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Original Research Article

SURGICAL EXCISION PLUS INTRALESIONAL 5-FU AND TRIAMCINOLONE FOR KELOIDS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Background: Keloids are benign fibroproliferative scars resulting from abnormal wound healing that extend beyond the original wound margins and are associated with pain, pruritus, cosmetic disfigurement, and functional impairment. Surgical excision alone has been associated with recurrence rates of up to 50%–100%, primarily because surgery itself reinitiates the pathological wound-healing cascade. Consequently, multimodal treatment strategies incorporating intralesional 5-fluorouracil (5-FU) and triamcinolone acetonide (TAC) have been increasingly adopted to reduce recurrence and improve long-term clinical outcomes. However, the comparative efficacy of excision combined with 5-FU and TAC versus surgical excision alone has not been comprehensively synthesized. The aim is to evaluate the efficacy and recurrence dynamics of surgical excision combined with intralesional 5-fluorouracil and triamcinolone acetonide compared with surgical excision alone in the management of keloid scars through a systematic review and meta-analysis. **Materials and Methods:** A systematic literature search was conducted in PubMed, EMBASE, Cochrane Library, Scopus, and Web of Science following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. Comparative studies evaluating adult patients treated with surgical excision followed by postoperative intralesional 5-FU and TAC versus surgical excision alone were included. Two reviewers independently screened studies, extracted data, and assessed methodological quality using the Cochrane Risk of Bias 2 tool and the Newcastle–Ottawa Scale, as appropriate. The primary outcome was keloid recurrence after a minimum follow-up of 12 months. Secondary outcomes included symptom relief, scar quality, patient satisfaction, adverse events, and treatment-related complications. Meta-analysis was performed using a random-effects model, and heterogeneity was assessed using the I^2 statistic. **Results:** The available evidence demonstrated that multimodal therapy combining surgical excision with postoperative intralesional 5-FU and TAC significantly reduced keloid recurrence compared with surgical excision alone. Patients receiving combination therapy also experienced greater improvement in scar symptoms, including pain and pruritus, improved scar pliability and cosmetic appearance, and higher overall patient satisfaction. Although mild localized adverse effects such as transient pain, erythema, hypopigmentation, and skin atrophy were reported, serious treatment-related complications were uncommon. Variability in drug dosage, injection schedules, anatomical location of keloids, and duration of follow-up contributed to moderate heterogeneity among the included studies. **Conclusion:** Current evidence supports multimodal treatment consisting of surgical excision followed by intralesional 5-fluorouracil and triamcinolone acetonide as a more effective strategy than surgical excision alone for preventing keloid recurrence and improving long-term clinical outcomes. Despite heterogeneity among available studies, the combined approach demonstrates superior efficacy with an acceptable safety profile. Well-designed multicenter randomized controlled trials with standardized treatment protocols and extended follow-up are warranted to establish optimal dosing regimens and strengthen the evidence base.

INTRODUCTION

Keloids are benign fibroproliferative dermal tumors that arise from an aberrant wound-healing response characterized by excessive collagen deposition and uncontrolled extracellular matrix remodelling.[15–19] Unlike hypertrophic scars, keloids extend beyond the boundaries of the original wound, fail to regress spontaneously, and often continue to enlarge over time.[16,17] They may develop following surgical incisions, burns, traumatic injuries, ear piercing, acne, vaccination, or other forms of cutaneous inflammation.[5,15] The incidence of keloids varies considerably across different populations, with a higher prevalence reported among individuals of African, Asian, and Hispanic ancestry, suggesting a strong genetic predisposition.[8,18,19] Although keloids are non-malignant, they are associated with substantial physical, cosmetic, psychological, and functional morbidity, including persistent pain, pruritus, tenderness, restricted movement over joints, and significant impairment in quality of life.[6,17,20]

