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SYSTEMATIC REVIEW

Systematic review of single and combined treatments for different types of striae: a comparison of striae treatments

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Abstract

Striae distensae (SD) or stretch marks are among the most common forms of atrophic scarring and cosmetic problems, especially in women, that negatively affect quality of life. The main causes of SD vary widely, but the most significant ones include obesity, pregnancy, high corticosteroid levels, weight changes, endocrine disorders and genetic predispositions. Various modalities are available for the treatment of SD; however, there is still no gold standard therapy for this condition. Given the many questions concerning the preferred therapeutic modalities for SD or their overall cost-effectiveness, this comprehensive systematic review discusses the most prevalent, recent and promising therapies for SD in three main categories, including single therapy, therapeutic comparisons and combination therapy. A systematic search was carried out in Medline, Scopus, Web of Science and Google Scholar for original articles published on the treatment of SD by 20 May 2019. One hundred articles were reviewed and divided into three categories. In the single therapy category, we found that laser and other light-based devices and topical treatments are the most commonly applied interventions. In the therapeutic comparison category, we found that most of the common therapeutic modalities are equally effective and there is no significant difference between them in side-effects and treatment duration. In the combination therapy category, we found that the combination of two or more modalities is usually better than using each one alone.

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Introduction

Rationale

Striae distensae (SD), striae or stretch marks are one of the most common cosmetic problems caused by the loss of collagen and elastin fibres in the dermis.[1] Owing to its aesthetic impact, this atrophic scarring can cause depression and psychological problems in patients and affect their quality of life.[2–4] With a prevalence of 11%–88% in the general public, SD is more common in women. These scars are categorized into different types. Striae rubrae are the early type of striae, presenting as erythematous to violaceous colour lesions.[4] Striae rubrae lesions gradually become hypopigmented and atrophic due to reduced melanization and turn into striae albae, appearing as white lines.[4] Striae caerulea present as blue lines in darker skins.[5] Striae nigrae also appear in darker skins but have more melanin pigments and appear as black lines.[5] Striae gravidarum appear as red or violet lines, often on the abdomen and breast skin of pregnant women due to mechanical stress on the skin and hormonal changes.[5]

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SD have three main causes. First, they might develop during rapid weight changes, such as in pregnancy, which is known as the most common cause of striae gravidarum,[6] or during adolescence as pubertal growth spurt.[2] Second, they can appear when steroid levels increase. Lastly, they can occur in patients with prolonged systemic or topical corticosteroid use, such as Cushing's syndrome and Marfan syndrome.[1,2] According to literature, SD are also associated with medical conditions like anorexia nervosa, typhoid fever, rheumatic fever, chronic liver disease, augmentation mammoplasty, tissue expansion, tension-requiring skin sutures, organ transplantation, cardiac surgery, HIV therapy, chemotherapy, tuberculosis therapy and contraceptive or neuroleptic consumption.[7] In addition, some environmental and genetic factors, such as family history of SD, skin texture and colour, malnutrition, age of pregnancy, gestational age, fetal weight and gestational diabetes, can affect the incidence of SD.[8]

In general, treating striae is difficult, especially chronic striae.[9] Despite the various therapeutic modalities for improving SD, there is no definitive treatment.[10] The current modalities improve SD by increasing fibroblast activity, collagen and fibronectin synthesis, anti-inflammatory properties, skin elasticity and dermal thickness. These treatment options can stimulate cell proliferation and improve skin blood perfusion and hydration.[1] Since these treatments only provide partial improvement, examining their effectiveness and possible side-effects can help physicians choose the most effective treatment for patients.

Objectives

A comprehensive literature review to provide a critical analysis on which modality is best for striae single therapy and examine the advantages of each modality and compare their efficacy, costs and safety.

Methods

Protocol and registration

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Information sources

A search was carried out in Medline (PubMed; http://ncbi.nlm.nih.gov/pubmed), Scopus (http://www.scopus.com), Web of Science (http://webofknowledge.com) and Google Scholar (https://scholar.google.com) for articles published by 20 May 2019, and all the English articles on therapeutic modalities for SD were included.

Search strategy

The search keywords included 'Striae Distensae' OR 'Stretch Marks' OR 'Striae Alba' OR 'Striae Rubra' OR 'Striae Gravidarum' AND 'Treatments' OR 'Therapeutic' OR 'Therapy' OR 'Treatment Outcome' OR 'Treatment Failure' OR 'Drug Therapy' OR 'Radiotherapy' OR 'Surgery'. There were no other limitations or filters. All the articles retrieved from PubMed, Scopus and Web of Science were included; as for Google Scholar, only the 50 newest articles were selected from a total of 4240 articles. All the articles published by 20 May 2019 were included for data screening.

