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Research Article

Assessment of Efficacy and Patient Satisfaction with Fractional CO_2 Laser in Vitiligo Treatment

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Abstract

Background: Vitiligo is a common acquired depigmenting disorder with substantial psychosocial consequences. Conventional treatments, topical immunomodulators, phototherapy, and surgical techniques often yield partial or slow repigmentation, and relapse remains frequent. ***Objective***: To assess the therapeutic efficacy of fractional carbon dioxide laser for vitiligo and to evaluate patient satisfaction. ***Method***: A single-arm interventional study was conducted in a private dermatology clinic in Iraq, from February 2024 to February 2025, enrolling consecutive adults with stable, non-segmental vitiligo of Fitzpatrick skin phototypes III–IV. Treatment consisted of fractional ablative carbon dioxide laser sessions scheduled every two to three weeks. Outcomes were evaluated at three and six months from the first session. ***Results***: Participants completed a median of six fractional CO_2 laser sessions (range 4–7). At three months, 50.0% achieved an excellent response, 26.7% a moderate response, and 23.3% a poor response. The mean patient-reported satisfaction score at three months was 3.6±1.0. By six months, 60.0% remained relapse-free. Compared with relapsers, non-relapsers were more often male (72.2% *vs*. 41.7%; p=0.018), had shorter disease duration (3.0±2.2 *vs*. 4.8±3.4 years; p=0.026), and reported higher satisfaction (4.0±0.6 *vs*. 2.9±1.1; p<0.001). The lesion site was highly correlated with outcomes (overall p<0.001). ***Conclusions***: The fractional carbon dioxide laser resulted in statistically meaningful repigmentation and was tolerated reasonably well, with favorable patient-reported satisfaction. Our findings supported site-specific counseling and treatment duration, as site-specific results differed by lesion and duration of disease.

Keywords: Ablative laser therapy; Fractional CO_2 laser; Non-segmental vitiligo; Patient satisfaction; Repigmentation; Vitiligo.

تقييم فعالية ورضا المرضى باستخدام ليزر CO_2 الجزئي في علاج البهاق

الخلاصة

الخلفية: البهاق هو اضطراب شائع لإزالة التصبغ المكتسب له عواقب نفسية اجتماعية كبيرة. غالبا ما تؤدي العلاجات التقليدية، وأجهزة تعديل المناعة الموضعية، والعلاج الضوئي، والتقنيات الجراحية إلى إعادة تصبغ جزئية أو بطيئة، ولا يزال الانتكاس متكررا. **الهدف**: تقييم الفعالية العلاجية لليزر ثاني أكسيد الكربون الجزئي للبهاق وتقييم رضا المرضى. **الطرائق**: أجريت دراسة تدخلية بذراع واحد في عيادة خاصة للأمراض الجلدية في العراق، من فبراير 2024 إلى فبراير 2025، حيث شملت بالغين متتاليين يعانون من بهاق مستقر وغير مجزئي من الأنواع الضوئية الجلدية من فيتزباتريك III–IV. تضمن العلاج جلسات ليزر ثاني أكسيد الكربون الجزئية المجدولة كل أسبوعين إلى ثلاثة أسابيع. تم تقييم النتائج بعد ثلاثة وستة أشهر من الجلسة الأولى. **النتائج**: أكمل المشاركون متوسط ست جلسات ليزر CO_2 جزئية (النطاق 4–7). بعد ثلاثة أشهر، حقق 50٪ استجابة ممتازة، و26.7٪ استجابة متوسطة، و23.3٪ استجابة ضعيفة. كان متوسط درجة الرضا المبلغ عنها من قبل المريض خلال ثلاثة أشهر 3.6. وبحلول ستة أشهر، بقي 60٪ منها خاليا من الانتكاس. مقارنة بالمكررين، كان غير الانتكاسي أكثر من الذكور (72.2٪ مقابل 41.7٪؛ p=0.018)، وكانت مدة المرض أقصر (3.0 مقابل 4.8 سنوات؛ p=0.026)، وأبلغ عن رضا أعلى (4.0 مقابل 2.9؛ ص<0.001). كان موقع الآفة مرتبطا ارتباطا وثيقا بالنتائج (p<0.001). **الاستنتاجات**: أدى ليزر ثاني أكسيد الكربون الجزئي إلى إعادة تصبغ ذات معنى إحصائي وتم تحمله بشكل معقول، مع رضا إيجابي أبلغ عنه المرضى. دعمت نتائجنا الاستشارة ومدة العلاج حسب الموقع المحدد، حيث اختلفت النتائج حسب الموقع حسب الآفة ومدة المرض.

