

New Progress in Therapeutic Modalities of Striae Distensae

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Abstract: Striae distensae (stretch marks/striae gravidarum) is one of the common cosmetic problems that can cause psychological distress and anxiety to patients due to its disfiguring damage, especially for women. The etiology of striae distensae is currently unknown, and risk factors include low maternal age, family history of stretch marks, excessive weight gain during pregnancy, and high neonatal weight. This article reviews the latest literature on the most commonly used, most popular, and novel treatment modalities and analyzes the hot spots and difficulties in striae distensae treatment in recent years. Topical treatment modalities are mainly used as an adjunctive treatment. Ablative lasers and non-ablative lasers are the most popular, among which picosecond has been tried in striae distensae treatment in the last two years. Combined treatment modalities are currently a hot spot for SD treatment, and microneedle radiofrequency and fractional CO₂ laser combined with other treatments are the most common. Microneedle radiofrequency is the most commonly used and achieved therapeutic effect among the combined treatment modalities.

Keywords: striae distensae, stretch marks, striae gravidarum, treatment

Introduction

Striae distensae (SD) (stretch marks/striae gravidarum) is a typical dermal lesion that can occur during pregnancy, adolescence, and obesity as well as disease (eg Cushing's syndrome/chronic steroid use). In the available literature, the prevalence of SD has been described as varying from 11% to 88%, with the vast majority of SD patients being pregnant women and adolescents and pregnancy-related SD, also known as SG (striae gravidarum). Research on the treatment of SD has been a hot topic due to its high prevalence and the psychosocial disorders it causes, which seriously affects patients' quality of life. SD is divided into striae rubrae (SR) and striae albae (SA). SR appears as red/purple, flat, or sometimes slightly convex striae in the early stage and become white striae called SA in the late stage due to melanin reduction and atrophy. SD is often located in the abdomen, breasts, buttocks, and thighs.¹⁻³ Studies have shown that maternal underage or weight gain during pregnancy is associated with SG formation. In contrast, fetal birth weight, gestational age at delivery, and family history of SG are associated with moderate and severe SG.⁴

The pathogenesis of SD is unclear, but the prevailing view is that it is related to changes in the extracellular matrix (ECM) components, including fibrillin, elastin, and collagens. These structures provide skin resistance to tension and elasticity. Compared to normal skin, patients with SD had increased glycosaminoglycan content and a significant decrease in vertical fibrillin fibres under the dermal-epidermal junction (DEJ) and elastic fiber dermis. The orientation of elastin and fibrillin fibres in the deep dermis was realigned.⁵ In the early stages of SD, the elastic fiber network is markedly disrupted, and the newly synthesized tropoelastin-rich fibrils are thin and disorganized and do not work like standard elastic fibers to produce the skin laxity of SD.⁶ Together with the significant separation of collagen bundles during this period, the newly disorganized collagen fibrils cannot repair the collagen bundles due to intense skin stretching, which together leads to atrophy of SD.⁷

There are various treatment modalities for SD, but there is still no "gold standard" for SD treatment. Single treatment modalities for SD include topical treatment, lasers, light devices, and others, with lasers and light devices being more

effective and widely used than topical treatment. In recent years, more combination therapies have been proposed and tried. In general, they are more clinically effective than single therapies, but it depends on the type of therapies combined.² Among the treatment modalities that have been explored so far, the therapeutic targets broadly include increasing collagen production, reducing vascularity, increasing pigmentation, and others.³

Topical Treatment

Tretinoin

Tretinoin is a recognized treatment for repairing skin damage associated with photoaged skin and histologic changes have been shown to be associated with reversal of photodamage, such as increased collagen production, fibroblast activity and angiogenesis. Therefore, some researchers tried to use tretinoin to treat skin damage caused by excessive stretching.⁸ A 0.1% retinoic acid has a good clinical outcome for pregnancy-related SD, and most of the current literature confirms its use in the treatment of SR.^{2,3} In a multicenter prospective study, 20 patients treated with 1% retinoic acid for 12 weeks showed a 20% reduction in SG length compared to the control group. Erythema, scarring, pruritus, and burning sensation were expected adverse effects, most of which appeared early in the treatment period and gradually resolved with emollients.⁹ Meanwhile, in the Hexsel et al¹⁰ study, the clinical effectiveness of 0.05% retinoic acid compared to superficial dermabrasion for SR was evaluated. The width and length of the treated SD were measured, which were the main outcomes. A 5-point scale was used to evaluate the Global Aesthetic Improvement Scale (GAIS: worse, no change, improved, much improved, very much improved) and patient satisfaction (very unsatisfied, unsatisfied, neither satisfied nor unsatisfied, satisfied, very satisfied) in the treatment area. The width and length of SD were significantly decreased in both groups after treatment. All the patients were satisfied or indifferent and no one was dissatisfied. Both showed significant improvements in clinical performance, patient satisfaction, and aesthetic scores in SR. Other studies demonstrated no significant improvement in SD after seven months of 0.025% retinoic acid treatment.¹¹ Low levels of tretinoin may be the primary cause.