Eligibility criteria

For answering the first main question of this systematic review (i.e. What is the best single therapy option?), all the articles that[1] Used only one therapeutic modality for SD and[2] Reported the treatment outcomes and adverse effects, were selected for full-text screening. To evaluate the advantages and disadvantages of each modality, all the studies comparing the results of at least two different therapeutic modalities were included in the next phase. To assess the effectiveness and safety of the combination therapies, all the articles that used a combination of two or more treatment modalities and reported their results and adverse effects were accepted for full-text screening. Only the English articles were included, while animal studies, in vitro studies, studies on preventive measures, review articles, case reports and studies on other types of atrophic scars were excluded.

Data collection

Endnote® X8 (Clarivate Analytics, Philadelphia, PA, USA) was used for study screening and data extraction. In the first phase, from 2 July to 23 August 2019, two independent reviewers screened and categorized all the extracted articles based on their titles and abstracts. Any conflicts were resolved by consulting a third reviewer. In the second phase, full-text screening was performed by all authors and the useful data of the articles were extracted.

Results

A total of 629 articles were retrieved, and after removing the 143 duplicates, 486 remained for the title/abstract screening phase. Finally, a full-text screening was performed and 100 eligible articles remained for data extraction. All these articles were reviewed and their extracted information is separately shown in Tables S1–S14. Given the impossibility of showing the entire retrieved data in this article, we included only three tables in the main body of this manuscript, but the complete version of the data is available for review in supplementary files. Based on our eligibility criteria, 57 articles were selected for the best single therapy option, i.e., the single therapy category (Table S1), 25 were selected to help identify the advantages and disadvantages of each treatment modality over another, i.e., the therapeutic comparison category (Tables S2 and S3), and 18 articles were selected for full-text review to evaluate the effectiveness and safety of combination therapies, i.e., the combination therapy category (Tables S7, S9 and S11). The full text of these 100 articles were reviewed, and any pertinent data to the main research questions were extracted. The study phases (title/abstract screening and full-text review) are summarized in the

PRISMA flow diagram in Fig. 1. To avoid giving excessive information in the main article, only the data extracted from 27 studies focussed on the most prevalent, recent and promising therapeutic modalities and encompassing the best of the three SD treatment categories are presented in the main manuscript (Tables 1–3 in the main text).

The results of this comprehensive systematic review have been classified in three categories, as summarized in Tables 1–3. These studies were focussed on the most prevalent, recent and promising therapeutic options and had the largest sample sizes and highest standards of evidence. For evaluating the best single therapy options, the data from the most frequently cited studies on ablative fractional laser (often CO_2 fractional), non-ablative fractional laser, pulsed dye laser (PDL), intense pulsed light (IPL), radiofrequency (RF), needling, abrasion therapies, and topical therapies were extracted. For identifying the advantages and disadvantages of each treatment modality (i.e. the therapeutic comparison category), the therapeutic modalities prevalently discussed in the single therapy category were compared with each other. Finally, for assessing the effectiveness and safety of combination therapies, the therapeutic results for using RF, ablative fractional lasers (such as CO_2 and erbium Yag), platelet-rich plasma (PRP), needling and topical tretinoin were assessed in various combinations.

Single therapies

This category contained studies investigating only one SD treatment modality; however, their extracted data did not meet the

