

# Review of picosecond lasers in non-pigmented disorders

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Based on the principles of the selective photothermolysis theory, picosecond lasers can enhance the therapeutic effect on the target tissue and minimize damage to the surrounding tissue. Therefore, picosecond lasers have significant advantages over conventional laser techniques in terms of effectiveness, safety, and therapeutic effect on the pigmented skin. Additionally, picosecond lasers induce intraepidermal and dermal vacuole formation through laser-induced optical breakdown, which is associated with dermal remodeling by increasing dermal collagen and elastin formation. Based on these additional findings, picosecond lasers are reportedly effective in treating non-pigmented disorders, scars, and in cutaneous rejuvenation. Herein, we review the literature on the treatment of non-pigmented disorders by a picosecond laser and confirm its efficacy.

## Key words

Lasers; Scar; Rejuvenation; Striae distensae

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## INTRODUCTION

In recent years, improved medical lasers with shorter pulse duration have been developed, which limit the therapeutic effect only to the target tissue and ensure safety by minimizing the damage to the surrounding tissues. This advancement in the laser systems is based on the theory of selective photothermolysis, which states the following: "When a targeted chromophore is selectively irradiated with a preferentially absorbed wavelength at an energy level capable of target destruction, delivered at a pulse duration shorter than the thermal relaxation time of the target, heat energy generated is limited to the target, thereby minimizing damage to the adjacent normal tissue."<sup>1</sup> Compared with the conventional nanosecond lasers, the picosecond laser has been expected to show a better therapeutic effect on pigmented skin because of the shorter pulse duration. As a result, picosecond laser treatments have been attempted for various pigmentary cutaneous disorders, such as melasma, freckles, cafe au lait spots, and nevus of Ota. Excellent results have been reported, especially for tattoo removal.<sup>2,3</sup> However, there are reports that the effect of the picosecond laser is not significantly superior to that of the conventional nanosecond laser to pigmented lesions.<sup>4,5</sup>

Recently, picosecond lasers were shown to be effective in not only treating non-pigmented disorders, including acne and scars, but also in aiding skin rejuvenation. Additionally, picosecond lasers induce intraepidermal and dermal vacuole formation through laser-induced optical breakdown (LIOB). LIOB results from multiphoton ionization due to high temperature and pressure created by high-energy irradiation with extremely short pulse durations. This localized damage is associated with dermal remodeling caused by increased dermal collagen and elastin formation.<sup>6-9</sup> In this paper, we reviewed the literature on the treatment of non-pigmented cutaneous disorders by a picosecond laser and confirmed its efficacy.

## CUTANEOUS REJUVENATION; WRINKLES, SKIN TEXTURE, AND ENLARGED PORES

The effects of picosecond lasers on cutaneous rejuvenation, particularly in treating wrinkles and enlarged pores and improving skin texture, have been actively reported (Table 1). Wu et al.<sup>10</sup> conducted a prospective, open-label study of 20 participants with Fitzpatrick skin types (FST) I-IV who had photodamaged skin on the anterior side of the chest and were treated with the diffractive lens array mode of a 755-nm picosecond pulsed alexan-

drite laser. The treatment was administered four times at 3-week intervals. The investigator evaluated the skin texture and wrinkles using a standardized 5-point scale, global aesthetic improvement 5-point scale, and subject satisfaction questionnaire at 1- and 3-month intervals after the treatment ended. Significant improvements in skin texture and wrinkles in comparison with the baseline were confirmed at the 1- and 3-month intervals. Weiss et al.<sup>11</sup> treated 40 patients with a 755-nm picosecond alexandrite laser four times in a 1-month cycle to confirm the safety and efficacy of picosecond laser in treating the wrinkles around the mouth and eyes. Along with evaluation by the Fitzpatrick wrinkle scale using clinical photographs, histological changes were confirmed from biopsies of mouth wrinkles in six patients before and at intervals of 1 month, 3 months, and 6 months after the treatment. Significant improvement was observed in the wrinkle scores and dyschromia. Similarly, the histological examination confirmed a gradual increase in collagen and elastin fibers. Ross et al.<sup>12</sup> treated facial wrinkles and dyschromia in parallel with a fractional picosecond laser of wavelength 532/1,064-nm. The 1,064-nm (350 mJ) laser was applied first, and immediately thereafter, the 532-nm (250 mJ) laser was used. Three sessions of treatment at 1-month interval were performed. At the 1-month follow-up visit, patients showed significant improvements in wrinkles (79%) and pigmentation (93%). The therapeutic effect on enlarged pores has also been studied. A retrospective study by Tran et al.<sup>13</sup> reported a reduction in the size and number of enlarged pores in all the 32 patients treated with a 755-nm picosecond alexandrite laser.

