WOUND HEALING, FORMATION OF HYPERTROPHIC SCARS AND KELOIDS, AND THEIR TREATMENT METHODS – A LITERATURE REVIEW

Gojenie ran, powstawanie blizn przerostowych i keloidów oraz metody ich leczenia – przegląd literatury

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Abstract

Background: This article reviews current knowledge on the pathogenesis and process of wound healing, highlighting the differences between scar types. It discusses the pathogenesis and characteristics of hypertrophic scars and keloids, along with therapeutic approaches, including adjuvant, targeted, and non-targeted therapies. Psychological aspects and their impact on patients' lives are also addressed. **Methods:** A comprehensive literature search was conducted in the PubMed and Cochrane databases to identify articles on scar pathogenesis and treatment methods, published between 2007 and 2025. **Results:** The wound healing process is complex and multistage, involving inflammation, proliferation, angiogenesis, and extracellular matrix remodelling. Various cells (including fibroblasts and immune cells) and growth factors such as TGF-β, PDGF, and VEGF, participate in this process. Disruptions to healing can lead to the formation of pathological scars, including keloids and hypertrophic scars. Despite advances in therapeutic approaches, the mechanisms underlying their formation are not fully understood. The best clinical outcomes are achieved through combination therapy. **Conclusion:** A wound represents a disruption of skin integrity, and its healing is a dynamic, multistage process encompassing inflammation, proliferation, cell migration, angiogenesis, remodelling, and extracellular matrix synthesis. Healing engages immune cells, connective tissue, epithelial cells, inflammatory mediators, and the vascular system. Abnormalities can lead to pathological scarring. The mechanisms of scar formation remain unclear, which complicates effective management. Hypertrophic scars and keloids, often occurring in high-tension areas, are particularly challenging. Scars cannot be completely eliminated, and no single therapy is universally effective; combined methods yield the best results.

Streszczenie

Wprowadzenie: Niniejszy artykuł stanowi przegląd aktualnej wiedzy na temat patogenezy i procesu gojenia ran. Omówiono różnice między poszczególnymi rodzajami blizn. Przedstawiono również patogenezę i charakterystykę blizn przerostowych oraz keloidów, a także podejścia terapeutyczne, w tym terapie wspomagające, ukierunkowane i nieukierunkowane. Omówiono także aspekty psychologiczne i ich wpływ na życie pacjentów. **Metody:** Przeszukano literaturę w bazach PubMed i Cochrane w celu zidentyfikowania artykułów dotyczących patogenezy blizn i metod ich leczenia, opublikowanych w latach 2007–2025. **Wyniki:** Proces gojenia jest złożony i wieloetapowy. Obejmuje stan zapalny, proliferację, angiogenezę i przebudowę macierzy zewnątrzkomórkowej. W procesie tym biorą udział różne komórki, w tym fibroblasty i komórki odpornościowe, a także czynniki wzrostu, takie jak TGF-β, PDGF i VEGF. Zaburzenia procesu gojenia mogą prowadzić do powstawania blizn patologicznych, w tym keloidów i blizn przerostowych. Pomimo rozwoju metod terapeutycznych mechanizmy ich powstawania nie są w pełni poznane. Najlepsze wyniki leczenia osiąga się dzięki terapii skojarzonej. **Wniosek:** Rana stanowi uszkodzenie ciągłości skóry, a jej gojenie jest dynamicznym, wieloetapowym procesem, obejmującym stan zapalny, proliferację, migrację komórek, angiogenezę, przebudowę i syntezę macierzy zewnątrzkomórkowej. W procesie

gojenia biorą udział komórki odpornościowe, tkanka łączna, komórki nabłonkowe, mediatory stanu zapalnego i układ naczyniowy. Nieprawidłowości w procesie gojenia mogą prowadzić do powstawania blizn patologicznych. Mechanizmy powstawania blizn pozostają niejasne, co utrudnia ich skuteczne leczenie. Blizny przerostowe i keloidy, często występujące w obszarach o dużym napięciu, stanowią szczególne wyzwanie terapeutyczne. Blizn nie można całkowicie usunąć i nie ma jednej terapii, która byłaby uniwersalnie skuteczna. Najlepsze wyniki daje połączenie różnych metod.

Keywords: keloids; wound healing; scars; hypertrophic scars; scar treatment

Słowa kluczowe: keloidy; gojenie ran; blizny; blizny przerostowe; leczenie blizn

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Wound healing process

The skin, composed of multiple tissues forming the body's outer covering, serves as a barrier against chemical, physical, and biological agents, regulates temperature, prevents water loss, supports immunity, and contributes to hormonal balance. Reparative processes within damaged tissues maintain organismal homeostasis [1]. The skin consists of three layers: the epidermis, dermis, and subcutaneous tissue. The epidermis contains densely packed keratinocytes with little extracellular matrix (ECM), whereas the dermis contains abundant ECM with dispersed fibroblasts as its principal cells, responsible for synthesising collagen that provides elasticity and strength. Type I collagen predominates in the dermis, and type IV collagen is characteristic of the basement membrane. Dermal proteoglycans, composed of glycosaminoglycans and proteins, bind water and interact with hyaluronic acid, maintaining turgor. The ECM is dynamic, undergoing continuous synthesis and degradation by enzymes such as metalloproteinases (MMPs), which are regulated by tissue inhibitors (TIMPs). Imbalance in these processes leads to pathological scarring. Fibroblast migration along the ECM, cell accumulation, and stem cell activity are crucial for wound repair, with cytokines also playing an active role [1–3].

