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ACNE SCARS MANAGEMENT: A REVIEW OF COMBINED THERAPEUTIC APPROACHES

Magdalena Badziąg[1] ✉, ***Martyna Kłossowska[2]***, ***Karolina Skonieczna[3]***, ***Paulina Szulc[4]***, ***Laura Kurczoba[3]***, ***Olimpia Wiciun[3]***, ***Olga Kądziołka[5]***, ***Kacper Ordon[3]***

[1]*University Clinical Center in Gdańsk, Poland*
[2]*Baltic Clinic Sp. z o.o. Gdynia, Poland*
[3]*Collegium Medicum, Nicolaus Copernicus University, Bydgoszcz, Poland*
[4]*Dr Jan Biziel's University Hospital No. 2, Bydgoszcz, Poland*
[5]*Independent Public Health Care Facility in Szamotuły, Poland*

✉ ***badziagmagdalena@gmail.com***

ABSTRACT

Background: Acne scars affect up to 80–90% of young adults and represent not only an aesthetic but also a psychosocial problem. They result from chronic inflammation and abnormal wound healing. The main types of acne scars are atrophic (icepick, rolling, and boxcar) and hypertrophic, including hypertrophic scars and keloids. Available therapies include chemical peels, lasers, microneedling, microneedle radiofrequency, fillers, and subcision. Recent studies indicate that combined approaches achieve better results than monotherapy.

Aim: This review summarizes the available evidence on combined treatment modalities for acne scars and highlights their clinical applicability.

Methods: Articles were searched in PubMed and Google Scholar using the keywords "acne scars," "acne scars overview," and "combined therapy." Studies published in English in peer-reviewed journals over the last ten years and evaluating combined approaches were included.

Results: The reviewed studies demonstrated the effectiveness of several combined modalities: energy-based devices with oral isotretinoin [25–29], microneedling with platelet-rich plasma or glycolic acid peels [31–33], fillers and biostimulators with lasers or radiofrequency [34–35], and subcision with platelet-rich plasma or fillers [36–40]. For hypertrophic scars, effective approaches included triamcinolone combined with 5-fluorouracil or laser-assisted corticosteroid delivery [22,41–42]. These combinations provided superior scar reduction, improved skin texture, and higher patient satisfaction compared with monotherapy. Reported adverse events were mild and transient, such as erythema, swelling, and post-inflammatory hyperpigmentation [20–21,27].

Conclusions: Combined therapies are more effective than single methods, including regimens performed during isotretinoin treatment, without increasing the risk of complications. An individualized therapeutic plan based on scar type, skin phototype, acne activity, previous treatments, and patient expectations is essential to achieve optimal results.

Keywords: Acne scars; Acne vulgaris; Combined therapy; Multimodal treatment; Scar management

INTRODUCTION

Scars develop as a natural consequence of inflammatory diseases, traumatic injuries, and surgical procedures, being an integral component of the wound healing process [1]. Beyond cosmetic disfigurement, scars frequently cause functional impairment, pain, pruritus, and psychosocial burden, substantially reducing quality of life in affected individuals [2,3]. Hypertrophic scars and keloids remain particularly problematic in regions of mechanical tension, such as the chest, back, neck, and face [4].

Among the etiological factors, acne vulgaris stands out as the leading cause of scarring, affecting approximately 80–90% of adolescents and young adults worldwide [1–3]. Even with timely treatment of acne lesions, the development of atrophic or hypertrophic scars is frequent, leading to long-term morbidity and persistent hyperpigmentation. Therapeutic options remain challenging, often yielding incomplete results and creating a perception of limited efficacy and permanent disfigurement among patients [5,6].

In recent years, there has been growing interest in combined therapeutic modalities that integrate energy-based devices, chemical agents, injectables, and surgical techniques. Compared with monotherapy, such multimodal approaches demonstrate superior outcomes, including greater scar reduction, improved skin texture, and higher patient satisfaction. Novel protocols that combine minimally invasive interventions with systemic therapy, particularly isotretinoin, are now being actively studied and have shown encouraging safety and efficacy profiles.

The relevance of this review lies in the high prevalence and psychological impact of acne scars, which continue to represent an unmet clinical need despite the expansion of therapeutic options. The novelty of the present work is the synthesis of recent evidence from the past decade, with a focus on emerging combined approaches, their mechanisms of action, and practical considerations in tailoring therapy to scar morphology, skin phototype, and individual patient factors.

The aim of this study is to critically review the available literature on combined treatment modalities for acne scars, highlighting the most effective therapeutic combinations and their mechanisms. The review is based on articles indexed in PubMed, Google Scholar, and other scientific databases, published in peer-reviewed journals over the last 10 years.

METHODS

This review was conducted through a structured literature search in PubMed, Scopus, and Google Scholar databases. The search covered the period from January 2013 to December 2023 in order to capture the most recent advances in the field of acne scar management. The following keywords and their combinations were used: "acne scars", "post-acne scars", "acne scar treatment", "combined therapy", "multimodal therapy", "isotretinoin and laser", "microneedling and PRP", "filler and energy-based devices". Boolean operators (AND, OR) and Medical Subject Headings (MeSH) terms were applied where appropriate.

Inclusion criteria were original articles, randomized controlled trials, meta-analyses, systematic reviews, and high-quality narrative reviews that reported clinical outcomes of combined therapeutic approaches for acne scars. Only studies published in peer-reviewed journals and written in English were considered. Exclusion criteria were case reports with fewer than five patients, non-peer-reviewed publications, conference abstracts without full text, and studies addressing monotherapy only without a combined treatment arm.

