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ORIGINAL ARTICLE

Long-pulsed 1064-nm and 755-nm lasers for C1 leg veins on skin type IV patients: a side-by-side comparison

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Abstract

Long-pulsed 1064-nm (LP1064) and 755-nm (LP755) lasers have been demonstrated as effective treatments for leg veins. However, few studies of these treatments on Asian skin type as well as direct comparison between two methods were reported. The aim of this study was to compare the clinical efficacy and safety of LP1064 with LP755 in the treatment of C1 leg veins on skin type IV patients. Patients with symmetric matched areas C1 leg veins were treated with single session of LP1064 for the right and LP755 for the left. Treated areas of every patient were divided into matrices of 2 × 2 cm squares. Vessels in the highest density squares were subjected to evaluation. Spot sizes were 5 mm fixed. Pulse durations and fluences were according to vessel diameters and endpoints, respectively. The clearances were evaluated at 1 and 3 months post treatment. Side effects were recorded immediately, 10 min, 24 h, and 1 and 3 months after treatment. Twenty-two patients were enrolled with total 96 vessels from 22 selected squares in the right and 106 vessels from 22 selected squares in the left. At 1-month follow-up, the clearances of LP1064 and LP755 were not significantly different (71.87% and 71.69%, respectively; $p = 0.99$). At 3-month follow-up, the efficacies were constant and no recurrence occurred. Pain levels of both methods were moderate and significantly lower in LP755. These findings suggest that LP1064 and LP755 laser treatments were comparatively effective and safe for C1 leg veins of skin type IV patients.

Keywords Clinical trial · Long-pulsed 1064-nm Nd:YAG laser · Long-pulsed 755-nm alexandrite laser · Telangiectasia · Reticular veins · Leg veins

Introduction

Chronic venous disorder (CVD) is a complex pathology resulting from a multifactorial etiology. Incompetent venous valves, reflux, hereditary, and gravity play major roles. Clinical manifestations of CVD range from dilated superficial vessels in the skin to chronic leg ulcers. The classification for CVD, which includes clinical manifestations (C), etiological factors (E), anatomic distribution of disease (A), and underlying pathophysiological findings (P), is known as CEAP. Of these, clinical manifestations including C0 to C6 are most commonly utilized. C0 refers to invisible or palpable signs of venous disease, while C1 refers to telangiectasia and reticular veins. Telangiectasia is defined as dilated intradermal venules less than 1 mm in caliber, and reticular veins are dilated bluish subdermal veins which have 1 mm up to 3 mm diameter with exclusion of normal visible veins in thin and transparent skin [1]. Various treatment options for CVD including invasive and noninvasive methods exist depending on disease stage. For C1, sclerotherapy with intravenous injection of a liquid or foamed sclerosants including hypertonic solution of sodium chloride, sodium tetradecyl sulfate, and polidocanol has been well demonstrated as a high benefit method and is considered first choice [2]. This method has limitations on very small vessel and complications such as telangiectatic matting, skin necrosis, potential allergy to sclerosants, and persistent residual hyperpigmentation [3, 4].

Laser therapy with vascular-specific wavelengths has been utilized since the inception of the selective photothermolysis theory in the early 1980s. Pulsed dye laser with the wavelengths of 585/595 nm and intense pulsed light are very

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effective for capillary lesions such as port wine stains, rosacea, and hemangiomas [5, 6]. Those light sources have less potent effect in the treatment of larger and deeper vessels such as leg telangiectasia and reticular veins due to shallow penetration [7–9]. Studies have shown that treatments using long-pulsed 1064-nm Nd:YAG (LP1064) and long-pulsed 755-nm alexandrite (LP755) are effective in telangiectasia and reticular veins [10, 11]. To the best of our knowledge, most studies of laser treatment for dilated leg veins were carried out on Caucasian skin type patients, and there is only one study directly comparing three wavelengths including LP1064 and LP755 in terms of efficacy and safety [12]. In this article, we present our findings comparing LP1064 to LP755 in the treatment of C1 leg veins in Vietnamese patients.

Materials and methods

This was an open-label prospective study conducted on skin type IV patients with C1 leg veins including telangiectasia and reticular veins. Exclusion criteria were pregnancy; lactation; anticoagulation agents uses; active skin infection; or history of herpes simplex infection, thrombosis, hypercoagulability, diabetes, hypertrophic/keloid scar, and cardiovascular, renal, and liver disease. Ethical approval was sought and granted by the Board of Ethics in Biomedical Research from the University of Medicine and Pharmacy at the University of Ho Chi Minh City in Vietnam in line with the Helsinki declarations for ethics and medical research. The study was issued a code 200/UMP-BOARD.