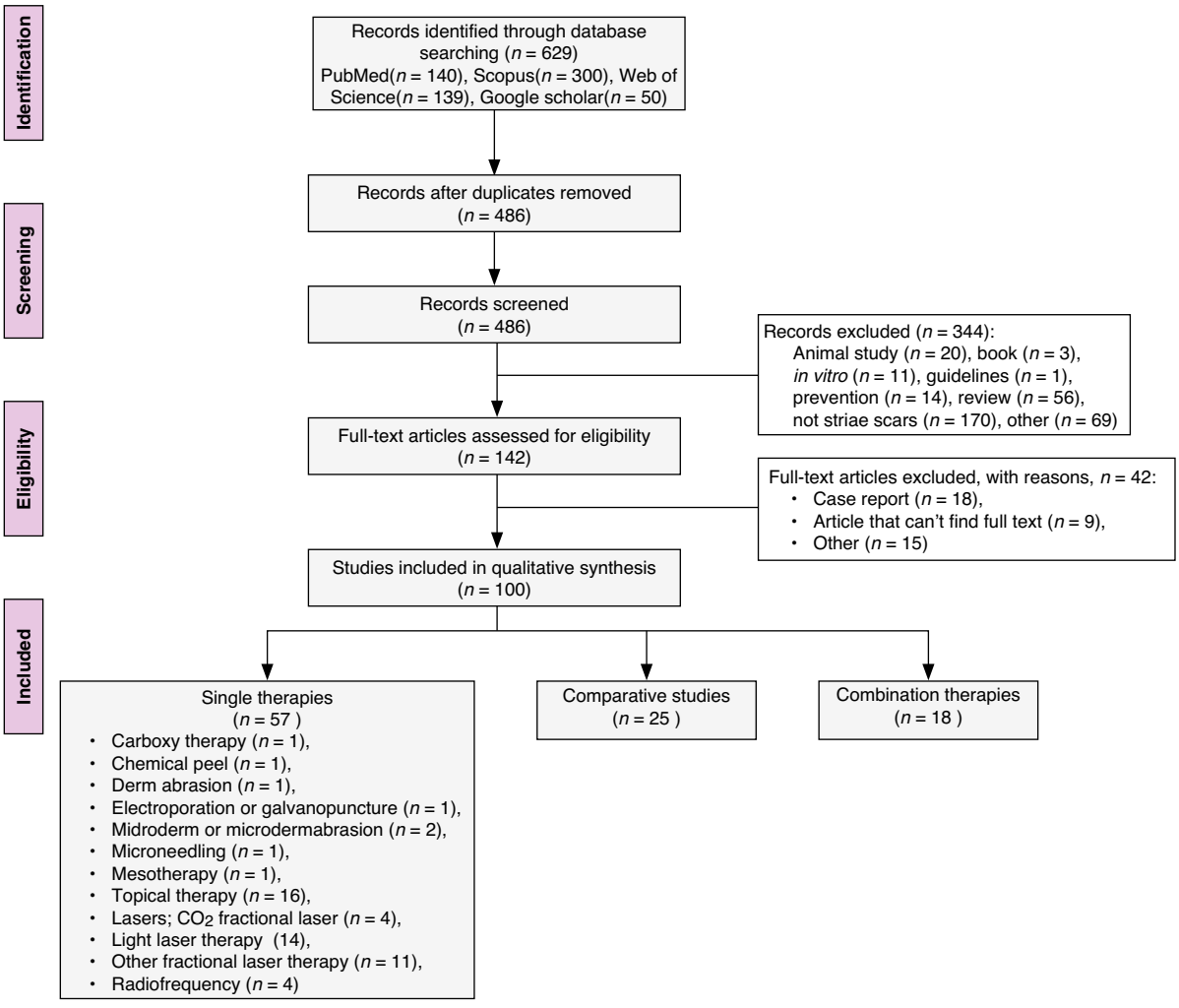

Figure 1 PRISMA flow diagram.

Table 1 Summarizing the original studies retrieved on striae treatment modalities, category1 (single therapies)

Reference	Title	Number of patients	Gender	Study group			Treatment duration	Method of measuring improvement	Type of striae	Adverse effects	Summary of results
				Group 1	Group 2	Group 3					
2	Treatment of striae distensae using an ablative 10,600-nm carbon dioxide fractional laser: A retrospective review of 27 participants	27	100% f	Fractional ablative CO_2 laser	-	-	One session	Before and after photographs and participant satisfaction	Distensae	Post-therapy erythema, PIH, transient pruritus, post-treatment crusting or scaling, and oozing	CO2 FS can significantly affect late-stage striae distensae.
11	Fractionated CO_2 laser in the treatment of striae alba in darker-skinned patients: A prospective study	30	90% f	Fractional ablative CO_2 laser	-	-	Two sessions with 4-week intervals	Cutaneous Resonance Running Time (CRRT) was measured by a reviscometer (MPA5 multi-probe adaptor)	Alba	Erythema, burns, PIH	The treatment of striae alba with fractional CO2 laser therapy led to minimal improvements and caused only mild side-effects.
12	An efficacy and safety of nanofractional radiofrequency for the treatment of striae alba	33	84.8% f	Radiofrequency	-	-	Three sessions with 4-week intervals	Measurement of total lesion surface area (using Pictzar™ digital software)	Alba	PIH	Non-fractional RF is highly effective and safe for treating striae alba.
13	Treatment of striae distensae with fractional photothermolysis	22	100% f	Fractional non-ablative laser therapy	-	-	Two sessions with 4-week intervals	Before and after photographs and skin biopsy samples	Distensae	Erythema and mild pigmentation	Fractional photothermolysis may be effective in treating striae distensae; the treatment outcomes were better in the patients with white rather than red striae.
14	Fractional non-ablative 1540-nm laser treatment of striae distensae in Fitzpatrick skin types II to IV: clinical and histological results	51	94% f	Fractional non-ablative laser therapy	-	-	Two to four sessions with 4- to 6-week intervals	Skin biopsies and before and after photographs	Rubra and alba	Transient erythema and oedema, PIH	Significant textural and pigment corrections were observed for a wide range of striae rubra and striae alba cases after treatment with a 1540-nm fractional non-ablative laser.
15	Treatment of striae distensae using needling therapy: A pilot study	16	87.5% f	Micro-Needling	-	-	Three sessions with 4-week intervals	Before and after photographs, skin biopsies, and patient satisfaction using the quartile grading scale	Alba and rubra	Mild pain, erythema, and spotty bleeding	Disk microneedle therapy system (DTS) can be safely and effectively used in the treatment of striae distensae.