The initial search yielded 1482 records. After removal of duplicates and screening of titles and abstracts, 134 full-text articles were assessed for eligibility. Of these, 42 studies met all inclusion criteria and were included in the final analysis. The types of included studies comprised randomized clinical trials, controlled observational studies, and systematic reviews. Data were extracted on study design, patient population, scar classification, type of combined interventions, treatment protocols, follow-up duration, and reported outcomes.

This methodological framework allowed for transparent synthesis of evidence regarding the efficacy and safety of combined therapeutic modalities in acne scar management.

FINDINGS

PATHOPHYSIOLOGY OF SCARRING

Wound healing and scar formation are divided into three stages: inflammation, proliferation and matrix remodeling/scar formation [7]. Immediately after the injury, local inflammation occurs and a fibrin plug is formed. Inflammatory cells and mediators, such as neutrophils and macrophages clear the wound, while the extracellular matrix and primary connective tissue accumulate along with the blood. This phase lasts up to 5-7 days. Then,

during the activation process, TGF-β (Transforming growth factor β) recruits fibroblasts. The fibrin plug is replaced by granulation tissue, containing fibroblasts, inflammatory cells, collagen, elastin and hyaluronic acid in the scar bed. PDGF (Platelet-drived growth factor) activates fibroblasts to proliferate and produce collagen III. Angiogenesis begins due to the activation of the extracellular matrix. The phase of scar formation and vasculature lasts 3-4 weeks. Interestingly, the normal healing process continues even up to 2 years after the wound is formed due to continuous scar reconstruction and maturation [1,8]. During this process, collagen I (instead of III) is restored, which adds strength and remodels the granulation tissue [7,9].

Each of the above processes is necessary for the formation of a mature, healthy scar. Disturbances in any phase of scarring lead to an abnormal final result [7]. In the formation of a keloid, the inflammatory phase and excessive amounts of proinflammatory cytokines, as well as the later processes of collagen and granulation tissue formation, lead to tissue hypertrophy [7,9].

ACNE SCARS CLASSIFICATION

Multiple therapeutic options for post-acne scar treatment are available, ranging from non-invasive topical treatments to more invasive surgical procedures. Therapies are selected based on individual skin examination, specific needs and scar types. There are two types of acne scars: atrophic (rolling, icepick and boxcar types) and hypertrophic (Fig. 1) [6,10,11]. Each type requires a different therapeutic approach. Patients' preferences should also guide the choice of therapy [2,12].

The most common are atrophic scars. They form due to damage to the dermal structures from inflammation and loss of collagen fibers. As a result, scars of various architectures are created. Out of atrophic scars, the most common are ice pick scars, which are narrow, but quite deep, reaching the dermal layer. Rolling scars are wider, but shallow, with normal skin structure. Boxcar scars are round scars with jagged edges, which can be either shallow or deep [13].

Hypertrophic scars (HS) result from abnormal collagen accumulation due to damage to the dermis during inflammation. Unfortunately, skin diseases associated with long-term inflammation often lead to the formation of hypertrophic or keloid scars. HS form as raised lesions that do not extend beyond the edges of the wound, whereas keloids form similar lesions that extend beyond the wound margins [13]. Hypertrophic scars, as well as keloids, occur less frequently in acne, mainly in men on the chest and back, as well as in patients with Fitzpatrick skin types II-V [14].

Most often, all three types of atrophic scars are visible in a single patient, which makes it difficult to differentiate between them and select the appropriate therapy [6]. As of this review's publication date, there are no official scales or gold standards for assessing scar severity and treatment. Clark et al. described available scales, but none of them allows for a comprehensive assessment of properties such as color, depth, or changes over time. According to the authors, this is an important factor limiting the development of a specific treatment plan for a particular grading of scarring [3].

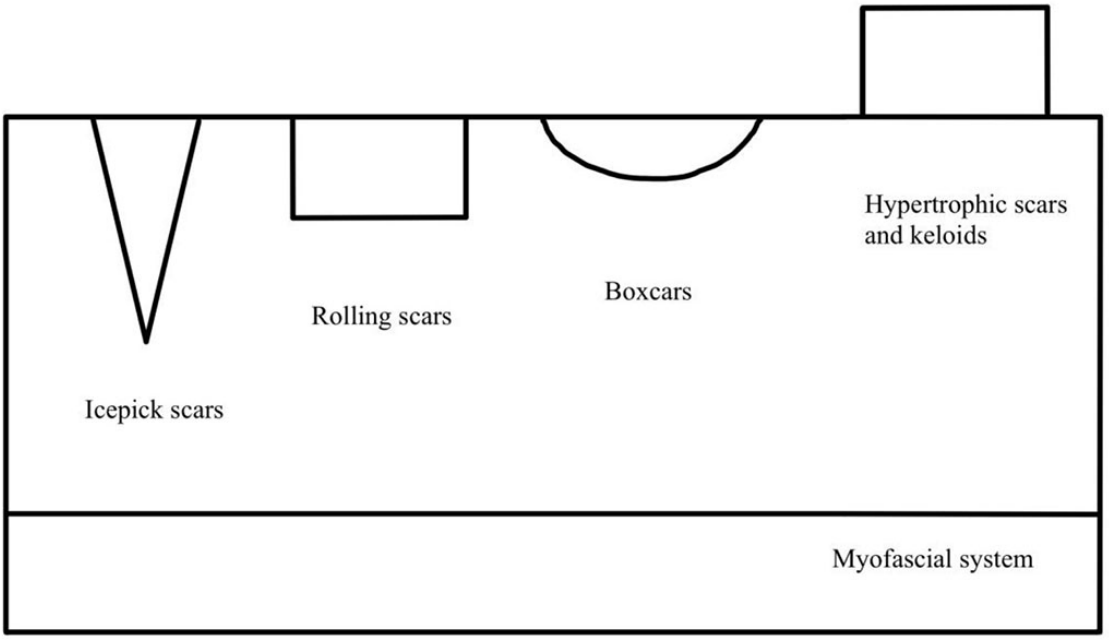

Figure 1. Types of acne scars depending on different depths.

