

Evaluating the Utility of Beta Blockers in Arteriovenous Malformations and Related Vascular Lesions: A Systematic Review

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Abstract Objectives: To synthesize the available clinical evidence on beta-blocker therapy for arteriovenous malformations (AVMs) and related vascular lesions and to clarify the distinction between evidence derived from true AVMs and evidence derived from infantile haemangioma (IH)-dominant cohorts. **Methods:** This systematic review was prepared in accordance with PRISMA. PubMed, Scopus and Web of Science were searched for studies published between January 2016 and October 2025, supplemented by bibliography screening and Google Scholar searching. Eligible studies included randomized trials, observational studies and case reports evaluating systemic or topical beta-blockers. Because the included literature was clinically heterogeneous, a narrative synthesis was performed. Primary outcomes were radiological or clinical lesion response and symptom improvement; secondary outcomes were adverse events, need for additional intervention, recurrence/progression and functional outcomes. **Results:** Eighteen studies were included (2 randomized controlled trials, 10 observational studies and 6 case reports). The evidence base was dominated by IH and related vascular lesions, whereas true AVM-specific evidence was limited to case reports and small retrospective series. Across AVM-focused reports, propranolol was generally used at 1-2 mg/kg/day or equivalent fixed doses, usually for several months and was associated more often with symptom improvement or lesion stabilisation than with consistent radiological shrinkage. The randomized trials addressed IH rather than true AVMs and both were judged to have high risk of bias. Adverse effects included bradycardia, hypotension, wheeze, hypoglycaemia and gastrointestinal intolerance. **Conclusion:** Current evidence strongly supports beta-blockers in IH, but does not establish them as definitive primary therapy for true AVMs. In selected AVM cases, beta-blockers may provide symptomatic benefit or short-term stabilisation; however, they should presently be regarded as adjunctive or exploratory treatment pending higher-quality AVM-specific studies.

Key Words Arteriovenous Malformations, Vascular Anomalies, Infantile Haemangioma, Propranolol, Timolol, Systematic Review

INTRODUCTION

Arteriovenous malformations (AVMs) are high-flow vascular lesions formed by abnormal direct shunts between arteries and veins without an intervening capillary bed. They may present with swelling, pain, bleeding, ulceration, thrombosis, disfigurement, or, in advanced cases, high-output cardiac failure. Diagnosis is clinical and radiological, commonly requiring Doppler ultrasonography, computed tomography, magnetic resonance imaging or angiography depending on lesion site and flow characteristics.

Management of AVMs remains difficult because recurrence after incomplete treatment is common and because

lesion behaviour varies by anatomical site, extent, haemodynamic profile and stage. Surgery combined with embolization remains the conventional approach when feasible, whereas systemic medical therapy is generally considered adjunctive. In contrast, propranolol and other beta-blockers have an established and reproducible role in infantile haemangioma (IH), where regression is attributed to vasoconstriction, down-regulation of angiogenic signalling and endothelial apoptosis. Whether those mechanisms translate meaningfully to true AVMs remains uncertain.

The literature on beta-blockers in AVMs is therefore clinically important but methodologically challenging. Published

studies frequently mix true AVMs with IH, arteriovenous fistulas, dural malformations or other vascular anomalies and outcomes are measured inconsistently across imaging response, colour change, softening, symptom relief and need for reintervention. This heterogeneity can lead to overinterpretation if IH data are generalized to AVMs.

The present review was undertaken to synthesize the available evidence on beta-blocker therapy in AVMs and related vascular lesions, while explicitly separating AVM-specific findings from IH-dominant evidence wherever possible. The review focused on lesion response, symptom relief, adverse effects and the clinical position of beta-blockers as either primary or adjunctive therapy.

METHODS

Study Design and Reporting Standard

This systematic review followed PRISMA 2020 reporting principles (Figure 1). Because the review protocol was not prospectively registered, this has been acknowledged as a limitation in the revised manuscript.

Review Question

The review question was: "What are the effects of beta-blockers in the treatment of arteriovenous malformations and related vascular lesions and how should AVM-specific findings be interpreted separately from IH-dominant evidence?"