Skin injuries result from physical, chemical, or thermal factors. Wounds, whether traumatic or surgical, trigger complex reparative mechanisms aimed at restoring structure and function [4]. Regeneration restores tissue without scarring, whereas healing replaces it with altered tissue. Wound healing progresses through three overlapping stages: inflammation, proliferation, and remodelling. Inflammation removes necrotic tissue and initiates haemostasis through clot formation [1–3]. Neutrophils and macrophages clear bacteria and release growth factors such as PDGF and TGF-β, which regulate fibroblast activity [1, 2, 5]. Fibroblasts produce collagen and differentiate into myofibroblasts that contract the wound, while epithelialisation restores the surface layer. The remodelling phase, which lasts up to a year, re-establishes tissue architecture [2, 5].

Healing depends on cytokines, growth factors, proteases, and ECM interactions. Disturbances in their balance can result in pathological scarring [2, 5, 6]. Key mediators include CTGF, TGF-β, PDGF, VEGF, IGF, EGF, and TNF-α. VEGF and PDGF initiate granulation and angiogenesis, while TNF-α and FGFs stimulate fibroblast and endothelial proliferation. ECM remodelling involves MMPs, and dysregulation of collagen deposition remains a major cause of impaired healing [5, 6].

Pathogenesis of hypertrophic scars and keloids

Hypertrophic scars and keloids arise from abnormal wound healing, which normally progresses through the inflammation, proliferation, and remodelling phases. Fibroblast migration, regulated by cytokines and stem cells, is a key element of tissue repair [1, 2, 7]. Scars, composed of fibrous connective tissue, replace damaged skin and reflect structural remodelling [2, 3]. Aberrant fibroblast and stem cell activity, along with dysregulated collagen deposition, underlie the development of hypertrophic and keloid scars [2, 5, 7].

An important aspect of scar pathogenesis not fully addressed in the original text is the role of collagen type III. Physiologically, the ratio of collagen I to III is tightly regulated during wound healing, with type III predominating in early proliferation and gradually replaced by type I during remodelling [2, 5, 7]. This transition ensures appropriate tissue elasticity and structural organisation. In hypertrophic scars and keloids, this balance is disrupted: type III collagen remains elevated, contributing to persistent stiffness, a disorganised ECM, and pathological scar maturation [2, 5, 7]. The abnormal persistence of collagen III, combined with excessive fibroblast activity and dysregulated TGF-β signalling, underlies the characteristic rigidity and raised appearance of these scars. TGF-β-activated fibroblasts drive excessive ECM and hypertrophy, while wounds healing without inflammation tend to scar less [5–8].

Mature scars differ from normal skin in elasticity, colour, and structure, lacking rete ridges, glands, and hair follicles,

and retaining capillaries for up to six months. Scarring reflects the balance between regeneration and restoration of the skin barrier [2, 3, 7]. Hypertrophic scars, confined to the wound area, usually develop around four weeks after injury [3, 7, 9]. Their formation involves excessive fibroblast activity, angiogenesis, delayed collagen breakdown, and chronic inflammation, with disorganised collagen and myofibroblast-mediated contracture [2, 5, 6, 8]. TGF-β overexpression, reduced MMP activity, and elevated CTGF and VEGF contribute to hypertrophy and delayed remodelling [5, 6, 10].

Keloids, in contrast, extend beyond the wound borders and do not regress [3, 7, 9, 11]. Their pathogenesis involves dysregulated fibroblast proliferation, impaired apoptosis, and abnormal ECM remodelling. A further critical element in scar pathophysiology is the role of myofibroblasts. These specialised fibroblasts mediate wound contraction through cytoskeletal tension and are normally removed by apoptosis during scar maturation. In hypertrophic scars and keloids, myofibroblasts persist abnormally, contributing to excessive contracture and raised scar morphology [2, 5, 12]. Their activation is strongly influenced by mechanical forces within the wound environment, including tension along skin lines, and is potentiated by TGF-β signalling, linking mechanotransduction to pathological ECM deposition. Dysregulated myofibroblast activity, together with aberrant persistence of collagen type III and fibroblast heterogeneity, underlies the characteristic rigidity, elevated contour, and functional impairment observed in hypertrophic and keloid scars [5, 7, 12]. Genetic predisposition also significantly contributes to keloid formation and abnormal scar healing. Variations in genes involved in TGF-β signalling, including TGF-β1 and TGFBR2, as well as polymorphisms in SMAD proteins and specific HLA alleles, have been associated with enhanced fibroblast proliferation, impaired apoptosis, and excessive ECM deposition. Moreover, keloids occur more frequently in individuals with certain connective tissue syndromes, such as Rubinstein-Taybi, Ehlers-Danlos, and Marfan syndrome, highlighting the influence of inherited abnormalities in collagen metabolism and tissue elasticity [5, 7, 9].

