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Efficacy and Safety of Topical Steroid with 1064 nm Long-pulsed Nd:YAG Laser compared to Topical Steroid Alone in the Treatment of Paronychia associated with EGFR Inhibitors: A Randomized Controlled Pilot Study

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Abstract

Paronychia is a common adverse event associated with epidermal growth factor receptor inhibitor (EGFRI) therapy, substantially affecting patients' quality of life and adherence to cancer treatment. Currently, there are no definitive guidelines for its management. This prospective randomized controlled study evaluated the efficacy and safety of a topical steroid combined with a long-pulsed 1064 nm Nd:YAG laser compared to topical steroids alone for treating paronychiae associated with EGFRIs. Each of the ten patients with two lesions (20 in total) was randomized to receive laser treatment with topical steroids on one lesion (n = 10), while the other lesion received topical steroids alone (n = 10). PSG grade, Atis grade, and pain scores were assessed at baseline (Day 0) and on Days 7, 14, and 21. Photographic documentation was obtained at each time point. The laser group demonstrated significantly greater improvements. The reduction in PSG grade from Day 0 to Day 21 was more pronounced in the laser-treated lesions (-1.40 ± 0.84) than in those treated with steroids alone (-0.50 ± 0.97, p = 0.045). The reduction in Atis grade was also greater in the laser group (-2.70 ± 0.82) than in the control group (-0.30 ± 1.70, p = 0.003). Pain reduction was also more significant in the laser group. Nd:YAG 1064 nm laser therapy combined with topical steroids demonstrates superior efficacy in reducing inflammation and pain in EGFRI-associated paronychia. This suggests that a combined treatment approach is a promising option. Further studies with larger sample sizes are warranted to confirm these findings.

Keywords: *epidermal growth factor receptor inhibitors; long-pulsed 1064 nm Nd:YAG laser; paronychia; topical steroid*

1. Introduction

Paronychia is an inflammatory condition affecting the proximal and/or lateral nail folds, and is classified as acute or chronic. A specific subtype, chemotherapy-associated paronychia (CAP), arises following treatment with anticancer agents such as Epidermal Growth Factor Receptor Inhibitors (EGFRIs). Paronychia is a common adverse effect of EGFRIs, along with papulopustular rashes, hair growth abnormalities, pruritus, and xerosis collectively termed PRIDE syndrome (Papulopustules and/or Paronychia, Regulatory abnormalities of hair, Itching, Dryness due to EGFRIs). EGFRIs are effective treatments for various malignancies, including non-small cell lung cancer, colorectal cancer, and pancreatic cancer, particularly in patients with EGFR mutations (Gupta, & Lipner, 2022; Li et al., 2022; Shaban et al., 2023). However, currently available treatments, especially for severe cases involving granulation tissue, are often inadequate, too slow-acting, or overly invasive to effectively relieve symptoms and maintain EGFRI adherence. This underscores the need for a rapid and minimally invasive alternative treatment.

Because EGFRIs affect normal epidermal cells as well as tumors, they provoke chronic periungual inflammation, often driven by cytokines such as tumor necrosis factor-alpha (TNF-α), chemokine (C-C motif) ligand 2 (CCL2), chemokine (C-C motif) ligand 5 (CCL5), and interferon gamma-inducible protein 10 (IP-10) (Fabbrocini et al., 2015, Li et al., 2022; Lulli et al., 2016). In some cases, excessive inflammation can lead to pyogenic granuloma-like lesions, which are highly vascularized and prone to bleeding (Lacouture, 2006; Yen et al., 2020). Severe paronychia can cause intense pain, marked periungual swelling, and, in extreme cases, functional impairment, which significantly affect patients' quality of life. These complications may necessitate dose reductions or discontinuation of EGFRIs, thereby compromising cancer control. Consequently, managing EGFRI-induced skin toxicities is essential to ensure both effective oncologic treatment and preserved patient quality of life.

At present, there is no standardized protocol for managing EGFRI-induced paronychia. Recommended strategies include meticulous nail care, povidone-iodine soaks, topical and oral antibiotics, topical steroids, surgical procedures, and phenol chemical matricectomy (PCM) (Goto et al., 2016; Gupta, & Lipner, 2022). However, these treatments often yield limited success, particularly in severe cases characterized by granulation tissue formation.

