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REVIEW

A Comprehensive Review of Predictive Precision in Scar Medicine: From Molecular Predictors to Machine Learning Models

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Abstract: Scars—including keloids, hypertrophic scars, and acne scars—pose substantial functional and psychosocial burdens that current empirical treatments often address by trial-and-error. Quantitative evidence now supports a precision framework. Validated clinical tools (eg, VSS, POSAS) and imaging modalities (3D photogrammetry; high-frequency ultrasound elastography) provide objective baselines, while emerging AI models deliver measurable gains: an automated scar-type classifier achieved precision 80.7%, recall 71.0%, AUC 0.846 for image-based categorization, and a clinical recurrence model for keloids reported AUC 0.889 with sensitivity 78.7% and specificity 86.8%, enabling earlier risk-stratified interventions and fewer ineffective treatment cycles in model-informed pathways. We synthesize cytokine/fibroblast signatures and genetic predisposition with multimodal (clinical-imaging-molecular) learning, detail validation challenges, and propose actionable safeguards (TRIPOD+AI-aligned reporting, internal-external validation, bias audits, SHAP-based interpretability, and federated learning to preserve privacy and improve generalizability). A pragmatic roadmap—including funding mechanisms, stakeholder roles, and a barrier-solution matrix—aims to accelerate translation toward predictive, preventive, and personalized scar care.

Keywords: scar management, predictive modeling, fibroblast phenotype, machine learning, precision medicine

Introduction: The Need for Predictive Precision in Scar Medicine

The Clinical Burden of Keloids, Hypertrophic Scars, and Acne Scars

Keloids, hypertrophic scars, and acne scars impose a substantial clinical burden on patients. Keloids and hypertrophic scars are fibroproliferative disorders resulting from abnormal wound healing.[1] These scars can be aesthetically disfiguring, functionally debilitating, and emotionally distressing.[2] Common causes include trauma, burn, surgery, and acne.[1] For instance, a retrospective study of 6,249 patients found that hypertrophic scars and keloids were more commonly associated with Black/African American individuals (OR = 1.74, $P < 0.01$).[3], highlighting ethnic disparities where individuals of African, Asian, and Hispanic descent exhibit higher prevalence due to genetic factors, skin pigmentation, and fibroblast hyperactivity. These disparities are linked to specific genetic pathways, such as TLR4 polymorphisms that modulate inflammatory responses, and susceptibility loci identified through genome-wide association studies (GWAS), including variants in genes like NEDD4 and FOXO1 that influence fibroblast activity and extracellular matrix regulation.[4] Acne scars, on the other hand, are a frequent sequela of acne vulgaris, which affects over 90% of adolescents and persists into adulthood in 12–14% of cases.[5] Acne scars can be classified into atrophic and hypertrophic types, with atrophic scars being more prevalent. They can cause significant psychological and social implications, negatively impacting patients' quality of life.[5] These distinct clinical features necessitate tailored therapeutic approaches based on

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scar type, location, and progression pattern. Figure 1 illustrates the morphological differences and typical anatomical locations of keloid, hypertrophic, and acne scars, emphasizing their clinical heterogeneity and patient impact.

Limitations of Current Empirical Treatment Approaches

Current empirical treatment approaches for scars have several limitations. These treatments often rely on a one - size - fits - all strategy, without considering individual patient characteristics. For example, corticosteroid injection, a common treatment for keloids and hypertrophic scars, may not be effective for all patients, and can lead to side effects such as skin atrophy.[6] Moreover, the lack of accurate prediction of treatment response means that patients may undergo multiple ineffective treatments, leading to delays in proper management. Existing methods also struggle to account for the complex interplay of genetic, biological, and environmental factors that influence scar formation and treatment outcomes. This lack of precision in treatment selection can result in suboptimal results, increased healthcare costs, and patient dissatisfaction.

Rationale for Predictive and Personalized Strategies

Predictive and personalized strategies in scar medicine are essential to overcome the limitations of current approaches. By leveraging a patient's genetic, molecular, and clinical characteristics, these strategies can tailor treatment plans to individual needs. For example, in lung adenocarcinoma, multi-omics and machine-learning approaches have been used to develop personalized treatment strategies based on B-cell-associated gene signatures.[7] Similarly, in dermatology, multi-modal integration has been applied in conditions like psoriasis, combining clinical imaging with biomarker profiles to predict flare-ups and treatment responses. In the context of scar medicine, understanding a patient's genetic predisposition, cytokine profiles, and fibroblast phenotypes can help predict treatment response. This enables the selection of the most appropriate treatment modality from the start, reducing the need for trial-and-error treatment and improving patient outcomes. Personalized strategies also have the potential to enhance patient satisfaction by providing more targeted and effective care.

