

Research Article

Comparison of Efficacy of Carbon Dioxide Laser Therapy with Cryotherapy for the Treatment of Palmoplantar Viral Warts

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Received: 19.04.26, Revised: 16.06.26, Accepted: 24.06.26

ABSTRACT

Background: Palmoplantar viral warts are common human papillomavirus-associated cutaneous lesions for which several destructive treatment modalities are available, but comparative evidence regarding the efficacy of carbon dioxide (CO₂) laser therapy and liquid nitrogen cryotherapy remains limited. This study compared the efficacy of CO₂ laser therapy with cryotherapy for the treatment of palmoplantar viral warts.

Methods: This randomized controlled trial included 100 patients aged 18-60 years with palmoplantar viral warts presenting to the Dermatology Outpatient Department of DHQ Hospital, Faisalabad. Participants were allocated equally to CO₂ laser therapy (n=50) or liquid nitrogen cryotherapy (n=50). The CO₂ laser group received ablative continuous-wave treatment at 4-8 weeks per lesion, while the cryotherapy group underwent two freeze-thaw cycles using liquid nitrogen, with treatment continued weekly until clearance or for a maximum of eight weeks. Efficacy was defined as complete clinical clearance of warts. Quantitative variables were summarized as mean $\pm$ standard deviation, categorical variables as frequencies and percentages, and treatment efficacy was compared using the chi-square test, using SPSS v.26.0 and the statistical significance set at p<0.05.

Results: The mean age was 32.42 $\pm$ 11.15 years in the CO₂ laser group and 35.22 $\pm$ 12.09 years in the cryotherapy group. Overall, 64% of participants were male. Complete clearance was achieved in 44/50 patients (88.0%) treated with CO₂ laser therapy compared with 27/50 (54.0%) treated with cryotherapy (p<0.001). The direction of the treatment difference was maintained across the prespecified strata of age, sex, lesion site, disease duration, and number of warts, although the comparison among patients with disease duration greater than six weeks did not reach statistical significance.

Conclusions: CO₂ laser therapy achieved a higher rate of complete clinical clearance than liquid nitrogen cryotherapy in patients with palmoplantar viral warts. These findings add randomized comparative evidence supporting CO₂ laser therapy as an effective treatment option, although larger multicenter studies with longer follow-up are required to evaluate recurrence, adverse effects, durability of response, and patient-reported outcomes.

Keywords: Palmoplantar Warts, CO₂ Laser, Cryotherapy, Liquid Nitrogen, Viral Warts, Human Papillomavirus.

INTRODUCTION

Cutaneous warts are benign proliferative lesions caused by human papillomavirus (HPV) infection of keratinocytes and occur across all age groups, with palmoplantar warts representing an important form of non-genital cutaneous disease.[1-4] Plantar warts are

associated with several HPV genotypes and typically present as hyperkeratotic lesions that may disrupt normal skin markings; although diagnosis is usually clinical, overlap with other plantar hyperkeratotic disorders can complicate recognition.[2,3,5,6] Nevertheless some warts regress spontaneously, persistent lesions may

spread, recur, and cause pain or functional discomfort, particularly on weight-bearing surfaces, prompting patients to seek treatment.[1,2,7] The principal therapeutic challenge is that no single intervention provides consistently high clearance across patients, and treatment response may vary according to lesion characteristics, chronicity, treatment intensity, and tolerability.[1,7,8]

Current therapeutic options include keratolytic and chemical agents, liquid-nitrogen cryotherapy, immunotherapy, intralesional treatments, laser-based procedures, electrosurgery, and excision, with cryotherapy remaining one of the most established destructive approaches.[1,7,9,10] However, comparative evidence for cryotherapy remains heterogeneous, with randomized studies against salicylic acid, monochloroacetic acid-based regimens, trichloroacetic acid, and nitric-zinc formulations producing variable clearance rates rather than identifying a uniformly superior treatment strategy.[11-15] Trials evaluating thermotherapy, intralesional measles-mumps-rubella vaccine, intralesional cryotherapy, and topical adapalene have likewise reported differing therapeutic responses, reflecting the continuing search for an optimal approach to palmoplantar warts.[16-19] Laser therapy permits targeted tissue destruction, yet systematic evidence demonstrates wide clearance ranges across laser modalities, while randomized evidence with long-pulsed Nd:YAG laser has not shown consistent superiority over cryotherapy.[20,21] Reports of CO₂ laser treatment for plantar and recalcitrant warts have shown encouraging outcomes, but much of this evidence derives from small or non-comparative studies, leaving uncertainty regarding its relative effectiveness under standardized conditions.[20,22,23]