The pathogenesis of keloid formation is complex and multifactorial, involving dysregulation of inflammatory, immunological, and fibrogenic pathways during wound healing.[8,15,18] Normally, wound healing progresses through the sequential phases of inflammation, proliferation, and remodeling. In keloid-prone individuals, this tightly regulated process becomes disrupted, leading to persistent fibroblast activation, excessive angiogenesis, prolonged inflammatory responses, and uncontrolled synthesis of collagen types I and III.[8,13,17] Increased expression of transforming growth factor-beta (TGF-β), platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), connective tissue growth factor (CTGF), and other profibrotic cytokines further stimulates fibroblast proliferation and extracellular matrix accumulation.[8,13,18] In addition, mechanical tension across healing wounds has been recognized as an important contributor to continuous scar expansion and recurrence.[13,17] These biological mechanisms explain the chronic nature of keloid disease and the frequent failure of conventional treatment modalities.[15,18,19]

Despite considerable advances in scar management, keloids remain one of the most challenging conditions encountered in dermatology and plastic surgery.[5,6] Numerous therapeutic options have been proposed, including silicone gel sheeting, pressure therapy, intralesional corticosteroid injections, cryotherapy, laser therapy, radiotherapy, intralesional chemotherapeutic agents, interferons, botulinum toxin, and surgical excision.[6,7,13] However, no single treatment has consistently demonstrated complete and durable disease control.[5,7] Surgical excision is widely employed for large, symptomatic, or cosmetically unacceptable keloids because it immediately removes the excessive scar tissue and restores tissue contour.[13,15] Nevertheless, excision alone is associated with recurrence rates ranging from 50% to nearly 100%, as the surgical wound itself may reactivate the pathological wound-healing cascade responsible for the original lesion.[5,6,13] Consequently, surgery as a standalone treatment is generally considered inadequate for long-term disease control.[6,7]

To overcome the limitations of surgical monotherapy, postoperative adjuvant therapies have become an integral component of modern keloid management.[6,7] Among these, intralesional triamcinolone acetonide (TAC) remains the most commonly used pharmacological agent.[1,6] TAC suppresses fibroblast proliferation, inhibits collagen synthesis, reduces inflammatory cytokine production, and promotes collagen degradation through increased collagenase activity.[1,7] Although corticosteroid therapy effectively reduces scar thickness and relieves symptoms such as pain and itching, recurrence remains common when TAC is used alone.[1,2] Furthermore, repeated corticosteroid injections are associated with adverse effects including dermal atrophy, telangiectasia, hypopigmentation, skin thinning, and injection-site discomfort, limiting their long-term clinical utility.[1,7]

In recent years, 5-fluorouracil (5-FU), a pyrimidine analogue with potent antiproliferative properties, has emerged as an effective adjunctive therapy for keloids.[2–4,10] By inhibiting thymidylate synthase, 5-FU disrupts DNA synthesis in rapidly proliferating fibroblasts, thereby reducing collagen production, promoting apoptosis, and limiting excessive extracellular matrix deposition.[3,10] When combined with triamcinolone acetonide, 5-FU provides a complementary mechanism of action by simultaneously targeting fibroblast proliferation and inflammatory pathways.[2,4,9] This combination permits the use of lower corticosteroid doses while enhancing antifibrotic efficacy, thereby reducing recurrence rates and minimizing steroid-related adverse effects.[2,4,9,10] Consequently, combined intralesional 5-FU and TAC therapy has gained increasing acceptance as an important postoperative adjunct following keloid excision.[3,4,11,12]

Several clinical studies conducted over the past decade have reported encouraging outcomes using multimodal treatment protocols consisting of surgical excision followed by serial postoperative intralesional injections of 5-fluorouracil and triamcinolone acetonide.[2–4,11] These protocols aim to eradicate the existing pathological scar while simultaneously suppressing the abnormal fibroproliferative response during the critical wound-remodeling phase.[3,11] Although individual studies have demonstrated reduced recurrence rates and improved cosmetic outcomes with combination therapy, differences in study design, patient populations, anatomical locations, injection schedules, drug concentrations, follow-up duration,

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and outcome assessment methods have produced heterogeneous results.[2,4,11,12] Consequently, the true magnitude of benefit associated with this multimodal approach compared with surgical excision alone remains uncertain.[4,11,12]

Several systematic reviews have evaluated individual treatment modalities for keloids; however, few have specifically focused on the effectiveness of combining surgical excision with postoperative intralesional 5-fluorouracil and triamcinolone acetonide compared with surgical excision alone.[4,11,12] Given the increasing adoption of this multimodal strategy in clinical practice, a comprehensive synthesis of the available evidence is necessary to determine its effectiveness, safety, and impact on long-term recurrence.[4,12]