Overview of Prognostic Tools and Modeling Methodologies

Prognostic tools and modeling methodologies in scar medicine aim to predict treatment outcomes and guide clinical decision - making. Methodological quality assessment tools are available to evaluate the reliability of diagnosis and prognosis research.[8] Machine - learning - based clinical prediction models, such as regression - based, non - regression - based, and ensemble models, are increasingly being developed.[9] These models can analyze a variety of data, including clinical, imaging, and molecular data, to predict scar recurrence, treatment response, and other outcomes. However,

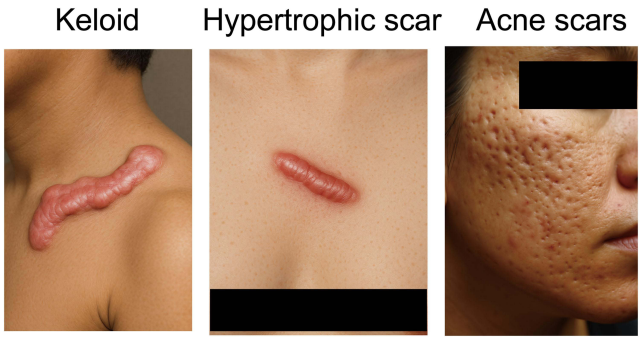

Figure 1 Illustrative comparison of the clinical presentations of keloid, hypertrophic, and acne scars, highlighting differences in morphology, location, elevation, and pigmentation. The keloid scar (left) appears as a raised, irregular, pink-to-red mass extending beyond the original wound boundaries, often seen on the neck or shoulders due to excessive collagen deposition. The hypertrophic scar (center) is elevated and firm but confined within the original wound margins, typically presenting as a linear, ridged lesion with variable pigmentation. Acne scars (right) are predominantly atrophic, manifesting as pitted or depressed areas on the face, with irregular texture and potential hyperpigmentation, resulting from inflammatory acne sequelae. These examples underscore the heterogeneous impact on aesthetics and function across scar types. All images were obtained with institutional review board (IRB) approval from Union hospital of Fujian Medical University (KY-2025-031-K01) and informed patient consent. Imaging protocols involved high-resolution digital photography (Canon EOS 5D Mark IV, 30.4 MP) unDer Standardized lighting (5000K LED, neutral background) at a fixed distance of 50 cm.

challenges such as sample size estimation, development and validation analysis methods, and ensuring model generalizability need to be addressed to improve the quality of these models.[9]

Aim and Structure of the Review

The aim of this review is to comprehensively explore the field of predictive precision in scar medicine. It will first examine validated scar assessment tools, followed by biological and molecular predictors of treatment response. Emerging machine - learning and AI - based prediction models will then be discussed, along with their integration into clinical decision - making. Ethical and regulatory considerations will be analyzed, and future directions for research will be outlined. The review is structured to provide a detailed and systematic overview of the current state - of - the - art in scar prediction, highlighting the need for further research and development to achieve a precision medicine framework in scar management.

Validated Scar Assessment Tools: Foundations of Prediction

Vancouver Scar Scale (VSS): Strengths and Limitations

The Vancouver Scar Scale (VSS) is a widely used tool for assessing scar characteristics. It evaluates scars based on four parameters: vascularity, pliability, thickness, and height.[10] One of its strengths is its simplicity, making it easy to use in clinical practice. A meta - analysis of 7 randomized controlled trials involving 216 participants found that the VSS could effectively evaluate the improvement of wounds treated with skin substitutes compared to skin grafts alone, with a mean change of 1.38 (95% CI: 0.13–2.63; $p = 0.03$).[10] However, the VSS also has limitations. It has been criticized for its subjectivity, as different raters may have varying interpretations of the scale. Additionally, it does not fully capture the patient's perspective on scar quality, such as pain and itching, which are important factors affecting patient satisfaction.[11]

Patient and Observer Scar Assessment Scale (POSAS)

