Original Research

Carbon Dioxide Nonablative Laser Compared with Topical Clobetasol for Lichen Sclerosus

A Randomized Controlled Trial

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OBJECTIVE: To compare nonablative carbon dioxide (CO_2) laser treatment with topical clobetasol propionate for symptom control in women with vulvar lichen sclerosus (LS).

METHODS: We conducted a prospective, randomized, open-label trial that included women with symptomatic LS. Participants were randomized to three courses of CO_2 laser treatment every 3 weeks or to a 3-month regimen of tapered topical clobetasol propionate 0.05%. The primary outcome was the change in the BIP (burn-itch-pain) score (range 0–30) from baseline to 3 months. Secondary outcomes included physician-rated visual improvement and overall improvement, and disease-specific quality of life (QOL). Ninety participants per group provided 90% power to detect a 2-point between-group BIP score difference (SD 4; 2-sided $\alpha=0.05$). Analyses were intention-to-treat. Prespecified multivariable linear regression adjusted for baseline symptom severity, age, body mass index (BMI), smoking status, previous corticosteroid use, and disease duration.

RESULTS: Between November 2021 and March 2025, 245 women were randomized (laser: n=123; clobetasol propionate: n=122). At 3 months, symptom improvement was greater in the laser group (median ΔBIP score −8 [IQR −13 to−3]) than in the clobetasol propionate group (−5 [IQR, −10.75 to 0]; P=.007). In the multivariable analysis, laser treatment remained independently associated with greater symptom improvement (adjusted β, −2.90; 95% CI, −4.64 to −1.15; P=.001). Physician-rated visual improvement and overall improvement, and disease-specific QOL change favored laser therapy. Both treatments were generally well tolerated, with no serious treatment-related adverse events. During an exploratory postrandomization phase after the 3-month primary endpoint assessment, participants could choose to cross over to the alternative treatment. Patients who crossed over from clobetasol propionate to laser experienced additional symptom improvement from 3 to 6 months. Results were robust to sensitivity analyses for missing outcome data.

CONCLUSION: Laser treatment resulted in greater symptom improvement than clobetasol propionate therapy for women with vulvar LS. Sequential treatment with clobetasol propionate followed by CO_2 laser may further improve clinical symptoms.

CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov, NCT05010421.

(Obstet Gynecol 2026;00:1–11)

DOI: 10.1097/AOG.0000000000006326

Lichen sclerosus (LS) is a chronic autoimmune disorder of the vulvar skin that affects anywhere from 1 in 70 women to 1 in 500 women and typically causes itching, burning, pain, and progressive anatomic distortion of the vulva.[1–4] Lichen sclerosus is associated with dyspareunia, chronic vulvar pain, reduced quality of life (QOL), and vulvar cancer risk via differentiated vulvar intraepithelial neoplasia, with a lifetime risk of 2–6%.[5,6]

The standard treatment of LS for decades has been high potency topical corticosteroids such as clobetasol propionate.[7,8] Clobetasol propionate

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The study was funded by the authors' institutional funds. No external funding or support was received.

Each author has confirmed compliance with the journal's requirements for authorship.

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Financial Disclosure

The authors did not report any potential conflicts of interest.

ISSN: 0029-7844/26

induces remission or significant improvement for around 75–85% of women.[9,10] Treatment typically consists of 3 months of daily or tapering clobetasol propionate therapy followed by once weekly maintenance to reduce symptomatic recurrence.[3,4,7,9,10]

Carbon dioxide (CO_2) laser treatment is a novel approach that may serve as an adjunct or alternative to clobetasol propionate for women with LS. Small retrospective and prospective case series report symptomatic improvement and histologic changes in sclerosis.[11–13] A systematic review of six studies (177 patients) found greater reduction in itching, pain, and dyspareunia with laser treatment compared with topical corticosteroids; histopathologic findings were largely similar except for increased collagen production; patient satisfaction was higher with laser therapy.[14]

To date, only four small, randomized controlled trials (RCTs; 40–66 women each) that compared laser treatment with topical corticosteroids have been published. In these studies, laser therapy showed greater improvement in QOL scores, symptom scores, and patient satisfaction in some trials; one sham-controlled trial found no significant histopathologic improvement after CO_2 laser treatment.[15–18]

Overall, existing evidence suggests that laser treatment may be a promising option for women with symptomatic LS, but the available RCTs are small and inconclusive, and laser therapy is not currently accepted as a standard treatment alternative or adjunct to topical corticosteroids.[19] Among the investigated modalities, fractional CO_2 laser therapy has been most widely studied and is commonly used in clinical practice for vulvar tissue remodeling. Therefore, we conducted a large RCT that compared CO_2 laser with topical clobetasol propionate to define the clinical value of CO_2 laser treatment for women with symptomatic LS.

METHODS

We conducted a prospective randomized, single-center, open clinical trial, at our tertiary referral center for vulvar disorders that included women referred for the treatment of symptomatic LS. The study was approved by the ethical review board of Ruhr-Universität Bochum (registration No. 21-7241-MPG §23b; approval date: July 7, 2021) and registered at ClinicalTrials.gov (NCT05010421).

Inclusion criteria included individuals aged at least 18 years with an established diagnosis of LS (vulva, perineum, or perianal region) made by experienced clinicians based on characteristic clinical findings, with histopathologic confirmation when clinically indicated, for patients who were willing to comply with study requirements and had sufficient language proficiency to understand study procedures and complete the questionnaires. Exclusion criteria included: patients with concurrent immunosuppressive treatment; a history of vulvar cancer, vulvar dysplasia, or vulvar surgery; contraindication to clobetasol treatment, known sunlight allergy; or a skin condition that interfered with local treatment, such as neurodermatitis or bullous pemphigoid.

