

# Fractional CO<sub>2</sub> laser therapy for vulvar lichen sclerosis in adults

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**Background:** The CO<sub>2</sub> laser has been used to treat vulvar lichen sclerosis (VLS) with a significant reduction in symptoms, and there is a paucity data on the efficacy, sexual function, and quality of life (QOL) improved. This study was to evaluate the efficacy of fractional CO<sub>2</sub> laser for VLS and assess sexual function and QOL from multi-centers. **Methods:** The women with biopsy-proved VLS who were treated with CO<sub>2</sub> fractional laser were enrolled between January 2017 and December 2018 from three centers. The visual analogue scale (VAS) was to assess clinical symptoms. The Female sexual distress scale-revised (FSDS) was to evaluate the patients' sexual activity, and the family Dermatology Life Quality Index (DLQI) was to evaluate the QOL. **Results:** A total of 119/122 patients (mean 44.5 years, 27–72 years) completed the treatment with fractional CO<sub>2</sub> laser and following-up. The clinical symptoms and QOL were improved significantly from baseline to follow-up (3 months and 12 months post-treatment) according to the following measures: itching score, 7.65 (1.07, 0–10) versus 4.52 (1.23, 0–10) versus 0.96 (1.49, 0–4); burning score, 6.9 (1.66, 0–10) versus 3.82 (1.79, 0–8) versus 0.98 (1.42, 0–4); DLQI score, 14.24 (5.64, 0–30) versus 8.7 (1.9, 0–15) versus 5.7 (2.3, 0–10); FSDS score, 15.48 (11.3, 0–51) versus 12.51 (10.59, 0–45) versus 7.87 (9.34, 0–50). **Conclusion:** In conclusion, the fractional CO<sub>2</sub> laser was effective and safe for treating VLS, which significantly ameliorated the annoying symptoms and improved the quality of life.

## Keywords

Fractional CO<sub>2</sub> laser; Vulvar lichen sclerosis; Efficacy

## 1. Introduction

Vulvar lichen sclerosis (VLS) (also named vulvar dystrophy) is characterized by atrophy of the vulva, hyperkeratosis, and scarring. VLS is an underrecognized and underdiagnosed disease [1], which occurs in all age groups. The mean age of onset is the mid to late 50 s, with approximately one-third of cases occurring in patients under 50 years old [2, 3]. Between 1991 and 2011, the incidence rate of VLS was 10.4 cases per 100,000 women-years and comparable incidence rates of VLS, ranging from 11.7 to 24.4 cases per 100,000 women-years, for patients between 50 and 59 years of age,

have been found [2]. The aetiology of VLS is still mostly unknown. The principal symptom is itching, followed by burning and dyspareunia, in its most severe form, pallor and scarring of the skin of the anogenital region is present [4]. VLS causes a deterioration in the quality of life and if untreated, it is associated with a 2–6% lifetime risk of squamous cell carcinoma of the vulva [5].

Though potent steroids are considered the most effective treatment, robust evidence concerning the superiority of potent steroid at least over calcineurin inhibitors is still lacking the field of VLS [4]. And it may increase the risk of malignant transformation [5]. The Fractional CO<sub>2</sub> laser could improve blood flow in vaginal tissues, improve the extracellular matrix of the mucosal structures, reduce frequent infection and chronic vaginitis [6]. It has been used to treat vaginal atrophy with a significant reduction in symptoms [7]. Laser therapy may result in remodelling of vaginal connective tissue and thickening and improved glycogen storage of the vaginal epithelium in women with vaginal atrophy [8]. However, the cohorts from previous studies were small or from a single centre. This study was to evaluate the efficacy of fractional CO<sub>2</sub> laser treatment for VLS and assessed sexual function and quality of life (QOL) from multi-centres.

## 2. Materials and methods

This multi-centre, open-label, non-comparative study was conducted between January 2017 and December 2018 at three centers. Women with biopsy-proven VLS who were treated with a CO<sub>2</sub> fractional laser procedure were enrolled. This study was approved by the Ethics Committee and the Institutional Review Board of our hospital (No: 2017-02) and written consent was obtained from each patient.