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INTRODUCTION

Vitiligo is the most prevalent acquired depigmenting skin disorder, affecting about 0.5–2% of the world population. The selective destruction of melanocytes results in distinct chalk-white patches on the skin [1]. While vitiligo does not pose a medical health risk, the disorder is highly visible and therefore can result in devastating psychosocial effects [2]. It is much more than a cosmetic disease, as we know that patients with vitiligo develop depressive moods, scarring of self-esteem, and social stigma [3]. This profound effect on mental health and quality of life highlights the need for effective treatment strategies that can enhance patients' well-being by inducing repigmentation [4]. Managing vitiligo remains challenging. The disease has an unpredictable course with a high tendency to recur; also, the spontaneous prognosis is generally poor, and long-term control is difficult [5]. Different treatment modalities such as topical and systemic corticosteroids, calcineurin inhibitors, phototherapy (narrowband UVB), and surgical approaches (punch grafting and melanocyte transplantation) are available, but results are often incomplete and variable [6]. Standard monotherapies often do not provide adequate or long-lasting repigmentation, and treatment courses may be lengthy and many monthly [7]. The unclear pathogenesis of vitiligo and the limited responses to

current treatments create a critical need for alternative modalities that can induce faster, stronger, and more durable repigmentation. As a result, researchers and clinicians are investigating adjunctive novel treatments to improve efficacy beyond what standard therapies are capable of achieving [8]. An example of this new trend is an application of fractional carbon dioxide (CO_2) laser therapy for vitiligo. Ablative fractional CO_2 lasers cause an overlapping grid of microscopic zones of thermal injury in untreated areas of skin, which initiates a wound-healing cascade that may help restore pigment. Micro-injuries from the laser lead to the release of cytokines and growth factors during healing that might enhance melanocyte activation and migration to vitiliginous areas [9]. Fractional photothermolysis is believed to aid in repigmentation by encouraging the self-multiplication of melanocytes and providing niche space for peripherally migrating pigment cells or hair follicle melanocytes to repopulate in depigmented areas [7]. Ablative fractional CO_2 laser treatment has been thus proposed to be a novel vitiligo therapy able to accelerate repigmentation and possibly do better in resistant cases with standard therapies [5]. Fractional laser is indeed one of the effective but less invasive interventions, which enhances the topical uptake of oxygenated mediators and promotes dermal remodeling and produces tracks of coagulation, enabling it to be either a stand-alone procedure or an adjuvant to other therapies to allow more efficient repigmentation compared to standard procedures [10]. A fractional CO_2 laser combined with conventional vitiligo therapies has yielded promising results according to early clinical trials. An evidence-based study showed that mixed fractional CO_2 laser treatment after narrowband UVB phototherapy has much higher repigmentation than phototherapy alone [11]. A faster answer also enhances clinical results and patient compliance and satisfaction, provided that long treatment cycles are recognized to foster dropout and frustration in vitiligo therapy. According to the above reason, based on its property of stimulating a faster pigmentation process, a fractional CO_2 laser may promote faster treatment adherence and visible effects [12]. While fractional CO_2 lasers have shown promise in some studies as a treatment for vitiligo, the benefit may depend on the nature of the treatment protocol, vitiligo subtype, site of action, and concomitant therapies [13]. In a randomized study, addition of fractional CO_2 laser to tacrolimus ± excimer light was well tolerated but did not lead to a significant increase in repigmentation [14]. Laser: Its efficacy is context-dependent, as mixed data indicate. Due to its mild-to-moderate, transient adverse event profile and reasonable patient acceptability, most of the data supports its use in a resistant setting, particularly for use in combination therapy [15]. There is also an increasing awareness that in addition to quantitative measures of repigmentation, the achievement of patient-reported outcomes, satisfaction, and quality of life improvements are integral components for success in the treatment of vitiligo [16]. Since the ultimate goal of therapy is not only to induce repigmentation but also to improve patients' self-image and psychosocial well-being, this provides the clinical relevance of interventions that are effective and well-tolerated. This study aimed to evaluate the clinical utility of fractional CO_2 laser in treating vitiligo and evaluate patients' satisfaction with such a modality to consider a role for this approach in vitiligo management by ensuring efficacy and being patient-oriented.

