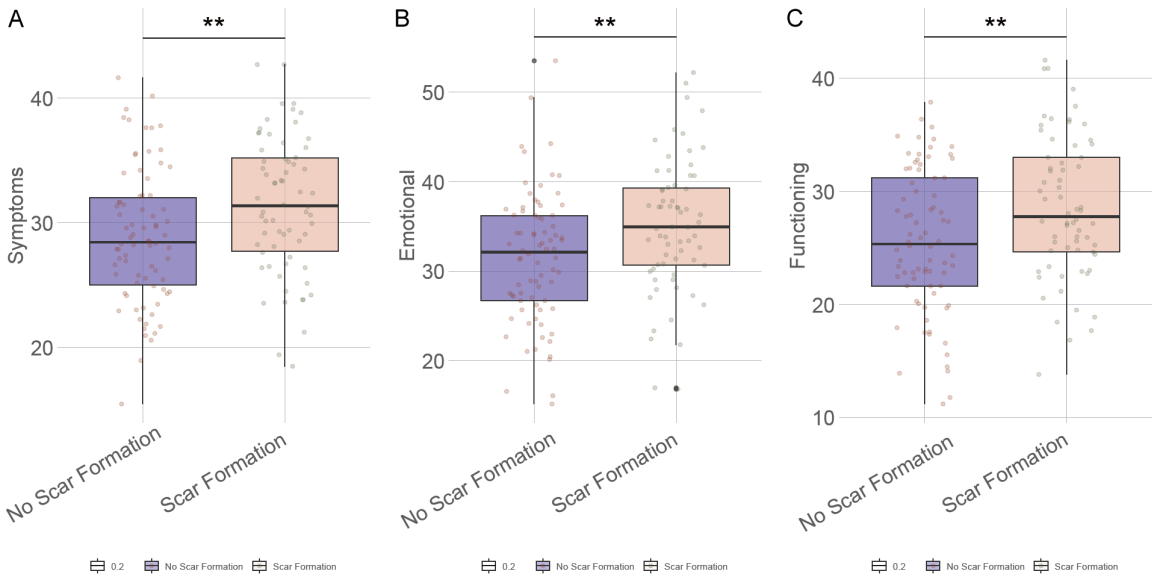

Figure 3. Comparison of Skindex-16 subscale scores between two groups of patients in the Test set. A: Symptoms; B: Emotional; C: Functioning. **: P < 0.01.

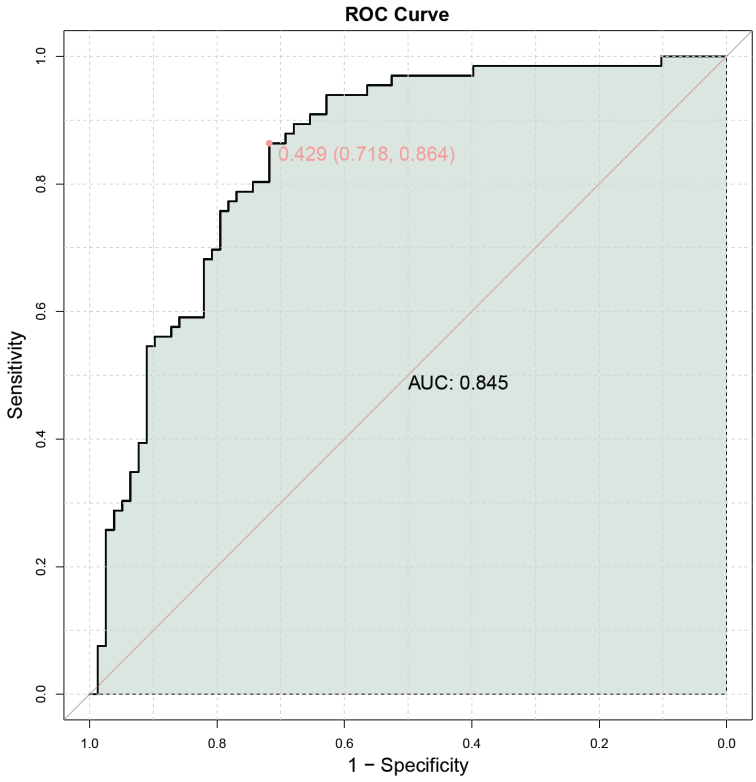

Figure 4. Validation of the model's predictive performance in the Test Set.

scarring. These results align with Oley et al.'s [24] observation that higher ICAM-1 levels correlate with more severe scarring outcomes. In summary, our study confirms the role of TNF-α and ICAM-1 in promoting scar formation and supports previous research indicating their involvement in persistent inflammatory responses following burns.

