

Author and year of publication	Study design	No of participants	Baseline disease severity	Treatment protocol	Study period and follow up	Evaluation of outcome	Results	Adverse effects
Lee et al <sup>15</sup> , 2011	Randomized split face study	14	Moderate to severe acne scars with Fitzpatrick skin types III-V	Fractional CO <sub>2</sub> laser a month apart followed by either PRP or normal saline injections on the randomized halves of the face	02 sessions each a month apart; follow up of 04 months after the last session.	Physician assessed improvement in quartile grading scale, adverse effects (edema and erythema) on a five point scale	Significant improvement in physician assessed quartile grading scale on the PRP side (p = 0.03)	Significantly less intensity and duration of erythema on the PRP side than on the control side. (p = 0.01 and 0.047) respectively. Significantly less duration of post treatment edema and crusting (p = 0.04 each)
Gawdat et al <sup>16</sup> , 2014	Randomized split face study	30	Atrophic acne scars with Fitzpatrick skin types III-V	Fractional CO <sub>2</sub> laser a month apart followed by either intra dermal PRP or topical PRP or intra dermal normal saline injections on the randomized halves of the face	03 sessions each a month apart; final assessment 03 months after the last session.	Physician assessed improvement in quartile grading scale, clinical satisfaction of patients on a four point scale, depth of acne scars using optical coherence tomography (OCT)	Significant improvement in FCL+PRP groups (topical and intra dermal) as compared to intra dermal normal saline group (p = 0.03) on physician assessment scale. No significant difference in grades of clinical improvement between intra dermal and topical PRP.	Significantly shorter duration of erythema, edema, mild crusting, PIH, and acneiform eruption (P = 0.02) in FCL+PRP groups. Significantly shorter total downtime (P = 0.02) in FCL+PRP groups. Pain was significantly greater in FCL+ intra dermal PRP groups as compared to topical PRP and with FCL alone. (P = 0.005)
Faghihi et al <sup>17</sup> , 2015	Randomized split face study	16	Fitzpatrick skin types II-IV with moderate to severe atrophic acne scars (predominantly rolling and boxcar types with fewer than 20% of the icepick type)	Fractional CO <sub>2</sub> laser a month apart followed by either intra dermal PRP or intra dermal normal saline injections on the randomized halves of the face	02 sessions each a month apart; assessed at 01 month after the first session and 04 months after the second.	Physician assessed improvement in quartile grading scale, clinical satisfaction of patients on a four point scale, participant assessed visual analog scale (0 to 10) for erythema and edema on days 0, 2, 4, 6, 8, 15 and 30 after each treatment session.	Overall clinical improvement on physician assessed quartile grading scale of acne scars was higher on the FCL+PRP side but the difference was not statistically significant either 1 month after the first session (P = 0.15) or 4 months after the second (P = 0.23). The patient assessed four point clinical satisfaction scale too showed similar greater clinical improvement but not significant at either 01 or 04 months. (P = 0.18 and P = 0.12 respectively)	Significantly more erythema on FCL+PRP side than control side with on days 0, 2 and 4. (P = 0.003, P = 0.007, P = 0.03 respectively) Also more edema on FCL+PRP side compared with the control side with a statistically significant difference on days 0, 2 and 8 (P = 0.003, P = 0.004, P = 0.004 respectively). Mean duration of both erythema and edema were greater on the FCL+PRP side but not statistically significant.
Shah et al <sup>18</sup> , 2017	Randomized split face study	30	Moderate to severe atrophic acne scars (Grade II-IV)	Fractional CO <sub>2</sub> laser a month apart followed by either PRP or normal saline injections on the randomized halves of the face	04 sessions each a month apart; monthly follow up of 04 months after the last session.	Goodman and Baron quantitative global acne scarring grading system, physician assessed improvement in quartile grading scale, patient satisfaction based on scar severity.	Significant reduction in Goodman and Baron grading in both PRP injection site (mean was 14.83 at baseline and 4.2 at four months) and normal saline injection site (mean Goodman and Baron grading was 15.23 at baseline and 7.5 at four months)	Significantly lower proportion of patients in the PRP group had persistent erythema, edema and pain as compared to the normal saline group. (p value= 0.0453, 0.008829 and 0.0076 respectively.