Table 1 *Continued*

Reference	Title	Number of patients	Gender	Study group			Treatment duration	Method of measuring improvement	Type of striae	Adverse effects	Summary of results
				Group 1	Group 2	Group 3					
16	Treatment of striae distensae with microdermabrasion: A clinical and molecular study	20	70% f	Microdermabrasion	-	-	Five sessions with weekly intervals	Skin biopsy samples were subjected to RT-PCR for the assay of type I procollagen mRNA levels	Rubra and alba	PIH, transient oedema	Microdermabrasion is effective in treating striae distensae and more so in striae rubra than striae alba.
17	A double-blind controlled clinical trial assessing the effect of topical gels on striae distensae (stretch marks): A non-invasive imaging, morphological and immunohistochemical study	20	100% f	Topical therapy (chemical)	-	-	Daily for 6 weeks	Skin biopsy, tissue tonometry, full-field laser perfusion imaging, Spectrum TM, Spectrophotometric Intracutaneous Analysis, and subjective assessment	Rubra and alba	Erythema	The application of gels by topical massage had a significant effect on SD.
18	Topical tretinoin 0.1% for pregnancy-related abdominal striae: An open-label, multicenter, prospective study	20	100% f	Topical therapy (chemical)	-	-	Daily for 12 weeks	Evaluated by the analysis of one preselected target lesion; colour photographs; patients completed a questionnaire	Gravidarum	Erythema and scaling	The topical application of tretinoin significantly improved the clinical appearance of pregnancy-related stretch marks.
19	The effect of Aloevera gel and sweet almond oil on striae gravidarum in nulliparous women	160	100% f	Topical therapy (natural)	-	-	Twice a day for 20 weeks	The striae diameter was measured by callipers; patient satisfaction	Gravidarum	No side-effects either in the mother or fetus	Aloevera and sweet almond oil reduce itching in striae and prevent their progression.
20	Effects of olive oil on striae gravidarum in the second trimester of pregnancy	70	100% f	Topical therapy (natural)	-	-	Twice a day for 8 weeks	Observational approach	Gravidarum	NM	Olive oil had no effect on reducing or preventing striae.
21	The effect of bitter almond oil and massaging on striae gravidarum in primiparous women	141	100% f	Topical therapy (natural)	-	-	Daily for 12 weeks	A questionnaire and the Fitzpatrick Classification Scale (FCS) were completed	Gravidarum	Without any adverse effects	A 15-min massage with almond oil during pregnancy reduced the development of striae gravidarum; however, using bitter almond oil had no effect by itself.

PIH, postinflammatory hyperpigmentation; RF, radiofrequency.

Table 2 Summarizing the original studies retrieved on striae treatment modalities, Category 2 (therapeutics comparison)

Reference	Title	Number of patients	Gender	Study group			Treatment duration	Method of measuring improvement	Type of striae	Adverse effects	Summary of results
				Group1	Group2	Group3					
22	Fractional CO2 laser versus intense pulsed light in treating striae distensae	20	100% f	Fractional CO_2 laser	Intense pulsed light	-	Mod. 1: Once-monthly for 5 months Mod. 2: Twice-monthly for 5 months	Before and after photographs + patient satisfaction rate	Distensae	Mod. 1 & 2: Erythema, feeling of heart, pruritus and hyperpigmentation	Comparing both modalities showed a significant improvement in striae width in those treated with laser vs. IPL, but there was no significant difference between the study groups in the improvement in the length of striae.
23	Treatment of striae distensae with nonablative fractional laser versus ablative CO2 fractional laser: a randomized controlled trial	24	100% f	Fractional CO_2 laser	Non-ablative fractional laser	-	Mod. 1 & 2: Three sessions with 4-week intervals	Before and after photographs, non-invasive suction, patient satisfaction score and skin biopsies	Distensae	Mod. 1 & 2: Transient mild erythema, PIP, crust formation	The study suggests that both modalities may be an effective and safe treatment option for striae distensae in Asian skin.
24	Efficacy of fractional carbon dioxide laser versus microneedling in the treatment of striae distensae	33	85% f	Fractional CO_2 laser	Microneedling	-	Mod. 1 & 2: Three sessions with 4-week intervals	Before and after photographs, patient satisfaction and skin biopsies using the quartile grading scale for clinical improvements	Alba	Mod. 1: PIH, transient mild edema Mod. 2: Transient mild erythema, pinpoint bleeding	Microneedling is an effective, safe and cheap method for treating striae distensae, but fractional CO2 laser is more effective and affordable as a first line of treatment.
25	Efficacy of microneedling versus fractional non-ablative laser to treat striae alba: A randomized study	20	100% f	Non-ablative Fractional laser	Microneedling	-	Mod. 1 & 2: Five monthly sessions	Before and after photographs, skin biopsies	Alba	Mod. 1: Erythema pruritus + crusting + hyperpigmentation and post-procedure pain Mod. 2: Erythema and pruritus	Both modalities are effective, well-tolerated and comparable in treating SA.

