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ORIGINAL ARTICLE

Treatment of acne scars with fractional carbon dioxide laser in Asians: a retrospective study to search for predicting factors associated with efficacy

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Abstract

Ablative fractional laser treatment has been extensively used for resurfacing atrophic acne scars. However, few studies have investigated how the parameters set during laser procedures affect efficacy. In this retrospective study, we examined the relationship between efficacy and Fitzpatrick skin type, gender, age, follow-up duration, energy, and treatment sessions utilizing ablative fractional carbon dioxide (CO_2) laser in Asians with Fitzpatrick skin types III–IV. We then analyzed the relationship between outcome and adverse effects including hyperpigmentation. Three blinded dermatologists used the ECCA (Echelle d'Evaluation Clinique des Cicatrices d'Acnluation Clinique des Cicospectively review 82 of 1034 patients who presented at our institution for atrophic acne scar treatment between August 2013 and August 2019. Factors associated with efficacy, including age, gender, Fitzpatrick skin type, energy, treatment sessions, follow-up duration, and pigmentation, were analyzed. 82 patients met inclusion criteria. Patients underwent one to three CO_2 laser treatment sessions. Parameter settings for individual patients were consistent across treatments. Mean ECCA scores decreased from 102.70 ± 24.95 to 87.28 ± 24.48 ($p \leq 0.001$). The number of treatment sessions and duration of pigmentation lasting shorter than 3 months positively correlated with better outcomes. All patients had erythema, which lasted longer than 3 months in 16 patients (19.51%). Post-inflammatory hyperpigmentation (PIH) affected 60 patients (73.17%) and lasted longer than 3 months in 26 patients (31.71%). One patient experienced hypopigmentation (1.22%), while 8 experienced acne flare-up (9.76%). Post-laser scars occurred in 2 patients (2.44%). Our data suggest that in atrophic acne scar treatment in Asians using fractional CO_2 laser, 3 treatment sessions and duration of hyperpigmentation within 3 months have better outcomes regardless of energy, gender, age, Fitzpatrick skin type, follow-up duration, and disease course.

Keywords Atrophic acne scars · Fractional CO_2 laser · Hyperpigmentation

Introduction

Atrophic acne scars usually develop as a result of aberrant collagen production and degradation during wound healing after inflammatory acne and causes significant physical and psychological distress [1]. Atrophic acne scars are classified as icepick, boxcar, and rolling scars based on depth and size of the destruction area [2].

Common atrophic acne scar treatments include lasers, dermabrasion, chemical peeling, fillers, subcision, radiofrequency, microneedling, and fat injections [3]. Relative to classical ablative CO_2 lasers, ablative fractional CO_2 lasers that create discrete columns of thermal damage known as the microthermal treatment zone (MTZ) spare the tissue surrounding each column, thereby minimizing side effects with similar efficacy. Although energy, treatment sessions, disease duration, and follow-up duration may influence efficacy, few studies have examined their relationship with efficacy, and it is unclear if efficacy is associated with side effects, including pigmentation. Here, we evaluated factors that can influence fractional CO_2 laser efficacy in patients

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that present with atrophic acne scars and analyzed the relationship between adverse effects and efficacy.

Materials and methods

Patients

This retrospective study included 82 of 1034 patients who came to our laser surgery department between August 2013 and August 2019 for atrophic acne scar treatment. Inclusion criteria were acne scar patients who accepted uniform therapy utilizing CO_2 laser with the same parameters across treatment sessions. Participants gave written informed consents prior to treatment. Exclusion criteria were history of pregnancy, lactation, immunosuppression, keloid scars, skin cancer, photosensitivity, allergy to lidocaine or prilocaine, laser resurfacing procedures within the preceding 6 months, and other treatments on affected skin areas.

Laser treatment

All patients received 1–3 sessions of single-pass ablative fractional CO_2 laser (AcuPulse 40AES, Lumenis Laser Corp., Santa Clara, CA) with the parameter settings of 4050–11,830 mJ/cm^2 maintained across treatment sessions. Topical anesthetic cream comprised of 2.5% lidocaine hydrochloric acid and 2.5% prilocaine (Tongfang Pharmaceutical Group CO. Ltd., Beijing, China) was applied to the treatment area for an hour before laser therapy. After treatment, ice packs were provided to alleviate heat and pain. Patients were prescribed 0.2% nitrofural ointment for 7-day use after the procedure and advised to avoid regular sun exposure.