Long-pulsed 1,064 nm Neodymium-doped Yttrium Aluminium Garnet (Nd:YAG) laser therapy, utilizing a 1064-nanometer wavelength, has demonstrated efficacy in various dermatological conditions, including vascular malformations and pigmented lesions (Hora et al., 2022; Serdar, & Izci, 2020). A pilot study by El-Komy, & Samir (2015) explored the use of long-pulsed 1064 nm Nd:YAG laser to treat chronic paronychia in women who frequently wash dishes. Their findings revealed significant reductions in inflammation severity with a favorable safety profile, as only mild, tolerable pain was reported during laser sessions. The proposed mechanisms of action include antifungal effects, modulation of immune responses, and enhancement of local microcirculation. Additionally, the 1064 nm Nd:YAG laser has been successfully used to treat pyogenic granulomas at finger and toe lesions (Hammes et al., 2012). The proposed mechanism is that light at this wavelength is effectively absorbed by hemoglobin, facilitating deep thermal damage and coagulation of neovascular structures, which are also present in EGFRI-associated paronychia (Dong et al., 2019; Gex-Collet et al., 2008).

Despite these promising findings, no studies have investigated the use of 1064 nm long-pulsed Nd:YAG laser therapy in patients with PRIDE syndrome-associated paronychia. This study aims to evaluate the efficacy and safety of combining long-pulsed 1064 nm Nd:YAG laser therapy with topical steroids compared to topical steroids alone in the treatment of EGFRI-induced paronychia.

2. Objectives

This study aimed to evaluate the efficacy and safety of combining long-pulsed 1064 nm Nd:YAG laser therapy with topical steroids compared to topical steroids alone for the treatment of EGFRI-associated paronychia. Outcomes included changes in paronychia severity grades, pain scores (VAS), and adverse events.

3. Materials and Methods

This was a single-center, prospective, randomized controlled trial involving adult cancer patients who developed paronychia associated with EGFR inhibitors. The study duration was three weeks, with in-person visits on Day 0, Day 7, and Day 21, and a telemedicine follow-up on Day 14 for digital imaging and adverse event reporting. All procedures complied with institutional ethical standards, and were approved by the Chulabhorn Royal Academy's Ethical Committee, approval no. EC080/2566. Written informed consent was obtained from all participants.

3.1 Patient Population

Eligible participants were adults aged 20 years or older, with paronychia developing during EGFR inhibitors therapy with involvement of at least 2 nail lesions on the hands or feet, and a PSG score of three or higher. Any ongoing treatment for paronychia at the time of screening was discontinued at least two weeks prior to study entry. All participants agreed not to use any topical products other than the topical steroid provided by the researcher and emollients. Participants who were already receiving antibiotics for conditions other than paronychia continued their treatment. Exclusion criteria included pregnancy or breastfeeding, conditions triggered by thermal exposure from laser (e.g., panic disorder, epilepsy), and prior use of topical steroids within the past two weeks.

3.2 Nd:YAG Laser Procedure

Participants received two sessions of long-pulsed 1,064 nm Nd:YAG laser treatment (GentleMax Pro®, Candela Corp., Wayland, MA, USA) on Days 0 and 7,

using a fluence of 100 J/cm², a 6-mm spot size, and a 10-ms pulse duration. A single pass was delivered over the lesion at each visit using these fixed parameters. Continuous cold air cooling was applied to minimize thermal damage to the surrounding tissues. The laser parameters were adapted from Dong et al., (2019), who reported favorable outcomes using similar settings (fluence 100–125 J/cm², 6-mm spot size, 10.5–13.5 ms pulse duration) for treating pyogenic granulomas at nail sites. Our parameters fall within this range, representing a balanced approach between efficacy and tolerability (Dong et al., 2019; Gex-Collet et al., 2008). Two sessions were selected based on prior studies showing clinical improvement after one to two treatments.

3.3 Topical Corticosteroids

All participants received betamethasone valerate 0.1% cream, classified as a potent steroid (US classification: Class III–V). Participants were instructed to apply the cream to all paronychial lesions, including the laser-treated sites, twice daily. Betamethasone valerate was selected based on evidence demonstrating clinical improvement in chronic paronychia with a three-week course of topical methylprednisolone aceponate 0.1%, a steroid of comparable potency (Tosti et al., 2002). Additionally, betamethasone valerate was preferred due to its favorable safety profile, particularly when used in combination with laser therapy.

3.4 Assessment Methods

3.4.1 Clinical Assessments

Assessments were performed at the baseline and weekly thereafter until the last follow-up (three weeks after the first treatment session or two weeks after the second treatment session).

For clinical scoring of the severity of paronychial lesions, we employed the Paronychia Severity Grading (PSG) scale with a total of six grades (shown in Table 1) and Atis et al.'s paronychia severity index with a total score of 14 (shown in Table 2). Both scoring systems were used to describe clinically relevant differences in disease severity and to enhance the precision of efficacy comparisons between treatment groups. The scoring systems were examined for the degree of inflammation of the periungual area, such as erythema, edema, discharge, and granulation tissue. Furthermore, pain levels were assessed separately at each evaluation point using a Visual Analog Scale (VAS).