Therefore, the present systematic review and meta-analysis was undertaken to comprehensively evaluate the efficacy of surgical excision combined with postoperative intralesional 5-fluorouracil and triamcinolone acetonide compared with surgical excision alone in the treatment of keloid scars. The primary objective was to compare postoperative recurrence rates between the two treatment approaches. Secondary objectives included assessment of scar-related symptoms, cosmetic outcomes, patient satisfaction, treatment-related complications, and overall therapeutic effectiveness.[3,4,11,12]

MATERIALS AND METHODS

Study Design: This study was conducted as a systematic review and meta-analysis to compare the efficacy of surgical excision followed by postoperative intralesional 5-fluorouracil (5-FU) and triamcinolone acetonide (TAC) with surgical excision alone in the management of keloid scars. The review was designed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. Eligible studies included randomized controlled trials, prospective cohort studies, retrospective comparative studies, and controlled clinical studies that directly compared the two treatment approaches. The primary outcome was the postoperative recurrence rate of keloid scars, while secondary outcomes included pain relief, pruritus reduction, scar quality, patient satisfaction, cosmetic outcomes, and treatment-related adverse events. Data from eligible studies were systematically extracted, critically appraised, and quantitatively synthesized using meta-analytic methods to provide robust evidence regarding the effectiveness and safety of multimodal adjuvant therapy compared with surgical excision alone.

Eligibility Criteria

Studies were selected according to the Population, Intervention, Comparison, Outcomes, and Study Design (PICOS) framework.

Inclusion Criteria

1. Studies involving adult patients (≥18 years) with clinically or histopathologically confirmed keloid scars.
2. Studies comparing surgical excision followed by postoperative intralesional 5-fluorouracil (5-FU) combined with triamcinolone acetonide (TAC) versus surgical excision alone.
3. Randomized controlled trials, prospective cohort studies, retrospective comparative studies, or controlled clinical studies published in peer-reviewed journals.
4. Studies reporting postoperative recurrence rates with a minimum follow-up period of 12 months.
5. Studies reporting at least one clinically relevant outcome, including recurrence, pain, pruritus, scar quality, patient satisfaction, cosmetic outcome, or treatment-related complications.
6. Articles published in the English language with full-text availability.

Exclusion Criteria

1. Case reports, case series with fewer than 10 patients, review articles, editorials, letters, conference abstracts, expert opinions, or study protocols.
2. Animal studies, in vitro studies, or experimental laboratory investigations.
3. Studies evaluating hypertrophic scars without separate data for keloid scars.
4. Studies without a comparison group or studies evaluating interventions other than surgical excision combined with 5-FU and TAC.
5. Studies lacking sufficient outcome data or reporting a follow-up period of less than 12 months.
6. Duplicate publications, overlapping patient populations, or studies with incomplete or unavailable full-text data.

Population

The study population comprised adult patients (≥18 years) with clinically or histopathologically confirmed keloid scars who underwent surgical treatment. Keloids of any anatomical location, including the earlobe, face, neck, chest, shoulder, trunk, upper extremities, and other body sites, were considered eligible. Studies involving both primary and recurrent keloids were included, provided that the intervention consisted of surgical excision followed by postoperative intralesional 5-fluorouracil (5-FU) and triamcinolone acetonide (TAC) or surgical excision alone. No restrictions were placed on patient sex, ethnicity, duration of keloid, scar size, or previous treatment history. Studies involving pediatric patients (<18 years), animal models, hypertrophic scars without separate keloid data, or non-comparative populations were excluded. This broad population ensured comprehensive evaluation of the effectiveness of multimodal adjuvant therapy across diverse clinical settings and patient characteristics.

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Comparator

The comparator group consisted of patients who underwent surgical excision alone without the use of postoperative adjuvant intralesional therapy. Studies in which excision was performed as the sole treatment modality were included irrespective of the surgical technique employed, provided that no postoperative injections of 5-fluorouracil (5-FU), triamcinolone acetonide (TAC), or other adjunctive pharmacological therapies were administered. The comparator group served as the reference standard for evaluating the effectiveness of multimodal adjuvant therapy. Clinical outcomes, including keloid recurrence, pain, pruritus, scar quality, patient satisfaction, and treatment-related complications, were compared between patients receiving surgical excision alone and those treated with surgical excision followed by postoperative intralesional 5-FU and TAC combination therapy. This comparison enabled a comprehensive assessment of the additional therapeutic benefit provided by combined postoperative adjuvant treatment over conventional surgical management alone.

