Evidence-Based Scar Management: How to Improve Results with Technique and Technology

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Background: Scars represent the visible sequelae of trauma, injury, burn, or surgery. They may induce distress in the patient because of their aesthetically unpleasant appearance, especially if they are excessively raised, depressed, wide, or erythematous. They may also cause the patient symptoms of pain, tightness, and pruritus. Numerous products are marketed for scar prevention or improvement, but their efficacy is unclear.
Methods: A literature review of high-level studies analyzing methods to prevent or improve hypertrophic scars, keloids, and striae distensae was performed. The evidence from these articles was analyzed to generate recommendations. Each intervention's effectiveness at preventing or reducing scars was rated as none, low, or high, depending on the strength of the evidence for that intervention.
Results: For the prevention of hypertrophic scars, silicone, tension reduction, and wound edge eversion seem to have high efficacy, whereas onion extract, pulsed-dye laser, pressure garments, and scar massage have low efficacy. For the treatment of existing hypertrophic scars, silicone, pulsed-dye laser, CO_2 laser, corticosteroids, 5-fluorouracil, bleomycin, and scar massage have high efficacy, whereas onion extract and fat grafting seem to have low efficacy. For keloid scars, effective adjuncts to excision include corticosteroids, mitomycin C, bleomycin, and radiation therapy. No intervention seems to have significant efficacy in the prevention or treatment of striae distensae.
Conclusion: Although scars can never be completely eliminated in an adult, this article presents the most commonly used, evidence-based methods to improve the quality and symptoms of hypertrophic scars, as well as keloid scars and striae distensae. (*Plast. Reconstr. Surg.* 138: 165S, 2016.)

The prevention and improvement of scars are goals that have inspired the development of numerous products and devices; many of which were later proven ineffective or even harmful. The literature on scar prevention and treatment contains many studies that have a high risk of bias or inadequate design. Nevertheless, the analysis of the studies that are well designed and unbiased affords us the ability to assess the efficacy of various interventions for scar treatment.

In this article, we begin by describing the validated scar assessment tools most commonly used in scar studies. We then discuss the evidence behind topical scar treatments, such as onion extract, vitamin E, and silicone, followed by lasers, injectables, pressure garments, emerging molecular therapies, and surgical technique. Finally, we briefly discuss the evidence-based treatment of keloid scars and striae distensae. After each section, we provide an evidence-based recommendation, along with the level of evidence of the studies on which the recommendation is based. The studies included in this review are summarized in Table 1, and the evidence is summarized in Table 2.

METHODS

A database search in PubMed was performed for all articles containing the terms "scar", "onion extract", "silicone", "quercetin", "pulse dye", "CO_2

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Table 1. Summary of the Articles Included in This Review

Study	Study Type	No. of Subjects	Intervention Evaluated	Outcomes of the Intervention
Hypertrophic scar prevention				
Chanprapaph et al[5]	RCT	20	Onion extract	Improved scar height and symptoms, no difference in scar redness, pliability, appearance
Jenwitheesuk et al[6]	RCT	60	Silicone + onion extract	Improved scar pigmentation and symptoms, no difference in scar redness, pliability, height
Wananukul et al[7]	RCT	39 (pediatric)	Onion extract	Reduced incidence of hypertrophic scars
Chung et al[8]	RCT	24	Onion extract	No difference from control (petrolatum)
Willital and Heine[9]	RCT	45	Onion extract	Improved scar width and pigmentation
Draelos et al[12]	RCT	44	Onion extract	Improved scar appearance, softness, texture and redness
Draelos[13]	RCT	60	Onion extract	Improved scar appearance, softness, texture and redness
Ocampo-Candiani et al[14]	RCT	61	Onion extract	Improved scar pigmentation, texture and redness
Jackson and Shelton[15]	RCT	17	Onion extract	No difference from control (petrolatum)
Baumann and Spencer[24]	RCT	15	Vitamin E	No difference from control (petrolatum), more contact dermatitis
Khoo et al[25]	RCT	122	Vitamin E	No difference from placebo
Jenkins et al[26]	RCT	159	Vitamin E	No difference from placebo
Zampieri et al[27]	RCT	428	Vitamin E (used preop and postop)	Improved scar cosmetic result compared with petrolatum
Chan et al[31]	RCT	50	Silicone	Improved scar pigmentation, vascularity, pliability, height and symptoms
Cruz-Korchin[34]	Prospective	20	Silicone	Reduced incidence of hypertrophic scars
Conologue and Norwood[46]	RCT	16	PDL	Improved scar redness, vascularity, overall appearance
Nouri et al[47]	RCT	11	PDL	Improved scar redness, vascularity, pliability, overall appearance
Davari et al[48]	RCT	10	PDL	No difference from control
Alam et al[49]	RCT	20	PDL	No difference from control
Chan et al[50]	RCT	29	PDL	Improved symptoms, but no difference in appearance from controls
Anzarut et al[80]	Meta-analysis of RCTs	316	Pressure garments	Improved scar height, but no difference in pliability, redness, overall appearance
Cho et al[82]	RCT	146	Massage	Improved scar height, pliability, redness, symptoms
Wray[104]	Prospective	7	Tension reduction	Decreased scar width
Lim et al[105]	RCT	12	Tension reduction	Improved scar appearance
Longaker et al[106]	RCT	65	Tension reduction	Improved scar appearance, height, pliability, redness, pigmentation
Moody et al[107]	RCT	55	Eversion	Improved scar appearance, decreased scar width
Hypertrophic scar treatment				
Campanati et al[10]	Prospective	30	Onion extract	Improved redness
Beuth et al[11]	Retrospective	771	Onion extract	Improved scar height and redness compared to intralesional corticosteroid
Hosnuter et al[16]	Prospective	60	Onion extract	Improved scar redness
Koc et al[17]	RCT	27	Onion extract	Improved scar height and symptoms with onion extract + steroids compared to steroids alone
Karagoz et al[33]	RCT	45	Silicone	Improved scar height, pigmentation
Momeni et al[35]	RCT	38	Silicone	Improved scar pliability, redness, pigmentation
Allison et al[2]	RCT	38	PDL	Improved symptoms
Chan et al[50]	RCT	27	PDL	Improved symptoms, but no difference in appearance from controls
Alster and Williams[52]	RCT	16	PDL	Improved symptoms, height, redness
Alster[53]	RCT	22	PDL	No benefit to adding corticosteroids to PDL
Walia and Alster[63]	Prospective	60	CO_2 laser	Improved acne scar appearance
Majid and Imran[64]	Prospective	60	CO_2 laser	Improved acne scar appearance