TREATMENT OPTIONS FOR ACNE SCARS

Retinoids in scar prevention

The best way to fight post-acne scars is to prevent them from forming and to stop the inflammation process accociated with acne [6,11]. The most effective method of treating the underlying disease is oral isotretinoin therapy. The drug's mechanism of action is based on blocking the activity of the sebaceous glands [6,15]. Isotretinoin is administered in doses of 0.5-1 mg/kg of body weight, with a cumulative dose of 120-150 mg/kg after several months of treatment. Common side effects include dryness of the skin and mucous membranes, reduction of sebum, headache, alopecia, arthralgia and muscle pain. The most dangerous side effect is teratogenicity. Additionally, improper wound healing, irritable bowel syndrome or depression may occur. According to the literature, the effect of isotretinoin on the development of depression was not confirmed in later studies [15]. However, acne as a dermatosis with visible skin lesions on the face is an obvious risk factor for the development of psychological disorders [16]. Even despite rapid isotretinoin therapy, acne lesions tend to scar and therapy may not be sufficient to avoid them. However, patients should be aware of the scarring process and the challenges in meeting their expectations [6].

Current recommendations for the treatment of mild acne suggest monotherapy with topical retinoids, such as adapalene, tretinoin and tazarotene. If ineffectiveness persists for more than 6 weeks, a component containing benzoyl peroxide or a topical antibiotic is added [17]. When used on acne scars, external retinoids have shown efficacy and improvement [18].

Despite the above methods, the treatment of acne and its consequences is unfortunately often ineffective. Thus, the treatment of acne scars relies on non-pharmacological methods [19].

Atrophic scars treatment

Atrophic scars treatment includes less-invasive methods, such as peels, as well as more invasive procedures like dermabrasion, microneedling, radiofrequency, lasers, and subcision [5,6,11]. The damage that stimulates collagen production and regenerates skin occurs at different depths, depending on the substance used and its concentration [7,9,11]. Table 1 presents the effectiveness of therapy depending on the type of acne scar [6,10,11].

Table 1. Effectiveness of available treatments for atrophic acne scars in monotherapy.

Treatment	Ice pick scars	Rolling scars	Boxcar scars
Chemical peels (TCA, CROSS)	++		++
AFL/NAFL		++	++
Fractional laser	++	++	++
Microneedling		++	++
Dermabrasion	+		+
Fillers	+	++	+
Subcision	++		+

++ effective; + less effective

Chemical peels based on acids differ in the depth of penetration and action within the layers of the skin. Lactic acid, salicylic acid, glycolic acid, trichloroacetic acid (TCA) at 10% and 25%, and Jessner solution (a mixture of resorcinol, salicylic acid, and lactic acid) are commonly used [6,11]. TCA can also be used in concentrations of 35-50%, where it reaches the papillary layer of the skin. In concentrations of 51-75%, TCA gives the best results in reducing scars and discolorations. Phenol, a very deep-acting acid, reaches the reticular layer and provides effects comparable to a CO2 laser [11]. Chemical peels should be used with caution in patients with Fitzpatrick phototypes IV-VI, as they are at increased risk of post-treatment pigmentation, especially after using high concentrations of deeply penetrating acids6. Other side effects, aside from hyperpigmentation, include prolonged redness, infection and even scarring, as it is difficult to control the depth of damage with peels. Phenol peels, due

to their deep penetration, can be absorbed into the systemic circulation and may cause cardiotoxic reactions. Currently, CO2 lasers are recommended instead of phenol, as they do not cause dangerous side effects and promote the formation of a thicker collagen layer [11].

The Chemical Reconstruction of Skin Scars technique (CROSS) is used in the treatment of icepick scars, where a TCA peel is applied at a concentration of 65-100%. It is applied directly to the bottom of the scar to provoke scar reconstruction. According to Connolly et al., after 3-6 sessions, improvement is observed in 90% of patients. An undesirable side effect of CROSS peeling is hyperpigmentation, which occurs in about 34% of cases [11].

Laser therapy is represented by the gold standard, the ablative laser, which provides noticeable results after just one session. However, treatment with traditional ablative lasers can be uncomfortable and painful [7,11]. Newer generations of CO2 lasers are increasingly less painful for patients, especially fractional lasers, which offer significantly fewer side effects [7]. Non-ablative lasers are better tolerated by patients, but require multiple sessions to show results. Typical side effects after laser treatment include erythema, particularly severe after ablative and fractional lasers, lasting up to a month. Laser therapy and the heat emitted by radiation can also cause pigment alteration, especially with strong ablative lasers [11]. The latest advanced picosecond lasers reduce known side effects due to their very short energy pulses delivered to the skin. In the case of rolling scars, picosecond lasers are compared to fractional lasers in terms of effectiveness [11,20]. The majority of specialists in the study by Samaleh et al. agree that CO2 lasers are more effective than Er:YAG in treating acne scars, while vascular lasers are the first-line treatment for flat erythematous scars [21].

Microneedling is a method based on stimulating collagen production in the skin and smoothing it, working best on rolling scars. The use of a needle during the procedure allows the delivery of active substances that further stimulate the scar area beyond the initial stimulation through damage. Some authors compare the effectiveness of microneedling to non-ablative lasers [11].