The Patient and Observer Scar Assessment Scale (POSAS) consists of two separate six - item scales, one for the patient and one for the observer. It assesses a wide range of scar characteristics, including pain, itch, color, stiffness, thickness, and surface. In a prospective study of 30 patients with facial scars, the POSAS was used to evaluate the outcome of treatment with self - drying silicone gel. The patient - rated scale reported the greatest improvement in color, stiffness, and thickness, while the observer - rated scale primarily reported improvement in vascularization, pigmentation, and pliability. Rasch analysis has demonstrated the POSAS to be a reliable and valid scale for measuring scar quality, with person reliability of the Observer Scale and Patient Scale being 0.82 and 0.77, respectively.[12]

Digital Imaging and 3D Volumetric Analysis Tools

Digital imaging and 3D volumetric analysis tools offer objective and quantitative assessment of scars. Digital holography, These tools allow clinicians to objectively assess scar progression and treatment response over time using quantitative metrics.As shown in Figure 2, traditional 2D tools offer basic measurements, while modern 3D imaging technologies provide comprehensive volumetric and structural assessments critical for precision monitoring.for example, can be used to obtain 3D images of scars and estimate their biovolume.[13] In a study of soft - tissue volumetric changes following monobloc distraction procedure, a digital 3D photogrammetry system was used to record volumetric changes for skeletal and soft - tissue midface structures. The results showed a mean increase in 3D volumetric soft - tissue changes of 99.5 ± 4.0 cm³ ($P < 0.05$) at 6 weeks and 94.9 ± 3.6 cm³ ($P < 0.05$) at 1 - year follow - up.[14] These tools can provide detailed information about scar volume, shape, and surface area, which is valuable for monitoring treatment response and predicting long - term outcomes.

Ultrasound and Elastography in Scar Evaluation

Ultrasound and elastography are useful for evaluating the elastic properties of scars. High - frequency ultrasound (HFUS) elastography, for instance, can estimate the elasticity of scars by using the Lamb wave model. In a study involving phantom and human studies, the estimated shear moduli were 12.8 ± 5.4 kPa and 74.8 ± 26.8 kPa for healthy skin and

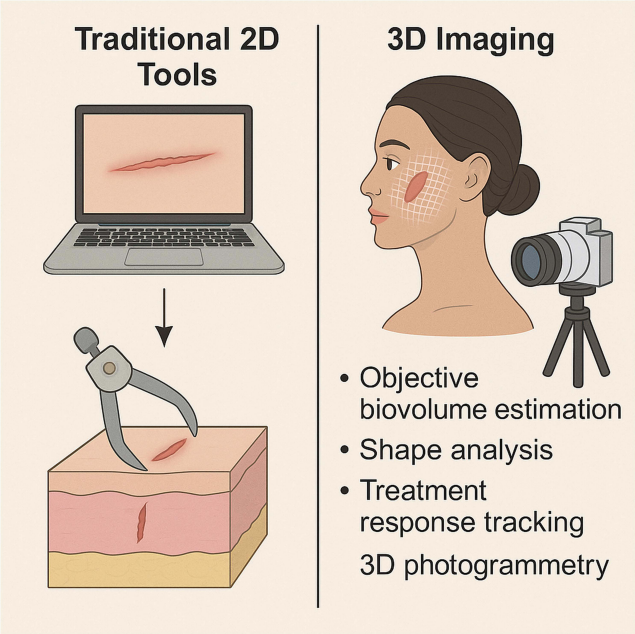

Figure 2 Advanced imaging tools in scar assessment. Diagram comparing traditional 2D scar evaluation with modern 3D volumetric imaging techniques, highlighting advantages such as objective biovolume estimation, shape analysis, and treatment response tracking using digital holography and 3D photogrammetry. No clinical images were used; schematic generated via software (Adobe Illustrator). Ethics approval not applicable.

scar tissue, respectively.[15] Evaluation of the uterine scar stiffness in women with previous Cesarean section by ultrasound elastography has shown that the stiffness of the uterine scar is higher than that of the surrounding myometrium, with a mean strain ratio of 1.8 ± 0.7.[16] These techniques can provide insights into the internal structure and mechanical properties of scars, which can help in treatment planning.

