

Patient, Lesion, and Surgical Predictors of Keloid Recurrence After Excision: A Systematic Review

Badariyatud Dini

Maulana Malik Ibrahim State Islamic University

Corresponding Author: Badariyatud Dini badariyatud_dini.dr@uin-malang.ac.id

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ABSTRACT

Keloid recurrence after surgical excision remains a significant clinical challenge due to its multifactorial nature involving patient susceptibility, lesion characteristics, and perioperative factors. This systematic review aimed to identify and synthesize prognostic factors associated with keloid recurrence following surgical excision. The review was conducted according to the PRISMA 2020 guidelines, including primary human studies published from January 2020 to September 2026. Relevant studies were retrieved from Scopus, PubMed/MEDLINE, Embase, Web of Science, and CENTRAL. Eligible studies included observational cohorts, case-control studies, and clinical studies reporting postoperative recurrence and prognostic factors. Risk of bias was assessed using the Quality In Prognosis Studies (QUIPS) tool, and findings were synthesized across patient, lesion, and surgical domains. The evidence indicates that recurrence risk is associated with multiple factors, including family history, age, lesion size, clinical activity, anatomical location, mechanical tension, postoperative infection, and wound-related complications. Lesion-related and perioperative factors demonstrated more consistent prognostic relevance than isolated systemic biomarkers. Postoperative therapies appeared mainly as treatment modifiers rather than intrinsic predictors of recurrence. This review provides an integrated prognostic framework by combining individual susceptibility, lesion characteristics, and modifiable surgical factors

INTRODUCTION

Keloids are pathological fibroproliferative scars characterized by excessive extracellular matrix deposition and persistent growth beyond the boundaries of the original injury. Their clinical burden extends beyond cosmetic deformity because they may cause pain, pruritus, functional impairment, and psychosocial distress. Surgical excision remains an important treatment option, particularly for bulky, symptomatic, anatomically deforming, or treatment-resistant lesions. However, excision alone does not eliminate the biological tendency toward abnormal scar formation, and recurrence remains a major clinical limitation. Contemporary management therefore frequently combines surgery with postoperative interventions such as radiotherapy, corticosteroid injection, compression therapy, or other adjuvant strategies to improve local control (Fu et al., 2024; Lawera et al., 2024).

The risk of recurrence after excision is unlikely to be determined by treatment modality alone. Keloid behavior reflects the interaction of patient susceptibility, lesion characteristics, anatomical and mechanical factors, surgical technique, wound healing, and postoperative management. Hao et al. (2023) showed that the Keloid Activity Assessment Scale and postoperative complications contributed to recurrence prediction in patients with chest keloids treated with surgery and radiotherapy. A subsequent study using logistic regression, decision tree, and random forest models identified clinical activity, postoperative complications, inflammatory cell proportion, and mean arterial pressure as potentially informative predictors of recurrence (Hao et al., 2025). These findings indicate that postoperative recurrence is a multifactorial outcome rather than a uniform response to a single therapeutic protocol.

Patient-related characteristics may contribute independently to this variability, although the evidence remains inconsistent. Lee et al. (2025) evaluated preoperative vitamin D status in patients undergoing keloid excision and found no significant association between serum vitamin D levels and recurrence, whereas younger age was associated with a higher recurrence risk after adjustment for relevant covariates. Such findings are important because they demonstrate that biologically plausible factors do not necessarily have consistent prognostic value. At the lesion level, anatomical location, lesion size, clinical activity, and mechanical tension may influence recurrence. Zhang et al. (2025) reported long-term outcomes following excision of large anterior chest keloids reconstructed with intercostal artery perforator propeller flaps, a strategy designed to reduce closure tension. In auricular keloids, Li et al. (2024) also demonstrated that recurrence may vary according to postoperative management following reconstructive surgery.

Surgical factors further complicate recurrence risk. The extent of excision, preservation of peripheral or overlying tissue, closure tension, reconstructive technique, and postoperative wound conditions may modify the inflammatory and mechanical stimuli involved in recurrent fibroproliferation. This concept has increased interest in intralesional and core excision techniques. Lawera et al. (2024) synthesized 608 keloids treated with intralesional excision and demonstrated that recurrence could be meaningfully assessed according to the

surgical approach. Ran et al. (2025) reviewed 20 studies involving 926 keloids treated with core excision and highlighted the unresolved influence of residual keloid tissue and other surgical factors on recurrence. These reviews confirm the relevance of surgical technique, but their primary focus remains the effectiveness of specific operative strategies rather than the broader identification of prognostic determinants across different surgical approaches.

A similar pattern is evident in studies of postoperative radiotherapy. Hwang et al. (2022) evaluated the association between biologically effective electron-beam radiation dose and recurrence after excision, while Fernandes et al. (2024) reported institutional recurrence outcomes following adjuvant radiation. More recent systematic reviews have focused on the timing and delivery of postoperative radiotherapy. Peng et al. (2025) assessed radiotherapy administered within the first 24 hours after excision and examined treatment timing, biologically effective dose, lesion length, and anatomical location, whereas Seth et al. (2026) synthesized the effectiveness and timing of post-excisional radiotherapy. These studies provide clinically important evidence for optimizing adjuvant treatment, but their central question is therapeutic rather than prognostic. They do not provide an integrated synthesis of the patient, lesion, and surgical characteristics that may explain why recurrence occurs despite apparently appropriate excision and postoperative care.

This distinction reveals the principal research gap. Recent systematic reviews have largely been organized around treatment modalities, including intralesional excision, core excision, postoperative radiotherapy, radiotherapy timing, perioperative corticosteroids, and combination therapies (Fu et al., 2024; Lawera et al., 2024; Peng et al., 2025; Ran et al., 2025; Seth et al., 2026). Such evidence is valuable for estimating average recurrence rates under specific treatment protocols, but it does not fully explain interindividual differences in recurrence. Existing prognostic studies provide fragmented evidence on factors such as age, clinical activity, anatomical location, postoperative complications, inflammatory features, lesion characteristics, and wound tension, yet these findings arise from heterogeneous populations, different anatomical sites, variable surgical techniques, inconsistent adjuvant regimens, and predominantly single-center observational designs (Hao et al., 2023; Hao et al., 2025; Lee et al., 2025). The lack of a unified prognostic framework makes it difficult to determine which predictors are consistent, which are site-specific or treatment-dependent, and which remain uncertain.