This therapeutic uncertainty provides a clear rationale for a direct, protocolized comparison of ablative CO₂ laser therapy with liquid-nitrogen cryotherapy using complete clinical clearance as the principal efficacy outcome.[1,7,20] Because treatment outcomes may be influenced by lesion characteristics, procedural technique, number of treatment sessions, and duration of follow-up, a head-to-head randomized evaluation in a defined palmoplantar wart population can provide clinically interpretable evidence.[13,15,20,21] Accordingly, the present study was undertaken to compare the efficacy of CO₂ laser therapy with liquid-nitrogen cryotherapy in adults with palmoplantar viral warts and to generate

context-specific comparative evidence relevant to routine dermatologic practice. The findings are intended to support evidence-informed selection between these commonly used destructive treatment modalities for palmoplantar warts.

METHODOLOGY

This randomized controlled trial was conducted in the Outpatient Department of Dermatology, DHQ Hospital, Faisalabad, from June 10, 2022, to December 9, 2022. Palmoplantar warts were diagnosed clinically as small, flesh-colored, white, pink, or tan-colored grainy papules or nodules with pinpoint black spots or bleeding on paring, representing thrombosed capillaries. Treatment efficacy was defined as complete clinical clearance of the warts, characterized by the absence of visible lesions on naked-eye examination with restoration of normal skin, assessed eight weeks after completion of treatment. Partial efficacy was defined in patients with multiple warts when only some of the lesions had cleared while others remained clinically visible.

A total sample size of 100 patients was calculated, with 50 participants allocated to each treatment group. The sample size was based on anticipated efficacy rates of 88.33% for CO₂ laser therapy and 60.0% for cryotherapy, using a statistical power of 90% and a 5% level of significance. Sample size estimation was performed using the World Health Organization sample size determination software. Patients of either sex, aged 18–60 years, with clinically diagnosed palmoplantar warts according to the predefined operational criteria were eligible for inclusion. Pregnant or lactating women were excluded, as were patients who had received topical treatment for warts during the preceding four weeks. Patients with immunodeficiency disorders, those receiving immunosuppressive therapy, and those with clinical or culture evidence of superadded infection were also excluded. Additional exclusion criteria included unwillingness to participate and the presence of phobia toward either of the study procedures. Patients presenting to the Dermatology Outpatient Department were screened for eligibility. Those fulfilling the selection criteria were enrolled after obtaining informed consent. Participants were subsequently randomized into two equal treatment groups using the lottery method. Group A received CO₂ laser therapy, whereas Group B underwent liquid nitrogen cryotherapy.

Participants allocated to Group A were treated with ablative CO₂ laser therapy in continuous-wave mode at a power setting of 4–6 W. Treatment was applied to each wart together with a surrounding margin of approximately 1–2 mm. Sessions were performed once weekly until complete clearance of the lesions or for a maximum treatment duration of eight weeks. The number and size of lesions were documented at weeks 4, 6, and 8 during the treatment period. Participants in Group B received cryotherapy using liquid nitrogen at –196°C with the cryospray technique. Two freeze-thaw cycles were applied during each treatment session. Cryotherapy was administered once weekly until complete clearance of all lesions or for a maximum of eight weeks. Wart counts were recorded at the end of weeks 4, 6, and 8 to assess the clinical response during treatment.

The primary outcome was treatment efficacy as per operational definition. Follow-up was maintained using participants' contact information, and all clinical and study-related information was recorded by the investigator on a structured data-collection proforma.