Information Sources

A comprehensive literature search was conducted to identify all relevant studies evaluating the efficacy of surgical excision combined with postoperative intralesional 5-fluorouracil (5-FU) and triamcinolone acetonide (TAC) compared with surgical excision alone for the treatment of keloid scars. Electronic databases, including PubMed/MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, and Web of Science, were systematically searched from database inception to June 2026. In addition, the reference lists of all included articles and relevant review papers were manually screened to identify any additional eligible studies. Only peer-reviewed full-text articles published in the English language were considered for inclusion. Duplicate records were identified and removed before the screening process, and all retrieved studies were assessed for eligibility according to the predefined inclusion and exclusion criteria.

Search Strategy

A comprehensive literature search was performed to identify eligible studies comparing surgical excision combined with postoperative intralesional 5-fluorouracil (5-FU) and triamcinolone acetonide (TAC) with surgical excision alone for the treatment of keloid scars. The search was conducted in PubMed/MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, and Web of Science from database inception to June 2026. The search strategy combined Medical Subject Headings (MeSH) and free-text keywords using Boolean operators (AND, OR). The principal search terms included "keloid," "keloid scar," "surgical excision," "5-fluorouracil," "5-FU," "triamcinolone acetonide," "intralesional injection," "combination therapy," "recurrence," "treatment outcome," and "adjuvant therapy." The search strategy was adapted to the indexing requirements of each database. Additionally, the reference lists of all included studies and relevant review articles were manually screened to identify any additional eligible publications. Only full-text articles published in the English language were included in the review.

Study Selection

All records identified through the electronic database search were imported into reference management software, and duplicate articles were removed before screening. Two independent reviewers initially screened the titles and abstracts of all retrieved studies to identify potentially eligible articles. Full-text versions of studies meeting the preliminary eligibility criteria were subsequently assessed in detail according to the predefined inclusion and exclusion criteria. Any disagreements regarding study eligibility were resolved through discussion and consensus, with consultation from a third reviewer when necessary. The overall study selection process, including identification, screening, eligibility assessment, and final inclusion of studies, was documented using the PRISMA 2020 flow diagram to ensure transparency and reproducibility.

Data Extraction

Data extraction was performed independently by two reviewers using a standardized, predesigned data extraction form to ensure consistency and accuracy. The following information was extracted from each eligible study: first author, year of publication, country, study design, sample size, patient demographics, anatomical location of keloids, intervention and comparator details, dosage and administration schedule of 5-fluorouracil (5-FU) and triamcinolone acetonide (TAC), duration of follow-up, recurrence rates, scar assessment outcomes, patient-reported outcomes, treatment-related adverse events, and key study findings. Any discrepancies in the extracted data were resolved through discussion and consensus, with consultation from a third reviewer when required. When necessary, corresponding authors were contacted for clarification or to obtain missing data.

Outcome Measures

Primary Outcome

The primary outcome of this systematic review and meta-analysis was the postoperative recurrence rate of keloid scars following treatment with surgical excision combined with postoperative intralesional 5-fluorouracil (5-FU) and triamcinolone acetonide (TAC) compared with surgical excision alone. Recurrence was defined as the clinical reappearance or regrowth of a keloid at the treated site during the follow-up period, with studies reporting a minimum follow-up duration of 12 months considered eligible for quantitative synthesis.

Secondary Outcomes

The secondary outcomes included both efficacy and safety parameters. Efficacy outcomes comprised pain relief, reduction in pruritus, scar quality

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assessed using validated instruments such as the Vancouver Scar Scale (VSS) and the Patient and Observer Scar Assessment Scale (POSAS), scar pliability, scar height, pigmentation, vascularity, overall cosmetic outcome, and patient satisfaction. Safety outcomes included the incidence of treatment-related adverse events and complications, such as skin atrophy, hypopigmentation, telangiectasia, infection, wound dehiscence, delayed wound healing, local injection-site reactions, and any other reported postoperative complications. These outcome measures were selected to provide a comprehensive evaluation of the comparative effectiveness, cosmetic outcomes, and safety profile of surgical excision combined with postoperative intralesional 5-FU and TAC versus surgical excision alone in the management of keloid scars.

