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Ablative vs Nonablative Laser Skin Resurfacing

Outcomes and Adverse Effects of Ablative versus Nonablative Lasers for Skin Resurfacing: A Systematic Review of 1093 Patients

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Manuscript Word Count: 3738 **Figure(s): 0** **Table(s): 4**

Abstract Word Count: 250 **Supplement(s):** ***Fig 1 Tab 2***

The authors have no conflicts of interest to report.

Author Contributions: Mirza, Mirza had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Mirza, Mirza, Khatri. *Acquisition, analysis, or interpretation of data:* Mirza, Mirza. *Drafting of manuscript:* Mirza, Mirza. *Critical revision of manuscript for important intellectual content:* Khatri. *Statistical Analysis:* N/A. *Obtained Funding:* N/A. *Administrative, technical, or material support:* Mirza, Mirza, Khatri. *Study supervision:* Khatri.

Funding/Support: This systematic review was conducted without financial support.

Role of the Sponsors:

	Funding/Sponsor was Involved?
Design and conduct of study	No
Collection, management, analysis, and interpretation of data	No
Preparation, review, or approval of the manuscript	No
Decision to submit the manuscript for publication	No

Financial Disclosure : None reported.

All Financial Interests (including pharmaceutical and device products): None reported.

Acknowledgement: N/A.

Data Availability Statement: Data are available in article supplementary material. The data that supports the findings of this study are available in the supplementary document included in this submission.

Abstract

Background. It is generally believed that ablative laser therapies result in prolonged healing and greater adverse events when compared to nonablative lasers for skin resurfacing.

Objective. To evaluate the efficacy of ablative laser use for skin resurfacing and adverse events as a consequence of treatment in comparison to other modalities.

Methods & Materials A PRISMA-compliant systematic review (Systematic Review Registration Number: 204016) of twelve electronic databases was conducted for the terms 'ablative laser' and 'skin resurfacing' from March 2002 until July 2020. Studies included meta-analyses, randomized control trials, cohort studies, and case reports to facilitate evaluation of the data. All articles were evaluated for bias.

Results. The search strategy produced 34 studies. Of 1093 patients included in the studies of interest, adverse events resulting were reported in a total of 106 patients (9.7%). Higher rates

of adverse events were described in nonablative therapies (12.2±2.19%, 31 events) when compared to ablative therapy (8.28±2.46%, 81 events). 147 patients (13.4%) reported no side effects, 68 (6.22%) reported expected, transient self-resolving events, and five (0.046%) presented with hypertrophic scarring. Excluding transient events, ablative lasers had fewer complications overall when compared to nonablative lasers (2.56±2.19% vs 7.48±3.29%).

Conclusions. This systematic review suggests ablative laser use for skin resurfacing is a safe and effective modality to treat everything from photo-damage and acne scars, to hidradenitis suppurativa and posttraumatic scarring from basal cell carcinoma excision. Further studies are needed, but these results suggest that ablative lasers are a superior, safe and effective modality to treat damaged skin.

Key Words: laser, phototherapy, acne, photosensitivity, therapy-topical, skin, resurfacing, photo-rejuvenation, fractional, ablative, adverse, events, side, effects, efficacy, CO2, erbium, versus, nonablative, resurfacing, erythema, pigmentation, photo-damage, scarring, scars, scar, revision, photodamage, burn, trauma, hypopigmentation, hand, safe, effective, systematic review

Abbreviations:

AFR, Ablative fractional resurfacing; AMF, Ablative Microfractionated; Comb, Combination; Er, Erbium; Er:YSGG , Erbium: Erbium-doped yttrium, scandium, gallium and garnet; Er:YAG, erbium-doped yttrium aluminium garnet; IPL, Intense Pulsed Light; MNRF, Microneedling with Radiofrequency; NAFR, Nonablative Fractional Resurfacing; Nd:YAG, neodymium-doped yttrium aluminum garnet; NSFU, Nonsequential fractional ultrapulsed; P-DOE, neodymium-doped yttrium aluminium garnet P-DOE; PIH, Post-

inflammatory hyperpigmentation; RFUP, Radiofrequency excited Ultrapulsed ; SE, Standard Error

Introduction

Laser skin resurfacing is an effective noninvasive tool for the removal of scars, pigmentation, and wrinkles in the skin. The use of lasers has a wide variety of applications clinically from reducing the visibility of traumatic postoperative scarring to closing of ulcerated wounds and infections and acne scarring. Lasers can be ablative or nonablative, each with its own set of advantages and best uses.[1]

Compared to nonablative lasers, ablative lasers have a prolonged recovery time and have been largely thought to have a significant complication risk. An intermediate method known as fractional resurfacing utilizes ablative technology, ablating microscopic portions of the skin resulting in a shorter recovery time. The least invasive of the laser modalities, nonablative lasers, cause dermal injury while preserving the epidermis resulting in the shortest recovery time.[2]

While generally more invasive, ablative procedures are thought to yield superior results in comparison to nonablative lasers.[3] However, the decision for clinicians to use a particular modality relies on a discussion of indication, effectiveness and potential adverse events.

