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Comparative evaluation of laser therapy for infantile hemangiomas: A systematic review of clinical outcomes and treatment considerations

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ABSTRACT

Background and objectives: Infantile hemangiomas (IHs) are the most common benign vascular tumors in infancy. While many resolve spontaneously, treatment is often required due to ulceration, functional impairment, or aesthetic concerns. Laser therapy, either alone or in combination with beta-blockers, has become a central therapeutic option. However, optimal laser parameters, efficacy for different IH types, and safety remain under investigation. This systematic review evaluates the effectiveness and safety of various laser treatments for IHs, focusing on lesion regression, treatment protocols, recurrence, and adverse events.

Study design/materials and methods: A systematic search was conducted following PRISMA guidelines in PubMed, Scopus, Web of Science, Embase, and the Cochrane Library. Studies published up to January 2025 were included. This review included 20 studies comprising a total of 2856 patients. Included clinical studies evaluated laser therapy—alone or combined with pharmacological agents—and reported outcomes such as lesion regression, treatment duration, recurrence, and adverse effects.

Results: The 595-nm pulsed dye laser (PDL) was the most studied and showed high efficacy for superficial IHs, with improvement rates up to 85 %. The 1064-nm Nd:YAG laser was more effective for deeper lesions, achieving up to 87.57 % regression. Combination therapies (e.g., PDL with propranolol or timolol) yielded better outcomes than monotherapy, with higher regression and lower recurrence. Dual-wavelength approaches also showed promise. Adverse effects were generally mild and infrequent.

Conclusion: Laser therapy is effective and well-tolerated for IHs. PDL is preferred for superficial lesions and Nd:YAG for deeper or mixed types. Standardized protocols are needed, and further research should refine therapeutic parameters and clinical guidelines.

1. Introduction

Background

Infantile hemangiomas (IHs) are the most common benign vascular tumors in infancy, exhibiting a wide spectrum of clinical presentations and biological behavior[1–5]. Recent studies have contributed significantly to understanding their pathogenesis and clinical management. Several studies [5–9](2024) described the heterogeneity of cellular components in IHs, including stem cells, pericytes, telocytes, and macrophages, all of which play critical roles in lesion development [10]. The involvement of angiogenic and vasculogenic pathways, including those mediated by the renin-angiotensin system, has been

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further elucidated [1,5,11,12] identified dysregulation in angiogenesis and endothelial signaling as central to IH proliferation. Sun and Greenberg al [12,13] emphasized the significance of hemangioma endothelial cells and their interactions with stem cells, while Kahn et al. [14] demonstrated the clonality of hemangioma-derived endothelial cells. Clinically, Ji et al. [15] confirmed through a large multicenter study that infants with ≥5 cutaneous lesions are at high risk of harboring hepatic IHs, highlighting the need for early ultrasound screening. Similarly, Mull et al. [16] and Dahan et al. [3] expanded the phenotypic characterization of IHs, underscoring their potential systemic complications. This growing body of evidence supports a paradigm shift toward individualized treatment strategies, integrating systemic therapies, imaging surveillance, and laser-based interventions as part of comprehensive IH management.

Infantile hemangiomas (IHs) are the most common benign vascular tumors in infancy. They affect approximately 4–10 % of newborns, with a higher incidence observed in premature and low-birth-weight infants [17]. These vascular anomalies result from **abnormal endothelial proliferation**, typically following a characteristic growth pattern of **rapid proliferation during the first year of life**, followed by spontaneous involution over several years. While many IHs regress without medical intervention, a subset requires treatment due to complications such as **ulceration, bleeding, airway obstruction, visual impairment, or permanent disfigurement** [17,18].

Recent studies have expanded the therapeutic landscape for infantile hemangiomas, exploring both well-established and novel pharmacological options. Propranolol remains the first-line treatment, with its clinical safety and efficacy well-documented [12,19,20]. However, itraconazole has emerged as a promising alternative due to its anti-angiogenic properties, demonstrating comparable or even superior outcomes in some pediatric cases [21,22]. Comparative analyses have shown that itraconazole can reduce hemangioma volume and angiopoietin-2 levels similarly or more effectively than beta-blockers [23]. In parallel, advanced imaging techniques such as cutaneous ultrasound are gaining traction as non-invasive tools for monitoring lesion evolution [24]. Reports also underscore the importance of recognizing segmental and syndromic variants of hemangiomas, which may involve complex clinical presentations and require multidisciplinary evaluation [2]. Notably, sirolimus has shown efficacy in refractory or unresectable vascular anomalies by targeting the mTOR pathway [25]. These insights underscore the dynamic evolution of clinical strategies for hemangioma management, reinforcing the need for individualized therapeutic approaches based on lesion type, depth, and systemic involvement [26,27].

Historically, systemic **corticosteroids** were the primary pharmacological treatment for IHs, but their use declined due to **significant adverse effects**, including **immunosuppression, growth retardation, and metabolic complications** [28,29]. The introduction of **propranolol in 2008** revolutionized IH management, offering superior efficacy in reducing lesion size with a favorable safety profile [17,28,30]. However, propranolol therapy requires **prolonged administration (6–12 months)** and may be associated with systemic side effects, such as **hypotension, bradycardia, and hypoglycemia** [17,28,30,31].

Infantile hemangiomas (IHs) are the most common benign vascular tumors in infancy and display a wide spectrum of clinical behaviors and therapeutic responses. While oral propranolol remains the gold standard for first-line treatment, evolving strategies increasingly emphasize individualized, lesion-specific approaches. A recent review by Rešić et al. [11] highlights the importance of individualized, lesion-specific treatment planning for IHs, incorporating both pharmacological and procedural options, including laser therapy as part of a broader multidisciplinary approach[11]. This paradigm shift recognizes that IHs often vary in depth, location, and response to treatment, necessitating tailored combinations of systemic therapy, topical agents, and laser interventions.

1.1. Laser therapy in IH management

Laser therapy has emerged as a promising **and** minimally invasive treatment alternative for IHs, particularly targeting superficial and cosmetically sensitive lesions[32]. Selective photothermolysis enables the targeted absorption of laser energy by oxyhemoglobin in blood vessels, resulting in thermal coagulation, vascular remodeling, and subsequent lesion regression [18]. Among various laser modalities, the **pulsed dye laser (PDL, 595 nm)** is widely regarded as the **gold standard** for superficial hemangiomas due to its **high specificity for hemoglobin** and ability to **selectively target abnormal vasculature while preserving surrounding tissues** [33]. For **deeper or mixed hemangiomas, Nd:YAG (1064 nm)** has demonstrated superior penetration and efficacy [34].