LITERATURE REVIEW

The novelty of the present review therefore lies in its prognostic rather than treatment-centered orientation. To our knowledge, recent systematic reviews have not specifically integrated patient-related, lesion-related, and surgery-related predictors of recurrence after keloid excision within a single structured framework. Previous reviews have primarily assessed recurrence according to particular excision techniques or postoperative interventions, while individual prognostic studies have developed models within restricted clinical populations (Hao et al., 2023; Hao et al., 2025). This systematic review therefore aims to identify, critically appraise, and synthesize the available evidence on patient, lesion, and surgical predictors of recurrence following keloid excision. By distinguishing intrinsic prognostic factors from treatment-related modifiers, this review seeks to support more precise preoperative risk assessment, surgical planning, postoperative surveillance, and the future development of validated recurrence prediction models for personalized keloid management.

METHODOLOGY

Study Design and Reporting Framework

This systematic review was designed to identify and synthesize prognostic factors associated with keloid recurrence following surgical excision. The review will be conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement and its Explanation and Elaboration document, which provide a 27-item framework for transparent reporting of study identification, selection, appraisal, and synthesis (Page et al., 2021a, 2021b). Because the review addresses prognostic factors rather than comparative treatment effectiveness, the methodological approach will also follow recommendations for systematic reviews and meta-analyses of prognostic factor studies proposed by Riley et al. (2019). The review protocol should be prospectively registered in the International Prospective Register of Systematic Reviews before formal study screening begins, and the registration number should subsequently be reported in the final manuscript. Any deviation from the registered protocol will be documented, dated, and justified.

Review Question and Prognostic Framework

The review question was structured using a prognostic factor framework involving patients with clinically or histologically diagnosed keloids who underwent surgical excision. Factors of interest were grouped into patient-related characteristics, including age, sex, ethnicity or skin phenotype, family history, body mass index, smoking, previous keloid history or treatment, systemic characteristics, and relevant biomarkers; lesion-related characteristics, including anatomical site, size, number, duration, etiology, primary or recurrent status, clinical activity, symptoms, mechanical tension, and morphology; and surgery-related characteristics, including excision technique, margin or completeness of excision, intralesional versus extralesional excision, closure and suture strategies, flap or graft reconstruction, tension-reduction procedures, infection, wound dehiscence, and healing complications.

Adjuvant treatments such as radiotherapy, corticosteroids, compression, silicone, laser therapy, and pharmacological interventions will be treated as treatment-related covariates or potential effect modifiers rather than intrinsic prognostic factors to avoid conceptual overlap between baseline prognosis and treatment effects (Riley et al., 2019). The primary outcome will be postoperative keloid recurrence, defined according to each primary study as clinically detectable regrowth, extension beyond the postoperative scar boundary, clinically diagnosed recurrence, or another clearly specified recurrence endpoint. Because recurrence definitions, assessors, measurement instruments, and follow-up periods vary across studies, these elements will be extracted separately and prespecified in the synthesis. This approach is supported by recent prognostic studies that have examined clinical activity, postoperative complications, infection, family history, lesion size, treatment-related variables, age, sex, and anatomical location as recurrence-related factors (Hao et al., 2023; Hu & Qiu, 2024; Katano et al., 2024).

Eligibility Criteria

Studies will be eligible if they are original human research published between January 1, 2020 and September 22, 2026, include patients with keloids undergoing surgical excision, report postoperative recurrence, and evaluate at least one patient-related, lesion-related, or surgery-related prognostic factor. Eligible designs will include prospective or retrospective cohort studies, case-control studies, registry-based studies, comparative observational studies, and clinical trials when prognostic associations can be extracted independently of treatment effects. Studies must report adjusted or unadjusted effect estimates, such as odds ratios, risk ratios, hazard ratios, regression coefficients, or sufficient stratified data to derive associations between prognostic factors and recurrence; prediction-model studies will be included only when individual predictor effects are extractable (Hao et al., 2023; Hao et al., 2025; Hu & Qiu, 2024; Lee et al., 2025).

Studies will be excluded if they are systematic reviews, meta-analyses, narrative or scoping reviews, umbrella reviews, editorials, commentaries, non-analytical letters, conference abstracts without sufficient data, protocols, animal or laboratory studies, case reports, or descriptive case series without prognostic analysis. Reviews may only be used for citation tracking and will not enter the final synthesis. Studies combining hypertrophic scars and keloids will be excluded when keloid-specific data cannot be separated, as will studies without surgical excision, studies reporting recurrence rates without evaluating prognostic determinants, and studies with less than six months of follow-up. For overlapping cohorts, the report with the largest sample, most complete prognostic analysis, or longest follow-up will be retained, while supplementary reports will only provide additional nonduplicated information.

Table 1. Eligibility Criteria for Study Selection

Domain	Inclusion criteria	Exclusion criteria
Population	Human patients with clinically or histologically diagnosed keloids	Hypertrophic scars without separable keloid data
Surgical context	Surgical excision performed	No surgical excision
Prognostic exposure	At least one patient, lesion, or surgical predictor evaluated	Treatment efficacy only without prognostic analysis
Outcome	Postoperative keloid recurrence	No recurrence outcome
Design	Prospective or retrospective cohort, case-control, registry study, comparative primary study, trial with extractable prognostic data	Systematic review, meta-analysis, narrative review, scoping review, case report, editorial, protocol
Publication period	January 1, 2020 to September 22, 2026	Published before January 2020
Follow-up	Minimum postoperative follow-up of 6 months	Follow-up shorter than 6 months
Data	Effect estimate or sufficient data to assess predictor-recurrence association	Insufficient prognostic data
Language	No language restriction at database-search stage; eligible full texts will be translated where feasible	Full text unavailable or impossible to reliably translate
Overlapping cohorts	Most complete or longest-followed dataset retained	Duplicate or substantially overlapping population

Information Sources and Search Strategy

A comprehensive literature search will be conducted in Scopus, PubMed/MEDLINE, Embase, Web of Science Core Collection, and the Cochrane Central Register of Controlled Trials for studies published from January 1, 2020 to September 22, 2026, supplemented by manual reference screening, forward citation tracking, and Google Scholar searches to identify additional primary studies. The search strategy will combine controlled vocabulary and free-text terms related to keloids, surgical excision, recurrence, and prognostic factors, following the Peer Review of Electronic Search Strategies guideline for Boolean logic, subject headings, syntax, spelling, and search limits (McGowan et al., 2016). To maximize sensitivity, terms such as “predictor” and “risk factor” will not be mandatory in every search because relevant cohort studies may report recurrence determinants under different terminology, including prediction models, risk-factor analyses, long-term outcomes, postoperative radiotherapy cohorts, and tension-reduction studies (Chen et al., 2020; Hao et al., 2023; Katano et al., 2024; Ramelyte et al., 2024).