Information Sources and Search Strategy

Studies published from January 2016 to October 2025 were searched in PubMed, Scopus and Web of Science. Additional records were sought through bibliography screening and Google Scholar. Search terms combined controlled vocabulary and keywords related to AVMs and related lesions ("arteriovenous malformation", "AVM", "haemangioma", "infantile haemangioma", "arteriovenous fistula", "vascular malformation", "dural malformation") with beta-blocker terms ("beta-blocker", "propranolol", "timolol", "atenolol", "metoprolol", "nadolol", "carteolol").

Eligibility Criteria

Eligibility was determined using PICOS. Population: patients of any age with AVMs or related vascular lesions evaluated in the

included literature. Intervention: systemic or topical beta-blockers. Comparator: placebo, standard care, alternative therapy or no comparator in descriptive studies. Primary outcomes: lesion size/volume change, flow reduction or symptom improvement. Secondary outcomes: adverse events, requirement for surgery or embolization, recurrence/progression and functional outcomes. Randomized trials, non-randomized studies, retrospective studies, case series and case reports were eligible. Review articles, preclinical studies, abstracts without full data, duplicate publications and unpublished studies were excluded.

Study Selection and Data Extraction

Two reviewers independently screened titles, abstracts and full texts. Disagreements were resolved by discussion and, where required, consultation with an additional reviewer. Extracted variables included lesion type, anatomical site, age, sample size, concomitant therapy, beta-blocker type and dose, treatment duration, outcome measurement method, therapeutic response and adverse events.

Risk-of-Bias Assessment and Synthesis

The Joanna Briggs Institute (JBI) critical appraisal tools were used for cross-sectional studies and case reports and RoB 2 was used for randomized trials. Owing to the marked heterogeneity of lesion types, co-interventions, outcome definitions and follow-up durations, quantitative pooling was not considered appropriate; therefore, results were synthesized narratively, with emphasis on separating true AVM findings from IH-focused evidence.

RESULTS

The literature search identified 196 records from electronic databases and 6 additional records through manual searching. After removal of duplicates and screening, 18 studies met the inclusion criteria: 2 randomized controlled trials, 10 observational studies and 6 case reports.

The included evidence base was clinically mixed. A minority of reports focused on true AVMs, arteriovenous fistulas or cerebral proliferative angiopathy, whereas the majority addressed IH or mixed vascular anomaly cohorts. This scope mismatch is central to the interpretation of the

Study	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Cheng et al., 2020 (26)	⊖	⊗	⊕	⊕	⊕	⊗
Kim et al., 2017(34)	⊗	⊗	⊕	⊕	⊕	⊗

Domains:
 D1: Bias arising from the randomization process
 D2: Bias due to deviations from the intended intervention
 D3: Bias due to missing outcome data
 D4: Bias in measurement of the outcome
 D5: Bias in selection of the reported results

