Research Article

Efficacy of Fractional CO_2 Laser in Management of Acne Scars: Systematic Review and Meta-Analysis

Bushra Mohammad Albluwi[1*], Mohammed Ali Alanka[2], Yassmeen Hmoud Alblowi[3], Mohammed Abdullah Albesher[4], Hadi Adnan Mohammed[5], Saad Abdulrahman Alotaibi[6], Faisal Abdullah Alghubaywi[7], Nawaf Ammash Alsubaie[8], Abdulrahman Fahad Alotaibi[9] and Rana Abdullhadi Bugshan[10]

[1]Department of Dermatology, Dammam Medical Complex, Dammam, Saudi Arabia; [2]Department of Service Resident, Qatif Central Hospital, Qatif, Saudi Arabia; [3]Department of Medicine, Tabuk University, Tabuk, Saudi Arabia; [4]Department of Medicine, Qassim University, Qassim, Saudi Arabia; [5]Department of Medicine, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia; [6]Department of Medicine, Shaqra University, Riyadh, Saudi Arabia; [7]Department of Medicine, King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia; [8]General Practitioner at PSBJ, Alahsa, Saudi Arabia ; [9]General Practitioner, King Khalid Hospital, Riyadh, Saudi Arabia; [10]General Practitioner, East Jeddah Hospital, Jeddah, Saudi Arabia

Corresponding author:
Bushra Mohammad Albluwi,
Department of Dermatology,
Dammam Medical Complex,
Dammam, Saudi Arabia;
Email: Derma_2010@yahoo.com

Abstract

Background: Different types of lasers, both ablative and non-ablative, are used to treat acne scars. Non-ablative lasers stimulate dermal fibroblasts to make new collagen (NdYAG and Diode lasers), while ablative lasers target water and vaporize injured scar tissue. **Aim:** This work aims to determine the efficacy and safety of fractional CO_2 laser in the management of patients with acne scars. **Methodology:** A systematic search was performed over different medical databases to identify Dermatology studies, which studied the outcome of the CO_2-laser group versus the Non-CO_2-laser group of acne scar patients. We conducted a meta-analysis process on improved observer assessment, and satisfied patient assessment as primary outcomes, and on post-inflammatory hyperpigmentation (PIH) as a secondary outcome. Eight studies were identified involving 288 patients, with 144 patients in the CO_2-laser group, and 144 patients in the Non-CO_2-laser group. Our meta-analysis process showed revealed a highly significant increase in improved observer assessment in the CO_2-laser group compared to the Non-CO_2-laser group (p=0.016). But, there was a non-significant difference regarding both satisfied patient assessment and PIH (p>0.05) respectively. **Conclusion:** To conclude, fractional CO_2 laser had a significant contribution in improving observer assessment along with clinical improvement, but PIH is still the most common side effect of laser therapy, and further studies are needed to assess the safety of CO_2 laser in the management of patients with acne scars.

Keywords: Fractional CO_2 laser; Acne scars; Dermal fibroblasts

Introduction

Acne is the most common skin disorder, and practically every teenager suffers from it to some extent. This condition, however, is not restricted to a specific age range. [1] It's so common that we think of it as a natural part of the developing process. It occurs in boys with the age of 16 years-17 years up to 95%-100% and in girls of these ages; the recurrence percent is 83%-85%. [2] Acne usually clears itself between the ages of 23 and 25; however, it can last up to 40 years in 1% of men and 5% of women. [3] Even though acne heals on its own after a few years, and we can't ignore it. Because untreated acne can leave unsightly scars on the skin. Acne develops when the sebaceous glands of the skin become clogged, and the condition worsens when infection and microbial elements are added to it. [4]

Inflammatory acne can result in a variety of scars. These scars have a negative impact on the patient's social and relationship life. Acne scars are caused by the aberrant creation or breakdown of collagen that happens throughout the healing process. Collagen degradation occurs at the dermal level in the majority of cases (80%-90%), resulting in atrophic scarring. Hypertrophic or keloid scars are more commonly caused by an increase in collagen production. [5] Ice pick scars (60%-70%), boxcar scars (20%-30%) and rolling scars (15%-25%) are the three types of atrophic acne scars. [6] Various approaches for classifying acne severity have been offered. [7] The Goodman and Baron Quantitative Global Acne Scarring Grading System (GBGS), which ranges from 0 to 84 points, is a clinically useful and straightforward system for grading the severity of acne scars. It is based on scar count (1-10, 11-20,>20), scar shape (atrophic, macular, boxcar, hypertrophic, keloidal), and scar severity (mild, moderate, severe). [8]

