Original Article

A Comparative Study on the Efficacy of Fractional CO2 Laser and Fractional CO2 Laser with Autologous Platelet-Rich Plasma in Scars

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Abstract

Context: Surgical correction of scars may not be an ideal solution in all cases and hence it is desirable to have a nonsurgical option available. Autologous platelet-rich plasma (PRP) and fractional carbon dioxide laser (FCL) offer an alternative treatment modality. **Aims:** To compare the efficacy and safety of FCL and intradermal PRP with FCL in the management of postburn and posttraumatic scars. **Settings and Design:** A prospective, randomized, observer-blinded, comparative study was conducted at a hospital skin centre from Oct 2016 to Sep 2018. **Subjects and Methods:** A total of 67 patients with scars were randomly divided into two groups; Group I was treated with four sessions of monthly FCL and Group II was treated with four sessions of PRP and FCL. The patients were assessed using the Patient and Observer Scar Assessment Scale (POSAS) at baseline and 4 weeks after each session. **Statistical Analysis Used:** For continuous variables, the summary statistics of mean ± standard deviation was used; for categorical data, number and percentage were used. Chi-square ($\chi 2$) test was used for association between two categorical variables. *P* value <0.05 was considered to be statistically significant. **Results:** Thirty cases in each group completed the study. There was a significant improvement in the total score of POSAS ($p < 0.001$) in both groups, but the final difference between the two groups was not statistically significant ($p = 0.793$ and $P = 0.278$, respectively). **Conclusions:** Fractional CO2 laser causes significant improvement in scar appearance. PRP in combination with FCL offers no additional advantage.

Keywords: *Fractional CO_2 laser, platelet-rich plasma, POSAS, scars*

Introduction

Scars are a common problem as they inevitably develop after cutaneous dermal injury.[1] Superficially, a scar may appear to be only a cosmetic problem; however, they can remarkably impact the patients on many different physical and psychological levels. Physically, scars can impede the patients' range of movements and can cause pain, dysesthesia, and pruritus.[2] Psychologically, low self-esteem and feelings of psychosocial alienation are felt.[3]

Various methods to improve the appearance of scars include pressure garments, intralesional corticosteroid therapy, dermabrasion, surgical corrections, chemical peels, laser treatment, and autologous platelet-rich plasma.[4]

Autologous platelet-rich plasma (PRP) is popular for posttraumatic, postburns, and acne scar treatment.[5-8] Platelet-rich plasma with platelet derived and other growth factors helps in regenerating damaged soft tissue.[9]

Fractional CO_2 laser (FCL) is now well established in scar management as it provides superior results and lower side effects compared to conventional ablative lasers.[1,2,10]

As FCL creates microthermal wounding of skin, PRP is added to aid in wound healing and promote scar resolution.[11] Discordant reports in literature about efficacy of PRP exist and hence we conducted this study to compare the use of FCL monotherapy and addition of PRP in postburn and posttraumatic scar treatment.

Subjects and Methods

The study was conducted over a period of two years from Oct 2016 to Sep 2018 at a skin center of a referral hospital after obtaining ethical clearance from the

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institutional ethics committee. Patients aged 18–60 years reporting to the dermatology department with postburns or posttrauma scars were enrolled in the study [Figure 1]. Those with scars less than 6 months duration, concurrent infections or inflammatory skin disorders, known connective tissue disorders or hypersensitivity to lidocaine, history of laser or any other procedure for scars in last 06 months, keloidal/bleeding tendencies, unrealistic expectations, history of malignancy, and pregnancy/lactation were excluded.

A written informed consent was obtained from each patient before recruitment. Patients who met the eligibility criteria were randomized by draw of cards into two groups, Group I and II by a dermatologist not engaged in this study.