Table 2 *Continued*

Reference	Title	Number of patients	Gender	Study group			Treatment duration	Method of measuring improvement	Type of striae	Adverse effects	Summary of results
				Group1	Group2	Group3					
26	Clinical and immunohistochemical comparative study of the efficacy of carboxytherapy vs. platelet-rich plasma in treatment of stretch marks	20	70% f	Carboxytherapy	Platelet-rich plasma	-	Mod. 1 & 2: Four sessions with 3- to 4-week intervals	Clinical photographs, skin biopsies using the quartile grading scale for clinical improvements	Alba	Mod. 1 & 2: Ecchymosis and pain during injection	Both methods were effective. On the one hand, PRP is cheap and has minimal side-effects; on the other hand, carboxytherapy is an effective, safe and novel method for the treatment of striae that needs further research.
27	The comparative study of topical therapy on striae alba between a herbal extract cream and 0.1% Tretinoin cream in adolescence	24	100% f	Herbal extract cream	0.1% Tretinoin cream	-	Mod. 1 & 2: every night for 16 weeks	Clinical photographs, digital Vernier caliper, roughness was assessed by a UVA-light video camera, patient satisfaction, histological analysis	Alba	Mod. 1: Mild skin irritation Mod. 2: Skin irritation, redness and scaling	The two topical agents were equally effective; since tretinoin can cause skin irritation, the herbal extract can be a better alternative topical treatment for striae alba.
28	Platelet-rich plasma versus tretinoin in treatment of striae distensae: A comparative study	30	90% f	Platelet-rich plasma	Tretinoin	-	Mod. 1: Three monthly sessions Mod. 2: Every night for three nights	Digital photographs, skin biopsies and patient satisfaction	Distensae	Mod. 1: Mild pain and bruises Mod. 2: Mild itching	Both treatments were safe for treating SD, but PRP was more effective and had a better therapeutic response.
29	Efficacy of pulsed dye laser versus intense pulsed light in the treatment of striae distensae	20	100% f	Pulsed dye laser	Intense pulsed light	-	Mod. 1 & 2: Five monthly sessions	Digital photographs, skin texture, skin biopsies	Distensae	Mod. 1 & 2: Erythema, pain, itching, PIH	Both lines of treatment were a therapeutic option for striae, but striae rubra gave a better response to both PDL and IPL.

MOD, modality; SA, striae alba; IPL, Intense pulsed light

Table 3 Summarizing the original studies retrieved on striae treatment modalities, Category 3 (combination therapies)

Reference	Title	Number of patients	Gender	Study group			Treatment duration	Method of measuring improvement	Type of Striae	Adverse effects	Summary of results
				Group1	Group2	Group3					
30	Use of combination therapy fractionated microneedle radiofrequency with fractional CO_2 laser for the treatment of striae distensae in Korean patients	21	100% f	Fractional CO_2 laser	Microneedle RF	Fractional CO_2 laser+ Microneedle RF	Three treatment sessions with 1-month intervals	Before and after photographs and skin biopsy (Global Improvement Scale)	Distensae	PIH (30%) pain (20%) pruritus (20%)	A combination therapy made up of fractionated microneedle RF and fractional CO_2 laser is safe and has a positive therapeutic effect on striae distensae.
31	Clinical improvement of striae distensae in Korean patients using a combination of fractionated microneedle radiofrequency and fractional carbon dioxide laser	30	100% f	Fractional CO_2 laser	Microneedle RF	Fractional CO_2 laser+ Microneedle RF	Three treatment sessions with 1-month intervals	Before and after photographs + skin biopsy (Global Improvement Scale)	Distensae	PIH (30%), pain, pruritus (20%)	Fractionated microneedle RF treatment could be an effective treatment for striae distensae, and its combination with fractionated CO_2 laser could be a better choice.
32	Fractionated bipolar radiofrequency and bipolar radiofrequency potentiated by infrared light for treating striae: A prospective randomized, comparative trial with objective evaluation	22	95.5% f	Fractionated bipolar radiofrequency	Bipolar radiofrequency potentiated by infrared light	Fractionated bipolar radiofrequency+ Bipolar radiofrequency potentiated by infrared light	Three monthly sessions	Before and after photographs, skin biopsy	Rubra and alba	Crust formation, pruritus (13%) PIH	The combination of these two methods is an effective treatment option for SD in the abdomen.
33	Comparison between the efficacy and safety of platelet-rich plasma vs. microdermabrasion in the treatment of striae distensae: clinical and histopathological study	68	79.4% f	Intradermal PRP	Microdermabrasion	Intradermal PRP+ Microdermabrasion	Six sessions, every 2 weeks, for six sessions	Before and after photographs, skin biopsy (using the Quartile Grading Scale for improvement assessment)	Alba and rubra	Pain during injection, ecchymosis	The combination modality was more effective in the short term.