(*Continued*)

Table 1. (*Continued*)

Study	Study Type	No. of Subjects	Intervention Evaluated	Outcomes of the Intervention
Asilian et al[70]	RCT	60	Corticosteroids, 5-FU, PDL	Improved scar appearance, redness, symptoms with combination of corticosteroids, 5-FU and PDL
Field et al[83]	RCT	20	Massage	Improved burn scar symptoms
Denton et al[92]	RCT	45	Anti–TGF-β1 antibodies	No improvement in skin thickness in systemic sclerosis
Caviggioli et al[94]	Case report	1	Fat grafting	Improved scar pliability in cicatricial ectropion
Rigotti et al[96]	Prospective	20	Fat grafting	Improved tissue morphology in radiated wounds
Khouri et al[101]	Retrospective	43	Fat grafting	Improved tissue pliability
Khouri et al[102]	Retrospective	31	Fat grafting	Improved tissue pliability in postburn contractures, radiation scars
Klinger et al[103]	Case series	3	Fat grafting	Improved overall appearance of postburn scars
Keloids (adjuncts to excision)				
Ketchum et al[116]	Retrospective	22	Corticosteroids	Decreased scar height and symptoms
Stewart and Kim[122]	Prospective	10	Mitomycin C	Effective at reducing keloid recurrence
Aggarwal et al[125]	Prospective	50	Bleomycin	Effective at reducing keloid recurrence
Recalcati et al[123]	Retrospective	60	Radiation	Effective at reducing keloid recurrence
Connell[128]	Prospective	10	PDL and steroids	Decreased scar height, redness, and symptoms
Striae prevention				
Buchanan et al[133]	RCT	300	Cocoa butter	No benefit
Taavoni et al[134]	RCT	70	Olive oil	No benefit
Striae treatment				
Trelles et al[130]	Prospective	10	Infrared	No benefit
Pribanich et al[131]	RCT	11	Tretinoin	No benefit
Kang et al[132]	RCT	22	Tretinoin	Decreased size of striae

laser", "fluorouracil", "pressure garment", and "scar massage". We only included English-language articles. The results were manually searched for relevant articles. All level I and II articles were analyzed. Level I studies were defined as high-quality randomized-controlled trials (RCTs) with adequate power, and level II studies were defined as lesser quality RCTs and nonrandomized prospective studies. For interventions that had no level I or level II published articles, lower level articles were included. The evidence from these articles was synthesized to generate recommendations. The rating of each intervention's effectiveness at preventing or reducing scars was developed as follows: if no high-quality study showed effectiveness, the effectiveness was rated as "none." If the majority of high-quality studies did not show effectiveness or only showed marginal effectiveness, the effectiveness was rated as "low." If the majority of high-quality studies showed effectiveness, the effectiveness was rated as "high."