METHODS

Study design and setting

This study was conducted in a private dermatology clinic in Tikrit city, Salah al-Din Province, Iraq. The data collection and treatment procedures were conducted over a period of 1 year, from February 2024 to February 2025. Sixty patients clinically diagnosed with non-segmental vitiligo affecting either cosmetic or functionally important areas were enrolled in the study population. The sample size represented all eligible consenting patients during the accrual window.

Sample size calculation

The sample size was estimated using Cochran's formula for a single proportion ($n=Z^2p(1-p)/d^2$). To ensure a robust estimate, an anticipated response rate (p) of 50% was used, as this maximizes the required sample size. Assuming a 95% confidence level ($Z=1.96$) and accepting a margin of error (d) of 12.7%, the calculated required sample size was 60 patients. Consequently, the study enrolled 60 eligible participants who presented during the study period.

Study population

We studied sixty patients with clinically diagnosed, non-segmental vitiligo affecting cosmetically or functionally relevant sites. The sample size accrued reflected all eligible, consenting patients who presented during the accrual window. Participants used a convenience sampling strategy to sequentially recruit all eligible consecutive adults with vitiligo presenting for fractional carbon-dioxide (CO_2) laser resurfacing.

Inclusion criteria

Adults aged ≥18, with Fitzpatrick skin phototype III–IV based on the patient history of sunburn/tan, were eligible, with stable disease for at least 6 months (no new lesions or increase in the size of any existing patches by >10%) and able to attend scheduled visits and utilize adequate photoprotection [17].

Exclusion criteria

The subjects were excluded if they had segmental vitiligo, active infection at the site of target, keloid diathesis, pregnancy, and lactation. Additional exclusion criteria were use of systemic retinoids within the last 6 months; topical steroids, calcineurin

inhibitors, or depigmenting agents on the target lesions within the last 2 weeks; photodermatoses; immunosuppressed patients; uncontrolled diabetes; and previous laser treatments to the same area in the last 3 months. Such criteria were selected to minimize procedure-related risk and to reduce confounding from concomitant therapies.

Laser treatment protocol

The fractional ablative CO_2 laser (wavelength: 10,600 nm) was used for all procedures, operating on the principle of fractional photothermolysis, which targets microscopic treatment zones that create areas of thermal injury, thus initiating epidermal and dermal remodeling while preserving the surrounding tissue. All target areas were cleansed, and topical aesthetic cream (lidocaine/prilocaine) was occluded for 45–60 minutes prior to treatment as necessary. Single- to dual-uniform passes were delivered over each low-to-moderate-density vitiliginous patch to minimize post-inflammatory hyperpigmentation risk in skin types III-IV and to control optimal clinical outcome. Homogeneous erythema with some pinpoint bleeding but no or little char was the clinical endpoint. Afterward, cooling treatment and a bland emollient were performed, and patients were instructed to use a gentle soap and petrolatum-based ointment within 3–5 days, not to manipulate the crusts, and to practice strict photoprotection with a broad-spectrum sunscreen. The sessions were performed every 2–3 weeks, with a planned total of 4–7 sessions based on the response of the lesions and tolerability by the patient; concomitant vitiligo therapies were temporarily discontinued during the active treatment period to isolate the effect of the laser.