In addition, heterogeneity among keloid fibroblasts has been observed, with distinct subpopulations displaying variable collagen synthesis, cytokine responsiveness, and proliferative capacity, which may explain differences in scar morphology, growth patterns, and treatment response [12]. These genetic and cellular factors interact with environmental and mechanical cues, such as wound tension and local inflammation, to determine the severity and persistence of hypertrophic and keloid scars. Risk is higher in individuals of African, Asian, and Hispanic descent, especially during puberty or pregnancy, and is rare in albinos [7, 9, 11]. Influencing factors include wound tension, pigmentation, immune dysregulation, and genetic background, along with cytokines such as TGF-β, PDGF, VEGF, IL-1, IL-6, and TNF-α [6–9]. Scar formation is also influenced by age, skin type, hormones, nutrition, systemic disease, circulation, infection, and wound depth or location [3, 7, 9]. Remodelling begins around three weeks after wound closure, and mature scars typically become flat and pearly within a year. Hypertrophic and keloid scars are more common in younger patients due to heightened fibroblast activity. A single patient may present with various scar types, classified by shape, cause (surgical, inflammatory, traumatic, burn, or striae), or underlying mechanism [3, 7, 13].

Characteristics of hypertrophic scars and keloids

Hypertrophic scars are thick, red, and raised, but remain confined to the original injury site. They result from prolonged healing and excessive collagen synthesis, often following burns or impaired collagen metabolism, and are more common in individuals genetically predisposed to pathological healing [3, 7, 9]. These scars frequently develop in areas of high skin tension, such as the chest (sternum), shoulder blades, joints, and other regions with steep mechanical force gradients along skin tension lines, which promote excessive fibroblast activity and collagen deposition. High mechanical tension in these anatomical areas contributes to scar formation by stimulating fibroblast proliferation and increasing collagen synthesis, making hypertrophic scars more likely to develop and become pronounced [5–7]. They may negatively affect quality of life due to pain, itchiness, appearance, or functional impairment [4, 9, 11].

Keloids are raised scars that extend beyond the original wound borders and do not regress. They involve excessive deposition of collagen and glycosaminoglycans, and differ in collagen composition (types I and III) from normal skin. Keloids may form after injury or spontaneously, appearing as protruding nodules that grow from a central core and may reach several centimetres. Common symptoms include burning, itching, redness, tension, pain, and impaired mobility. Keloids typically occur on the chest, back, shoulders, and earlobes, and may also arise from minor injuries such as insect bites or injections. They are more frequent in younger individuals due to active fibroblast proliferation. Similar to hypertrophic scars, areas subjected to high mechanical forces and tissue tension, such as the chest, back, and joints, are particularly predisposed to keloid formation [5, 7, 9, 11, 14]. Mechanical stress in these regions amplifies fibroblast activity and excessive collagen deposition, contributing to the aggressive growth and protrusion characteristic of keloids [5–7].

Acne keloidalis increases the risk of both keloid and hypertrophic scarring. These lesions lack hair follicles, sebaceous glands and sweat glands, and show abnormal fibroblast activity, with increased synthesis of elastin, fibronectin, and proteoglycans, as well as an aberrant cytokine response. The overlying epidermis may appear normal or atrophic [8, 9]. A spontaneous form of keloid occurs in predisposed individuals, presenting with multiple foci and rich vascularisation during the growth phase, giving a pink or red appearance that gradually fades over time [9, 11].

Hypertrophic scars and keloids differ in their response to light- and energy-based treatments. Keloids, with higher vascularity and fibroblast activity, exhibit more pronounced inflammatory reactions, whereas hypertrophic scars are more localised [10, 15, 16]. In patients with darker skin phototypes (Fitzpatrick IV–VI), post-inflammatory hyperpigmentation is a common and clinically relevant complication, limiting the use of aggressive

laser modalities and medium- to deep-depth chemical peels [11, 15, 16]. Consequently, current reviews and clinical guidelines emphasise cautious patient selection, preference for less aggressive or fractional approaches, and individualised treatment protocols adjusted to scar type, anatomical location, and skin phototype to balance therapeutic efficacy with safety [11, 16].

According to Mustoe's classification, scars are divided as follows:
- Normal scar – pale, flat;
- Abnormal scar – painful, red, slightly raised above the surrounding skin;
- Linear hypertrophic scar – red, confined to the area of surgical incision, may be painful;
- Widespread hypertrophic scar – large, raised, flat, sometimes itchy;
- Small keloid – raised, localised, itchy, extends beyond the original wound;
- Large keloid – itchy or painful, large, raised, extends beyond the wound margins [14].

Scars can also be classified based on shape:
- Linear scars – the least visible, tend to fade quickly, typically occurring at surgical or traumatic incision sites;
- Atrophic scars – result from skin thinning; often caused by inflammation such as acne or chickenpox; may be singular or numerous;
- Hypertrophic scars – raised, firm, fibrotic thickening of various shapes and sizes, confined to the original area of trauma, surgery, inflammation, or burn;
- Keloids – typically occurring at sites of skin damage such as injections, surgeries, burns, or post-inflammatory lesions.