After informed consent, women randomized to the experimental arm received three courses of nonablative CO_2 laser treatment every 21 days that used a nonablative laser (AcuPulse) at the following settings: 0.9 mm spot size; 10 mJ, 10×10 spots; two to four passes over all affected areas. Local anesthesia was provided with a topical cream containing lidocaine 25 mg/g and prilocaine 25 mg/g (EMLA), applied 45 minutes before laser treatment. Women in the control arm received topical clobetasol 0.05% (Dermoxin) daily for 1 month, then every other day for 1 month, then three times per week for 1 month. Patients received no compensation.

The primary outcome was the BIP (burn-itch-pain) score, a summary score of the three cardinal symptoms of LS (ie, vulvar burning, itching, and pain), each measured on an 11-step numerical rating scale (min 0=no symptom; max 10=extreme symptom), yielding a total score between 0 and 30. Secondary outcomes included a vulvar disease-related QOL assessment before therapy and at 3 months that used a standardized, validated questionnaire (VQLI [Vulvar Disease Quality of Life Index]),[20] overall improvement rated by the treating physicians, and visual improvement rated by a physician unaware of study assignment (both on an 11-step numerical rating scale after 3 months). Patient-reported adverse events were assessed at the 3-month visit by a standardized yes or no question about undesirable side effects, with a free-text description when applicable. In the CO_2 laser group, an additional structured physician-assessed safety evaluation was performed during and immediately after laser sessions to capture intraoperative and perioperative adverse events. These data were summarized descriptively at the patient level across the laser treatment course.

The sample size was calculated based on the hypothesis that CO_2 laser treatment, when compared with topical clobetasol propionate, would produce a clinically relevant 2-point difference in the BIP score at 3 months. Based on previously published studies, we assumed a mean BIP score of approximately 12 with an SD of 4 on the 0–30 scale.[16–18] With 180

participants, the study had more than 90% power to detect a difference of at least 2 points with an SD of 4 at a significance level of 0.05 through the use of a nonparametric test such as the Mann-Whitney *U* test. Assuming a 10% dropout rate after randomization, we aimed to recruit 198 patients.

Randomization used a computer-generated allocation list with permuted blocks of variable size (4 and 6), generated before study initiation.[21] Participants were stratified according to previous treatment with topical corticosteroids to ensure balanced distribution between study arms. Study assignments were contained in sealed, sequentially numbered opaque envelopes prepared by an independent study coordinator and opened after patients presented to the outpatient clinic for study discussion and provided informed consent.

Study data were collected and managed using REDCap.[22] After collection, exported data were further processed for statistical analyses in Microsoft Excel.

The primary outcome was the change in the BIP score from baseline to 3 months. Between-group comparisons used nonparametric methods because distributions were nonnormal. Continuous variables are presented as medians with IQRs. For adjusted analyses of the primary outcome, multiple linear regression models prespecified in the study protocol were applied. The dependent variable was the symptom score at 3 months. Independent variables included study group (CO_2 laser vs clobetasol propionate), baseline symptom severity, age, body mass index (BMI, calculated as weight in kilograms divided by height in meters squared), current smoking status, prior topical corticosteroid treatment, and disease duration (years from the first diagnosis of LS to study entry). This model was chosen a priori based on clinical considerations and literature that suggested associations of these variables with LS course and treatment response.[3–7,9,10] Although symptom scores are bounded, showing deviation from normality, linear regression was retained because it provides interpretable estimates of between-group differences and is robust to moderate deviations from normality in samples of this size. Secondary outcomes were analyzed descriptively and through the usage of nonparametric methods, as appropriate.

After the completion of the randomized treatment phase at 3 months, participants could choose further therapy according to protocol: no further protocol treatment; continuation of the originally assigned therapy; or cross over to the alternative treatment. Follow-up assessment occurred at 6 months. Analyses of this postrandomization phase were prespecified as secondary and exploratory. All statistical tests were 2-sided with a significance level of 0.05. For the three prespecified secondary outcomes (physician-rated visual improvement, physician-rated overall improvement, and VQLI change), *P* values were adjusted for multiple testing by using the Holm-Bonferroni procedure. Within-group comparisons over time (eg, from 3 months to 6 months during the crossover phase) were evaluated by using paired nonparametric tests (Wilcoxon signed-rank test). Analyses were performed using SigmaPlot 16. Violin plots were generated using Matplotlib.[23]

RESULTS

Between November 2021 and March 2025, 381 patients were screened. Twenty-two patients declined to participate, and 114 patients did not meet the inclusion criteria. Thus, 245 patients were recruited and randomized to the experimental arm (n=123) or standard arm (n=122). In the intention-to-treat population, 26 participants withdrew consent before the 3-month assessment and 11 were lost to follow-up. Reasons for withdrawal were the side effects of clobetasol propionate (n=2), the side effects of laser treatment (n=2), no more symptoms (n=1), dissatisfaction with counselling (n=1), diagnosis of cancer (n=2), personal reasons (n=3), dissatisfaction with assignment to clobetasol propionate (n=1), and no reason given (n=14). Thus, 208 patients were included in the final analysis. Figure 1 shows the patient flow through the study. Baseline characteristics by study allocation are shown in Table 1 and were comparable between the two treatment groups. Baseline symptom scores did not differ between groups (Table 2).