Gaps in Traditional Scoring Systems for Predicting Outcomes

Traditional scoring systems for predicting scar outcomes have several gaps. They often rely on limited clinical and morphological features, without incorporating molecular or genetic information. For example, in other medical fields, conventional scoring systems for predicting the severity and outcomes of acute pancreatitis have shown varying degrees of accuracy, with some scoring systems being better at predicting severity while others at predicting mortality.[17] In scar medicine, existing scoring systems may not accurately account for the complex biological processes underlying scar formation and treatment response. This lack of comprehensiveness can lead to inaccurate predictions, limiting their utility in guiding personalized treatment decisions. There is a need for more comprehensive scoring systems that integrate multiple data sources to improve the prediction of scar outcomes.The summary of different assessment tools were showed in Table 1.

Biological and Molecular Predictors of Treatment Response

Cytokines and Inflammatory Biomarkers (eg, IL - 4, IL - 13, TGF - β)

Cytokines and inflammatory biomarkers play a crucial role in scar formation and treatment response. In trauma patients, high levels of pro - inflammatory cytokines such as IL - 6, IL - 8, and TGF - β, and low levels of anti - inflammatory cytokine IL - 4 were found to be reliable markers of immune reactivity.[18] In asthma, the presence of a Th2 endotype, indicated by markers such as eosinophil count, fraction of exhaled nitric oxide, and immunoglobulin E, is associated with the role of cytokines like IL - 5, IL - 13, and IgE.[19] In the context of scarring, TGF - β is known to be involved in fibroblast activation and extracellular matrix deposition. Understanding the role of these cytokines can help in developing targeted therapies and predicting treatment response.

Table 1 Summary of Validated Scar Assessment Tools

Tool	Parameters Assessed	Strengths and Limitations
Vancouver Scar Scale (VSS)	Vascularity, pliability, thickness, height	Strengths: Simple and widely used; Limitations: Subjective, lacks patient perspective[9,10]
Patient and Observer Scar Assessment Scale (POSAS)	Pain, itch, color, stiffness, thickness, surface	Strengths: Includes patient and observer views, reliable (reliability 0.77–0.82); Limitations: Time-consuming[11]
Digital imaging and 3D volumetric analysis	Volume, shape, surface area	Strengths: Objective, quantitative; Limitations: Requires specialized equipment[12,13]
Ultrasound and elastography	Elasticity, stiffness	Strengths: Non-invasive, measures internal properties; Limitations: Operator-dependent[14,15]

Fibroblast Phenotypes and Collagen Remodeling Markers

Fibroblast phenotypes and collagen remodeling markers are important determinants of scar characteristics. Keloid dermal fibroblasts exhibit a fibrotic phenotype with high levels of skin fibrosis markers, ECM remodeling enzymes, and migration ability.[20] In a study on fibroblast - populated collagen lattices, tissue transglutaminase was found to dominate early calcium - dependent remodeling, while lysyl oxidase contributed more at later stages.[21] In idiopathic pulmonary fibrosis, changes in collagen macro/supramolecular structure, as characterized by second harmonic generation microscopy, were observed, suggesting that these alterations could serve as biomarkers for disease diagnosis and progression.[22] These markers can provide insights into the underlying mechanisms of scar formation and help predict how scars will respond to treatment.

Genetic Predisposition and Epigenetic Modulation

Genetic predisposition and epigenetic modulation influence scar formation and treatment response. In some progeroid syndromes, causative mutations have been linked to epigenetic age acceleration.[23] In Alzheimer's disease, genetic features play a role in the formation of the epigenetic landscape, and non-coding regulatory SNPs have been identified that may affect epigenetic mechanisms.[24] In the context of scarring, certain genetic variants may predispose individuals to develop keloids or hypertrophic scars. Epigenetic modifications, such as DNA methylation and histone acetylation, can also regulate gene expression related to scar formation, with recent studies showing hypermethylation of anti-fibrotic genes in keloid fibroblasts, leading to persistent fibrosis.[20] Understanding these genetic and epigenetic factors can aid in predicting an individual's risk of developing abnormal scars and their response to treatment. These molecular and genetic elements interact in complex ways, influencing scar formation and persistence. Figure 3 summarizes key biological mechanisms—including fibrotic fibroblasts, TGF-β signaling, and genetic susceptibility—that drive pathological scarring and extracellular matrix remodeling.