Scar Assessment

Validated tools have been developed to standardize scar assessment. Although there is no gold standard, the Vancouver Scar Scale is a commonly used tool that uses clinician rating of pigmentation, pliability, vascularity, and height (Table 3).[1] The Patient and Observer Scar Assessment Scale is another commonly used tool, which, like the Vancouver Scar Scale, not only includes a clinician assessment but also adds patient assessment of pain, pruritus, color, stiffness, thickness, and irregularity (Table 4). The added patient perspective in the Patient and Observer Scar Assessment Scale is particularly informative, as hypertrophic scars are often accompanied by pruritus and discomfort, because of their increased levels of substance P and calcitonin gene-related peptide.[2]

To facilitate quantitative comparisons in research studies, attempts have been made to augment these scales with objective measures. Such objective measurement devices include spectrophotometers to measure scar erythema, elastomers to measure pliability, and calipers to measure height/thickness. Histopathologic examination of scar biopsies is also often performed to describe the cellular changes seen with a given intervention.

Topical Products and Dressings

Many over-the-counter products have been marketed as tools to prevent scars or to improve their appearance and symptoms. The 3 most

Table 2. Summary of Evidence for Scar Prevention and Treatment

	Effectiveness	Level of Evidence	References
Hypertrophic scars			
Prevention strategies			
Onion extract	Low	I and II	5–9,12–15
Vitamin E	None	I	24–27
Silicone	High	I and II	31,32,34
PDL	None to low	I	46–50
Pressure garments	Low	I	80
Scar massage	Low	II	82
Recombinant TGF-β3	None	I	87
Tension reduction	High	I	104–106
Wound edge eversion	High	I	107,108
Treatment strategies			
Onion extract	Low	I	10,11,16,17
Silicone	High	I	33,35
PDL	High	I	2,50–53
CO_2 laser	High	II	63,64
Corticosteroids	High	I	70
5-FU	High	I	70
Bleomycin	High	I	73
Scar massage	High	I	82,83
Anti–TGF-β1 antibodies	None	I	92
Fat grafting	Low	III, IV, and V	94,96,98–103
Keloid scars			
Adjuncts to excision			
Corticosteroids	High	III	116–118
Mitomycin C	High	III	122
Bleomycin	High	III	125
Radiation	High	III	123
PDL	Low	III	128
Striae distensae			
Prevention strategies			
Cocoa butter	None to low	II	133
Olive oil	None to low	II	134
Treatment strategies			
Infrared	None	IV	130
PDL	None	IV	126
Tretinoin	None to low	II	131,132

Table 3. Vancouver Scar Scale

Scar Characteristic	Score
Vascularity	
Normal	0
Pink	1
Red	**2**
Purple	**3**
Pigmentation	
Normal	0
Hypopigmentation	**1**
Hyperigmentation	**2**
Pliability	
Normal	0
Supple	1
Yielding	**2**
Firm	**3**
Ropes	**4**
Contracture	**5**
Height	
Flat	0
<2 mm	1
2–5 mm	**2**
>5 mm	**3**
Total score	13

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common ingredients in those products are onion extract, silicone, and vitamin E.[3]

Onion Extract

Quercetin extracted from *Allium cepa* is the main ingredient in 2 commonly used onion-based gels: Mederma and Contractubex (Merz Pharmaceuticals, Raleigh, N.C.). Mederma is the American formulation and contains 10% onion extract and 1% allantoin, whereas Contractubex is the European formulation and contains 50 U/g heparin in addition. Most studies on onion extract recommend applying the ointment 3 times daily starting around 1 week postoperatively, for up to 12 weeks. Onion extract gels have been evaluated in multiple studies, which have found conflicting evidence.[4]

We found 4 split-scar, RCTs with scar evaluators who were blinded to the treatment assigned to each scar segment. Chanprapaph et al[5] found that onion extract improved scar height and itchiness

Table 4. The POSAS

POSAS Patient Scale	Score	
Has the scar been painful the past few weeks?	1–10 (1 = not at all, 10 = very much)	
Has the scar been itching the past few weeks?	1–10 (1 = not at all, 10 = very much)	
Is the scar color different from the color of your normal skin at present?	1–10 (1 = not at all, 10 = very much)	
Is the stiffness of the scar different from your normal skin at present?	1–10 (1 = not at all, 10 = very much)	
Is the thickness of the scar different from your normal skin at present?	1–10 (1 = not at all, 10 = very much)	
Is the scar more irregular than your normal skin at present?	1–10 (1 = not at all, 10 = very much)	
What is your overall opinion of the scar compared with normal skin?	1–10 (1 = like normal skin, 10 = very different)	
POSAS Observer Scale	Score	Categories
Vascularity	1–10 (1 = like normal skin, 10 = worst scar imaginable)	Pale, pink, red, purple, mix
Pigmentation	1–10 (1 = like normal skin, 10 = worst scar imaginable)	Hypo, hyper, mix
Thickness	1–10 (1 = like normal skin, 10 = worst scar imaginable)	Thicker, thinner
Relief	1–10 (1 = like normal skin, 10 = worst scar imaginable)	More, less, mix
Pliability	1–10 (1 = like normal skin, 10 = worst scar imaginable)	Supple, stiff, mix
Surface area	1–10 (1 = like normal skin, 10 = worst scar imaginable)	Expansion, contraction, mix
Overall opinion	1–10 (1 = like normal skin, 10 = worst scar imaginable)	