Judgement
 ⊕ Low
 ⊖ Some concerns
 ⊗ High

Figure 1: PRISMA flow chart

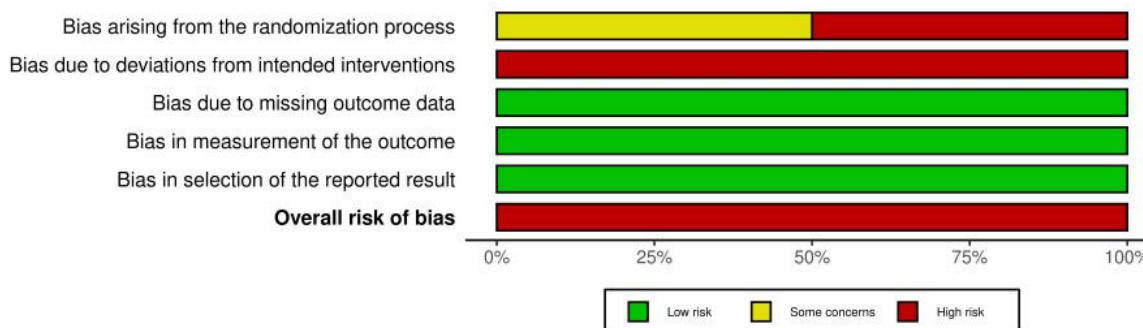


Figure 2: Risk-of-bias figures retained from source

Table 1: Summary of AVM-specific versus IH-dominant findings

Evidence domain	Main revised interpretation
True AVM/arteriovenous fistula reports	Evidence is limited to case reports and small retrospective series; benefits are mainly symptom relief, softening, stabilization, or partial response in selected cases.
Extracranial AVM series	No consistent radiological volume reduction was demonstrated; self-reported improvement may still occur.
Infantile haemangioma studies	These constitute the majority of the included evidence and show stronger efficacy for propranolol, timolol, carteolol, and topical propranolol.
Usual systemic propranolol range	Commonly 1-2 mg/kg/day, with treatment courses often extending for several months.
Topical beta-blockers	Studied mainly in superficial IH cohorts; generally safer systemically, but not supported as equivalent evidence for true AVMs.
Safety profile	Adverse events include bradycardia, hypotension, wheeze/bronchospasm, gastrointestinal intolerance, and hypoglycaemia; topical therapy is usually better tolerated.
Overall practice implication	Use beta-blockers as standard therapy for IH and only as adjunctive/exploratory therapy for selected AVMs pending better evidence.

review findings, because the strongest quantitative outcomes were derived from IH studies rather than AVM-specific studies.

A total of 1750 patients were represented across the included studies. Most participants were infants, particularly in the IH literature, while AVM-specific reports included neonates, children and adults. Propranolol was the most frequently studied agent. Across studies, the usual starting oral dose ranged from 1 to 2 mg/kg/day, with treatment duration commonly spanning 5 to 12 months, although several AVM-focused reports used fixed doses or longer courses. Topical timolol, carteolol and 2% propranolol preparations were evaluated primarily in superficial IH cohorts.

AVM-specific outcomes were modest and inconsistent. Small case reports and retrospective series suggested possible symptom improvement, lesion softening, colour reduction, headache control, stabilization or partial radiological improvement in selected patients. However, the extracranial AVM series by Chastanet *et al.* reported no meaningful reduction in lesion volume despite some self-reported symptom benefit, supporting the interpretation that beta-blockers may stabilize or palliate symptoms rather than reliably shrink true AVMs.

IH-focused studies showed substantially stronger efficacy signals. The randomized trials and several observational studies demonstrated clinical response, lower complication rates in selected superficial lesions or non-inferiority of propranolol relative to steroids. These findings support established IH practice, but they should not be extrapolated directly to true AVMs.

Concomitant treatments were common, including steroids, furosemide, surgery, embolization, radiotherapy and migraine-directed medication. This reduces certainty about the isolated effect of beta-blockers in many AVM-focused reports. Safety events across the included literature included bradycardia, hypotension, wheeze/bronchospasm, gastrointestinal intolerance, hypoglycaemia and sleep or behavioural disturbance; topical agents were generally associated with fewer systemic adverse effects (Table 1).

Risk-of-bias assessment showed that both randomized trials had high risk of bias, primarily due to limitations in randomization and blinding. The observational and case-report literature provided useful descriptive information on dose, duration and adverse effects, but was inherently limited by small sample sizes, incomplete demographic reporting, confounding from co-interventions and non-standardized outcome assessment (Figure 1).

DISCUSSION

The principal finding of this review is that the apparent therapeutic promise of beta-blockers depends heavily on which lesion type is being considered. The most convincing evidence relates to IH, for which propranolol is already an accepted therapy. In contrast, the evidence base for true AVMs remains sparse, highly heterogeneous and dominated by case reports or small retrospective series.

This distinction is clinically important because IH and AVMs differ biologically and haemodynamically. Mechanisms proposed for propranolol in IH - including vasoconstriction, reduced angiogenic signalling and endothelial apoptosis - may not translate fully to high-flow

AVMs. Accordingly, the reviewed AVM literature more commonly suggested symptom relief or lesion stabilization than consistent structural regression.