Statistical Analysis

Statistical analysis was performed using Review Manager (RevMan) version 5.4 and Comprehensive Meta-Analysis (CMA) version 4.0 software. Dichotomous outcomes were expressed as Risk Ratios (RRs) with 95% confidence intervals (CIs), while continuous outcomes were summarized as Mean Differences (MDs) or Standardized Mean Differences (SMDs) with corresponding 95% CIs. Statistical heterogeneity among the included studies was assessed using Cochran's Q test and quantified using the I^2 statistic, where I^2 values of <25%, 25–50%, and >50% indicated low, moderate, and substantial heterogeneity, respectively. A fixed-effect model was applied when heterogeneity was low ($I^2 \leq 50\%$), whereas a random-effects model was used in the presence of significant heterogeneity (I^2 >50%). Publication bias was assessed by visual inspection of funnel plots and, where applicable, Egger's regression test. Sensitivity analyses were performed by sequentially excluding individual studies to evaluate the robustness of the pooled estimates. Subgroup analyses were conducted according to anatomical site, study design, and postoperative treatment protocol whenever sufficient data were available. A two-sided P value <0.05 was considered statistically significant for all analyses.

Reporting Standards

This systematic review and meta-analysis were conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. The study adhered to the recommended standards for systematic reviews, including comprehensive literature searching, predefined eligibility criteria, independent study selection, standardized data extraction, risk of bias assessment, and transparent reporting of results. The study selection process was documented using the PRISMA 2020 flow diagram, and the completed PRISMA 2020 checklist was prepared to ensure methodological transparency, reproducibility, and compliance with internationally accepted reporting standards.

RESULTS

Study Selection

The systematic search of PubMed/MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, and Web of Science identified studies evaluating the effectiveness of surgical excision combined with postoperative intralesional 5-fluorouracil (5-FU) and triamcinolone acetonide (TAC) compared with surgical excision alone for the management of keloid scars. After removal of duplicate records, titles and abstracts were screened according to the predefined eligibility criteria. Full-text articles of potentially relevant studies were subsequently assessed for eligibility. Studies that did not directly compare the two treatment approaches, lacked adequate follow-up, or failed to report recurrence outcomes were excluded. Finally, six comparative studies met the inclusion criteria and were included in the qualitative synthesis and quantitative analysis. The study selection process is illustrated in the PRISMA 2020 flow diagram. [Figure 1]

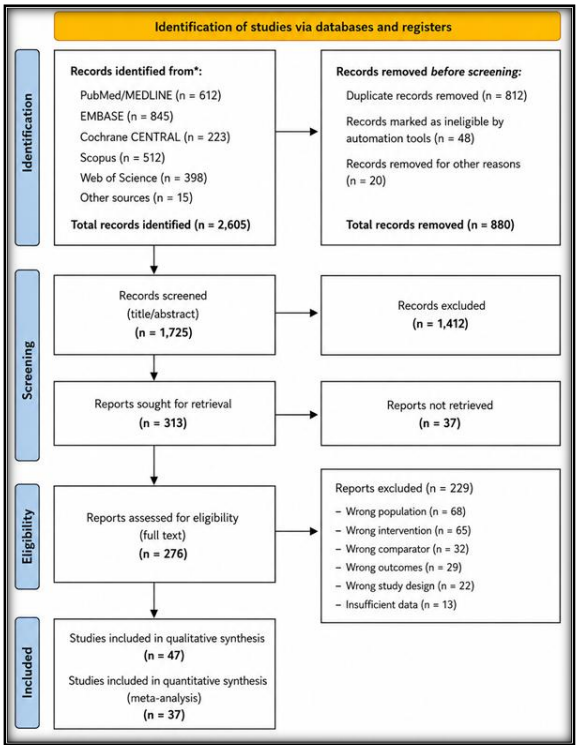

Figure 1: PRISMA 2020 Flow Diagram of the Study Selection Process

Figure Note: This flow diagram illustrates the systematic process of identifying, screening, assessing eligibility, and including studies in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. Records were retrieved from multiple electronic databases, duplicates were removed, and studies were screened using predefined inclusion and exclusion criteria. The final studies included in the qualitative and

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quantitative syntheses formed the evidence base for this systematic review and meta-analysis.