Chemical peels, dermal abrasion/microdermal abrasion, laser treatments, punch methods, and combined therapies for atrophic scars: silicone gel, intralesional steroid therapy, cryotherapy, and surgery for hypertrophic scars and keloids are different methods of treatments. [9] Different types of lasers, both ablative and non-ablative, are used to treat acne scars. Non-ablative lasers stimulate dermal fibroblasts to make new collagen (NdYAG and

How to Cite this Article: Albluwi BM, et al. Efficacy of Fractional CO_2 Laser in Management of Acne Scars: Systematic Review and Meta-Analysis. Ann Med Health Sci Res. 2021;11:S5:27-31.

Diode lasers), while ablative lasers target water and vaporize injured scar tissue (carbon dioxide laser, Erbium YAG laser). [10] This work aims to determine the efficacy and safety of fractional CO_2 laser in the management of patients with acne scars.

Study Methodology

Our review came following the (PRISMA) statement guidelines. [11]

Study eligibility

The included studies should be in english, a journal published article, and a human study describing acne scar patients. The excluded studies were either animal or non-english studies or articles describing children.

Study identification

Basic searching was done over the pubmed, cochrane library, and google scholar using the following keywords: fractional CO_2 laser, acne scars.

Data extraction

Comparative studies, clinical trials, and Randomized Controlled Trials (RCTs), which studied the outcome of the CO_2-laser group versus the Non-CO_2-laser group of acne scar patients, will be reviewed. Outcome measures included improved observer assessment, and satisfied patient assessment as primary outcomes, and Post-Inflammatory Hyperpigmentation (PIH) as a secondary outcome.

Study selection

We found 150 records, 100 excluded because of the title; 50 articles are searched for eligibility by full-text review; 22 articles cannot be accessed; 11 studies were reviews and case reports; 9 were not describing the functional outcome. The studies which met all inclusion criteria were 8 studies.

Statistical analysis

Pooled Odds Ratios (OR), Proportions (%), with 95% Confidence Intervals (CI) assessed, using a statistical package (MedCalc, Belgium). The meta-analysis process was established *via* I^2-statistics (either the fixed-effects model or the random-effects model), according to the Q test for heterogeneity.

The included studies were published between 2011 and 2020. Regarding patients' characteristics, the total number of patients in all the included studies was 288 patients, with 144 patients in the CO_2-laser group, and 144 patients in the Non-CO_2-laser group, while their average follow-up time was (6.3) months. The mean age of all patients was (28.1 years) [Table 1]. Our meta-analysis included 8 studies comparing 2 different groups of patients; with a total number of patients (N=288) [Table 2].

Each outcome was measured by

Odds Ratio (OR):

- For improved observer assessment.
- For satisfied patient assessment.
- For PIH.

Concerning the primary outcome measures, we found 6 studies that reported improved observer assessment. I^2 (inconsistency) was 0%, Q test for heterogeneity (p=0.886), so fixed-effects model was carried out; with overall OR=2.12 (95% CI=1.149 to 3.924). The fixed-effects model of the meta-analysis process revealed a highly significant increase in improved observer assessment in the CO_2-laser group compared to the non-CO_2-laser group (p=0.016) [Figure 1]. We found 5 studies that reported satisfied patient assessment. I^2 (inconsistency) was 0%, Q test for heterogeneity (p=0.620), so fixed-effects model

Table 1: Patients and study characteristics.

N	Author	Number of patients			Age	Follow-up time
		Total	CO_2-laser group	Non-CO_2-laser group	(average years)	(average months)
1	Asilian et al. [12]	64	32	32	26.5	9
2	Hedelund et al. [13]	26	13	13	33	9
3	Azzam et al. [14]	20	10	10	28	6
4	Manuskiatti et al. [15]	48	24	24	29.5	8
5	Mohammed [16]	28	14	14	22.7	6
6	Reinholz et al. [17]	28	14	14	28.6	3
7	Abou Eitta et al. [18]	20	10	10	33.2	3
8	Kaçar et al. [19]	54	27	27	23.9	---

Table 2: Summary of outcome measures in all studies.