On every patient, two matched areas on both legs were chosen for treatment. The treated areas were divided into matrices of 2 by 2 cm^2. Vessel numbers of the squares with highest vascular density were counted for evaluation of efficacy. Vessel diameters were measured by a 1-mm-scale ruler. Treatment was set up with LP1064 or LP755 of duo-wavelength system (CLARITY, Lutronic Aesthetic Ltd., Korea). Patients were treated with LP1064 on the right and LP755 on the left sides. In the LP1064 side, a single pass with 5 mm fixed spot size, pulse width of 20 ms for telangiectasias, and 30 ms for reticular veins and fluences of 120 to 220 J/cm^2 was used. In the LP755 side, a single pass with 5 mm fixed spot size, pulse width of 12 ms for telangiectasia, and 20 ms for reticular veins and fluences of 55 to 140 J/cm^2 was used. In all cases, fluence levels were adjusted to achieve clinical endpoints of vessel blanching or grayish color within the vessel. The parameters were selected based on the clinicians' experience and the selective photothermolysis theory with larger vessels requiring a longer pulse duration. We chose the 5 mm spot size as it has the advantage of good penetration particularly considering the larger vessels. The fluence was chosen depending on the pulse duration and size of the vessel with the aim of achieving the desired clinical endpoint. Intelligent cooling device at 10/20/10 ms and additional post-treatment cooling with ice packs within a minute were applied. Immediately post laser, pain levels were measured by visual analog scale (VAS, 0–10) with 0 being reported as totally painless and 10 as unbearable painful sensation. Within 10 min, any focal skin changes were considered to be early side effects. Patients were instructed to avoid sun exposure during this study. Follow-up was scheduled at 24 h and 1 and 3 months post treatment. Efficacy was evaluated by clinical examination and comparison of pre- and post-treatment standardized photos. Proportion of disappeared vessels to baseline was defined as clearance. All results were independently evaluated by two authors (TNH.N. and TT.V.).

Statistical analysis was performed with R language. Median and interquartile range (IQR) were calculated. The Mann-Whitney signed rank test, chi-square test, or Fisher's exact test were used when applicable. A p value of less than 0.05 was considered significant difference in this study.

Results

Twenty-two Vietnamese patients, three males and nineteen females, with median age of 32 were enrolled and all patients completed the study. The distribution of treated areas was as follows: thigh in 7 patients (34%), ankle in 6 patients (27%), popliteal fossa in 5 patients (23%), and lower leg in 4 patients (18%). All treated areas were matched anatomically to be as symmetrical as possible. There was no significant difference of treated area between the two sides, in which the IQR of LP1064-treated areas was 6.5–17.5 cm^2 and the IQR of LP755-treated areas was 8–15 cm^2, $p = 0.4$, Mann-Whitney signed rank test.

In total, 44 squares of 22 patients were selected for counting vessel number. The total vessel numbers of 22 squares on the right were 96 with the median of 4 (IQR: 3–5.75) and on the left were 106 with the median of 4.5 (IQR: 3–6.75) (Table 1). Vessels with diameter of less than 1 mm accounted for 82.7% vessels of 44 squares.

At 1-month evaluation using clinical examination and standardized photography, the overall clearance in both groups were identical (71.87% and 71.69% in the LP1064 and LP755 groups, respectively; $p = 0.99$). The clearance of vessels with diameter of 1–3 mm was significantly higher than that of < 1 mm in the LP1064 side. The same tendency was also observed in the LP755 treatment group, though there was no significant difference (Table 2; Figs. 1 and 2). At the final follow-up at 3 months, there was no change of vessel appearance as compared with the first month visit.

To clarify the efficacy on each patient, medians of clearance were calculated. Data showed that the number of vessels treated by either method dramatically decreased. The medians of clearance were 100% and 93.75% in the LP1064 and

Table 1 Number of vessel on evaluated squares before treatment

Diameter	Right side		Left side		*p
	No. of vessel of 22 patients	Median [IQR]	No. of vessel of 22 patients	Median [IQR]	
< 1 mm	73	3 [0–4.75]	94	4 [3–6]	0.54
1–3 mm	23	0 [0–2]	12	0 [0–0.75]	0.70
Total	96	4 [3–5.75]	106	4.5 [3–6.75]	0.34

The vessels were mainly telangiectasias. There were no significant differences between two sides regardless of diameters. IQR, interquartile range; *, Mann-Whitney signed rank test

LP755 sides, respectively. There was no significant difference between the two methods ($p = 0.31$) (Table 3).