Glycolic Acid (GA)

Glycolic acid is an effective peeling agent, and topical application of 25% AHAs (glycolic, lactic, and citric acid) can increase the thickness of the epidermis and papillary dermis, increase acid mucopolysaccharide, improve the quality of elastic fibers, and increase collagen density. The combination of GA and the tretinoin mentioned above is effective in reducing photodamaged skin, as is AHAs, and the combination is a safe and effective treatment for acne vulgaris. It is not hard to see GA being mainly used in combination with other treatments. For example, in a study by Ash et al⁸ 10 SA samples of different Fitzpatrick skin types (I–IV) were selected. The objective blind method is done by visual grading method and histopathologic analysis was performed. Both treatments increased the epidermal thickness compared to untreated striae distensae. The application of 20% GA in combination with 0.05% retinoic acid or 10% L-ascorbic acid was safe and effective in improving the clinical performance of SA. The side effects were less than mild irritation. Glycolic acid can co-regulate collagen synthesis through cytokines released by fibroblasts and keratin-forming cells. In a double-blind controlled study, the treatment of 40 SD patients with 70% GA for six months was effective in reducing the striae width and hemoglobin content of SR and significantly reducing SA striae width and increasing melanin deposition, but not wholly repairing SD.¹²

Lasers and Light Devices

Ablative Lasers

Fractional CO₂ Laser (FrCO₂)

The Fractional Ablative CO₂ laser is the most commonly used laser treatment for SD and has satisfactory efficacy in promoting the regeneration and remodeling of collagen and elastin fibers.² In the study by Crocco et al,¹³ 13 SG patients were treated with a 10,600-nm Fractional CO₂ laser, and each patient experienced four sessions of increasing pulse energy levels (80, 90, 100 and 110 m J/MTZ), respectively. Maximum striae widths and skin tissue biopsies were measured before and after treatment. Biopsies of untreated normal skin were also obtained, and superficial and deep skin

tissue samples for analysis of collagen fibers and recent, intermediate, and mature elastic fiber changes. The width of the largest striae was significantly reduced after treatment, with significant thickening of the epidermal cell layer and a significant increase in collagen fibers, which were not significantly different from normal untreated skin. However, no significant increase in the number of elastic fibers was seen in all periods, which the researchers speculate may be related to the additional thermal stability of elastic and collagen fibers. It was reported that clear boundary lines and parallel collagen fibers appeared in the distorted dermo-epidermal junction area as potential markers of SD improvement when the treated skin was observed by reflectance confocal microscopy. Of concern is that the higher the laser energy, the greater the risk of post-inflammatory hyperpigmentation, and in some patients, PIH can last up to a year.¹⁴ Studies have also shown comparable efficacy of FrCO₂ laser and micro-needling for SR.¹⁵

Fractional Er:YAG Laser

Fractional Er:YAG laser has similar treatment effects to the Fractional Ablative CO₂ laser described above, but the 2940 nm Er:YAG causes less thermal damage to the surrounding tissues and thus allows for faster wound healing causing milder side effects such as erythema, edema, and PIH. PIH is more difficult to accept for Fitzpatrick skin type IV–V people so it can be used as favorable alternative treatment for darker skin people.¹⁶ It was reported that the researchers applied short pulse (SP) mode plus smooth (SM) mode to treat one side of SD and the other side with two short pulses (SP) modes for two months. All SD volumes were significantly reduced, and all patients showed more than 25% improvement. There was no significant difference between the two modalities regarding treatment effect. However, at the 6-month follow-up, the incidence of PIH in the SM&SP model was only 12.5% compared with 23.5% in SP&SP. Researchers believe this is related to the SM mode slowly penetrating heat from the skin surface into the deeper tissues, resulting in minor thermal damage. Therefore, to prevent and reduce PIH in dark-skinned people, it is necessary to apply SM mode and topical preparations of the affected area pre- and post-treatment.¹⁷ Interestingly, two years later, Meningaud et al¹⁸ explored an alternative treatment modality to reduce PIH and shorten recovery time. Applying a 2940 nm Er:YAG laser with an SMA module to split the laser beam into several micro spots scanning patterns, which only penetrate the epidermis by 50 mm, while also inducing acoustic waves generation to promote tissue regeneration. A 85% of patients reported great improvement, with significant improvements in skin thickness, elasticity, and quality in the affected areas by instrumental analysis. Only 15% reported average or slight improvement. These patients had late-stage and mature SD, which the researchers believe could be improved by increasing the number of treatment sessions or decreasing the interval between each treatment, but this would also require a larger RCT trial to demonstrate. The study suggests that the 2940 nm Er:YAG laser requires at least six treatments to be effective and that no side effects occurred in the 20 patients with long-term follow-up while recovery time was only five days. In addition, another study evaluated the efficacy of laser treatment of SA with a 2940 nm Er:YAG laser for six sessions, supplemented with bovine basic fibroblast growth factor (rb-bFGF) for one week light-emitting diode-red light (LED-RL) every seven days between laser treatments. At 6-month follow-up, 27 of 30 patients reported more than 50% improvement. At the same time, biopsies suggested thickening of both epidermis and dermis and an increase in the density of both elastic and collagen fibers.¹⁶