Prior to treatment, a topical anesthetic cream containing a combination of topical lidocaine and prilocaine (EMLA) in a cream base was applied for 1 hour on and 1 cm around the scar area. Under aseptic precautions, Group I was treated with a single pass of FCL (Cis F1-Fractional CO2 Laser, Sellas, Korea) using a pulse energy of 25 mJ, spot density of 144/cm^2, pulse interval of 0.5 mm, and pulse duration of 0.1 milliseconds. The second group was treated with FCL using the Group I settings and, in addition, intradermal injections at 1cm intervals of 0.1 ml PRP were given.[8] A two-stage centrifuge process was performed using an R8C centrifuge device (REMI Sales & Engineering Ltd. Goregaon (East), Mumbai, India) to obtain PRP. The spin speed determined using the device radius was 2316 RPM for 5 minutes-1st spin and 3538 RPM for 17 minutes-2nd spin.[12]

Four sessions of treatment were administered to each group at 4-week intervals and patients were assessed at baseline and after 4 weeks of each session by a third observer (blinded) using the Patient and Observer Scar Assessment Scale (POSAS) into the observer scale and patient scale to obtain the total POSAS score.[13] Requisite permission was obtained from POSAS group to use and quote the scale.

POSAS consists of an observer scale [Figure 2] and a patient scale [Figure 3] which includes a comprehensive list of items, based on the clinically relevant scar characteristics. Each item has a 10-point scoring ranging from "1" corresponding to normal skin to "10" implying the worst imaginable scar. The total score is calculated by adding up the scores of six items for both scales, the final score ranging from 6 to 60. An "Overall Opinion" of the scar quality is scored separately although it is not part of the total score.

Statistical analysis

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean ± standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square ($\chi 2$) test was used to find the association between two categorical variables. If the *P* value was <0.05, then the results were considered to be statistically significant; otherwise, it was considered as not statistically significant. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) software v. 23.0 and Microsoft Office 2007.

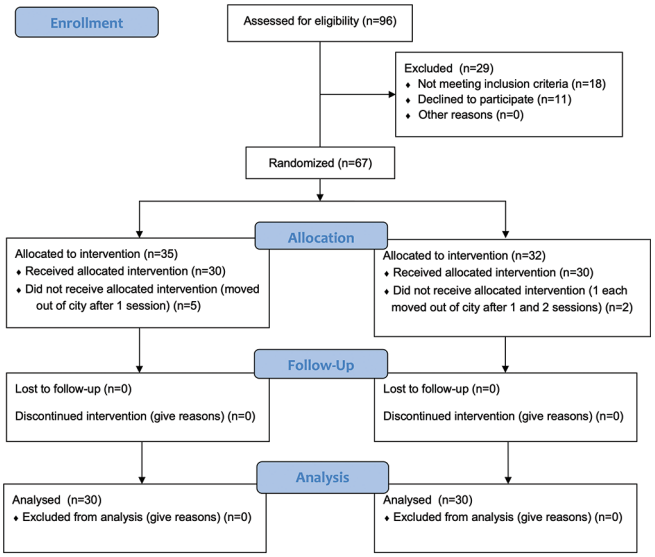

Figure 1: Study consort flow diagram

POSAS Observer Scale										
Parameter	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Vascularity										
Pigmentation										
Thickness										
Relief										
Pliability										
Surface area										
Total Score										
What is your overall opinion of the scar compared to normal skin?										

Figure 2: Observer-scale POSAS

POSAS Patient Scale										
Patient questions	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Has the scar been painful the past few weeks?										
Has the scar been itching the past few weeks?										
Is the scar color different from the color of your normal skin at present?										
Is the stiffness of the scar different from your normal skin at present?										
Is the thickness of the scar different from your normal skin at present?										
Is the scar more irregular than your normal skin at present?										
Total Score										
What is your overall opinion of the scar compared to normal skin?										

Figure 3: Patient-scale POSAS

Results

A total of 96 patients were screened and 67 were randomized into the two groups. A total of 60 completed the study [Figure 1]. Both groups were age and gender

matched with no statistical difference in number, location, and duration of scars between them [Table 1]. The commonest location of scars in both groups was the face. The mean duration of scars in Group I was 3 years and in Group II, 2.4 years.

Statistically significant difference in the quality of scars was seen when the baseline individual parameters and total scores of observer part of POSAS were compared with the final scores in each group. Before and after scores were statistically significant ($P < 0.001$) in Group I [Figures 4a, b and 5a, b] and similar results ($P < 0.001$) were seen in Group II [Tables 2 and 3] indicating improvement in the quality of scars [Figures 6a, b and 7a, b].