The efficacy of ablative versus nonablative lasers has been discussed extensively in the literature, however, there has not been a direct comparison between the use of ablative lasers versus nonablative lasers for skin resurfacing. Therefore, our aim was to conduct a systematic review evaluating the efficacy of ablative lasers for skin resurfacing alongside adverse events that may help to shape clinical practice for the benefit of the patient.

Methods

Protocol registration was conducted via the PROSPERO International prospective register of systematic reviews, adhering to PRISMA guidelines with additional resources included in the supplement (Systematic Review Registration Number: 204016).

Search Strategy & Study Selection

The authors conducted a search of twelve databases for published studies with the terms 'ablative laser' and 'skin resurfacing' from March 2002 until July 2020. The search strategy for PubMed included ((ablative versus nonablative*) AND (skin resurfacing) [all]). Language restriction was not applied with translations included and assessed according to inclusion and exclusion criteria, further explained in Supplemental Table 1. Two review authors (H.N.M, F.N.M.) independently screened and retrieved studies from the search. All study models were eligible in the search including meta-analyses, randomized controlled trials, cohort studies, and case series and reports. Utilizing the Oxford Center for Evidence-Based Medicine Levels of Evidence, we looked for and assigned appropriate values to meta-analyses, randomized control trials, cohort studies, and case series and reports to facilitate evaluation of the data.

Quality Assessment

Risk of bias was assessed by two review authors (H.N.M, F.N.M.) utilizing the Cochrane Methods Bias Group's Risk of Bias in Non-Randomized Studies – of Interventions

(ROBINS-I) Tool. Upon comparison, disagreements on quality ratings were resolved by a third author (K.K.). The tool allowed the authors to assess whether the risk of bias is low, moderate, serious, or critical. Declaration of a particular level of risk of bias for an individual domain means that the study as a whole has a risk of bias at least this severe, reflected in the determination of the overall risk of bias, as presented in Supplemental Table 2.

Data Synthesis

Two researchers (H.N.M., F.N.M.) extracted data. The outcomes related to the review question considered the efficacy (e.g. physical and psychosocial improvement) or adverse events (e.g. pigmentation, scarring, infection, etc) associated with the use of ablative lasers, and if a control group was provided, the comparison of these outcomes between groups.

Results

Study selections are detailed in Figure 1 with exclusion criteria presented in Supplemental Table 1. After eliminating duplicates and following exclusion criteria, 31 studies met the inclusion criteria.

Of the selected 34 studies, seven studies were case reports, four were retrospective analyses, fourteen were prospective clinical trials, and six were randomized controlled trials, and three

were split face clinical trials. All together, this systematic review includes an aggregate of 1093 patients. Majority of adverse events resulting from therapy were transient, regardless of treatment modality. Ablative lasers had fewer complications overall when compared to nonablative lasers (2.56% vs 7.48%). Results of are displayed in Tables 1-4.

Randomized controlled trials

Three studies considered the difference between ablative lasers and Nd:YAG nonablative laser treatments. Robati et al[4] studied the use of Er:YAG lasers compared to Nd:YAG lasers for the treatment of hand wrinkles in 33 patients. No significant difference was found between the two modalities in terms of efficacy ($p<0.05$), and patient satisfaction ($p<0.05$). Mild discomfort was noted after Nd:YAG treatment, though no other side effects of treatment were noted. Both treatments resulted in a major improvement from baseline ($31.02\% \pm 5.01\%$, $p<0.001$). Azim et al[5] studied the use of a fractional CO2 ablative laser in combination with a long pulsed Nd:YAG laser in comparison to only a Nd:YAG laser in 20 patients with hidradenitis suppurativa. No patient reported adverse events with the exception of spontaneously resolving erythema. Statistically significant improvement was noted in with the combination treatment compared to Nd:YAG alone ($p=0.011$). Vachiramon et al[6] performed CO2 laser therapy and Q switched Nd:YAG therapy on 25 patients with two solar lentigines. 7 receiving the CO2 therapy and 6 receiving the Nd:YAG laser developed post inflammatory hyperpigmentation, while two individuals developed

hypopigmentation from both lasers. Faster healing was noted with CO2 therapy, though Nd:YAG lesions showed statistically significant lightening compared to CO2 lesions ($p<0.001$).

Three studies considered the difference between ablative lasers versus a nonablative lasers/control for skin resurfacing in the treatment of acne scarring, photoaging, or perioral rhytides. Fourteen patients reported adverse events.

Hedelund et al[7] enrolled thirteen patients for laser resurfacing for acne scars in two intraindividual areas with one receiving three monthly CO2 fractional laser treatments and the other receiving no treatment. Prior to treatment, there was no statistical difference in the degree of acne scars, uneven texture, nor atrophy. One month, three months, and six months after treatment scar texture and atrophy both significantly improved ($p<0.0001$). No major adverse events were reported. Transient events included mild erythema and superficial wounds resolving 2-3 days postoperatively.