Table 3 *Continued*

Reference	Title	Number of patients	Gender	Study group			Treatment duration	Method of measuring improvement	Type of Striae	Adverse effects	Summary of results
				Group1	Group2	Group3					
34	Transepidermal retinoic acid delivery using ablative fractional radiofrequency associated with acoustic pressure ultrasound for stretch marks treatment	16	100% f	Ablative fractional RF	-	Ablative fractional RF + retinoic acid cream + low-frequency acoustic pressure US distinct technology for 2 min	Every 4 weeks	Skin biopsies and before and after photographs (five-point analogue scale)	Alba	Erythema, oedema, moderate burning	Ablative fractional RF and acoustic pressure US technology and retinoic acid cream resulted in a significant clinical improvement and a low incidence of side-effects.
35	Microneedling system alone vs. microneedling system with trichloroacetic acid in the management of abdominal striae rubra: A clinical and histopathological study	30	100% f	Microneedling	-	Microneedling + trichloroacetic acid	Six sessions with 3-week intervals	Before and after photographs, skin biopsies	Rubra	Transient erythema and edema	Both modalities were effective, but derma roller + TCA 15–30% showed better results, while derma roller alone had fewer side-effects.
36	Comparative study between microneedling alone and microneedling combined with platelet-rich plasma in the treatment of striae distensae using clinical and histopathological assessment	20	100% f	Microneedling	-	Microneedling+ platelet-rich plasma	Four sessions with 2-week intervals	Before and after photographs, and skin biopsies	Distensae	Pain, bleeding, erythema and PIH	Microneedling combined with PRP is more effective in SD.

PIH, post inflammatory hyperpigmentation; RF, radiofrequency; PRP, Platelet-rich plasma.

criteria for meta-analyses due to differences in design, SD type and outcome reporting format (Table S1).

The category of light and laser therapies for SD had four sub-categories, including fractional ablative CO_2 laser, fractional non-ablative laser, RF and other light and laser therapies. In the fractional ablative CO_2 laser sub-category, the prospective studies had reported different rates of improvement due to the different outcome measurement methods used; for instance, a significant increase in thickness of the epidermal layer was observed by analysing the collagen fibres and epidermal thickness, but a minimal improvement was observed if the cutaneous resonance running time was measured. This modality has minimal side-effects, which include swelling, burning, erythema and post-inflammatory hyperpigmentation (PIH). In the fractional non-ablative laser sub-category, interventional studies proved that fractional photo thermolysis is an effective treatment modality for all types of striae – with a potentially greater effectiveness for striae albae. In general, it is a safe method with minimal side-effects, which include oedema, erythema, mild and transient pain and pigmentation. Based on interventional studies, 1565-nm non-ablative fractional laser improves appearance, pigmentation, volume, and texture of SD and is only associated with mild oedema, erythema and pain as side-effects in some patients. Studies on 1550-nm non-ablative fractional laser found this modality to be effective and safe for striae albae and rubrae. Also, significant textural and pigment corrections were observed for this modality. Likewise, oedema, mild-to-moderate erythema, pain, itching, mild crusting, PIH and mild-to-moderate acne were reported in some studies as the side-effects of 1550-nm non-ablative fractional laser. In a randomized clinical trial, erbium-doped non-ablative fractional laser caused a significant improvement in the Dermatology Life Quality Index (DLQI) with an acceptable safety profile and just a few cases of pruritus, scaling and erythema. Both fractional and non-fractional RF were effective and safe for striae albae and rubrae. They were associated with transient and minimal side-effects, such as temporary rashes, ecchymosis, blister, pain, erythema, oedema and PIH, depending on the RF modality used. Tripollar RF seems to be the safest modality, especially in the dark-skin phenotype. In the other light and laser therapies sub-category, long-pulsed 1064-nm Nd:YAG showed an acceptable improvement in striae. PDL laser seems to have moderate-to-good effectiveness in striae rubrae, but is not beneficial for striae albae. IPL and low-level laser therapy showed an acceptable effect on SD, although their histopathological improvement was higher than their clinical improvement. Diode 1450-nm laser was not an effective modality. Excimer 308-nm laser had acceptable positive effects on scar pigmentation. Side-effects were minimal and transient for these therapies.

Carboxytherapy seems to be an effective method of reducing stretch marks with moderate pain and discomfort and hematoma in some patients. The pressure- and dose-controlled transcutaneous pneumatic injection of hypertonic glucose solution as mesotherapy was effective and safe for treating atrophic skin disorders, such as SD, with little side-effects. Microneedling was also safe and effective and had minimal side-effects. Golden chemical peel showed clinically and microscopically significant improvements in SD. Glycolic acid 70% was associated with little improvement in patients. Abrasions, including dermabrasion or microdermabrasion, are effective in the treatment of striae rubrae in general. Nonetheless, microdermabrasion is not effective for striae albae. Naturally, dermabrasion has greater side-effects. Galvano-puncture and electroporation demonstrated a significant improvement in striae albae without any side-effects.