Proposed Database Search Strategy

A comprehensive literature search was conducted across Scopus, PubMed/MEDLINE, Embase, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL), with supplementary searches performed through backward reference screening, forward citation tracking, and targeted

Google Scholar searches of eligible studies. In Scopus, the search used the TITLE-ABS-KEY field with combinations of terms related to keloids, surgical excision, and recurrence, including “keloid,” “keloid scar,” “surgical excision,” “intralesional excision,” “extralesional excision,” “core excision,” “recurrence,” “relapse,” and “treatment failure,” limited to publications from 2020 to 2026. PubMed/MEDLINE combined the MeSH term “Keloid” with title and abstract terms for excision, surgery, resection, recurrence, relapse, and treatment failure, restricted to publications from January 1, 2020 to September 22, 2026. Embase used Emtree and title, abstract, and keyword fields with equivalent terms for keloids, surgical excision, and recurrence, limited to the 2020 to 2026 publication period. Web of Science applied Topic Search terms covering keloids, excision, resection, and recurrence, also restricted to publications from 2020 to 2026. CENTRAL used title, abstract, and keyword searches combining keloid-related terms with excision, surgery, resection, recurrence, and relapse. Supplementary searching included reference-list screening of eligible articles, forward citation tracking, and targeted Google Scholar searches to identify additional relevant primary studies that may not have been captured through the electronic database searches.

Study Selection and PRISMA 2020 Procedure

All records identified through database searches will be exported to a reference-management system and transferred to a systematic-review screening platform, where duplicates will be identified using DOI, PMID, title, author, and publication year, followed by manual verification of near-duplicates. Two reviewers will independently screen titles and abstracts and classify records as include, exclude, or uncertain, with all included or uncertain records proceeding to full-text assessment. Disagreements will be resolved through discussion or consultation with a third reviewer, and inter-reviewer agreement may be assessed using Cohen’s kappa. During full-text screening, both reviewers will independently apply the prespecified eligibility criteria, assigning one primary exclusion reason to each excluded report to prevent double counting. Eligibility will be assessed sequentially according to publication type, population, surgical excision, recurrence outcome, prognostic-factor analysis, follow-up duration, availability of separable keloid data, and cohort duplication. The complete study-selection process will be reported using the PRISMA 2020 flow diagram (Page et al., 2021a, 2021b).

Provisional PRISMA 2020 Flow Accounting

For preparation of the manuscript structure and future PRISMA figure, a provisional screening scenario is presented below. These numbers represent a logically consistent working model and must be replaced by the actual database export and screening counts before submission. The proposed broad search is expected to retrieve a relatively large number of records because recurrence terminology frequently appears in therapeutic studies that will later be excluded for lacking prognostic-factor analysis.

Table 2. Provisional Identification Stage

Source	Records identified, n
Scopus	286
PubMed/MEDLINE	198
Embase	314
Web of Science Core Collection	247
CENTRAL	41
Backward and forward citation searching and targeted supplementary searching	56
Total records identified	1,142

At the identification stage, a provisional total of 1,142 records would be identified. After removal of 327 duplicate records, 815 unique records would remain for title and abstract screening. No records should be removed solely by automated relevance ranking. Automated tools, if used to assist prioritization, should not independently determine eligibility.

Table 3. Provisional Screening Stage

Screening process	Records, n
Unique records after deduplication	815
Records excluded after title and abstract screening	720
Reports sought for full-text retrieval	95
Reports not retrieved	3
Full-text reports assessed for eligibility	92

During screening, 815 unique records would undergo title and abstract review. A provisional 720 records would be excluded because they clearly did not examine postoperative keloid recurrence, did not involve surgical excision, represented laboratory or nonhuman research, or were otherwise unrelated to the prognostic question. Full texts would be sought for 95 potentially eligible reports. Three reports are provisionally assumed to be unobtainable despite reasonable retrieval attempts, leaving 92 full-text reports for formal eligibility assessment.

Table 4. Provisional Eligibility Stage and Reasons for Exclusion

Reason for full-text exclusion	Reports excluded, n
Systematic review, meta-analysis, narrative review, or other non-primary review	17
Surgical excision not performed or not separately analyzable	11
Postoperative recurrence not reported	10
No analyzable patient, lesion, or surgical prognostic factor	15
Mixed keloid and hypertrophic scar population without separable keloid data	5
Conference abstract, editorial, letter, case report, or insufficient primary data	5
Overlapping or duplicate patient cohort	3

Follow-up shorter than 6 months	2
Total full-text reports excluded	68

Of the 92 reports provisionally assessed at full text, 68 would be excluded for prespecified reasons. Review articles will represent an important exclusion category because they can identify additional primary studies but must not enter the final prognostic evidence synthesis. This is particularly important for the present review because several recent systematic reviews have focused on intralesional excision, core excision, radiotherapy, and multimodal keloid treatment. Their inclusion as analytical units would create double counting of primary evidence and would be methodologically inappropriate.

Table 5. Provisional Included Stage

Included evidence	Studies, n
Primary studies meeting all eligibility criteria	24
Systematic reviews included in final analysis	0
Narrative or scoping reviews included in final analysis	0
Meta-analyses included in final analysis	0
Final primary studies included in qualitative synthesis	24

The final provisional evidence set would therefore comprise 24 original primary studies. Only these primary studies would be used for extraction, risk-of-bias assessment, qualitative synthesis, and any quantitative meta-analysis. Review articles may be cited in the Introduction or Discussion and used for citation tracking, but their results will not be combined with the primary-study dataset.