Moon et al[8] enrolled 44 patients with photoaged skin with 19 receiving ablative fractional Er:YAG resurfacing and 15 receiving nonablative fractional 1550nm Er:glass laser resurfacing. Both cohorts received three sessions at four-week intervals. The ablative arm had significant improvement in pigmentation, uneven tone, and erythema while the

nonablative arm showed greater overall improvement in wrinkle score reduction. Two ablative (10.5%) and nine nonablative patients (60%) experienced adverse events. The Er:YAG cohort had fewer adverse events than the Er:glass cohort, though all adverse events were reversible and consisted primarily of erythema, which is specified as not a true adverse event but rather an expected result of ablative therapy.

Hedelund et al[3] enrolled 27 female patients with perioral rhytides receiving 3 monthly treatments of CO2 or IPL laser resurfacing evaluated at baseline and up to 12 months postoperatively. Compared to IPL, ablative CO2 laser treatment resulted in higher degrees of patient satisfaction and clinical rhytide reduction ($p<0.05$) though both groups had improved skin elasticity. Only ablative patients (n=3, 25%) experienced transient adverse events. No long-term adverse events were noted, though a higher incidence of trans epidermal water loss and skin redness was noted in the ablative arm one month postoperatively.

Prospective split face trials

Three studies used a split-face model. Seven patients reported adverse events across two studies. Li et al[9] and Jung et al[10] studied 20 and 13 patients for photodamaged skin and facial scarring respectively using a CO2 ablative laser on half of the face. Li et al[9] used no treatment on the other half of the face, while Jung et al[10] used a nonablative nd Er.YAG

laser. Li et al[9] found significant improvement in both patient satisfaction and blinded investigator global improvement. Jung et al[10] found roughly ¼ of patients reported better outcomes from ablative treatment, with almost ½ reporting more pain and the other half equal pain from both treatments. Both noted no significant side effects. Jung et al[10] reported the majority of adverse events on both sides with the exception of some pinpoint bruising in one patient on the ablative half.

Kwon et al[11] studied 25 patients receiving a randomly assigned P-DOE ablative laser to half the face and nonablative fractional laser to the other half for acne scarring. Adverse events were only reported in the NAFL group (n=4, 16%) consisting of hyperpigmentation. The P-DOE half was reported to have achieved a significantly better improvement in acne appearance with less severe pain, with lower side effects ($p<0.05$).

Prospective clinical trials

Fourteen studies were prospective clinical trials evaluating the efficacy of ablative lasers for skin resurfacing, of which four studied acne scarring, five studied photodamage, four studied facial resurfacing, and one studied traumatic scars. Adverse events were reported in 51 patients across eight studies.

Kimura et al[12], Lee et al[13], Hwang et al[14], and Walgrave et al[15] conducted single arm prospective clinical trials in 5, 22, 24, and 30 patients respectively using ablative laser skin resurfacing for acne scarring. Their respective adverse events were reported as 0%, 22.7%, 0%, and 10% of patients (See Table 1). The first two utilized Er:YSGG and Er:YAG lasers respectively, with the later two studying fractional CO2 lasers. All cohorts found improvement ranging from over three fold mean improvement noted by Lee et al[13] to a 30% increase in skin elasticity after 4 weeks by Kimura et al[12]. No serious complications were reported, with the most common report of transient erythema or serosanginous oozing. Lee et al[13] included the most descriptive adverse events including post inflammatory hyperpigmentation, acne flare up, and time to complete wound healing, averaging 6-9 days.

Chan et al[16], Marini et al[17], Boonchai et al[18], and Trelles et al[19] studied the use of ablative lasers for facial resurfacing enrolling 9, 10, 60, and 102 patients respectively. Adverse events were reported at a rate of 11.1%, 20%, 66.7%(AFR)/30% (NAFL), and 7.8% of patients respectively (See Table 1). Chan et al[16] used a CO2 fractional ablative laser and found statistical improvement in skin texture, wrinkles, laxity, and acne scars though noted postinflammatory hyperpigmentation in over half of subjects, dropping to a single patient by 6 months. Boonchai et al[18] found studied the adverse events post ablative therapy, finding higher sensitization to sunscreen in ablative patients. Marini et al[17] used a combination of two passess with a Nd:YAG nonablative laser followed by two passess with a Er:YAG

ablative laser noting prolonged improvement in facial telangiectasias, lentigines, pigmentation, lines, and skin texture. No significant adverse effects were noted with most commonly crusting lasting 6-8 days and at worse, 20 days of self-resolving localized hyperpigmentation. Trelles et al[19] similarly applied Er:YAG ablative laser resurfacing followed by Nd:YAG nonablative therapy with all patients seeing an improvement, 67 of which reported very good results with minor transient milia and hyperpigmentation in four patients.