The review also highlights the interpretive challenge created by mixed vascular anomaly populations. Several included studies enrolled patients with haemangiomas, vascular malformations, fistulas or unspecified anomalies under a broad AVM-oriented search strategy. While this broad search was useful for capturing all potentially relevant beta-blocker experience, it also limited the certainty of AVM-specific conclusions and explains why a narrative synthesis was more appropriate than meta-analysis.

Another important observation is the frequent use of co-interventions. Beta-blockers were often administered alongside steroids, surgery, embolization, supportive heart-failure treatment or other medications. In such settings, therapeutic response cannot be attributed confidently to beta-blockade alone. Similarly, outcome measurement varied widely across studies, ranging from MRI-based lesion assessment to subjective cosmetic or symptomatic improvement.

From a practical standpoint, current evidence supports the established use of beta-blockers for IH and suggests that selected AVM patients may experience symptom benefit, short-term stabilization or improved tolerance of adjunctive treatment. However, current data do not justify routine use of beta-blockers as definitive stand-alone therapy for true AVMs. Careful counselling is needed so that changes in colour, softness or symptoms are not misinterpreted as durable cure.

The present review has strengths, including a structured PRISMA-based search, use of multiple databases, manual searching and formal risk-of-bias assessment. Its limitations include English-language restriction, probable publication bias toward positive case reports, inclusion of mixed lesion types, heterogeneity of outcomes, lack of protocol registration and the predominance of low-level evidence. These limitations should temper any clinical recommendation.

Future AVM-specific studies should use standardized lesion definitions, protocol registration, reproducible search reporting and uniform outcomes such as MRI-measured volume change, flow metrics, bleeding frequency, pain, need for reintervention and quality of life. Comparative work against other medical options, including targeted therapies, would also strengthen decision-making.

CONCLUSIONS

Beta-blockers remain strongly supported for infantile haemangioma, but evidence for true arteriovenous malformations is scarce and inconsistent. In selected AVM cases, propranolol or related agents may provide symptomatic relief or short-term stabilization, yet they do not currently demonstrate reliable AVM volume reduction across the limited published literature. Until better AVM-specific trials become available, beta-blockers should be

regarded as adjunctive or exploratory therapy rather than definitive primary treatment for AVMs.

Strengths and Limitations

Strengths include transparent study identification, use of multiple databases, manual searching and formal bias assessment.

The main limitations are lesion-type heterogeneity, English-only inclusion, frequent co-interventions, non-standardized outcomes and the predominance of low-level evidence for true AVMs.

Implications for Practice

Beta-blockers should continue to be interpreted as standard therapy for IH, not as established curative therapy for AVMs.

For selected AVM patients, a monitored trial of beta-blocker therapy may be considered for symptom control or short-term stabilization, with explicit counselling regarding uncertainty, follow-up imaging and stopping rules if there is no response or if adverse effects occur.

Data Availability

The review was based on published studies. The study-selection decisions, extracted variables and bias assessments are available from the corresponding author upon reasonable request.