Data collection

The data were collected through a standardized case-report form filled out at baseline and each visit. In particular, the variables recorded were age (years), sex, duration of disease (years), positive family history of vitiligo, Fitzpatrick skin type, anatomical location of lesions (face, face/neck, hands, wrist, neck, legs, chest, and abdomen), number of sessions delivered, and adverse effects. Self-reported immediate effects, erythema, burning, and superficial peeling were assessed at every treatment visit and during telephone follow-up in the week after treatment.

Outcome measurement

Outcome assessment combined clinician-reported response and patient-reported satisfaction, timed to minimize early procedural confounding. The primary effectiveness endpoint was treatment response at three months from the first session, judged clinically from standardized photographs under consistent lighting and camera settings. The response was categorized as excellent (50–75% repigmentation), moderate (25–50%), or poor (<25%), using lesion-level visual estimation aggregated to the patient level. Secondary outcomes included a 5-point patient satisfaction score at three months—anchored as 5 “very satisfied” (excellent repigmentation/cosmetic outcome), 4 “satisfied” (good repigmentation >50% with minor residual patches), 3 “neutral” (moderate improvement), 2 “dissatisfied” (minimal improvement <25%), and 1 “very dissatisfied” (no improvement or worsening). Another secondary outcome was relapse status at six months from the first session, defined as re-loss of pigment in a previously repigmented treated area (≥25% decrease from peak repigmentation) or the appearance of new depigmented macules contiguous with the treated border, confirmed clinically against photo-documentation.

Ethical considerations

The study protocol was approved by the Research Ethics Committee of the College of Medicine, Tikrit University (Certificate No. 430 in January 2024), and conducted in accordance with the Declaration of Helsinki. Consent was obtained from each participant before enrollment in the study.

Statistical analysis

R software packages were used for data processing, visualization, and statistical analysis ("R version 4.2.2"). Descriptive statistics summarized continuous variables as mean ± SD, and, where skewed, median (range); categorical variables were tabulated as counts and percentages. Between-group comparisons used Welch’s t-test for unequal variances, Pearson’s chi-square test, or Fisher’s exact test as appropriate. Comparisons across the three response categories used one-way ANOVA for continuous variables and chi-square/Fisher’s exact tests for categorical outcomes, and two-sided $p< 0.05$ denoted statistical significance.

RESULTS

The cohort’s age averaged 36.7 ± 12.2 years with a median of 36.5 years (range, 19–55). Males constituted 60.0% (n=36) and females 40.0% (n=24). Over half of the patients reported a positive family history (56.7%), with a mean disease duration of 3.7 ± 2.8 years. Skin phototypes were predominantly type 4 (60.0%), followed by type 3 (40.0%). Lesions most frequently involved the face and hands (each 26.7%), with additional involvement of the face/neck (20.0%) and less commonly the legs, neck, and wrist (each 6.7%); the abdomen (3.3%); and the chest (3.3%) as presented in Table 1. Table 2 summarized therapeutic dosing and short-term outcomes following fractional CO_2 laser. Participants completed a median of six sessions (mean: 5.5 ± 0.8; range: 4-7). Over the three months, approximately half achieved an excellent clinical response, with the remainder split between moderate and poor improvement. The mean patient-reported satisfaction on a five-point scale was 3.6 ± 1.0, reflecting generally favorable perceptions.