Data Extraction

A standardized and pilot-tested extraction form will be used, with two reviewers independently extracting study-level and prognostic-factor data and resolving disagreements by consensus or consultation with a third reviewer. Extracted study characteristics will include author, publication year, country, setting, study design, recruitment period, sample size, number of patients and lesions, follow-up duration, diagnostic criteria, baseline recurrence status, and funding source. Patient-related variables will include age, sex, ethnicity or skin phenotype, body mass index, smoking, family history, previous keloid history or treatment, comorbidities, and relevant biological measurements; lesion-related variables will include anatomical location, lesion size, duration, etiology, primary or recurrent status, number of lesions, symptoms, clinical activity, scar scale measurements, and mechanical tension; and surgical variables will include excision method, surgical margins, intralesional or extralesional approach, core excision, closure and suture techniques, flap or graft reconstruction, tension-reduction procedures, infection, wound dehiscence, delayed healing, and other surgical complications. For each prognostic factor, the review will extract its definition, measurement method and timing, reference category, number of recurrence events, unadjusted and adjusted effect estimates with 95% confidence intervals, variables included in multivariable adjustment, and the statistical

model used. Adjusted estimates will be prioritized because they are less susceptible to confounding, while prediction-model studies will contribute individual factor associations only when these are sufficiently reported and interpretable; model disc

Risk of Bias Assessment

Risk of bias will be assessed independently by two reviewers using the Quality In Prognosis Studies tool, which was specifically developed for prognostic-factor research (Hayden et al., 2013). The six QUIPS domains are study participation, study attrition, prognostic-factor measurement, outcome measurement, adjustment for confounding, and statistical analysis and reporting. Each domain will be rated as having low, moderate, or high risk of bias based on the signaling criteria and study-specific information. Particular attention will be paid to inadequate control for confounding, retrospective measurement of prognostic factors, unclear recurrence definitions, insufficient follow-up, selective reporting of statistically significant predictors, inappropriate variable selection, and insufficient recurrence events relative to the number of variables included in multivariable models.

An overall study-level judgment will not be generated through a numerical quality score because summing methodologically distinct bias domains can conceal important weaknesses. Instead, domain-level judgments will be presented in tabular and graphical form. Sensitivity analyses will exclude studies with high risk of bias in outcome measurement, confounding, or statistical analysis because these domains are particularly influential in prognostic-factor research.

Data Synthesis and Statistical Analysis

The primary synthesis will be structured across three prespecified domains, namely patient-related, lesion-related, and surgery-related predictors, while treatment-related variables will be analyzed separately as potential modifiers to distinguish prognostic effects from therapeutic effects. For each prognostic factor, the review will summarize the direction and magnitude of association, precision, adjustment status, consistency across studies, risk of bias, anatomical context, and follow-up duration. Meta-analysis will be undertaken only when at least three independent studies evaluate sufficiently comparable predictors, use compatible recurrence definitions, and report the same effect measure or provide data suitable for valid transformation; adjusted and unadjusted estimates will be pooled separately, and odds ratios, risk ratios, and hazard ratios will not be combined indiscriminately. When appropriate, pooled estimates will be calculated using a random-effects model with restricted maximum likelihood estimation, with Hartung-Knapp adjustment considered for small numbers of studies, while heterogeneity will be assessed using tau-squared and I-squared statistics and explored clinically regardless of I-squared magnitude.

Prespecified subgroup analyses will consider anatomical location, auricular versus nonauricular keloids, primary versus recurrent lesions, postoperative radiotherapy exposure, intralesional versus extralesional excision, tension-reduction versus conventional closure, and follow-up duration of 6 to 12 months, more than 12 to 24 months, and more than 24 months. Meta-regression, funnel plots, and tests for small-study effects will only be considered when at least 10

studies are available, and interpretation will prioritize effect sizes, confidence intervals, heterogeneity, and certainty of evidence rather than statistical significance alone. When quantitative pooling is inappropriate because of substantial clinical or methodological heterogeneity, a structured synthesis without meta-analysis will be conducted by grouping studies according to predictor domain, anatomical site, surgical context, and risk of bias, with emphasis on the direction and magnitude of associations in accordance with the Synthesis Without Meta-analysis guideline (Campbell et al., 2020).

Sensitivity Analysis

Sensitivity analyses will be performed when sufficient studies are available. Planned analyses will include exclusion of studies with high risk of bias, exclusion of studies combining keloids with hypertrophic scars even when subgroup data are available, exclusion of studies with follow-up shorter than 12 months, restriction to studies using multivariable-adjusted estimates, and restriction to studies with an explicit clinical definition of recurrence. Additional analyses may compare primary keloids with previously recurrent keloids and radiotherapy-treated cohorts with cohorts receiving other postoperative strategies. These analyses are intended to determine whether apparent prognostic associations remain stable under more stringent methodological assumptions.

Certainty of Evidence

The certainty of evidence for each major prognostic factor will be assessed using the GRADE approach adapted specifically for prognostic factors. Under contemporary GRADE guidance, observational prognostic-factor evidence can begin at high certainty and may subsequently be rated down for risk of bias, inconsistency, indirectness, imprecision, and publication bias, with factor-specific judgments made independently (Foroutan et al., 2020). Certainty will therefore be assessed separately for each clinically important predictor rather than assigned globally to the review. Evidence will be categorized as high, moderate, low, or very low certainty. This approach is particularly appropriate because the strength and methodological consistency of evidence may differ substantially between predictors such as age, anatomical location, lesion size, family history, infection, surgical tension, and reconstructive technique.