Assessment of responses and complications

The information associated with acne scars, including age at onset, disease duration, Fitzpatrick skin type, treatment sessions, outcomes, and follow-up, was recorded. High-resolution photos taken at baseline and at the last visit were independently evaluated by 3 blinded investigators using ECCA scoring system. Consistency between the 3 dermatologists was assessed using intraclass correlation coefficient (ICC: poor ≤ 0.50, $0.50 <$ moderate ≤ 0.75, $0.75 <$ good ≤ 0.90, and $0.90 <$ excellent). Patients were asked to score their satisfaction with improvement on a 5-point scale (-1 = worse, 0 = no change, 1 = satisfied, 2 = very satisfied, 3 = extremely satisfied). Subjective pain scores from 0 (no pain) to 10 (unbearable pain) were also obtained. Adverse events secondary to laser resurfacing, including erythema, hyperpigmentation, hypopigmentation, acne flare-up, and post-laser scar, were recorded.

Statistical Analysis

Statistical analysis was performed on SPSS version 18.0 (IBM). Data were shown as mean ± SD, median (interquartile range; IQR), and proportion (%), as appropriate. Hypothesis tests were performed by paired t test, with $p \leq 0.05$ indicating statistical significance. Spearman correlation analysis was adopted, for the dependent variables of the study did not meet the normal distribution. Multiple variable linear regression analysis was used to analyze the relationship between independent and dependent variables.

Results

The demographics of the 82 patients (36 females and 46 males, mean age 23.52 ± 3.36 years) involved in this study are summarized on Table 1. Of this, 6 were classified as having Fitzpatrick skin type III, while 76 were classified as having Fitzpatrick skin type IV. ECCA scoring by the investigators revealed a statistically significant reduction in acne scars after laser therapy (Table 1, Figs. 1 and 2). Patient satisfaction assessment revealed that 32 (39.02%)

Table 1 Patient and treatment characteristics

Patient characteristics	
Age (y), mean (SD)	23.52 (3.36)
Gender, *n* (%)	
Female	36 (43.90)
Male	46 (56.10)
Course (y), median (IQR)	4.5 (2–7.25)
Fitzpatrick skin type, *n* (%)	
III	6 (7.32)
IV	76 (92.68)
Treatment characteristics	
Energy density (mJ/cm^2), mean (SD)	7074.27 (1535.75)
Number of sessions, *n* (%)	
1	64 (78.05)
2	17 (20.73)
3	1 (1.22)
Pain, mean (SD)	6.61 (1.92)
Follow-up (y), mean (SD)	0.64 (0.40)
Patient satisfaction, *n* (%)	
Extremely satisfied	6 (7.32)
Very satisfied	44 (53.66)
Satisfied	32 (39.02)
ECCA score, mean (SD)	
Pre-treatment	102.70 (24.95)
Post-treatment	87.28 (24.48)

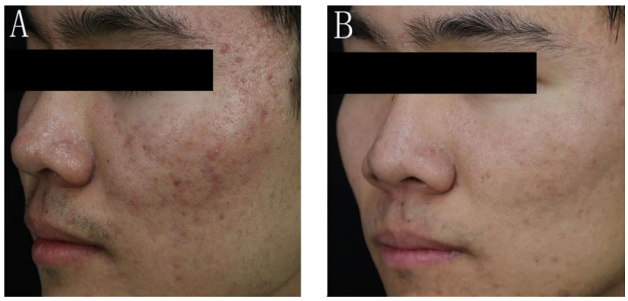

Fig. 1 Pre-treatment (**A**) and post-treatment (**B**) photographs of a 19-y-old male patient. Pre-treatment ECCA score was 113.33, and post-treatment ECCA score was 66.67

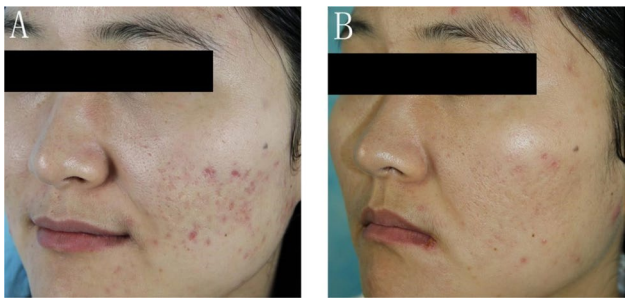

Fig. 2 Pre-treatment (**A**) and post-treatment (**B**) photographs of a 23-y-old male patient. Pre-treatment ECCA score was 116.67, and post-treatment ECCA score was 73.33

were "satisfied," 44 (53.66%) were "very satisfied," and 6 were "extremely satisfied" (7.32%) (Table 1).