Stebbins and Hanke[20], Kaplan and Kaplan[21], Clementoni et al[22], Waibel et al[23], and Clementoni et al[24] enrolled 10, 14, 24, 34, and 55 into prospective clinical trials on ablative laser skin resurfacing for photodamage respectively. Adverse events were reported at 10%, 0%, 0%, 5.9%, and 0% of patient respectively. Stebbins and Hanke[20] studied the use of ablative fractional CO2 lasers on the hand applying three treatments to one hand in 4-6 week intervals. After 1 month, the researchers found over 50% improvement in pigment, and over 26% improvement in wrinkles and texture with only transient erythema and edema, which are expected with ablative therapy. One patient however did have significant edema after the first treatment, though no long-term alteration was noted. Kaplan and Kaplan[21] applied 8 nonablative treatments followed by 4 ablative treatments noting over 43% of patients experiencing over a 50% improvement, 18% 25-50%, and 39% mild with no reported adverse events. Clementoni et al[22] applied 1 multimodal fractional ablative CO2 laser

treatment evaluating patients with 3D imagining, noting an average of 42% improvement of wrinkles and 40.1% improvement in melanin variation with no reported adverse events. Similarly, Clementoni et al[24] performed a single session full face ablative CO2 laser treatment with imaging and found significant differences between baseline and 1 and 3 months post-treatment in all areas except telangiectasias, with improvement of wrinkles occurring only after a double-pass. Adverse side effects were minimal with low downtime. Waibel et al[23] treated patients with two treatments spaced 4-6 weeks apart with a hybrid approach using a nonablative and ablative laser noting 80% of patients having significant improvement on photographic analysis and pain averaging 4/10. Notably satisfaction was 100%, with the only adverse effects being two patients with post inflammatory hyperpigmentation resolving within 90 days.

Kim et al[25] performed a prospective clinical trial on 12 patients receiving four Er:YAG ablative laser skin resurfacing treatments at one month intervals for facial lacerations repaired by sutures. Adverse events were reported in 0% of patients. Improvement was noted in all patients, confirmed by the patients themselves as well as 10 blinded and 10 non-blinded physicians with an average improvement of 7.0/10 by the blinded physicians. Adverse events were recorded and none were reported post-treatment.

Retrospective clinical trials

Four of the selected studies were retrospective analyses of ablative lasers for skin resurfacing. Lederhandler et al[26], Naouri et al[27], Alajlan and Alsuwaidan[28], and Clementoni et al[29] studied 10, 46, 82, and 312 patients respectively. Adverse events were reported in 0%, 21.7%, 0%, and 2.2% of patients respectively (See Table 1). Lederhandler et al[26] analyzed outcomes of 10 pediatric patients undergoing fractional ablative CO2 laser resurfacing treatment for traumatic facial scarring, with 6 receiving additional nonablative laser treatment. Patients had gradual improvement of scar appearance and texture after fractional ablative laser resurfacing. All resurfacing was well tolerated with short-term erythema in 6 patients and hyperpigmentation in one treated with alternative devices. Naouri et al[27] conducted facial skin resurfacing with a fractional ablative CO2 laser and found the average length of erythema was 5.2 days and average pain was 3.3 and 4.1/10 for premedicated and nonpremedicated patients. Adverse events were recorded including 10.6% of patients having facial herpes despite antiviral prophylaxis, 8.7% with inflammatory reactions and 2.2% with acne, all resolving quickly. Alajlan and Alsuwaidan[28] analyzed patients receiving nonablative or ablative fractional laser therapy for acne scarring and found overall satisfaction as higher in the nonablative cohort (71% vs 65%) with less downtime in the nonablative cohort. However, transient postinflammatory hyperpigmentation was higher in the nonablative cohort compared to the ablative cohort. Clementoni et al[29] evaluated the use of an ultrapulsed CO2 laser with computer imaging finding 76.74% of patients having an improvement of 75% or more. Adverse events were limited with mean pain during

treatment reported as 4.1/10, with burning felt for no more than 15-25 minutes post treatment. 21 patients of 301 had mild swelling post treatment and mean healing time was 3.9 ± 1.1 days.

Case Reports

Six of the included studies were case reports. Adverse events were reported in 6 patients from 2 case reports. Basnett et al[30]reported the use of ablative fractional laser resurfacing for a 16-year-old female with several nonhealing cuteaneous leishmaniasis on the bilateral and upper extremities. After two treatments, the patient's wound healed completely without evidence of infection and with minimal scarring.

Tierney and Hanke[31] reported the use of a series of three treatments at eight week intervals using an ablative fractionated CO2 laser for head and neck hypopigmentation wherein a 75% improvement was achieved with no adverse effects.

Krakowski et al[32] reported the use of ablative fractional CO2 laser resurfacing for nonhealing wounds in two pediatric patients, whereby a single treatment in one patient, and two treatments one month apart in a second patient, resulted in complete wound healing in the shin and forearm respectively with no complications.

Zaouak et al[33] reported two treatments with a fractionated resurfacing laser at one month intervals used for the treatment of a perioral burn scar in a 48-year-old woman. Treatment resulted in HSV reactivation five days after her second therapy, which was treated with IV acyclovir for 10 days resulting in the clearing of her vesicular eruption.

Krakowski and Ghasri[34] reported the use of an ablative fractional CO2 laser for the treatment of a recessive dystrophic epidermolysis bullosa on the left upper back of a 22-year-old male. Treatment resulted in a 92% decrease in wound surface area with mild discomfort and near complete re-epithelization after two treatments, improved well being, and relief from chronic pain with no adverse effects.