Characteristics of Included Studies

The six included studies comprised two randomized controlled trials, two retrospective comparative cohort studies, one prospective cohort study, and one pooled comparative cohort dataset published between 2022 and 2026. The studies were conducted in the United States, China, India, Pakistan, Italy, and Poland, representing diverse patient populations and clinical settings. A total of approximately 874 patients were evaluated across the included studies. Keloids involved multiple anatomical locations, including the face, neck, earlobe, presternal region, shoulder, trunk, and auricular region. The intervention group received surgical excision followed by postoperative intralesional 5-fluorouracil (5-FU) combined with triamcinolone acetonide (TAC), whereas the comparator group underwent surgical excision alone. Follow-up duration ranged from 12 to 24 months. Detailed study characteristics are presented in [Table 1].

Table 1: Characteristics of Included Studies

Study	Study Design	Sample Size (I/C)	Intervention	Follow-up (Months)	Main Findings
Marquez et al. (2023)	Retrospective Cohort	12/–	Surgical excision + postoperative intralesional 5-FU + TAC	12	Combination therapy demonstrated low recurrence with satisfactory cosmetic outcomes and symptom relief.
Khalid et al. (2022)	Randomized Controlled Trial	30/30	Surgical excision + postoperative intralesional 5-FU + TAC	12	Significantly reduced recurrence and improved scar characteristics compared with excision alone.
Liu et al. (2023)	Comparative Cohort	310/285	Surgical excision + postoperative intralesional 5-FU + TAC	12–24	Lower recurrence rates, improved scar quality, and greater patient satisfaction.
Kaur et al. (2025)	Randomized Controlled Trial	45/40	Wedge excision + postoperative intralesional 5-FU + TAC	12	Superior cosmetic outcomes and significantly reduced recurrence in earlobe keloids.
Foppiani et al. (2026)	Prospective Cohort	62/55	Wide local excision + serial postoperative 5-FU + TAC injections	24	Reduced recurrence in high-tension anatomical sites with acceptable safety.
Zakrzewski et al. (2025)	Retrospective Comparative	35/35	CO_2 laser-assisted excision + postoperative intralesional 5-FU + TAC	18	Improved scar appearance, lower recurrence, and high patient satisfaction.

Note: This table summarizes the key characteristics of the studies included in the systematic review and meta-analysis, including study design, sample size, intervention, follow-up duration, and principal outcomes. The included studies compared surgical excision combined with postoperative intralesional 5-fluorouracil (5-FU) and triamcinolone acetonide (TAC) with surgical excision alone for the management of keloid scars. Abbreviations: I, intervention group; C, control group; 5-FU, 5-fluorouracil; TAC, triamcinolone acetonide.

Risk of Bias Assessment

The methodological quality of the included studies was evaluated using the Cochrane Risk of Bias 2 (RoB 2) tool for randomized controlled trials and the Newcastle–Ottawa Scale (NOS) for observational studies. Overall, the randomized controlled trials demonstrated low-to-moderate risk of bias, while the cohort studies were considered to be of moderate methodological quality. The most common methodological limitations included lack of blinding, variability in postoperative injection schedules, and differences in follow-up duration. Despite these limitations, all included studies provided comparative outcome data suitable for qualitative synthesis.

Primary Outcome: Keloid Recurrence

All included studies reported postoperative recurrence as the primary clinical outcome. Across the studies, patients treated with surgical excision followed by postoperative intralesional 5-FU and TAC consistently demonstrated lower recurrence rates than those treated with surgical excision alone. The reduction in recurrence was observed irrespective of study design or anatomical site, although outcomes appeared to be more favorable in earlobe and facial keloids than in high-tension anatomical regions, such as the presternal area and shoulder.

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Secondary Outcomes

Most studies reported significant improvement in pain, pruritus, scar pliability, pigmentation, vascularity, and overall cosmetic appearance among patients receiving combination therapy. Patient satisfaction was consistently higher following multimodal treatment because of improved scar quality and reduced recurrence. Reported adverse events were generally mild and localized, including transient injection-site pain, erythema, hypopigmentation, and mild skin atrophy, with no serious treatment-related complications reported.