The primary endpoint was the change in symptom sum score from baseline to 3 months, corresponding to completion of the initial treatment phase in both groups (negative values indicate improvement). Symptom improvement occurred in both groups but was greater in the laser group (Table 2 and Fig. 2A). Baseline-adjusted and more extensive, prespecified multivariable linear regression models supported the main finding (Table 2 and Fig. 2B; for full model details see Appendix 1, available online at http://links.lww.com/AOG/E690). Symptom trajectories are illustrated in Figure 2C (and in more detail in Appendix 2, available online at http://links.lww.com/AOG/E690). To assess robustness of the primary outcome to missing data, a conservative baseline-carry-forward sensitivity analysis was performed and showed that laser treatment remained associated with greater symptom improvement than

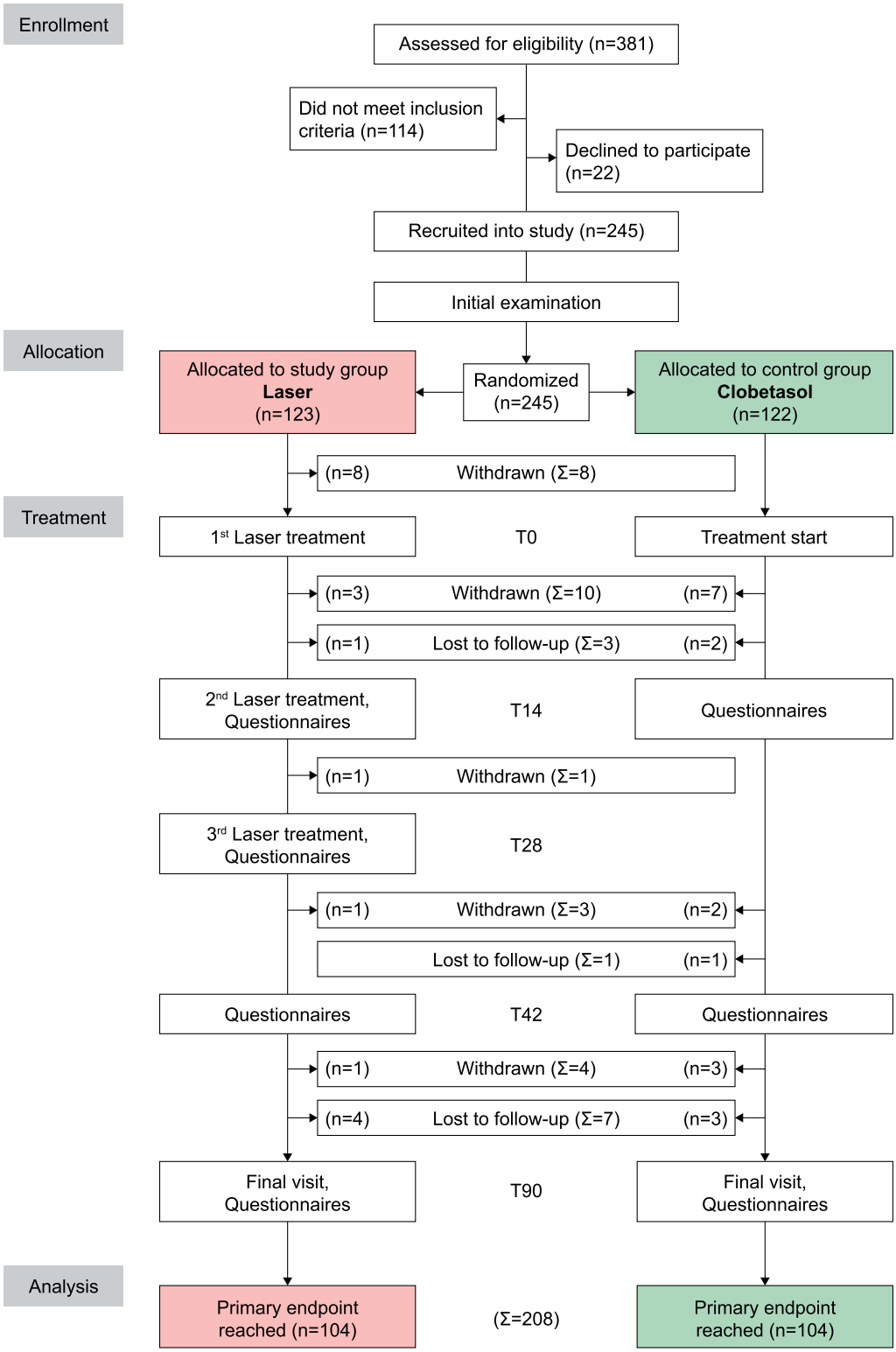

Fig. 1. Study flow diagram.

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Table 1. Patient Characteristics

Characteristic	Laser	Clobetasol
No. of patients	123 (50.2)*	122 (49.8)*
Age (y)	57.4 (47.8–63.0)	56.4 (44.0–64.9)
BMI (kg/m^2)	25.9 (21.7–30.1)	24.9 (22.1–28.3) [1]
Parity	1 (0–2) [2]	1 (0–2) [1]
Currently pregnant	0	0
Allergies (yes/no)	41 (33.3)	51 (41.8)
Skin condition (yes/no)	14 (11.4)	14 (11.5)
Tobacco use	[1]	
Currently smoking	17 (13.9)	17 (13.9)
Ever smoked	41 (33.6)	44 (36.1)
Never smoked	81 (66.4)	78 (63.9)
Alcohol consumption (yes/no)	78 (63.4)	67 (54.9)
Substance use disorder (yes/no)	0	0
Concomitant disease (yes/no)	97 (80.2) [2]	91 (75.2) [1]
Prescription drug use (yes/no)	105 (86.1) [1]	94 (77.0)
LS		
Localization†		
Vulva	119 (96.7)	113 (92.6)
Perineum	82 (66.7)	82 (67.2)
Perianal	43 (35.0)	46 (37.7)
Clitoris or periclitoral	7 (5.7)	6 (4.9)
Other	2 (1.6)	5 (4.1)
Years since LS diagnosis	2 (0.9–5) [5]	2 (0.25–4) [5]
Years since LS symptom onset	4 (2–7.75) [19]	5 (2–10) [22]
Years between symptom onset and diagnosis	1 (0–3) [22]	1 (0–4) [27]
Prior treatment with corticosteroids	101 (82.1)	101 (82.8)
Duration of corticosteroid treatment (mo)	11 (4–48) [2]	12 (4–24) [1]

BMI, body mass index; LS, lichen sclerosus.
Data are n (%) or median IQR. Numbers in square brackets indicate the number of missing values.
* Percentage across row.
† Multiple localizations possible.

clobetasol propionate (Appendix 3, available online at http://links.lww.com/AOG/E690).