Additional assessment included photography using a digital phone camera (iPhone 14 Pro, Apple Inc.). To minimize variation in color, white balance, and scale across images, all participants were photographed against a black plate with a white background scale. This setup ensured consistent evaluation of erythema intensity and edema size. All images were independently evaluated by one unblinded investigator and two blinded dermatologists using predefined grading criteria. If a discrepancy of two or more points occurred between evaluators, the case was excluded from analysis. For discrepancies of less than two points, consensus was used to resolve differences, ensuring consistency and accuracy in severity grading.

3.4.2 Patients' Self-assessment

Patients were asked to report the degree of pain they felt during the first and second sessions for Nd:YAG laser through the pain visual assessment score (0–10) where "0" =no pain, "1–3" =mild pain, "4–6" =moderate to severe, "7–9" =very severe and "10" =worst pain possible. At the final follow-up, compliance with topical medication was assessed, and a satisfactory score was recorded.

Table 1 Six-Point Paronychia Severity Grading (PSG) Scale[1]

Grade 0	No sign or symptoms of paronychia
Grade 1	Erythema of periungual skin
Grade 2	Erythema, edema of periungual skin
Grade 3	Erythema, edema, discharge from periungual skin
Grade 4	Erythema, edema, discharge, periungual granulation tissue
Grade 5	Erythema, edema, discharge, subungual granulation tissue

[1]Note: Adapted from Capriotti et al. (2019)

Table 2 Atis et al.'s Chronic Paronychia Severity Index[1]: A grading system assessing nail folds involvement, edema, erythema, nail plate change, and cuticle integrity

Component	Description	Score
Nail fold involvement	Involvement of 1 nail fold (proximal or lateral)	1
	Involvement of 2 nail folds (proximal and/or lateral)	2
	Bilateral lateral nail folds involvement and proximal nail fold involvement	3
Edema	Absent	0
	Mild	1
	Moderate	2
	Severe	3
Erythema	Absent	0
	Mild	1
	Moderate	2
	Severe	3
Nail plate change	Absent	0
	Mild	1
	Moderate	2
	Severe	3
Cuticle	Normal	0
	Damaged	1
	Absent	2

[1]Note: Adapted from Atış et al., (2018).

3.5 Safety

Safety was evaluated for all treated patients using physical examinations. Cutaneous adverse effects were evaluated and recorded by the investigator, including edema, vesiculation, bullae, and necrosis.

3.6 Blinding and Randomization

One lesion per participant was randomly allocated to laser therapy combined with topical steroid via computer-generated randomization, while the other served as the control (topical steroid alone). Due to the visible nature of the interventions, blinding of participants and treating investigators was not feasible. However, to minimize observer bias, outcome assessments were conducted by independent evaluators who were blinded to treatment allocation. This approach ensured objective evaluation of outcomes while addressing the practical limitations of blinding in this study design.

3.7 Statistical Methods

Statistical analyses were performed using STATA (version 17; StataCorp LLC, College Station, TX, USA). Continuous variables are presented as mean ± standard deviation (SD), while categorical variables are reported as frequencies (%). The normality of continuous data was assessed using the Shapiro–Wilk test. Participants were randomized into Control and Laser groups and evaluated on Days 0, 7, 14, and 21. Primary outcomes (PSG grades, Atis grades, and pain scores) were treated as ordinal measures. Between-group comparisons at each time point were analyzed using the Mann–Whitney U test. Within-group changes over time were assessed using the Friedman test, followed by Wilcoxon signed-rank tests with Bonferroni correction for multiple comparisons. Post hoc power calculations were conducted for between-group and repeated-measures comparisons. Statistical significance was set at $p < 0.05$.

4. Results

4.1 Demographics and Clinical Characteristics

A total of 10 patients (8 women and 2 men; mean age 69.3 ± 9.5 years) with EGFR inhibitor-associated paronychia were enrolled, providing 20 nail lesions (2 lesions per patient). All patients had lung cancer (n=10), with most received erlotinib (50%), followed by osimertinib (40%) and afatinib (10%). The mean body mass index was 20.1 ± 4.7 kg/m^2. Nine patients (90%) were never smokers, and one (10%) was a former smoker. Regarding lesion distribution, 80% of patients presented with both

fingernail and toenail involvement, while the remaining 20% had lesions restricted to either fingernails or toenails only. Other dermatologic complications included papulopustular eruptions (40%), abnormal hair growth (40%), itching (80%), and dryness (100%) (Table 3). Each patient contributed one lesion to the Laser group (Nd:YAG + topical steroid) and another to the Control group (topical steroid alone), ensuring balanced both baseline demographic and clinical characteristics across both groups