POSAS, Patient and Observer Scar Assessment Scale.
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but not erythema, pliability, or overall appearance, compared with placebo.[5] Jenwitheesuk et al[6] found that silicone gel sheeting combined with onion extract resulted in improved pruritus and pigmentation compared with silicone gel sheeting and placebo ointment, with no difference in scar pliability or height. Wananukul et al[7] found that onion extract gel resulted in fewer hypertrophic scars than placebo in pediatric median sternotomies. Chung et al[8] found no difference between onion extract gel and moisturizer in the prevention of hypertrophic scars after surgery.

Several other studies were nonrandomized, not properly controlled, or did not have blinded evaluators. Some of those studies found that onion extract gel resulted in decreased scar width,[9] decreased scar erythema,[10–13] decreased pruritus,[11] and overall improved scar appearance.[12–14] Other studies found that onion extract was no more effective than antibiotic ointment for scar prevention[15] and less effective than silicone gel sheeting.[16] For the treatment of established hypertrophic scars and keloids, Koc et al[17] found that intralesional steroid combined with topical onion extract resulted in improved scar pruritus and height compared with steroids alone.

The mechanism of action of onion extract is unclear. In vitro, it has been found to have a dose-dependent inhibitory effect on the proliferation of fibroblasts,[18–20] while inhibiting histamine[6] and upregulating the expression of matrix metalloproteinase-1.[19] These effects result in histologic changes in the scar: Saulis et al[21] found that onion extract improved collagen organization histologically in the rabbit ear model, although this did not translate clinically into reduced scar hypertrophy.

Recommendation: Although onion extract may have beneficial molecular effects on scars, its clinical efficacy in scar prevention and treatment remains largely unproven (level I and II studies).

Vitamin E

Vitamin E is a family of lipid-soluble tocopherols and tocotrienols,[22] which have a modest inhibitory effect on collagen synthesis.[23] Of the 4 blinded RCTs on vitamin E that we identified, 3 found that vitamin E provided no benefit compared with plain moisturizer in the treatment of recent surgical scars and in fact had a higher rate of contact dermatitis.[24–26] Only Zampieri et al[27] found that vitamin E applied for 15 days preoperatively and 30 days postoperatively improved patient-reported scar cosmetic outcomes in pediatric surgical incisions.

Recommendation: Available evidence suggests that vitamin E is not effective for scar prevention and may have harmful effects (level I evidence).

Silicone, Ointments, and Creams

Polydimethylsiloxane, the most commonly used medical silicone, is an inert polymer that can be applied to scars in the form of sheets or gel.[22]

Most authors recommend starting silicone application as soon as the second week after surgery and continuing it for at least 3 months.[28] Multiple studies have shown that the use of silicone, in either of its forms, over fresh surgical incisions, reduces the incidence of hypertrophic scarring.[29] Both products are efficacious, although silicone gel may be preferred because of ease of application.[30]

In a prospective, blinded RCT, Chan et al[31] found that silicone gel was superior to control in the prevention of hypertrophic scarring after median sternotomies, resulting in improved pigmentation, vascularity, pliability, height, pain, and pruritus. Lee et al[32] found that silicone gel was superior to onion extract for the prevention of hypertrophic scars in the rabbit ear. Similarly, Karagoz et al[33] found that both silicone gel and silicone sheets were superior to onion extract gel in the prevention of hypertrophic scarring after burns. In a prospective study of women undergoing bilateral reduction mammoplasty, Cruz-Korchin et al[34] treated the incisions on 1 breast, but not the other, with silicone sheeting. The rate of hypertrophic scars was much lower when silicone sheeting was used (25% vs 60%).

Silicone has also been found to be effective in the treatment of established hypertrophic scars. In a randomized, double-blind, split scar study, Momeni et al[35] compared silicone sheets with placebo in the treatment of hypertrophic burn scars. They found that silicone sheets significantly improved scar pigmentation, vascularity, pliability, and pruritus.