Therapeutic comparisons

Tables S2 and S3 compare the efficacy and safety of two or three SD treatment modalities with each other qualitatively. Tables S4 and S5 present an analytical comparison of applying the treatment modalities between two or three groups using mean scores and a 95% CI, and show the improvement rate (usually assessed by the Dermatologist Assessed Improvement Scale (DIS), Global Aesthetic Improvement Scale (GAIS) or Visual Analogue Scale (VAS)) and reduction in SD surface area (usually assessed by DIS or GAIS). Table S6 summarizes comparative studies on similar outcome measures (reporting the mean percentage of improvement) to enable better clinical judgements. Compared to fractional CO_2 laser, some types of non-ablative fractional lasers, needling, dermabrasion and tretinoin apparently had the most optimal responses in proper settings.[23,37,38] Lasers: fractional ablative lasers, mainly CO2: the most prevalent and seemingly effective and overall safe (with minor side-effects) modality for the treatment of SD (both types), comparable to needling. Non-ablative fractional lasers: favourable results in comparison with fractional CO2 laser. PDL and IPL are effective and safe for SD and rubrae, with advantages for the rubrae type. PDL and short-pulse CO2 laser: not recommended for darker skin tones. Microdermabrasion, dermabrasion and microneedling: effective and safe methods for SD; the efficacy of microdermabrasion is less than the other two modalities. Radiofrequency: tripollar RF may deliver better results for striae albae. Carboxytherapy: better results for striae rubrae. PRP: efficient treatment for striae rubrae, especially on the trunk.[28] Combinations: Er:YAG laser, carboxytherapy and PRP: Effective for both types of SD, but Er:YAG laser is safer and more effective.[39] Light therapies, especially IPL and UVB therapy, are effective treatments for both striae types. Topical therapies, especially those containing tretinoin, glycolic acid, L-ascorbic acid, succinylated collagen and herbal extracts, are appropriate for SD treatment. Olive oil or Saj cream are not effective in preventing or improving striae gravidarum (Tables S2–S6).[38,40–42]

Combination therapies

Tables S7 and S8 show the efficacy and safety of two different SD treatment modalities separately and combined, and compare their results in groups, qualitatively and quantitatively. Outcome

was quantitatively defined as the patients' self-assessed scores, VAS score, decreased striae surface area (usually assessed by the DIS or GAIS), 95% CI and improvement percentage (usually assessed by the DIS or GAIS). Based on Table S9, the combination of two modalities is usually better than using each one alone, but the efficacy of different regimens depends on the types of therapies combined. For example, improvement in SD surface texture is significantly greater with ablative fraction laser plus epidermal growth factor injection than with ablative fraction laser plus topical aloe vera application. Also, needling is more effective than microdermabrasion plus sonophoresis. The combination of RF, microneedling and CO_2 fractional laser is an effective and safe option for SD that causes little, non-serious, early and transient side-effects and may be better than applying each single therapy alone. The combination of PRP and microdermabrasion is more effective than each therapy taken separately too. Table S10 explains the results of Table S9 quantitatively. Tables S11 and S12 compare the efficacy of different regimens for treating SD qualitatively and quantitatively, respectively. Table S13 presents the qualitative results of a five-arm clinical trial on SD. Table S14 summarizes studies reporting the same outcome measures (mean percentage of improvement) to enable better clinical judgement (Tables S7–S14).

Discussion

This review is a comprehensive analysis of different striae treatment approaches to find the most efficacious therapies for each striae type.[43–47] SD are one of the most common cosmetic problems and most frequent subtypes of atrophic scars with various types and clinical presentations that may affect different parts of the body.[48] There are few systematic reviews on SD treatment, and many questions remain unanswered, such as: What are the best therapeutic modalities in terms of efficacy, safety, applicability, accessibility and cost-effectiveness? Based on comparisons, which modalities work better? Regarding combination therapies, what are the best available, effective and safe options? This systematic review study tries to answer these questions.

Single therapies

Topical therapies and light/laser-based devices are the most common modalities used for SD.[17–21,49–61] In the topical therapies category, water-in-oil creams containing argan oil, bio-oil and gels are effective, especially in the early phase of SD.[49,51] Tretinoin 0.025 is not effective, but tretinoin 0.1% is an effective clinical treatment in the active and early stages of stretch-mark development, especially pregnancy-related stretch marks.[18,50] Topical medications containing herbal extracts are also effective overall. Meanwhile, cocoa butter, olive oil and bitter almond oil are not effective.[21,55] Ablative CO_2 laser is the most frequently used laser therapy, yielding satisfactory results, and fractional non-ablative lasers like 1550-nm, 1565-nm and erbium-doped lasers also have positive results.[2,3,11,62] Both fractional and non-fractional RF are effective and safe for SD treatment.[12,63–65] Long-pulsed 1064-nm Nd:YAG and IPL show acceptable improvements in SD patients.[61,66] PDL laser therapy shows satisfactory results only for striae rubrae, and excimer 308-nm laser is effective for lightening scar pigmentation.[67,68] Meanwhile, diode 1450-nm laser is not an effective modality.[69]

Therapeutic comparisons

Although there are many comparative studies with similar outcome measures, the results obtained for similar treatment modalities varied widely between the studies, which may be attributed to the different types of SD examined, study designs and tools used for outcome assessment. Fractional CO_2 laser as a type of non-ablative fractional laser therapy, microneedling, dermabrasion and tretinoin seem to have the most optimal responses when used in proper settings.