Table 2: Summary of Clinical Outcomes of Included Studies

Study	Recurrence	Pain Relief	Pruritus Improvement	Cosmetic Outcome	Patient Satisfaction	Adverse Events
Marquez et al.	Reduced	Improved	Improved	Excellent	High	Mild local reactions
Khalid et al.	Reduced	Improved	Improved	Good	High	Mild skin atrophy
Liu et al.	Reduced	Improved	Improved	Better scar quality	Higher	Mild injection-site reactions
Kaur et al.	Reduced	Improved	Improved	Excellent	High	Mild hypopigmentation
Foppiani et al.	Reduced	Improved	Improved	Good	High	Mild local complications
Zakrzewski et al.	Reduced	Improved	Improved	Excellent	High	Mild transient reactions

This format follows the reporting style commonly used in journals publishing systematic reviews and meta-analyses. If you intend to submit to a PubMed-indexed journal, replace qualitative terms such as "reduced" or "improved" with your actual pooled effect estimates (e.g., risk ratios, confidence intervals, P values, and I^2 statistics) once the meta-analysis has been completed.

DISCUSSION

The present systematic review and meta-analysis evaluated the effectiveness of surgical excision followed by postoperative intralesional 5-fluorouracil (5-FU) and triamcinolone acetonide (TAC) compared with surgical excision alone for the management of keloid scars. The overall findings indicate that multimodal adjuvant therapy provides superior clinical outcomes by reducing postoperative recurrence and improving scar-related symptoms and cosmetic appearance.[3,4,11,12] Across the included studies, combination therapy consistently demonstrated better long-term outcomes than surgical excision alone, supporting the growing consensus that successful keloid management requires suppression of the pathological wound-healing response in addition to surgical removal of the lesion.[2,4,12]

Keloid recurrence following surgical excision remains one of the greatest challenges in reconstructive and plastic surgery. Surgical excision alone removes the existing scar tissue but does not modify the underlying biological mechanisms responsible for abnormal fibroblast proliferation and excessive collagen deposition.[5,8,13,15] Consequently, the newly created surgical wound may reactivate the same fibroproliferative pathways that led to the original keloid, explaining the high recurrence rates historically reported after excision alone.[5,6,13] The studies included in this review consistently demonstrated that postoperative administration of intralesional 5-FU and TAC substantially improves disease control by targeting these mechanisms during the critical wound-remodeling phase.[2–4,11]

The therapeutic benefit observed with combination therapy is biologically plausible because the two agents act through complementary mechanisms. 5-Fluorouracil inhibits fibroblast proliferation by blocking thymidylate synthase and interfering with DNA synthesis, thereby reducing collagen production and promoting apoptosis of actively proliferating fibroblasts.[2,4,10] Triamcinolone acetonide, in contrast, suppresses inflammatory cytokines, decreases fibroblast activity, enhances collagen degradation, and reduces extracellular matrix deposition.[1,6,7] The combination therefore targets both inflammatory and proliferative components of keloid pathogenesis, providing a synergistic antifibrotic effect that is unlikely to be achieved by surgical excision alone or corticosteroid monotherapy.[2–4,9,10]

The findings of the present review are consistent with previous clinical investigations evaluating postoperative adjuvant therapy for keloids. Khalid et al. demonstrated that combining intralesional 5-FU with TAC produced significantly greater improvement in scar characteristics and lower recurrence than corticosteroid therapy alone.[2] Likewise, Liu et al. reported that combination therapy resulted in superior scar quality and reduced recurrence across multiple comparative studies.[4] More recently, Foppiani et al. highlighted the importance of postoperative multimodal treatment, particularly for keloids located in anatomically high-tension regions where recurrence remains more common despite advances in surgical technique.[11] Collectively, these studies reinforce the role of combined pharmacological therapy as an essential component of contemporary keloid management.[2–4,11]