Physician-rated visual improvement as well as overall improvement at 3 months, after Holm-Bonferroni correction, significantly favored laser therapy (Table 3).

Quality of life improved significantly in both groups. Absolute VQLI scores did not differ between groups at baseline or at 3 months, but improvement was greater in the laser group (Table 3). Baseline-adjusted analyses supported this finding.

Patient-reported side effects at 3 months were uncommon in both groups: 18 of 104 (17.3%) in the laser group and 15 of 104 (14.4%) in the clobetasol propionate group (P=.569, χ^2 test). In the laser group, the most commonly reported side effects were transient vulvar pain, burning, or pruritus, often occurring in the days after the procedure. Several patients reported temporary dyspareunia, fissures, or localized irritation, which generally resolved over time. Isolated reports included discomfort related to topical anesthetic use and procedural pain during or shortly after laser sessions. In the clobetasol propionate group, reported side effects mainly involved local irritation, dryness, pruritus, or cyclical exacerbations. Isolated events included yeast infection, increased vaginal discharge, and systemic discomfort attributed to topical corticosteroid use. One reported adverse event was unrelated to study treatment. No serious treatment-related adverse events were reported in either group.

In the randomized laser group, physician-assessed intraoperative and perioperative adverse events occurred in 30 of 115 patients (26.1%) who underwent at least one laser procedure (Table 4). The most frequent events were minor wound bleeding (15.7%) and local pain that required systemic analgesia (12.2%). Less common events included wound healing disturbances (1.7%) and wound infection (0.9%). No unplanned readmissions occurred. A small number of adverse events occurred intraoperatively (2.6%). Other reported events were infrequent and included transient severe pruritus immediately after laser treatment, vulvovaginal fungal infection, and malodorous vaginal discharge. No serious procedure-related adverse events were observed.

Table 2. Symptom Outcomes at Baseline and 3 Months

Outcome	Laser	Clobetasol	Adjusted Effect (β) (95% CI)*	P†
Primary outcome				
Change in symptom score from baseline to 3 mo‡				
n (complete cases)	104	104	208	
ΔBIP	−8 (−13 to−3) −8.2±7.4	−5 (−10.75 to 0) −5.4±8.3		.007
ΔBurn	−3 (−5 to 0)	−1 (−4 to 0)		.009
ΔItch	−3 (−5 to 0)	−2 (−5 to 0)		.040
ΔPain	−2 (−5 to 0)	−1 (−4 to 0)		.122
Adjusted analyses				
Minimal (supportive)§			−2.67 (−4.42 to−0.91)	.003
Prespecified multivariable analysis (confirmatory)‖			−2.90 (−4.64 to−1.15)	.001
Secondary and supportive analyses				
Baseline symptom score				
n (all randomized)	123	122		
BIP_T0	15 (10 to 20)	16 (8 to 21)		.863
3-mo symptom score				
n (complete cases)	104	104		
BIP_T90	5.5 (2 to 12)	8 (2 to 14)		.079

BIP, burn-itch-pain; T0, baseline; T90, 3-month.
Data are median (IQR) or mean±SD unless otherwise specified.
* β<0 indicates greater improvement (larger negative ΔBIP) in the laser group.
† Between-group comparisons for unadjusted outcomes were performed using the Mann-Whitney U test. Adjusted analyses used linear regression models.
‡ ΔBIP=BIP_T90−BIP_T0; negative values indicate symptom improvement.
§ Multiple linear regression with ΔBIP as the dependent variable and baseline symptom score (BIP_T0) as covariate.
‖ Prespecified multivariable regression model including study group, baseline symptom score (BIP_T0), age, body mass index (BMI), current smoking status, prior topical corticosteroid treatment, and disease duration (years since diagnosis).

After the randomized treatment phase at 3 months, participants could choose no further protocol treatment, continuation of assigned therapy, or cross over to the alternative treatment (Fig. 3). Of the 104 patients originally assigned to laser who reached 3 months, 75 chose no further treatment, six received additional laser treatment, and 23 crossed over to clobetasol propionate. Of the 104 individuals originally assigned to clobetasol propionate, 74 crossed over to laser and 30 chose no further protocol treatment.

Among participants initially randomized to clobetasol propionate with 6-month data, those who crossed over to laser showed further symptom improvement from 3 months to 6 months. However, they also had substantially higher symptom scores at 3 months than those who did not cross over, indicating postrandomization treatment selection (Table 5). These findings therefore suggest, but do not establish, an additional benefit of sequential laser after clobetasol propionate. Consistently, significant within-group improvement from 3 months to 6 months was observed only in patients who crossed over from clobetasol propionate to laser (Wilcoxon signed-rank test, $P<.001$), whereas no significant change was seen in participants who did not change therapy or in other crossover pathways (all $P\geq.097$). Individual BIP score trajectories are shown in Appendix 2 (http://links.lww.com/AOG/E690).

Quality of life changes from 3 months to 6 months did not differ by postrandomization treatment strategy, and VQLI scores at 3 months were similar between groups (Table 5). At 6 months, however, absolute VQLI scores were lower for participants who received no further protocol treatment than for those crossing over to laser. This pattern is consistent with postrandomization treatment selection and differences in assessment timing relative to active treatment and should be interpreted cautiously. Physician-rated overall and visual improvement at 6 months were similar across treatment pathways.