Skin Phototype and Ethnicity as Predictive Factors

Skin phototype and ethnicity can be predictive factors in scar management. Self - reported pigmentary phenotypes and race are significant but incomplete predictors of Fitzpatrick skin phototype.[25] In an Ecuadorian population, ethnicity, eye color, and hair color were found to be significant independent predictors of Fitzpatrick skin phototype scale (FSPTS).[26] Different ethnic groups may have varying susceptibilities to certain types of scars, and skin phototype can influence the risk of sunburn and subsequent scarring. For example, individuals with lighter skin phototypes may be more prone to sun - related scarring. Considering these factors can help in tailoring preventive and treatment strategies.

Response Biomarkers for Steroid, Laser, and Immune - Targeted Therapy

Response biomarkers for different therapies can help predict treatment efficacy. In metastatic melanoma patients treated with targeted therapy, genes involved in immune re - induction, such as CXCL - 10, SERPING1, PDL1, and PDL2, were identified as potential biomarkers of response.[27] For steroid therapy in scar treatment, understanding the molecular pathways affected by steroids can help identify biomarkers that predict which patients will respond well. In laser therapy,

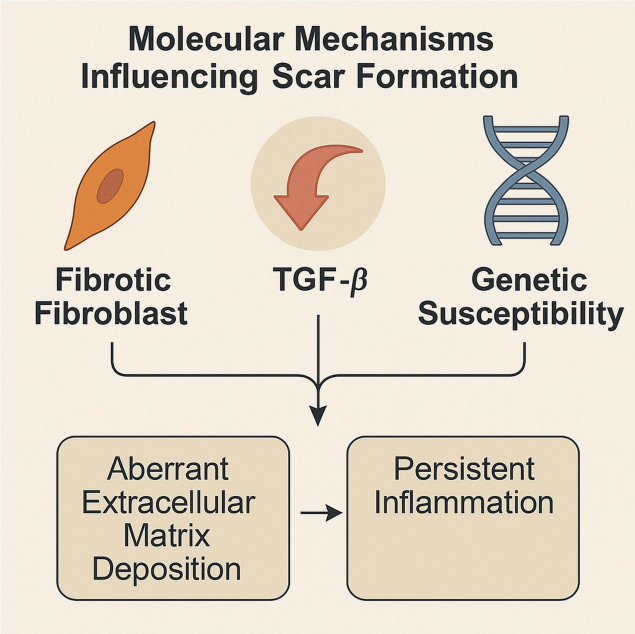

Figure 3 Molecular mechanisms influencing scar formation. Schematic of key biological and genetic factors involved in scar development. Includes representation of fibrotic fibroblast phenotypes, TGF-β signaling, and genetic susceptibility contributing to aberrant extracellular matrix deposition and persistent inflammation. No clinical images were used; schematic generated via software (Adobe Illustrator). Ethics approval not applicable.

biomarkers related to tissue repair and remodeling may indicate the likelihood of a positive outcome. Identifying these response biomarkers can optimize treatment selection and improve patient outcomes.

Emerging Machine Learning and AI - Based Prediction Models

Overview of Machine Learning in Dermatology and Scar Research

Machine learning has the potential to revolutionize dermatology and scar research. In dermatology, it has been applied in various areas, such as disease classification using clinical and dermatopathology images, assessment of skin diseases using mobile applications, and facilitating large - scale epidemiology research.[28] In scar research, machine - learning algorithms can analyze a large amount of data, including clinical, imaging, and molecular data, to predict scar outcomes. For example, a study developed a computer vision algorithm using automated machine learning to diagnose four scar types, achieving an average precision of 80.7%, an average recall of 71%, and an area under the curve (AUC) of 0.846.[29] These applications can assist in early diagnosis, treatment planning, and predicting treatment response.

Supervised Models for Scar Recurrence Prediction (eg, Logistic Regression, Random Forest)

Supervised models, such as logistic regression and random forest, can be used for scar recurrence prediction. A logistic regression analysis of 132 keloid scar patients identified infection, family history of keloid scars, relatively large scar size, and the absence of radiotherapy and local hormone therapy as independent risk factors for postoperative recurrence.[30] The prediction based on these joint independent risk factors yielded an area under the ROC curve of 0.889, with a sensitivity of 78.72%, a specificity of 86.84%, and an accuracy of 81.06%.[30] Another study compared logistic regression, decision tree, and random forest models for keloid recurrence prediction. The logistic regression model showed the best performance in terms of the area under the ROC curve, highlighting the significance of factors like KAAS, mean arterial pressure levels, postoperative complications, and the proportion of inflammatory cells.[31]

Neural Networks for Image - Based Scar Classification and Outcome Prediction

Neural networks, especially convolutional neural networks (CNNs), have shown promise in image - based scar classification and outcome prediction. In other medical imaging applications, CNNs have been used for tasks such as detecting myocardial scar from electrocardiogram data, achieving an area under the curve score of 0.89, sensitivity of 70.0%, specificity of 84.3%, and accuracy of 78.0%.[32] For scar classification, neural networks can analyze the morphological and texture features of scar images. By training on a large number of scar images, these networks can learn to distinguish different types of scars and predict treatment outcomes. They can potentially provide more accurate and objective predictions compared to traditional methods.