Brightman et al[35] used an ablative fractional CO2 laser in an 82-year-old male with recurrent basal cell carcinoma receiving a paramedian forehead flap from plastic surgery. After 1 month, the patient had improved alar rims, nasal sidewall contour, and diminished surgical scars. No severe adverse effects were reported, with mild oozing occurring post therapy, even after clinical follow-up two years post-treatment.

Avram et al[36] presented follow-up on five patients who developed scarring after receiving fractional CO2 laser resurfacing for the treatment of photodamage to the neck. These

patients developed hypertrophic scarring which was largely reversible through attentive care with nonablative fractional laser therapy.

Discussion

Summary

Thirty-one studies considering the study of ablative laser efficacy were identified consisting of evaluation of 1093 patients, the largest systematic review of ablative laser effectiveness and adverse effects. Of these, ablative lasers were used in 519 patients for photoaging and photodamage, 240 patients for facial resurfacing, 201 patients for acne scarring, 33 for hand wrinkles, 27 patients for perioral rhytides, 25 for solar lentigines, 24 patients for traumatic scars, 20 for hidradenitis suppurativa, and single patients for leischmaniasis, perioral burns, forehead flaps, and recessive dystrophic epidermolysis bullosa respectively.

All thirty-four studies reported improvement after treatment with ablative laser resurfacing. While the range of improvement varied from study to study, only six studies consisted of randomized controlled trials, including one split face trial, comparing the efficacy of ablative to nonablative laser therapy. All found superior clinical results with ablative therapy with the exception of Vachiramon et al who found less improvement with fewer reported adverse events.[6] Moon et al[5] found greater improvement in all parameters except wrinkles, alongside

fewer side effects in the ablative arm compared to the nonablative arm ($p<0.05$). Hedelund et al[3] also found greater improvement with ablative laser treatment ($p<0.05$) but noted higher levels of skin redness. Jung et al[10] found 53.8% of patients reporting better outcomes from ablative resurfacing, though noted higher levels of pain with similar adverse events in both cohorts. Kwon et al[11] found ablative modalities to have superior improvement, less pain, and lower side effects ($p<0.05$). Robati et al found no significant difference between ablative therapy and nonablative therapy, while Azim et al found statistically significant improvement in combined therapy versus nonablative therapy.[4,5]

All studies demonstrated ablative laser resurfacing to be an effective means of treating patients for a variety of ailments. Many studies, including Kaplan and Kaplan[21], Waibel et al[23], and Trelles et al[19] amongst others found significant improvement utilizing a mixture of ablative and nonablative hybrid therapies.

Adverse Events

Excluding transient events, ablative lasers had fewer complications overall when compared to nonablative lasers (2.56±2.19% vs 7.48±3.29%). Specific adverse events resulting from laser skin resurfacing were reported in a total of 106 patients (9.70%). Of these, 81 adverse events were described in ablative therapy (8.28±2.46%), and 31 were described in nonablative therapy (12.2±4.80%). Majority of adverse events resulting from therapy were

transient, regardless of treatment modality. Of the 1015 patients, no patient presented with severe adverse events as a result of ablative laser skin resurfacing. Many of these studies reported no adverse events while a majority reported transient self-resolving hyperpigmentation, erythema, and milia (See Table 2).

Two studies with the lowest quality of evidence reported the most significant adverse events as a result of ablative laser skin resurfacing. Zaouak et al[33] presented a case report of an elderly female with reactivation of HSV after her second laser treatment while Avram et al[36] presented a case series of five patients known to have had hypertrophic scarring seeking additional treatment. Due to the low quality of evidence it is difficult to discern whether additional factors predisposed these patients to these phenomenon. However, both authors noted that these events, with proper medical attention were minor and had no long-term effects.

Quality Assessment

Recommendation on the use of ablative lasers in comparison to nonablative modalities for skin resurfacing is limited by the number of comparative randomized controlled trials. This systematic review contains nine level 2, fourteen level 3, four level 4, and seven level 5 reports.

As this review draws the majority of evidence from studies level 3 and higher, this analysis considers a greater body of evidence than that used to formulate current guidelines.

Limitations of all studies included in this review exist and range from selection and confounding in pre-intervention, to post intervention reports of adverse events and missing data resulting in bias. Seven studies were critically biased due to the inherent limitations of case reports while the remainder of studies were moderately biased. Critically biased studies were the only to report severe reactivation of HSV, as well as hypertrophic scarring resulting from treatment, whereas moderately biased studies largely reported transient adverse events, if any.

From a study level, limitations include a limited spectrum of inclusion criteria, limited number of comparative studies, and incomplete retrieval of all studies related to the efficacy of ablative laser use for skin resurfacing. No language restrictions as well as searching through twelve databases help to counteract these forms of bias.

Recommendation

Majority of studies determined that ablative laser use for skin resurfacing is a safe and effective modality for the treatment of a variety of ailments, whether for promoting healing post surgical or nonsurgical wound to acne scar revision.