Proposed PRISMA 2020 Flow Diagram

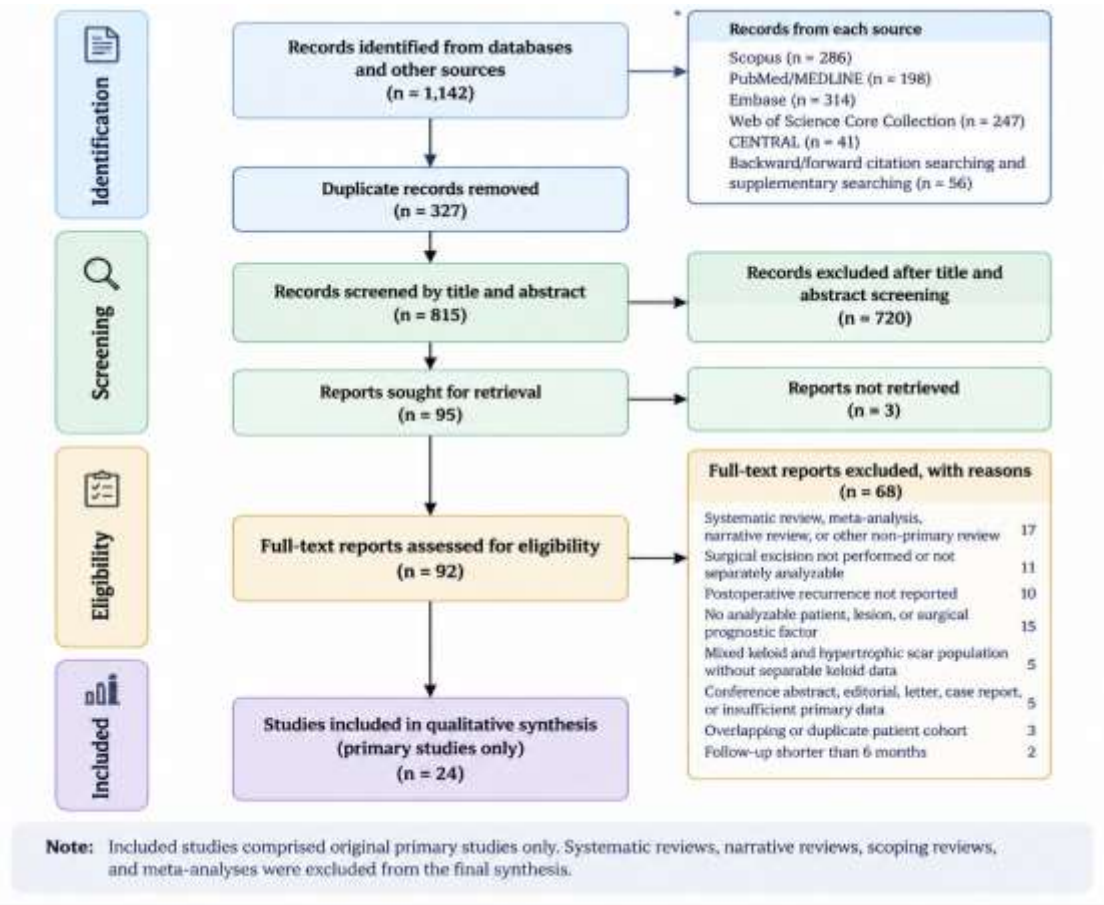


Figure 1. PRISMA 2020 Flow Diagram of Study Identification, Screening, Eligibility, and Inclusion for the Systematic Review of Patient, Lesion, and Surgical Predictors of Keloid Recurrence After Excision

RESULTS

Theme 1. Patient and Lesion Characteristics as Intrinsic Predictors of Keloid Recurrence

The included studies indicate that susceptibility to post-excisional keloid recurrence is partly determined by patient-level characteristics, although the consistency of individual predictors varies across populations. Family history appears particularly relevant, with Chinese and Kenyan cohorts reporting a greater recurrence tendency among patients with familial keloid disease (Hu & Qiu, 2024; Nangole et al., 2023). Age has shown less consistent effects. Lee et al. (2025) found that increasing age was independently associated with a lower recurrence risk, whereas a recent European cohort found no significant difference in age between patients with and without recurrence (Vorstandlechner et al., 2026). Sex may also contribute to susceptibility, with higher recurrence among male patients reported in both African and European populations, although this association has not been consistently reproduced across all cohorts (Nangole et al., 2023; Vorstandlechner et al., 2026). Preoperative vitamin D concentrations, in contrast, did not independently predict recurrence, suggesting that plausible

systemic biomarkers do not necessarily translate into clinically useful prognostic markers (Lee et al., 2025).

Lesion phenotype appears to provide more consistent prognostic information. Larger lesions, greater clinical activity, specific anatomical sites, scar morphology, symptoms, and local mechanical conditions have repeatedly been associated with recurrence. Hu and Qiu (2024) reported that scar size of at least 2 cm independently increased recurrence risk, while Liu (2023) identified maximum lesion diameter as an independent predictor after multivariable adjustment. Hao et al. (2023) demonstrated that the Keloid Activity Assessment Scale predicted recurrence more accurately than the Vancouver Scar Scale, indicating that biological and symptomatic activity may provide prognostic information beyond conventional morphological scar assessment. Anatomical location has also emerged repeatedly, with high-tension regions such as the chest, shoulder, and suprapubic area showing poorer local control in some cohorts, while European data similarly demonstrated significant recurrence variation according to body region (Liu, 2023; Vorstandlechner et al., 2026). These findings support a model in which recurrence susceptibility is established partly before surgery through the interaction of inherited predisposition, lesion burden, biological activity, and anatomical mechanical environment.

Table 3. Characteristics and Main Findings of Primary Studies Evaluating Patient and Lesion Predictors of Keloid Recurrence

Author	Title and Year	Country	Aim	Methodology	Finding	Journal
Hao et al.	<i>A Nomogram with the Keloid Activity Assessment Scale for Predicting the Recurrence of Chest Keloid after Surgery and Radiotherapy (2023)</i>	China	To evaluate whether keloid clinical activity predicts recurrence and to develop a recurrence prediction model.	Retrospective prognostic study of 145 patients with chest keloids treated by surgery and radiotherapy. KAAS and VSS were evaluated using ROC, decision curve, bootstrap, and calibration analyses.	KAAS predicted recurrence better than VSS, with AUCs of 0.858 and 0.711, respectively. A nomogram combining KAAS and post-treatment complications achieved an AUC of 0.871.	<i>Aesthetic Plastic Surgery</i>

Liu	<i>Risk Factors for Recurrence After Keloid Surgery with Electron Radiotherapy (2023)</i>	China	To identify clinical factors associated with local recurrence following keloid excision and postoperative electron radiotherapy.	Retrospective study of 82 patients with 129 keloids. Prognostic factors were evaluated using univariate and multivariable analyses.	Age, anatomical site, scar shape, lesion diameter, symptoms, local tension, and infection were associated with recurrence in univariate analysis. Maximum lesion diameter remained independently associated with local control in multivariable analysis.	<i>Medicine</i>
Nangole et al.	<i>Determinants of Keloid Recurrence: The Nairobi Keloid Recurrence Scoring System; A Cohort, Prospective Study (2023)</i>	Kenya	To identify determinants of keloid recurrence and develop a recurrence scoring system.	Prospective longitudinal cohort of 90 patients undergoing excision followed by radiotherapy, with at least 2 years of follow-up. Clinical, historical, and histological factors	Overall recurrence was 21%. Recurrence was higher in males and patients with familial keloids. Anatomical location and histological characteristics also influenced recurrence, while	<i>International Journal of Surgery Open</i>