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APPENDIX

Appendix Table 1: Retained source table

Author-Year	Geographical location	Study design	Sample size	Male/Female	Age
Gupta 2023 ¹⁸	India	Prospective interventional study	382	159/223	Up to 15 years of age
Jong-A-Liem <i>et al.</i> , 2023 ²¹	Brazil	CR	1	1/0	29 years
Panda <i>et al.</i> , 2023 ²¹	India	CR	1	1/0	3-day
Chastanet <i>et al.</i> , 2022 ²⁴	France	Retrospective monocentric study	7	5/2	Median: 55 years Range: 20-67 years
Ba <i>et al.</i> , 2020 ²⁵	China	CR	2	2/0	Case 1: 4-day old Case 2: 2-hour old
Cheng <i>et al.</i> , 2020 ²⁶	China	RCT	41	TTM: 9/15 Non-TTM: 5/12	TTM: 2.89±1.91 months Non-TTM: 2.67±1.76 months
Diociaiuti <i>et al.</i> , 2020 ²⁷	Multicenter (European regions)	Retrospective	7	0/7	3.7 months
Singh <i>et al.</i> , 2020 ²⁸	India	CR	1	1/0	8 years
Tani <i>et al.</i> , 2020 ²⁹	Japan	Cross-sectional	5	3/2	3-6 months
Xu <i>et al.</i> , 2020 ³⁰	China	Retrospective	81	24/57	3.12±1.64 months
Igarashi <i>et al.</i> , 2018 ³¹	Japan	CR	1	1/0	26 days
Lu <i>et al.</i> , 2018 ³⁰	USA	CR	1	0/1	19 years
Wu <i>et al.</i> , 2018 ³²	China	Cross-sectional	724	191/533	5.8 months
Xu <i>et al.</i> , 2018 ³³	China	Clinical cross-sectional study	Topical carteolol: n=16 Oral propranolol: n=134 Intralesional Beta- methasone: n=35	156/29	3.9 months
Goss <i>et al.</i> , 2017 ³⁴	USA	Retrospective study	Group 1: Those correctly labeled as IH (n=91) Group 2: Those inappropriately diagnosed as IH (n=49) Group 3: Those appropriately diagnosed as having vascular anomaly other than IH (n=96).	NR	NR
Kim <i>et al.</i> , 2017 ³⁴	Korea	RCT	34	15/19	3.3 months
Wang <i>et al.</i> , 2017 ³⁵	China	Cross-sectional	40	12/28	30 days to 12 months (median: 4.5 months)
Yu <i>et al.</i> , 2017 ³⁶	China	CR	1	0/1	One month

Appendix Table 2: Retained source table

Author- Year	Type and site of arteriovenous malformation	Outcome measurement methods and previous treatments, if any	Duration and dose of treatment	Concomitant therapy or comparison group if clinical trial	Adverse drug reactions	Study inference
Gupta 2023 ²¹	IH, congenital hemangioma, vascular malformations	Ultrasoundography and/or CT scan	The initial dosage was 0.5 mg/kg/day, which was then escalated to 2 mg/kg/day in two or three separate doses during the follow-up	Oral prednisolone (5 mg/5 ml syrup), topical steroid (beclomethasone dipropionate/hydrocortisone ointment), and surgery.	Diarrhoea, nausea, vomiting, dullness, lethargy, somnolence, transient peripheral coolness, and hypersensitivity reaction characterised by extensive urticarial rashes	The research confirms the efficacy of propranolol hydrochloride as the primary treatment for IHs and congenital haemangiomas. It might serve an adjunctive function in lymphatic and venous malformations within a multimodal therapeutic strategy for vascular anomalies
Jong-A-Liem <i>et al.</i> , 2023 ²²	Cerebral proliferative angiopathy	Contrast-enhanced MRI of the brain, cerebral angiographic study	80 mg of propranolol for seven years	10 mg of nortriptyline and triptans	NR	Seven years after, a cerebral arteriography revealed a reduction in the vascular network and a notable enhancement in the abnormal cerebral flow, indicating that propranolol may have contributed to the regression of the vascular lesion.
Panda <i>et al.</i> , 2023 ²³	IHs (hepatic AVM)	CT abdomen	Oral propranolol 2 mg/kg/day in two separate doses for 6 months	Oral furosemide for congestive cardiac failure	NR	Propranolol proved beneficial in symptomatic HAVM cases prior to the initiation of intensive therapy.
Chastanet <i>et al.</i> , 2022 ²⁴	AVM on the face, head, upper and lower limbs	MRI	Propranolol was administered at doses ranging from 7 to 80 mg per day for five cases, while atenolol was given at doses between 25 to 50 mg for two cases, for 14 to 36 months; treatment remained continuous for four patients.	Embolization, radiotherapy, ligation, surgery	Bradycardia, Raynaud's syndrome, reduced libido, sadness, cough, and chilliness	An overall enhancement in self-reported efficacy was noted. Beta-blockers may be incorporated into the therapeutic approach for managing AVM due to their satisfactory safety profile.
Ba <i>et al.</i> , 2020 ²⁵	Congenital hepatic arteriovenous fistula	Enhanced CT, Doppler ultrasound of the liver	Commenced oral propranolol at a dosage of 1 mg/kg/day, eventually escalating to 2 mg/kg/day over a duration of 8 to 9 months for case 1; initiated metoprolol at 0.5 mg/kg/day, subsequently increasing to 1.5 mg/kg/day after 2 weeks for case 2.	Case 1: Digitalis and diuretics for heart failure Case 2: dopamine, milrinone, and furosemide for heart failure, and sildenafil for pulmonary hypertension.	Bronchospasm	Propranolol and metoprolol can effectively manage hepatic arteriovenous fistula in newborns.
Cheng <i>et al.</i> , 2020 ²⁶	IH of face, neck, scalp, acral and buttocks regions	NR	0.5% TTM solution twice daily (one drop/10mm in length or width of lesion) for 12 months	Laser treatment	Ulceration	A 0.5% TTM solution is a safe and efficacious for infants with tiny superficial IH, particularly in high-risk regions, to mitigate problems and decrease IH volume.