The mechanism of action of silicone has been hypothesized to involve multiple factors: inhibition of fibroblast activity via hydration and occlusion, activation of collagenase via warming, and polarization of the scar tissue via the static negative charge of silicone.[28] However, 2 facts argue toward hydration and occlusion as the main mechanisms explaining silicone's efficacy: first, several nonsilicone occlusive dressings have been found to result in equivalent results to silicone-containing dressings.[31,36,37] Second, silicone cream combined with an occlusive dressing has been found to be much more effective than silicone cream alone.[38] Moist wound environments are known to be conducive to faster epithelialization and fewer scar-related symptoms of pain and pruritus.[39] Injury to the stratum corneum, such as after a surgical incision, results in increased evaporative losses and enhanced collagen synthesis.[40] A dry environment also causes increased nociceptive activity and neurogenic inflammation, resulting in pain and pruritus.[41]

Creams and ointments are often used on wounds and incisions to provide a moist healing environment. Those include antibiotic ointment, Moist Exposed Burn Ointment, and petrolatum, among others. Many surgeons prefer antibiotic ointments because of the widespread belief that they reduce infectious complications. However, it has been shown that in clean surgical incisions, antibiotic ointments are no more effective than petrolatum at reducing infection and in fact have a higher risk of contact dermatitis.[42] Atiyeh et al[43,44] have shown that Moist Exposed Burn Ointment produced faster reepithelialization and superior long-term cosmetic outcome in split-thickness skin graft donor sites and surgical incision closures, compared with a dry healing environment. Overall, it seems that the contents of the cream or ointment are not consequential, as long as it provides a moist healing environment.

Recommendation: Occlusive dressings, such as silicone, are efficacious in the prevention and treatment of scars (level I and II evidence). The action of ointments and creams on scars may be mediated by their scar hydration effect.

Lasers

The use of lasers has grown to include the prevention and treatment of hypertrophic, keloid, and acne scars. Jin et al[45] performed a meta-analysis of 28 studies and found that, among all lasers, the pulsed-dye laser (PDL) had the highest efficacy in both the prevention and treatment of hypertrophic scars.

PDL

The 585- and 595-nm PDL selectively targets oxyhemoglobin. The prophylactic treatment of new surgical scars with PDL has been evaluated in several studies, and the results are mixed. Conologue and Norwood [46] and Nouri et al[47] found that treating surgical scars with PDL starting on the day of suture removal resulted in an improvement in erythema, pliability, and overall appearance, whereas other studies did not show any long-term improvement.[48–50]

In contrast, studies on the treatment of established hypertrophic scars with PDL are more conclusive.[51] In a split-scar RCT of hypertrophic median sternotomy scars, Alster et al[52] demonstrated that treatment with PDL resulted in an improvement in scar height, pliability, and erythema, compared with untreated areas. In addition, untreated hypertrophic scars had dense sclerosis and thick hyalinized dermal collagen with haphazardly arranged fibroblasts, whereas

PDL-treated scars had looser, less coarse collagen fibers.[52] Allison et al[2] compared PDL with control in the treatment of burn scars and found that PDL resulted in a sustained decrease in pruritus. Alster et al[53] found that hypertrophic inframammary fold scars after reduction mammaplasty benefit from a combination of intralesional steroids and PDL.

The timing of scar treatment with PDL has been studied. PDL seems to be most effective in immature hypertrophic scars, which are still hypervascular and erythematous, early in the remodeling phase.[54] Goldman et al[55] found that scars younger than 1 year were much more likely to improve with PDL and required fewer treatments, than scars older than 1 year. Other PDL variables, such as fluence and treatment frequency, have also been studied. Manuskiatti et al[56] found that fluences ranging from 3 to 7 J/cm^2 achieved comparable efficacy and that repeated treatments every 6 to 8 weeks were more efficacious than a single treatment.

Because PDL only penetrates about 1 mm deep, thick hypertrophic scars may not respond well to PDL.[57] Combining PDL with intralesional steroids or 5-fluorouracil (5-FU), which can thin the scar, may result in synergistic action.[58]

The mechanism of action of PDL on scars is unclear but has been hypothesized to involve the destruction of microvasculature, leading to scar hypoxia and decreased fibroblast proliferation and neocollagenesis,[57,59] an increase in the concentration of collagenase,[57] a decrease in transforming growth factor (TGF)-β1,[60] and heat-induced collagen fiber realignment.[53] This hypoxia-induced reduction in scar burden may mimic fetal wound healing: fetal skin is relatively hypoxic compared with adult skin, with a partial pressure of oxygen around 16 mm Hg, compared with 60 mm Hg in adults.[36] This relative hypoxia causes upregulation of hypoxia-inducible factor I, which in turn upregulates vascular endothelial growth factor and TGF-β3,[61] both of which decrease fibroblast activity.