Non-Ablative Lasers

Er:Glass Laser

Given that histologically SD and scar healing are very similar, the 1540-nm Er:glass laser can enable dermal remodeling to treat atrophic scarring, which has recently been attempted in studies to treat SD. The researchers applied treatment 2 to 4 times, and after a one-month follow-up biopsy comparison, the epidermis and dermis were thickened, and collagen fibers and elastic fibers were increased. After three months, image comparison revealed a 50–75% improvement in all SD. After six months and even longer follow-up, patients had more than 50% improvement by visual assessment, and none had a recurrence. In addition, the study suggests that the optimal treatment parameters for the laser are 30 to 50 mJ/cm², and it is hypothesized that the stamping mode energy pattern is more suitable for SD treatment, ensuring the effectiveness and consistent distribution of microbeams into the skin. Also, this study selected 51 patients (II–IV), including SR and SA, in which 14% striae of more than 20 years and the farthest years were 40 years. Because of the experience with the treatment of the striae ranging in maturation age from 1 to 40 years, the researchers propose a

different view from the previous treatment of SD. They concluded that the superiority of the treatment effect lies more in the length, width, and density of Striae compared to the maturity of SD.¹⁹ In a prospective study, the Fractional 1565-nm Er:glass with picosecond 1064 nm or 532nm Nd:YAG laser was evaluated to be equally effective in treating SA.²⁰

Picosecond Lasers

In the study by Fusano et al²¹ after 27 Caucasian women with SA were treated with the 1064 nm picosecond laser over four months, clinicians observed clinical improvement in 81.4% of patients and 66.6% of patients perceived clinical improvement and satisfactory outcomes. Meanwhile, at the 6-month follow-up, the 3D analysis showed a significant improvement in the overall texture and depth of the striae. However, no significant reduction in width and collagen remodeling and dermal papillae were observed at Reflectance Confocal Microscopy (RCM), all of which indicate that 1064 nm picosecond laser treatment is an effective treatment option for SA but not a complete cure. After one year, the same conclusions were reached in another study evaluating the efficacy of 1064-nm picosecond laser treatment in 20 patients with dark-skinned (IV–V) SA. At 6-month follow-up, more than 90% of patients reported moderate to significant improvement, sustained improvement in skin texture, more evenness of striae color, and side effects of only mild erythema, edema, crusting, and PIH, with a 10% incidence of PIH.²²

Pulsed Dye Laser (PDL)

PDL increases collagen fiber production and reduces the degree of erythema in SR, which significantly improves SR.^{23,24} Based on the high affinity of hemoglobin for 585 nm PDL during treatment, all can effectively reduce the degree of erythema of SR.²³ Also, because melanin as a chromogenic group competes with hemoglobin for the light energy from the 585 nm PDL, dark-skinned people are highly susceptible to PIH, so even low-energy lasers are not recommended for use in dark-skinned (IV–V) people. The study by GLORIA et al²⁴ demonstrated that 585 nm PDL was effective in improving SR but had no significant clinical efficacy in SA, even though an increase in collagen fibers was detected in SA after treatment. This conclusion was similarly supported in another study, confirming that IPL and PDL are equally effective for SR.

Nd:YAG Laser

In a study conducted by Elsaie et al²⁵ comparing the efficacy of two energies (75 and 100 J/cm²) of long-pulsed Nd:YAG laser in the treatment of SD, it was confirmed that 100 J/cm² improved the appearance of SA significantly, while 75 J/cm² was more effective for SR, with a significant increase in collagen fibers and elastic fibers in post-treatment sample, and satisfactory changes were observed from both clinical and histological evaluation. The skin color of the 45 patients in this study sample included III–V, where the dark-skinned population did not show significant PIH.

Lights

Intense Pulsed Light (IPL)

In a prospective study evaluating the efficacy of IPL for SA at wavelengths between 515 nm and 1200 nm, all 15 patients reported satisfactory outcomes, with the average number of SD per patient decreasing from 7.8 to 6.26. The average length of SD decreased from 25 cm to 15.93 cm. There was an increase in both epidermal and dermal thickness under the microscope, confirming the effectiveness of IPL for the treatment of SA.²⁶

Others

Radiofrequency (RF)