Research was also conducted to determine the parameters that could ensure safety while maximizing the therapeutic effect. Dierickx<sup>14</sup> conducted a split-face study on seven participants and applied a 755-nm picosecond alexandrite laser to one side of the face with a standard treatment protocol of approximately 3,000-6,000 pulses and five treatment sessions at 1-month interval. A significant improvement in wrinkles was noted on both sides of the face, with no significant difference between the sides. In a study by Kirsanova et al.,<sup>15</sup> a 1,064-nm picosecond Nd:YAG laser with energy intensities varying from 1.1 J/cm<sup>2</sup> to 2.1 J/cm<sup>2</sup> was used to treat 28 participants with signs of advanced photoaging such as wrinkles and pigmentation on the face and neck. The clinical and histological effects on cutaneous rejuvenation were compared and found to be particularly pronounced in the patient group treated with the strongest energy intensity at 2.1 J/cm<sup>2</sup>. Additionally, no significant side effects were reported due to the administration of laser with increased

**Table 1.** Rejuvenation

Authors	Lesion	N	Skin type	Devices	Parameter	Outcomes
Wu et al. <sup>10</sup>	Photodamaged skin on the anterior side of the chest	20	I-IV	755-nm PS alexandrite (Picosure <sup>®</sup> ; Cynosure, USA)	6 × 6 mm spot; 0.71 J/cm <sup>2</sup> ; 750 ps; Fractionated; 2-4 passes; 4 treatment sessions; 3-wk intervals	Significant improvement in dyspigmentation, skin texture, and rhytides
Weiss et al. <sup>11</sup>	Facial wrinkles	40	I-IV	755-nm PS alexandrite (Picosure <sup>®</sup> ; Cynosure)	6 × 6 mm spot; 0.71 J/cm <sup>2</sup> ; 750 ps; Fractionated; 5,000 pulses; 4 treatment sessions; 1-mon interval	Significant improvement in wrinkles and dyschromia Increase in collagen and elastin fibers was detected on histological examination
Ross et al. <sup>12</sup>	Facial wrinkles and dyschromia	18	I-III	1,064/532-nm PS (PiQo4 <sup>®</sup> ; Lumenis, Israel)	10 mm hexagonal spot (100 microbeams); 800 ps; Fractionated; 1,064-nm (350 mJ) → 532-nm (250 mJ) 3 treatment sessions; 1-mon interval	Significant improvement in wrinkles (79%) and dyschromia (93%)
Tran et al. <sup>13</sup>	Enlarged pores	32	I-III	755-nm PS alexandrite (Picosure <sup>®</sup> ; Cynosure)	6 × 6 mm spot; 0.71 J/cm <sup>2</sup> ; Fractionated; 5,000-13,660 pulses; 1-3 treatment sessions; 1-mon interval	All participants showed reductions in pore count and size and improvement in pore scores in comparison with the baseline
Dierickx <sup>14</sup>	Facial wrinkles	7	II-IV	755-nm PS alexandrite (Picosure <sup>®</sup> ; Cynosure)	6 × 6 mm spot; 0.57 J/cm <sup>2</sup> ; 750 ps; Fractionated; 3,000-6,000 pulses; 5 treatment sessions; 1-mon interval	Both sides showed mild to moderate improvement in wrinkles No significant clinical difference was observed in either group
Kirsanova et al. <sup>15</sup>	Photodamage on face and neck	28	N/A	1,064-nm PS (Picoway <sup>®</sup> ; Candela, USA)	6 × 6 mm spot; 1.1-2.1 J/cm <sup>2</sup> ; 450 ps; Fractionated; 4 passes; 1 treatment session	Significant clinical improvements were observed in signs of photoaging skin and a more pronounced effect on clinical and histological assessment of facial skin rejuvenation with higher energy (2.1 J/cm <sup>2</sup> )

PS, picosecond; N/A, not available.

energy levels within that range.