Fractional Microneedle Radiofrequency (FMRF) involves the delivery of electric current through micro-punctures, which stimulates collagen production and smooths scars, especially icepick and boxcar scars. Traditional unipolar and monopolar radiofrequency (RF) works on all layers of the skin during puncture, causing significant pain during the procedure. Modern fractional RF targets specific layers of the skin during puncture, reducing pain and allowing work at the correct depth, giving improvement with up to 75% scar reduction after 3-4 treatment sessions [11].

Dermabrasion is a procedure involving the mechanical abrasion of the epidermis and upper dermis layers. It allows for precise abrasion of scar edges and is particularly effective for scars with jagged edges, such as shallow boxcar scars. Side effects include discomfort and pain during the procedure, as well as an increased risk of hyperpigmentation, since the skin is deprived of its epidermis and requires photoprotection [11].

Fillers are used to fill soft tissues. In post-acne atrophic scars, they fill the scar space while also stimulating collagen production and improving skin quality. This method works best with rolling and boxcar scars. Among the substances used, hyaluronic acid and biostimulants such as poly-lactic acid and calcium hydroxylapatite stand out. Side effects of the procedure may include pain, infection, redness, lumps, swelling and abscesses. The effects of fillers can last from several months to even several years, which should be considered when choosing this treatment method [11].

Scar subcision is a method that uses a needle placed in the dermis to cut the fibers that cause the scar to collapse. This results in a lift, especially in the case of rolling scars. The destruction of tissue also stimulates collagen production, skin regeneration and more controlled healing. Side effects include facial swelling, bruising, bleeding during the procedure and infection [11].

Punch excision/elevation is a procedure in which a punch instrument is used to excise tissue.

The instrument must be adapted to the size of the scar, most often a deep icepick scar or a wide boxcar scar. The excision reaches the depth of the subcutaneous tissue and is closed with sutures. This procedure allows for lifting the skin and leveling the Surface [11].

The above methods are mostly based on skin revitalization by stimulating collagen production, which takes time. The activation of fibroblasts and collagen rebuilding may take several months to a year, depending on the procedure performed, and the effects should be assessed after this period [11].

Hypertrophic scars and keloids treatment

These scars occur much less frequently as acne scars. To the best of our knowledge, there are currently no official recommendations [22]. General recommendations for the treatment of HS are applied. It should be noted that hypertrophic scars tend to spontaneously regress over time, unlike keloids [23].

Topical silicone gels are the first-line therapy and prevention method, as well as steroid tapes and plasters for larger scars [13,23].

Injections of corticosteroids, such as triamcinolone (at a dose of 5-10 mg per session) are the next line of treatment [13].

Cryosurgery can also be used as a supplementary treatment or as an alternative to injections [23].

Pulsed-dye or ablative lasers are considered second-line treatments. Most authors agree on their effectiveness, especially after corticosteroid injections, when the scar is flatter, but erythematous [13]. It is recommended to start laser therapy during the early stages, when the hypertrophic scar is forming [24].

Ablative fractional laser (AFL) reduces scar volume and redness, as well as has a positive effect on the patient's subjective experience, such as reducing itching, pain, and stiffness [10].

Surgical excision remains a controversial therapeutic option. Any surgical intervention in a hypertrophic scar carries the risk of recurrence or even enlargement of the initial scar. Ogawa et al. propose appropriate suturing techniques, such as zig-zag stitching or the use of local flap transfer [13].

Figure 2 shows a flow chart for scar treatment depending on its type [2, 5, 7, 9-14, 20-24, 30-31, 33-42].

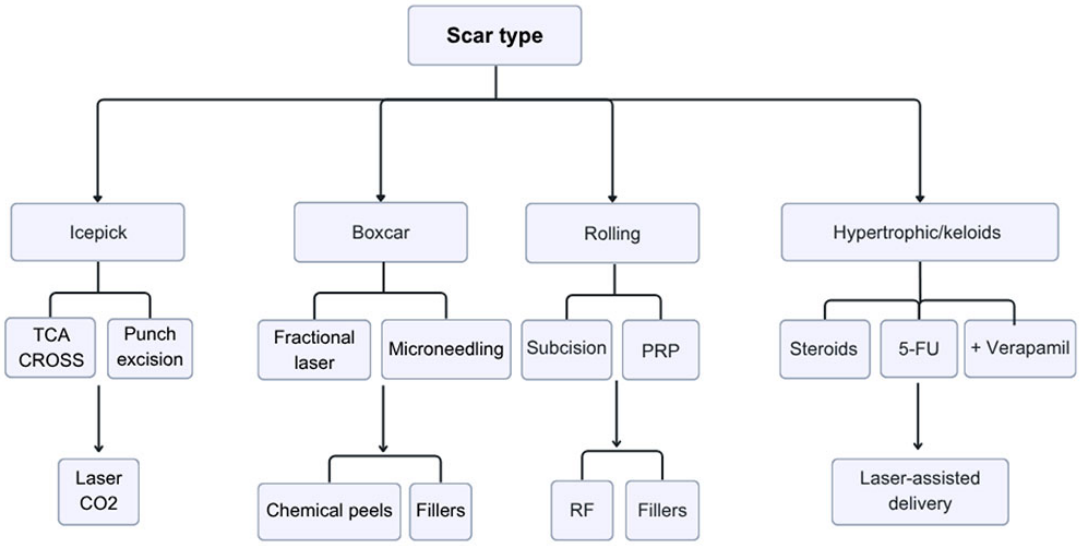

Figure 2. Algorithm scheme: classification of scars and suggested treatments.

Table 2 presents common adverse effects of scar treatment [5,7,9-10, 13, 15, 20, 24, 26-38, 40-42].

Table 2. Adverse effects of scar treatments.