The inclusion criteria included women older than 18 years, were diagnosed by biopsy with VLS, ever treatment or not, being symptomatic such as itching, burning, leukoderma (pallor), or hyperkeratosis. The exclusion criteria included

**Table 1. Demographic and clinical characteristics of the patients enrolled.**

Number	Mean age	Mean duration	Previous topical therapies used			
	(years)	(years)	Corticosteroids n (%)	Herbs n (%)	Hormones n (%)	Focused ultrasound n (%)
Patients	Range (SD)	Range (SD)				
119	44.5 ± 13.1 (27–72)	3.5 ± 5.1 (1–10)	89 (74.8)	78 (65.5)	20 (16.8)	27 (22.7)

women who had received medications during treatment cycles or during follow-up, and women who had acute genital infections or vulvar neoplasia.

The following characteristics were recorded for all patients: historical features, including age and menopausal status (premenopausal, postmenopausal with/without hormone therapy, duration of symptoms, and previous treatment). Objective parameters, including itching, burning, leukoderma (pallor), and hyperkeratosis, were considered to assess the clinical features and severity of the disease. Objective evaluation of each parameter was performed by the researchers using the visual analogue scale (VAS) to assess vulvar symptoms, where 0 indicated no symptoms and 10 indicated very severe symptoms, or the following 4-point scale was used: 0 = absence of symptoms, 1 = mild symptoms, 2 = moderate symptoms, and 3 = severe symptoms. The female sexual distress scale-revised (FSDS-R) was used to evaluate the patients' sexual activity on a scale of 0 (not at all relevant) to 4 (extremely relevant) [9]. The family Dermatology Life Quality Index (DLQI) was used to evaluate the patients' quality of life (QOL) on a scale of 0 (not at all) to 3 (very much) [10].

The treatment utilized a hand-held, forked probe that facilitated an accurate focal length of the delivered laser beam. The laser was scanned in a boxlike pattern to encompass the entirety of the involved vulva tissue. Settings for the vulvar laser treatment were as follows: watts, 20; time, 1000 microseconds; and width, 1000 micrometres. Treatment cycles included 3 laser treatment sessions at monthly intervals. Follow-ups occurred at 3 months and 12 months posttreatment. The CO<sub>2</sub> laser equipment was provided by Cynosure, Westford, MA and was manufactured by DEKA, Florence, Italy, under the trade name Monalisa Touch® SmartXide V2LR.

At the follow-up visits, the following features were recorded: subjective symptomatic response to treatment, objective clinical response to treatment, and adverse effects. The mean scores of the symptoms and disease indicators as well as the prevalence of each clinical parameter were evaluated.

ANOVA and Pearson correlation coefficient were used to determine the correlation of the continuous scales with categorical and continuous variables respectively, which was conducted using SPSS, version 20.0 (SPSS version 22.0; SPSS Inc, Chicago, IL, USA). A *p* value < 0.05 defined statistical significance.

### 3. Results

122 patients were enrolled in the study. The fractional CO<sub>2</sub> laser treatment was performed in three sessions with 30 days between each treatment session. Every patient underwent history and physical examination before laser therapy. The examination included a pathological examination of the vulva. During the treatment, three patients experienced redness and swelling; the treatments were stopped, and they withdrew from the study. Ultimately, a total of 119 patients (mean age, 44.5 years; range, 27–72 years) completed the fractional CO<sub>2</sub> laser treatment and follow-up.