Based on these results, picosecond lasers may be considered to be excellent for rejuvenation, particularly for treating wrinkle and elongated pores and improving skin texture.

## ACNE SCARS

Picosecond lasers has also demonstrated clinical efficacy for improving the appearance of acne scarring (Table 2). Brauer et al.<sup>9</sup> treated 20 patients with acne scars with FST I-V using a 755-nm picosecond fractional laser six times at 4- to 8-week intervals. Three months after the last treatment, scar imaging and histology were

**Table 2.** Scars

Authors	Lesion	N	Skin type	Devices	Parameter	Outcomes
Brauer et al. <sup>9</sup>	Acne scars	20	I-V	755-nm PS alexandrite (Picosure <sup>®</sup> ; Cynosure, USA)	6 × 6 mm spot; 0.71 J/cm <sup>2</sup> ; 750 ps; Fractionated; 3,072 mean pulses; 6 treatment sessions; 4- to 8-wk intervals	A 27% (max) reduction in scar volume was observed Significant improvement in skin texture and pigmentation Increased dermal collagen level and elastin fibers
Bernstein et al. <sup>16</sup>	Acne scars	27	I-VI	1,064/532-nm PS (Picoway <sup>®</sup> ; Candela, USA)	6 × 6 mm spot (100 microbeams); Fractionated; A. 19 patients 1,064-nm (450 ps) (1.3-2.9 mJ/microbeam) 2 passes; 4 treatment sessions; 1-mon interval B. 8 patients 532-nm (375 ps) (0.16-1.5 mJ/microbeam); 2 passes; 4 treatment sessions; 1-mon interval	Significant improvement in acne scar scores Well tolerated and little to no downtime
Zhang et al. <sup>17</sup>	Acne scars	20	IV-V	755-nm PS alexandrite (Picosure <sup>®</sup> ; Cynosure)	6 × 6 mm spot; 0.71 J/cm <sup>2</sup> ; 750 ps; Fractionated; 5 passes; 3 treatment sessions; 4- to 6-wk intervals	Significant improvements in ECCA grading scale (197.75 ± 35.26 → 142.00 ± 35.92, <i>p</i> = 0.000) and IGA scores (mean improvement-3.03 ± 0.75) Satisfaction scores obtained from patient self-assessment showed improvements (2.30 ± 0.98)
Manuskiatti et al. <sup>18</sup>	Acne scars	26	III-IV	1,064-nm PS (Enlighten <sup>™</sup> ; Cutera, USA)	8 × 8 mm spot; 1.0 J/cm <sup>2</sup> ; 750 ps; Fractionated; 2-4 passes (1,000-2,500 pulses); 6 treatment sessions; 1-mon interval	Significant improvements in scar volume by 9.29%, 8.5%, and 10.78% and skin texture by 5.9%, 4.8%, and 7.9% from baseline at 1, 3, and 6 months after the final treatment (analyzed by Antera 3D <sup>®</sup> CS [Miravex Limited, Ireland])
Kwon et al. <sup>19</sup>	Acne scars	25	III-IV	1,064-nm PS (PicoLO <sup>®</sup> ; LASEROPTEK, Republic of Korea)	10 × 10 mm spot; 130-430 mJ/cm <sup>2</sup> ; 450 ps; Fractionated; 4-8 passes; 4 treatment sessions; 3-wk intervals	Significant improvement in acne appearance (ECCA percent reduction: 55%), IGA score, and subjective satisfaction with less severe pain Elongation and increased density of collagen, elastic fiber, and mucin deposition throughout the dermis

performed to evaluate the changes. The scar volume decreased by an average of 27%, and the histologic examination confirmed that the elastic fibers, collagen, and mucin in the dermis increased compared with those before the treatment. These results were similar to those

obtained after conventional fractional laser treatments, and this study was the first to show the potential of picosecond lasers for treating acne scars. Later, Bernstein et al.<sup>16</sup> used a 532-nm or 1,064-nm picosecond fractional laser, four times at monthly intervals, to treat 27 patients