Other Lasers and Light Devices

Similar to the action of a mechanical dermabrader, CO_2 and erbium:yttrium-aluminum-garnet lasers act to superficially ablate tissue with each pass. Their thermal energy, however, also results in collagen remodeling. These lasers have been found to be effective in treating acne scars, although their resulting downtime and erythema are cited as disadvantages.[62] Walia and Alster [63] demonstrated immediate and prolonged clinical improvement of acne scars, as well as continued collagenesis and dermal remodeling, after treatment with a high-energy pulsed CO_2 laser. Fractional CO_2 lasers are also helpful, with 68% achieving excellent or good response.[64] Similar to the high-energy laser, fractional CO_2 lasers also generate thinner, better organized collagen.

In the treatment of established hypertrophic scars, different lasers can be used to target specific goals. PDL lasers are best suited for the treatment of pruritus and erythema, whereas the CO_2 laser is most useful to improve scar pliability and contour.[65,66] Nevertheless, lasers may also function in a synergistic manner: Alster et al[67] found that, when treating hypertrophic scars, the combination of CO_2 and PDL lasers was superior to CO_2 laser alone. Intense pulsed light has also been used to target scar dyschromia, with good results.[68]

Recommendation: The PDL is effective in the treatment of established scars (level I evidence). The CO_2 laser, with its deeper penetration, is best suited for the treatment of irregular scar contour (level II evidence).

Injections

Intralesional injections of substances that inhibit cell proliferation have been used in the treatment of hypertrophic scars for many years. The most common substances used are corticosteroids, 5-FU, and bleomycin. All of these substances are effective in the treatment of established hypertrophic scars.[69]

Corticosteroids function by inactivating TGF-β1,[1] leading to collagenase activation and collagen degradation.[70,71] They are efficacious at softening scars.[72] The usual recommended dose of triamcinolone is 0.5 cc per cm^2. Dark-skinned individuals should be counseled about the risk of hypopigmentation. In those individuals, intralesional bleomycin may be a superior option.[73]

5-FU is an antimetabolite that inhibits fibroblast proliferation.[70] Haurani et al[74] found that intralesional 5-FU achieved long-term reduction in scar size. Asilian et al[70] evaluated the combination of intralesional triamcinolone, 5-FU, and PDL in the treatment of hypertrophic scars. They found that triamcinolone (10 mg/mL) injected weekly for 8 weeks significantly improved scar pliability and thickness and that the addition of intralesional 5-FU weekly for 8 weeks had additional benefit in scar height and pliability. The addition of 3 PDL treatments produced further benefit in scar pliability and thickness. 5-FU, however, can result in wound ulceration, hyperpigmentation, and pain, as it is generally reserved for treatment of aggressive keloids.

Bleomycin is an antitumor agent that induces breaks in DNA, leading to cell apoptosis[72] and reducing fibroblast activity.[75] It has been used as a treatment for hypertrophic scars and keloids. The total dose of bleomycin should remain below 9 IU to avoid risks of pulmonary and cutaneous fibrosis.[72] Payapvipapong et al[73] found that bleomycin was equally effective as triamcinolone in achieving flattening and softening of hypertrophic scars.

Recommendation: Intralesional steroids, 5-FU, and bleomycin are proven to improve scar thickness and pliability (level I evidence).

Pressure Garments

Pressure has been a commonly used treatment modality for hypertrophic scars and keloids, ever since Nason[76] reported that postoperative pressure reduced recurrence rates after excision of keloids in 1942. Pressure earrings were subsequently shown to reduce the recurrence of earlobe keloids.[39,77,78] The presumed mechanisms of action of pressure include reduction of edema[22,28] and hypoxia-induced fibroblast apoptosis,[28] although some studies have shown an increase in blood flow with pressure therapy.[79]

Pressure garments for the prevention of postburn scar hypertrophy is another common application. The evidence of pressure for this indication is mixed. Anzarut et al[80] performed a meta-analysis of 6 RCTs evaluating the effectiveness of pressure garments in the prevention of hypertrophic scarring after burn injury. They found that pressure garments achieved a small reduction in scar height but no difference in scar pliability, vascularity, or overall appearance. Factors that limit the effectiveness of pressure therapy in the prevention of hypertrophic scars are limited patient compliance and the need to frequently procure new garments, as garments lose elasticity after 6 to 8 weeks.[81] A pressure of at least 24 mm Hg and almost complete compliance are needed to achieve significant scar improvement with pressure garments after burns.[28]

Recommendation: Pressure garments may be effective at reducing the thickness of hypertrophic scars but require high levels of patient compliance (level I evidence).

Scar Massage

Scar massage is commonly recommended after burn injury. Cho et al[82] performed an RCT of burn wounds and compared scar massage (30-min sessions, 3 times a week) with no massage. They found that scar massage significantly improved scar-related pain and pruritus, as well as scar pliability and thickness. Scar massage was also found to result in decreased pain, pruritus, and anxiety by Field et al.[83]

Scar massage is also commonly used for the prevention of hypertrophy in postsurgical scars. Shin et al[84] reviewed the literature and noted that massage seems to be more effective in postsurgical scars than in traumatic and burn scars. The mechanism of scar massage is unclear, although there is some evidence that cyclical pressure may induce fibroblast apoptosis.[85]

Recommendation: There is some evidence that scar massage may prevent and improve hypertrophic scars (level I and II evidence).