Data were analyzed using IBM SPSS Statistics version 26.0. Quantitative variables, including age, duration of disease, and number of warts, were summarized as mean $\pm$ standard deviation. Categorical variables, including sex, site of warts, and treatment efficacy, were presented as frequencies and percentages. The chi-square test was used to compare treatment

efficacy between the CO₂ laser and cryotherapy groups. Potential effect modifiers, including age, sex, duration of disease, site of warts, and number of warts, were assessed through stratified analyses, followed by post-stratification chi-square testing. A p-value of <0.05 was considered statistically significant.

RESULTS

Participant Characteristics

A total of 100 participants aged 18–60 years were included, with 50 allocated to CO₂ laser therapy and 50 to cryotherapy. The mean age was 32.42 ± 11.15 years in the CO₂ laser group and 35.22 ± 12.09 years in the cryotherapy group. Overall, 72 participants (72.0%) were aged 18–40 years and 28 (28.0%) were aged 41–60 years. There were 64 males (64.0%) and 36 females (36.0%); males comprised 66.0% of the CO₂ laser group and 62.0% of the cryotherapy group.

Mean disease duration was 6.46 ± 3.25 weeks in the CO₂ laser group and 6.52 ± 3.66 weeks in the cryotherapy group. Disease duration was ≤ 6 weeks in 32/50 (64.0%) and 34/50 (68.0%) participants, respectively. Lower-limb lesions were present in 35/50 (70.0%) participants receiving CO₂ laser therapy and 32/50 (64.0%) receiving cryotherapy. The corresponding mean numbers of warts were 3.92 ± 1.10 and 3.98 ± 1.13 , with more than three warts present in 32/50 (64.0%) and 33/50 (66.0%) participants, respectively. Baseline characteristics are summarized in Table 1.

Table 1. Baseline characteristics of participants according to treatment group

Characteristic	CO ₂ laser therapy (n=50)	Cryotherapy (n=50)
Age, years, mean $\pm$ SD	32.42 ± 11.15	35.22 ± 12.09
Age 18–40 years, n (%)	37 (74.0)	35 (70.0)
Age 41–60 years, n (%)	13 (26.0)	15 (30.0)
Male, n (%)	33 (66.0)	31 (62.0)
Female, n (%)	17 (34.0)	19 (38.0)
Disease duration, weeks, mean $\pm$ SD	6.46 ± 3.25	6.52 ± 3.66
Disease duration ≤ 6 weeks, n (%)	32 (64.0)	34 (68.0)
Disease duration > 6 weeks, n (%)	18 (36.0)	16 (32.0)
Upper-limb lesion site, n (%)	15 (30.0)	18 (36.0)
Lower-limb lesion site, n (%)	35 (70.0)	32 (64.0)
Number of warts, mean $\pm$ SD	3.92 ± 1.10	3.98 ± 1.13
≤ 3 warts, n (%)	18 (36.0)	17 (34.0)
> 3 warts, n (%)	32 (64.0)	33 (66.0)

Primary Efficacy Outcome

At the efficacy assessment, complete clearance was recorded in 44/50 participants (88.0%) in

the CO₂ laser group and 27/50 (54.0%) in the cryotherapy group (Figure 1)