Scars may also be categorised by injury mechanism: post-surgical, post-burn, post-acne, post-traumatic, or striae. Another classification is based on aetiology: post-surgical, post-burn, post-inflammatory, or post-traumatic [3, 9, 14, 17].

Two main types of factors influence scar appearance:
- General factors: Fitzpatrick skin type, patient age, kidney or liver disease, diabetes, overall health, comorbidities, hormonal imbalances, nutrition, circulatory disorders, vitamin deficiencies.
- Local factors: neuropathy, impaired wound perfusion, wound infection, and the location, shape, depth, and width of the wound [7, 9, 11, 13].

In clinical practice and research, scar severity and treatment outcomes are commonly assessed using validated scar assessment scales. The Vancouver Scar Scale (VSS) focuses on observer-based evaluation of vascularity, pigmentation, pliability, and scar height, providing an objective measure of scar maturity and severity. In contrast, the Patient and Observer Scar Assessment Scale (POSAS) incorporates both clinician-rated parameters (including vascularity, pigmentation, thickness, surface roughness, and pliability) and patient-reported symptoms such as pain, pruritus, stiffness, and overall scar perception. The combined use of observer- and patient-based assessments allows for a more comprehensive evaluation of hypertrophic scars and keloids, particularly when monitoring therapeutic efficacy and impact on quality of life [14, 18, 19].

Therapeutic methods

Adjunctive therapy

Scar treatment depends on scar type, characteristics, and time since healing. Surgical correction is usually avoided during the first year, with conservative approaches such as massage, emollients, or specialised ointments used instead [4, 7, 13]. Recurrence rates are high with monotherapy. The aim of treatment is to reduce scar prominence and symptoms (e.g. pain, burning, restricted movement), particularly in visible areas that affect quality of life [7, 11, 18].

Flavonoids are plant-derived compounds used to prevent severe scar formation. Products such as gels and ointments containing flavonoids have shown variable efficacy. Quercetin, a flavonoid, may act by inducing MMP-1 or inhibiting SMAD2/3/4 expression [20].

Deep oscillation is a non-invasive technique using electrostatic fields to generate deep tissue vibrations that enhance fluid transport and tissue healing. Effective in early scar remodelling, it uses frequencies between 5 and 250 Hz. Reported benefits include improved blood flow, scar pigmentation, and elasticity. It is particularly useful after grafts, surgery, or trauma, and in cases where conventional mechanical therapy is contraindicated [21].

Laser therapy

Laser therapy has become the gold standard in scar management, used either alone or in combination with other modalities [4, 11, 16]. Ablative lasers (e.g. Er:YAG, CO_2) remove the epidermal and upper dermal layers, whereas non-ablative lasers (e.g. Er:Glass, PDL, diode, Nd:YAG) remodel collagen without disrupting the epidermis [11, 15, 16]. The Er:YAG laser (2940 nm) corresponds to the peak absorption coefficient of water, producing a superficial and precisely controlled ablative effect with minimal thermal injury and fewer adverse effects. In contrast, CO_2 lasers penetrate more deeply, generating a broader zone of thermal impact that induces more pronounced collagen remodelling but carries a higher risk of side effects.

Skin phototype, commonly classified according to the Fitzpatrick scale, is an important clinical factor influencing both the selection and safety of therapeutic modalities for hypertrophic scars and keloids. Several reviews and clinical guidelines emphasise that darker skin phototypes are associated with an increased risk of pigmentary complications, particularly post-inflammatory hyperpigmentation (PIH), when treated with laser- and energy-based devices. Consequently, treatment strategies should be individualised according to skin phototype, with careful adjustment of laser parameters, preference for less aggressive modalities, and increased caution in patients with higher Fitzpatrick phototypes to optimise outcomes and minimise adverse effects.

Laser therapy therefore carries a higher risk of PIH in individuals with darker skin phototypes (Fitzpatrick IV–VI), making careful selection of laser type, wavelength, and fluence essential. The absorption characteristics of different lasers influence their safety and efficacy: Er:YAG

(2940 nm) energy is strongly absorbed by water, resulting in a superficial and highly controlled ablative effect with minimal thermal spread, whereas CO_2 lasers (10,600 nm) penetrate more deeply, producing a broader zone of thermal impact and more extensive collagen remodelling, but with a higher risk of PIH, scarring, or delayed healing, particularly in dark-skinned patients. For hypertrophic scars and keloids, lower fluences are generally recommended to reduce the risk of adverse effects while still promoting collagen remodelling.

Fractional non-ablative lasers are often preferred in darker skin types because they deliver energy in microthermal zones, allowing surrounding tissue to remain intact and promoting faster re-epithelialisation. Pre-treatment skin preparation, including topical depigmenting agents or careful photoprotection, may further reduce the risk of hyperpigmentation and optimise outcomes, particularly in individuals prone to abnormal pigmentary responses.