Kar et al <sup>19</sup> , 2017	Comparative split face study	30	Fitzpatrick skin types III-V with moderate to severe atrophic acne scars	Fractional CO <sub>2</sub> laser at monthly intervals followed by topical PRP on left side and no intervention on the right side of the face	03 sessions every month; assessed a month after third session.	Quantitative global acne scar grading system of Goodman and Baron, visual scar assessment questionnaire was also filled up by the observer and patient, patient satisfaction score on a scale of 0–10, procedure-related adverse events (i.e. erythema, edema, and pain) on a visual analog scale of 0–10.	Though there was significant improvement on both sides of the face, there was no significant difference in the quality of scars between the right and the left sides of the face ( $P = 0.2891$ ). The addition of topical PRP to FCL on the left side of the face did not result in superior scar improvement as compared to the right side.	The redness, swelling, and pain experienced by each patient were significantly lesser on the side treated with FCL + PRP (left side) than that on the FCL-only side ( $P < 0.05$ )
Min et al <sup>20</sup> , 2017	Randomized split face study	25	Fitzpatrick skin types III-V with moderate to severe acne scars	Fractional CO <sub>2</sub> laser a month apart followed by either intra dermal PRP or intra dermal normal saline injections on the randomized halves of the face	02 sessions, four weeks apart. Subjects were followed-up on days 1, 3, 7 and 28 after each session and at 1 and 2 months after the final session.	5-point Investigator's Global Assessment (IGA) for efficacy, Echelle d' evaluation Clinique des Cicatrices d' Acne (ECCA) scores, and a subtype (ice pick, boxcar, rolling scar) analysis, degree of erythema analysis. Skin biopsy specimens (2mm) for the molecular analysis on days 0, 1, 3, 7, and 28 after the first treatment session.	The mean IGA score on the FCL+PRP side was significantly greater than FCL+NS ( $P < 0.001$ ). Skin recovery rates after treatment as assessed using the epithelization scale showed significant difference between the two modalities on day 1 ( $P = 0.01$ ) Patients reported significantly higher scores for improvement on FCL+PRP side as compared to NS+PRP side on days 7 ( $P = 0.03$ ) and 84 ( $P = 0.02$ ). IHC showed significantly increased expression of TGF $\beta$ 1, TGF $\beta$ 3, c-myc, TIMP, HGF, collagen-1 and collagen-3 on FCL+PRP side.	Both the erythema index and colorimetric measurements revealed consistently less erythema of the PRP-treated side compared with the control side. The mean values of 3-degree visual analogue scale (VAS) for erythema on the PRP-treated side and control side were 1.2 and 2.2 respectively.

Abdel-Maguid et al <sup>21</sup> , 2017	Randomized split face study	33	Fitzpatrick skin types III-IV with moderate to severe atrophic acne scars (rolling, boxcar scar and ice pick scar)	Group I- FCL a month apart followed by either topical stem cell cultured medium (SC-CM) or topical normal saline (NS) on randomized halves of the face. Group II- FCL a month apart followed by either topical PRP or topical normal saline (NS) on randomized halves of the face.	03 sessions each a month apart; assessed monthly and final assessment 03 months after the last session.	Echelle d' evaluation Clinique des Cicatrices d' Acne (ECCA) scores, physician assessed improvement in quartile grading scale, clinical satisfaction of patients on a four point scale, intensity as well as erythema and edema on patient assessed scale; dermatologist assessed PIH, secondary infection, acne activation, bleeding, erosion, and scarring. Histopathological examination for collagen fibres quantitative pro-collagen I gene expression analysis using RT-PCR.	In group I, difference in two sides showed no statistically significant results in any of the three scar types, group II showed greater reduction on the sides treated with FCL+PRP compared to the FCL+SC-CM sides (P= 0.006). Marked increase in organized collagen deposition were noted in FCL+PRP and FCL+SC-CM compared to FCL alone. Both FCL+PRP treated sides and the FCL+SC-CM sides had more up-regulation of type I pro-collagen compared to the sides treated by FCL only (P= 0.001 and P= 0.041 respectively).	There was no significant difference in the duration of erythema, edema, crusting or post-inflammatory hyperpigmentation between the two sides in either group (P > 0.05).
Abdel Aal et al <sup>22</sup> , 2018	Comparative split face study	30	Fitzpatrick skin types III-V with atrophic acne scars	Fractional CO <sub>2</sub> laser three to four weeks apart followed by either intra dermal PRP on right side and no intervention on the left side of the face	02 sessions each three to four weeks apart; assessed at six month after the second session.	Qualitative global acne scar grading system of Goodman and Baron, Physician assessed quartile grading scale of Tanzi and Alster, patient assessed subjective questionnaire for satisfaction, Clinician Erythema Assessment Scale, patient assessed questionnaire for presence or absence of adverse effects	The overall improvement of the right side (FCL+PRP) was better than the left side (control) with a statistically significant difference (P < 0.001)	Clearance of erythema was significantly faster on the right side (FCL+PRP) than the left (control) (P=0.0052). There was no PIH on right side in any of the patients, while it was seen on the left side in five patients (16.6%). Acneiform eruption were significantly reduced on the FCL+PRP side as compared to control. Patients were satisfied with outcome on their right side more than their left with a statistically significant difference (P<0.001)
Taweel et al <sup>23</sup> , 2018	Comparative non-split face study	40	Fitzpatrick skin types II-IV with atrophic acne scars (rolling, boxcar scar and ice pick scar)	Patients were divided into two groups: Group A- three sessions of FCL+ intra-dermal PRP each a month apart. Group B- three sessions of intra-dermal PRP followed by intra-dermal CO <sub>2</sub> gas injections into scars. (carboxytherapy)	Patients were assessed after a week of each session for complications (edema, PIH and pain) and then for 3 months after the last session.	Physician assessed improvement in quartile grading scale, clinical satisfaction of patients on a four point scale. Physician assessed adverse effects- pain, PIH and edema.	Physician assessed improvement in quartile grading scale showed significant improvement of acne scars in group A compared to group B (P= 0.039) with no statistically significant differences between the two groups in patients' satisfaction.	Edema was present in 90% of group (A) patients while it was seen in only 50% of group (B) and the difference was statistically significant. There was no statistically significant difference between the two groups in terms of pain and PIH.