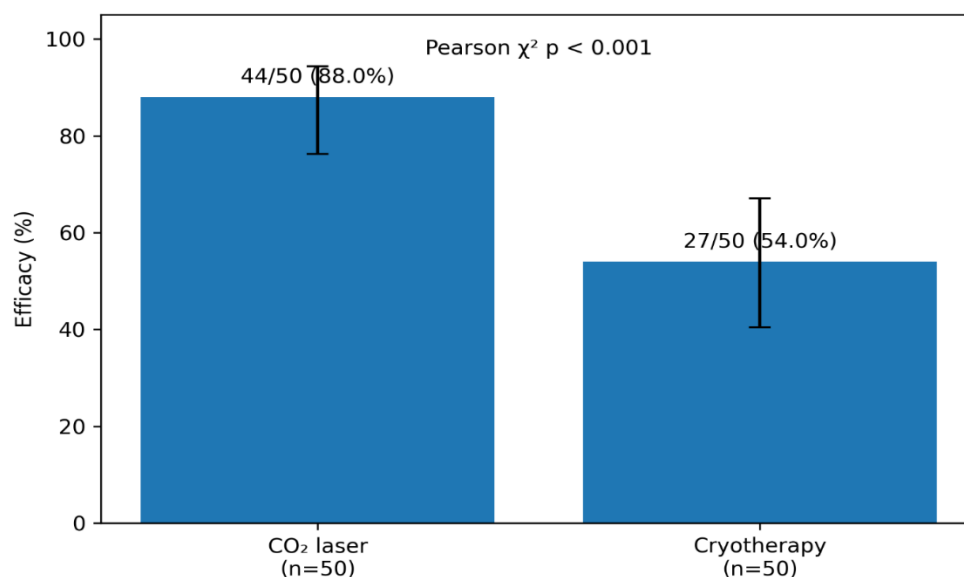


Figure 1: Efficacy of CO₂ laser therapy versus cryotherapy

Efficacy of CO₂ laser therapy compared with cryotherapy for palmoplantar viral warts. Bars represent the percentage of participants achieving complete clearance, with error bars indicating 95% Wilson confidence intervals. Complete clearance occurred in 44/50 (88.0%) participants receiving CO₂ laser therapy and 27/50 (54.0%) receiving cryotherapy. The between-group comparison was performed using Pearson's chi-square test ($p < 0.001$). The corresponding 95% confidence intervals for the

efficacy proportions were 76.2%–94.4% and 40.4%–67.0%, respectively. The absolute between-group difference was 34.0 percentage points (95% CI: 16.4–49.0 percentage points), and the relative risk was 1.63 (95% CI: 1.24–2.15). The prespecified Pearson chi-square comparison yielded $p < 0.001$ (reported source value, $p = 0.0002$) (Table 2). The numbers without complete clearance were 6/50 (12.0%) and 23/50 (46.0%), respectively.

Table 2. Primary efficacy outcome according to treatment group

Outcome	CO ₂ laser therapy (n=50)	Cryotherapy (n=50)	Effect estimate	p-value
Complete clearance, n (%)	44 (88.0)	27 (54.0)	RR 1.63 (95% CI: 1.24–2.15)	<0.001
95% CI for efficacy proportion	76.2%–94.4%	40.4%–67.0%	—	—
No complete clearance, n (%)	6 (12.0)	23 (46.0)	—	—
Absolute difference in efficacy	—	—	34.0 percentage points (95% CI: 16.4–49.0)	—

CI = confidence interval; RR= risk ratio. The p-value was obtained from the prespecified Pearson chi-square comparison; the original calculated value was $p = 0.0002$. The treatment-specific confidence intervals were calculated using the Wilson method; the confidence interval for the absolute risk difference used the Newcombe method; and the relative-risk confidence interval was calculated on the logarithmic scale. These additional effect-size estimates were derived directly from the reported 44/50 and 27/50 outcome counts.

Stratified Efficacy Analyses

Stratified treatment-group comparisons according to age, sex, disease duration, lesion site, and number of warts are presented in Table 3 and Figure 2. For participants aged 18–40 years, efficacy was recorded in 31/37 (83.8%) in the CO₂ laser group and 21/35 (60.0%) in the cryotherapy group ($p = 0.024$); among participants aged 41–60 years, the corresponding proportions were 13/13 (100.0%) and 6/15 (40.0%) ($p < 0.001$).

Table 3. Stratified efficacy according to participant and disease characteristics

Stratum	CO ₂ laser therapy n/N (%)	Cryotherapy n/N (%)	RR (95% CI)	p-value
Overall	44/50 (88.0)	27/50 (54.0)	1.63 (1.24–2.15)	<0.001
Age 18–40 years	31/37 (83.8)	21/35 (60.0)	1.40 (1.03–1.90)	0.024
Age 41–60 years	13/13 (100.0)	6/15 (40.0)	2.50 (1.35–4.65)	<0.001
Male	30/33 (90.9)	20/31 (64.5)	1.41 (1.06–1.87)	0.011
Female	14/17 (82.4)	7/19 (36.8)	2.24 (1.19–4.19)	0.006
Disease duration ≤6 weeks	30/32 (93.8)	19/34 (55.9)	1.68 (1.23–2.29)	<0.001
Disease duration >6 weeks	14/18 (77.8)	8/16 (50.0)	1.56 (0.90–2.69)	0.091
Upper limb	14/15 (93.3)	10/18 (55.6)	1.68 (1.09–2.59)	0.015
Lower limb	30/35 (85.7)	17/32 (53.1)	1.61 (1.13–2.30)	0.004
≤3 warts	17/18 (94.4)	11/17 (64.7)	1.46 (1.01–2.11)	0.028
>3 warts	27/32 (84.4)	16/33 (48.5)	1.74 (1.19–2.55)	0.002

CI = confidence interval; RR= risk ratio. p-values are Pearson chi-square p-values from the prespecified post-stratification analysis and

have been standardized to three decimal places, with values <0.001 presented accordingly.