Treatment	Reported Adverse Effects	Typical Duration / Severity
Fractional laser (CO_2, 1064 nm, picosecond, NAFL)	Erythema, edema, post-inflammatory hyperpigmentation (PIH), crusting, transient pain	Mild to moderate; resolves within days to 2 weeks
Microneedling (alone or with PRP / peels)	Erythema, pinpoint bleeding, transient swelling, discomfort	Mild; 1–3 days
Radiofrequency (microneedling RF)	Redness, swelling, mild pain, rare cases of PIH	Transient; usually mild
Chemical peels (e.g., glycolic acid)	Burning, redness, peeling, PIH, especially in darker skin types	PIH risk increases without sun protection
PRP (Platelet-Rich Plasma) injections	Swelling at injection sites, mild bruising, discomfort	Mild, short-term

Subcision	Bruising, swelling, temporary nodularity, discomfort	Mild to moderate; may last up to 1 week
Isotretinoin (oral, low-dose)	Dryness (skin, lips), photosensitivity, mucosal irritation, possible delay in wound healing	Common but manageable
Isotretinoin + laser/ light treatments	Concern about delayed wound healing or increased PIH; however, low-dose shown to be safe in combination	Risk minimized with proper protocol
Injectable fillers (HA, CaHA)	Swelling, tenderness, bruising, rare granuloma formation	Mild, temporary; rare serious events
Steroid injections (e.g., triamcinolone)	Skin atrophy, telangiectasia, hypopigmentation, rebound hypertrophy with overuse	Depends on dose/ frequency
Laser-assisted drug delivery	Similar to fractional laser (erythema, swelling), plus local irritation from active drugs	Mild; depends on drug used
5-FU (injected for keloids)	Pain, ulceration, local irritation, possible pigmentary changes	Localized; requires monitoring

COMBINED MODALITIES IN ACNE SCARS THERAPY

For the last several years, the topic of combined therapies using various methods that provide a synergistic effect and improve the skin has been widely discussed [2]. Currently, there is no official consensus on combined modalities for managing acne scars, only individual studies on specific methods. We present selected studies related to combined acne scar treatments. It should be noted that only a few of the many reports on various therapeutic approaches have been cited. Many studies are still under investigation.

ENERGY-BASED DEVICES COMBINED WITH ORAL ISOTRETINOIN

Recent studies have demonstrated the beneficial effects of initiating laser treatment during oral isotretinoin therapy, even at a stage when the patient's skin is free from inflammatory lesions. A systematic review by Xu et al. evaluated 16 studies on the effects of this combination treatment. The majority of these studies concluded that patients well tolerated side effects such as erythema, dryness and discomfort during the procedure. Additionally, they achieved significantly better results and patient satisfaction was higher [25]. As Karmisholt's study shows, early laser treatment positively impacts proper scar formation [26].

There is ongoing debate regarding the timing of invasive procedures during oral retinoid therapy. Earlier recommendations suggested waiting up to 6 months after the last dose of isotretinoin before starting aesthetic treatments [21,27]. However, more recent consensus among practitioners suggests waiting about 1 month to 12 weeks [21,28]. The primary concerns are side effects, such as irritation and the induction of hyperpigmentation. Nevertheless, newer-generation lasers reduce the risk of these side effects. For instance, pulsed dye lasers (PDL) have shown a positive effect on reducing erythema. While there is still a lack of research on the long-term effects of combined therapy, many dermatologists report successful management of patients [25].

He et al. compared two contradictory approaches to laser treatment during isotretinoin therapy. Their meta-analysis confirmed the common side effects, such as erythema, dryness and hyperpigmentation. However, the study also indicated statistically better treatment outcomes with the combination of oral isotretinoin and laser therapy compared to monotherapy [28].

Interestingly, Xue observed that the use of picosecond lasers in combination with a low dose of oral isotretinoin led to improvements, highlighting the importance of early intervention for acne scars during the initial stages of treatment [27].

In a study by Kim et al., the efficacy and safety of combining CO2 laser with fractional microneedle radiofrequency (FMRF) during oral isotretinoin therapy were evaluated. Initially, patients received combined radiofrequency and fractional CO2 laser therapy every 4-6 weeks, with an average of 3.3 sessions. Two independent dermatologists assessed the results using patient photographs and the Scar Global Assessment scale (SGA) and the Grade of Acne Severity. Of the 71 patients in the study, the 43 who received additional low-dose oral isotretinoin showed

the most significant improvement in scarring. Notably, none of the patients reported a noticeable delay in wound healing. The most common side effects were erythema and swelling, which lasted approximately 7 days [19].

COMBINED APPROACH FOR MICRONEEDLING AND RADIOFREQUENCY

In the study by Kim et al., the safety and effectiveness of combining oral isotretinoin therapy with ablative fractional laser (AFL) treatment and fractional microneedle radiofrequency (FMRF) were demonstrated. The study highlighted the synergistic effect of photothermal damage to the sebaceous glands caused by the laser, which helps even out skin texture. The authors followed a protocol of three sessions, using a CO2 laser treatment regimen followed by FMRF. Adverse effects were mainly limited to irritation, erythema and edema after the procedure, which were well tolerated by patients. Interestingly, when compared to the control group that did not undergo isotretinoin therapy, no significant differences were observed in delayed healing time or other side effects. The authors proposed an early combination approach for treating both acne and acne scars, as these conditions often co-occur in most patients [29].