Analysis was done for association between treatment response and the patient gender, age, duration of course, Fitzpatrick skin type, energy density, number of treatment sessions, satisfaction, pain, erythema within or beyond 3 months, PIH within or beyond 3 months, hypopigmentation, acne flare-up, and post-laser scar. Erythema and PIH are demarcated by 3 months at which the curative effect began. This analysis showed that the number of treatment sessions and PIH within 3 months positively correlated with treatment effects ($p \leq 0.05$), with those undergoing more treatment sessions or experiencing PIH within 3 months having better results (Table 2). No significant correlation was observed between other factors and the treatment efficacy.

Table 3 Adverse effects following laser resurfacing

Adverse effects	No. of patients (%)
Erythema (< 3 months)	66 (80.49)
Prolonged erythema (> 3 months)	16 (19.51)
Hyperpigmentation (< 3 months)	34 (41.46)
Persistent pigmentation (> 3 months)	26 (31.71)
Hypopigmentation	1 (1.22)
Acne flare-up	8 (9.76)
Post-laser scar	2 (2.44)

The most common adverse effects were pain, erythema, and pigmentation (Table 3). All patients had a pain level of 6.61 ± 1.92. Post-treatment erythema occurred in all subjects studied (100%), appearing in 80.49% of the patients lasting < 3 months and in 19.51% lasting > 3 months. PIH occurred in 60 patients (73.17%), appearing in 41.46% of the patients lasting < 3 months and in 31.71% lasting > 3 months. One patient experienced hypopigmentation (1.22%). Acne flare-up affected 8 patients (9.76%). Post-laser scars occurred in 2 patients (2.44%, Fig. 3). No other side effects, including contact dermatitis, HSV outbreak, or bacterial infection, were observed.

Discussion

Ablative fractional laser resurfacing is crucial for atrophic acne scar treatment and is associated with up to 80% improvement and minimal adverse events [4]. Here, 1–3 treatments with the single-pass fractional CO_2 laser (energy density range, 4050–11,830 mJ/cm^2) significantly improved acne scars. However, treatment efficacy is also

Table 2 Regression analysis of CO_2 laser efficacy on atrophic acne scar

Model	Unstandardized coefficient		Standardized coefficient	*t*	*p*	Multicollinearity	
	B	Standard error	*β*			Tolerance limits	VIF
Constant	0.094	0.067		1.400	0.165		
Hyperpigmentation (< 3 months)	0.064	0.025	0.271	2.591	**0.011**	0.914	1.094
Number of sessions	0.079	0.026	0.305	3.023	**0.003**	0.985	1.015
Energy density	−9.501E−6	0.000	−0.124	−1.196	0.235	0.926	1.080

B unstandardized regression coefficient, *β* standardized regression coefficient, *VIF* variance inflation factor. Multiple variable linear regression analysis

The bold values indicate statistically significant values

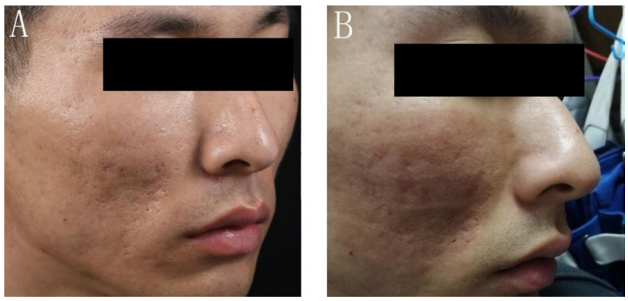

Fig. 3 Pre-treatment (A) and post-treatment (**B**) photographs of a 22-y-old male patient. About 1 month after treatment, cord scars appeared on the face

influenced by scar type [5] and severity [6], Fitzpatrick skin type [7], onset age [8], disease duration [9], follow-up [10], and timing [11] and methodology [12] of assessment. Few studies have assessed the relationship between these factors.