Appendix Table 2: Continued

Author-Year	Type and site of arteriovenous malformation or intracranial IH	Outcome measurement methods and previous treatments, if any	Duration and dose of treatment	Concomitant therapy or comparison group if clinical trial	Adverse drug reactions	Study inference
Diociaiuti <i>et al.</i> , 2020 ⁷	Intracranial IH	Brain or spinal MRI	Propranolol 2-3 mg/kg/day for 6-14 months	NR	NR	There was total clearance of IH without any adverse consequences.
Singh <i>et al.</i> , 2020 ⁸	Scrotal AVM	Color Doppler Ultrasonography, computerized tomography (CT) angiography of scrotum and penis	Oral propranolol 2 mg/kg for 11 months	NR	NR	Rapid healing of the ulcer and a gradual although significant reduction in the size of the scrotal enlargement were observed during the 11-month follow-up, although the patient subsequently became lost to follow-up.
Tani <i>et al.</i> , 2020 ⁹	IH of cheek, forehead, abdomen, head and buttocks	Chest X-ray, electrocardiogram, and 2-dimension echocardiogram	Oral propranolol 3 mg/kg/day for 3-5 months	NR	NR	Propranolol inhibits PDGF-BB synthesis in monocytes and macrophages, facilitating the regression of haemangioma.
Xu <i>et al.</i> , 2020 ¹⁰	IH of lip and vermilion border	echocardiography, electrocardiogram, blood pressure, blood glucose, and routine blood tests, and tests of hepatic and renal functions	Oral propranolol 2 mg/kg/day (in 2 divided doses for 8.5 months)	Surgery and laser treatment	Cold extremities, sleeping disorders, and diarrhea	Lesions affecting the vermilion border exhibited poorer outcomes and prognosis compared to those restricted to one side of the vermilion
Igarashi <i>et al.</i> , 2018 ¹¹	IH	Whole- body computed tomography and abdominal MRI	Oral propranolol 1-3 mg/kg/day for 10 months	Laser therapy	NR	Propranolol treatment can efficiently restore thyroid function and induce haemangioma regression
Lu <i>et al.</i> , 2018 ¹²	AVM: large erythematous patch and right lower limb hypertrophy	Duplex ultrasound	Oral propranolol 20 mg 3 times/day and later was reduced to 20 mg 2 times daily, continued for 5 months	NR	dizziness and bradycardia	Complete regression of the hypertrophy in the right lower limb was noted, resulting in a resemblance to the normal left leg
Wu <i>et al.</i> , 2018 ¹³	IH	NR	0.5% topical timolol group and oral propranolol 2 mg/kg/day in two divided doses for 6.7 months	NA	Local pruritus and skin blemishes.	The study suggested that topical timolol may serve as the primary treatment for superficial IH owing to its superior efficacy and enhanced safety profile compared to oral propranolol
Xu <i>et al.</i> , 2018 ¹⁴	IH	Cardiac, liver, and renal functions, hepatic enzymes, glucose, electrolyte, and electrocardiogram	2% Carteolol Hydrochloride for follow up of 8 months	The patients switched to systemic oral propranolol (1.5 mg/kg/d, in 2 divided doses) treatment if the tumors showed no obvious change	Soft tissue atrophy, diarrhea, moon face, bradycardia, and liver enzyme abnormalities	Timely intervention for haemangioma can yield favourable outcomes and prevent functional damage. The authors advocate for personalised treatment based on the size and location of tumours in various patients
Goss <i>et al.</i> , 2017 ¹⁵	IH and other vascular anomalies	Comparison of study center's diagnosis with the referral diagnosis based on prior history, photographs, imaging, or histopathology	Dosage of propranolol not reported	NR	bradycardia, hypotension, hypoglycemia, hyperkalemia	Propranolol is utilised for the treatment of vascular abnormalities excluding IH. No discernible data of the efficacy of propranolol for other forms of vascular abnormalities was observed.