In another study, the use of FMRF to deliver superficially applied polylactic acid (PLA) into deeper skin layers was examined. The combined therapy showed a significant improvement in the appearance of acne scars, skin smoothness, and patient satisfaction compared to monotherapy. Notably, none of the 36 patients experienced post-inflammatory hyperpigmentation, which is a major concern in energy-based treatments. Erythema, pain, and swelling were observed in patients, but these side effects were well tolerated. In their discussion, the authors concluded that radiofrequency (RF) treatment reduces the risk of hyperpigmentation by acting only within the dermis, bypassing the epidermal layers. Therefore, the proposed protocol is considered much safer for patients with phototypes III and IV. The polylactic acid used in the protocol acts as a biostimulator, promoting collagen production [30].

In a study by Ismail et al., 30 patients were compared: 15 received microneedling with dermapen and platelet-rich plasma (PRP) on one side of their face and microneedling alone on the other, while the remaining 15 received microneedling with PRP on one side and PRP injections on the other. The results showed significant improvement in skin appearance with all three treatments, but microneedling with dermapen and PRP was the most effective [31]. Similar conclusions were drawn by other researchers, including Ibrahim et al., who used the same protocol. Their study also found significant improvement in the appearance of scars when combining microneedling with topically applied PRP [32].

Rana et al. studied the effects of microneedling with a dermaroller combined with 70% glycolic acid, using a protocol of microneedling at 0, 6 and 12 weeks, followed by peeling at weeks 3, 9 and 15. The group that received both microneedling and the glycolic acid peel showed better treatment outcomes. Notably, the protocol is simple to perform, does not require additional devices and does not damage the epidermis, making it affordable for most patients [33].

FILLERS AND BIOSTIMULATORS IN COMBINED APPROACH

Fillers, such as hyaluronic acid (HA), can be effectively combined in the treatment of atrophic scars. The study by Behrangi et al. examined the efficacy and compared the use of cross-linked and non-cross-linked HA. Additionally, botulinum toxin type A (BTA) was used to reduce muscle tension around the scars. Two groups of patients received either cross-linked HA diluted with BTA or non-cross-linked HA diluted with BTA. No significant differences were found between the two preparations, but cross-linked HA was more effective in terms of pore reduction [34].

An interesting study by Koren et al. involved a large group of 352 patients who underwent combined therapy with four different energy-based devices (EBD) along with the injection of calcium hydroxyapatite (CaHA) just before the device procedure or 2–4 weeks prior. The devices used included fractional ablative CO2 laser (FACL), non-ablative fractional laser (NAFL), and microneedle radiofrequency (MNRF). The therapy lasted 2–4 weeks, and 80% of patients did not experience any side effects. The study showed that adding CaHA to each EBD procedure gave positive results, regardless of the timing of filler administration. However, it was found that administering CaHA before the procedures had a more beneficial impact on the final outcome. The greatest improvement in reducing acne scars was observed in the FACL + CaHA group, although this was also the group, where hyperpigmentation occurred most frequently [35].

The consensus of Salameh et al. on laser therapy for acne scars also includes the topic of combined therapies. Regarding fillers and biostimulators, the authors recommend performing EBD treatments first to smooth out the scars, followed by filler injections [21]. This approach, among other benefits, allows for the use of a smaller amount of filler. The most commonly used filler among specialists in the study was HA [21,35].

COMBINED SURGICAL/INJECTIONAL METHODS

In the study by Faghihi et al., 25 patients underwent subcision for atrophic acne scars on one cheek. Two weeks after the procedure, patients received radiofrequency treatment on both cheeks. Subsequent RF sessions were

performed at 4-week intervals. Both clinical evaluations by two independent dermatologists and the patients' self-assessments indicated improvement and greater satisfaction with the results on the side, where the combined treatment was applied. In the discussion, the authors emphasized the strong synergistic effect of both treatments in stimulating collagen production [36].

Deshmukh et al. investigated the potential enhanced effectiveness of scar reduction when combining scar subcision with subsequent platelet-rich plasma (PRP) injections. In the study, patients who had undergone subcision received PRP injections on the right cheek, leaving the left cheek as a control. All patients received four PRP injection sessions over a 4-month period. The results clearly demonstrated the benefit of the combined therapy, especially for rolling and boxcar scars. Adverse reactions, such as redness and swelling, lasted an average of less than 4 days. Scar subcision with PRP injections is a simple and relatively inexpensive method that does not pose a risk of hyperpigmentation in patients with phototypes III, IV and V [37].

In the field of combined therapy with subcision and PRP, Bhargava et al. examined the effectiveness of combining these procedures with microneedling for grade 4 atrophic scars. PRP can be used not only as an injection during microneedling, but also as a superficial application in the microneedling procedure with a dermaroller. Patients were divided into two groups: the first group had microneedling performed after subcision, while the second group received additional local PRP application after the procedures. The treatments were repeated three times at 3-week intervals. After 3 months, results were assessed based on photographs and patients' self-assessment. In the group that received additional PRP, 66.67% showed improvement, with patients rating the results as "very good." Not a single patient rated the results as poor. Undesirable symptoms such as erythema and swelling, lasted an average of 16 hours in the study group (compared to 32 hours in the control group). The authors highlight the strong synergistic effect of PRP with subcision and microneedling, with PRP's growth factors optimizing healing and improving scar appearance [38].

Rullan et al. proposed a new combined therapy involving chemical peeling, microneedling and surgical subcision for scars. Peeling with 88% carbolic (phenolic) acid was performed using the CROSS procedure, followed by subcision and microneedling. The effects were assessed based on photographs. The case series presenting this combined method suggested it could be effective in treating atrophic acne scars [39].