Energy is thought to impact acne scar laser resurfacing the most as it influences MTZ, subsequent neocollagenesis, and final treatment outcome [13]. It is reported that ablation depth in fractional resurfacing was correlated to the used energy [14]. An evaluation of response to high (50–70 mJ) and low (15–35 mJ) energy in fractional CO_2 laser revealed that the average scar improvement score was better with high energy (5.8) relative to low energy (4.0) [15]. However, our analysis of correlation between efficacy and demographic characteristics and parameter settings revealed that the number of treatments was statistically significant to resurfacing outcome whatever energy, age, gender, Fitzpatrick skin type, disease duration, and follow-up are. Similarly, Tatliparmak et al. revealed the number of treatment sessions was positively correlated to the change in ECCA scores no matter what the energy was [7]. This may be attributable to penetration defects of fractional laser as ice pick acne type, which accounts for 70% of acne scars, lies deep in the dermis [16]. Therefore, differences in energy are often not enough to make statistically significant difference in a single treatment. Indeed, Mahmoud et al. reported the same degree of acne improvement using 10 mJ and 40 mJ energy settings on Er:YAG laser [17]. Besides, all the patients in this study only received 1 to 3 treatment sessions, and there is no relevant study on whether there is a plateau of efficacy when the treatment is more than 3 times. The author suggests that patients with acne scar can be given 3 laser treatment sessions to observe whether there is efficacy, otherwise other methods need to be selected.

To our knowledge, this is the first study reporting that pigmentation duration within 3 months positively correlates with treatment efficacy. Although previous studies have shown that energy heavily affects pigmentation after laser procedure [18], given that our data indicate that energy has no effect on efficacy, pigmentation may be used as a single-factor predictor of efficacy. Once the repair has started, fibroblasts migrate to the local area and secrete various cytokines, including hepatocyte growth factor (HGF), stem cell factor (SCF), and Sema7a, to promote melanocyte proliferation, leading to pigmentation [19]. Furthermore, melanocytes secrete alpha-melanocyte-stimulating hormone (a-MSH), which not only causes pigmentation but also exerts a strong anti-inflammatory effect. It can promote collagen rearrangement and increase collagen III by mediating the inflammatory phase of wound healing, thereby reducing scar formation. [20].

Here, hyperpigmentation was significant, probably due to the sensitivity of Asian Fitzpatrick skin types to injury. One case of hypopigmentation and 8 cases of acne flare-up were observed, and 2 patients reported post-laser net-like scars on the margin of the cheek near the eyelids. Hence, clinicians should be prudent when resurfacing thin skin, such as the periorbital area.

This study has some limitations. Firstly, being a retrospective study, it is difficult to determine the cause and effect between variables. Secondly, clinical photographs used for analysis were taken prior to treatment, rather than at fixed timepoints after each treatment. Thirdly, the majority of the participants in this study are Asian. Nevertheless, our findings make valuable contribution given the paucity of studies investigating this field.

Conclusion

This study indicates that the efficacy of ablative fractional CO_2 laser on atrophic acne scars in Asians with Fitzpatrick skin types III–IV positively correlates with treatment sessions, other than energy, gender, age, and follow-up time. Additionally, the duration of hyperpigmentation within 3 months may predict efficacy. Evidence-based prospective studies are needed to explore the relationship between efficacy and age, gender, Fitzpatrick skin type, energy, treatment sessions, follow-up duration, and pigmentation.

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Declarations

Conflict of interest The authors declare no conflicts of interest.