A prospective randomized controlled study conducted by Harmelin et al²⁷ evaluated the effect of Fractionated Bipolar Radiofrequency versus Bipolar Radiofrequency Potentiated by Infrared Light for the treatment of SD. The abdomen was divided into four quadrants representing the four groups: the blank group, the two separate RF groups, and the combined treatment group. At the 6-month follow-up of the combined treatment group, 3D photography showed a 21.6% decrease in mean streak depth and a 1.73% increase in the control group. The distribution of collagen fibers was more uniform than in pre-treatment, and the distribution of elastic fibers was reduced. Both the physician and the patient reported significant improvement in SD but not in the width of the striae. The efficacy of combination therapy is superior to

monotherapy in all aspects and is an effective treatment modality for SA and SR. Side effects were mainly associated with Fractionated Bipolar Radiofrequency, and the presence of PIH in two patients suggests caution in dark-skinned people. Interestingly, in a study by Manuskiatti et al²⁸ it was noted that TriPollar RF is an excellent alternative treatment even for dark-skinned people. Improvement of more than 50% was perceived by 11.8% of patients after just one week of treatment, and persistent improvement was found at a follow-up kind of 6 weeks later. The clinical outcome of 1 patient with SR was better than all other SA patients, with 65% of patients reporting satisfactory treatment results. Even more satisfying for patients is that TriPollar RF side effects are only brief and mild erythema and edema while being essentially painless. From the results of the two research experiments mentioned above, the authors concluded that the treatment of SD requires developing an individualized treatment plan. Selecting treatment parameters and frequency and intervals needs to be considered thoroughly according to various aspects such as the patient's skin color, striae depth, clinical response, and tolerance level.

Micro-Needling

Unlike laser treatments, micro-needling does not cause thermal injury to the skin, so it reduces the risk of post-inflammatory hyperpigmentation, especially for darker skin phototypes. The advantages of fewer side effects, shorter recovery time, and lower cost have made it a hot spot for SD treatment in the last two years. The principle of action is similar to that of laser in that it promotes new collagen synthesis and dermal remodeling through dermal damage. In a recent study of 25 SD patients (I–V) treated with 1–3 consecutive Micro-needling sessions, all striae improved by more than 50%, and 28% of SD patients demonstrated more than 75% improvement. There was no significant difference in efficacy between patients with different skin types and no difference between thicker and thinner skin areas.²⁹ West et al³⁰ applied micro-needling to treat SR. Biopsies showed many regular collagen fiber bundles and dermal fibroblast proliferation but an insignificant increase in elastic fibers. Except for one case of Fitzpatrick type VI skin with PIH that resolved with topical treatment such as retinoic acid, no distant PIH appeared. In another study, micro-needling was shown to be as effective as 1340 nm Nd: YAP non-ablative fractional laser in the treatment of SA, and it was also observed that pain was more pronounced in the micro-needling group, so it was suggested that when the penetration depth was greater than 3 mm, local anesthetics were needed to pre-treatment.³¹ Studies have also shown that a combination of micro-needling with PRP is more effective than micro-needling alone.³²

Platelet-Rich Plasma (PRP)

PRP is a concentrated platelet centrifuged and sunk into a small amount of plasma. PRP induces extracellular matrix remodeling, collagen fiber, and elastic fiber formation.

Studies have shown that local PRP injections are more effective than 0.05% retinoic acid for SA, especially striae alba. Of the 30 SD patients, 86.6% of the PRP group reported improvement, and patient satisfaction was 89.9%, compared with 60% in the retinoic acid group in both areas. At the same time, PRP also had the advantages of easy access and no risk of hyperpigmentation or infection.³³ It has also been shown that PRP and carboxytherapy are essentially equivalent in the treatment of SA.³⁴ This year, Ebrahim et al³⁵ researchers tried the superiority of PRP combined with subcision or peeling/medium-depth peeling (GA 70% + TCA 35%) compared to PRP alone. After clinical improvement, patients' satisfaction and Dermatology Life Quality Index (DLQI), and skin biopsy assessments, it was confirmed that both combined treatments were superior to PRP alone. At the same time, subcutaneous separation was superior in the treatment of SA and safer in dark-skinned populations.

Microdermabrasion (MDA)

Microdermabrasion removes aged skin cells through mechanical damage and stimulates new cell production, collagen fiber, and elastic fiber synthesis. In an RCT involving 48 SA, it was demonstrated that both Galvano-puncture and MDA effectively reduced the length and width of SA, with thermography showing more significant improvement with Galvano-puncture and no statistically significant difference in pain.³⁶ In another single-center clinical trial, Hexsel et al¹⁰

evaluated the efficacy of Superficial Dermabrasion versus 0.05% retinoic acid for the treatment of 32 SR. Confirmed by comparing the width and length of the striae, Global Aesthetic Improvement Scale scores, patient satisfaction, and histological analysis, both treatments were significantly effective and did not differ. In addition, histological analysis showed a reduction in elastolysis, collagen fragmentation, epidermal atrophy, and an improvement in dermis and epidermis, confirming the clinical presentation. Both exhibited pruritus, erythema, and scaling. However, the incidence was higher in the retinoic acid group, which led to better patient compliance and safety in superficial dermabrasion, which the researchers concluded could be used for early and localized SR.