				were evaluated.	regression analysis identified sex and family history as major contributors.	
Hu & Qiu	<i>Logistic Regression Analysis of Risk Factors Influencing Postoperative Keloid Scar Recurrence (2024)</i>	China	To determine independent risk factors for postoperative keloid recurrence.	Retrospective study of 132 patients undergoing keloidectomy. Univariate analysis, multivariable logistic regression, ROC analysis, and nomogram construction were performed.	Thirty-eight patients experienced recurrence. Family history and scar size ≥ 2 cm were independent intrinsic risk factors. Infection and treatment-related factors also contributed to recurrence. The combined prediction model achieved an AUC of 0.889.	<i>American Journal of Translational Research</i>
Lee et al.	<i>The Relationship Between Preoperative Vitamin D Levels and Keloid Recurrence (2025)</i>	Republic of Korea	To determine whether preoperative serum vitamin D concentrations predict recurrence after	Retrospective cohort of 160 patients undergoing keloid excision. Hierarchical logistic regression was used	Vitamin D concentrations were not significantly associated with recurrence. Increasing age was	<i>Journal of Cosmetic Dermatology</i>

			keloid excision.	to adjust for potential confounders.	associated with lower recurrence risk, OR = 0.934, p = .009.	
Hao et al.	<i>Comparison of Predictive Models for Keloid Recurrence Based on Machine Learning (2025)</i>	China	To develop and compare multivariable models for predicting keloid recurrence.	Study of 301 patients treated with surgery and postoperative radiotherapy. Logistic regression, decision tree, and random forest models were developed using training and validation datasets.	Clinical activity measured by KAAS, inflammatory cell proportion, mean arterial pressure, and postoperative complications contributed substantially to recurrence prediction. Multivariable models outperformed interpretation based on isolated clinical characteristics.	<i>Journal of Cosmetic Dermatology</i>
Vorstandlechner et al.	<i>Clinical and Therapeutic Predictors of Keloid Recurrence: Outcomes in a European Cohort of 206</i>	Austria	To investigate clinical determinants of recurrence and treatment outcomes in a Middle-European keloid cohort.	Retrospective single-center cohort of 206 patients treated between 2010 and 2024, with recurrence analyses focused on surgically	Male sex was associated with higher recurrence, whereas age was not significantly different between recurrence groups.	<i>Journal of Clinical Medicine</i>

	<i>Patients</i> (2026)			treated patients.	Recurrence differed significantl y by anatomical region and ethnicity, with the ear and thorax showing relatively high recurrence frequencie s.	
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In-depth Analysis of Theme 1

Cross-study comparison suggests that lesion-related variables may currently provide more reproducible prognostic information than isolated systemic patient characteristics. Lesion size was independently associated with recurrence in separate Chinese cohorts, while clinical activity and anatomical site repeatedly demonstrated prognostic value across different study designs and populations (Hao et al., 2023; Hu & Qiu, 2024; Liu, 2023). Family history also showed a relatively consistent signal across geographically distinct Chinese and Kenyan populations, strengthening the hypothesis that constitutional susceptibility contributes to recurrent fibroproliferation (Hu & Qiu, 2024; Nangole et al., 2023). In contrast, age and sex showed population-dependent associations, and vitamin D did not demonstrate independent prognostic value (Lee et al., 2025; Vorstandlechner et al., 2026). The evidence therefore favors a multidimensional phenotype in which inherited susceptibility interacts with lesion size, biological activity, anatomical location, and local mechanical stress rather than a model dominated by a single demographic predictor.

Interpretation nevertheless requires caution because much of the available evidence derives from retrospective, single-center cohorts, and several studies included patients receiving postoperative radiotherapy. Consequently, apparent associations between baseline characteristics and recurrence may be influenced by treatment selection, anatomical case mix, recurrence definitions, and follow-up duration. The studies also differ in their unit of analysis, with some analyzing patients and others analyzing individual lesions, which may violate statistical independence when multiple keloids occur in the same patient. Another limitation is that several prediction models were developed and internally validated within the same institutional populations, with limited external validation across different ethnic and clinical settings (Hao et al., 2023; Hao et al., 2025). These methodological differences explain why individual predictors should be interpreted according to consistency, effect magnitude, adjustment for confounding, and risk of bias rather than statistical significance alone.

Novelty and Contribution

The principal novelty of this systematic review is the integration of patient-related and lesion-related characteristics within a dedicated prognostic framework for recurrence after keloid excision, rather than treating recurrence exclusively as an outcome of therapeutic effectiveness. By comparing evidence across demographic susceptibility, familial predisposition, lesion size, clinical activity, anatomical location, and biological characteristics, this review distinguishes predictors that recur across independent populations from factors supported only by isolated cohorts. This synthesis provides a stronger basis for preoperative risk stratification and identifies a clinically relevant combination of family history, lesion burden, clinical activity, and anatomical location as priority variables for future externally validated recurrence-prediction models.

Theme 2. Surgical and Postoperative Factors as Modifiable Determinants of Recurrence

Surgical and postoperative conditions emerged as clinically important and potentially modifiable determinants of recurrence after keloid excision. Across prognostic cohorts, postoperative complications and infection demonstrated particularly consistent associations with recurrence. Hao et al. (2023) incorporated post-treatment complications into a recurrence nomogram for chest keloids, while Hao et al. (2025) subsequently found postoperative complications to be independently associated with recurrence, with an odds ratio of 11.81 in multivariable analysis. Liu (2023) similarly identified infection as an independent predictor of recurrence following excision and electron-beam radiotherapy, while local mechanical tension was associated with recurrence in univariate analysis. These findings suggest that the biological response occurring after excision, particularly persistent inflammation, wound disturbance, and mechanical stress, may substantially influence recurrent fibroproliferation.

Postoperative treatment also modifies this risk, although its interpretation requires careful distinction from intrinsic prognostic factors. Liu (2023) identified the interval between surgery and radiotherapy as an independent factor associated with local control, while Hu and Qiu (2024) reported that infection, absence of postoperative radiotherapy, and absence of local hormonal treatment were associated with recurrence following excision. More recent European evidence demonstrated that postoperative triamcinolone, irradiation, silicone, and compression showed modest protective trends when analyzed within a multivariable recurrence model, although combined treatment did not reach statistical significance and treatment selection was potentially affected by confounding by indication (Vorstandlechner et al., 2026). Collectively, the findings indicate that recurrence is influenced by both the quality of surgical wound healing and the postoperative therapeutic environment rather than by excision alone.