References

1. Taylor M, Gonzalez M, Porter R (2011) Pathways to inflammation: acne pathophysiology. Eur J Dermatol 21(3):323–333. https://doi.org/10.1684/ejd.2011.1357
2. Bhargava S, Cunha PR, Lee J, Kroumpouzos G (2018) Acne Scarring Management: Systematic Review and Evaluation of the Evidence. Am J Clin Dermatol 19(4):459–477. https://doi.org/10.1007/s40257-018-0358-5
3. Sadick NS, Cardona A (2018) Laser treatment for facial acne scars: a review. J Cosmet Laser Ther 20(7–8):424–435. https://doi.org/10.1080/14764172.2018.1461230
4. Ortiz AE, Tremaine AM, Zachary CB (2010) Long-term efficacy of a fractional resurfacing device. Lasers Surg Med 42(2):168–170. https://doi.org/10.1002/lsm.20885
5. Sardana K, Manjhi M, Garg VK, Sagar V (2014) Which type of atrophic acne scar (ice-pick, boxcar, or rolling) responds to nonablative fractional laser therapy? Dermatol Surg 40(3):288–300. https://doi.org/10.1111/dsu.12428
6. Alexiades-Armenakas MR, Dover JS, Arndt KA (2008) The spectrum of laser skin resurfacing: nonablative, fractional, and ablative laser resurfacing. J Am Acad Dermatol 58(5):719–740. https://doi.org/10.1016/j.jaad.2008.01.003
7. Tatlıparmak A, Aksoy B, Shishehgarkhaneh LR, Gökdemir G, Koç E (2020) Use of combined fractional carbon dioxide laser and fractional microneedle radiofrequency for the treatment of acne scars: a retrospective analysis of 1-month treatment outcome on scar severity and patient satisfaction. J Cosmet Dermatol 19(1):115–121. https://doi.org/10.1111/jocd.13004
8. Helou J, Korkomaz J, Stephan F, Soutou B (2020) Searching predictive factors of efficacy and safety in a fractional CO_2 laser. Dermatol Ther 33(6):e13985. https://doi.org/10.1111/dth.13985
9. Karmisholt KE, Haerskjold A, Karlsmark T, Waibel J, Paasch U, Haedersdal M (2018) Early laser intervention to reduce scar formation - a systematic review. J Eur Acad Dermatol Venereol 32(7):1099–1110. https://doi.org/10.1111/jdv.14856
10. Bjørn M, Stausbøl-Grøn B, BraaeOlesen A, Hedelund L (2014) Treatment of acne scars with fractional CO_2 laser at 1-month versus 3-month intervals: an intra-individual randomized controlled trial. Lasers Surg Med 46(2):89–93. https://doi.org/10.1002/lsm.22165
11. Fournier N, Mordon S (2005) Nonablative remodeling with a 1,540 nm erbium:glass laser. Dermatol Surg 31(9 Pt 2):1227–1236. https://doi.org/10.1111/j.1524-4725.2005.31931
12. Ong MW, Bashir SJ (2012) Fractional laser resurfacing for acne scars: a review. Br J Dermatol 166(6):1160–1169. https://doi.org/10.1111/j.1365-2133.2012.10870.x
13. Paasch U, Haedersdal M (2011) Laser systems for ablative fractional resurfacing. Expert Rev Med Devices 8(1):67–83. https://doi.org/10.1586/erd.10.74
14. Helbig D, Bodendorf MO, Grunewald S, Kendler M, Simon JC, Paasch U (2009) Immunohistochemical investigation of wound healing in response to fractional photothermolysis. J Biomed Opt 14(6):064044. https://doi.org/10.1117/1.3275479
15. Kim S, Cho KH (2009) Clinical trial of dual treatment with an ablative fractional laser and a nonablative laser for the treatment of acne scars in Asian patients. Dermatol Surg 35(7):1089–1098. https://doi.org/10.1111/j.1524-4725.2009.01193.x
16. Kim HJ, Kim TG, Kwon YS, Park JM, Lee JH (2009) Comparison of a 1,550 nm Erbium: glass fractional laser and a chemical reconstruction of skin scars (CROSS) method in the treatment of acne scars: a simultaneous split-face trial. Lasers Surg Med 41(8):545–549. https://doi.org/10.1002/lsm.20796
17. Mahmoud BH, Srivastava D, Janiga JJ, Yang JJ, Lim HW, Ozog DM (2010) Safety and efficacy of erbium-doped yttrium aluminum garnet fractionated laser for treatment of acne scars in type IV to VI skin. Dermatol Surg 36(5):602–609. https://doi.org/10.1111/j.1524-4725.2010.01513.x
18. Yuan XH, Zhong SX, Li SS (2014) Comparison study of fractional carbon dioxide laser resurfacing using different fluences and densities for acne scars in Asians: a randomized split-face trial. Dermatol Surg 40(5):545–552. https://doi.org/10.1111/dsu.12467
19. Upadhyay PR, Ho T, Abdel-Malek ZA (2021) Participation of keratinocyte- and fibroblast-derived factors in melanocyte homeostasis, the response to UV, and pigmentary disorders. Pigment Cell Melanoma Res 34(4):762–776. https://doi.org/10.1111/pcmr.12985
20. de Souza KS, Cantaruti TA, Azevedo GM Jr et al (2015) Improved cutaneous wound healing after intraperitoneal injection of alpha-melanocyte-stimulating hormone. Exp Dermatol 24(3):198–203. https://doi.org/10.1111/exd.12609
21. Mu YZ, Jiang L, Yang H (2019) The efficacy of fractional ablative carbon dioxide laser combined with other therapies in acne scars. Dermatol Ther 32(6):e13084. https://doi.org/10.1111/dth.13084