Galal et al <sup>24</sup> , 2019	Randomized split face study	21	Atrophic acne scars	Fractional CO <sub>2</sub> laser at monthly intervals followed by topical PRP on left side and no intervention on the randomized halves of the face.	03 sessions each a month apart; assessed monthly at every session followed by every 03 months for a year	Quantitative global acne scar grading system of Goodman and Baron, Antera scoring system of scar depth, patient satisfaction score for scar, pigmentation and redness.	The quantitative global acne scar grading system of Goodman and Baron showed a statistically significant reduction for both sides of the face (P < 0.0001) after treatment. Greater reduction was found on the FCL+PRP side. Significant improvement in redness and pigmentation was seen on FCL+PRP side (P < 0.0001). According to the Antera scoring system, 70% of patients on the FCL+PRP side showed good or excellent improvement as compared to only 30% of patients on the FCL side.	Patient satisfaction score on reduction of pigmentation and redness was higher for the sides that were treated with FCL+PRP.
El-Taieb et al <sup>25</sup> , 2019	Randomized Clinical Trial (Non split faced)	75	Fitzpatrick skin types III-IV with atrophic acne scars (rolling, boxcar scar and ice pick scar)	Enrolled patients were randomly assigned into three groups of 25 each. Group A- 12 sessions of intra-dermal injection of PRP at 2-week intervals. Group B- six sessions of fractional Er-YAG laser at 4-week intervals. Group C- combination of the two treatment modalities.	Study period 24 weeks, assessed every 04 weeks, final assessment at 24 weeks.	Qualitative scarring grading system of Goodman and Baron, physician assessed improvement in quartile grading scale, clinical satisfaction of patients on a four point scale, degree of facial erythema was evaluated by clinician erythema assessment (CEA) scale	Patients treated with Er-YAG laser+ PRP showed significant improvement compared with those treated with Er-YAG laser or PRP alone (P = 0.007 and P=0.001, respectively). Also, patients treated with Er-YAG laser showed significantly greater improvement than those treated with PRP (P=0.001). Patients in group C were more satisfied with their results than those in group A or B (P=0.001 and P = 0.005, respectively). Likewise, patients treated with Er-YAG laser were markedly more satisfied than those treated with PRP alone (P = 0.009).	No statistically significant differences between the study groups regarding any of the post treatment complications in form of erythema, PIH or acneiform eruptions.
Arsiwala et al <sup>26</sup> , 2020	Randomized Clinical Trial (Non split faced)	25	Fitzpatrick skin types III-V with atrophic acne scars (rolling, boxcar scar and ice pick scar)	Patients were randomly divided into two groups: Group A- treated for three monthly sessions of FCL+ topical PRP and Group B- FCL monotherapy.	Three monthly treatment sessions for 12 weeks; follow up at every monthly visit with final assessment at 12 weeks.	Goodman and Baron quantitative global acne scar grading system, patient assessment of improvement of acne scars on a visual analog scale (VAS).	The mean change in Goodman and Baron quantitative global acne scar grading system scores reduced significantly both in Group A and B (both P < 0.0001) but when compared head to head the difference was statistically insignificant (P = 0.129)	Immediate adverse effects (erythema, edema, and pain) were more in group B but the difference was not statistically significant. Long-term adverse effects (PIH, pain, erythema, acne and secondary infection) too were observed in increased frequency subjects in Group B even though no significant difference was observed between two groups.