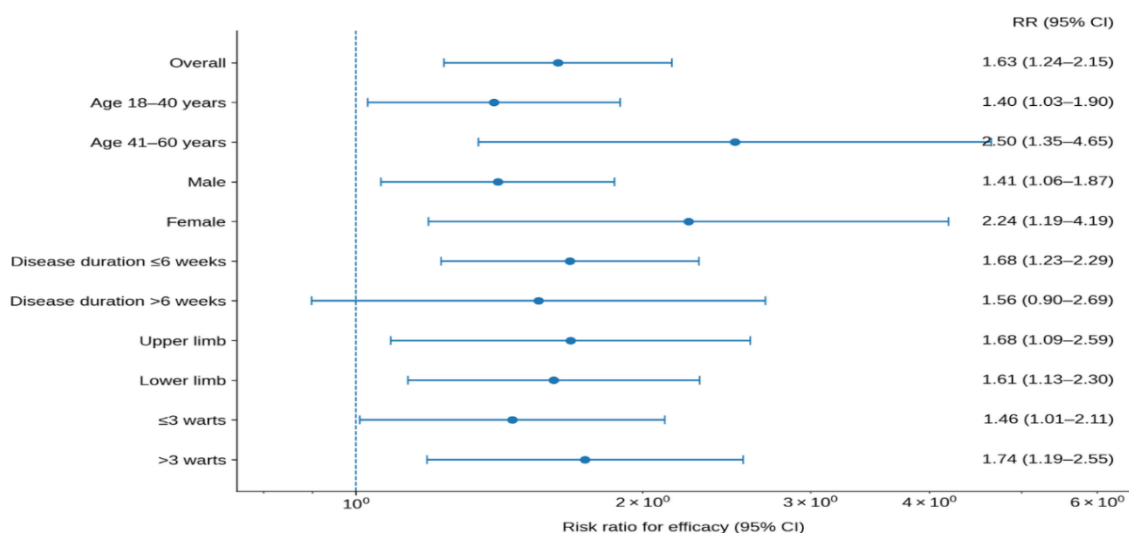


Figure 2: Forest plot of efficacy across prespecified strata

Relative risks for efficacy with CO₂ laser therapy compared with cryotherapy overall and according to prespecified age, sex, disease-duration, lesion-site, and wart-number strata. Points represent risk ratios and horizontal lines represent 95% confidence intervals. The vertical reference line corresponds to a risk ratio of 1.00. Exact subgroup counts and

prespecified Pearson chi-square p-values are provided in Table 3.

Among males, efficacy was recorded in 30/33 (90.9%) and 20/31 (64.5%) participants, respectively (p=0.011), while among females the corresponding proportions were 14/17 (82.4%) and 7/19 (36.8%) (p=0.006). For disease duration of ≤6 weeks, efficacy occurred

in 30/32 (93.8%) and 19/34 (55.9%) participants ($p < 0.001$). For disease duration > 6 weeks, the proportions were 14/18 (77.8%) and 8/16 (50.0%), respectively ($p = 0.091$).

For upper-limb lesions, efficacy was recorded in 14/15 (93.3%) participants in the CO₂ laser group and 10/18 (55.6%) in the cryotherapy group ($p = 0.015$); for lower-limb lesions, the corresponding proportions were 30/35 (85.7%) and 17/32 (53.1%) ($p = 0.004$). Among participants with ≤ 3 warts, efficacy occurred in 17/18 (94.4%) and 11/17 (64.7%) participants ($p = 0.028$), whereas among those with > 3 warts it occurred in 27/32 (84.4%) and 16/33 (48.5%), respectively ($p = 0.002$).