Table 2. Continued

Authors	Lesion	N	Skin type	Devices	Parameter	Outcomes
Choi et al. <sup>21</sup>	Hypertrophic scars	24	III-V	1,064-nm PS (PICO plus 4 <sup>®</sup> ; Lutronic, Republic of Korea)	4 × 4-8 × 8 mm spots; 0.4-2.0 J/cm <sup>2</sup> ; 750 ps; 3-5 passes; 1-7 treatment sessions; 3- to 13-wk intervals	Significant decrease in average VSS scores (5.33 ± 2.77, <i>p</i> < 0.001) Moderate improvement in the average GAS (3.02 ± 0.93) and patient satisfaction scores (6.88 ± 2.66)
Guida et al. <sup>22</sup>	Hypertrophic scars	16	II-III	1,064-nm PS (Discovery PICO <sup>®</sup> ; Quanta System, Italy)	8 × 8 mm spot; 1.2 ± 0.2 J/cm <sup>2</sup> ; Fractionated; 450 ps; 3 passes; 3 treatment sessions; 1-mon interval	Significant improvement in pigmentation, vascularization, and skin texture ( <i>p</i> = 0.0001); collagen remodeling and reduced epidermal thickness ( <i>p</i> < 0.01)

PS, picosecond; ECCA, échelle d'évaluation clinique des cicatrices d'acné; IGA, Investigator's Global Assessment, VSS, Vancouver Scar Scale; GAS, Global Assessment Scale.

with acne scars. A blind review revealed a mean improvement of 1.4 in the score for all subjects on a 10-point scale. Clinically significant improvements were observed in both groups with good tolerance and no downtime. No differences were noted with respect to improvements and side effects when comparing subjects treated with the 1,064-nm laser and those treated with the 532-nm laser.

Studies have also explored the safety and efficacy of treatments for scarring due to acne in people of color. Zhang et al.<sup>17</sup> administered treatment for acne scar to 20 Asian patients with FST IV-V using a 755-nm picosecond alexandrite fractional laser. The mean échelle d'évaluation clinique des cicatrices d'acné (ECCA) scores decreased from 197.75 ± 35.26 to 142.00 ± 35.92, and the change was significant (*p* = 0.000). The mean Investigator's Global Assessment (IGA) score was 3.03 ± 0.75, and based on the patient's self-assessment, the improvement scores were 2.30 ± 0.98. Mild transient erythema, edema, and scabbing were reported, and no serious adverse events were observed. In a study conducted by Manuskiatti et al.,<sup>18</sup> the scar volume and skin texture—analyzed by three-dimensional (3D) photography and ultraviolet A-light video camera in 26 patients with acne with FST III-IV—improved when treated with a 1,064-nm picosecond Nd:YAG fractional laser (scar volume: 9.29%, 8.5%, and 10.78%; skin texture: 5.9%, 4.8%, and 7.9% from baseline at 1, 3, and 6 months after the final treatment).

Comparative studies using non-ablative fractional lasers for treating acne scars have also been conducted. Kwon et al.<sup>19</sup> conducted a prospective, randomized, split-

face, controlled trial of 25 Korean patients with acne scars. A 1,064-nm picosecond laser was used on one side of the face, and a 1,550-nm non-ablative fractional laser was used on the other. After four treatments at three-week intervals, the final treatment was completed. Eight weeks later, the ECCA grading, IGA, and histologic assessment were performed for evaluation and comparison. The side of the face treated with the 1,064-nm picosecond fractional laser showed better improvement in the resolution of the acne scar (ECCA score reduction: 55% vs. 42%, *p* < 0.05). Additionally, patients reported experiencing lesser pain (4.3 vs. 5.6, *p* < 0.05) during the 1,064-nm laser application compared with the 1,550-nm laser. Furthermore, the histological examination showed that both treatment sites were found to have increased collagen, elastic fibers, and mucin deposits across the entire dermis.

Several studies have demonstrated the safety and efficacy of picosecond fractional lasers of various wavelengths for treating acne scars. Compared with the conventional non-ablative fractional lasers, better efficacy, safety, and reduced treatment-related pain have been documented. Picosecond lasers are also considered an excellent treatment option for people of color, such as Asian patients, who did not show a significant increase in the incidence of side effects such as hyperpigmentation.