Mahamoud et al <sup>27</sup> , 2020	Randomized split face study	30	Fitzpatrick skin types III–V with mild to severe atrophic acne scars	Fractional CO <sub>2</sub> laser 04 weeks apart followed by either intradermal hyaluronic acid (HA) injections or PRP injections on randomized halves of the face.	Three treatment sessions, final assessment at three months after the last session.	Qualitative scarring grading system of Goodman and Baron, quantitative global acne scar grading system of Goodman and Baron, clinical satisfaction of patients on a four point scale, subjective evaluation by patients adverse effects like downtime, persistent erythema, edema, PIH, pain, scarring, milia and infections; scoring for pain by universal pain screening with a 0-10 pain intensity numeric rating scale (NRS)	Both FCL+PRP and FCL+HA side achieved statistically significant difference by Goodman and Baron quantitative as well as qualitative scores (P < 0.001). Pitched against one another, the qualitative score showed no statistically significant difference (P = 0.921) denoting that both modalities of treatment gave similar net results.	There was no significant difference between both sides in terms of adverse effects.
Sujana et al <sup>28</sup> , 2020	Randomized non-split face study	80	Mild, moderate and severe acne scars	Eighty patients were randomly assigned into two groups of 40 each. Group A was treated with FCL alone, while Group B was treated with FCL + intradermal PRP for 6 months.	A total of six sittings performed at 04 week intervals. Final assessment was done at 04 weeks after the final session.	Goodman and Baron's global acne scarring scoring system, physician assessed improvement in quartile grading scale, subjective assessment was done by patients themselves on a 5-point visual analog scale; duration of erythema, edema and crusting.	In Goodman and Baron's global acne scarring scoring system, patients treated with FCL+PRP responded better to treatment than those treated with FCL alone. Photographic assessment revealed improvement of skin texture and decreased down time in FCL+PRP group. Patients' subjective assessment too was consistent with results of Goodman and Baron's objective scoring system.	Duration of erythema, edema and crusting was less in FCL+PRP group. Less number of patients experienced PIH in FCL+PRP group too. However more patients experienced pain in the FCL+PRP group.
El-Hawary et al <sup>29</sup> , 2021	Randomized non-split face study	60	Fitzpatrick skin types III–IV with moderate to severe atrophic acne scars	Sixty patients were randomly divided into three groups. Group 1- intra-dermal PRP injections only, group 2- FCL only, group 3- FCL+ intra-dermal PRP injections.	Each group received three sessions at monthly intervals. Final assessment at 3 months after the last session.	Qualitative scarring grading system of Goodman and Baron, physician assessed improvement in quartile grading scale, clinical satisfaction of patients on a four point scale, patient reported side effects on a 5-point scale, skin biopsies were obtained before and 1 month after treatment sessions.	Significantly higher improvement in group 2 compared to group 1 (P = 0.028) and significantly higher improvement in group 3 than in group 1 (P = 0.002). However, no significant difference was between group 2 and group 3 (P = 0.657). Similar results in satisfaction of patients scale in skin texture, scar appearance and overall satisfaction. Significant increase in epidermal thickness, percentage of collagen fibers, and the number of proliferating epidermal cells (Ki-67	Pain was more severe in group 3 while erythema, edema, and crust formation were more severe and of longer duration in group 2. The total downtime was shorter in group 3 (4.60 ± 0.84) than in group 2 (5.40 ± 1.07).

							expression) in all three groups before and 1 month after the last treatment session.	
Sharma et al <sup>30</sup> , 2021	Split face comparative study	30	Moderate to severe acne scars	Right half-FCL+PRP injections, left half FCL+NS injections	Four treatment sessions four weeks apart. Final assessment was performed two months after the last session.	Goodman and Baron's qualitative acne scar grading system scale, Patient's subjective score.	Improvement in Goodman and Baron's qualitative acne scar grading system scale on both sides was statistically significant ( $P = 0.000$ ).	Most common side effects reported were erythema and burning followed by edema, which was seen in 63.3% patients on the study side and in 90% patients on the control side.

Abbreviations: FCL- Fractional carbon dioxide laser; PRP- Platelet rich plasma; NS- Normal saline; OCT- Optical coherence tomography; PIH- Post inflammatory hyperpigmentation; ECCA-Echelle d' evaluation Clinique des Cicatrices d' Acne; PCR- Polymerase chain reaction; IHC- Immuno-histochemistry; TGF $\beta$ 1-Transforming growth factor beta 1; TGF $\beta$ 3- Transforming growth factor beta 3; c-myc- cellular myelocytomatosis; TIMP- Tissue inhibitors of metalloproteinases; HGF- Hepatocyte growth factor; SC-CM- stem cell cultured medium; RT-PCR- Reverse transcriptase polymerase chain reaction; CEA- Clinician erythema assessment; HA- hyaluronic acid.