Subcision can also be combined with the injection of fillers and biostimulants, such as hyaluronic acid (HA) and polylactic acid (PLLA). Ebrahim et al. studied the effects of combining subcision with cross-linked HA in one group of patients and subcision with PLLA in another. Patients who underwent three subcision procedures within 3 months were divided into groups, with one group receiving HA and the other PLLA on one of their cheeks. Clinical assessments showed improvement in 67.3% of patients who only underwent subcision. In the group treated with PLLA, improvement occurred in 82.4% of patients, while in the group treated with HA, improvement was seen in 94.1%, both in clinical evaluations and patients' self-assessments. The authors concluded that both preparations are highly effective in reducing acne scars, with HA showing a slight advantage [40].

COMBINED MODALITIES FOR HYPERTROPHIC SCARS

HS (hypertrophic scars) are discussed in a separate subsection due to the different therapeutic approaches required compared to atrophic scars. As previously described, atrophic and hypertrophic scars develop through different mechanisms and exhibit distinct clinical characteristics, which necessitate different treatment strategies.

Currently, multimodal therapy is recommended over single-modality treatment for keloids and hypertrophic scars. In both monotherapy and combined therapies, drugs such as 5-fluorouracil, bleomycin, and botulinum toxin type A are used, but there is no established gold standard for treatment. Bernabe et al. conducted a systematic review comparing potential therapies to triamcinolone injection monotherapy [22] . Many combinations showed efficacy, with the most potent being the combination of triamcinolone and 5-fluorouracil [4,22].

Nowadays, combined therapy for hypertrophic scars is increasingly used, involving the combination of lasers with the external application of glucocorticosteroids, also known as laser-assisted topical delivery. As demonstrated by Park et al., AFL laser treatments followed by the external application of a glucocorticosteroid improve the drug's permeability, reduce pain and produce results comparable to intralesional corticosteroid injections [41].

In a study by Kant et al., volunteers received three injections of a combination of triamcinolone and verapamil at intervals of 1 and 2 weeks, respectively. After 39 days, efficacy and results were assessed by a panel of experts and patients using the Patient and Observer Scar Assessment Scale (POSAS). Adverse events, such as scar hardening, dimpling, and itching, occurred in several patients immediately after the injections. The results showed significant improvement in hypertrophic and keloid scars in terms of surface area, pigmentation, pain and itch relief and elasticity [42].

In the EBD consensus for the treatment of acne scars, Salameh et al. mention combining energy-based devices in the therapy of hypertrophic scars and keloids, particularly combining vascular lasers with triamcinolone injections. According to the authors, pulsed dye lasers are the most commonly chosen vascular lasers and require 3–6

sessions to reduce erythematous hypertrophic scars. The majority of experts in the consensus recommend combining PDL with fractional lasers. It is advised to use the PDL first, followed by the fractional laser to minimize tissue damage and avoid potential adverse effects associated with the vascular laser [21]. Table 3 shows the combinations of methods used in scar treatment [13,27-38, 40-42].

Table 3. Combination therapies for acne and hypertrophic/keloid scars

Combination therapy	Treatment goals	Examples
Isotretinoin + laser/ radiofrequency	Reduces sebum production and inflammation; lasers promote collagen remodeling and scar texture improvement.	Oral isotretinoin + fractional laser, microneedle radiofrequency
Microneedling + PRP / chemical peel	Microneedling stimulates collagen; PRP accelerates healing; peels assist exfoliation and skin renewal.	Microneedling + PRP / 70% glycolic acid peel
Fillers + laser/ radiofrequency	Fillers address volume loss in atrophic scars; energy-based devices improve skin texture and tone.	Calcium hydroxyapatite + energy-based devices
Subcision + PRP / fillers	Subcision breaks fibrotic strands under scars; PRP or fillers support skin regeneration and volumization.	Subcision + PRP / hyaluronic acid / threads
Hypertrophic scars: steroids + 5-FU, laser-assisted delivery	Targets fibroblast activity; corticosteroids and 5-FU reduce fibrosis; laser enhances transdermal drug delivery.	Triamcinolone + verapamil / 5-FU + fractional laser
Laser + microneedling / radiofrequency	Combined skin resurfacing techniques; stimulate dermal remodeling and collagen production.	CO_2 laser + fractional microneedle RF
Isotretinoin + chemical peels / IPL	Effective for active acne with post-acne marks; retinoid reduces activity, peel/light improves tone and texture.	Isotretinoin + chemical peels / intense pulsed light (IPL)
Subcision + microneedling + PRP	Multilayered approach for deep atrophic scars: release fibrotic strands, stimulate skin, and boost healing.	Subcision + microneedling + PRP
Laser-assisted drug delivery (keloids)	Laser creates channels for deeper penetration of drugs like corticosteroids.	Fractional laser + topical corticosteroids
Steroids + verapamil (keloids)	Combination reduces collagen deposition and inflammation in hypertrophic/keloid scars.	Intralesional triamcinolone + verapamil

SUMMARY

A total of 42 studies published between 2013 and 2023 were analyzed, including randomized clinical trials, observational studies, and systematic reviews. Combined therapeutic modalities consistently demonstrated superior outcomes compared with monotherapy. Energy-based devices combined with oral isotretinoin showed significantly better scar reduction and patient satisfaction, with acceptable safety profiles [25–29]. Microneedling combined with platelet-rich plasma or chemical peels resulted in marked improvement in skin texture and scar

appearance compared with monotherapy [30–33]. Fillers and biostimulators combined with lasers or radiofrequency enhanced outcomes, reduced the required volume of filler, and provided longer-lasting effects [34–35]. Subcision combined with radiofrequency, platelet-rich plasma, or fillers proved particularly effective for rolling and boxcar scars, achieving improvement in the majority of patients [36–40]. For hypertrophic and keloid scars, combined regimens such as triamcinolone with 5-fluorouracil, or laser-assisted corticosteroid delivery, demonstrated efficacy in reducing scar thickness, erythema, and symptoms such as pain and itching [22,41–42]. Reported adverse events were generally mild and transient, most commonly erythema, swelling, and post-inflammatory hyperpigmentation, with higher risk noted after ablative laser procedures in patients with darker phototypes [20–21,27]. Table 4 summarizes the most important studies used in the review [1, 4-5, 12-14, 21, 25, 27, 42].