DISCUSSION

In this randomized trial, we demonstrate that three courses of CO_2 laser are superior to 3 months of standard treatment with topical clobetasol propionate across several outcome measures, including BIP scores, visual improvement, physician assessment, and VQLI. Furthermore, crossover-phase data suggest that clobetasol propionate followed by CO_2 laser may reduce symptoms to levels comparable with laser

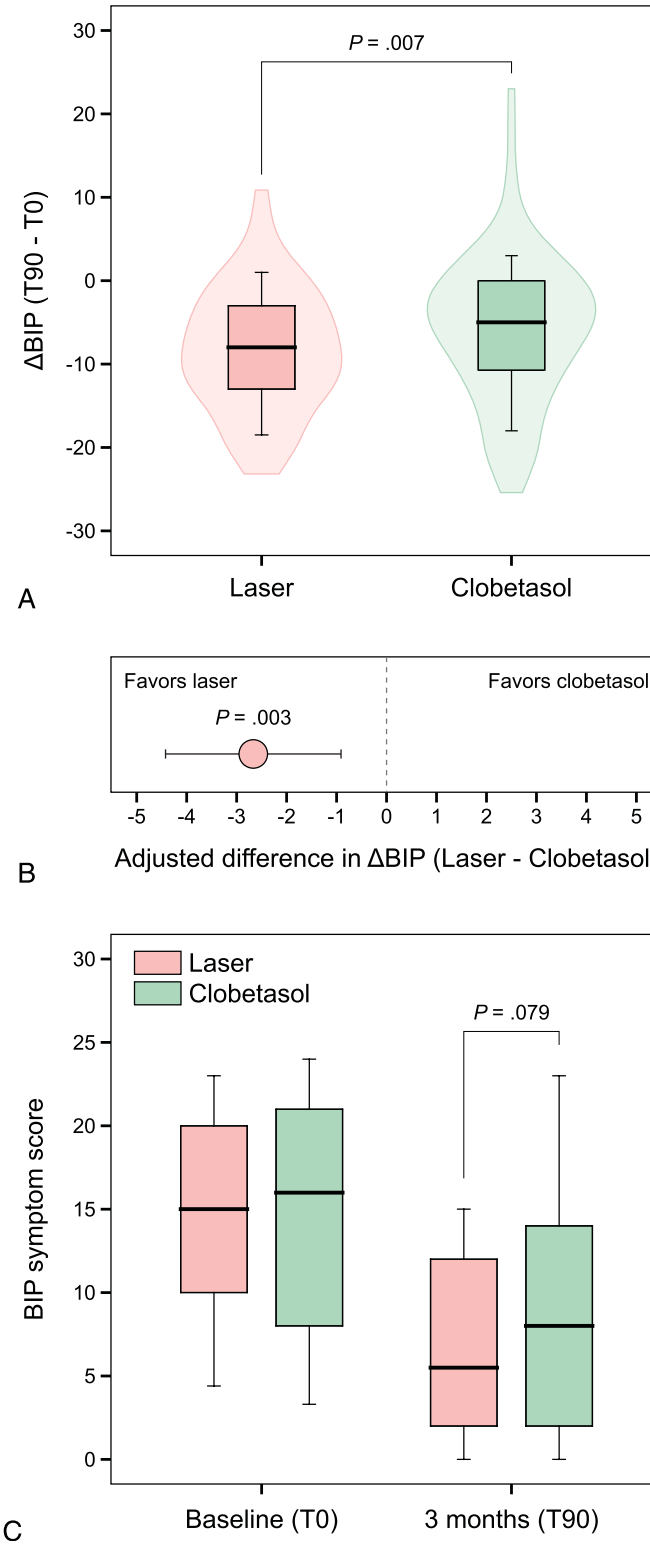

Fig. 2. Changes in symptom scores and adjusted treatment effects at 3 months (T90). **A**. Distribution of change in symptom score (ΔBIP=BIP at T90−BIP at T0 [baseline]) for laser and clobetasol. *Negative values* indicate improvement. *Violin plots* display kernel density estimates of the full distribution. **B**. Adjusted between-group difference in ΔBIP from linear regression (β=−2.67; 95% CI, −4.42 to −0.91). *Dotted vertical line* indicates no difference. **C**. Symptom scores at T0 and T90. T0 values were similar; T90 scores were lower in the laser group. *Box plots* show medians, IQRs, and 10th/90th percentile whiskers. BIP, symptom sum score (burning, itching, pain; range 0–30; lower score means less severe symptoms).

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Table 3. Secondary Outcomes at 3 Months

Outcome	Laser	Clobetasol	*P**
Physician-rated visual improvement†			
n (available)	96	98	
Score	6 (3–8)	3.5 (2–7)	.003
Physician-rated overall improvement†			
n (available)	104	102	
Score	7 (5–8)	5 (2–7)	<.001
QOL (VQLI)			
Baseline QOL			
n (available)	102	103	
VQLI_T0	24 (17–32)	23 (16–30)	.206
3-mo QOL			
n (available)	101	100	
VQLI_T90	16 (8.5–24)	17 (9–24.75)	.783
Within-group change in VQLI from baseline to 3 mo			
n (paired)	101	100	
ΔVQLI‡	−7 (−15 to−2)	−5 (−10 to 0)	
P (Wilcoxon signed-rank test)	<.001	<.001	
Between-group comparison of change in VQLI from baseline to 3 mo			
n (complete cases)	99	99	
ΔVQLI	−7 (−15 to−2)	−5 (−10 to 0)	.020

QOL, quality of life; VQLI, Vulvar Disease Quality of Life Index.
Data are median (interquartile range) unless otherwise specified.
* Mann-Whitney *U* test.
† Higher values indicate greater improvement (physician-assessed).
‡ ΔVQLI=VQLI_T90 − VQLIT0 (negative values indicate improved quality of life).

alone. The treatment effect of laser therapy was consistent across unadjusted, baseline-adjusted, and prespecified multivariable analyses, which supports the robustness of the primary findings. Among the prespecified covariates, higher BMI and longer disease duration were associated with worse outcomes, whereas age, smoking, and previous corticosteroid treatment were not independently predictive after accounting for baseline severity. Therefore, we conclude that CO_2 laser may be a reasonable additional treatment option for women with symptomatic LS.