Table 1: Baseline demographic characteristics of the study cohort clinical profile and lesion distribution at baseline (n=60)

Characteristic	Result
Age (year)	36.7±12.2
Median (range)	36.5(19-55)
Sex	
Male	36(60)
Female	24(40)
Positive Family history	34(56.7)
Duration of vitiligo (year)	3.7±2.8
Skin type	
Type 3	24(40)
Type 4	36(60)
Location of the lesion	
Face	16(26.7)
Hands	16(26.7)
Face and neck	12(20)
Legs	4(6.7)
Neck	4(6.7)
Wrist	4(6.7)
Abdomen	2(3.3)
Chest	2(3.3)

Values are presented as frequency, percentage, and mean±SD.

Table 2: Treatment exposure, early response, satisfaction, and six-month relapse (n=60)

Characteristic	Result
Number of CO_2 laser sessions	5.5±0.8
Median (range)	6.0(4.0-7.0)
Co_2 laser response	
Excellent	30(50)
Moderate	16(26.7)
Poor	14(23.3)
Patient's satisfaction score (after 3 months)	3.6±1.0
Relapse rate (after 6 months from last cession)	
No relapse	36(60)
Relapse	24(40)

Values are presented as frequency, percentage, and mean±SD.

Table 3: Comparative characteristics by six-month relapse status

Characteristic	No relapse (n=36)	Relapse n=24)	*p*-value*
Age (year)	38.1±12.4	34.6±11.8	0.3
Sex			
Male	26(72.2)	10(41.7)	0.018
Female	10(27.8)	14(58.3)	
Duration (year)	3.0±2.2	4.8±3.4	0.026
Location			
Face	16(44.4)	0(0.0)	<0.001
Hands	2(5.6)	14(58.3)	
Face and neck	10(27.8)	2(8.3)	
Legs	0(0.0)	4(16.7)	
Neck	4(11.1)	0(0.0)	
Wrist	4(11.1)	0(0.0)	
Abdomen	0(0.0)	2(8.3)	
Chest	0(0.0)	2(8.3)	
Positive family history	20(55.6)	14(58.3)	0.8
Skin type			
Type 4	22(61.1)	14(58.3)	0.8
Type 3	14(38.9)	10(41.7)	
Number of sessions	6(4.0-7.0)	5(4.0-6.0)	0.015
Treatment response			
Excellent	30(83.3)	0(0.0)	<0.001
Moderate	6(16.7)	10(41.7)	
Poor	0(0.0%)	14(58.3)	
Satisfaction score (after 3 months)	4.0±0.6	2.9±1.1	<0.001

Values are presented as frequency, percentage, and mean±SD. *Welch two sample t-test; Pearson's Chi-squared test; Fisher's exact test.

At six months after the last session, 60% remained relapse-free, whereas 40% exhibited relapse. When six-month outcomes were compared, age did not differ significantly between groups (p= 0.3), whereas sex distribution did, with a higher proportion of males in the no-relapse group and more females among relapsers (p= 0.018). Disease duration was longer in the relapse group (4.8 ± 3.4 *vs*. 3.0 ± 2.2 years; p= 0.026). The lesion site showed strong divergence: facial lesions predominated in the no-relapse group, while hand, leg, abdominal, and chest involvement was concentrated among relapsers (overall p< 0.001). Patients without relapse completed more sessions (median 6.0 *vs*. 5.0; p= 0.015), achieved markedly better clinical responses (83.3% excellent *vs*. 0.0%; p< 0.001), and reported higher satisfaction at three months (4.0 ± 0.6 *vs*. 2.9 ± 1.1; p< 0.001). Family history and Fitzpatrick skin type distributions were comparable (both p= 0.8) as seen in Table 3. Across treatment-response strata, age differed only nominally and did not reach statistical significance (p= 0.064) and sex distribution did not differ (p= 0.30). Disease duration was longest among poor responders (5.6 ± 3.1 years) versus excellent and moderate groups (3.3 ± 2.3 and 2.9 ± 2.9 years; p= 0.010). The lesion site was strongly associated with the outcome (p< 0.001); facial involvement predominated in excellent responders (46.7%), whereas hand lesions characterized the poor-response group (100%).