Similarly, a statistically significant difference in the quality of scars was noted when the baseline individual parameters and total scores of patient part of POSAS were compared with the final scores of each group, except for the parameter "painful scar."

The baseline total scores of the observer and patient part of POSAS for Groups I and II indicated that the severity of scars was similar in both the groups and that they were comparable at the initiation of treatment. However, the final scores also indicated no significant difference in the quality of scars between the two groups. This indicated that although there was a significant improvement in both the groups, the addition of PRP to FCL in Group II did not result in superior scar improvement posttreatment as compared to Group I that was treated with FCL only [Tables 4 and 5].

Pain and erythema were the commonest side effects observed in both groups with 11 affected in Group I and all 30 in Group II.

Discussion

Scar treatment is a challenge and a number of therapeutic options exist for the treating dermatologist. Among the treatment options available, literature reports successful use of lasers and nonablative devices in the management of acne scars, traumatic scars, and atrophic and hypertrophic burn scars with or without the use of PRP as an alternative to surgical correction.[7,14,15] The use of FCL in improving traumatic and burn scars is reportedly useful.[16,17] The rational for the clinical use of PRP is based on its ability to stimulate the production and subsequently, increase the concentration of growth factors and secretion of proteins which are able to improve the healing process at cellular level.[14]

We reviewed studies [Table 6] using FCL and PRP in traumatic and burn scars and also included postacne scars

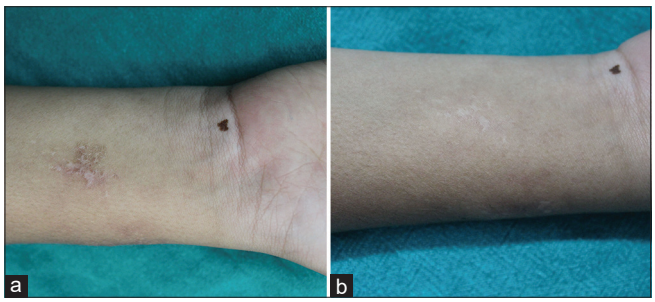

Figure 4: (a) Baseline (POSAS Observer scale 28 and Patient scale 26); (b) at 16 weeks (POSAS Observer scale 20 and Patient scale 17) in a patient of Group I

Table 1: Profile of patients

	Group I	Group II
Age (Years)*		
≤20	8	7
21-25	14	14
26-30	7	7
>30	1	2
Number of scars*		
1	23	21
2	4	7
3	2	1
>3	1	1
Location of scars*		
Face	21	21
Lower limb	3	2
Trunk	2	0
Upper limb	4	7
Cause of scars*		
Post burn	4	4
Post traumatic	26	26

*Difference between group I and II not significant (P>0.05)

Table 2: Mean POSAS observer scale parameters at baseline and week 16

POSAS observer scale parameters	Baseline		Week 16	
Group I	Mean	SD	Mean	SD
Vascularity	3.57	1.07	2.40*	0.67
Pigmentation	4.57	1.33	3.37*	0.72
Thickness	4.87	1.17	3.27*	0.94
Relief	5.23	1.01	3.47*	0.78
Pliability	4.63	1.25	3.57*	0.90
Surface area	4.97	0.61	4.47*	0.78
Overall opinion	5.50	0.73	3.77*	0.90
Total score	27.83	4.36	20.53*	3.42
POSAS observer scale parameters Group II				
Vascularity	3.52	0.96	2.29*	0.86
Pigmentation	4.32	1.25	3.26*	0.73
Thickness	5.19	1.05	3.45*	0.81
Relief	5.26	0.68	3.35*	0.80
Pliability	4.84	1.10	3.55*	0.89
Surface area	4.97	0.55	4.39*	0.84
Overall opinion	5.48	0.72	3.71*	1.04
Total score	28.10	3.91	20.29*	3.77