The fractional Er:Glass laser (1550 nm) creates microthermal zones that stimulate collagen regeneration, reducing scars and stretch marks with minimal discomfort and rapid recovery [11, 15, 16]. PDL (585–600 nm) targets haemoglobin to treat the vascular components of scars. Compared with other methods, such as microneedling or CO_2 lasers, non-ablative lasers offer lower pain and shorter downtime. Lasers generally outperform IPL (intense pulsed light) devices in pain relief, anti-inflammatory action, and wound healing [10, 11, 16].

IPL enhances microcirculation, stimulates fibroblasts, and improves oxygen exchange through low-energy electromagnetic radiation (500–2500 nm), leading to reduced scar thickness, greater elasticity, and improved appearance. However, IPL delivers broad-spectrum, non-coherent light with limited penetration and selectivity, restricting its ability to target deeply located fibroblasts and the excessive collagen production characteristic of keloids. Consequently, IPL may improve scar appearance and vascularity but has limited impact on the key pathophysiological mechanisms underlying keloid formation and persistence [20, 22].

Fractional lasers, used in atrophic acne scars, hypertrophic scars, and stretch marks, create micro-injuries while sparing surrounding tissue, enabling rapid re-epithelialisation and a lower risk of post-inflammatory hyperpigmentation. Fractional laser therapy is indicated for atrophic acne scars, remodelling hypertrophic surgical and traumatic scars, and improving stretch marks. Contraindications include the use of skin-sensitising medications, and potential adverse effects comprise scarring, depigmentation, hyperpigmentation, and blistering. In clinical practice, individualised treatment protocols that consider skin phototype, scar type, and anatomical location are essential for maximising efficacy and minimising complications, particularly when treating dark-skinned patients with hypertrophic or keloid scars [11, 15, 16, 20, 22].

Acids peels

Chemical peels are classified by depth: superficial (stratum corneum to spinous layer), medium and deep (epidermis to reticular dermis). Acid strength depends on pH and pKa, and treatment choice is guided by photodamage, skin type, scar characteristics, and therapeutic goals. Agents such as trichloroacetic acid (15–40%), pyruvic acid, salicylic acid, glycolic acid, lactic acid, mandelic acid, Jessner's solution, and phenol are used to reduce scars. Combined peels may reduce adverse effects [23–25].

Hydroxy acids (AHAs and BHAs) provide gentle exfoliation at concentrations below 5%. Mandelic acid is notable for its antibacterial properties and suitability for all skin types. BHAs such as salicylic acid have anti-inflammatory benefits. Newer agents, including gluconic acid and polyhydroxy acids (PHAs) such as lactobionic acid, provide gentle exfoliation, antioxidant effects, and suitability for sensitive skin [23–25].

Special caution is required in patients with darker skin phototypes (IV–VI), who are particularly susceptible to complications. High-concentration formulations, especially trichloroacetic acid (TCA) 35–40%, may induce PIH, exacerbate scarring, prolong inflammation, and potentially worsen the overall appearance of scars. For this reason, pre-treatment prior to chemical peeling is particularly important in patients with Fitzpatrick skin types IV–VI and in the management of hypertrophic scars and keloids, as it helps reduce the risk of PIH and excessive inflammatory response. Recommended pre-treatment for a period of 2–4 weeks includes hydroquinone at a concentration of 2–4% to inhibit melanogenesis, cautious use of a retinoid to normalise keratinisation, mandatory application of broad-spectrum SPF 50+ sunscreen, and avoidance of skin irritation.

Acid peels are used primarily for acne scars and atrophic scars rather than hypertrophic scars or keloids. They are not first-line therapy, should be applied with caution, and are mainly used as adjunctive treatment [17, 26, 27].

Chemotherapeutic agents

Main chemotherapeutic agents used in scar management include antimetabolites and steroids, such as 5-fluorouracil (5-FU), mitomycin C, bleomycin, and corticosteroids, which inhibit fibroblast proliferation by disrupting cell cycles [28].

5-FU blocks thymidylate synthase and suppresses TGF-β-induced collagen expression, showing particular efficacy when combined with other therapies. Weekly or biweekly intralesional injections are effective, with adverse effects including pain, ulceration, and hyperpigmentation, although systemic toxicity has not been reported [11, 28].

Mitomycin C inhibits nucleic acid and protein synthesis, reducing fibroblast activity, but topical use application has not prevented keloid recurrence and may delay wound healing, indicating the need for further research.

Bleomycin reduces collagen and lysyl oxidase (LOX) synthesis, and may induce fibroblast apoptosis, with similar side effects and rare systemic toxicity [11, 28].

Corticosteroids, particularly triamcinolone acetonide (TAC), are widely used for their anti-inflammatory and

antifibrotic effects. They reduce collagen and glycosaminoglycan synthesis, and modulate growth factors such as TGF-β, IGF-1, and VEGF. TAC (10–40 mg/ml) is injected intralesionally every 4–6 weeks, inhibiting TGF-β1 and increasing bFGF expression. When combined with surgery, recurrence rates drop to 10–30%, making TAC the current gold standard [11, 29]. Monotherapy with TAC achieves a 50–100% response rate, but combining it with agents such as 5-FU, interferon-α2b, or pulsed dye laser further improves scar outcomes.