The results of this systematic review are promising for patients considering ablative laser therapy for skin resurfacing. We conclude that though there may be a risk associated with ablative lasers, the body of evidence indicates that this risk is relatively small or absent and confined to rare cases and patients with other contraindications for treatment. Further comparative studies should be conducted to provide additional evidence guiding clinical practice and outcomes.

Conclusion

The data presented demonstrated the efficacy of ablative lasers for skin resurfacing in various patients from those suffering traumatic scarring to those with nonhealing-ulcerated wounds. This systematic review suggests ablative modalities for skin resurfacing in these patients results in superior clinical results with fewer adverse events when compared to nonablative laser therapy, while also demonstrating safety and long-term efficacy of such interventions. Further high-quality randomized controlled trials with direct comparisons between ablative and nonablative lasers must be performed before advising against ablative therapy solely based upon modality.

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Table 1. Analysis of Studies with Major Adverse Effects.

Author(s)	Study Type	Treatment	N	Laser Cohort 1	Laser Cohort 2	# Adverse Events	% Adverse Events	Adverse Events
Moon et al 2015	RCT	Photoaging	44	AFR Er:YAG laser	NAFR 1550-nm Er:glass laser	2/19 [AFR], 9/15 [NAFR]	10.5% [AFR], 60.0% [NAFR]	In the AFR group, one patient had PIH, and one patient experienced prolonged erythema. In the NAFR group, five patients had an acneiform eruption with irritation and four patients presented with prolonged erythema or aggravation of reddish skin after the laser treatment. All events were reversible.
Hedelund et al 2006	RCT	Perioral rhytides	27	CO2 laser	IPL	3/12 [CO2], 0/15 [IPL]	25% [CO2],0 % [IPL]	Erythema, dyspigmentation, and milia in AFR, with no side effects observed after IPL rejuvenation.
Hedelund et al 2012	RCT	Acne scars	13	AFR CO2 laser	No Treatment	0/13, 0/13	0%, 0%	None reported.
Robati et al 2017	RCT	Hand wrinkles	33	Er:YAG 2940-nm laser	long pulse Nd:YAG 1064-nm laser	0/33 [Er:YAG], 0/33 [Nd:YAG]	0% [Er:YAG], 0% [Nd:YAG]	Some pain from Nd:YAG, no other side effects
Azim et al 2018	RCT	Hidradenitis suppurativa	20	AFR CO2 Laser and long pulsed Nd : YAG laser	long pulsed Nd : YAG laser	0/20 [Comb], 0/20 [Nd: YAG]	0% [Comb], 0% [Nd: YAG]	Spontaneously resolving erythema.
Vachiramon et al 2016	RCT	Solar lentigines	25	AFR CO2 laser	Q-switched Nd:YAG	7/25 [CO2], 6/25 [Nd:YAG]	28% [CO2], 24% [Nd:YAG]	PIH (6 Nd:YAG, 7 in CO2). Pain noted in all patients. 2 patients developed hypopigmentation from both lasers.
Boonchai et al 2015	CT	Facial resurfacing	60	AFR + sunscreen	NAFL + sunscreen	20/30 [AFR], 9/30 [NAFL]	66.7%, 30%	Sensitization after treatment, no other reported adverse event.

Kwon et al 2020	SFRCT	Acne scars	25	1064-nm P-DOE	NAFL	0/25 [P-DOE], 4/25 [NAFL]	0% [P-DOE], 16% [NAFL]	Lower treatment related side-effects (erythema) in the P-DOE group ($P < 0.05$). Mild hyperpigmentation noted only in the NAFL side.
Li et al 2010	SFCT	Photodamage	20	NSFU CO2 laser	No Treatment	0/20, 0/20	0%, 0%	None reported, rapid healing noted.
Jung et al 2013	SFCT	Facial Scars	13	AFR CO2	Er:YAG lasers	3/13 [AFR], 3/13 [Er:YAG]	23% [AFR], 23% [Er:YAG]	No significant side effects were noticed following the laser procedure except for post-procedural erythema, reactive acne (3 patients on both sides), and pin-point bruising (1 patient, on both sides and 2 patients, only on the fractional Er:YAG treated side)
Trelles et al 2002	PC	Facial resurfacing: Perioral and Periocular	102	Er: YAG pulse, NAFR CO2 laser shot		8/102	7.8%	Milia in three full face patients and hyperpigmentation in one periocular patient, all successfully resolved. Eight of 28 periocular patients had residual rhytides, which were still visible 2 months after the procedure though improved.
Clementoni et al 2007	PC	Photodamage	55	NSFU CO2 laser with CPG		0/55	0%	None reported, low downtime.
Waibel et al 2018	PC	Photodamage	34	Hybrid 1470nm NAFR, 2940nm AFR laser		2/34	5.9%	PIH in two patients resolving within 90 days.
Walgrave et al 2009	PC	Acne scars	30	10600nm AFR CO2 laser		3/30	10%	Serosanguinous oozing, transient erythema. 3 patients experienced PIH at 3 months follow-up. Post-operative downtime was significantly decreased compared to traditional ablative resurfacing.
Clementoni et al 2012	PC	Photodamage	24	AFR CO2 laser		0/24	0%	None reported
Hwang et al 2013	PC	Acne scars and wrinkles	24	AFR CO2 laser		0/24	0%	None reported after 3 months post treatment
Lee et al 2014	PC	Acne scars	22	Er:YAG laser		5/22	22.7%	Prolonged erythema in two patients, prolonged PIH in one patient, and one patient experienced mild hypopigmentation. Mild to moderate acne flare-up noted in five patients (22.7%).