## HYPERTROPHIC SCARS

Hypertrophic scars are treated with various vascular

lasers and intralesional injections of triamcinolone acetonide. However, treatment selection is difficult due to adverse effects such as local skin atrophy and telangiectasia and the side effect of hypopigmentation.<sup>20</sup>

Recently, various studies have been conducted to determine the therapeutic effect of picosecond lasers on hypertrophic scars to overcome these limitations (Table 2). In a retrospective study published by Choi et al.,<sup>21</sup> 24 Asian patients with hypertrophic scars were treated with a 1,064-nm picosecond laser and evaluated for clinical improvement and patient satisfaction. A significant decrease in the Vancouver Scar Scale (VSS) scores ( $5.33 \pm 2.77$ ,  $p < 0.001$ ) was observed, and improvements in the Global Assessment Scale scores ( $3.02 \pm 0.93$ ) and patient satisfaction ( $6.88 \pm 2.66$ ) were also reported. Guida et al.<sup>22</sup> enrolled 16 patients with FST II-III with atrophic and hypertrophic scars to assess changes in the appearance of scars after

picosecond fractional laser treatment using VSS and 3D imaging, and the histological changes were evaluated using a reflex confocal microscope (RCM). After six months, ten patients with hypertrophic scar showed significant improvements in the VSS scores, scar pigmentation, vascularization, and skin texture, as well as significant reductions in epidermal thickness and collagen deposition.

These studies allow us to consider the efficacy of a picosecond laser for the treatment of hypertrophic scars. However, since there are only a few studies on these treatments, large-scale studies, including studies comparing the picosecond laser with the existing laser treatments with respect to efficacy, histologic features, and long-term follow-up data, are required.

**Table 3.** Striae distensae

Authors	Lesion	N	Skin type	Devices	Parameter	Outcomes
Zaleski-Larsen et al. <sup>26</sup>	Striae alba	16	II-III	1,064/532-nm PS (Picoway <sup>®</sup> ; Candela, USA)	A: Rt. abdomen: 1,565-nm Er:glass fractional lasers; 12 × 12 mm spot; 400 mb/cm <sup>2</sup> spot density; 40 J; 1 pass; 3 treatments; 3-wk intervals B: Lt. abdomen: 6 × 6 mm spot; Fractionated; 1,064-nm: 1.3 mJ/microbeam with 4 passes; → 532-nm: 0.4 mJ/microbeam with 2 passes; 3 treatment sessions; 3-wk intervals	Significant improvement in skin texture (31% with both groups), the degree of atrophy (35% with the picosecond laser and 30% with the Er:glass laser), and overall subjective assessment (45% with the picosecond laser and 48% with the Er:glass laser) Equally efficacious in improving striae alba in comparison with non-ablative fractional 1,565-nm Er:glass laser
Fusano et al. <sup>27</sup>	Striae alba	27	II-III	1,064-nm PS (Discovery Pico <sup>®</sup> ; Quanta System, Italy)	8 × 8-mm spot; Fractionated; 450 ps; 0.6 ± 0.2 J/cm <sup>2</sup> ; 4 passes; 4 treatment sessions; 1-mon interval	Clinical improvements (81%) Significant improvements in skin texture and mean depth Collagen remodeling and the appearance of new dermal papillae
Kaewkes et al. <sup>28</sup>	Striae alba	20	IV-V	1,064-nm PS (Enlighten <sup>™</sup> ; Cutera, USA)	8 × 8 mm spot; Fractionated; 750 ps; 0.6 J/cm <sup>2</sup> ; 2 passes; 4 treatment sessions; 1-mon interval	Significant improvement in skin texture; moderate to marked improvement of striae appearance was observed in 90% (18) of the patients Two (10%) developed transient post-inflammatory hyperpigmentation

PS, picosecond; Rt, right; Lt, left.