Moreover, recent studies suggest that combining laser therapy with pharmacological agents, such as topical timolol or systemic propranolol, significantly enhances treatment outcomes [35]. Propranolol-induced vasoconstriction effectively reduces blood flow, thereby making hemoglobin more accessible to laser-induced photocoagulation[17]. Additionally, propranolol's **anti-angiogenic effects** complement laser therapy by promoting **endothelial apoptosis and limiting further vascular proliferation** [36].

1.2. Challenges and need for a systematic review

Despite the increasing use of laser therapy for IHs, variability in treatment protocols—including differences in laser parameters (wavelength, fluence, pulse duration), combination therapies, and timing of intervention—complicates the establishment of standardized guidelines. While several studies have demonstrated the effectiveness of PDL monotherapy, others have reported superior outcomes with combination approaches, particularly PDL + propranolol or dual-wavelength lasers [28]. Furthermore, questions remain regarding long-term recurrence rates, safety profiles, and optimal treatment strategies [37,38].

Given the widespread use of laser therapy for IHs and the growing interest in combination treatments, a **systematic review** is essential to consolidate current evidence and provide **clinical guidance** [18]. This study aims to evaluate:

- The comparative efficacy of laser monotherapy versus combination therapy (e.g., PDL + propranolol) [39].
- The outcomes of different laser modalities (e.g., PDL, Nd:YAG, and dual-wavelength approaches) [29].
- The safety profile and adverse effects associated with various laser protocols [40].
- The impact of early versus late intervention on treatment efficacy and recurrence rates [34].

By systematically analyzing available data, this review seeks to **refine treatment protocols, improve patient outcomes, and contribute to the development of standardized clinical guidelines** for IH management.

2. Materials and methods

2.1. Study design and eligibility criteria

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [41]. The objective was to assess the efficacy and safety of various laser therapies for infantile hemangiomas (IHs), with or without pharmacological combination treatments. The study protocol was registered in **PROSPERO (Registration Number: CRD420250635593)** prior to initiating the review process.

2.2. PICO question

To guide the systematic review, the following **PICO** (Population, Intervention, Comparison, Outcome) question was formulated:

- **Population (P):** Infants diagnosed with infantile hemangiomas requiring treatment.
- **Intervention (I):** Laser therapy (Pulsed dye laser, Nd:YAG laser, diode laser, CO2 laser, intense pulsed light) alone or in combination with pharmacological agents.
- **Comparison (C):** Different laser types, laser monotherapy vs. combination therapy, or laser therapy vs. pharmacological treatments alone (e.g., systemic propranolol).
- **Outcome (O):** Lesion regression, treatment duration, recurrence rates, patient satisfaction, and adverse effects.

2.3. Inclusion criteria

To be included in this review, studies had to meet the following criteria:

1. **Study Design:** Randomized controlled trials (RCTs), prospective cohort studies, and retrospective observational studies.
2. **Population:** Infants diagnosed with IHs requiring intervention.
3. **Intervention:** Use of laser therapy as monotherapy or in combination with pharmacological agents such as propranolol or timolol.

Comparators: Studies comparing different laser types, combination therapy versus laser monotherapy, or laser therapy versus other treatment modalities (e.g., systemic propranolol alone).

Outcome Measures: Studies had to report at least one of the following clinical outcomes—lesion regression, treatment duration, recurrence rates, patient satisfaction, or adverse effects.

1. **Publication Status:** Only peer-reviewed articles were included, ensuring data reliability and scientific rigor.
2. **Language:** Studies published in English to maintain consistency in data interpretation.

2.4. Exclusion criteria

Studies were excluded if they:

1. Were non-clinical (e.g., animal studies, in vitro research).
2. Were case reports, editorials, narrative reviews, or conference abstracts.
3. Lacked clear outcome measures or statistical analysis.
4. Were duplicate studies analyzing the same patient population as a previously included study.

2.5. Search strategy

A systematic literature search was performed across five major databases: **PubMed, Scopus, Web of Science (WOS), Embase, and Cochrane Library**. The search aimed to identify all relevant studies published up to **January 2025**. The search strategy incorporated a combination of Medical Subject Headings (MeSH) terms and Boolean operators to ensure comprehensive retrieval of relevant literature.

Database	Formulation
Pubmed = 121	((('Laser therapy' [Title/Abstract]) OR ('Laser treatment' [Title/Abstract]) OR ('Red light therapy' [Title/Abstract]) OR (Laser [Title/Abstract]) OR ('Laser application' [Title/Abstract]) OR (ablation [Title/Abstract]) OR ('esthetic treatment' [Title/Abstract]) OR ('Lasers' [MeSH Terms]) OR ('Low-Level Light Therapy' [MeSH Terms])) AND (('Hemangioma' [Title/Abstract]) OR ('Capillary hemangioma' [Title/Abstract]) OR ('Infantile hemangioma' [Title/Abstract]) OR ('Vascular tumor' [Title/Abstract]) OR ('Benign vascular tumor' [Title/Abstract]) OR ('Hemangioma' [MeSH Terms]) OR ('Capillary Hemangioma' [MeSH Terms]) OR ('Vascular Neoplasms' [MeSH Terms])) AND (('Size reduction' [Title/Abstract]) OR (Shrinkage [Title/Abstract]) OR ('Reduction in size' [Title/Abstract]) OR ('Volume reduction' [Title/Abstract]) OR (reduction [Title/Abstract]) OR ('Mass regression' [Title/Abstract]) OR ('Dimensional decrease' [Title/Abstract]) OR ('Size contraction' [Title/Abstract]) OR (diminution [Title/Abstract]))))
Scopus = 259	TITLE-ABS-KEY(("Laser therapy" OR "Laser treatment" OR "Red light therapy" OR Laser OR "Laser application" OR ablation OR "esthetic treatment") AND ("Hemangioma" OR "Capillary hemangioma" OR "Infantile hemangioma" OR "Vascular tumor" OR "Benign vascular tumor" OR "Vascular neoplasms") AND ("Size reduction" OR Shrinkage OR "Reduction in size" OR "Volume reduction" OR reduction OR "Mass regression" OR "Dimensional decrease" OR "Size contraction" OR diminution))
WOS = 64	TS=("Laser therapy" OR "Laser treatment" OR "Red light therapy" OR Laser OR "Laser application" OR ablation OR "esthetic treatment") AND TS=("Hemangioma" OR "Capillary hemangioma" OR "Infantile hemangioma" OR "Vascular tumor" OR "Benign vascular tumor" OR "Vascular neoplasms") AND TS=("Size reduction" OR Shrinkage OR "Reduction in size" OR "Volume reduction" OR reduction OR "Mass regression" OR "Dimensional decrease" OR "Size contraction" OR diminution)
Cochrane Library= 105	(("Laser therapy" OR "Laser treatment" OR "Red light therapy" OR "Laser" OR "Laser application" OR "Ablation" OR "Esthetic treatment")):ti,ab,kw AND (("Hemangioma" OR "Capillary hemangioma" OR "Infantile hemangioma" OR "Vascular tumor" OR "Benign vascular tumor")):ti,ab,kw
Embase= 239	('laser therapy':ti OR 'laser treatment':ti OR 'red light therapy':ti OR 'laser':ti OR 'laser application':ti OR 'ablation':ti OR 'esthetic treatment':ti) AND ('hemangioma':ti OR 'capillary hemangioma':ti OR 'infantile hemangioma':ti OR 'vascular tumor':ti OR 'benign vascular tumor':ti)