Carboxytherapy

Carboxytherapy, meaning cutaneous and subcutaneous injection of carbon dioxide gas, has been popular in dermal rejuvenation treatments since 1995. Water molecules react with carbon dioxide to produce molecular carbonic acid, which reduce the pH of tissue. According to the Bohr effect, this causes hemoglobin to release oxygen and microcirculatory vasodilation, while increasing peripheral blood flow (Bohr effect: A decrease in pH can cause a decrease in the affinity of hemoglobin and oxygen). Tissue stretching during carbon dioxide injection induces subclinical inflammation that activates macrophages, fibroblasts and endothelial cells. This stimulates neovascularization and extracellular matrix remodeling for skin repair and tissue regeneration.³⁷ Studies have shown carboxytherapy effectively improves the skin elasticity of SD, reducing the width and length of striae. At the same time, the color of SD becomes more like the natural skin, with hematoma being the most significant side effect.³⁸ In recent years, Elmorsy et al³⁷ demonstrated no significant difference in efficacy between carboxytherapy and FrCO₂. Up to 80% of SD patients had significant clinical improvement with carboxytherapy. SR was more effective than SA. The mean striae length decreased from 13.1 cm to 9.3 cm after only one month of treatment, and no patient in the carboxytherapy group had more severe striae than FrCO₂. The majority of the sample population in this study was Fitzpatrick skin type IV. No patients experienced PIH with carboxytherapy. Only temporary erythema and bruising at the injection site. Another study suggested that the clinical improvement of the carboxytherapy was comparable to the PRP. However, patients' satisfaction was higher with carboxytherapy. Because PRP was more likely to have pain and ecchymosis, carboxytherapy was effective for any part of the body and both types of SD.³⁹ Some of the clinical trials of single treatment modalities have been tabulated in [Table 1](#).

Combination Therapies

RF Plus Others

Microneedling and radiofrequency (MRF) have been successfully applied to treat atrophic scarring and facial wrinkles in recent years. Many researchers have tried to use it to treat SD, given the similarity between them, the histological characteristics of SD, and atrophic scarring. In the study by Al-Murish et al⁴⁰ non-insulated MRF with FrCO₂ indicated an improvement and no statistical difference in the treatment of SD as assessed by the Global Aesthetic Improvement Scale, dermoscopy, and VISIA imager (3D images). The VISIA system uses virtual shadow overlaps to provide reproducible targeting to accurately observe changes before and after treatment at the same position, generate corresponding regular and rendered 3D images. Regular images include skin tone and grayscale photograph to measure the depth and range of skin color changes. Red and yellow color in rendered 3D images represent the elevation of the skin, in this case SD lesions. These 3D images can make up for the deficiencies visual contrast in 2-dimensional images. Both groups after treatment, rendered 3D images showed a decrease in red and yellow color, while grayscale and skin tone color showed flatten of SD. Dermoscopy revealed a 5–32% reduction in striae width in the MRF group and a 6–31% reduction in the FrCO₂ group. The pain index was significantly higher in the MRF group but was tolerated by both patients, and although PIH occurred in both groups, it was more likely to occur in the FrCO₂ group. The above findings are generally consistent with those of Sobhi et al.⁴¹ The only difference is the absence of PIH in the MRF group in the latter study, which the authors suggest is related to the choice of the treatment protocol and instrumentation as well as pre- and post-treatment

Table 1 Clinical Trials of Single Treatment Modalities

Study Method	Treatment Protocol	Striae Type	Sample Size (Fitzpatrick Skin Type)	Results Measurement	Results
FrCO ₂ laser vs blank control	10600 nm 80, 90, 100 and 110 mJ/MTZ 4 sessions 30 days intervals	SG	13 (NM)	The width of largest striae Skin biopsy (stains: NM) Patient satisfaction assessment Epidermis thickness	Treated region 1. Reduction in the striae width 2. Increase in the amount of collagen fibers, no significant changes in the number of mature intermediate and recent elastic fibers 3. 92% patients considered results “good” or “very good” 4. Increase in the thickness of the epidermis
Er:YAG laser	2940 nm 2.3 J/cm ² 3 Hz 0.3 milliseconds 6 sessions 50 µm 30 days intervals	SD	20 (I–IV)	Skin elasticity and dermis thickness Patient satisfaction scale: very good; moderate; slight Patient and observer scar assessment scale (POSAS) scores	1. Significantly improved skin elasticity and increased average the dermal thickness 2. 70% participants reported good improvements in SD scarring; 15% very good; 10% moderate; 5% slight 3. Significantly decreased POSAS Score, reflecting improved skin quality
Erbium: glass laser	1540 nm 2–3 passes 35–55 mJ/mb (10-mm) or 12–14 mJ/mb (15-mm) 4–6 weeks intervals	SA & SR	51 (II–IV)	Clinical improvements: 5 = 100%; 4 = 76–99%; 3 = 51–75%; 2 = 26–50%; 1 = 1–25%; 0 = 0% Histologic analysis (stains: collagen fiber analysis with hematoxylin and eosin staining, elastic fiber analysis with Orcein-Giemsa staining)	1. Nonblinded clinical assessment: 50% improvement or more 2. Blinded evaluators assessment: 51–75% improvement 3. Thickening of neocollagenesis, dermis and epidermis, increased of elastin deposition
Picosecond laser	1064 nm 0.6 J/cm ² 750 ps pulse width 10 Hz 8 mm 4 sessions 4 weeks intervals	SA	20 (IV–V)	Skin texture Average melanin index (MI) and melanin variation score Clinical improvement (no improvement, less than 25% = minimal, 25–50% = moderate, 51–75% = marked, more than 75% = excellent improvement) Patient's satisfaction	Significantly improvement of skin texture Average MI increased significantly and the melanin variation score decreased 90% subjects: moderate to marked improvement in striae distensae appearance 85% patients: 25–50% improvement; 5% patients: over 75% improvement

(Continued)

Table 1 (Continued).