Dexamethasone also slows fibroblast proliferation and reduces VEGF expression, whereas topical corticosteroids alone are ineffective for prevention. Adverse effects such as atrophy, pigment changes, telangiectasia, pain, and ulceration may be reduced by combining low doses with 5-FU [11, 29].

Targeted therapy

Targeted therapies aim to block specific factors involved in pathological scar formation, particularly those driving fibrosis. Key targets include fibronectin (FnEDA), cytokines, and enzymes involved in collagen cross-linking. Antisense oligonucleotides (ASOs) directed against TGF-β mRNA have shown promise in vitro by downregulating fibrosis-related markers such as MMP-9, SMAD2, and SMAD4. ASOs targeting HIF-1α reduce PAI-1 levels. However, these therapies remain experimental and are not yet applicable in clinical practice.

Collagen cross-linking inhibitors such as beta-aminopropionitrile (BAPN) inhibit LOX, an enzyme responsible for collagen fibre stabilisation. BAPN has shown efficacy in reducing severe scarring following keloid excision. Other agents, including copper chelators (e.g. D-penicillamine) and proline analogues, also aim to reduce collagen deposition but require further study before clinical use [5, 30].

Surgical treatment

Every surgical intervention results in scar formation as a normal component of wound healing, and even well-healed scars differ structurally from normal skin [3, 6]. Excision of hypertrophic scars may improve aesthetic outcomes but carries a risk of recurrence; a scar is generally considered successfully treated if no recurrence occurs within two years. Importantly, surgical excision itself may trigger recurrence of hypertrophic scars and keloids, occasionally producing lesions larger than the original, and should therefore be undertaken with caution, except in cases of minor hypertrophic scars.

The first-line surgical approach involves scar excision combined with modification of scar shape, most commonly through Z- or W-plasty, to reduce linear tension. Effective recurrence prevention relies on tension-minimising strategies, including subcutaneous or fascial tension-reduction sutures, which address the dermal origin of pathological scarring. Dermal sutures alone are insufficient to offload dermal tension, whereas engagement of the superficial and deep fascia enables effective stress redistribution and controlled approximation of wound edges, a key factor in preventing postoperative pathological scarring. Zig-zag techniques, including Z-plasty, further facilitate release of linear contractures, accelerate scar maturation, and reduce pathological scarring, particularly when scars cross joints.

Surgical management is commonly complemented by adjuvant therapies, including 5-fluorouracil, corticosteroids, laser therapy, topical steroids, and silicone-based products, to limit excessive connective tissue proliferation. Local flap techniques may be employed in selected cases, particularly for elevated scars or those that restrict movement [6, 31–33]. Compared with skin grafts, which frequently result in secondary circumferential contractures, local flaps offer better postoperative adaptability and a lower risk of contracture formation. Although historically avoided due to concerns about donor-site keloid formation, multimodal strategies incorporating tension-reduction sutures and radiotherapy can mitigate these risks, rendering flap reconstruction a viable option for severe keloids. In patients predisposed to keloid formation, surgical incisions should be oriented along relaxed skin tension lines and performed using atraumatic techniques. Despite appropriate management, keloids frequently recur following excision and may increase in size [6, 31–33].

Radiotherapy

Superficial X-ray therapy, low- or high-dose-rate brachytherapy, and electron-beam irradiation have demonstrated favourable outcomes in scar-reduction protocols, most commonly as adjuncts to surgical excision of keloids. The therapeutic and preventive effects of radiotherapy are mediated through suppression of neovascular sprouting and inhibition of fibroblast proliferation, leading to reduced collagen synthesis and, consequently, decreased inflammation. Radiotherapy used as monotherapy should be reserved for elderly patients or those with very large keloids, as effective treatment requires relatively high radiation doses. This approach provides rapid relief from pain and pruritus, while gradual improvements in scar pigmentation and thickness are typically observed over the following year. Radiotherapy is particularly effective when combined with surgical excision, with combined therapy associated with lower recurrence rates than radiotherapy alone. Advances in surgical techniques, radiation delivery, and postoperative management likely contribute to these improved outcomes.

Although superficial or orthovoltage x-rays (photons) were previously employed, many centres now favour electron-beam (β-ray) therapy because of its reduced impact on internal organs. High-dose-rate brachytherapy, primarily using γ-rays, is increasingly utilised; however, further evaluation of its safety with respect to internal organs is required [6, 31–34]. Electron-beam irradiation is typically initiated 24–48 hours after keloid excision. The maximum biologically effective dose for keloid treatment is 30 Gy, as higher doses do not improve efficacy and instead increase the risk of secondary carcinogenesis and adverse effects, including hypo- and hyperpigmentation, erythema, telangiectasia, and tissue atrophy. Because recurrence risk varies by anatomical location, a biologically effective dose of 30 Gy is not always necessary. To further reduce carcinogenic risk, postoperative irradiation may be tailored to the treated site, with

protocols including 18 Gy in three fractions over three days for high-recurrence areas, 8 Gy in a single fraction for earlobes, and 15 Gy in two fractions over two days for other body sites. Over the past 70 years, only a limited number of cases of malignant transformation following keloid radiotherapy have been reported. Nevertheless, as radiation carries an inherent carcinogenic risk, particularly in sensitive regions such as the breast and thyroid, its use should be approached with appropriate caution [31, 33, 34].