The reference lists of included articles were also manually reviewed to identify additional relevant studies that were not retrieved through the database search.

2.6. Study selection and data extraction

Two independent reviewers (EF and AC) screened all retrieved studies in a two-stage process:

1. **Title and Abstract Screening:** Non-relevant studies were excluded based on titles and abstracts.
2. **Full-text Review:** Articles were assessed for eligibility based on the inclusion and exclusion criteria.

A standardized data extraction form was used to collect key study characteristics, ensuring consistency across reviewers. The following data points were extracted:

- **Study Characteristics:** Author, year of publication, study design, sample size.
- **Patient Demographics:** Age, gender, lesion type, Fitzpatrick skin type and baseline characteristics.

- **Intervention Details:** Laser type, wavelength, fluence, pulse duration, treatment frequency, and session intervals.
- **Comparative Interventions:** Inclusion of propranolol, timolol, or other medical treatments.
- **Outcome Measures:** Lesion regression, treatment duration, recurrence rates, adverse effects, and patient satisfaction.

Any discrepancies in study selection or data extraction were resolved through consensus discussion with a third reviewer (RC) to minimize bias.

2.7. PICO-Based framing of the review question

For example, a representative PICO question guiding this review is: In infants with superficial infantile hemangiomas (P), does pulsed dye laser therapy (I), compared to propranolol monotherapy (C), lead to greater lesion regression and fewer side effects (O)?

2.8. Quality assessment and risk of bias evaluation

To evaluate the methodological quality of the studies included, different tools were used based on study design:

- **Randomized Controlled Trials (RCTs):** Assessed using the Cochrane Risk of Bias (RoB 2.0)[42] tool, which evaluates factors such as randomization procedures, allocation concealment, blinding, incomplete outcome data, and selective reporting.
- **Observational Studies:** Assessed using the Newcastle-Ottawa Scale (NOS)[43], which rates studies based on selection bias, comparability of groups, and outcome assessment.

Studies were categorized as having a **low, moderate, or high risk of bias**. A risk of bias summary was generated to visually present the methodological quality of the included studies.

2.9. Data synthesis and statistical analysis

Due to the heterogeneity of study designs, treatment protocols, and outcome measures, a **qualitative synthesis** was performed instead of a meta-analysis. Descriptive statistics were used to summarize study characteristics and clinical outcomes.

Comparative analyses were conducted for studies evaluating:

- **Different laser modalities** (PDL vs. dual-wavelength vs. Nd:YAG).
- **Combination therapies** (Laser + propranolol vs. Laser + timolol vs. Laser monotherapy).