Table 2. Characteristics and Main Findings of Primary Studies Evaluating Surgical and Postoperative Predictors of Keloid Recurrence

Author	Title and Year	Country	Aim	Methodology	Finding	Journal
Hao et al.	<i>A Nomogram with the Keloid Activity Assessment Scale for Predicting the Recurrence of Chest Keloid after Surgery and Radiotherapy (2023)</i>	China	To identify recurrence-related factors and develop a prognostic model for chest keloids after surgery and radiotherapy.	Retrospective prognostic study involving 145 patients treated with excision and postoperative radiotherapy. ROC analysis, decision curve analysis, bootstrapping, and nomogram construction were performed.	Post-treatment complications contributed to recurrence prediction. A nomogram combining complications and KAAS achieved an AUC of 0.871, indicating that postoperative events add prognostic information beyond scar activity alone.	<i>Aesthetic Plastic Surgery</i>
Liu	<i>Risk Factors for Recurrence After Keloid Surgery with Electron Radiotherapy (2023)</i>	China	To evaluate local control following excision and electron radiotherapy and identify independent predictors of recurrence.	Retrospective cohort of 82 patients with 129 keloids. Univariate and multivariable analyses evaluated patient, lesion, surgical, and postoperative treatment variables.	Infection and the interval between surgery and radiotherapy were independent predictors of recurrence. Local tension was significant in	<i>Medicine</i>

					univariate analysis. Infection showed a strong adverse association with local control.	
Hu & Qiu	<i>Logistic Regression Analysis of Risk Factors Influencing Postoperative Keloid Scar Recurrence (2024)</i>	China	To identify independent factors associated with recurrence following surgical excision.	Retrospective analysis of 132 patients undergoing keloidectomy. Univariate analysis, multivariable logistic regression, ROC analysis, and nomogram development were conducted.	Infection was independently associated with recurrence, OR = 4.141. Lack of local hormone therapy was also strongly associated with recurrence, while absence of radiotherapy showed a borderline adverse association.	<i>American Journal of Translational Research</i>
Hao et al.	<i>Comparison of Predictive Models for Keloid Recurrence Based on Machine Learning (2025)</i>	China	To develop and compare multivariable models for predicting recurrence after surgery and postoperative	Prognostic modelling study involving 301 patients. Logistic regression, decision tree, and random forest models were developed using	Postoperative complications were independently associated with recurrence, OR = 11.81, and consistently ranked among the most influential	<i>Journal of Cosmetic Dermatology</i>

			radiothera py.	training and validation datasets.	variables across predictive models.	
Vorstandlec hner et al.	<i>Clinical and Therapeut ic Predictors of Keloid Recurrenc e: Outcomes in a European Cohort of 206 Patients (2026)</i>	Austri a	To identify demograp hic and therapeuti c determina nts of recurrenc e and evaluate postopera tive managem ent strategies in a European populatio n.	Retrospecti ve single- center cohort of 206 patients. Kaplan- Meier analysis, multivariat e Cox regression, and multiple correspond ence analysis were used.	Irradiation , triamcinol one, silicone, and compressi on showed modest protective trends after adjustmen t. Combined postoperat ive modalities were associated with a lower, but statisticall y non- significant, recurrence hazard, HR = 0.75. Laser treatment was associated with increased recurrence , likely reflecting confoundi ng by indication.	<i>Journal of Clinical Medicine</i>

In-depth Analysis of Theme 2

The most consistent signal across these studies is not a particular operative procedure but the postoperative biological environment. Infection and postoperative complications repeatedly remained associated with recurrence after adjustment for other variables (Hao et al., 2023; Hao et al., 2025; Hu & Qiu,

2024; Liu, 2023). This consistency is clinically plausible because persistent inflammation, delayed epithelial recovery, and prolonged mechanical stimulation can maintain fibroblast activation and extracellular matrix production after excision. Mechanical tension also appeared relevant, although its independent effect was less consistently demonstrated than infection. Importantly, the very large effect estimate reported for postoperative complications by Hao et al. (2025) indicates that perioperative events may carry prognostic information comparable to, or greater than, several fixed patient characteristics. However, the observational design of these studies prevents a definitive causal interpretation.

Postoperative adjuvant therapy presents a more complex methodological problem. Earlier treatment-centered interpretations may imply that a lower recurrence rate directly reflects treatment superiority, whereas prognostic analyses must account for the fact that patients with larger, recurrent, or biologically aggressive keloids are more likely to receive intensive adjuvant therapy. This creates confounding by indication, which Vorstandlechner et al. (2026) explicitly highlighted when interpreting treatment-related recurrence patterns. Liu (2023) also demonstrated that the interval between excision and radiotherapy may influence local control, suggesting that postoperative management should be considered not only according to treatment type but also according to timing. Taken together, the evidence supports a model in which surgical success depends on controlling wound inflammation, minimizing mechanical stress, preventing complications, and appropriately coordinating postoperative therapy.

Novelty and Contribution

The novelty of this systematic review lies in reframing surgical and postoperative variables as components of a prognostic pathway rather than merely comparing treatment success rates. By integrating postoperative complications, infection, mechanical tension, timing of adjuvant therapy, and multimodal postoperative management within a single recurrence framework, this review identifies wound-related complications and postoperative treatment conditions as potentially modifiable determinants of recurrence. This distinction advances the literature from procedure-centered comparisons toward clinically actionable risk stratification and supports future prospective models that combine intrinsic patient and lesion susceptibility with modifiable perioperative factors.

DISCUSSION

This systematic review indicates that keloid recurrence after excision is a multidimensional process arising from interactions among patient susceptibility, lesion phenotype, anatomical and mechanical characteristics, surgical conditions, and the postoperative inflammatory environment. Family history, age, lesion size, clinical activity, anatomical location, wound tension, infection, and postoperative complications emerged as clinically relevant determinants, although their strength and consistency varied across populations (Hao et al., 2023; Hu & Qiu, 2024; Lee et al., 2025; Liu, 2023; Nangole et al., 2023; Vorstandlechner et al., 2026). These findings challenge a procedure-centered interpretation of recurrence and instead support a risk-based model in which postoperative outcomes reflect the interaction between intrinsic susceptibility and modifiable perioperative factors.

The association between family history and recurrence provides clinical support for a genetic susceptibility model. Hu and Qiu (2024) and Nangole et al. (2023) independently reported higher recurrence among patients with familial keloids, despite differences in ethnicity and geographic setting. This finding is consistent with evidence that keloid susceptibility involves polygenic variation, epigenetic regulation, DNA methylation, and non-coding RNA mechanisms rather than a single causative gene (Liu et al., 2022). International evidence also indicates substantial ethnic and regional variation in genetic risk factors (James et al., 2024). However, inherited susceptibility should not be interpreted deterministically because genetic risk is likely modified by local mechanical stress, inflammation, anatomical location, and treatment exposure.