DISCUSSION

This randomized controlled trial addressed the limited direct comparative evidence on CO₂ laser therapy and liquid nitrogen cryotherapy for palmoplantar viral warts, particularly within the local Pakistani population. The principal finding was that CO₂ laser therapy produced a substantially higher rate of complete wart clearance than cryotherapy, with the direction of effect remaining consistent across the prespecified clinical and demographic strata. This finding adds to the existing literature by providing randomized, locally derived evidence supporting a meaningful difference in short-term clinical efficacy between two commonly used destructive treatment modalities. In our study of 100 adults with palmoplantar viral warts, complete clearance was achieved in 44 of 50 patients (88.0%) treated with CO₂ laser therapy compared with 27 of 50 (54.0%) treated with liquid nitrogen cryotherapy. This corresponded to an absolute difference of 34 percentage points and a relative risk of 1.63 for complete clearance with CO₂ laser therapy. The between-group difference was statistically significant ($p < 0.001$). Numerically higher clearance with CO₂ laser therapy was also observed across the prespecified strata of age, sex, disease duration, lesion site, and number of warts. The only stratified comparison that did not reach the prespecified threshold for statistical significance was among patients with a disease duration of more than six weeks, in whom clearance occurred in 77.8% of the CO₂ laser group and 50.0% of the cryotherapy group ($p = 0.091$). The subgroup analyses, however, were not formal tests of interaction and therefore should not be interpreted as demonstrating that the relative treatment effect differed according to these patient characteristics.

These findings are relevant in the context of the therapeutic difficulty associated with palmoplantar warts. Their hyperkeratotic nature can complicate treatment, and no single modality has consistently provided complete clearance in all patients. The literature reviewed for this study describes both cryotherapy and laser ablation as established destructive approaches, with treatment selection influenced by lesion number, site, patient characteristics, adverse effects, and practical considerations. Cryotherapy produces tissue destruction through repeated freezing and thawing, whereas the CO₂ laser is absorbed by tissue water and produces controlled vaporization and coagulative tissue injury. The present study evaluated these modalities using complete clinical clearance as the efficacy endpoint rather than surrogate changes in lesion size or number.

The results are particularly consistent with those reported by Anwar et al. [24] in a Pakistani population with palmoplantar warts. In that study, 120 patients were treated with either ablative CO₂ laser or liquid nitrogen cryotherapy using treatment protocols closely resembling those used in the present trial. Complete clearance was documented in 53 of 60 patients (88.3%) receiving CO₂ laser therapy compared with 36 of 60 (60.0%) receiving cryotherapy ($p = 0.0004$). The 88.0% clearance rate observed with CO₂ laser therapy in the present study is therefore nearly identical to the 88.3% reported by Anwar et al., while the cryotherapy clearance rate in the present study was somewhat lower at 54.0% compared with 60.0%. The similarity is clinically relevant because both studies evaluated palmoplantar disease and used comparable CO₂ laser and cryotherapy protocols, making this a more direct comparison than studies involving genital, periungual, or treatment-resistant warts.

A randomized trial by Boroujeni and Handjani [22] also directly compared CO₂ laser therapy with cryotherapy in 60 patients with plantar warts. That study differed from the present investigation in its principal comparison because it emphasized the number of treatment sessions required for complete resolution. The median number of sessions was one with CO₂ laser therapy and three with cryotherapy, with a statistically significant difference between groups ($p \leq 0.001$). Recurrence after three months did not differ significantly between the two treatment groups. These findings complement the current

results but should not be considered directly equivalent: the present trial primarily compared the proportion of patients achieving complete clearance, whereas the earlier trial focused substantially on the number of treatment sessions and subsequent recurrence.

The direction of the present findings is also comparable with the randomized trial by Azizjalali et al. [25], although that investigation involved external genital rather than palmoplantar warts. Among 160 participants, complete clearance was reported in 95% of patients treated with CO₂ laser and 46.2% treated with cryotherapy ($p < 0.001$). The magnitude of the between-treatment difference in that trial resembles the pattern observed here, but differences in anatomical site, wart phenotype, treatment response, and study population limit direct comparison. Its findings therefore provide supportive evidence regarding the relative ablative effects of the two interventions rather than direct confirmation of efficacy specifically for palmoplantar disease.