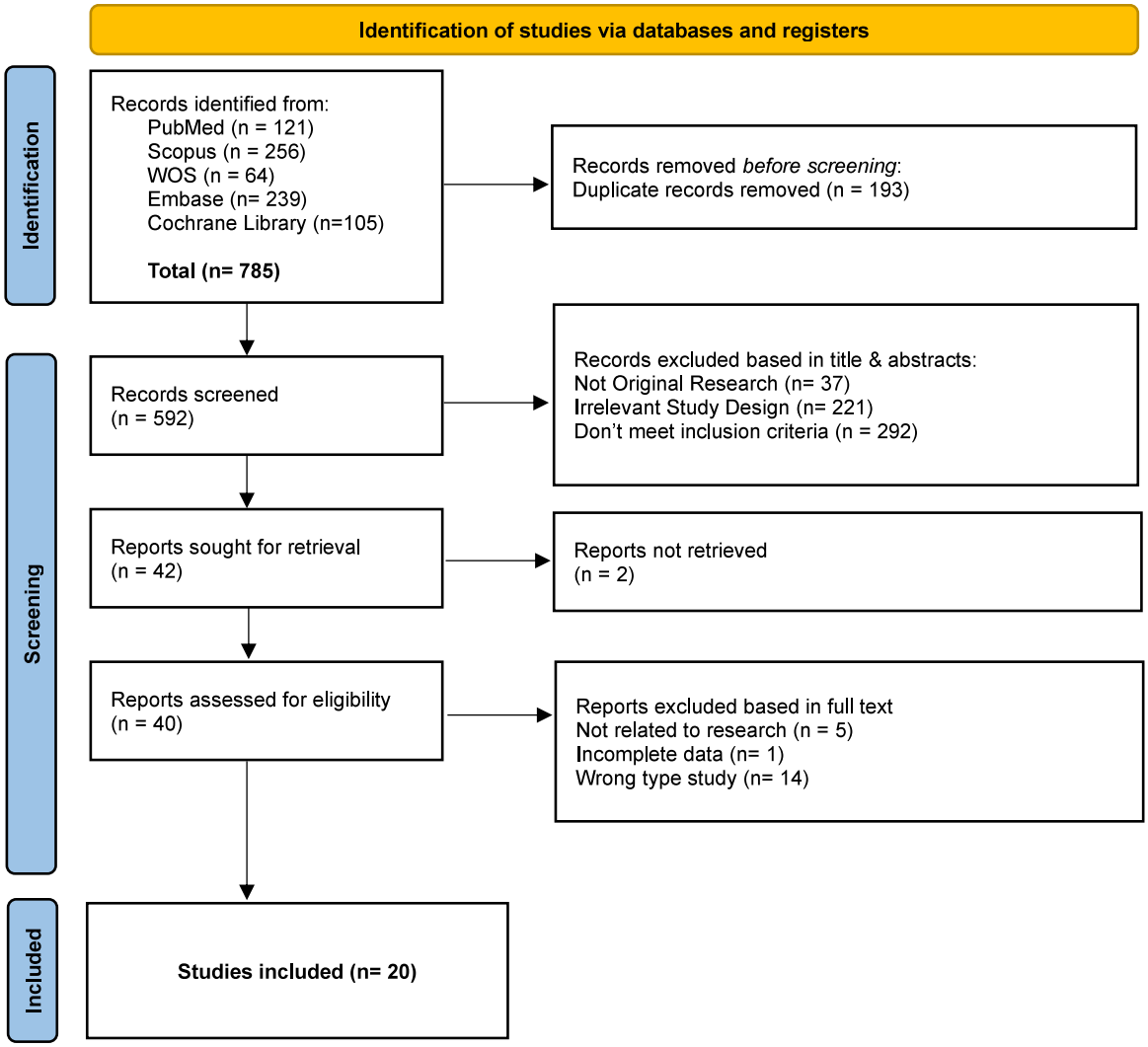

Fig. 1. PRISMA Flow Diagram for Study Selection. This flow diagram illustrates the process of identifying, screening, and selecting studies for inclusion in the systematic review. It details the number of records retrieved from databases and registers, the number of records excluded at each stage, and the final number of studies included in the analysis.

- **Timing of treatment initiation** (early vs. late intervention).

A sensitivity analysis was performed to assess the impact of study quality and risk of bias on overall findings.

2.10. Ethical considerations

As this study was a systematic review of published data, no institutional review board (IRB) approval was required. The study adhered to ethical guidelines for systematic reviews and ensured transparency in data collection and reporting.

3. Results

3.1. Study characteristics

This systematic review included 20 studies (Fig. 1), which evaluated the efficacy and safety of various laser therapies for infantile hemangiomas. The included studies comprised randomized controlled trials, prospective cohort studies, and retrospective analyses. The treatment modalities investigated included pulsed dye laser, Nd:YAG laser, diode laser, CO2 laser, and intense pulsed light, either as monotherapy or in combination with pharmacological agents [44–46]. Tables 1 and 2

Table 1
Summary of Studies on Hemangioma Treatment Using Laser and Other Therapies.

Author and Year	Study Type	Number of Patients	Treatment Type	Control Group	Follow-up Duration	Main Findings
Garden et al., 1992	Prospective	24	FPDL 585 nm	Not applicable	5 to 11 months	Best results observed in hemangiomas ≤3 mm elevation. Recommended for patients with functional impairment risk or ulceration areas.
Barlow et al., 1996	Observational	7	585 nm FPDL	Not applicable	Not mentioned	Significant reduction in vascular lesions. No significant side effects.
Waldorf et al., 1997	Experimental	47	FPDL 585 nm with cooling	FPDL without cooling	6–8 weeks	Dynamic cooling reduces pain without compromising efficacy.
Fuchs et al., 2001	Prospective	10	Diode laser 810 nm, 300–1100 mW (circumscribed choroidal hemangioma)	Not applicable	3 months	Transpupillary thermotherapy effectively treats some choroidal hemangiomas, preventing fluid leakage if the lesion does not involve the fovea.
Hohenleutner et al., 2001	Retrospective	617	FPDL	Not applicable	Up to 55 months (mean: 17)	Total regression achieved in almost half of hemangiomas. Progression was halted or regression induced in the majority.
Offergeld et al., 2003	Observational	55	Doppler-guided Nd:YAG laser	Not applicable	3 months	Complete regression in 62 % of cases, partial regression in 38 %.
Nicolai et al., 2005	Retrospective	46	CO2 laser (3.5–5 W) vs. Nd:YAG (20 W) vs. tracheostomy and steroids	Not applicable	Not applicable	CO2 laser was superior to Nd:YAG and tracheostomy in terms of morbidity reduction, speech development delay, and quality of life.
Ulrich et al., 2005	Retrospective	15	Nd:YAG (600–900 W/cm^2)	Not applicable	Up to 8 years	Application of Nd:YAG produced positive results in most cases.
Angiero et al., 2008	Prospective	136	810 nm diode laser (2.5–6 W)	Not applicable	Up to 8 years	Forced dehydration with induced photocoagulation is a safe and effective treatment for oral hemangiomas up to 2 × 2 cm with low relapse rates.
Angiero et al., 2009	Prospective (?)	160	980 nm diode laser (3–12 W, endolesional)	Not applicable	2–3 years	Effective for pediatric patients in terms of aesthetic results and lesion resolution.
Crisan et al., 2010	Prospective	70	980 nm diode laser, Er:YAG laser	Not applicable	6–12 months	Laser treatment for oral and maxillofacial hemangiomas reduces size and minimizes intraoperative and postoperative risks.
Kagami et al., 2013	Prospective	27	Propranolol 1 mg/kg/day, then 2 mg/kg/day, then 0.5 mg/kg/day	PDL 585 nm and cryosurgery	Up to 287 days	Propranolol induced significantly earlier involution and redness reduction compared to pulsed dye laser and cryosurgery.
Kessels et al., 2013	Prospective, randomized, controlled clinical trial	22	PDL 595 nm	Observation group	12 months	Significant color improvement with PDL compared to observation.
Zhong et al., 2015	Prospective	794	Nd:YAG 1064 nm	Not applicable	12 months	Nd:YAG laser is a safe and efficacious treatment for infantile hemangiomas. The curative effect depends on patient age and hemangioma classification.
Crisan et al., 2016	Controlled clinical study	92	980 nm diode laser (9–11 W)	Sclerotherapy	6–12 months	Laser therapy was more efficient than sclerotherapy in terms of aesthetics and size reduction.
Zeng et al., 2017	Prospective randomized study	181 (165 final)	PDL 595 nm + 5-ALA	PDL alone	6 months	Higher efficacy with 5-ALA combination. Minor adverse effects in both groups.
Nammour et al., 2020	Retrospective	143	Nd:YAG, CO2, Diode lasers, Er,Cr:YSGG	Not applicable	12 months	Laser-assisted aesthetic treatment of lip vascular lesions is effective regardless of wavelength used. No recurrence with CO2 and Er:YAG lasers.
Jin et al., 2020	Prospective	194	Alexandrite Laser + PDL	Not applicable	6 months	Combination of lasers effectively treats hemangiomas.
Filaj et al., 2021	Retrospective	202	IPL 590–595 nm	Not applicable	Not mentioned	Direct correlation between adverse effects and Fitzpatrick IV phototype. Importance of patient selection and accurate wavelength measurement.
Khamaysi et al., 2023	Prospective cohort study	30	Nd:YAG on residual hemangioma after propranolol	Not applicable	Not mentioned	No patients had an unsatisfactory response. No serious side effects observed; only minor side effects reported.