Legs, abdomen, and chest were observed only among moderate responders, and neck lesions appeared only in the excellent group. Skin phototypes distribution (type IV *vs*. III) and number of sessions (median: 6.0 *vs*. 5.0) were not significantly different (p= 0.10 and p= 0.40, respectively). Patient-reported satisfaction followed a clear gradient (4.2 ± 0.4 excellent; 3.4 ± 0.7 moderate; 2.4 ± 1.1 poor; p< 0.001), mirrored by relapse rates at follow-up (0.0%, 62.5%, and 100.0%; p< 0.001) as presented in Table 4. Visual Assessment of Repigmentation As shown in figure 1, successful treatment was defined as the return of color in the repigmented area. In the representative example (Figure 1A), the baseline presentation was comprised of sharply demarcated, ivory white macules, appearing chalky compared to the patient's Fitzpatrick IV skin.

Table 4: Patient and treatment characteristics stratified by three-month response

Characteristic	Excellent (n=30)	Moderate (n=16)	Poor, (n=14)	*p*-value*
Age (year)	39.2±12.6	30.6±11.4	38.1±10.4	0.064
Sex				
Male	20(66.7)	10(62.5)	6(42.9)	0.3
Female	10(33.3)	6(37.5)	8 (57.1%)	
Duration (year)	3.3±2.3	2.9±2.9	5.6±3.1	0.010
Positive family history	16(53.3)	12(75)	6(42.9)	0.2
Location				
Face	14(46.7)	2(12.5)	0(0.0)	<0.001
Hands	2(6.7)	0(0.0)	14(100)	
Face and neck	8(26.7)	4(25)	0(0.0)	
Legs	0 0.0)	4(25)	0(0.0)	
Neck	4(13.3)	0(0.0)	0(0.0)	
Wrist	2(6.7)	2(12.5)	0(0.0)	
Abdomen	0(0.0)	2(12.5)	0(0.0)	
Chest	0 (0.0)	2(12.5)	0(0.0)	
Skin type				
Type 4	20(66.7)	6(37.5)	10(71.4)	0.10
Type 3	10(33.3)	10(62.5)	4(28.6)	
Number of sessions	6(4.0-7.0)	5(4.0-7.0)	5(4.0-6.0)	0.4
Satisfaction Score	4.2±0.4	3.4±0.7	2.4±1.1	<0.001
Relapse rate	0(0.0)	10(62.5)	14(100)	<0.001

Values are presented as frequency, percentage, and mean±SD. *Welch two sample t-test; Pearson's Chi-squared test; Fisher's exact test.

According to the treatment protocol (Figure 1B), the lesions showed significant follicular and marginal response with coalescing islands of pigment replacing zones of the earlier depigmented patches. Long-term follow-up confirmed that no atrophy or scarring had occurred and that significant post-inflammatory hyperpigmentation had not developed, supporting the safety of the fractional CO_2 parameters used, with smooth post-treatment skin texture. While some patients exhibited diffuse marginal repigmentation, others demonstrated a distinct perifollicular pattern, as seen in Figure 2. In these cases, the fractional CO_2 laser successfully stimulated melanocytes residing in the hair follicle bulges. This is clinically evidenced by the appearance of numerous pigmented macules ("islands") appearing centrally within the white vitiligo patches (Figure 2B). Over the three-month follow-up, these follicular islands expanded and began to coalesce, reducing the overall surface area of the depigmentation and confirming the preservation of the follicular reservoir in these responders. Following fractional CO_2 laser treatment, post-procedural complications were common but predominantly mild and self-limiting. Erythema and pinpoint bleeding each affected all 60 patients (100%); erythema was mostly mild to moderate (50.0% and 41.7%, respectively) with only 8.3% severe, while pinpoint bleeding was uniformly mild in every case. Post-inflammatory hyperpigmentation was the next most notable effect, occurring largely in mild form (83.3%), with moderate (11.7%) and severe (5.0%) presentations being uncommon. Importantly, no scarring was recorded in any patient (0%), indicating a favorable safety profile for the procedure.