Molecular Therapies

Advanced knowledge of the molecular biology of scars and the differences between fetal and adult wound healing are being used to develop new scar prevention and treatment strategies. Wounds that occur after the second trimester of gestation differ from wounds that occur during the first 2 trimesters by the presence of scarring rather than regeneration.[36,86] Fetal skin is capable of healing wounds with minimal inflammation,[87] and collagen is rapidly deposited in a fine reticular pattern that appears identical to uninjured skin. Fetal extracellular matrix is arranged in a loose pattern and contains high concentrations of hyaluronic acid, which promotes cellular migration and inhibits fibroblast proliferation.[36] In contrast, adult scars have thick, disorganized collagen bundles with more crosslinking.

TGF-β is one of the major drivers of wound healing and scarring.[88] It exists in 3 forms in mammals, with TGF-β1 and TGF-β2 causing increased fibroblast activity and collagen production and TGF-β3 inhibiting fibroblast activity.[60] TGF-β1 is capable of autocrine function, increasing its own production, which may explain the excessive scarring seen in some individuals.[86] Fetal wounds have a higher ratio of TGF-β3 to TGF- β1 and TGF- β2 compared with adult wounds.[36] Animal models have shown that upregulation of TGF-β1 and TGF-β2 results in increased scarring, whereas neutralizing antibodies against them result in decreased scar formation.[89] In contrast, addition of exogenous TGF-β3 results in decreased scarring in animal models.[90,91] The translation of these animal studies into human clinical trials, however, have failed to produce effective molecular scar treatments. Antibodies against TGF-β1 failed to demonstrate efficacy in the treatment of the excessive scarring seen in systemic sclerosis,[92] and phase III clinical trials of human recombinant TGF-β3

(Avotermin, Renovo, Manchester, United Kingdom) injected intradermally after scar revision failed to demonstrate efficacy.[87]

The emergence of fat grafting has found some applications in scar treatment. Rapp et al[93] found that injection of either lipoaspirate or adipose-derived stem cells into fresh wounds in swine reduced the incidence of hypertrophic scarring. Fat grafting has also been found to improve scar quality in cicatricial ectropion,[94] acne scarring[95] and even radiated surgical scars.[96] The exact mechanism of action of grafted fat on scars is unclear. Kim et al[97] demonstrated the use of fat grafts in the filling of depressed scars. The effect of fat grafting on scars, however, is thought to involve more than just a volumetric filling effect.[94] Neoangiogenesis induced by adipose-derived stem cells contained within the fat graft may play a role in scar improvement.[96] Several authors have found that fat grafting into radiated tissue resulted in decreased fibrosis and collagen thickness.[98–100] Others have noted improvement in scar quality after the release of the scar from the underlying tissues ("rigottomy") and lipofilling.[101,102] Similarly, Klinger et al[103] have shown improvement in burn scar pliability, thickness, and texture after fat grafting.

Recommendation: Molecular targeting of TGF-β has not proven efficacious (level I evidence). Grafting of fat seems effective in scar treatment (level III, IV, and V evidence).

Technique

Proper surgical technique has been found to reduce scar width and hypertrophy. This includes minimization of tension on the closure and meticulous closure with wound edge eversion.

Wray[104] demonstrated, in reduction mammaplasty, that incisions closed under greater tension resulted in wider scars. Tension results in compensatory, overabundant collagen production,[40] leading to scar hypertrophy. Therefore, care should be taken to minimize orthogonal tension on the closure by undermining adjacent tissues to the extent necessary to avoid tension and by applying tension to the underlying fascial layer rather than the skin. One device that is designed to offload pressure is the embrace device (Neodyne Biosciences Inc, Menlo Park, Calif.). The device combines a silicone dressing and tapes that offload pressure off the incision. In 2 split-scar RCTs, Longaker et al[105] found that the embrace device, applied between postoperative days 1 to 4 and reapplied weekly for 12 weeks, resulted in a significant improvement in scar appearance after scar revision surgery and after abdominoplasty.[106] It is unclear whether the benefit of this device stems from its occlusive silicone portion, the pressure offloading, or both.