Table 2
Summary of Selected Laser Treatment Outcomes.

Author/Year	Laser Type	Wavelength (nm)	Treatment Conditions	Reported Efficacy	Adverse Effects
Garden et al., 1992	FPDL	585	2–10 sessions, 3–4 week intervals	All lesions reported lightening and decreased thickness.	Transient hyperpigmentation, hypopigmentation, cutaneous atrophy.
Barlow et al., 1996	FPDL	585	Up to six sessions, 1–2 month intervals, topical/general anesthesia	Significant reduction in vascular lesions.	Scarring, feeding difficulty, auditory obstruction.
Waldorf et al., 1997	FPDL	585	Cooling vs non-cooling	Fewer adverse effects with cooling.	Purpura, pain, hyperpigmentation, hypopigmentation.
Hohenleutner et al., 2001	FPDL	585	Up to 12 sessions (mean 2.5), every 4–6 weeks, no anesthesia	Growth stopped in 67.9 %, marked regression in 14.9 %, total resolution in 13.8 %, progression in 3.4 %.	Blisters, crusts, swelling, hypopigmentation, hyperpigmentation, atrophic scars, granuloma teleangiectaticum.
Offergeld et al., 2003	Nd:YAG	Not mentioned	Doppler-guided, 1–3 sessions	Complete regression in 62 % of cases, partial regression in 38 %.	Not mentioned.
Nicolai et al., 2005	CO2 vs Nd:YAG	10,600 / Not found	Tracheostomy required if laser treatment was ineffective.	CO2 laser had fewer complications, shorter hospitalization, and fewer tracheostomies required.	Laser-induced scars, glottic and subglottic stenosis from Nd:YAG.
Ulrich et al., 2005	Nd:YAG	1064	1–3 sessions, topical or general anesthesia	7 % showed no effect, 7 % showed tumor growth.	Transient swelling, scars, hyperpigmentation, hypopigmentation, atrophy, wrinkled texture.
Angiero et al., 2008	Diode	810	1–2 sessions, no anesthesia	98.53 % had complete remission.	Transient swelling.
Angiero et al., 2009	Diode	980	1–5 sessions, sedation or anesthesia	17 % reduction in lesion size at 3 months.	Minimal side effects.
Crisan et al., 2010	Diode, Er:YAG	980, 2940	Multiple stages, 6-week intervals, interstitial and irradiation technique	45–95 % lesion size reduction.	No adverse effects reported.
Kagami et al., 2013	PDL	585	1 to 10 sessions, combined with cryosurgery	Propranolol induced significantly earlier involution and redness reduction compared to PDL and cryosurgery.	Not reported.
Kessels et al., 2013	PDL	595	<1 Min per session, 3–4 week intervals, 1–9 sessions	46 % of patients showed significant improvement.	Mild purpura, minimal crusting, pain.
Zhong et al., 2015	Nd:YAG	1064	Up to 5 sessions, 2-month intervals, spot size 3–7 mm, local anesthesia for larger lesions	Higher efficacy in older patients; worse for deeper subcutaneous and mixed lesions.	Blisters, skin texture changes, hyperpigmentation, atrophic scarring, secondary ulcers, hypopigmentation.
Zeng et al., 2017	PDL + 5-ALA	595	6 sessions, 4–6 week intervals, antibiotic cream post-treatment	67.4 % complete clearance in experimental group, 37 % in control group.	Atrophic scars, hyperplastic scars, pigmentation changes.
Nammour et al., 2020	Nd:YAG, CO2, Diode, Er, Cr: YSGG	1064, 10,600, 980, 2780	Multi-laser therapy, local anesthesia	CO2 and Er:YAG prevented recurrence.	Modest pain.
Jin et al., 2020	PDL, Alexandrite Laser	595, 755	4-week intervals, topical anesthesia	36.1 % efficacy for PDL, 76.3 % for Alexandrite laser.	Depigmentation, ulcers, blisters.
Filaj et al., 2021	IPL	590–595	4 sessions, fluence 11–12 J/cm^2, duration 1.5 ms	Effective in selected cases; efficacy depends on patient selection and settings.	Hypopigmentation, hyperpigmentation, superficial burns, edema, erythema.
Khamaysi et al., 2023	Nd:YAG	1064	1–3 sessions, no anesthesia	18 patients had >75 % improvement, 10 had 51–75 % improvement, 2 had <50 % improvement.	Erythema, edema, pain, hypopigmentation, hyperpigmentation, loose skin, blisters.

3.2. Types of studies and their contributions (Table 1)

The studies varied in design, with some employing randomized controlled trials to compare different treatment modalities, while others used prospective cohort designs to follow patients over time. Retrospective analyses were also included to evaluate long-term outcomes based on patient records. Randomized controlled trials provided the highest level of evidence, particularly those that compared laser therapy with pharmacological interventions such as propranolol or timolol [34,39]. Prospective cohort studies contributed valuable data on treatment efficacy and safety in real-world clinical settings, tracking patient progress over extended follow-up periods [28,40]. Retrospective studies helped identify trends in treatment response and adverse effects but were limited by potential biases in data collection and patient selection [29,33].