All 10 patients completed baseline and Day 21 visits. One patient missed visits on Days 7 and 14 but returned for the final visit, resulting in complete endpoint data on Day 21 for all lesions (Figure 1). Data from this patient were included in the Day 21 endpoint analysis without imputation of the missing intermediate data. This decision was made in consideration of the study's small sample size and exploratory nature, with the aim of maintaining the integrity of the observed data

Table 3 Patient Demographic data

Age, y/o	
Range (mean ± SD)	48-81 (69.3 ± 9.5)
Gender, n (%)	
Women	8 (80%)
Men	2 (20%)
BMI, kg/m^2	
mean ± SD	20.1 ± 4.7
Smoking status, n (%)	
Never	9 (90%)
Ex-smoker	1 (10%)
Primary cancer, n (%)	
Lung	10 (100%)
Breast	0 (0%)
Colon	0 (0%)
Neoplasia treatment	
Afatinib	1 (10%)
Erlotinib	5 (50%)
Osimertinib	4 (40%)
Lesion localization	
Fingernails only	1 (10%)
Toenails only	1 (10%)
Both	8 (80%)
Number of fingers involvement, Mean (range)	
Hands	2.3 (0-8)
Feet	2.1 (0-3)
Other toxic effects, No (%)	
Papulopustular eruption	4 (40%)
Abnormal hair growth	4 (40%)
Itch	8 (80%)
Dryness	10 (100%)

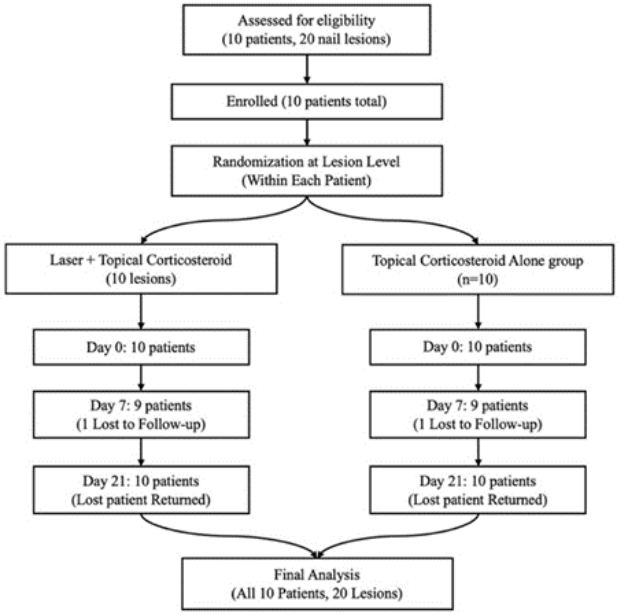

Figure 1 CONSORT diagram of the patients

Table 4 Comparison of Clinical Outcomes Between Laser and Control Groups: PSG grade, Atis grade, and pain scores over time.

	Control		Laser		P-value	Power
	n	**Mean** ± SD	**n**	**Mean** ± SD		
PSG grade						
Day 0	10	3.70 ± 0.48	10	3.90 ± 0.32	0.276	0.178
Day 7	9	3.78 ± 0.44	9	3.56 ± 0.53	0.331	0.147
Day 14	9	3.78 ± 0.44	9	3.78 ± 0.44	1.000	-
Day 21	10	3.20 ± 0.79	10	2.50 ± 0.85	0.062	0.439
Atis grade						
Day 0	10	6.80 ± 1.14	10	7.60 ± 0.84	0.166	0.391
Day 7	9	7.00 ± 1.00	9	6.78 ± 0.44	0.635	0.086
Day 14	9	7.44 ± 1.42	9	6.56 ± 1.13	0.157	0.276
Day 21	10	6.50 ± 1.58	10	4.90 ± 0.88	0.007	0.740
Pain score						
Day 0	10	4.80 ± 1.87	10	6.00 ± 2.00	0.221	0.259
Day 7	9	4.44 ± 1.81	9	4.78 ± 1.86	0.929	0.066
Day 14	9	4.00 ± 1.87	9	4.00 ± 1.80	0.822	-
Day 21	10	3.50 ± 1.90	10	2.80 ± 1.81	0.357	0.126

4.2 Efficacy

4.2.1 Comparison between Groups at each Time Interval

The mean PSG grade, Atis grade, and pain score at each time point by group were illustrated in Table 4. Although no statistically significant differences emerged between groups at Day 0, 7, or 14 (all $p > 0.05$), the Laser group demonstrated lower (better) mean PSG grade, Atis grade, and pain scores at Day 21, with the difference in Atis grade reaching statistical significance ($p = 0.007$).