Integration of Multimodal Data: Clinical, Imaging, and Molecular

The integration of multimodal data, including clinical, imaging, and molecular data, can enhance prediction models in scar medicine. In oncology, harnessing multimodal data integration has the potential to advance precision oncology beyond genomics.[33] In scar research, combining clinical information (such as patient demographics and medical history), imaging data (eg, 3D volumetric images and ultrasound), and molecular data (eg, cytokine profiles and genetic markers) can provide a more comprehensive understanding of scar formation and treatment response. The integration of multimodal datasets is a critical step toward precision scar medicine, enabling a holistic view of patient-specific scar dynamics. Figure 4 outlines how clinical, imaging, and molecular data are fused through machine learning workflows to predict outcomes, stratify patients, and support real-time clinical decision-making. This integrated approach can improve the accuracy of prediction models and enable more personalized treatment strategies. Different machine learning models for scar prediction was showed in Table 2.

Challenges in Model Validation and Generalizability

Model validation and generalizability are significant challenges in machine-learning-based prediction models for scars. Internal-external cross-validation can be used to evaluate the generalizability of prediction models in large clustered datasets.[34] However, many studies on prediction models for scars lack external validation, limiting their generalizability.[35] Additionally, issues such as data heterogeneity, overfitting, lack of interpretability (eg, the "black

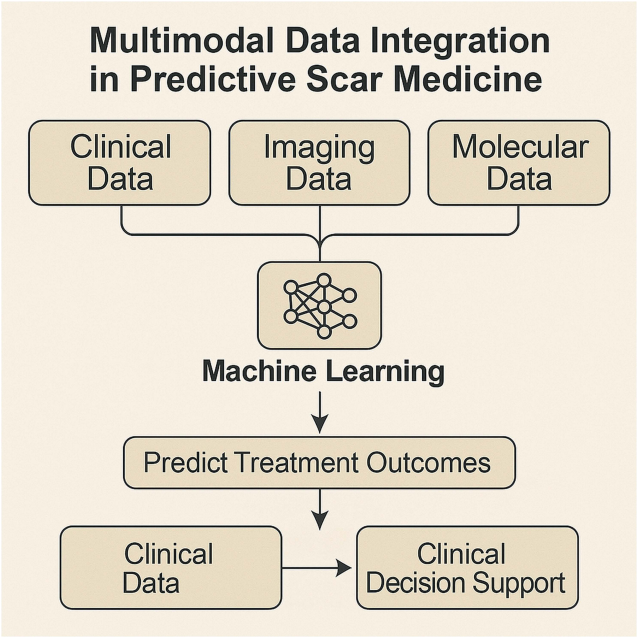

Figure 4 Multimodal data integration in predictive scar medicine. Visual workflow depicting how clinical, imaging, and molecular data are combined in machine learning algorithms to predict treatment outcomes, stratify patients, and support real-time clinical decision-making in scar management. No clinical images were used; schematic generated via software (Adobe Illustrator). Ethics approval not applicable.

Table 2 Summary of Machine Learning Models for Scar Prediction

Model Type	Examples	Performance Metrics and Limitations
Supervised (eg, Logistic Regression, Random Forest)	Keloid recurrence prediction[29,30]	AUC 0.889; Limitations: Risk of overfitting, needs large datasets
Neural Networks (eg, CNNs)	Image-based scar classification[31]	AUC 0.89; Limitations: 'Black box' interpretability, data bias[31]
Multimodal Integration	Clinical + imaging + molecular[32]	Improved accuracy; Limitations: Heterogeneity, lack of external validation[33,34]

box" nature of neural networks making clinical adoption difficult), and potential biases in training data (eg, under-representation of ethnic minorities leading to skewed predictions) can affect the quality of the models. To mitigate overfitting, techniques such as k-fold cross-validation, regularization (eg, L1/L2 penalties), and ensemble methods can be employed. For addressing bias, diverse and representative datasets, along with federated learning approaches that allow model training across decentralized data sources without sharing sensitive information, are recommended. Interpretability can be enhanced using explainable AI tools like SHAP (SHapley Additive exPlanations) values or LIME (Local Interpretable Model-agnostic Explanations), which provide insights into feature contributions and improve clinician trust. Ensuring the reliability and generalizability of these models is crucial for their clinical implementation, as inaccurate models may lead to inappropriate treatment decisions.