3.3. Wavelengths used in laser therapy (Table 2)

The laser wavelengths used in the included studies varied depending on the type of laser and targeted lesion characteristics. Pulsed dye lasers typically operated at 585–595 nm, which corresponds to the absorption peak of oxyhemoglobin, making them particularly effective for treating superficial hemangiomas [36,46]. This wavelength allows for selective photothermolysis, leading to vascular coagulation while minimizing damage to surrounding tissues. The Nd:YAG laser, commonly used at 1064 nm, penetrates deeper into tissues due to its lower absorption by hemoglobin and higher scattering properties, making it highly effective for treating thicker or subcutaneous hemangiomas [18,47]. Diode lasers in the 810–980 nm range have demonstrated efficacy for smaller vascular lesions, particularly in mucosal areas, due to their moderate penetration depth and hemostatic properties [35,37]. CO_2 lasers, operating at 10,600 nm, were primarily employed for ablative purposes, flattening ulcerated hemangiomas and reducing bulkier lesions [48]. Intense pulsed light, typically in the 590–595 nm range, was also investigated as a broad-spectrum option for vascular lesions, showing efficacy in lesion clearance with a lower risk of thermal damage [29].

3.4. Efficacy of laser monotherapy vs. combination therapy

Combination therapies provide superior lesion regression, shorter treatment durations, and lower recurrence rates when compared to laser monotherapy. Asilian et al. [39] reported a 71.8 % lesion regression rate with pulsed dye laser and timolol, significantly higher than pulsed dye laser monotherapy. Zeng et al. [34] found that pulsed dye laser combined with 5-ALA photodynamic therapy resulted in 67.4 % complete lesion clearance, compared to lower rates in monotherapy. Lu et al. [17] reported that Nd:YAG laser combined with propranolol achieved enhanced lesion regression and lower recurrence rates compared to propranolol alone. Kagami et al. [28] showed that propranolol was more effective than pulsed dye laser and cryosurgery in reducing hemangioma volume and promoting earlier involution. Overall, laser monotherapy was effective, but combination approaches, particularly pulsed dye laser with beta-blockers, were associated with faster lesion resolution and lower recurrence rates.

3.5. Comparison of different laser modalities

Studies comparing different laser types revealed varying efficacy depending on hemangioma depth and composition. Pulsed dye laser at 595 nm demonstrated 71–85 % improvement, particularly in superficial hemangiomas and residual erythema [44,45]. Nd:YAG laser at 1064 nm achieved the highest efficacy for deeper or thicker lesions, with an 87.57 % regression rate [18,31]. Dual-wavelength therapy combining pulsed dye laser and Nd:YAG showed promise for treating mixed hemangiomas with lower recurrence rates [40]. The CO_2 laser was effective for flattening ulcerated hemangiomas, while diode laser at 810 nm achieved a 70 % lesion reduction, particularly in labial hemangiomas and small vascular lesions [35,37,38,49].

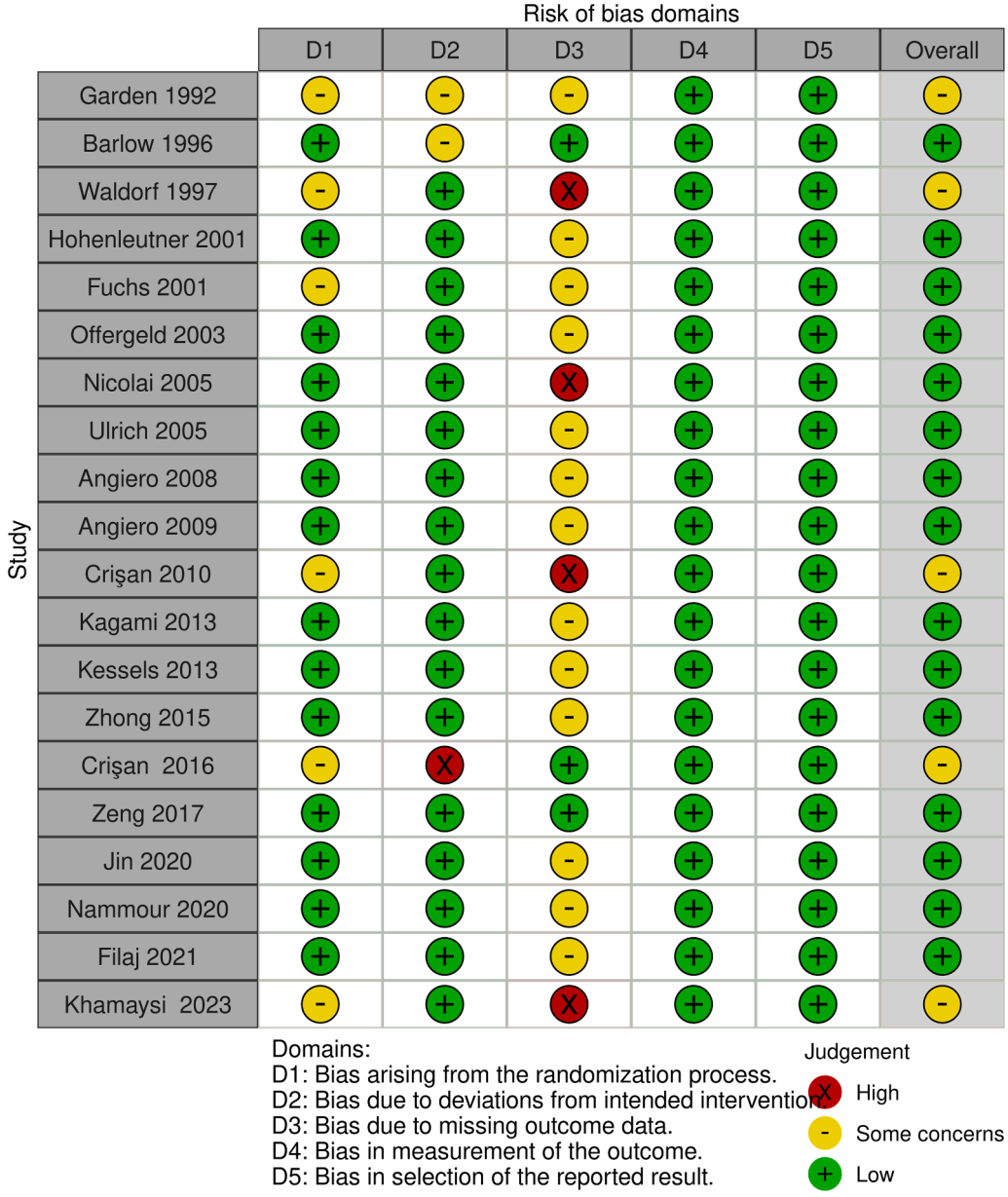

Fig. 2. Risk of Bias Assessment for Included Studies. This figure presents the risk of bias evaluation for each included study across five domains: (D1) bias arising from the randomization process, (D2) bias due to deviations from intended interventions, (D3) bias due to missing outcome data, (D4) bias in the measurement of the outcome, and (D5) bias in the selection of the reported result. Green (+) indicates a low risk of bias, yellow (-) represents some concerns, and red (X) denotes a high risk of bias. The overall risk assessment for each study is shown in the last column.