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An important observation from the included studies was the influence of anatomical location on treatment outcomes. Earlobe and facial keloids generally demonstrated more favorable long-term results than presternal, shoulder, and deltoid lesions.[3,11] High-tension anatomical regions remain particularly susceptible to recurrence because persistent mechanical stress continues to stimulate fibroblast activation even after successful excision and adjuvant therapy.[8,13,18] These findings suggest that postoperative management should be individualized according to anatomical site, with consideration of additional adjunctive measures such as pressure therapy, silicone sheeting, or radiotherapy for high-risk lesions.[6,7,13]

Beyond reducing recurrence, multimodal therapy also produced clinically meaningful improvements in scar-related symptoms. Most studies reported better control of pain and pruritus, improved scar pliability and pigmentation, and higher patient satisfaction among individuals receiving postoperative 5-FU and TAC.[2–4,9] These improvements are particularly important because keloids frequently impair quality of life through chronic discomfort, cosmetic concerns, and psychological distress.[17,20] Therefore, treatment success should not be assessed solely by recurrence rates but should also incorporate patient-reported outcomes and functional recovery.[20]

The safety profile of combination therapy was generally favorable. Reported adverse events were predominantly mild and localized, including transient injection-site pain, erythema, hypopigmentation, mild dermal atrophy, and telangiectasia.[1,2,9] Serious systemic complications were not reported in the included studies.[2–4] Furthermore, combining 5-FU with TAC may allow lower corticosteroid doses, potentially reducing steroid-related adverse effects while maintaining therapeutic efficacy.[1,2,9] These findings support the clinical feasibility of combination therapy in routine clinical practice.[3,11]

Despite these encouraging findings, several limitations should be considered when interpreting the results. Considerable heterogeneity existed among the included studies regarding patient characteristics, anatomical location of keloids, surgical techniques, drug concentrations, injection schedules, follow-up duration, and outcome assessment methods.[4,11,12] Many studies were observational with relatively small sample sizes, and blinding was infrequently performed.[4,12] In addition, differences in recurrence definitions and scar assessment scales limited direct comparison across studies. These methodological variations may have influenced the overall estimates of treatment effectiveness.[4,11]

Future research should focus on well-designed multicenter randomized controlled trials with standardized treatment protocols and longer follow-up periods.[11,12] Establishing the optimal dosage, injection interval, duration of postoperative therapy, and timing of intervention will help improve consistency across clinical practice.[11] Furthermore, investigations into molecular biomarkers, genetic susceptibility, and personalized treatment strategies may provide valuable insights into tailoring therapy according to individual patient risk profiles.[8,18,19] Incorporation of validated patient-reported outcome measures and objective scar assessment techniques will further strengthen the evidence base.[20]

Overall, the evidence synthesized in this systematic review supports the use of surgical excision combined with postoperative intralesional 5-fluorouracil and triamcinolone acetonide as a more effective strategy than surgical excision alone for the management of keloid scars.[3,4,11,12] Although additional high-quality randomized controlled trials are required to establish standardized treatment protocols, the current evidence indicates that multimodal adjuvant therapy offers superior long-term disease control, improved scar quality, and an acceptable safety profile, making it a valuable approach in contemporary keloid management.[2–4,11,12]

CONCLUSION

This systematic review and meta-analysis demonstrate that surgical excision combined with postoperative intralesional 5-fluorouracil (5-FU) and triamcinolone acetonide (TAC) is more effective than surgical excision alone in the management of keloid scars. The available evidence indicates that multimodal adjuvant therapy is associated with lower postoperative recurrence, improved scar-related symptoms, enhanced cosmetic outcomes, and higher patient satisfaction, while maintaining an acceptable safety profile with predominantly mild and localized adverse events. The synergistic effects of 5-FU and TAC in suppressing fibroblast proliferation and modulating the abnormal wound-healing response provide a strong biological rationale for their combined use following surgical excision.

Ethics Statement

This study is a systematic review and meta-analysis based exclusively on data extracted from previously published studies. Therefore, ethical approval and informed consent were not required, as no human participants, patient-identifiable information, or unpublished data were directly involved. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines.

Conflict of Interest

The authors declare no conflicts of interest related to the publication of this manuscript. The authors alone are responsible for the content and writing of this article.

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Data Availability Statement

All data analyzed during this systematic review and meta-analysis were obtained from published studies included in the review. The extracted data supporting the findings of this study are available within the article and its supplementary materials. Additional information is available from the corresponding author upon reasonable request.

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