4.2.2 Comparison of Mean Differences in Changes of Paronychia Severity and Pain Over Time between Groups

Mean changes in PSG grade, Atis grade, and pain over time between groups are shown in Table 5. By Day 21, the laser group showed significantly greater improvements in PSG grade ($p = 0.045$), Atis grade ($p = 0.003$), and pain ($p = 0.009$) compared with the control group. The findings highlighted the adjunctive benefit of Nd:YAG laser in resolving inflammation and discomfort.

Table 5 Mean Differences in Paronychia Severity and Pain Over Time: Comparative analysis of laser and control groups

	Control		Laser		P-value	power
	n	**Mean** ± SD	**n**	**Mean** ± SD		
PSG grade						
Day 0 - Day 7	9	0.00 ± 0.50	9	-0.33 ± 0.50	0.176	0.261
Day 0 - Day 14	9	0.00 ± 0.50	9	-1.11 ± 0.60	0.654	0.979
Day 0 - Day 21	10	-0.50 ± 0.97	10	-1.40 ± 0.84	**0.045**	0.554
Atis grade						
Day 0 - Day 7	9	0.00 ± 0.71	9	-0.89 ± 1.05	0.079	0.510
Day 0 - Day 14	9	0.44 ± 1.13	9	-1.11 ± 1.45	0.037	0.658
Day 0 - Day 21	10	-0.30 ± 1.70	10	-2.70 ± 0.82	**0.003**	**0.960**
Pain score						
Day 0 - Day 7	9	-0.67 ± 1.12	9	-1.44 ± 1.24	0.130	0.255
Day 0 - Day 14	9	-1.11 ± 1.36	9	-2.22 ± 1.20	0.056	0.407
Day 0 - Day 21	10	-1.30 ± 1.42	10	-3.20 ± 1.32	**0.009**	**0.834**

Within-group repeated-measures analyses further supported these findings. Figure 2 shows the changes in PSG grade, Atis grade, and pain score in the laser and control groups over time. In Figure 2a, the laser group showed a significant reduction in PSG grade from Day 0 to Day 21 ($p < 0.001$, Friedman test), with post hoc comparisons revealing significant improvements between Day 7 and Day 21 ($p = 0.048$) and Day 14 and Day 21 ($p = 0.004$). In contrast, the control group did not exhibit significant PSG improvements ($p = 0.125$), suggesting that Nd:YAG laser therapy facilitated faster lesion resolution compared to topical steroids alone.

Changes in Atis grade in the laser and control group over time, shown in Figure 2b, further confirmed the beneficial effects of Nd:YAG laser therapy. The laser group demonstrated a significant reduction in Atis grade between baseline and last visit ($p < 0.001$, Friedman test), with significant post hoc differences observed between Day 7 and Day 21 ($p = 0.010$) and Day 14 and Day 21 ($p = 0.024$). In contrast, the control group did not show significant improvement ($p = 0.622$), indicating that standard treatment with topical steroids alone was insufficient for achieving meaningful reductions in lesion severity. These findings reinforce the superior efficacy of Nd:YAG laser therapy in improving chronic paronychia symptoms.

Pain levels were assessed using VAS. The laser group showed a significant reduction in pain between Day 0 and Day 21 ($p = 0.003$, Friedman test) (Figure 2c). However, other post hoc comparisons did not reach statistical significance ($p > 0.05$), indicating that the most substantial pain reduction occurred over the entire study duration rather than at earlier time points. Similarly, the control group also experienced a significant reduction in pain from Day 0 to Day 21 ($p = 0.006$), though the magnitude of improvement was less pronounced compared to the Laser group. These results suggest that Nd:YAG laser therapy provides superior pain relief in EGFRI-associated paronychia compared to steroids alone.

An example of clinical progression is shown in Figure 3, which illustrates the comparative lesion response in Patient No. 2 across the 3-week treatment period.