Study Method	Treatment Protocol	Striae Type	Sample Size (Fitzpatrick Skin Type)	Results Measurement	Results
PDL	585 nm 3 J/cm ² 0.45 ms PD 10 mm spot 1 passe 2 sessions 42 days intervals	SA & SR	20 (II–VI)	Visual analog scale 0 to 5: 0 = normal, 1 = light pink, 2 = pink, 3 = light brown, 4 = brown, and 5 = white hydroxyproline assay (collagen changes)	Striae rubra: Moderately beneficial for reducing erythema; striae alba: no apparent clinical improvement Total collagen per gram of dry weight increased (one striae alba and one striae rubra)
IPL	650 nm vs 590 nm 13.0–15.5 J/cm ² 6 ms PD Two pulses, 20 ms delay 10 × 50 mm 5 sessions 2 weeks intervals	SR	20 (III–IV)	Sum of striae length and width Degree of erythema: 7–10 severe; 4–7 moderate; 1–4 mild; 0–1 white Patient's satisfaction: weak, partial, very good	1. The length and width of both sides significantly reduced 2. 590-nm wavelength erythema significantly reduced with high patient's satisfaction scores
Nd:YAG laser	1064 nm 75 vs 100 J/cm ² 5 mm spot size 15 ms pulse duration 1 Hz 2 sessions 3 weeks intervals	SD	45 (III–IV)	Global Aesthetic improvement scale (GAIS): 1 = very much improved to 5 = no change Patient satisfaction score: 1 = very satisfied to 5 = very unsatisfied Histological analysis: (stains: hematoxylin and eosin, orcein and Masson's trichrome)	Both doctors and patients are satisfied with clinical improvement. Striae alba: significant improvement with 100 J/cm ² ; striae rubra: improved more with 75 J/cm ² . Both collagen and elastin fibres increased

RF	1.bipolar RF potentiated with IR light: five passes 100 J/cm ² 20–30% overlap 2.fractional bipolar RF: two passes 50% overlap 50–65 mJ/ pin 3 sessions of two types	SD	22 (II–V)	Width and depth of the striae distensae Scale of global assessments: –1 = worsening of lesion; 0 = no change; 1 = slight improvement; 2 = moderate improvement; 3 = marked improvement; 4 = complete clearance Histological analysis (stains: hematoxylin, eosin, safran, orcein and Verhoeff) Reflectance Confocal Microscopy Pain: 0 = no pain to 4 =maximum pain	1. Striae distensae depth decreased by 21.64% in the combination group and increase by 1.73% in control group 2. No significant differences in striae distensae width 3. Global assessment showing greater progress in combination therapy compared to control areas 4. Dermal papilla becoming more roundish and collagen fibers more reticulated pattern in combination treated and fractional bipolar RF-treated areas 5. Thicker collagen fibers in all treated areas 6. The median pain score = 3 in combination treated and fractional bipolar RF-treated areas
Micro-needling	1.5–3 mm needle depths 4–10 passes 30 days intervals	SD	25 (I–V)	Clinical improvement of a 5-point scale (4 = 76–100% improvement, 3 = 51–75% improvement, 2 = 26–50% improvement, 1 = 1–25% improvement, 0 = no change) Global assessment score (GAS)	Clinical improvement of at least 50% for all striae and more than 75% for 28% of patients No significant differences in clinical responses to different skin phototypes of patients Striae in thicker skin regions showed comparable clinical Different Different skin thickness for the same treatment regimen with same clinical improvement
PRP vs Tretinoin	1.PRP: every month for 3 sessions 2.Tretinoin (0.05%): every night for 3 months	SD	30 (NM)	Clinical improvement (digital photographs pre and after treatment) Patient's satisfaction Histological analysis (stains: collagen with hematoxylin, eosin, Masson Trichrome and elastic fibers with Van Gieson stain)	Significantly improvement in both sides and PRP-treated side had 86.6% of patient improvement, tretinoin-treated side had 60% Patient's satisfaction: more improvement in the PRP-treated side Collagen and elastic fibers increased in both sides
Dermabrasion vs Tretinoin	1.Superficial dermabrasion: 16 weekly sessions 2.Tretinoin (0.05%): daily for 16 weeks	SR	32 (I–IV)	Length and width of the striae distensae Histological analysis (NM) Patient's satisfaction: very unsatisfied, unsatisfied, neither satisfied nor unsatisfied, satisfied, very satisfied Global aesthetic improvement scale: very much improved, much improved, improved, no change, worse	1. The length and width of striae distensae decreased significantly in two treated areas but no significant difference between two treatments 2. Dermabrasion group:Improvement of dermal and epidermal layers 3. Satisfaction scores in two treated areas but no significant difference between two treatments 4. Global aesthetic improvement scale (Dermabrasion vs Tretinoin): Very much improved 7.7% vs 33.3%, Much improved 38.5% vs 55.6%, Improved 53.8% vs 11.1%

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Table 1 (Continued).