The postrandomization crossover phase of our trial provides exploratory insight into symptom trajectories beyond the randomized treatment period. Because treatment choices during this phase were not randomized but determined by participants after completion of the randomized treatment phase, these analyses should be interpreted descriptively. Among participants initially assigned to clobetasol propionate, those who crossed over to laser showed greater improvement in symptom scores from 3 months to 6 months than those who received no further protocol treatment. This pattern was observed both in between-group comparisons and within-group paired analyses, with significant symptom improvement detected only among patients who crossed from clobetasol propionate to laser. These findings occurred in the context of substantially higher symptom burden at the end of the randomized phase among crossover patients, suggesting marked postrandomization treatment selection.

Although early QOL improvement favored laser therapy, absolute scores at 3 months were similar between groups, suggesting that this did not immediately translate into separation of patient-reported QOL. The absolute difference in symptom improvement was

Table 4. Physician-Assessed Intraoperative and Perioperative Adverse Events in the Laser Group (115 Patients Originally Randomized to Carbon Dioxide Laser Who Underwent at Least One Procedure)

Adverse Event (Predefined)	No. of patients (%)
Any physician-assessed adverse event	30 (26.1)
Minor bleeding from wound	18 (15.7)
Local pain requiring systemic analgesia	14 (12.2)
Wound healing disturbance	2 (1.7)
Wound infection	1 (0.9)
Unplanned re-admission	0 (0.0)
Other adverse events*	4 (3.5)
Events occurring intraoperatively	3 (2.6)
Need for sedation during the procedure	4 (3.5)

* Includes severe pruritus immediately after laser treatment (n=2), vulvovaginal fungal infection (n=1), and malodorous vaginal discharge (n=1).

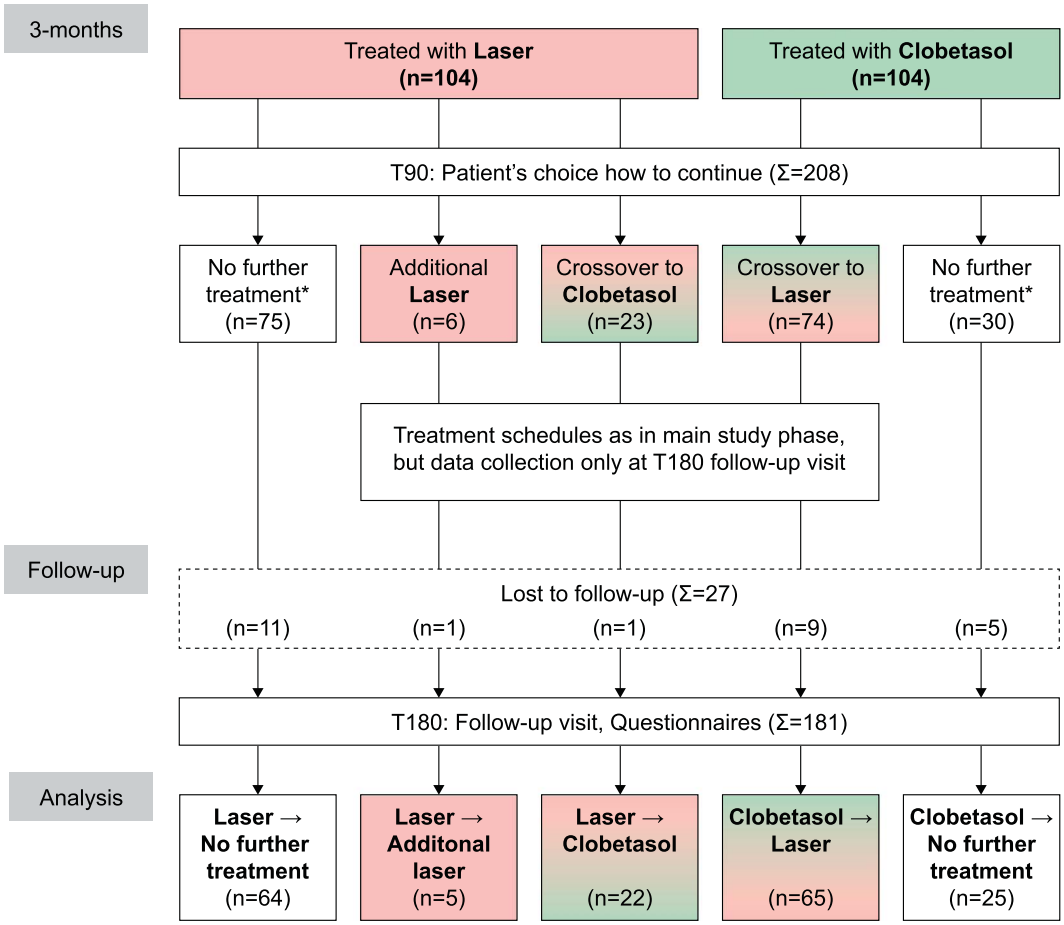

Fig. 3. Patient flow during the crossover phase from 3 months (T90) to 6 months (T180). *No further treatment refers to the absence of additional protocol treatment and may include low-dose or low-frequency clobetasol maintenance therapy.
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modest and should be interpreted in the context of the overall improvement seen in both treatment arms. During the postrandomization phase, QOL changes from 3 months to 6 months did not differ by treatment strategy; however, absolute 6-month scores were lower for participants who received no further protocol treatment than for those who crossed over to laser. This likely reflects postrandomization treatment selection and differences in timing of assessments relative to active treatment and recovery, rather than a true