3.6. Treatment duration and recurrence rates

Studies consistently reported that combination therapy significantly reduced overall treatment duration and minimized recurrence rates. Lu et al. [17] found that concurrent propranolol-laser therapy resulted in lesion clearance within approximately nine months, compared to fourteen months for sequential therapy. Ke et al. [40] observed that Nd:YAG laser monotherapy achieved the lowest recurrence rates, with long-term efficacy. Ehsani et al. [31] reported that multiple Nd:YAG sessions resulted in lower recurrence rates compared to single-session treatments. These findings suggest that early intervention and combination therapy optimize treatment outcomes by accelerating lesion regression and reducing the risk of recurrence.

3.7. Risk of bias assessment

The risk of bias assessment (Fig. 2) revealed that most studies had a low risk of bias, particularly in the domains of outcome measurement and selection of reported results [34,36]. However, some concerns were identified in randomization processes and missing outcome data. High risk of bias was observed in a few studies due to deviations from intended interventions or incomplete data reporting [29,33]. Notably, studies with the lowest risk of bias demonstrated consistent findings, reinforcing the reliability of the overall conclusions. These results suggest that, while some methodological limitations exist, the majority of the included studies provide robust and high-quality evidence supporting the efficacy and safety of laser therapy for infantile hemangiomas.

3.8. Limitations: inability to perform a meta-analysis

Despite the extensive data gathered in this review, a formal meta-analysis could not be conducted due to the significant heterogeneity across studies. Variability in study designs, laser protocols, treatment durations, outcome measures, and patient populations made it challenging to synthesize quantitative data in a statistically meaningful way. Additionally, differences in follow-up periods and assessment criteria further limited the ability to standardize results across studies. Given these discrepancies, a narrative synthesis was deemed the most appropriate approach to accurately reflect the findings and provide a comprehensive evaluation of laser therapy for infantile hemangiomas.

3.9. Clarification of outcome assessment

Complete resolution was defined by clinical examination in the majority of included studies, typically through visual assessment and palpation of lesion flattening and color normalization. A subset of studies (approximately 25 %) employed adjunctive imaging techniques—such as high-frequency ultrasound or Doppler imaging—to confirm vascular regression and rule out deeper residual components.

4. Discussion

4.1. Efficacy of laser therapy for infantile hemangiomas

The findings of this systematic review confirm that laser therapy remains an effective treatment modality for infantile hemangiomas (IHs), particularly when used in combination with pharmacological agents. Pulsed dye laser (PDL) continues to be the most widely studied and utilized laser therapy for superficial hemangiomas due to its selective absorption by oxyhemoglobin, allowing precise targeting of vascular structures while minimizing damage to surrounding tissues [39,46]. However, for deeper or mixed hemangiomas, Nd:YAG laser has demonstrated superior penetration and efficacy, achieving higher lesion regression rates [18,40].

Combination therapy, particularly PDL with beta-blockers such as propranolol or timolol, has been shown to enhance treatment efficacy, reducing lesion size more rapidly and lowering recurrence rates compared to laser monotherapy [28,34]. This synergistic effect is likely due to the vasoconstrictive and anti-angiogenic properties of beta-blockers, which decrease blood flow to hemangiomas, making them more susceptible to laser-induced coagulation and regression [17].

4.2. Comparison of laser modalities

Different laser modalities vary in their efficacy depending on the depth, size, and vascular composition of the hemangioma. The 595 nm PDL remains the gold standard for superficial hemangiomas, providing up to 85 % improvement in lesion appearance [45,46]. Nd:YAG at 1064 nm, with its deeper penetration, has proven more effective for thicker or subcutaneous lesions, with studies reporting up to 87.57 % regression rates [18,47].

Diode lasers, operating in the 810–980 nm range, have shown particular efficacy for small, mucosal, and labial hemangiomas due to their moderate penetration and hemostatic properties [35,38]. CO_2 lasers, at 10,600 nm, have primarily been used in ulcerated or bulky lesions where tissue ablation is required [48]. Meanwhile, intense pulsed light (IPL) at 590–595 nm has been explored as an alternative, providing a non-coherent broad-spectrum approach that has shown promising results in certain cases [29].

Dual-wavelength approaches, such as PDL combined with Nd:YAG, have emerged as a promising treatment strategy for mixed hemangiomas, offering improved clearance rates while addressing both superficial and deep vascular components [40]. However, further comparative studies are needed to standardize protocols and optimize laser parameter settings for these combination therapies.

4.3. Effectiveness of different wavelengths

Among the wavelengths employed in laser therapy for IHs, specific ranges have demonstrated superior effectiveness based on lesion characteristics. The most effective wavelengths identified in this review include PDL at 595 nm and Nd:YAG at 1064 nm. The 595 nm wavelength is highly selective for hemoglobin, making it particularly effective for superficial hemangiomas, while the 1064 nm wavelength provides deeper penetration, making it ideal for treating thick or subcutaneous lesions [18,47]. Additionally, dual-wavelength strategies, such as combining PDL with Nd:YAG, have been shown to optimize outcomes for mixed hemangiomas [40].

Conversely, other wavelengths have shown variable efficacy depending on lesion type. Diode lasers, operating in the 810–980 nm range, have demonstrated effectiveness for small vascular lesions but are less commonly used as first-line treatments for IHs due to their limited selectivity and higher risk of thermal damage [35,38]. CO_2 lasers at 10,600 nm are primarily used for ablation rather than vascular targeting, limiting their utility for non-ulcerated hemangiomas [48]. Intense pulsed light, while showing promise in some studies, lacks the specificity of monochromatic lasers and requires further validation before being considered a standard treatment option [29].