Integrative Prediction in Clinical Decision - Making

Stratifying Patients for Intralesional, Surgical, or Laser Interventions

Stratifying patients for different interventions is essential for optimal scar management. Intralesional diode laser pretreatment has been shown to facilitate surgery for orbital venous malformations. In a study of 23 consecutive patients, the mean volume of the malformations dropped significantly from 2366 ± 1887 to 129 ± 119 mm^3 ($t = 5.716$; $p < 0.001$) after intralesional laser treatment, and symptom scores improved significantly from 6.5 ± 1.4 to 1.2 ± 1.0 ($p < 0.001$).[36] For scars, understanding factors such as scar type, location, and patient - specific characteristics can help determine whether intralesional, surgical, or laser interventions are most appropriate. This personalized approach can improve treatment outcomes and reduce the risk of complications.

Risk Calculators and Treatment Algorithms in Development

Risk calculators and treatment algorithms are being developed to aid in clinical decision - making for scar management. In the context of melanoma, risk calculators have been developed to predict the likelihood of cancer recurrence in patients with thin melanomas. These calculators, developed using data from 25,930 Dutch patients and validated in 2,968 Australian patients, provide estimates of the risk of melanoma returning and are freely available online.[37] In scar medicine, similar risk calculators could be developed to predict the risk of scar recurrence, the likelihood of response to different treatments, or the development of complications. Treatment algorithms can then be based on these risk predictions to guide the selection of the most appropriate treatment.

Monitoring Therapeutic Response with Longitudinal Predictive Models

Longitudinal predictive models can be used to monitor therapeutic response in scar treatment. In oncology, longitudinal monitoring of KRAS - mutated circulating tumor DNA has been shown to enable the prediction of prognosis and therapeutic responses in patients with pancreatic cancer.[38] In scar treatment, longitudinal data, such as changes in scar characteristics (eg, size, texture, and color) over time, can be analyzed using predictive models. These models can help clinicians assess whether a treatment is effective, adjust treatment plans if necessary, and predict long - term outcomes. For example, changes in collagen remodeling markers or cytokine levels over time can be used to predict the response to a particular therapy.

Real - Time Prediction Platforms and Digital Health Integration

Real - time prediction platforms and digital health integration have the potential to transform scar management. In the digital health era, machine - learning and artificial intelligence approaches can be used to develop real - time stroke risk prediction and integrated care management systems.[39] Similarly, for scars, real - time prediction platforms could analyze data from wearable devices, mobile applications, or in - clinic measurements to provide immediate predictions of treatment response or the risk of scar progression. Digital health integration can also enable better communication between patients and healthcare providers, remote monitoring of scars, and more efficient management of patient data.

Ethical and Regulatory Considerations in Predictive Scar Medicine

Ethical and regulatory considerations are crucial in predictive scar medicine. The increased predictive power of modern diagnostic interventions in personalized medicine raises questions about personal responsibility for health - related behavior and lifestyle.[40] In the context of scar medicine, issues such as the use of genetic and molecular data for prediction, patient consent for data collection and use, and the potential for discrimination based on predicted scar outcomes need to be addressed. Regulatory frameworks are needed to ensure the ethical use of predictive technologies, protect patient privacy, and promote equitable access to personalized scar treatment.

Future Directions and Research Gaps

From Descriptive to Prescriptive Scar Analytics

There is a need to move from descriptive to prescriptive scar analytics. Current research often focuses on describing the characteristics of scars and the factors associated with their formation. However, prescriptive analytics aims to provide actionable recommendations for treatment. For example, in elite sports, the transition from descriptive to prescriptive data analytics has been proposed to guide training process decisions.[41] In scar medicine, prescriptive analytics could use data from scar assessment tools, biological predictors, and prediction models to recommend the most appropriate treatment for an individual patient. This would require integrating multiple data sources and developing more sophisticated algorithms to translate data into treatment recommendations.