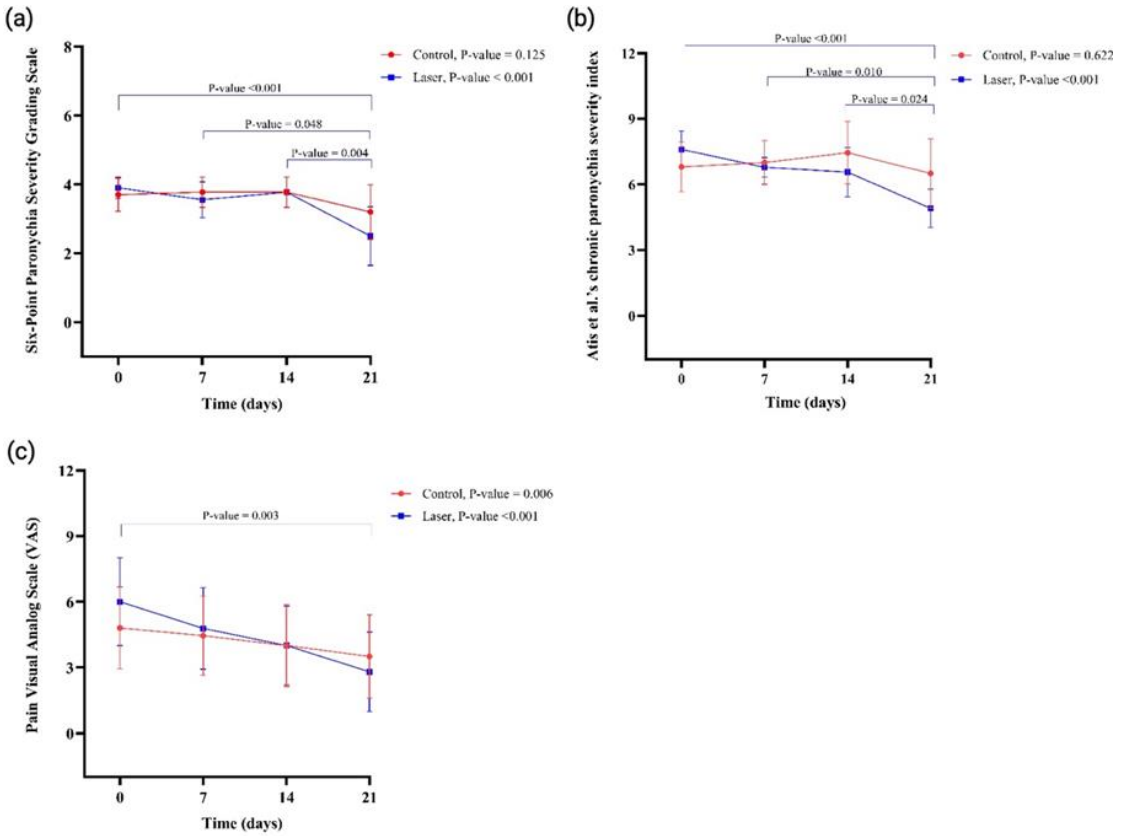

Figure 2 Changes in (a) Paronychia Severity Grading (PSG) Scale (b) Atis et al.'s Chronic Paronychia Severity Index (c) Pain Visual Analog Scale (VAS) scores in the Laser and Control groups over time

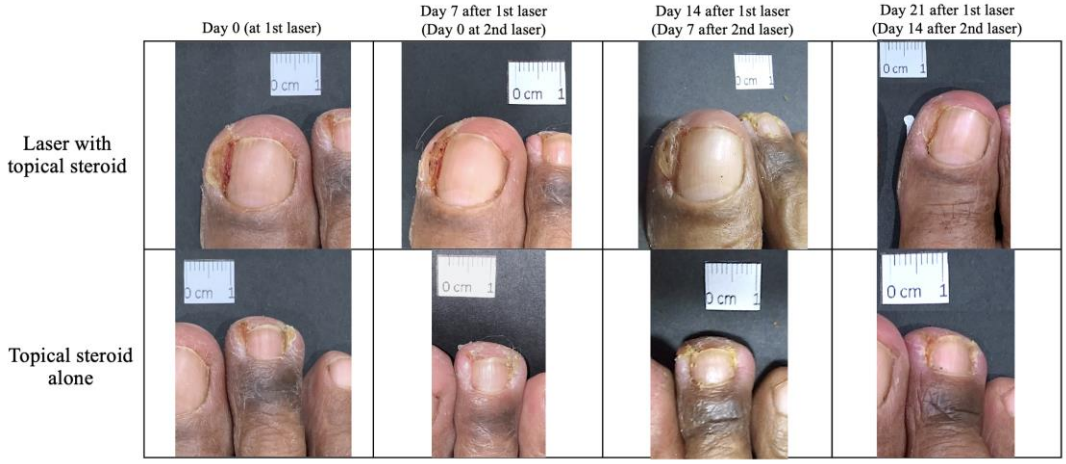

Figure 3 Clinical course of EGFRI-associated paronychia in Patient No. 2. The top row shows the lesion treated with Nd:YAG laser plus topical steroid at Day 0 and Days 7, 14, and 21. The bottom row shows the lesion treated with topical steroid alone over the same time points