The mean duration of symptoms before presentation was 3.5 years (range, 1–10 years). A total of 64 (53.8%) patients were premenopausal, 35 (29.4%) patients were postmenopausal and not using hormone therapy, and 20 (16.8%) patients were postmenopausal using either topical or systemic hormone therapy. Most of these patients had undergone previous treatment for VLS, such as corticosteroids, herbs, hormones, and focused ultrasound. Most of the patients had previously undergone more than one therapeutic method (see Table 1). Symptoms were present in all patients at the beginning of the study; the most frequent symptom was itching (105 patients, 88.2% of total), while 87 patients (73.1%) complained of burning. Leukoderma (pallor) was the most frequent finding (92 patients, 77.3% of total). Hyperkeratosis was found in 45 patients (37.8%). During the 12-month follow-up, 4 patients did not improve, and 115 patients improved the symptoms with different degree. These 4 patients had a history of more than 3 years of VLS and undergone treatments with corticosteroids, herbs and hormones. The mean baseline itching score was 7.65 (1.07, range 0–10), and post-treatment, it was 4.52 (1.23, range 0–10) (3 months post-treatment) and 0.96 (1.49, range 0–10) (12 months post-treatment), which indicated significant improvement (*p* < 0.001). The mean baseline burning score was 6.9 (1.66, range 0–10), and post-treatment, it was 3.82 (1.79, 0–8) (3 months post-treatment) and 0.98 (1.42, range 0–4) (12 months post-treatment), which indicated significant improvement (*p* < 0.001). The mean baseline leukoderma (pallor) score was 2.45 (0.81, range 0–3), and post-treatment, it was 1.26 (0.75, range 0–3) (3 months post-treatment) and 0.5 (0.7, range 0–4) (12 months post-treatment), which indicated significant improvement (*p* < 0.001). The mean baseline hyperkeratosis score was 1.24 (0.73, range 0–3), and post-treatment, it was 0.53 (0.58, range 0–2) (3 months post-treatment) and 0.34 (0.51, range 0–4) (12 months post-treatment), which indi-

**Table 2. Tertiary efficacy endpoint: mean symptom and sign improvement at 3 and 12 months compared with baseline.**

Parameter	Baseline mean value	3 months mean value	12 months mean value	p value
	(SD) [range]	(SD) [range]	(SD) [range]	
Itching <sup>a</sup>	7.65 ± 1.07 (0–10)	4.52 ± 1.23 (0–10)	0.96 ± 1.49 (0–10)	<0.001
Burning <sup>a</sup>	4.51 ± 1.66 (0–10)	2.35 ± 1.79 (0–8)	0.76 ± 1.42 (0–4)	<0.001
Leukoderma <sup>b</sup> (pallor)	2.45 ± 0.81 (0–3)	1.26 ± 0.75 (0–3)	0.5 ± 0.7 (0–3)	<0.001
Hyperkeratosis <sup>b</sup>	1.24 ± 0.73 (0–3)	0.53 ± 0.58 (0–2)	0.34 ± 0.51 (0–2)	0.016*

SD, Standard deviation. <sup>a</sup> Calculated as VAS from 0 to 10. <sup>b</sup> Calculated with a 4-point scale: 0 = absence, 1 = mild, 2 = moderate, 3 = severe. \*The score of 3 months and the baseline was 0.016, and the score of 12 months and the baseline was <0.001.

**Table 3. Outcomes of DLQI and FSDS at 3 and 12 months compared with baseline.**

Parameter	Baseline mean value	3 months mean value	12 months mean value	p value
	(SD) [range]	(SD) [range]	(SD) [range]	
DLQL	14.24 ± 5.64 (0–30)	8.7 ± 1.9 (0–15)	5.7 ± 2.3 (0–10)	<0.001
FSDS	15.48 ± 11.3 (0–51)	12.51 ± 10.59 (0–45)	7.87 ± 9.34 (0–50)	0.031 0.001*

\*the score of 3 months and the baseline was 0.016, and the score of 12 months and the baseline was 0.001.

cated significant improvement ( $p = 0.016$  and  $p < 0.001$ , respectively). The above results were shown in Table 2.

The mean baseline DLQL score was 14.24 (5.64, range 0–30), and post-treatment, it was 8.7 (1.9, range 0–15) (3 months post-treatment), and 5.7 (2.3, range 0–10) (12 months post-treatment), which indicated significant improvement ( $p < 0.001$ ). The mean baseline FSDS score was 15.48 (11.3, range 0–51), and it was 12.51 (10.59, range 0–45) (3 months post-treatment), and 7.87 (9.34, range 0–50) (12 months post-treatment), which indicated significant improvement ( $p = 0.031$  and  $p = 0.001$ , respectively). The above results were shown in Table 3.

#### 4. Discussion

Our study found that itching, burning and leukoderma (pallor) were the most common features of VLS, in accordance with similar studies, and that itching was the most common symptom based on the VLS, mean score, also in accordance with previous reports [11, 12]. The fractional CO<sub>2</sub> laser treatment significantly decreased the bothersome symptoms (itching, burning, leukoderma and hyperkeratosis) of VLS and improved the physical and mental QOL scores of most patients, which was consistent with previously published studies [7, 13, 14].