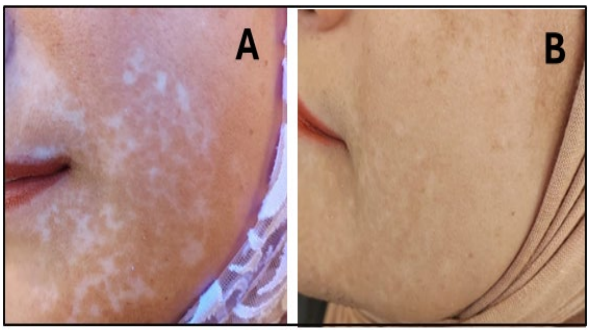

Figure 1: Representative vitiligo lesion pre-treatment (**1A**) and 3 months post-treatment (**1B**) following fractional CO_2 laser therapy.

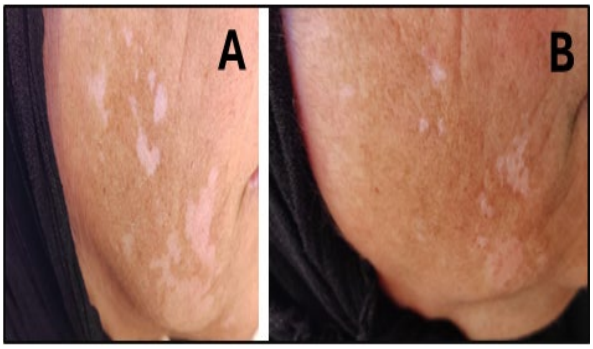

Figure 2: Representative vitiligo lesion pre-treatment (**A**) and 3 months post-treatment (B) following fractional CO_2 laser therapy.

Overall, the pattern suggests that adverse effects are frequent yet generally low-grade and transient, with serious complications being rare, as presented in Table 5.

Table 5: Frequency and severity of complications following fractional CO_2 laser treatment (n=60)

Side Effect	Mild	Moderate	Severe	Total
Erythema	30(50)	25(41.7)	5(8.3)	60(100)
Pinpoint bleeding	60(100)	0(0.0)	0(0.0)	60(100)
Post-inflammatory hyperpigmentation	50(83.3)	7(11.7)	3(5)	50(100)
Scarring	0(0.0)	0(0.0)	0(0.0)	0(0.0)

Data are presented as number (percentage). n= total number of patients.