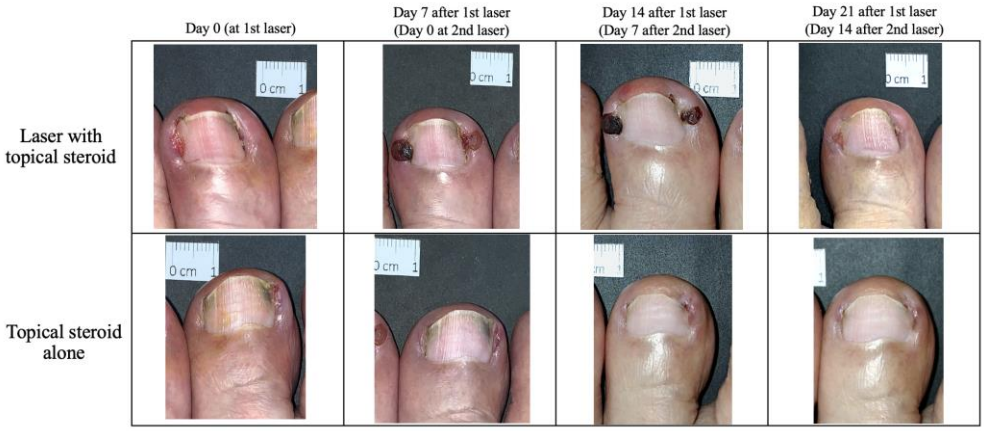

Figure 4 Blister formation as an adverse event of Nd:YAG laser is shown in the top row. The blister resolved spontaneously by the third week

4.3 Adverse Events

No serious adverse events were reported. One participant developed a blister at the laser-treated site (Figure 4), which dried and resolved spontaneously by week three. Other participants reported only mild discomfort, such as transient pain or heat sensation during laser sessions, along with mild edema and erythema. These symptoms resolved within one day and were well tolerated. No participant discontinued the study due to adverse effects.

4.4 Patient Satisfaction

At the final visit, all participants reported a high level of satisfaction, with an average rating of 8 out of 10. Additionally, all participants noted that the laser-treated side experienced less pain and exhibited a drier, improved appearance compared to the non-laser-treated side.

5. Discussion

Paronychia is a frequent and often debilitating side effect of EGFRIs, significantly affecting patients' quality of life and adherence to cancer treatment. Our findings show that adjunctive Nd:YAG laser therapy with topical steroids significantly lowers lesion severity and pain than topical steroids alone.

EGFRIs are widely used in the treatment of various malignancies, including lung, liver, and breast cancers. These agents target the epidermal growth factor receptor on cancer cells, leading to the inhibition of tumor proliferation (Shaban et al., 2023). However, EGFRIs also affect normal epidermal cells. They provoke inflammatory cell infiltration and capillary formation, resulting in chronic paronychia and pyogenic granuloma-like lesions (Lacouture, 2006; Li et al., 2022; Yen et al., 2020).

In the absence of standardized treatment protocols, expert consensus recommends a severity-based, multimodal approach for managing EGFRI-induced paronychia (Califano et al., 2015; Lu et al., 2024). Mild cases may be treated with potent topical steroids, often in combination with topical antibiotics or antifungals and antiseptic soaks. For moderate cases, oral antibiotics such as doxycycline or minocycline are commonly introduced. Severe or refractory cases may necessitate EGFRI dose adjustment or temporary discontinuation, in conjunction with surgical interventions such as partial nail avulsion or phenol matrixectomy. However, surgical procedures may be too invasive for some patients and carry a risk of complications, underscoring the need for less invasive, yet effective, alternatives, such as Nd:YAG laser therapy

Our study demonstrated that long-pulsed 1064 nm Nd:YAG laser therapy may help relieve both the inflammatory and vascular components of paronychia associated with EGFRIs. The therapeutic effects of the laser likely arise from its ability to modulate cytokine activity and induce vascular coagulation. Our findings are consistent with previous research by El-Komy, & Samir (2015), which demonstrated that Nd:YAG laser treatment suppresses interleukin-8 (IL-8) levels while increasing transforming growth factor-beta (TGF-β), thereby reducing local inflammation in chronic paronychia caused by frequent exposure to water or irritants (El-Komy, & Samir, 2015; Rocha et al., 2023). Additionally, the 1064 nm wavelength is selectively absorbed by hemoglobin, resulting in thermal coagulation of abnormal neovascular structures. This mechanism may explain the regression of pyogenic

granuloma-like lesions, as observed in studies by Dong et al., (2019) and Gex-Collet et al. (2008), where lesions resolved after one or two treatment sessions. These findings reinforce the potential applicability of Nd:YAG laser therapy in managing EGFRI-induced paronychia. However, it should be noted that most comparative studies involved similar but not identical conditions, such as chronic paronychia or periungual pyogenic granulomas, and only one prior study directly addressed paronychia unrelated to EGFRI therapy.