Kaplan and Kaplan 2016	PC	Photodamage/fac skin resurfacing	14	NARF, AFR, MN RF Comb		0/14	0%	None reported
Kim et al 2012	PC	Traumatic scars	12	AFR 2,940-nm Er:YAG		0/12	0%	None reported
Marini 2009	PC	Facial resurfacing	10	Nd:YAG laser, Er:YAG laser		2/10	20%	Irregular crusting areas lasting 2 days, and localized hyperpigmentations lasting 20 days in two patients.
Stebbins and Hanke 2011	PC	Photodamage (hands)	10	AFR CO2 Laser		1/10	10%	Significant edema in one patient. Other patient side effects were limited to transient erythema and edema, with no long-term scarring or pigmentary alteration.
Chan et al 2010	PC	Facial resurfacing	9	AFR CO2 laser		1/9	11.1%	Post-inflammatory hyperpigmentation at 1 month (55.5%) and 6 months (11.1%) post-treatment.
Kimura et al 2012	PC	Acne scars	5	Er:YSGG laser		0/5	0%	None reported
Tretti Clementoni et al 2013	RC	Photodamage	312	RFUP CO2 laser w/ CPG		7/312	2.2%	Prolonged erythema lasting no more than 37 days (n=7). Infections, milia, scars or other adverse side effects were not observed.
Alajlan and Alsuwaidan 2011	RC	Acne scars	82	AFR CO2 laser	NAFR 1550nm laser	0/37 [AF CO2], 0/45 [NAF]	0% [AF CO2] , 0% [NAF]	Transient post-inflammatory hyperpigmentation (PIH) in both cohorts
Naouri et al 2011	RC	Facial skin resurfacing	46	AFR CO2 laser		10/46	21.7%	Facial herpes (n=5), inflammatory reactions including facial swelling (4), and acne (1), all resolving quickly
Lederhandler et al 2020	RC	Traumatic scars	10	AFR Laser		0/10	0%	Short-term erythema with no additional scarring, infection, or hypopigmentation
Avram et al 2009	CR	Photodamage (neck)	5	AFR CO2 laser		5/5	100%	Hypertrophic scarring
Krakowski and Ghasri 2015	CR	Traumatic scars	2	AMF CO2 laser		0/2	0%	Wounds remained epithelialized after 9 months in one patient and 4 months in the other. No complications.

Basnett et al 2015	CR	Leischmaniasis	1	AMF 10,600 nm CO2 laser		0/1	0%	Full healing with minimal scarring
Brightman et al 2011	CR	Forehead flap (paramedian)	1	AFR CO2 laser		1/1	100%	Mild oozing for 12 hours following the procedure with erythema and mild edema resolving within one week.
Krakowski et al 2016	CR	Recessive Dystrophic Epidermolysis Bullosa	1	AMF 10 600-nm CO2 laser		0/1	0%	None reported
Tierney, Hanke 2010	CR	Face hypopigmentation	1	AFR CO2 laser		0/1	0%	None reported
Zaouak et al 2019	CR	Perioral burn	1	AFR CO2 laser		1/1	100%	HSV reactivation, resolving after IV treatment

Abbreviations: AFR, Ablative fractional resurfacing; AMF, Ablative Microfractionated; Comb, Combination; CR, Case Report; CT, Clinical Trial; Er, Erbium; Er:YSGG , Erbium: Erbium-doped yttrium, scandium, gallium and garnet; Er:YAG, erbium-doped yttrium aluminium garnet; IPL, Intense Pulsed Light; MNRF, Microneedling with Radiofrequency; NAFR, Nonablative Fractional Resurfacing; Nd:YAG, neodymium-doped yttrium aluminum garnet; NSFU, Nonsequential fractional ultrapulsed; PC, Prospective Cohort; P-DOE, neodymium-doped yttrium aluminium garnet P-DOE; PIH: Post-inflammatory hyperpigmentation; RC, Retrospective Cohort; RCT, Randomized Controlled Trial; RFUP, Radiofrequency excited Ultrapulsed SFCT; Split Face Clinical Trial SFRCT: Split Face Randomized Controlled Trial

Table 2. Adverse Events Experienced in Ablative vs Nonablative Procedures

Event	Number of Patients	Percent of Patients Experiencing Event
Ablative Complication (excluding transient)	25	2.56%, SE 2.19%
Nonablative Complication (excluding transient)	19	7.48%, SE 3.29%
Ablative Complications (all)	81	8.28%, SE 2.46%
Nonablative Complication (all)	31	12.20%, SE 4.80%

Complications include all adverse events unless otherwise denoted. Number and percent of adverse events are reported.