N	Author	Primary outcome				Secondary outcome	
		Improved observer assessment		Satisfied patient assessment		Rate of PIH	
		CO_2-laser group	Non-CO_2-laser group	CO_2-laser group	Non-CO_2-laser group	CO_2-laser group	Non-CO_2-laser group
1	Asilian et al.	28	24	26	24	0	10
2	Hedelund et al.	---	---	---	---	0	0
3	Azzam et al.	---	---	3	2	2	0
4	Manuskiatti et al.	13	11	12	14	10	7
5	Mohammed	5	3	12	9	2	9
6	Reinholz et al.	4	1	---	---	---	---
7	Abou Eitta et al.	10	10	7	8	---	---
8	Kaçar et al.	11	6	---	---	---	---

was carried out; with overall OR=1.18 (95% CI=0.614 to 2.27). The fixed-effects model of the meta-analysis process revealed a non-significant difference in satisfying patient assessment in the CO_2-laser group compared to the non-CO_2-laser group (p>0.05) [Figure 2].

Concerning the secondary outcome measure, we found 5 studies that reported post-inflammatory hyperpigmentation. I^2 (inconsistency) was 77.5%, Q test for heterogeneity (p=0.004), so random-effects model was carried out; with overall OR=0.42 (95% CI=0.0465 to 3.906). The random-effects model of the meta-analysis process revealed a non-significant difference in post-inflammatory hyperpigmentation in the CO_2-laser group compared to the Non-CO_2-laser group (p>0.05) [Figure 3].

Discussion

This work aims to determine the efficacy and safety of fractional CO_2 laser in the management of patients with acne scars. The included studies were published between 2011 and 2020. Regarding patients' characteristics, the total number of patients in all the included studies was 288 patients, with 144 patients in

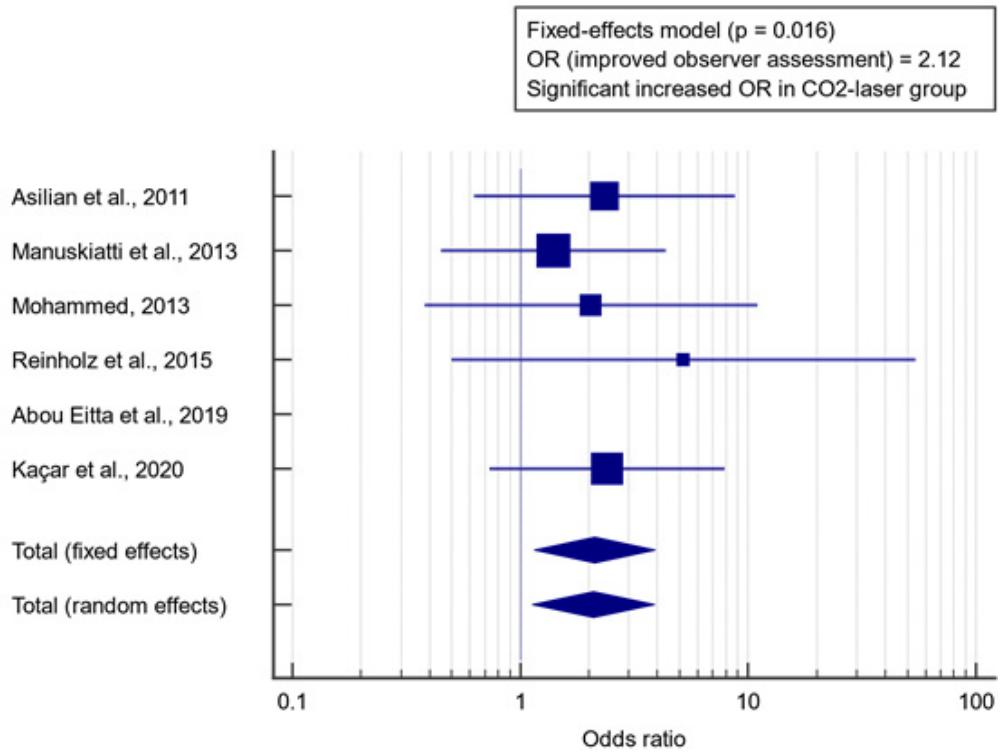

Figure 1: Forest plot (improved observer assessment).