4.4. Mechanisms of affinity and removal of hemangiomas in laser therapy

The mechanism of affinity and removal of hemangiomas in the context of laser therapy is based on the interaction of light with hemoglobin and its ability to modulate oxygen release, promoting the progressive involution of abnormal vascular tissue. The absorption of specific wavelengths, such as low-intensity laser in the 800–1060 nm range, induces photoexcitation of hemoglobin, facilitating oxygen dissociation and improving tissue oxygenation, thereby contributing to hemangioma regression [50]. Additionally, pulsed dye laser (PDL, 585 nm) optimizes the selective coagulation of blood vessels through photothermolysis, reducing cellular proliferation and preventing vascular recanalization [51]. Moreover, the application of Nd:YAG 1064 nm and

long-pulsed lasers, such as the 755 nm alexandrite laser, not only induce thermal destruction of blood vessels but also modulate signaling pathways such as VEGF/PI3K/Akt, leading to endothelial cell apoptosis and reducing aberrant angiogenesis [32,40]. These strategies have demonstrated efficacy in reducing tumor volume and improving aesthetic outcomes in patients with residual hemangiomas following pharmacological treatments such as propranolol [47].

4.5. Timing of treatment and recurrence rates

The timing of laser therapy initiation has a significant impact on treatment outcomes. Studies suggest that early intervention, particularly within the first year of life, leads to more effective lesion resolution and improved aesthetic outcomes [17,28]. Early treatment can prevent complications such as ulceration, bleeding, and functional impairments, which are more common in untreated hemangiomas that persist beyond infancy [40].

In terms of recurrence, Nd:YAG laser has shown the lowest recurrence rates, particularly in cases where multiple sessions were administered [31]. Combination therapy also plays a role in minimizing recurrence, with studies showing that PDL combined with propranolol or timolol led to lower relapse rates compared to monotherapy [34]. The use of multiple laser sessions, tailored to the size and depth of the lesion, appears to be a crucial factor in achieving sustained treatment effects.

4.6. Recommendations and clinical guidelines

Based on the available evidence, clinicians should prioritize laser selection based on hemangioma characteristics. PDL should be the first-line option for superficial hemangiomas, while Nd:YAG should be considered for thicker or deeper lesions. Dual-wavelength approaches may be beneficial for mixed lesions. Treatment should ideally begin within the first year of life to maximize efficacy and minimize complications. Combination therapy with beta-blockers, particularly propranolol, should be considered in cases where rapid lesion regression is required or when treating complex lesions. Standardized laser parameters, including fluence, pulse duration, and session intervals, should be established to ensure consistency across clinical settings.

Additionally, patient selection should be guided by lesion type, size, location, and risk factors for recurrence. Clinicians should employ imaging modalities, such as high-frequency ultrasound, to assess lesion depth and optimize laser application. Post-treatment care should include sun protection and follow-up evaluations to monitor regression and identify potential complications early. Further research is needed to refine laser protocols and assess the long-term efficacy of different treatment strategies.

4.7. Strength of evidence and study design considerations

While randomized controlled trials (RCTs) provided high-quality evidence supporting the efficacy of laser treatments—particularly pulsed dye laser (PDL) monotherapy and combination therapies with propranolol or timolol [31,34,39] retrospective studies exhibited greater variability in design and outcome assessment [29,46,47]. Many retrospective analyses lacked standardized treatment protocols, consistent follow-up intervals, and control groups, which limits the generalizability of their findings. Furthermore, retrospective designs are prone to selection bias and incomplete data reporting. Therefore, conclusions drawn from these studies should be interpreted with caution, and greater weight should be placed on findings from prospective and randomized investigations when developing clinical guidelines.

4.8. Limitations and future perspectives

Despite the promising outcomes observed in this review, several limitations must be acknowledged. One of the main challenges was the heterogeneity among studies regarding treatment protocols, laser settings, and outcome measures, which hindered direct comparisons and the ability to perform a meta-analysis [40]. The lack of standardized guidelines for laser fluence, pulse duration, and session intervals further complicates the establishment of optimal treatment protocols [34]. Additionally, many studies had relatively short follow-up periods, making it difficult to assess long-term recurrence rates and post-treatment skin alterations [31].

Future research should focus on conducting large-scale, multi-center, randomized controlled trials with standardized laser parameters to enhance the comparability of results. The integration of imaging technologies such as high-frequency ultrasound and optical coherence tomography could improve lesion assessment and allow for more precise laser application [29]. Additionally, novel combination therapies, including the use of vascular endothelial growth factor (VEGF) inhibitors alongside laser therapy, warrant further investigation to determine their potential for reducing recurrence rates and improving long-term outcomes [28]. Establishing consensus guidelines for laser treatment of IHs will be crucial in optimizing patient care and ensuring consistent clinical outcomes across different settings.

5. Conclusion

This systematic review highlights the efficacy and safety of laser therapy for IHs, particularly when combined with propranolol or timolol. Combination therapies result in superior lesion regression, shorter treatment duration, and lower recurrence rates compared to laser monotherapy. However, heterogeneity in laser parameters and treatment protocols necessitates further high-quality studies to establish standardized clinical guidelines for optimal IH management.

Future studies should focus on **optimizing treatment strategies, investigating long-term outcomes, and evaluating newer laser technologies** for **improved IH management**.

Future randomized controlled trials should aim to define standardized laser parameters, treatment intervals, and patient selection criteria. Moreover, consistent outcome measures—including lesion clearance rates, patient-reported satisfaction, and long-term recurrence—are essential for enabling meaningful cross-study comparisons.

5.1. Ethics and integrity statements

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- Clinical Trial Registration:

This systematic review is registered in PROSPERO under the registration number CRD420250635593.

CRediT authorship contribution statement

Alain Chaple Gil: Writing – original draft, Investigation, Formal analysis, Data curation. **Rodrigo Caviedes:** Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation. **Leonardo Díaz:** Data curation, Formal analysis, Methodology, Supervision, Validation, Writing – review & editing. **Alfredo Von Marttens:** Conceptualization, Investigation, Writing – original draft, Writing – review & editing. **Claudio Sotomayor:** Data curation, Methodology,

Writing – original draft, Writing – review & editing. **Javier Basualdo:** Investigation, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. **Víctor Beltrán:** Data curation, Methodology, Supervision, Validation, Writing – review & editing. **Gilbert Jorquera:** Formal analysis, Investigation, Validation, Writing – original draft, Writing – review & editing. **Cristian Bersezio:** Writing – review & editing, Writing – original draft, Supervision, Software, Resources, Investigation, Formal analysis. **Pablo Angel:** Writing – review & editing, Writing – original draft, Software, Resources, Project administration, Formal analysis. **Rodrigo Cabello Ibacache:** Writing – original draft, Project administration, Investigation, Data curation. **Eduardo Fernández:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation.

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