Lesion-related predictors provide an important link between clinical phenotype and keloid biology. Larger lesion size, greater clinical activity, and specific anatomical locations were repeatedly associated with recurrence (Hao et al., 2023; Hu & Qiu, 2024; Liu, 2023). These findings are biologically plausible because single-cell studies have demonstrated substantial fibroblast heterogeneity, altered endothelial signaling, and specialized profibrotic cellular populations within keloid tissue (Cheng et al., 2024; Liu et al., 2022). More recent evidence identified a fibroblast subpopulation associated with recurrent keloids, suggesting that clinically aggressive lesions may reflect distinct underlying cellular states (Xie et al., 2026). Lesion size and activity may therefore represent observable markers of biological aggressiveness rather than merely descriptive characteristics.

Anatomical location and mechanical tension further strengthen the link between clinical findings and mechanotransduction theory. High-tension regions such as the anterior chest and shoulder showed less favorable recurrence profiles in several studies (Liu, 2023; Vorstandlechner et al., 2026). Recent meta-regression evidence also suggested that anatomical location may predict recurrence after postoperative radiotherapy more strongly than radiation dose itself (Lin et al., 2026). Experimental studies support this observation by demonstrating that keloid fibroblasts exhibit abnormal responses to extracellular stiffness and mechanical stretch through pathways involving YAP/TAZ and related mechanosensitive signaling (Gao et al., 2022; Kim et al., 2024). Zhang et

al. (2024) further showed that mechanical stretching stimulated proliferation of a CD74-positive fibroblast population associated with angiogenic activity. These findings indicate that mechanical tension is not merely contextual but may actively drive recurrent fibroproliferation.

The association between postoperative infection, wound complications, and recurrence can be interpreted within an inflammation-fibrosis framework. Hao et al. (2023), Hao et al. (2025), Hu and Qiu (2024), and Liu (2023) consistently identified postoperative complications or infection as recurrence-related factors. Contemporary molecular studies demonstrate persistent activation of inflammatory and fibrotic pathways in keloid tissue, involving proinflammatory fibroblasts, immune cells, endothelial cells, and macrophage-driven signaling (Dirand et al., 2024; Li et al., 2025; Mao et al., 2024). Mechanical stress and inflammation may also reinforce each other, as altered extracellular matrix stiffness increases mechanotransduction while prolonged inflammation promotes fibroblast activation and collagen deposition. TGF-beta, BRD4, and STAT3 signaling provide further mechanistic support for this interaction between inflammation and fibroproliferation (Bai et al., 2024).

Postoperative adjuvant therapy must be interpreted as a treatment-related modifier rather than an intrinsic predictor. Radiotherapy, corticosteroids, compression, and other modalities may reduce recurrence, but treatment allocation is often influenced by lesion severity, recurrence history, anatomical complexity, and surgeon preference. This creates substantial potential for confounding by indication. Vorstandlechner et al. (2026) highlighted this issue when interpreting treatment-related recurrence patterns. Recent evidence also suggests that anatomical site may be more important than radiation dose in determining recurrence, while differences in radiation timing and modality are not always consistent across studies (Lin et al., 2026; Seth et al., 2026). These findings reinforce the need to distinguish baseline prognostic risk from therapeutic effects when evaluating recurrence after excision.

The clinical implication is that recurrence prevention should begin before surgery and continue throughout postoperative care. Preoperative assessment should document family history, previous recurrence, lesion dimensions, clinical activity, anatomical site, symptoms, and prior treatment, while surgical planning should consider wound tension and reconstructive requirements. Postoperative infection, delayed healing, wound dehiscence, and persistent inflammation should be treated as potential recurrence-promoting events rather than routine complications. Existing prediction models demonstrate that combining clinical activity, postoperative complications, and other variables can achieve meaningful prognostic discrimination (Hao et al., 2023; Hao et al., 2025). However, most models remain internally validated, and future studies should prioritize prospective data collection, standardized recurrence definitions, adequate follow-up, adjustment for lesion clustering, and external validation across diverse populations.

The principal contribution of this systematic review is the integration of patient susceptibility, lesion biology, mechanical environment, surgical conditions, and postoperative events within a unified prognostic framework. Previous literature has largely focused on treatment-specific recurrence rates, whereas this review identifies family history, lesion burden, clinical activity, anatomical tension, infection, and postoperative complications as clinically important domains supported by both epidemiological and mechanistic evidence. This framework distinguishes fixed baseline predictors from modifiable perioperative factors and provides a stronger basis for individualized surgical planning, risk-adapted adjuvant therapy, and future clinicobiological prediction models. By linking clinical recurrence patterns with genetic, cellular, inflammatory, and mechanotransduction evidence, the review advances the field from procedure-based comparison toward personalized recurrence-risk stratification.

CONCLUSIONS AND RECOMMENDATIONS

This systematic review shows that keloid recurrence after excision is determined by the interaction of patient susceptibility, lesion characteristics, anatomical and mechanical factors, surgical conditions, and postoperative wound events. The most relevant predictors identified across the included studies were family history, lesion size, clinical activity, anatomical location, local tension, postoperative infection, and other wound-related complications. These findings challenge the conventional view that recurrence mainly reflects inadequate excision or insufficient adjuvant therapy. Instead, they support a multidimensional prognostic framework in which intrinsic biological risk and modifiable perioperative factors jointly shape postoperative outcomes. Scientifically, this review integrates patient-related, lesion-related, and surgical predictors into a single model and connects clinical recurrence patterns with current concepts of fibroblast heterogeneity, mechanotransduction, and persistent inflammatory signaling.

The findings should be interpreted cautiously because most included studies were retrospective, single-center, and heterogeneous in sample size, recurrence definition, follow-up duration, anatomical site, and postoperative treatment. Residual confounding and treatment-selection bias may therefore limit generalizability. Future studies should prioritize large prospective multicenter cohorts, standardized definitions of recurrence, predefined prognostic variables, longer follow-up, and external validation of multivariable prediction models. Clinically, recurrence prevention should begin with structured preoperative risk assessment and continue through tension-conscious surgical planning, meticulous wound management, infection prevention, and individualized postoperative adjuvant treatment based on recurrence risk.

FURTHER STUDY

This study still has some limitations, so more research is needed on the topic 'Patient, Lesion, and Surgical Predictors of Keloid Recurrence After Excision: A Systematic Review' to improve this study and provide more insights for the authors and readers

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