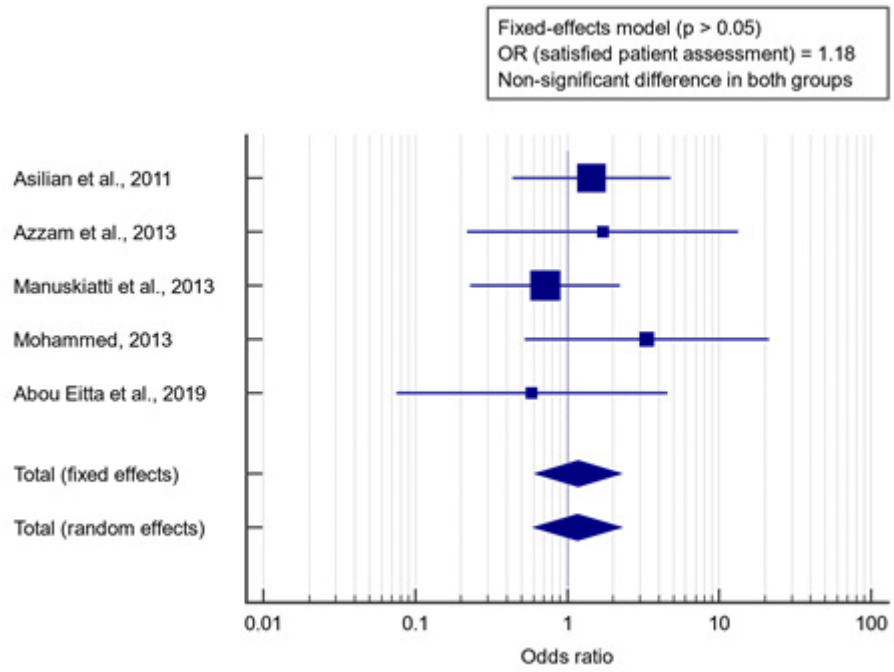

Figure 2: Forest plot (satisfied patient assessment).

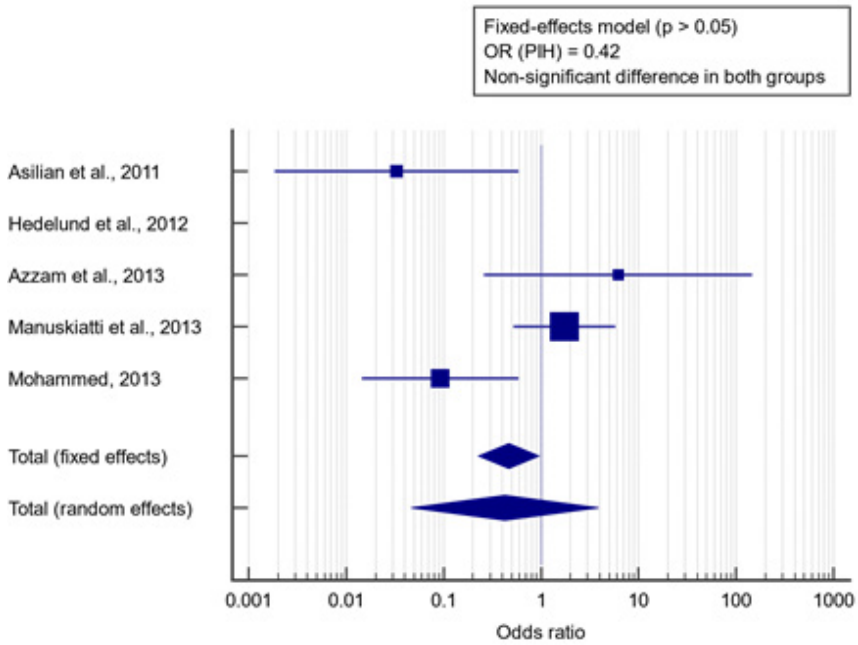

Figure 3: Forest plot (post-inflammatory hyperpigmentation).

the CO_2-laser group, and 144 patients in the non-CO_2-laser group, while their average follow-up time was (6.3) months. The mean age of all patients was (28.1 years). Our meta-analysis included 8 studies comparing 2 different groups of patients; with a total number of patients (N=288). Concerning the primary outcome measures, we found 6 studies that reported improved observer assessment. Using the Fixed-effects model of the meta-analysis process revealed a highly significant increase in improved observer assessment in the CO_2-laser group compared to the non-CO_2-laser group (p=0.016) which came in the agreement of Tatlıparmak et al. [20]