Table 5. Outcomes During the Postrandomization Crossover Phase (3–6 Months) in Participants Initially Randomized to Clobetasol

Outcome	Clobetasol → No Further Protocol Treatment (n=25)	Clobetasol → Laser (n=65)	*P**
BIP_T90	1.0 (0.0 to 7.5)	10.0 (4.5 to 15.5)	<.001
BIP_T180	2.0 (0.0 to 8.0)	7.0 (2.5 to 11.0)	
ΔBIP (T180−T90)†	0 (−1 to 2)	−3 (−7 to 1)	
VQLI_T90	14.0 (9.0 to 19.0)	14.5 (10.0 to 26.0)	
VQLI_T180	7.0 (2.0 to 13.0)	15.0 (8.0 to 24.0)	
ΔVQLI (T180−T90)†	−6.0 (−17.0 to 2.0)	−0.5 (−14.5 to 10.25)	

BIP, burn-itch-pain; T90, 3-month; T180, 6-month; VQLI, Vulvar Disease Quality of Life Index.
Data are median (IQR) unless otherwise specified.
* Mann-Whitney *U* test.
† Indicates change from 3 months to 6 months; negative values indicate improvement.

disadvantage of laser therapy. Participants initially treated with clobetasol who did not receive further intervention effectively represent an additional posttreatment follow-up period, suggesting that longer follow-up may be needed to determine whether early differences in QOL improvement lead to sustained divergence. Physician-assessed overall and visual improvement at 6 months were comparable across treatment pathways, indicating that clinician-rated outcomes were less sensitive than patient-reported symptom measures.

The results of our study are consistent with previous observational studies and small RCTs that consistently showed a measurable treatment effect of CO_2 laser for women with symptomatic LS.[11–13,16–18] Specifically, three out of four small RCTs reported improvement in Skindex-29 score,[16] clinical symptoms including burning, itching, pain, and dyspareunia,[17] and patient satisfaction.[18] Together with our findings, these data suggest that CO_2 laser is an effective treatment for LS, with an effect size similar to or greater than that of standard topical corticosteroid therapy. Because the primary outcome in our trial was based on patient-reported symptoms, placebo effects may have contributed to improvement in this device-based intervention. However, both groups in the present study received active treatments with established clinical effects rather than placebo or sham therapy. The exact mechanism of action of laser treatment remains unclear. Some histopathologic studies show an improvement in skin texture after CO_2 laser, with a significant increase in collagen content and reduction of sclerosis,[11,14,17] whereas others found no improvement in histopathology scale scores between pretreatment and posttreatment biopsies.[15] It therefore remains uncertain whether such histopathologic changes are occasional surrogate markers of treatment success or necessary for clinical benefit. Importantly, given the established role of long-term topical corticosteroid maintenance therapy in disease control and reduction of vulvar cancer risk, CO_2 laser should not be considered a substitute for corticosteroids, particularly with respect to maintenance treatment.[4] Moreover, it is unknown whether specific patient subgroups preferentially benefit from CO_2 laser. In any case, adverse events associated with laser therapy in our study were generally mild and transient, with no serious procedure-related complications observed.

Strengths of our study include its randomized design, large sample size, and the use of multiple measurements, including symptom scores, visual improvement, physician assessment, and QOL assessment. Furthermore, crossover allowed us to assess outcomes associated with sequential use of clobetasol propionate followed by CO_2 laser. In addition, the study population was a homogenous cohort of patients with LS, prospectively recruited using predefined criteria. We therefore believe the internal validity of our findings is strong. However, because the trial was conducted at a single center, confirmation in multicenter studies will be important to further establish generalizability.

Limitations include the use of a specific laser type (ie, a CO_2 laser). We therefore cannot exclude that other laser devices, such as Nd:YAG lasers, may have superior or inferior effects. Our findings cannot be extrapolated to alternative laser treatments. In addition, we did not assess the histopathologic effects of CO_2 laser by serial vulvar biopsies because this was prohibited by the local ethics committee. We therefore cannot confirm previous reports that show improved skin texture and increased collagen content after CO_2 laser.[14,17] Nor can we answer the mechanistic question of whether clinical benefit depends on, or is limited to, patients with increased skin collagen. Finally, the BIP score used as the primary endpoint is a composite of three numerical rating scale-based symptom measures (burning, itching, and pain) and has not been formally validated as a standalone instrument.

In summary, our study supports the hypothesis that CO_2 laser is a valid treatment for women with symptomatic LS. In the largest randomized trial to date, we found that CO_2 laser treatment is superior to the standard treatment with clobetasol propionate for women with symptomatic LS. Sequential treatment with clobetasol propionate followed by CO_2 laser may further improve clinical symptoms. Based on our findings, CO_2 laser may be a reasonable option in clinical practice as an adjunct to standard treatment with topical clobetasol propionate.