Pressure therapy

Pressure therapy employs mechanical compression using garments, cuffs, or clips [3, 6]. Treatment duration ranges from 6 to 24 months. This method is widely recommended for post-burn scars to prevent the formation of contractile fibrous bands, also known as "bridges". It requires the continuous use of custom-made compression garments, worn for 23 hours per day with a one-hour break for hygiene and skincare routines [13, 22, 31]. The mechanism of action involves inducing tissue hypoxia (limiting the supply of blood and oxygen), modulating fibroblast activity, and promoting collagen breakdown [5, 13, 31].

Post-surgical scar care follows three phases. Phase 1: no scar manipulation; dressings and manual lymphatic drainage (MLD) support healing. During the first 7 days, a mature scar has not yet formed, and the wound remains protected under a dressing. This first week is critical for the development of postoperative adhesions. By 6 to 8 weeks post-surgery, Phase 2 begins: MLD continues, with scar-area treatments and dynamic taping to minimise tension. Phase 3: scar management occurs from approximately 6–8 weeks to 0.5–2 years post-operation, and focuses on scar remodelling. A mature scar should move freely; adhesions indicate abnormal healing [21, 31]. Therapeutic techniques applied during this phase are significantly more intensive than in earlier stages.

Current guidance on pressure levels and treatment duration is largely derived from empirical experience and recommends sustained compression in the range of 15–40 mmHg; however, pressures between 15 and 25 mmHg are generally considered therapeutic, whereas higher values approaching 40 mmHg are associated with an increased risk of tissue ischaemia and adverse effects [13, 21, 22, 31].

Silicone

Silicone, a biomedical polymer, is applied topically in the form of gels or dressings that remain on the skin surface. Available formulations include gels, oils, elastomers, rubbers, and resins, with their properties influenced by polymerisation processes and alkylsiloxane content. Silicone reduces itching and pain, maintains hydration, and improves scar texture and colour. It conforms well to scar contours and is non-invasive. Gels create a transparent occlusive layer suitable for visible scars, whereas creams are more appropriate for small, fresh lesions. Silicone elastomer patches adhere through Van der Waals forces and may remain in place for up to a month.

Silicone increases skin temperature by approximately 1.7°C, potentially activating collagenase and altering fibroblast activity, although its exact mechanism is unclear due to the absence of systemic absorption. Silicone gels and patches demonstrate better efficacy for hypertrophic scars than keloids. However, occlusion may still reduce keloid density, pain, and pruritus [22]. This approach is primarily used as a preventive measure against the formation of hypertrophic scars and keloids and has not been shown to be effective in the treatment of established or mature lesions. In high-risk patients, early initiation of silicone therapy is a key preventive strategy. Silicone may also help with neurogenic inflammation and stabilise scars by addressing mechanotransduction.

Therapy may be initiated approximately two weeks after complete wound closure. Silicone sheets should be worn for a minimum of 12 hours per day, and preferably continuously, for at least two months. In anatomical regions with frequent movement or poor adherence of sheets, silicone gel is the preferred option and should be applied twice daily [18, 22].

Therapeutic algorithms for hypertrophic scars and keloids

Management of hypertrophic scars and keloids requires a stepwise, individualised approach that integrates scar type, stage, anatomical location, patient-specific risk factors, and prior treatment response [7, 18]. Both Ogawa and Mustoe emphasise prevention as the initial step, including meticulous wound closure, minimisation of mechanical tension, early silicone therapy, and pressure application to high-risk areas. Ogawa's algorithm combines preventive measures with active interventions tailored to scar severity and recurrence risk. Initial therapy for established scars commonly involves intralesional corticosteroids, frequently combined with 5-FU or laser therapy, to reduce fibroblast proliferation and abnormal ECM deposition. Surgical excision is reserved for refractory, functionally limiting, or cosmetically significant scars, and must be accompanied by adjuvant therapy to prevent recurrence.

Novel approaches, including stem cell modulation, growth factor targeting, and biologics, aim to normalise collagen deposition and TGF-β-mediated signalling. Treatment decisions are guided by scar location, size, patient age, skin type, and the heterogeneity of fibroblast subpopulations. Mustoe's algorithm similarly emphasises classification by scar type (hypertrophic versus keloid), stage (proliferative versus mature), and risk profile. Preventive strategies include silicone sheeting, pressure therapy, and early recognition of high-risk wounds [13, 22, 29]. Active scars are primarily managed with intralesional corticosteroids, with adjunctive therapies such as cryotherapy, laser therapy, and superficial chemical peels selected according to scar morphology and patient tolerance [11, 18, 29]. Surgery is considered for scars resistant to conservative measures, again followed by adjuvant therapy to minimise recurrence [11, 18]. Mustoe highlights the importance of continuous monitoring using validated assessment tools, such as the Vancouver Scar Scale (VSS) and Patient and Observer Scar Assessment Scale (POSAS), to guide ongoing therapy and optimise functional and aesthetic outcomes [14, 18, 19]. In practice, both algorithms underscore that scar treatment should be individualised,

combining preventive and active interventions and guided by pathophysiological understanding, including fibroblast heterogeneity, persistent myofibroblast activity, collagen type III dysregulation, mechanical tension, and genetic predisposition [5, 7, 12, 18].