Table 4. Key study characteristics on acne and hypertrophic/keloid scar treatments.

Author (Year)	Study design	Number of patients	Method	Outcome
Salameh et al. (2021)	International consensus	N/A	Energy-based devices (EBDs) for acne scars	Developed treatment recommendations; confirmed safety and efficacy of fractional lasers, RF, and microneedling for various scar types
Hay et al. (2016)	Cochrane systematic review	24 RCTs included	Multiple interventions for acne scars	Evidence supports laser therapies, dermabrasion, chemical peels; limited evidence for newer modalities
Lubczyńska et al. (2023)	Review	N/A	Manual scar therapy	Reviewed effectiveness of massage and manual techniques in scar remodeling
Renzi et al. (2024)	Review (procedural focus)	N/A	Surgical and procedural treatments	Compared surgical vs non-surgical acne scar treatments; favored combination therapies
Chilicka et al. (2022)	Literature review	N/A	Dermatological and cosmetological methods	Summarized efficacy of lasers, peels, microneedling, PRP for acne scars
Xue et al. (2024)	Systematic review	not specified	Isotretinoin + EBDs	Combining isotretinoin with laser/light-based treatments improved acne and scarring outcomes
Xue et al. (2023)	RCT	80	Isotretinoin vs isotretinoin + picosecond laser	Combination therapy more effective for acne scar improvement
Behrangi et al. (2020)	Review	N/A	Scar treatment (acne and burn)	Covered treatments like lasers, steroids, silicone; emphasized combination approaches

Ogawa et al. (2021)	Protocol-based review	N/A	NMS protocol for keloids/ hypertrophic scars	Described stepwise strategy using surgery, steroids, radiation, laser, and compression
Kant et al. (2018)	Retrospective study	67	Triamcinolone + verapamil for keloids	Showed improved scar flattening and reduced recurrence with combination over steroid monotherapy

DISCUSSION

The reviewed evidence supports the superiority of multimodal approaches over monotherapy in acne scar management. The enhanced outcomes are attributed to synergistic mechanisms including collagen remodeling, release of fibrotic adhesions, and modulation of vascular and inflammatory responses [19,21]. Recent clinical studies indicate that initiating laser or radiofrequency procedures during low-dose isotretinoin therapy is both safe and effective, contradicting earlier concerns regarding impaired wound healing [25,27–29]. Nevertheless, significant limitations remain. Many studies involved small patient cohorts, short follow-up, and heterogeneity in treatment protocols, which reduces the comparability of results [14,21,22]. Head-to-head trials comparing different combined regimens are scarce, and standardized protocols have yet to be established. Furthermore, variations in outcome measures and subjective assessment tools complicate the objective evaluation of treatment efficacy. Some studies also fail to adequately control for confounding factors such as concurrent skincare regimens or previous treatments, which may bias results. Additionally, differences in scar classification systems and inconsistent reporting of adverse events hinder meta-analytical synthesis. Moreover, the psychological impact of acne scarring and patient-reported outcomes are often underrepresented in clinical trials, despite their importance for holistic management. The rapid development of novel technologies such as picosecond lasers, combined energy-based devices, and advanced delivery systems also requires thorough investigation to validate their long-term benefits and safety. Lastly, current evidence is predominantly derived from limited ethnic populations, highlighting the need for inclusive research to ensure efficacy across diverse skin types. Future research should include large multicenter randomized studies with longer follow-up to better define the efficacy, safety, and optimal sequencing of combined treatments. Until such evidence is available, individualized therapy tailored to scar type, skin phototype, acne activity, and patient expectations remains essential [2,6,12].

CONCLUSIONS

Available evidence indicates that combined therapeutic modalities achieve superior outcomes in acne scar management compared with monotherapy. Studies on combinations of energy-based devices, microneedling with platelet-rich plasma or chemical peels, subcision with fillers or platelet-rich plasma, and multimodal approaches for hypertrophic scars consistently demonstrate greater scar reduction, improved skin texture, and higher patient satisfaction. Importantly, recent trials confirm the safety of performing laser and radiofrequency procedures during low-dose isotretinoin therapy, challenging earlier concerns about impaired wound healing. Nevertheless, the current body of evidence remains heterogeneous, with small sample sizes, short follow-up periods, and a lack of standardized treatment protocols. More high-quality randomized trials and long-term studies are required to establish clear guidelines and define optimal therapeutic algorithms. Individualized therapy remains crucial. Treatment choice should consider scar type, Fitzpatrick skin phototype, acne activity, and previous interventions, as well as patient expectations and financial possibilities. Such an approach maximizes both clinical efficacy and patient satisfaction.

AUTHORS' CONTRIBUTIONS

Conceptualization: Magdalena Badziąg, Martyna Kłossowska;

Methodology: Oliwia Wiciun, Karolina Skonieczna, Karol Ordon;

Investigation: Magdalena Badziąg, Laura Kurczoba, Paula Szulc, Oliwia Wiciun;

Writing - rough preparation - Magdalena Badziąg, Martyna Kłossowska, Karolina Skonieczna; Writing - review and editing - Magdalena Badziąg, Martyna Kłossowska, Karol Ordon, Olga Kądziołka;

Visualization: Magdalena Badziąg, Laura Kurczoba, Paula Szulc;

Project administration: Magdalena Badziąg, Olga Kądziołka, Oliwia Wiciun;

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