Most patients enrolled in previously published studies were postmenopausal women [7, 8, 13, 14], however, most patients in our study were premenopausal women (mean age 44.5 ± 13.1 years). In addition, one study from China also showed that the age of onset of VLS peaked at 25–30 years; the reason for this might be that most of the patients

were urban females who had better health-care awareness and more timely diagnosis of VLS [15]. Most of these patients had undergone previous treatment, such as corticosteroids, herbs, hormones, and focused ultrasound, for VLS, and most of them had undergone more than one therapeutic method. There was an interesting phenomenon in that four patients with VLS, who were premenopausal (mean age 35 ± 5.6 years), underwent fractional CO<sub>2</sub> laser treatment, and the VLS remained recalcitrant.

Lichen sclerosis was characterized by the creation of inflammation and eventually severe scar tissue formation leading to shrinkage, or atrophy, of the tissue. It was well known that topical corticosteroid (TCS) was an effective and safe treatment for VLS [16]; however, even potent TCS cannot achieve complete control of the disease in some VLS cases [17]. CO<sub>2</sub> laser treatment had been approved for various conditions by the FDA and the scientific literature dating back to the 1980s had demonstrated the advantages of the CO<sub>2</sub> laser wavelength with respect to safety as well as precision vaporization and cutting [18, 19]. Since the 1980s, a number of studies had shown that CO<sub>2</sub> laser therapy was an effective method of treatment in VLS [7, 8, 13, 14, 17, 20, 21].

The mechanism of the carbon dioxide action is that the laser absorbs light energy through water molecules in the epidermis, leading to heat accumulation and subsequent ablation of the epidermis and superficial dermis [20]. Fractional CO<sub>2</sub> laser treatment not only ablated the hyperkeratotic epidermis but also had a residual thermal effect on the underlying dermis [17], which could stimulate the production of new collagen and elastic fibres, thus remodelling tissue prop-

erties [22]. In theory, fractional CO<sub>2</sub> laser treatment may be more effective for recalcitrant VLS. In 2015, Lee reported 4 patients with recalcitrant VLS in which carbon dioxide laser was successful in achieving remission and maintained on topical steroids to prevent recurrence [17], and 3 of the 4 patients were postmenopausal. Whether fractional CO<sub>2</sub> laser treatment of premenopausal VLS patients is necessary and effective should be further studied.

This study demonstrated that fractional CO<sub>2</sub> laser treatment was associated with significant improvement in the quality of sex life, which was consistent with previous publications [13, 14]. However, more than half of the women in our study were premenopausal, and the mean baseline FSDS scores (15.48 ± 11.3) were less than those of similar studies [23–25]. This might be due to cultural reasons as sexual intercourse is relatively taboo in elderly women in China, and most women were unwilling to discuss their sexual activity.

One strength of our study was the use of specific standardized questionnaires to evaluate patients' quality of life and sexual function. We also added a subjective evaluation based on patients' perception of VLS symptoms, however, there may be low intrarater reliability in scoring activity of VLS patients. Compared with other single-centre studies, the patients enrolled in our study were from three hospitals. However, the follow-up in our study was completed at 12 months post-treatment, which was relatively shorter than in previous studies. And the future studies should emphasize patient age and VLS-duration stratification with longer follow-up.

## 5. Conclusions

In conclusion, the fractional CO<sub>2</sub> laser treatment was effective and safe for treating VLS, and it significantly ameliorated the annoying symptoms associated with VLS and improved patients' quality of life.

## Author contributions

XJW: Data acquisition, writing initial draft, and statistical analysis. YSC, LWW and ZL: CO<sub>2</sub> laser performed, data analysis and interpretation; YSC and KQH: Conception and design; KQH: Writing critical revision, and supervision. All authors read and approved the final manuscript.

## Ethics approval and consent to participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Institutional Review Board and Ethics Committee of Obstetrics and Gynecology Hospital of Fudan University (No: 2017-02).

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## Conflict of interest

The authors declared no conflict of interest.

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