Study Method	Treatment Protocol	Striae Type	Sample Size (Fitzpatrick Skin Type)	Results Measurement	Results
Carboxytherapy vs FrCO ₂ laser	1. Carboxytherapy: 50 to 80 mL/min. 45° needle 3–5 cm apart repeated once every 2 weeks 2. FrCO ₂ laser 10,600 nm 8 W pitch 600 µm 3000 microseconds Micro-diameter 120 µm 6 sessions 4 weeks intervals	SD	40 (III–IV)	Length and width of the striae distensae Clinical improvement (Digital photography of striae): –1 = worse, 0 = no change, 1 = weak (1–24% improvement), 2 = moderate (25–49%), 3 = good (50–74%) 4 = excellent (75–100%) Patients' satisfaction	Significant improvement in both the width and length in both group and no statistically difference between them No statistical significance difference in clinical improvement between both groups but 2 patients became worse in fractional CO ₂ group only Patients' satisfaction between the two groups was comparable

Abbreviations: FrCO₂ laser, fractional ablative CO₂ laser; SG, striae gravidarum; SA, striae albae; SR, striae rubrae; PDL, pulsed dye laser; IPL, intense pulsed light; RF, radiofrequency; PRP, platelet-rich plasma; NM, not mention; PIH, post-inflammatory hyperpigmentation; SD, striae distensae; MTZ, microscopic treatment zone; NM, not mention.

management. In another study, they asked whether the combination of FrCO₂ and MRF for SD could improve efficacy and reduce side effects, given the paradox that high-energy FrCO₂ is more effective for SD and has a greater risk of causing PIH. The results showed a slightly more significant improvement with the combination treatment than the conventional FrCO₂ treatment. The hyperpigmentation and erythema severity were more severe than in the MRF group. At the same time, the side effects are similar to the FrCO₂ group. After a combined treatment, the skin ultrasound scanner showed an increase in average skin thickness of 204.9 µm and an increase in dermal density of 8.8%, indicating that the dermal improvement would last for a more extended time.⁴² In addition, it has been shown that the efficacy of MRF and Er:YAG treatment for SA is comparable. However, the dermal and epidermal thickening in the MRF group was more significant but not statistically different in the optical coherence tomography instrument.⁴³ It is noteworthy that no PIH was reported in the MRF group in the latter two studies, in keeping with Sobhi above. MRF is more capable of stimulating SA collagen fiber regeneration than NAFL but is more painful.⁴⁴

Ablative Fractional radiofrequency combined with Acoustic Pressure Ultrasound transdermal delivery of 0.05% retinoic acid cream is also an effective treatment modality for SA. Combining the two devices can increase the penetration of retinoic acid and improve the clinical efficacy with an improvement of up to 76–100% with fewer side effects and only one case of PIH.⁴⁵ Sublative bipolar fractional radiofrequency combined with 0.1% retinoic acid is a promising treatment modality for SG.⁴⁶

FrCO₂ Plus Others

A randomized, double-blind study compared the efficacy of FrCO₂ combined with recombinant human epidermal growth factor (AFXL-rhEGF) and FrCO₂ combined with aloe vera gel (AFXL-Aloe) in the treatment of SA. Human epidermal growth factor and aloe vera gel are hydrophilic substances that can penetrate deeper into the skin through the MTZ produced by FrCO₂ to achieve better efficacy. The results showed a significant improvement in both subjective and objective assessments, which lasted for up to 6 months. At 6-month follow-up, up to 50% of patients reported significant improvement in patient satisfaction with AFXL-rhEGF compared with only 25% with AFXL-Aloe. At the same time, both had better efficacy in the SD of the buttocks than the thighs and abdomen. With little difference in efficacy, AFXL-Aloe is significantly more economical. Notably, the 24 SA involved in this study were all dark-skinned (III–IV) and had a high incidence of PIH of 95.8%, but hyperpigmentation improved at the 6-month follow-up.⁴⁷ In the last two years, it has been shown that FrCO₂ combined with PRP is also an effective treatment for SD and is superior to FrCO₂ alone or PDL combined with PRP.^{48,49} Some of the clinical trials of combined treatment modalities have been tabulated in Table 2.

Conclusion

Different skin types have different reactions and side effects to the same treatment. Despite some positive results, the treatment of SD is still a great challenge, especially for SA (end-stage of SD). Despite the limitations of the existing literature, combined treatment is generally more effective than single treatment. Tretinoin, FrCO₂ laser, Er:YAG laser, radiofrequency and microneedling were clinically responsive to proper settings or concentrations in single treatment. FrCO₂ laser remains the most popular and effective treatment, but the side effects of PIH deserve our attention, especially in dark-skinned people. The combination of radiofrequency and microneedling was the most common treatment with good clinical response and fewer side effects. In the future, a universal SD grading scale and a standardized way of assessing post-treatment outcomes are expected to be established before definitive conclusions can be obtained for more accurate comparative treatment. Combining therapy is currently a hot topic in SD treatment and more combinations can be tried to improve the efficacy, reduce side effects to achieve a better treatment effect and increase patient compliance. The study's design requires samples for different skin types, optimal parameters, and protocols for various treatment modalities, and follow-up of long-term results are directions that can be worked on in the future.