Next, we analyzed whether clinical endpoints from the two wavelengths were different and could predict a meaningful response. Our data showed that LP1064 induced higher incidence of blanching, whereas LP755 induced higher incidence of grayish change (Table 4). Interestingly, we found that in LP1064 group, the blanching endpoint was significantly more indicative than grayish endpoint to subsequently induce clearance of vessels < 1 mm ($p = 0.00$) (Table 5). In case of LP755-treated vessels, we could not find significant difference between the 2 endpoints (data not shown).

All patients reported transient painful sensation. Pain caused by LP1064 with median of 7 (ranged 2–8) was significantly higher than pain caused by LP755 with median of 5 (ranged 2–8) ($p = 0.00$). For physical side effects, Table 6 shows that at 10-min post treatment, erythema was present in 45.45% and 13.64% in both LP1064 and LP755 legs, respectively. The percentages of patients with erythema significantly increased over 24 h, however remarkably decreased at 1 month and completely resolved at 3 months post treatment in both groups. Hyperpigmentation occurred in half or more of the patients at 1 month of observation, with no significant difference between the two groups (63.64% and 50% for LP1064 and LP755, respectively; $p = 0.36$). Hypopigmentation was seen in only one case treated with LP755. After 3 months, the proportions of hyperpigmentation dramatically decreased, and the case of hypopigmentation almost completely recovered. Purpura presented in 2 cases of the LP1064 group and vesicle in 5 cases of the LP755 group. No scars or ulcers were observed. All patients were reviewed and there were no patients lost to follow-up.

Table 2 Efficacy on 22 evaluated squares of each side

Diameter	LP1064	LP755	*p
< 1 mm	69.86%	70.21%	0.57
1–3 mm	95.65%	83.33%	0.26
Total	71.87%	71.69%	0.98
*p	0.01	0.3	

Clearances of two methods in either total vessel numbers or vessel diameters were not significantly different. *, chi-square test or Fisher's exact test

Discussion

Chronic venous disorder is a common condition of the lower limbs and has various clinical manifestations. Telangiectasia and reticular veins which are defined as C1 affect approximately 21.6% of the general population [13]. While sclerotherapy is a simple and effective technique for treatment of C1 leg veins, it is associated with a number of complications.

Vascular lasers have been widely used in primary vascular conditions, and its efficacy depends on variables such as underlying pathology, anatomic location, and types and parameters of lasers used. Hemoglobin is a main chromophore in vascular laser treatments with absorption peaks in certain wavelengths such as 532 and 585/595 nm. Leg veins are characterized by varying diameters and thicker vessel wall and

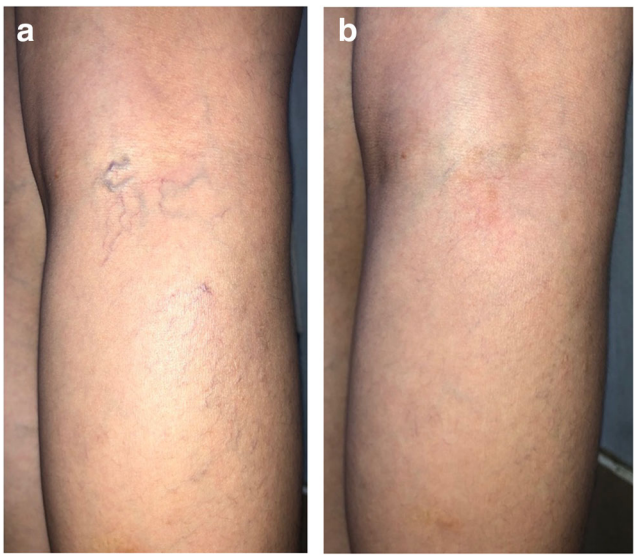

Fig. 1 Representative case of patient treated with LP1064. **a** Before treatment. **b** 3 months post treatment. Reticular veins were treated at fluences of 200 J/cm^2, pulse width of 30 ms; telangiectasia was treated at 140 J/cm^2, pulse width of 20 ms