Other studies of CO₂ laser treatment demonstrate that clearance rates vary according to patient selection, lesion characteristics, treatment technique, and duration of follow-up. Mitsuishi et al. [26] treated 35 plantar-wart lesions in 31 patients using CO₂ laser combined with artificial dermis and reported complete clearance of 31 lesions (88.6%) after one treatment, with local recurrence in four lesions during three to 12 months of follow-up. This clearance proportion is close to the 88.0% observed in the present study, although the addition of artificial dermis and the use of a lesion-level rather than patient-level outcome prevent direct equivalence. Conversely, Ockenfels and Hammes [27] reported cure rates of up to 75% with CO₂ laser in treatment-resistant common warts, while Sloan et al. [28] reported a 64.1% 12-month cure rate in a retrospective cohort of patients with resistant verrucae vulgaris. These lower estimates are not necessarily inconsistent with the current findings because treatment-resistant populations and longer follow-up periods represent substantially different clinical settings. The attached literature review similarly notes considerable variation in laser outcomes according to the population studied and duration of observation.

The stratified findings provide additional information regarding the consistency of the observed treatment difference. Among patients aged 18–40 years, clearance was 83.8% with CO₂ laser and 60.0% with cryotherapy, while

the corresponding rates among those aged 41–60 years were 100.0% and 40.0%. Among males, clearance was 90.9% versus 64.5%, and among females it was 82.4% versus 36.8%. A similar numerical pattern was present according to lesion site and wart burden: clearance with CO₂ laser versus cryotherapy was 93.3% versus 55.6% for upper-limb lesions, 85.7% versus 53.1% for lower-limb lesions, 94.4% versus 64.7% among patients with three or fewer warts, and 84.4% versus 48.5% among those with more than three warts. For disease duration of six weeks or less, the corresponding proportions were 93.8% and 55.9%; among patients with disease lasting more than six weeks, they were 77.8% and 50.0%. These data show that the numerical direction of the primary comparison was maintained across all examined strata. However, some strata contained relatively few patients, including only 13 patients aged 41–60 years in the CO₂ laser arm. Moreover, no treatment-by-subgroup interaction tests were performed. Consequently, differences in the magnitude or statistical significance of individual subgroup comparisons cannot establish that age, sex, disease duration, site, or wart number modifies the treatment effect.

The apparently lower clearance of longer-duration disease in both groups deserves similar caution. Although the between-treatment comparison was not statistically significant among patients with disease lasting more than six weeks, this subgroup comprised only 34 participants overall. Failure to reach statistical significance therefore cannot be interpreted as evidence that the two treatments were equivalent in patients with longer-standing warts. Previous evidence is also inconsistent regarding the influence of disease duration. For example, Sloan et al. found no significant relationship between wart duration and cure after CO₂ laser treatment in patients with resistant verrucae. Accordingly, the present study does not establish disease duration as a predictor of differential response and would require a substantially larger study with formal interaction or multivariable analyses to address that question.

The difference in complete clearance observed in the present trial may be related to differences in the manner in which the two modalities destroy infected tissue, although this study was not designed to investigate a biological mechanism. CO₂ laser permits localized vaporization of water-containing tissue and control over the area of ablation, whereas liquid

nitrogen produces cellular injury through freezing and subsequent thawing. The literature also describes cryotherapy as requiring repeated applications in many patients, while laser ablation may achieve removal in fewer sessions in selected populations. These procedural differences provide a plausible context for the observed findings but should not be presented as a demonstrated explanation for the treatment effect in this study because depth of tissue destruction, HPV clearance, immune response, and other mechanistic variables were not measured.