Table 3. Reported Complications of Ablative Lasers.

Study Authors	Treatment	Reported Complications*
Stebbins and Hanke 2011	Photodamage (hands)	Edema, transient erythema
Kwon et al 2020	Acne scars	Erythema
Hedelund et al 2006	Perioral rhytides	Erythema, dyspigmentation, and milia
Robati et al 2017	Hand wrinkles	Erythema.
Azim et al 2018	Hidradentis suppurativa	Erythema, transient pain.
Vachiramon et al 2016	Solar lentignes	Hypopigmentation, post-inflammatory hyperpigmentation.
Naouri et al 2011	Facial skin resurfacing	Facial herpes, inflammatory reactions, facial swelling, acne, all resolving quickly
Zaouak et al 2019	Perioral burn	HSV reactivation, resolving after IV treatment
Avram et al 2009	Photodamage (neck)	Hypertrophic scarring
Marini 2009	Facial resurfacing	Irregular crusting, small blisters, and localized hyperpigmentations
Brightman et al 2011	Forehead flap (paramedian)	Mild oozing, erythema, and mild edema
Trelles et al 2002	Facial resurfacing: Perioral and Periocular	Milia, hyperpigmentation, and residual rhytides
Basnett et al 2015	Leischmaniasis	None reported
Clementoni et al 2007	Photodamage	None reported
Li et al 2010	Photodamage	None reported
Hedelund et al 2012	Acne scars	None reported
Kimura et al 2012	Acne scars	None reported
Kaplan and Kaplan 2016	Photodamage/facial skin resurfacing	None reported
Clementoni et al 2012	Photodamage	None reported

Kim et al 2012	Traumatic scars	None reported
Tierney, Hanke 2010	Face hypopigmentation	None reported
Krakowski et al 2016	Recessive Dystrophic Epidermolysis Bullosa	None reported
Hwang et al 2013	Acne scars and wrinkles	None reported
Krakowski and Ghasri 2015	Traumatic scars	None reported
Waibel et al 2018	Photodamage	Post-inflammatory hyperpigmentation
Moon et al 2015	Photoaging	Post-inflammatory hyperpigmentation, prolonged erythema
Jung et al 2013	Facial Scars	Post-procedural erythema, reactive acne, and pin-point bruising
Chan et al 2010	Facial resurfacing	Post-inflammatory hyperpigmentation
Tretti Clementoni et al 2013	Photodamage	Prolonged Erythema
Lee et al 2014	Acne scars	Prolonged erythema, postinflammatory hyperpigmentation, mild hypopigmentation, mild to moderate acne flare-up
Walgrave et al 2009	Acne scars	Serosanguinous oozing, transient erythema
Lederhandler et al 2020	Traumatic scars	Short-term erythema
Alajlan and Alsuwaidan 2011	Acne scars	Transient post-inflammatory hyperpigmentation
Boonchai et al 2015	Facial resurfacing	Transient sensitization post treatment

*Erythema and edema are expected outcomes of ablative laser skin resurfacing, not true complications

Table 4. Most Common Reported Complications of Ablative Lasers.

Reported Complication	Number of Studies	Study Authors
None Reported	12	Basnett et al 2015, Clementoni et al 2007, Clementoni et al 2012 , Hedelund et al 2012, Hwang et al 2013 , Kaplan and Kaplan 2016, Krakowski et al 2016, Krakowski and Ghasri 2015, Kim et al 2012, Kimura et al 2012, Li et al 2010, Robati et al 2017, Tierney and Hanke 2010
Erythema*	10	Azim et al 2018, Brightman et al 2011, Hedelund et al 2006, Jung et al 2013, Kwon et al 2020, Lederhandler et al 2020, Lee et al 2014, Moon et al 2015, Stebbins and Hanke 2011, Tretti Clementoni et al 2013, Walgrave et al 2009
Post-inflammatory hyperpigmentation	5	Alajlan and Alsuwaidan 2011, Chan et al 2010, Lee et al 2014, Moon et al 2015, Vachiramon et al 2016, Waibel et al 2018
Edema*	3	Brightman et al 2011, Naouri et al 2011, Stebbins and Hanke 2011
Acne Flare	3	Jung et al 2013, Lee et al 2014, Naouri et al 2011
Seroanginous oozing	2	Brightman et al 2011, Walgrave et al 2009
Milia	2	Hedelund et al Trelles et al 2002
Hypo/dyspigmentation	2	Hedelund et al Lee et al 2014
Hyperpigmentation	2	Marini 2009, Trelles et al 2002
HSV Reactivation	2	Naouri et al 2011, Zaouak et al 2019
Transient Sensitization	1	Boonchai et al 2015
Residual Rhytides	1	Trelles et al 2002
Pinpoint Bruising	1	Jung et al 2013
Hypertrophic Scarring	1	Avram et al 2009
Crusting/Blisters	1	Marini 2009

*Erythema and edema are expected outcomes of ablative laser skin resurfacing, not true complications