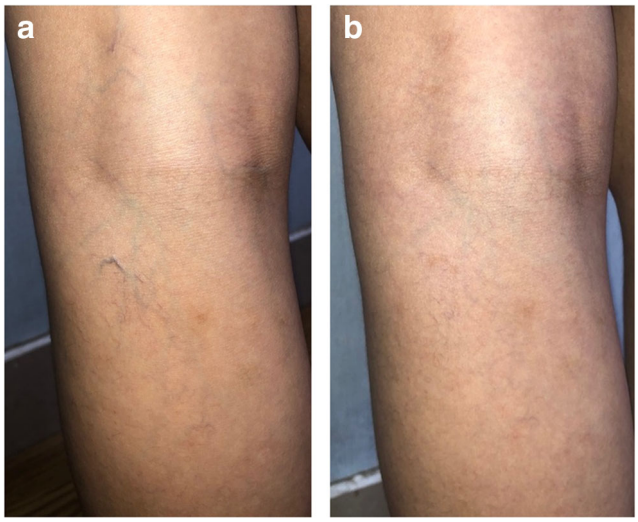

Fig. 2 Representative case of patient treated with LP755. **a** Before treatment. **b** 3 months post treatment. Reticular veins were treated at fluences of 110 J/cm^2, pulse width of 20 ms; telangiectasia was treated at 70 J/cm^2, pulse width of 12 ms

tend to be deeper than the reach of short wavelengths such as 532/595 nm, particularly in cases with vessels greater than 1 mm in diameter and at a depth greater than 1 mm. Studies have shown that treatments using LP1064 and LP755 are effective in telangiectasia and reticular veins [10, 14]. Moreover, Parlar B et al. reported that LP1064 treatment provided equal percentage of clearance but significantly lower percentage of post-inflammatory hyperpigmentation (PIH) as compared with sclerotherapy [15].

Efficacy of LP1064

Current trend in laser treatment for leg veins (C1) is the LP1064 owing to its relative low melanin absorption and greater depth of penetration. A series of studies demonstrated that LP1064 has superior results in comparison with other wavelengths. In a study by Ozden MG et al., the data showed that LP1064 was significantly higher in comparison with long-pulsed 532 nm laser in treatment of vessels smaller than 3 mm [16]. Eremia S et al. performed a side-by-side comparative study of three wavelengths including LP755, 810 nm diode, and LP1064 lasers and concluded the superiority of LP1064 in terms of vessel clearance and a lower profile of complications [12]. Another study by Sadick NS et al. on 13 patients with leg reticular veins and venulectasias showed that 62% of patients manifested 75 to 100% clearance of treated vessel surface areas after one treatment with LP1064 [17]. Similar results were found by Omura NE et al. on 20 patients with 1–3 vessels following a single LP1064 session [18]. In contrast, data from one study showed that there was only 4% of marked improvement after one session of LP1064, and five sessions were required to obtain 80.8% of marked improvement [19]. The authors applied 1.5–3 mm spot sizes for vessels up to 3 mm in diameter. This spot size may not be wide enough to effectively heat vessels. Supporting this notion, published studies showed that there was a difference in temperature and depth with different spot sizes [20, 21].

In our study, we treated patients with single treatment of LP1064 at 20–30 ms and 5 mm fixed beam, the overall clearance of total treated vessels of 22 evaluated squares was 71.87% at 1-month follow-up, and this clearance was constant at least 3 months post treatment (Table 2). These data suggest that single treatment with LP1064 is effective for reticular veins and telangiectasia.

Table 3 Reduction of vessel number on each patient at 1 month after treatment

	LP1064 Median [IQR]	LP755 Median [IQR]	*p
No. of vessels at baseline	4 [3–5.75]	4.5 [3–6.75]	
No. of vessels at 1 month	0 [0–1]	0.5 [0–2.75]	
Clearance (%)	100 [83.33–100]	93.75 [71.25–100]	0.31
^{+}p	0.00	0.00	

Numbers of vessels treated by either method were significantly lower than baseline. There was no significant difference of clearances on each patient between two wavelengths. *, $^{+}$, Mann-Whitney signed rank test

Table 4 Clinical endpoints of LP1064 and LP755

Clinical endpoints	No. of vessels		*p
	LP1064	LP755	
Grayish	56	94	0.00
Blanching	40	12	

Significant difference of clinical endpoints between LP1064 and LP755 treatment was observed. *, chi-square test

Table 5 Relevance of clinical endpoints and appearances of vessels treated with LP1064 at 1-month and 3-month follow-up

Diameter		Clinical endpoints		*p
		Grayish	Blanching	
< 1 mm				
	Absent	15	32	0.00
	Present	19	7	
1–3 mm				0.83
	Absent	21	1	
	Present	1	0	