A key strength of this study was its randomized controlled design, which enabled a direct comparison of CO₂ laser therapy and liquid nitrogen cryotherapy under a predefined treatment protocol. Equal allocation of 50 participants to each treatment group provided a balanced framework for evaluating the primary efficacy outcome, while the use of a clearly defined endpoint of complete wart clearance improved consistency in outcome assessment. The study also incorporated prespecified stratified analyses according to age, sex, disease duration, lesion site, and number of warts, allowing the overall treatment effect to be examined across clinically relevant subgroups without altering the primary comparison. In addition, both interventions were delivered using standardized procedural approaches, which reduced variation in treatment administration and strengthened the internal consistency of the comparison. The inclusion of patients with palmoplantar warts specifically, rather than a heterogeneous mixture of wart types, further improved the clinical relevance of the findings. Finally, the study contributes locally generated randomized evidence from a Pakistani population, addressing the relative scarcity of direct comparative data on CO₂ laser therapy versus cryotherapy for palmoplantar warts and thereby adding context-specific evidence to the existing literature.

Several limitations should be considered. First, this was a single-center study with 100 participants and consecutive recruitment, which may limit generalizability to populations with different demographic or clinical characteristics. Second, although allocation to treatment groups was randomized, blinding of participants or outcome assessors was not described, and complete clearance was determined clinically; this introduces the possibility of assessment bias for an outcome based on visual

examination. Third, the study evaluated treatment efficacy but did not provide comparative data on pain, scarring, dyspigmentation, healing time, treatment burden, patient satisfaction, or other adverse effects. These outcomes are relevant when comparing destructive procedures and should be incorporated into future trials. The literature itself emphasizes that the potential efficacy of ablative laser therapy must be considered alongside pain and other procedure-related effects. In addition, recurrence was not reported as an outcome in the present dataset. This limits conclusions to the observed period of clinical clearance and prevents assessment of whether the initial difference between treatments persists over longer follow-up. This distinction is important because HPV may persist in clinically normal surrounding tissue and recurrence can occur after apparently successful treatment. Previous investigations have therefore evaluated recurrence for several months after treatment, including the randomized studies by Hemmatian Boroujeni and Handjani and Azizjalali et al. Finally, the subgroup analyses involved multiple comparisons and relatively small cell sizes. They should therefore be considered supportive or exploratory rather than evidence for selecting treatment according to a particular age, sex, lesion site, disease duration, or wart burden.

Within these limitations, the present randomized comparison adds locally derived evidence to the relatively limited literature directly comparing CO₂ laser therapy with liquid nitrogen cryotherapy for palmoplantar warts. The observed complete-clearance rate with CO₂ laser therapy was consistent with the 88.3% reported in a previous Pakistani study of palmoplantar warts and with the approximately 89% clearance reported in selected studies of plantar warts. The current findings support a difference in short-term clinical clearance between the two treatment strategies in the population studied. Whether this difference is accompanied by advantages in recurrence, safety, treatment burden, patient-reported outcomes, or cost requires further evaluation before broader conclusions regarding treatment preference can be made.

CONCLUSION

In this randomized controlled trial of adults with palmoplantar viral warts, CO₂ laser therapy resulted in a higher rate of complete clinical clearance than liquid nitrogen cryotherapy.

Complete clearance was achieved in 88.0% of patients treated with CO₂ laser therapy compared with 54.0% of those receiving cryotherapy, corresponding to an absolute difference of 34 percentage points. The direction of this treatment difference was maintained across the prespecified strata of age, sex, lesion site, disease duration, and number of warts, although these subgroup analyses were not designed to establish treatment-effect modification. These findings provide randomized, locally derived evidence supporting CO₂ laser therapy as an effective treatment option for palmoplantar warts and add to the limited direct comparative literature evaluating CO₂ laser therapy against cryotherapy in this clinical setting. Larger multicenter trials with standardized outcome assessment and longer follow-up are therefore warranted to confirm these findings and to determine whether the observed difference in clearance is accompanied by sustained clinical and patient-reported benefits.

Acknowledgment

Grammarly for grammar check, Turnitin for plagiarism, Quilbot for paraphrasing and SPSS version 23.0 for statistical analysis.

Declaration of Patient's Interest

Patients' consent was not required as patients were not physically enrolled in this study.

Financial Support and Sponsorship

None. The whole project was self-funded by the authors.

Conflicts Of Interest

There are no conflicts of interest.

Use of Artificial Intelligence (AI)-Assisted Technology for Manuscript Preparation

The authors confirm that there was ethical use of artificial intelligence (AI)-assisted technology for assisting in the writing of this manuscript.

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