Multiple split-scar RCTs have shown that wound eversion is more likely to achieve a fine, flat scar than planar repair, which tends to result in a depressed scar.[107,108] Scar depression can be particularly disturbing to patients, as the depression tends to capture light and be quite visible.[109] Wound eversion is best achieved using deep dermal sutures. Many surgeons place a second, more superficial layer of suture in a running fashion (subcuticular suture). Interestingly, recent studies have shown that the subcuticular layer may be replaced with tissue adhesive, with similar cosmesis and a shorter operative time.[110,111] Similarly, it has been shown that surgical incision closure using deep dermal sutures followed by self-adhering mesh and octyl-2-cyanoacrylate (PRINEO, Ethicon, Raleign, N.C.) produced equivalent scar aesthetic results in breast surgery and abdominoplasty to deep dermal sutures followed by subcuticular sutures.[112–114] Deep dermal sutures relieve tension off the epidermis and produce skin edge eversion, whereas the subcuticular suture or the tissue adhesive simply reapproximates the epidermis. It is unclear whether tissue adhesives play a role in scar hydration.

Recommendation: Wound eversion and tension minimization are both proven to improve scar appearance (level I and II evidence). The subcuticular suture may be replaced with tissue adhesives, with or without a self-adhering mesh (level I evidence).

Keloids

The treatment of keloids is a complex topic that deserves its own review article, but we present a brief overview of the commonly accepted treatment principles.

Unlike hypertrophic scars, keloids have the ability to spread beyond the boundaries of the original wound.[1] They contain thick, acellular bands of collagen. Keloid fibroblasts exhibit greatly increased collagen synthesis and decreased collagenolysis.[1]

Surgical and laser-aided excision alone is known to have a recurrence rate up to 100%.[1,71] Some studies have attempted to use over-the-counter dressings and ointments alone for the treatment of keloids, but the results were poor.[115] Multimodal treatment is therefore the standard of care.

A commonly used multimodal approach is excision and repeated corticosteroid injections. It is known that adding intralesional corticosteroids

to surgical excision significantly decreases recurrence rates.[116–118] Another adjunct to excision is mitomycin C, an antimetabolite that has been shown to suppress fibroblast proliferation.[119] Mitomycin C has been used to reduce scarring in a variety of conditions, including esophageal strictures.[120,121] Studies have shown that intraoperative application of mitomycin C (0.4 mg/mL) to the open wound for 3 to 5 minutes after keloid excision, followed by saline irrigation and wound closure, decreases keloid recurrence rates.[122]

Another, less common, approach is excision followed by radiation therapy. The addition of radiation therapy to surgical excision decreases recurrence rates to 1% to 35%.[71] Radiation damages proliferating fibroblasts directly. Radiation is usually initiated 1 to 3 days after excision, with a total dose of 10 to 15 Gy.[123] Although radiation therapy carries the risk of carcinogenesis and wound healing problems,[123] those seem to be rare.[71]

Intralesional injection of bleomycin has shown some effectiveness in the treatment of keloids.[124] Aggarwal et al[125] achieved significant to complete keloid flattening in two third of patients after bleomycin injections into keloids and hypertrophic scars.

Ablative and nonablative laser treatment for keloids has been reported with variable success. Nonablative lasers, such as PDL, have been used to reduce symptoms of pain and pruritus.[126] PDL has been found to result in a downregulation of TGF-β1, although this did not translate into a decrease in type I collagen accumulation.[127] Because of its shallow penetration into tissues, PDL has a limited ability to affect the size of keloids, and therefore, combining it with corticosteroids may have synergistic effects. Connell and Harland[128] found that the combination of intralesional corticosteroids and PDL resulted in 60% reduction in height, 40% reduction in erythema, and 75% reduction in pruritus.

Recommendation: Multimodal treatment is necessary for keloids. This includes surgical or laser-assisted excision, intralesional steroids, mitomycin C, bleomycin, PDL, silicone compression, and radiation (level III evidence)

Striae Distensae

Striae are caused by elastolysis and dermal thinning.[129] Precipitating factors may include rapid weight gain, pregnancy, systemic corticosteroids, and estrogen.[126] They have scar-like features, namely an early erythematous phase, followed by a late hypopigmented phase.[130] Numerous treatment modalities have been attempted to prevent or treat striae, including infrared,[130] PDL,[126] tretinoin,[131,132] cocoa butter,[133] and olive oil.[134] None have demonstrated reproducible success.

Recommendation: Short of excision, there are no known effective treatments for striae distensae (level III and IV evidence).

CONCLUSIONS

The risk of development of hypertrophic or aesthetically unpleasant scars can be reduced with tension-free closure, wound edge eversion, the use of occlusive dressings, such as silicone gel, and early PDL treatment. The appearance and symptoms of established hypertrophic scars may be improved with injection of substances that cause scar atrophy, PDL treatment, pressure garments, and scar massage. Molecular therapies based on the knowledge of the cytokines involved in scar formation are emerging but have yet to be proven effective in humans. A multimodal approach is the standard of care in the treatment of keloids. Striae distensae remain a difficult problem without a proven solution.

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