Table 2 Clinical Trials of Combined Treatment Modalities

Study Method	Striae Type	Sample Size (Fitzpatrick Skin Type)	Results Measurement	Results	Adverse Effects	Limitations	References
MRF vs FrCO ₂ laser	SD	14 (III–IV)	Global aesthetic improvement scale: very much improved (76–100%) = 4, much improved (51–75%) = 3, improved (25–50%) = 2, no change (improvement of <25%) = 1, worse = 0 Width of striae Patients' satisfaction: 4 = extremely satisfied, 3 = very satisfied, 2 = satisfied, 1 = slightly satisfied, 0 = not satisfied	1. Global aesthetic improvement scale score showing a significant improvement and without a significant difference between the two groups 2. Significantly decreased of width in both groups 3. Patients' satisfaction: MFR = 3.3, FrCO ₂ = 2.5	Both groups: PIH, pain mean pain score: MRF = 5.35, FrCO ₂ = 2.35 (MRF-treated side had a higher score than the FrCO ₂ , which was a significant difference)	1. Small sample size 2. Lack of histologic assessment	[40]
MRF vs FrCO ₂ laser	SD	19 (III–IV)	Reduce width of the largest striae; blinded physician evaluation; skin texture; patient satisfaction; overall appearance and all of them with the same scale: No improvement = 0, < 25% minimal improvement = 1, 25–50% good improvement = 2, 50–75% very good improvement = 3, > 75% excellent improvement = 4	1. Both techniques effective, but MRF had a slight better efficacy and the difference was not statistically significant 2. MRF and FrCO ₂ laser equally effective in the treatment of striae rubra and striae alba	PIH was more evident in FrCO ₂ compared to FMR, and the difference was statistically significant	1. Small sample size and all participants were female 2. Lack of skin biopsy	[41]
MRF vs Er: YAG laser	SA	20 (NM)	Width of the largest striae Epidermal thickness Physician Scar Improvement Scale (PSIS) Self-Assessed Scar Improvement Scale (SASIS) Clinician Global Aesthetic Improvement Scale (CGAIS) All the scales above using Likert scale: 0 = no improvement, 1 = minimal (1–25% improvement), 2 = good (25–50% improvement), 3 = very good (50–75% improvement), and = for excellent (>75% improvement)	1. In both groups, the width of the largest striae decreased significantly and no significant difference between them 2. The average epidermal thickness increased significantly in all patients Significantly better results in FMR group 3. Scar improvements in both groups did not associate with duration, skin type, or site of the striae distensae	PIH	NM	[43]

Group1 (FrCO ₂ laser plus PRP) vs Group2 (PDL laser plus PRP)	SD	30 (V–IV)	Clinical assessment (including width of largest striae, improvement of skin texture) using Quartile Grading Scale: No improvement, Mild: < 25% improvement, Moderate: 26–50% improvement, Marked: 51–75% improvement, Excellent: >75% improvement Patient satisfaction: very satisfied, satisfied, slightly satisfied, unsatisfied Histological analysis (stains: hematoxylin, eosin stain and Masson's trichrome stain)	1. Both treatment groups: significant improvement of skin texture and reduction of width of striae lesions 2. Significantly higher clinical improvements in combined FrCO ₂ laser with PRP group than the other group so does patient satisfaction 3. Improvement of epidermal thickness and dermal thickness in both treatment groups and more significant improvement of combined PRP with FrCO ₂ laser group	Mild PIH (100%)	NM	[48]
Group1 (FrCO ₂ laser plus rhEGF) Vs Group2 (FrCO ₂ laser plus Aloe vera)	SA	24 (NM)	Melanin variation Average melanin Patient satisfaction Histological analysis (stains: hematoxylin and eosin, Masson trichrome, and Verhoeff–van Gieson)	1. Significant improvement in texture, without statistically significant difference in both groups 2. Participants satisfaction greater marked improvement in group 1 than group 2 3. Both groups improved melanin variation 4. Both groups showed statistically significant increases in epidermal thickness and decreases in elastic fragmentation	PIH (95.8%)	1.Small sample size. 2. The effect of FrCO ₂ laser treatment alone was not evaluated.	[47]

Abbreviations: MRF, micro-needling radiofrequency; FrCO₂ laser, fractional ablative CO₂ laser; SD, striae distensae; SA, striae albae; rh EGF, recombinant human epidermal growth factor; NM, not mention; PIH, post-inflammatory hyperpigmentation; PRP, platelet-rich plasma; PDL, pulsed dye laser.

Consent for Publication

All authors have read and approved the final manuscript for submission.

Disclosure

The authors report no conflicts of interest in this work.

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