*Significant with level of significance (P<0.001). SD: Standard deviation

Table 3: Mean POSAS patient scale parameters at baseline and week 16

POSAS Patients scale parameters	BASELINE		WEEK 16	
Group I	**Mean**	**SD**	**Mean**	**SD**
Painful scar	1.37	0.85	1.10**	0.31
Scar itching	2.03	0.93	1.50*	0.73
Scar color different from normal skin	4.63	1.30	3.37*	0.93
Stiffness of the scar different from normal skin	4.80	1.03	3.63*	0.85
Thickness of the scar different from normal skin	4.93	1.01	3.57*	0.86
Irregular scar	5.33	1.06	3.73*	0.58
Overall opinion	5.27	0.87	3.70*	0.79
Total score	23.10	4.12	16.90*	2.77
POSAS Patients scale parameters Group II				
Painful scar	1.07	0.25	1.00**	0.00
Scar itching	1.67	0.66	1.13*	0.35
Scar color different from normal skin	4.30	1.47	3.17*	0.83
Stiffness of the scar different from normal skin	4.90	0.84	3.60*	0.93
Thickness of the scar different from normal skin	5.07	0.98	3.53*	0.86
Irregular scar	5.07	0.74	3.67*	0.76
Overall opinion	5.27	0.78	3.57*	0.82
Total score	22.07	3.26	16.10*	2.88

**Not significant with level of significance (P>0.05). *Significant with level of significance (P<0.05). SD: Standard deviation

Table 4: Mean total score of the observer part of POSAS between study groups on follow up

Total score	Group I		Group II	
	Mean	**SD**	**Mean**	**SD**
BASELINE	27.83	4.36	28.10*	3.91
WEEK 4	26.77	4.23	26.94*	4.08
WEEK 8	24.13	3.89	24.16*	4.07
WEEK 12	22.70	3.69	22.81*	3.29
WEEK 16	20.53	3.42	20.29*	3.77

*Not significant with level of significance (P>0.05). SD: Standard deviation

Table 5: Mean total score of the patient part of POSAS between study groups at different weeks

Total score	Group I		Group II	
	Mean	**SD**	**Mean**	**SD**
BASELINE	23.10	4.12	22.07*	3.26
WEEK 4	22.37	3.58	21.67*	3.11
WEEK 8	20.43	3.62	19.33*	3.10
WEEK 12	18.73	3.12	18.10*	2.90
WEEK 16	16.90	2.77	16.10*	2.88

*Not significant with level of significance (P>0.05). SD: Standard deviation

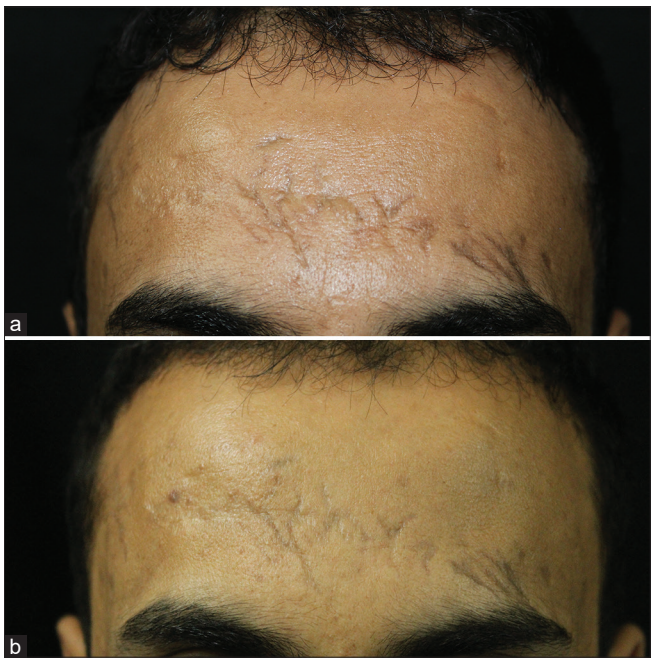

Figure 5: (a) Baseline picture (POSAS Observer scale 26 and Patient scale 20); (b) at 16 weeks (POSAS Observer scale 18 and Patient scale 16) in a patient of Group I

as fewer studies exist in the former. Acne scars are usually atrophic and thinner while posttraumatic and postburn scars are usually thicker.[16] While studies report FCL improves scars, discordance exists when PRP and FCL combination is compared to FCL alone. In studies, acne scars were noted to improve better when treated with FCL and topical PRP[6,7] or when PRP was injected.[5,7,8] Another comparative split face study done in acne scars comparing FCL and FCL with PRP did not reveal any additional PRP benefit.[18] A study conducted on posttraumatic scars showed that more than 50% treated showed moderate to excellent response,[11,19] while Faghihi *et al*. noted better scar correction on the PRP side but no statistical difference compared to FCL monotherapy.[20]