Tatlıparmak et al. reported that, after an average of five treatments, there was a considerable reduction in scars and a much higher rate of pleased patients compared to baseline. The number of treatments and clinical improvement was found to have a favorable relationship. [20] On the other hand, our result came in disagreement with Cho et al. study who reported that follow-up three months following the final laser treatment, 27 (25.5%) of the 100 patients showed moderate improvement, 61 (57.5%) patients showed significant improvement, and 12 (11.3%) patients showed near-total improvement. The mean clinical improvement grades were 2.64-0.76 for FPS, 2.60-0.68 for CO_2 FS, and 2.94-0.83 for FPS+CO_2 FS, based on clinical photography assessment. There were no significant differences in mean values amongst laser devices (p=0.249). [21]

Concerning the primary outcome measures, we found 5 studies that reported satisfied patient assessment. Using Fixed-effects model of the meta-analysis process revealed a non-significant difference in satisfying patient assessment in the CO_2-laser group compared to the non-CO_2-laser group (p>0.05) which came in the agreement of Cho et al.; van Drooge et al.; Hedelund et al.; Zhang et al. [22-25] Cho et al. reported that overall patient satisfaction was measured in surveys. Four of the eight patients (50.0%) were slightly satisfied after treatment with carbon dioxide fractional laser systems, two (25.0%) were very satisfied, one (12.5%) was slightly satisfied, and one (12.5%) was unsatisfied. Overall, there was no significant difference in satisfaction scores between the two groups (P>0.05). [22]

Van Drooge et al. reported that the total POSAS score did not differ significantly between the observer (p>0.05) and patient parts of the scale, according to statistical analysis. [23] Hedelund et al. reported that patients were satisfied with their treatments, and satisfaction levels at 1 month, 3 months, and 6 months after surgery were similar (P>0.05). The scar texture was rated as mild to moderately improved by the patients, and the evaluation scores did not alter significantly over time. [24] Zhang et al. who reported that, with fractional CO_2 laser therapy, acne scars can be improved clinically. [25]

Concerning the secondary outcome measure, we found 5 studies that reported post-inflammatory hyperpigmentation. Using the Random-effects model of the meta-analysis process revealed a non-significant difference in post-inflammatory hyperpigmentation in the CO_2-laser group compared to the Non-CO_2-laser group (p>0.05) which came in the agreement of Boen et al.; Davis et al. [26,27] Boen et al. reported that in 29% of patients, post-inflammatory hyperpigmentation occurred, and all patients had persistent erythema. Davis et al. reported that in dark-skinned people, PIH is still the most common side effect of laser therapy.

Conclusion

To conclude, fractional CO_2 laser had a significant contribution in improving observer assessment along with clinical improvement, but PIH is still the most common side effect of laser therapy, and further studies are needed to assess the safety of CO_2 laser in the management of patients with acne scars.

Acknowledgments

All the listed authors contributed significantly to the conception and design of study, acquisition, analysis, and interpretation of

data and drafting of the manuscript, to justify authorship.