For vessels <1 mm, blanching endpoint involved significantly higher efficacy than grayish endpoint. *, chi-square test

Table 6 Physical side effects caused by long-pulsed lasers at various time of examination

	Immediate	10 min *n* (%)	24 h *n* (%)	1 month *n* (%)	3 months *n* (%)
LP1064					
Erythema	0	10 (45.45)	17 (77.27)	1 (4.55)	0
Hyperpigmentation				14 (63.64)	5 (27.27)
Hypopigmentation				0	0
Purpura	0	0	2 (9.09)		
Vesicle	0	0	1 (4.55)		
LP755					
Erythema	0	3 (13.64)	13 (59.09)	3 (13.64)	0
Hyperpigmentation				11 (50)	4 (22.73)
Hypopigmentation				1 (4.55)	0
Purpura	0	0	0		
Vesicle	0	0	5 (22.73)		

Erythema and hyperpigmentation were mainly observed. There was significant difference of percentages of erythema between two methods at the 10th minute ($p = 0.02$) and significantly increased over 24 h in both groups ($p = 0.00$). There was no significant difference of hyperpigmentation proportion between the two groups ($p = 0.36$); Fisher's exact test. Other side effect occurred with low incidences

Comparison of efficacy between LP1064 and LP755

Although several studies have demonstrated the efficacy of LP755 for leg veins [22–24], treatment using this laser remains uncommon for this condition. This may come from its limitation due to higher absorbance of melanin. In the study of Eremia S et al., a regimen of 3 ms, 755 nm at 60–70 J/cm^2, and 8 mm spot size was effective for leg veins but caused significant complications including inflammatory response, purpura and matting [12].

Generally, in order to obtain efficient results, clinicians must address a number of factors that may influence outcomes. Optimal pulse duration is required to be long enough to warm up gently but short enough to avoid excessive bulk heating of the surrounding tissue [23]. Larger beam diameters provide greater optical penetration as a result of reduced scattering. Experience and recognition of warning signs are essential as larger spot sizes can increase the volumetric heating [21, 25].

We extrapolated that LP755 with longer pulse duration could heat vessels more gently and our chosen spot size could fully match vessels up to 3 mm in diameter with less risk of over coverage or excessive deep bulk heating, therefore providing optimal results with least damage of adjacent tissue. In our study, the clearance of LP755 was 71.69% at 1 month with minimal further change at 3-month follow-up. This result was comparative to efficacy of LP1064 ($p = 0.98$) (Table 2). Moreover, we also found that the medians of clearance were not significantly different between the two methods ($p = 0.31$) (Table 3).

The importance of pulse duration can be observed in 2 studies which used a 3–5 ms with LP755 which showed inferior results [12, 24] when compared with a study by Ross EV et al. using a longer pulse duration of up to 60 ms and a 6 mm spot. The latter achieved a higher clearance in line with our findings that shorter pulse durations than 60 ms were found effective in our study compared with previously published data on longer pulse durations [23].

Sizes of vessels and clearance

Large vessels have longer time to maintain a high temperature which leads to increased efficacy of intraluminal coagulation. In a study by Kauvar et al., the efficacy of treatment was higher in larger vessels when compared with smaller vessels despite appropriate selection of parameters [10]. These findings were reiterated in another study using LP1064 showing the highest clearance rate in reticular veins and the lowest rate with smaller spider veins [26].

Consistent with published studies, our results showed that clearance rate in vessels with 1–3 mm in diameter was significantly higher than that in smaller vessels in the LP1064 side. Although we could not find this significant difference in LP755, the tendency of higher clearance was also observed in 1–3 mm vessel (Table 2). Taken together, our results as well as the published literature show that larger diameter vessels are more responsive to laser therapy than smaller vessels.

Some studies described the increased clearance of vessels over time. A single session protocol of LP1064 in a study by Omura NE et al. showed the clearance of reticular veins at 3 months was higher than that at 1-month follow-up (65%

vs. 46%) [18]. In contrast, findings in a different study showed no difference at 1 month when compared with the 3-month follow-up [22].

The mechanism of laser-induced vessel clearance depends on heat-induced vessel constriction with spasm as well as on intraluminal thrombosis [27]. In comparison with smaller vessels, large vessels have a higher ratio of intraluminal thrombosis to vessel constriction, and this explains the time required for the subsequent inflammatory reaction with fibrosis and clearance. This concept was corroborated by our finding in which clearance of telangiectasia (constituted 82.7%) occurred in the first month with little ongoing change at 3-month follow-up.