Importantly, no serious adverse events were reported, and all patients tolerated the procedure well. Most participants experienced only mild, transient discomfort during the treatment, along with minor edema and erythema that spontaneously resolved within one day. One patient with pre-existing vesicles and severe lesions developed a blister, which resolved without intervention. This suggests that Nd:YAG laser therapy should be used with caution in patients with skin fragility and vesiculobullous changes, as they may have a higher risk of blister formation. For such cases, alternative treatments, such as topical or oral antibiotics, should be considered until the vesicles resolve, after which laser therapy may be introduced. Despite this, our findings align with existing literature on the safety profile of Nd:YAG laser therapy, supporting its role in EGFRI-associated paronychia management.

The findings of this study suggest that Nd:YAG laser therapy is an effective, well-tolerated treatment for EGFRI-associated paronychia. Unlike conventional approaches, which often require prolonged topical or systemic therapies and, in severe cases, surgical intervention, laser therapy offers a non-invasive alternative that may accelerate healing, enhance adherence to EGFRI therapy, and improve patients' quality of life. Lesions treated with laser therapy demonstrated faster reductions in size, swelling, and pain compared to the control group, with quicker overall healing, particularly during the second and third weeks. However, the potential contribution of placebo effects to pain reduction cannot be entirely excluded. High patient satisfaction scores further support its feasibility as a practical treatment option. Although statistical significance was primarily observed on Day 21, this may reflect the cumulative therapeutic effect of Nd:YAG laser treatment. This delayed response is consistent with the gradual healing process typical of chronic inflammatory conditions. The pattern observed in our study suggests that meaningful clinical differences may become more apparent following repeated treatment or sufficient time for tissue recovery.

To the best of our knowledge, this is the first randomized controlled trial (RCT) evaluating the efficacy of 1064 nm Nd:YAG laser therapy for EGFRI-associated paronychia. Previous research has demonstrated the efficacy of Nd:YAG laser in treating periungual pyogenic granuloma and paronychia from prolonged inflammation after dishwashing, further validating its use in this context.

Despite promising findings, this study has several limitations. First, the small sample size (10 patients, 20 lesions) may have limited the study's statistical power, particularly at early time points when changes were more gradual and less pronounced. This limitation also reduces the generalizability of the results, as findings from a small cohort may not be representative of the broader patient population. Furthermore, while moderate to high statistical power was achieved for late-stage comparisons, larger-scale studies are warranted to validate these results. Nevertheless, the observed clinical improvements are encouraging. Second, the short follow-up period may not fully capture recurrence or long-term outcomes. While this study was specifically designed to evaluate the short-term efficacy of Nd:YAG laser, future studies should extend the follow-up period to assess the durability of response and recurrence rates. Third, only participants with moderate to severe paronychia (PSG score $\geq$3) were included, as this study focused on evaluating Nd:YAG laser therapy as a less invasive treatment option for severe cases. Milder cases, which may respond to standard treatments alone, were not included. Lastly, in Thailand, although Nd:YAG laser is widely available in tertiary medical centers and dermatology practices, access to smaller or resource-limited clinics may be restricted. Nevertheless, our findings may offer a viable, non-invasive treatment option that could be integrated into care at tertiary centers, which are typically responsible for administering EGFRI therapy. Given the inflammatory nature of many nail disorders, the therapeutic effects of Nd:YAG laser particularly its anti-inflammatory and vascular coagulation mechanisms may extend beyond paronychia associated with EGFR inhibitors, ensuring its continued relevance in clinical practice.

6. Conclusion

The 1064 nm long-pulsed Nd:YAG laser therapy, in combination with topical steroids, shows promise as a noninvasive therapeutic option for EGFRI-associated paronychia, particularly in moderate to severe cases. While the treatment demonstrated favorable

short-term outcomes and good patient tolerance, the clinical implications should be interpreted with caution due to the small sample size and limited follow-up duration. Long-term safety and recurrence outcomes remain unknown. Nonetheless, this approach may expand therapeutic options in dermatologic and oncologic supportive care. Further investigation of Nd:YAG laser therapy for EGFRI-associated paronychia may offer additional benefits for patients undergoing cancer treatment. Future research should include larger patient populations, a laser-only treatment arm, extended follow-up periods, and comparative assessments of alternative laser parameters to establish optimal protocols and confirm sustained efficacy.

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