Appendix Table 2: Continued

Author-Year	Type and site of arteriovenous malformation	Outcome measurement methods and previous treatments, if any	Duration and dose of treatment	Concomitant therapy or comparison group if clinical trial	Adverse drug reactions	Study inference
Kim <i>et al.</i> , 2017 ³⁴	IH	MRI	Oral Propranolol: 2 mg/kg/d for 3 times/day for 20 weeks Prednisolone syrup: 1 mg/mL	NA	Hypotension, hypoglycemia, bradycardia, Gastroesophageal reflux, Hypertension	Propranolol was not inferior to steroids regarding therapeutic efficacy in IH.
Wang <i>et al.</i> , 2017 ³⁵	Proliferating IH	Cardiac color ultrasound images	2% topical propranolol cream 3 times per day	NR	Mild diarrhea and loss of appetite	The administration of 2% topical propranolol is a safe and effective method for treating proliferating infantile strawberry haemangiomas.
Yu <i>et al.</i> , 2017 ³⁶	IH	MRI, CT angiography, electrocardiogram, full ultrasonic cardiogram, full endocrine, antinuclear antibodies and ophthalmological evaluations	Propranolol (2 mg/day)	NR	NR	One month later, the haemangiomas exhibited a softer hue and a little reduction in prominence

Appendix Table 3: Retained source table

Question	Gupta ⁸	Chastanet <i>et al.</i> ³³	Goss <i>et al.</i> ³	Diociaiuti <i>et al.</i> ²⁷	Tani <i>et al.</i> ²⁹	Xu <i>et al.</i> ³⁰	Wu <i>et al.</i> ³⁵	Xu <i>et al.</i> ³⁵	Wang <i>et al.</i> ³⁵
Were the inclusion criteria explicitly delineated?	Yes	Yes	No	Unclear	No	Yes	Yes	Yes	Yes
Were the details of the study subjects and setting mentioned?	Yes	Yes	Yes	Unclear	No	Yes	Yes	Unclear	Yes
Was the exposure measurement valid and reliable?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were objective and standardised criteria employed for measurements?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the confounding variables described?	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Were the methods of dealing with confounding factors described?	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Were the evaluated outcomes valid and reliable?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was a suitable statistical evaluation employed?	No	No	No	No	No	Yes	Yes	No	Yes

Appendix Table 4: Retained source table

Question	Jong-A-Liem <i>et al.</i> , 2023 ³²	Panda <i>et al.</i> , 2023 ³³	Ba <i>et al.</i> , 2020 ³⁵	Singh <i>et al.</i> , 2020 ³⁶	Lu <i>et al.</i> , 2018 ³⁰	Igarashi <i>et al.</i> , 2018 ³¹	Yu <i>et al.</i> , 2017 ³⁵
Concise delineation of the patient's demographic attributes	No	No	No	No	No	No	No
Detailed timeline of the patient's medical history	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Concise delineation of the patient's present clinical status	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Concise delineation of the diagnostic evaluations or assessment techniques and their outcomes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Explicit delineation of the intervention or treatment protocols	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Concise delineation of the clinical status following intervention	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Concise delineation of unfavourable or unforeseen events	Yes	No	Yes	Yes	Yes	Yes	No
Clear description of the inference of the report	Yes	Yes	Yes	Yes	Yes	Yes	Yes