Clinical endpoint and types of laser

Clinical endpoint is considered an important sign in laser treatment. In our study, blanching and grayish changes presented with different incidences in both methods, in which the proportion of blanching was higher in the group treated by LP1064 compared with LP755. This might come from the deeper penetration of LP1064, which induces higher intravascular temperatures, especially in small and superficial vessels such as telangiectasia [28]. This thermal effect in vessels smaller than 1 mm in diameter could enable blanching to occur as an endpoint with subsequent clearance, most likely as a result of heat-induced muscular contraction of the vessel wall. Interestingly, clearance achieved from blanching was significantly higher than that from grayish endpoint in LP1064 group (Table 5). These results suggested that in the treatment of telangiectasia with LP1064, blanching endpoint could be positive sign of clearance but notably overheating should be avoided. In contrast, in the LP755 treatment side, grayish change was predominant (Table 4); however, there was no significant difference of clearance between the two endpoints (data not shown). These data indicated that physicians should not attempt to reach blanching endpoint with too high energy or multi-passes of LP755, which may increase the risk of complications.

Side effects of laser treatment

Normally, noninvasive lasers such as LP1064 and LP755 do not cause severe complications. We used cooling and avoiding sun exposure to minimize potential side effects. We found moderate but tolerable pain levels with no patients abandoning the treatment. Noticeably, pain levels caused by LP1064 were significantly higher than that caused by LP755. Higher fluence and deeper penetration as well absorption by water of LP1064 could be responsible for this observation.

Post-inflammatory hyperpigmentation (PIH) is a major concern with the use of vascular lasers, particularly on darker skin. Studies showed a wide range of pigmentation rates in both LP1064 and LP755. In two studies in the treatment with LP1064 on skin type II to V and I to IV, percentages of PIH were 16% at 1 month post treatment and 62% at 3 months, respectively [11, 26]. In a study using LP755 on skin types I to III, 19/20 and 15/20 cases had PIHs at 1 and 3 month post treatment [22], whereas another study found 35% of patients having PIH at 3-month follow-up [10]. In our investigation on skin type IV patients, percentages of PIH by LP1064 and LP755 were 63.64% and 50% at 1-month follow-up, respectively. These two proportions were not significantly different and resolved in more than half of the patients after 3 months.

Other complications including vesicle, purpura, and hypopigmentation occurred in very few cases. All of these complications recovered without scar formation.

Limitation of our study was the relative short follow-up at 3 months although we do not envisage this to drastically alter our observations. The strength of our study is that it is the only reported study on Asian skin type comparing LP755 with LP1064. To the best of our knowledge, such a study has previously not been reported.

Conclusion

Our study showed that both wavelengths are comparatively effective in treatment for leg veins in Asian skin type patients. Particularly, LP755 could provide better advantage in terms of causing lower pain levels. Our findings suggest that single treatment with either LP755 or LP1064 is effective and safe for C1 leg vein in skin type IV patients.

Authors' contributions Conceptualization: Van The Trung
Data curation: Nguyen Tran Ngoc Huyen and Van The Trung
Formal analysis: Nguyen Tran Ngoc Huyen and Van The Trung
Investigation: Nguyen Tran Ngoc Huyen and Van The Trung
Methodology: Nguyen Tran Ngoc Huyen and Van The Trung
Project administration: Van The Trung
Resources: Nguyen Tran Ngoc Huyen and Van The Trung
Software: Nguyen Tran Ngoc Huyen and Van The Trung
Supervision: Van The Trung
Validation: Nguyen Tran Ngoc Huyen, Van The Trung, and Al-Niaimi Firas
Visualization: Nguyen Tran Ngoc Huyen and Van The Trung
Writing (original draft): Nguyen Tran Ngoc Huyen and Van The Trung
Writing (review and editing): Van The Trung and Al-Niaimi Firas

Data availability Data is available within the article.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethics approval This research was approved by The Board of Ethics in Biomedical Research at University of Medicine and Pharmacy at Ho Chi Minh City.

Consent to participate "I have read and understand the above consent form, I certify that I am 18 years old or older, and by selecting "Yes" below, I indicate my willingness to voluntarily join in the study."

Consent for publication "I understand that the information will be published without my name attached, but that full anonymity cannot be guaranteed. I understand that the text and any pictures published in the article will be available on the internet and may be seen by the general public. The pictures and text may also appear on other websites or in print, may be translated into other languages or used for commercial purposes."

Code availability Not applicable

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