We used POSAS, a validated tool which includes both the patients' and physician's perspective, for outcome

Table 6: Review of studies on use of fractional CO_2 laser and autologous platelet rich plasma in post acne, post traumatic and post burn scars

Study	Type of study	Indication	Treatment modality	Number of patients	Duration of treatment/sessions	Scoring system used	Results
Lee JW *et al*. 2011[5]	Split-face randomized comparative study	Acne scars	Autologous PRP with Ablative CO_2 Fractional resurfacing vs Fractional CO_2 laser only	14	01 session	Chromometer Quartile grading scale	PRP and FCL: enhanced recovery of laser-damaged skin, better clinical outcomes
Gawdat H I *et al*. 2014[6]	Split-face randomized study	Atrophic acne scars	FCL and (Intradermal or topical) PRP vs FCL monotherapy	30	3 monthly sessions	GBQS	Combined PRP and FCL- significantly better response - no significant differences between intradermal and topical PRP
Arsiwala *et al*. 2019[7]	Randomized comparative study	Atrophic acne scars	FCL monotherapy versus FCL plus topical PRP	25	03 monthly sessions	GBQS VAS	FCL plus topical PRP more effective
Majid *et al*. 2015[10]	Observational study	Nonhypertrophic traumatic and burn scar	FCL	25	04 sessions at 06 weekly interval	Quartile grading scale	Excellent results with minimal adverse effects
Elsaie ML *et al*. 2018[14]	Randomized controlled trial	Postacne atrophic scars	Nonablative fractional erbium-doped glass 1540 nm and fractional ablative 10600 nm CO_2 laser	58	4 treatment sessions at 3 weeks interval	4-grade satisfaction scale	Fractional ablative laser showed higher efficacy while nonablative laser offered less pain and shorter downtime
El-Hoshy K *et al*. 2017[15]	Uncontrolled, open-label clinical trial	Mature burn scars	FCL monotherapy	20	03 sessions, at 4 to 8 weeks interval	VSS, POSAS	Effective and safe treatment method
Tawfic S *et al*. 2019[16]	Randomized study	Hypertrophic burn scars	Low, medium, and high-density FCL	25	03 monthly sessions	VSS, POSAS	High-density fractional CO_2: provides more improvement in burn scars both clinically and histopathologically
Kar BR, Raj C 2018[17]	Split-face comparative study	Acne scars	FCL and topical PRP vs FCL monotherapy	30	03,monthly sessions	GBQS	Addition of PRP - better clinical outcome (but not statistically significant)
Faghihi G *et al*. 2015[19]	Split-face randomized controlled trial	Acne scars	FCL and PRP vs FCL monotherapy	16	02 monthly session	VAS	FCL and PRP: no statistically significant synergistic effects
Present study	Randomized controlled study	Posttraumatic and postburn scars	FCL monotherapy vs FCL and PRP	67	04 monthly sessions	POSAS	Statistically significant results in both groups; difference between both groups not statistically significant

GBQS: Goodman and Baron qualitative scarring grading system, VAS: Visual Analogue Scale, VSS: Vancouver Scar Scale, POSAS: Patient and Observer Scar Assessment Scale, FCL: Fractional CO2 laser, PRP: Autologous Platelet rich plasma

assessment, by a blinded observer and demonstrated that FCL is an effective modality in posttraumatic and postburn scar treatment. The addition of PRP to FCL offered no additional benefit and was accompanied with greater side effects in the form of pain and erythema in all cases. This worsening of erythema and pain could be attributed to the accumulating evidence that demonstrates that platelets contribute to the initiation and propagation of the inflammatory process.[21] Dermal scar pain is a complex issue and it is hypothesized that nerve growth factors which