Combined therapy

Combining surgical excision with adjunctive therapies such as pulsed dye laser, radiotherapy, CO_2 laser, or pressure therapy reduces recurrence rates and underscores the need for personalised treatment plans that account for individual scar-risk factors. Patients prone to dystrophic scarring should avoid procedures that disrupt skin integrity, and no single modality guarantees success, making combined therapies preferable. Hypertrophic scars are often managed in stages, beginning with pressure therapy – frequently combined with corticosteroids – and, in some cases, skin expansion to facilitate closure. Keloid treatment is more challenging and may involve corticosteroid injections, vitamin A, surgery, or radiotherapy [18, 32, 35]. Because keloid pathophysiology remains incompletely understood, prevention is essential.

Monotherapies (e.g. excision, intralesional chemotherapy, laser, cryotherapy, silicone, pressure) yield variable and often temporary results with high recurrence rates (≈50–70%). Intralesional corticosteroids, commonly used alongside surgery, reduce collagen synthesis and fibroblast activity, and suppress pro-inflammatory mediators, although they typically soften rather than eliminate keloids. Combined treatments generally produce superior outcomes. When prophylaxis fails, options include corticosteroids, 5-FU, radiotherapy, laser therapy, or surgery, ideally applied in a tailored, combinatorial manner. Emerging techniques such as laser-assisted drug delivery or advanced topical formulations may benefit refractory cases. Microdermabrasion combined with AHA/BHA peels can improve texture and regeneration via stimulation of collagen, elastin, and glycosaminoglycan synthesis, and is more effective when performed in series than as a standalone treatment [23, 26]. Although standardised guidelines are lacking, evidence supports that combining excision with triamcinolone (TAC), pulsed dye laser, or 5-FU reduces recurrence and side effects. Treatment should remain flexible and tailored to each patient's response [29, 35].

Psychological aspects

Smooth skin is a key component of aesthetic appearance and self-esteem, and a clear link exists between dermatological conditions and mental health. Scars pose cosmetic, psychological, and physical challenges. Keloid lesions may cause functional impairment and significant psychosocial burden. They can be hypersensitive to touch and may represent a significant clinical problem [9, 34]. Scars, especially extensive ones, often serve as reminders of traumatic or unfortunate life events, and scarring in visible areas may provoke negative reactions from others. Scars in conspicuous places, such as the face, are particularly difficult for patients to accept. Scars are frequently perceived as disfiguring; individuals with visible scarring may be judged less attractive, which can lead to psychological distress. Scars can also be a source of anxiety, sleep problems, and even depression. Patients with scars should therefore be provided with optimal holistic treatment [33, 34].

Summary

Because of the complexity of the healing process, disturbances may occur, leading to the formation of various types of pathological scars. These lesions are characterised primarily by increased collagen synthesis and decreased collagen degradation. Scars have a diverse morphological presentation. Despite significant advances in medicine and aesthetic dermatology in recent years, the mechanisms involved in scar pathogenesis have not been fully elucidated, which complicates therapy.

Scar treatment is a challenging clinical problem. The complexity of scar pathogenesis, encompassing dysregulated fibroblast activity, excessive collagen deposition, and altered extracellular matrix remodelling, makes it unlikely that any single therapy can address all pathological mechanisms. Treatment often relies on direct and indirect modulation of skin fibroblast proliferation and collagen synthesis. Hypertrophic scars and keloids, most commonly located in areas of increased tissue tension, represent a distinct subgroup. It should be emphasised that only improvement in scar appearance and reduction in size are achievable. No currently available method is effective for all patients, regardless of differences in therapeutic goals and levels of invasiveness. Clinical studies have consistently shown that monotherapies, whether surgical, pharmacological, or physical, often result in incomplete resolution or high recurrence rates, particularly in hypertrophic scars and keloids. Complete scar removal is not achievable.

The most commonly used therapeutic approaches include pharmacological methods (local corticosteroid injections, systemic and topical preparations), surgical treatment, and physical modalities including laser therapy and pressure therapy. Each therapeutic method can be used as monotherapy; however, combining multiple methods yields significantly better therapeutic outcomes.

Combination therapy leverages complementary mechanisms: for example, surgery can remove bulky scar tissue, corticosteroids reduce fibroblast proliferation, and physical modalities such as laser or pressure therapy remodel collagen and improve vascularisation. This multimodal approach addresses multiple aspects of scar pathophysiology, leading to improved functional and aesthetic outcomes.

Therefore, for most patients, multiple methods should be combined to achieve the most effective treatment. Personalised multimodal strategies should be planned for each patient, taking into account scar type, anatomical location, and risk of recurrence, to optimise therapeutic efficacy and minimise complications. Patients should be informed that the goal of treatment is to reduce aesthetic and physical impairment rather than achieve complete scar elimination.

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