## STRIAE DISTENSAE

Striae distensae is a type of dermal scar that occurs during pregnancy, with rapid weight changes during growth, hormonal abnormalities, and as a side effect of long-term steroid use. It first appears red (striae rubra), gradually changing over time to become white and atrophied (striae alba).<sup>23,24</sup> Striae distensae undergoes various histological changes, including thinning of the epidermis, flattening of the dermal papilla and rete ridge, and an overall reduction in the extracellular matrix of collagen, fibronectin, and elastin. Therefore, despite various treatments, it is difficult to obtain satisfactory results.<sup>25</sup>

Zaleski-Larsen et al.<sup>26</sup> compared the therapeutic effects of 1,565-nm non-abrasive fractional lasers to 1,064/532-nm non-ablative picosecond fractional lasers on striae alba in a split-body study. Thrice at 3-week intervals, 16 patients with striae alba were treated with a 1,565-nm non-ablative fractional laser on one side and 1,064/532-nm non-ablative picosecond fractional laser on the other. A significant improvement of 31% in skin texture was observed; atrophy also significantly improved by 35% and overall subjective assessment by 45%. Thus, picosecond lasers show similar therapeutic efficacy in treating striae alba as 1,565-nm non-abrasive fractional lasers. Fusano et al.<sup>27</sup> used a 1,064-nm picosecond fractional laser to treat 27 Caucasian women four times at monthly intervals. Subsequently, clinical improvement, subjective satisfaction, changes in lesions using 3D images, and histological changes using RCM were evaluated. Clinical improvement was confirmed in approximately 81% of patients, and a significant improvement in skin texture and reduction in the depth of the lesion was observed. Additionally, the histologic assessment identified a remodeling of collagen in the dermal papillae. Kaewkes et al.<sup>28</sup> administered the picosecond fractional laser treatment in Asian patients with FST IV-V and analyzed the safety and efficacy of striae alba treatment. Four treatment sessions were administered at 1-month interval in 20 patients, and a significant improvement in skin texture was observed. Eighteen patients (90%) showed moderate or marked clinical improvement. Post-inflammatory hyperpigmentation was reported in two patients (10%).

Therefore, picosecond fractional lasers could be an effective and safe treatment option for old striae alba (Table 3). However, since limited research has been conducted, it is necessary to objectively establish the efficacy and safety of picosecond fractional lasers through large-scale studies in the future.

## SEBORRHEIC DERMATITIS

Liu et al.<sup>29</sup> reported that picosecond laser treatment was effective for patients with seborrheic dermatitis. Sixty-three Asian patients with facial seborrheic dermatitis were randomly assigned to two groups. The control group received only tacrolimus cream, while the experimental group was additionally administered the 1,064-nm picosecond laser in the first week. Clinical improvement, skin barrier function-related data, and the microbial status of the skin were evaluated at 2, 4, 8, and 12 weeks. A significant decrease in erythema and scaliness was observed in the experimental group. In addition, significant improvements were observed in transepidermal water loss and seborrhea content, with substantial reductions in epidermal *Pityrosporum furfur* and Demodex. The authors hypothesized that these improvements were achieved through the death of epidermal *Pityrosporum furfur* and Demodex due to the photothermal effects and the induction of fibroblast growth factor secretion in blood vessels to heal the wounds. While it is interesting to explore the impact of picosecond lasers by applying them to skin disorders other than pigments and scars, the results must be supported by subsequent studies to test the asserted hypothesis.

## CONCLUSION

The studies cited in this paper confirmed the therapeutic effect of picosecond lasers on several non-pigmented disorders other than pigmented disorders. Till date, a considerable amount of scientific data has accumulated on the effect of picosecond lasers on skin rejuvenation and scars, thus suggesting that the safety and efficacy of picosecond lasers are equal to or better than those of conventional laser treatments. The previous trials primarily used lasers with wavelengths ranging from 700- to 1,064-nm to induce LIQB formation in dermal layers, subsequently inducing the dermal remodeling process. In addition, based on the selective photothermolysis theory, picosecond lasers can enhance the therapeutic effect on the target tissue and minimize damage to the surrounding tissue. Therefore, picosecond lasers have important advantages over conventional laser techniques in terms of effectiveness and safety. This means that it is a safer choice for treating patients with dark skin (skin types above FST grade IV). In the future, it is hoped that the treatment of various skin disorders by picosecond lasers will confirm their safety and efficacy and help establish appropriate treatment guidelines accordingly.

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## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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Concept and design: JKH, KL, BJK, KHY. Analysis and interpretation: JS, SYC. Data collection: JKH. Writing the article: JKH, JS, KHY. Critical revision of the article: SYC, KL, BJK, KHY. Final approval of the article: KHY. Overall responsibility: JKH, KHY.

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