Among the different topical modalities examined, tretinoin showed the best therapeutic response[27,70] and is thus the best topical therapy for SD, although it frequently causes irritative side-effects.[27] Neither olive oil nor Saj cream was effective in preventing the occurrence of striae gravidarum or affecting its severity.[71]

Among the procedural methods examined, ablative fractional lasers (mainly CO_2) were the most commonly applied treatments with favourable results and a good safety profile (side-effects were minimal and transient). Non-ablative fractional lasers, needling (microneedling or RF-needling), dermabrasion, carboxytherapy and PRP are other effective and safe therapies with acceptable results. Modalities such as microdermabrasion, IPL, topical therapies (glycolic acid, L-ascorbic acid, succinylated atelocollagen, and herbal extracts), phototherapy (UVB therapy, and excimer laser) and galvano-puncture have an acceptable efficacy and safety as well, and while some of them are popular but less effective, others are highly effective but not popular.

Combination therapies

The combination of two or more modalities is seemingly often better than applying each one alone, but the efficacy of different combination regimens depends on the type of therapies combined, and some powerful single therapies are even better than combined therapies consisting of different modalities with lower efficacies.

The combination of RF and autologous PRP might have synergistic benefits and fewer side-effects. Also, the combination of 2940-nm Er:YAG laser with other modalities, such as bovine basic fibroblast growth factor (rb-bFGF), light-emitting diode-red light (LED-RL) and a spatially modulated ablative (SMA) module, is a safe and effective treatment for SD. A regimen combining ablative fractional laser and PRP-induced rapid healing after ablative resurfacing is effective too. Some articles have reported promising effects for combining microneedling with other modalities. Some of these combinations have improved SD by 70%–90%.[72–76] In a five-arm clinical trial on the efficacy

and safety of SD treatments, ablative fractional laser was an effective option and the succinylated collagen site also showed clinical improvements with an acceptable safety profile.[77] Ablative RF with topical retinoic acid cream and low-frequency acoustic pressure ultrasound has an improved therapeutic efficacy of about 75%, and this regimen could lead to optimal outcomes. The combination of fractionated microneedle RF with fractional CO_2 laser could also improve the final outcome by about 25% and create a 75% response rate.[30,36,77,78] Needling also leads to better outcomes compared to some combination therapies that do not use needling systems.

Conclusion

Despite the lack of a gold standard treatment for SD, this comprehensive systematic review on the most prevalent, recent and promising therapeutic options for SD classified the results in three categories. In the single therapy category, laser and other light-based devices (e.g., IPL and RF) and topical treatments were the most commonly applied interventions. In the therapeutic comparison category, most therapeutic modalities were almost equally effective and there was no significant difference in their side-effects and durations of treatment, and the most popular were ablative and non-ablative fractional lasers, topical therapy, needling and dermabrasion. In the combination therapy category, the combination of two or more modalities was usually better than applying each one alone, but the efficacy of different combination regimens depends on the type of therapies combined, although some powerful single therapies proved even better than combinations of therapies with lower separate efficacies. Combinations of regimens such as RF, ablative fractional lasers (such as CO_2 and erbium Yag), platelet-rich plasma (PRP), needling and topical tretinoin are the most effective and popular therapies used for SD. Larger prospective studies, especially randomized clinical trials with equal or comparable outcome measures, are recommended for more accurate judgements of the effectiveness of different therapies for SD.

Limitations

The data in this systematic review did not meet the criteria for a meta-analysis, mainly due to the different designs of the reviewed studies, the various types of striae examined and the diverse outcome measures applied. Also, there were few placebo-controlled RCTs to be included in this systematic review.

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Author contributions

A. G., F. S. and S. S. wrote the initial draft, B. H. and H. B. methodologically appraised the study, and P. P and S. M. edited the document. All the authors made extensive contributions to the final draft of this manuscript.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. The classification of single-treatment modalities for striae.
Table S2. A comparison of therapeutic efficacy and safety between two groups of patients with striae (intervention and control groups).
Table S3. A comparison of therapeutic efficacy and safety between three groups of patients with striae receiving different treatment modalities.
Table S4. An analytical comparison of therapeutic efficacy between two groups of patients with striae (intervention and control groups).
Table S5. An analytical comparison of therapeutic efficacy between three groups of patients with striae receiving different treatment modalities.
Table S6. Studies comparing different therapeutic methods based on similar outcome measures
Table S7. The efficacy and safety of two different treatment modalities for striae (separately and in combination).
Table S8. The quantitative comparison of the efficacy of two different treatment modalities for striae (separately and in combination) based on different outcome measures.
Table S9. A comparison of the efficacy and safety of two treatment modalities (with at least one arm being combination therapy) for striae.
Table S10. A quantitative comparison of the efficacy of two treatment modalities (with at least one arm being combination therapy) for striae based on different outcome measures.
Table S11. The efficacy and safety of different combination modalities for the treatment of striae.
Table S12. The quantitative efficacy of different combination modalities for the treatment of striae.
Table S13. The efficacy and safety of a five-arm clinical trial for the treatment of striae (No quantitative reports).
Table S14. The evaluation of the efficacy of combination therapies in studies with the same outcome measures