REFERENCES

1. Nair PA. Vulvar Lichen Sclerosus et Atrophicus. J Midlife Health 2017;8:55–62. doi: 10.4103/jmh.JMH_13_17
2. Goldstein AT, Marinoff SC, Christopher K, Srodon M. Prevalence of vulvar lichen sclerosus in a general gynecology practice. J Reprod Med 2005;50:477–80.
3. Lee A, Fischer G. Diagnosis and treatment of vulvar lichen sclerosus: an update for dermatologists. Am J Clin Dermatol 2018;19:695–706. doi: 10.1007/s40257-018-0364-7
4. Lee A, Bradford J, Fischer G. Long-term management of adult vulvar lichen sclerosus: a prospective cohort study of 507 women. JAMA Dermatol 2015;151:1061–67. doi: 10.1001/jamadermatol.2015.0643
5. Halonen P, Jakobsson M, Heikinheimo O, Riska A, Gissler M, Pukkala E. Lichen sclerosus and risk of cancer. Int J Cancer 2017;140:1998–2002. doi: 10.1002/ijc.30621

6. Preti M, Borella F, Ferretti S, Caldarella A, Corazza M, Micheletti L, et al. Genital and extragenital oncological risk in women with vulvar lichen sclerosus: a multi-center Italian study. Maturitas 2023;175:107767. doi: 10.1016/j.maturitas.2023.04.010
7. Edwards L. Corticosteroids for vulvar lichen sclerosus. J Reprod Med 1999;44:992.
8. Krapf JM, Mitchell L, Holton MA, Goldstein AT. Vulvar lichen sclerosus: current perspectives. Int J Womens Health 2020;12:11–20. doi: 10.2147/IJWH.S191200
9. Pérez-López FR, Vieira-Baptista P. Lichen sclerosus in women: a review. Climacteric 2017;20:339–47. doi: 10.1080/13697137.2017.1343295
10. Smith YR, Haefner HK. Vulvar lichen sclerosus pathophysiology and treatment. Am J Clin Dermatol 2004;5:105–25. doi: 10.2165/00128071-200405020-00005
11. Dieter AA, Iglesia CB, Lee JH, Etcheverry MJ, Gonzales MK, Sokol AI, et al. A prospective pilot study to assess for histologic changes on vulvar biopsies in postmenopausal women with lichen sclerosus treated with fractionated CO_2 laser therapy. Lasers Surg Med 2023;55:521–7. doi: 10.1002/lsm.23669
12. Gil-Villalba A, Ayén-Rodríguez Á, Naranjo-Díaz MJ, Linares-González L, Ruiz-Villaverde R. Efficacy of fractional CO_2 laser therapy in improving symptoms and quality of life in women with refractory vulvar lichen sclerosus: a prospective observational study. Life (Basel) 2024;14:1678. doi: 10.3390/life14121678
13. Siliquini GP, Giorgi M, Strano C, Accomasso F, Pennati BM, Fusco I, et al. Retrospective study on CO2 laser for second-line treatment of vulvar lichen sclerosus. J Obstet Gynaecol Res 2025;51:e70098. doi: 10.1111/jog.70098
14. Gil-Villalba A, Ayen-Rodriguez A, Naranjo-Diaz MJ, Ruiz-Villaverde R. Laser therapy for vulvar lichen sclerosus, a systematic review. Life (Basel) 2023;13:2146. doi: 10.3390/life13112146
15. Mitchell L, Goldstein AT, Heller D, Mautz T, Thorne C, Joyce Kong SY, et al. Fractionated carbon dioxide laser for the treatment of vulvar lichen sclerosus: a randomized controlled trial. Obstet Gynecol 2021;137:979–87. doi: 10.1097/AOG.0000000000004409
16. Burkett LS, Siddique M, Zeymo A, Brunn EA, Gutman RE, Park AJ, et al. Clobetasol compared with fractionated carbon dioxide laser for lichen sclerosus: a randomized controlled trial. Obstet Gynecol 2021;137:968–78. doi: 10.1097/AOG.0000000000004332
17. Bizjak Ogrinc U, Senčar S, Luzar B, Lukanović A. Efficacy of non-ablative laser therapy for lichen sclerosus: a randomized controlled trial. J Obstet Gynaecol Can 2019;41:1717–25. doi: 10.1016/j.jogc.2019.01.023
18. Zivanovic I, Gamper M, Fesslmeier D, Walser C, Regauer S, Viereck V. Nd:YAG/Er:YAG dual laser compared with topical steroid to treat vulvar lichen sclerosus: a randomised controlled trial. BJOG 2024;131:740–9. doi: 10.1111/1471-0528.17737
19. Preti M, Vieira-Baptista P, Digesu GA, Bretschneider CE, Damaser M, Demirkesen O, et al. The clinical role of LASER for vulvar and vaginal treatments in gynecology and female urology: an ICS/ISSVD best practice consensus document. Neurourol Urodyn 2019;38:1009–23. doi: 10.1002/nau.23931
20. Felmingham C, Chan L, Doyle LW, Veysey E. The vulval disease quality of life index in women with vulval lichen sclerosus correlates with clinician and symptom scores. Australas J Dermatol 2020;61:110–8. doi: 10.1111/ajd.13197
21. Sealed Envelope Ltd. Create a blocked randomisation list. Accessed January 12, 2026. https://www.sealedenvelope.com/simple-randomiser/v1/lists
22. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81. doi: 10.1016/j.jbi.2008.08.010
23. Hunter JD. Matplotlib: a 2D graphics environment. Comput Sci Eng 2007;9:90–5. doi: 10.1109/MCSE.2007.55

Authors' Data Sharing Statement

- Will individual participant data be available (including data dictionaries)?

Individual participant data, including data dictionaries, will not be publicly available.

- What data in particular will be shared?

Deidentified individual participant data underlying the analyses reported in this article may be made available on reasonable request.

- What other documents will be available?

No additional documents beyond those reported in this article will be made available.

- When will data be available (start and end dates)?

Data may be made available upon reasonable request after publication of the article, with no predefined end date.

- By what access criteria will data be shared (including with whom, for what types of analyses, and by what mechanism)?

Requests should be directed to the corresponding author. Requests will be evaluated on a case-by-case basis to ensure compliance with ethical approvals, patient confidentiality requirements, and institutional data-protection and data-use policies. Approved data will be shared via secure transfer mechanisms.

PEER REVIEW HISTORY

Received January 13, 2026. Received in revised form March 14, 2026. Accepted March 19, 2026. Peer reviews and author correspondence are available at http://links.lww.com/AOG/E691.