References

1. Fife D, Zachary CB. Combining techniques for treating acne scars. Curr Dermatol Rep. 2012;1:82-88.
2. Fife D. Practical evaluation and management of atrophic acne scars: Tips for the general dermatologist. J Clin Aesthet Dermatol. 2011;4:50.
3. Hwang E, Suh D, Lee J. The efficacy and safety of new total combination techniques compared with classic sequential combination therapy with punch, fractional and long-pulsed Er-YAG laser for the treatment of acne scars: P3506. J Am Acad Dermatol. 2011;64.
4. Kang WH, Kim YJ, Pyo WS, Park SJ, Kim JH. Atrophic acne scar treatment using triple combination therapy: Dot peeling, subcision and fractional laser. J Cosmet Laser Ther. 2009;11:212-215.
5. Connolly D, Vu HL, Mariwalla K, Saedi N. Acne scarring-pathogenesis, evaluation, and treatment options. J Clin Aesthet Dermatol. 2017;10:12.
6. Fabbrocini G, Annunziata MC, D'arco V, Vita VD, Lodi G, Mauriello MC, et al. Acne scars: Pathogenesis, classification and treatment. Dermatol Res Pract. 2010;2010.
7. Melina A, Dinh NN, Tafuri B, Schipani G, Nisticò S, Cosentino C, et al. Artificial intelligence for the objective evaluation of acne investigator global assessment. J Drugs Dermatol. 2018;17:1006-1009.
8. Goodman GJ, Baron JA. Postacne scarring-a quantitative global scarring grading system. J Cosmet Dermatol. 2006;5:48-52.
9. Mercuri S, Brianti P, Cestone E, Dattola A, Nisticò SP. Effective use of non-ablative fractional laser on multiple whip scars. Photomed Laser Surg. 2018;36:337-339.
10. Mercuri SR, Brianti P, Dattola A, Bennardo L, Silvestri M, Schipani G, et al. CO_2 laser and photodynamic therapy: Study of efficacy in periocular BCC. Dermatol Ther. 2018;31:e12616.
11. Liberati A, Altman D, Tetzlaff J, Mulrow C, Gøtzsche P, Ioannidis J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions. BMJ 2009;339.
12. Asilian A, Salimi E, Faghihi G, Dehghani F, Tajmirriahi N, Hosseini SM. Comparison of Q-switched 1064-nm Nd: YAG laser and fractional CO_2 laser efficacies on improvement of atrophic facial acne scar. Res J Med Sci. 2011;16:1189.
13. Hedelund L, Haak CS, Togsverd-Bo K, Bogh MK, Bjerring P, Hædersdal M. Fractional CO_2 laser resurfacing for atrophic acne scars: A randomized controlled trial with blinded response evaluation. Lasers Surg Med. 2012;44:447-452.
14. Azzam OA, Atta AT, Sobhi RM, Mostafa PI. Fractional CO (2) laser treatment *vs.* autologous fat transfer in the treatment of acne scars: A comparative study. J Drugs Dermatol. 2013;12:e7-e13.
15. Manuskiatti W, Iamphonrat T, Wanitphakdeedecha R, Eimpunth S. Comparison of fractional erbium-doped yttrium aluminum garnet and carbon dioxide lasers in resurfacing of atrophic acne scars in Asians. Dermatol Surg. 2013;39:111-120.
16. Mohammed G. Randomized clinical trial of CO_2 laser pinpoint irradiation technique with/without needling for ice pick acne scars. J Cosmet Laser Ther. 2013;15:177-182.
17. Reinholz M, Schwaiger H, Heppt MV, Poetschke J, Tietze J, Epple A, et al. Comparison of two kinds of lasers in the treatment of acne scars. Facial Plast Surg. 2015;31:523-1531.
18. Eitta RSA, Ismail AA, Abdelmaksoud RA, Ghezlan NA, Mehanna RA. Evaluation of autologous adipose-derived stem cells *vs.* fractional carbon dioxide laser in the treatment of post acne scars: A split-face study. Int J Dermatol. 2019;58:1212-1222.
19. Kaçar N, Dursun R, Akbay M, Gökşin Ş. The early and late efficacy of single-pass fractional carbondioxide laser, fractional radiofrequency, and their combination in acne scars: A prospective, split-face, single-blinded, controlled clinical study. Dermatol Ther. 2020;33:e14444.
20. Tatlıparmak A, Aksoy B, Shishehgarkhaneh LR, Gökdemir G, Koç E. 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. 2020;19:115-121.
21. Cho S, Jung JY, Shin JU, Lee JH. Non-ablative 1550 nm erbium-glass and ablative 10,600 nm carbon dioxide fractional lasers for various types of scars in Asian people: Evaluation of 100 patients. Photomed Laser Surg. 2014;32:42-46.
22. Cho SB, Lee SJ, Cho S, Oh SH, Chung WS, Kang JM, et al. Non-ablative 1550-nm erbium-glass and ablative 10 600-nm carbon dioxide fractional lasers for acne scars: a randomized split-face study with blinded response evaluation. J Eur Acad Dermatol Venereol 2010;24:921-925.
23. Drooge AMV, Vrijman C, Veen WVD, Wolkerstorfer A. A randomized controlled pilot study on ablative fractional CO_2 laser for consecutive patients presenting with various scar types. Dermatol Surg. 2015;41:371-377.
24. Hedelund L, Haak CS, Togsverd-Bo K, Bogh MK, Bjerring P, Hædersdal M. Fractional CO_2 laser resurfacing for atrophic acne scars: A randomized controlled trial with blinded response evaluation. Lasers Surg Med. 2012;44:447-452.
25. Zhang DD, Zhao WY, Fang QQ, Wang ZC, Wang XF, Zhang MX, et al. The efficacy of fractional CO_2 laser in acne scar treatment: A meta-analysis. Dermatol Ther. 2021;34:e14539.
26. Boen M, Jacob C. A review and update of treatment options using the acne scar classification system. Dermatol Surg. 2019;45:411-422.
27. Davis EC, Callender VD. Postinflammatory hyperpigmentation: A review of the epidemiology, clinical features, and treatment options in skin of color. J Clin Aesthet Dermatol. 2010;3:20.