Prospective Clinical Trials with Built - in Prediction Components

Prospective clinical trials with built - in prediction components are essential for validating prediction models and improving treatment outcomes. In drug discovery, inClinico, a transformer - based artificial intelligence software platform, has been used to predict the outcome of Phase II clinical trials, achieving 0.88 ROC AUC in a quasi - prospective validation dataset.[42] In scar medicine, prospective clinical trials could enroll patients based on their predicted risk of developing certain types of scars or their predicted response to treatment. By incorporating prediction components, these trials can provide more accurate information about the effectiveness of different treatments in specific patient populations, leading to the development of more personalized treatment strategies.

Development of International Predictive Registries and Datasets

The development of international predictive registries and datasets is crucial for advancing scar medicine. In oncology, the implementation of ICD - 11 in European cancer registries aims to revolutionize cancer data collection, although challenges remain.[43] In scar medicine, international registries could collect standardized data on scar characteristics, patient demographics, treatment outcomes, and biological predictors from multiple centers. These datasets can be used to develop more accurate prediction models, validate existing models across different populations, and identify factors that influence scar formation and treatment response on a global scale.

Multidisciplinary Collaboration in AI - Scar Medicine Interface

Multidisciplinary collaboration is essential at the AI - scar medicine interface. In exoskeleton development, multidisciplinary collaboration adopting user - centered design has been shown to be beneficial, although challenges such as low stakeholder engagement and lack of standard measurement exist.[44] In scar medicine, collaboration between

Table 3 Barriers and Solutions in Implementing Precision Scar Medicine

Barrier	Solution
Limited data availability and heterogeneity	Develop international registries with standardized protocols for data collection and sharing.
Overfitting and bias in ML models	Use federated learning, diverse datasets, and explainable AI tools like SHAP values.
Lack of funding and resources	Secure grants from NIH/ERC and partner with industry for AI tool development.
Ethical and regulatory hurdles	Establish multidisciplinary ethics committees and comply with GDPR/HIPAA standards.
Low stakeholder engagement	Define clear roles (eg, clinicians for validation, researchers for innovation) and conduct workshops.
Translation to clinical practice	Pilot online risk calculators and integrate into electronic health records (EHRs).

dermatologists, plastic surgeons, molecular biologists, data scientists, and other experts is needed. Dermatologists can provide clinical insights, molecular biologists can contribute knowledge of biological mechanisms, and data scientists can develop and validate machine - learning models. This interdisciplinary approach can lead to a more comprehensive understanding of scars and the development of more effective predictive and treatment strategies.

Roadmap Toward a Precision Scar Medicine Framework

A roadmap toward a precision scar medicine framework should include several key steps. First, there is a need to improve the accuracy and generalizability of prediction models by integrating more data sources and validating models in diverse populations. Second, ethical and regulatory issues need to be addressed to ensure the responsible use of predictive technologies. Third, international collaboration in the form of registries and multicenter trials should be promoted to advance the field, with priority given to establishing global scar registries for standardized data sharing and model validation. Fourth, multidisciplinary research should be encouraged to bring together different perspectives. Finally, the translation of research findings into clinical practice should be facilitated to improve patient outcomes, such as through the development of freely accessible online risk calculators similar to those in melanoma.[37] Practical steps include securing funding from sources like the National Institutes of Health (NIH), European Research Council (ERC), or private foundations focused on dermatology; defining stakeholder roles, such as clinicians leading trial design, data scientists handling model development, and ethicists overseeing privacy protocols; and piloting implementation in high-burden regions like Asia and Africa to address ethnic disparities. To operationalize this roadmap, it is essential to recognize the key barriers that currently hinder the implementation of precision scar medicine and to propose pragmatic solutions. Table 3 summarizes these barriers and outlines potential strategies to overcome them, providing a structured framework to guide future research, clinical translation, and policy-making. In contrast to previous reviews emphasizing clinical treatments, such as Bronte et al's focus on non-surgical interventions for hypertrophic and keloid scars in skin of color,[45] this work prioritizes multimodal AI integration for predictive precision, bridging biological insights with computational modeling to enable proactive rather than reactive scar management. This comprehensive approach can help achieve a precision medicine framework in scar management.

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Jinzhao Su and Jingbin Chen contributed equally to this work as co-first authors.

Disclosure

The authors have no competing interests to disclose.

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