DISCUSSION

The study documents clinically relevant repigmentation after fractional CO_2 laser delivered over a median of six sessions, with approximately half of patients classified as excellent responders at three months and a mean satisfaction score indicative of a generally positive patient experience. Relapse at six months affected two in five patients and was patterned by baseline and procedural variables: superior outcomes in facial lesions, poorer outcomes in hand lesions, longer disease duration among poor responders and relapsers, and a higher median session count in the non-relapse group. These observations are consistent with major biological and clinical determinants of vitiligo response described previously [18]. Modern syntheses classify fractional CO_2 as a viable choice, particularly in combination as an adjuvant for stable, treatment-refractory vitiligo, exploiting microthermal zones to incite melanocyte travel from follicular reserves and to modulate local cytokine milieus. The effectiveness of fractional CO_2 is supported by meta-analytic evidence from Acta Dermato-Venereologica [10], although protocols varied greatly and it was often used in combination with other treatments. Narrative reviews by Post et al. [18] have similarly highlighted the improved outcomes in selected patients, as well as careful parameter tailoring for dark phototypes, with promising results. Short-term response rates now follow these trends, and the satisfaction gradient (excellent > moderate > poor responders) is methodologically aligned with patient-centered measurement guidance (favoring 5-point Likert anchors) and the Vitiligo Noticeability Scale (VNS) [10,18-21]. Our results describing an anatomical gradient in response to therapy better response in facial lesions vs. hands are consistent with previous as well as recent findings [22,23]. The high density of follicular units serving as melanocyte reservoirs and those that aid in re-epithelialization and dispersion of pigment after fractional photothermolysis are biologically favorable in facial skin compared to acral sites, which are poorly represented by appendageal structures, and a thicker stratum corneum, which is known to inhibit repigmentation [24]. This finding supports reviews and distribution studies that regularly demonstrate strong facial and truncal responses, in contrast to the recalcitrance of the hands and feet to most treatment modalities including laser and phototherapy [18,25,26]. This anatomical limitation may explain the relative burden of negative outcomes and recurrence in hand lesions in this population, highlighting the need for site-stratified patient counseling and intervention protocol [27]. The negative correlation between disease duration and early repigmentation and the positive correlation between disease duration and relapse argue for a pathophysiologic basis, given the likelihood of persistence of autoimmune damage to melanocytes within the skin and depletion of follicular melanocyte reserves over time. Comparison of durability across studies is complicated because, and this hampers direct comparisons, relapse is variably defined (e.g., greater than 10% re-depigmentation compared to new lesions adjacent to treated borders) [28]. In any event, the greater median session number for non-relapsers in this cohort suggests a cumulative-dose effect, more macro- and microthermal coverage, and repeated *in vivo* activation of regenerative pathways—although confounding by indication (i.e., easier sites receiving more sessions) cannot be excluded. Several recent works, including those that focus on candidate biomarkers and imaging-based predictors of recurrence, underscore the need to harmonize definitions of relapse, as well as extended follow-ups in future studies [29, 30]. Evidence from randomized and prospective studies, as well as syntheses, indicates that pairing a fractional CO_2 laser with narrowband UVB, topical corticosteroids or calcineurin inhibitors, or platelet-rich plasma can achieve greater repigmentation than single-modality therapy, including on difficult sites. Superior improvements on the Vitiligo Area Scoring Index have been reported when fractional CO_2 is used as an adjunct, and recent systematic reviews highlight additional benefits with PRP combinations [7,10,31,32]. Because the present protocol deliberately withheld concomitant treatments to isolate the laser effect, the observed response and relapse figures likely represent conservative estimates relative to optimized combination regimens; this helps contextualize the six-month relapse rate and suggests a practical, testable route to improving durability. The adverse-event profile of transient erythema, burning, and superficial peeling matches expectations for fractional ablative CO_2. Reviews emphasize cautious parameter selection in Fitzpatrick III–IV to mitigate post-inflammatory hyperpigmentation and to avoid over-treatment, supporting the study's conservative density and 2–3-week spacing. This alignment with safety guidance reinforces the generalizability of the observed tolerability [33].

Study Limitations

This study has several limitations that should be considered when interpreting the findings. First, the single-arm design without a control or comparator group limits causal inference and precludes direct comparison with established therapies such as narrowband UVB phototherapy or topical tacrolimus. Second, the nonrandomized convenience sampling from a single center may introduce selection bias and limit the generalizability of the results. Third, treatment outcomes were assessed using a combination of clinician-evaluated photographs and patient-reported satisfaction measures rather than exclusively validated vitiligo-specific outcome instruments, which may affect the consistency of efficacy assessment. In addition, laser parameters were individualized according to clinical requirements, reducing protocol standardization and limiting dose–response analysis. The six-month follow-up period was sufficient to evaluate short-term efficacy and safety but inadequate to determine the long-term durability of repigmentation or relapse rates. Finally, variations in lesion location

and disease duration may have acted as potential confounding factors influencing treatment response.

Conclusion

Fractional CO_2 laser appears to be a potentially effective and well-tolerated modality for inducing repigmentation in selected patients with vitiligo. However, controlled studies with standardized outcome measures and longer follow-up are required to confirm these findings.

Conflict of interests

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Data sharing statement

The data that supports the findings of this study are available from the corresponding author upon a reasonable request.

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