Conversely, our study found that high levels of IL-10, EPO, and TGF-β1 were inversely related to scar formation, implicating their protective roles. IL-10 is known for its anti-inflammatory properties, often acting to inhibit the synthesis of pro-inflammatory cytokines and reducing tissue damage [25]. The inverse relationship between IL-10 levels and scar formation highlights its regulatory role in maintaining inflammatory equilibrium, potentially preventing excessive scar tissue development. EPO's protective effects might be attributed to its non-hematopoietic activities, including anti-apoptotic effects and promotion of angiogenesis, which contribute to proper wound healing and prevention of scar tissue formation [26, 27]. TGF-β1, while historically linked to fibrosis and scarring, it also plays a

complex role in wound healing; at certain levels, it facilitates appropriate tissue repair and regeneration without leading to fibrosis [28, 29]. Research by Elbialy et al. [30] similarly demonstrated that controlled levels of TGF-β1 can promote healing without excessive scarring. This study underscores the protective roles of IL-10, EPO, and TGF-β1 in mitigating scar formation, highlighting their potential as therapeutic targets in managing scar formation following burn injuries.

This study also contributes to the understanding of the psychosocial aspects of scar formation as evidenced by the Skindex-16 scores. Patients with scar formation experienced higher levels of symptoms, emotional distress, and impaired functioning [31, 32]. These results underline the multidimensional impact of scarring, which extends beyond physical disfigurement to affect psychological and social well-being. The chronic psychological stress associated with visible scars might exacerbate inflammatory processes through neuroendocrine pathways, thereby creating a feedback loop that could maintain an inflammatory environment conducive to scar formation [33, 34]. Research by Jeschke et al. [35] has shown that psychological stress can indeed modulate immune responses, potentially influencing the healing process and scar outcome. These highlight the necessity for a holistic approach to burn treatment, incorporating psychological support as an integral part of the therapeutic regimen. In summary, our findings emphasize the importance of addressing both physical and psychosocial factors in burn care to improve overall patient outcomes.

From a clinical perspective, the findings of this study emphasize the importance of early interventions aimed at modifying inflammatory responses in burn patients. This could involve the use of anti-inflammatory treatments during the acute phase of burn care to modulate cytokine profiles, accelerate wound healing, and minimize scar tissue formation. The predictive model developed herein could be instrumental in identifying high-risk patients who would benefit the most from such targeted interventions. Moreover, studies like ours provide support for the development of personalized medicine approaches, where treatment protocols are tailored to individual patient characteristics and biomarker profiles [36-38]. Additionally, the robust association of serum markers like PIV with scar risk could pave the way for developing diagnostic assays that offer rapid and reliable risk stratification based on immunoinflammatory profiles. Our study suggests the potential utility of PIV as a biomarker for predicting scar risk.

Logistic regression analysis identified several independent predictors of scar formation, strengthening the validity of the model by accounting for confounding factors. However, while these statistical models were effective for prediction and provided insight into the relative importance of different variables, they should be complemented by mechanistic studies. Future research should focus on experimental models to clarify the precise biological mechanisms through which these cytokines and growth factors influence scar formation at the molecular and cellular levels. Understanding these pathways could lead to the identification of new therapeutic targets or modification of existing treatment protocols. For instance, work by Kim et al. [39] explored how specific signaling pathways are activated during scar formation, offering promising directions for future investigations. In summary, while our study provides valuable insights into predicting scar risk, further research is necessary to uncover the underlying biological mechanisms.

This study has limitations that should be considered when interpreting the results. Being retrospective in nature, the study is subject to inherent biases such as selection and observational bias. Moreover, the model was developed using data from a single institution, which may limit its generalizability across different populations and geographic regions. Multi-center studies with larger sample sizes and diverse patient demographics are needed to validate the model's predictive capability. Furthermore, while we have considered major inflammatory and anti-inflammatory markers, the complex dynamics of wound healing and scar formation involve a broader range of cytokines, chemokines, and growth factors that may not have been captured in this study. Therefore, the findings in this study should be interpreted within the context of these limitations, and further validation is necessary to confirm the model's effectiveness in broader settings.

Conclusion

In conclusion, this study highlights the intricate relationship between PIV and scar formation in facial burn patients, emphasizing both biological and psychosocial dimensions. The predictive model developed serves as a valuable tool for clinicians to assess scar risk and tailor patient management accordingly. By integrating advanced wound care technologies with psychosocial support and targeted modulation of immune responses, there is significant potential to improve outcomes for individuals recovering from facial burns. Continued exploration into the molecular mechanisms underlying scar formation is crucial for refining therapeutic strategies that mitigate scarring while promoting optimal wound healing.

Disclosure of conflict of interest

None.

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