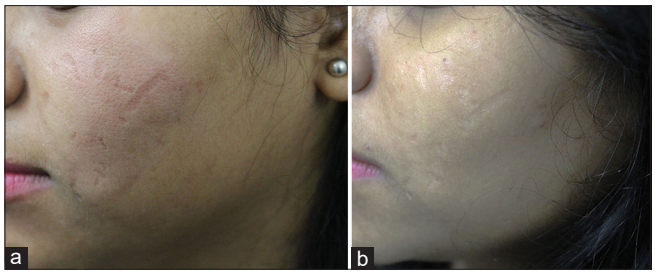

Figure 6: (a) Baseline (POSAS Observer scale 22 and Patient scale 22); (b) at 16 weeks (POSAS Observer scale 19 and Patient scale 17) in a patient of Group II

stimulate C-fibers not only play an important role in wound healing but also promote inflammation.[22] PRP despite its initial proinflammatory property is reported to help reduce this pain in the long run.[23] However, central sensitization results in long lasting pain despite adequate healing.[22] This may be the cause why our patients had persisting pain despite scar improvement on treatment. Patients in both groups observed stiffness of scar responded earliest followed by itching, thickness, and color response. The observer felt pliability and vascularity responded earlier than other parameters. We did not observe any long-term side effects.[7,10]

Thus, from this study, we concluded that the fractional CO_2 laser alone was as effective as the combination of fractional CO_2 laser with PRP. Avoiding PRP shall help reduce side effects, additional interventional procedures, and the overall cost.

Our study was limited due to the small sample size. The laser parameters were kept fixed for all scars to maintain consistency and avoid bias. This may have affected the end result as some scars may have been under or overtreated. An ideal assessment would include an ultrasonographic assessment of scar thickness to decide the laser type and its parameters.[24] Larger numbers of patient cohort, especially, for postburn scars, shall be needed to derive a final conclusion about the discordance in PRP effect and its usage.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

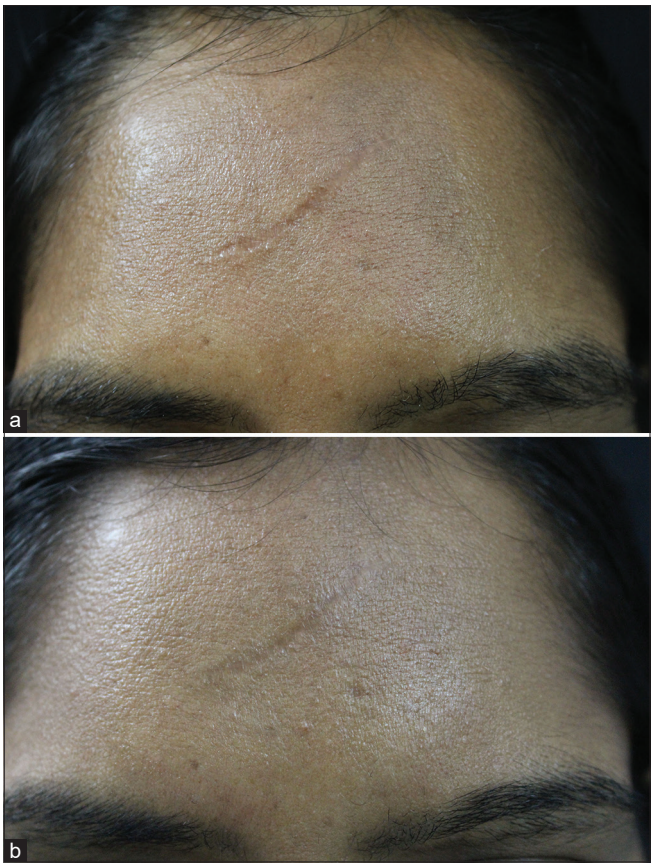

Figure 7: (a) Baseline picture (POSAS Observer scale 23 and Patient scale 19); (b) at 16 weeks (POSAS Observer scale 19 and Patient scale 15) in a patient of Group II

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