REVIEW

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Infantile hemangiomas screening modalities for primary care physicians

Stylianos Roupakias[1] | Eirini Kostopoulou[2] | Despoina Gkentzi[2] | Sotirios Fouzas[2] | Xenophon Sinopidis[1]

[1]Department of Pediatric Surgery, University of Patras School of Medicine, Patras, Greece
[2]Department of Pediatrics, University of Patras School of Medicine, Patras, Greece

Correspondence
Xenophon Sinopidis, Department of Pediatric Surgery, University of Patras School of Medicine, 26504 Patras, Greece.
Email: xsinopid@upatras.gr

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ABSTRACT

Infantile hemangiomas are the most common benign vascular tumors in children. They present a characteristic natural history of spontaneous involution after a phase of initial proliferation. A small but significant minority demonstrates incomplete regression or complications and requires prompt intervention. Prediction of the evolution of infantile hemangiomas is challenging because of their morphological and behavioral heterogeneity. The decision between referral for treatment and observation is sometimes difficult, especially among non-expert physicians, with the risk of missing the period for optimizing outcomes in case of delayed intervention. The aim of this review is to update our knowledge, especially of the primary care providers, regarding the ongoing difficulties of the early clinical evaluation of infantile hemangiomas, and to outline the importance of current practical scoring tools for the identification of the lesions which require expert consultation and referral.

KEYWORDS

Diagnosis, Infantile hemangioma, Scoring tool, Screening, Vascular tumor

INTRODUCTION

The term hemangioma is frequently used inaccurately to describe an array of different vascular anomalies.[1,2] The International Society for Vascular Anomalies categorized the vascular lesions in tumors (proliferation and hyperplasia) and malformations (dysplasia).[1–4] Infantile hemangiomas (IHs) comprise the most common benign vascular tumors in childhood, with an incidence of 5%.[5–7] They range from small, localized papules to large vascular dermal tumors in the skin, and rarely in internal organs.[7]

While certain types such as deep IHs may not be easily distinguished from other vascular anomalies without radiologic or histopathologic assistance, those of superficial or mixed type may be clinically diagnosed.[8] Typically, IHs are absent at birth.[9] Their growth cycle is divided into early and late proliferative, plateau, and involuting phases, but their duration may vary among different subtypes.[10] They often appear during the first weeks of life, and after a rapid proliferation phase between one and three months of age, often until five months, they resolve spontaneously without significant consequences.[11] Involution usually begins

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between 6 and 12 months, until the age of four years.[6] Some present a minimal, arrested, or prolonged growth phase.[12,13]

IHs must be distinguished from congenital hemangiomas which are present and fully formed at birth.[6] Congenital hemangiomas do not proliferate postnatally and may remain unchangeable.[6] Vascular malformations are not involuting congenital non-tumor lesions but may appear later in life.[6] Bleeding superficial lymphatic malformations may also be mistaken for IHs.[6] Expert opinion should be requested if the diagnosis is unclear.[14]

Decision for intervention is difficult, due to clinical IH heterogeneity. Most are small, harmless, and self-resolving.[7] Approximately 25%–70% of untreated IHs leave behind residual skin lesions (telangiectasia, fibrofatty tissue, depigmentation),[12,13] and about 10% are associated with long-term effects which may impact development and socialization.[14] However, depending on size and location, rapid outgrowth may occur, resulting in pain, anatomic distortion, functional impairment, or permanent disfigurement.[6,15,16] Complications vary from residual scarring to ulceration and bleeding, ocular dysfunction, airway obstruction, feeding difficulties, congestive heart failure, or hypothyroidism.[6,7,17] Therefore, primary care physicians should be able to determine which IH lesions must be referred to specialists.[6,15]

Incorrect identification, underestimation of possible complications, and delayed referral are associated with improper management. A wait-and-see approach may result in a missed window of opportunity to prevent adverse outcomes.[7] Early assessment in the first month of life is essential to decide which requires close monitoring or intervention.[12,18,19] Early treatment during the proliferative phase results in higher response rates, and better outcomes.[20–22] All IHs cause significant parental anxiety and concern.[7] Updated knowledge improves primary care providers' ability to an individualized risk-based management approach.

CLINICAL PRACTICE RECOMMENDATIONS

Several medical organizations have developed clinical practice guidelines for the management of IHs, recommending pediatricians and other primary care clinicians to monitor frequently infants with IHs during the first few weeks and months of life, to educate the parents about their clinical course (growth and complications), and to refer infants with high-risk IHs to specialists as early as the age of one month.[3,23–25] They provided a framework of clinical recommendations, without establishing a strong guideline protocol for all infants with IHs. They emphasized the importance of prompt recognition of the lesions in potentially high morbidity risk, increased vigilance, appropriate consultation, and timely referral to specialists. Clinicians should classify an IH as high risk if there is evidence of potentially life-threatening complications, associated structural anomalies, functional impairment, ulceration, or permanent skin changes, according to the disease heterogeneity and unique growth characteristics.[7] Either propranolol or surgical intervention has been proven essential options in such cases, and they should be timely applied upon indication.[26–28] Nevertheless, follow-up is adopted by most physicians. It is also a fact that recommendations suggest a more conservative approach in cases of controversy.[28]

Clinical features

Depending on the depth of the lesion from the surface of the skin, IHs are classified during their proliferative phase as superficial, confined in the epidermis and dermis, deep with a subcutaneous location, or mixed types.[5,6] Superficial IHs (formerly known as "strawberry" hemangiomas) have a red surface and little to no discernible subcutaneous component.[6] Deep IHs (formerly known as "cavernous" hemangiomas) are blue and located below the skin surface.[6] Superficial IHs usually appear earlier and tend to involute sooner than deep ones, which require a longer period of monitoring.[6] When components from both types are observed, they are called combined, mixed, or compound.[6] IHs can also be classified by their anatomic appearance as localized (well-defined that arises from a single focal point), segmental (involving a larger surface area of skin that is often plaque-like with a diameter greater than five cm), intermediate, or partial segmental (they are not definitively focal or segmental), and multifocal (focal lesions occurring at more locations than one).[6,7] Compared to localized IHs, segmental IHs which involve an anatomic area from one or more developmental units are related to a higher risk of morbidity and life-threatening complications.[7] Segmental IHs tend to have longer proliferative phases, are more commonly involved in syndromes, and are associated with comorbidities.[6]

Imaging investigation

The diagnosis of IHs is usually based exclusively on history and clinical observation.[8,19] Most can be distinguished easily from vascular malformations according to the age of manifestation, proliferation, and regression phase.[19] Imaging of the lesion is required when the diagnosis is uncertain.[6,7] Ultrasound with Doppler sonography is recommended and magnetic resonance imaging (MRI) may be required for large subcutaneous hemangiomas.[17] Ultrasound imaging of the liver and brain or other organs is required in cutaneous IHs with a diameter $\geq$ 5 cm, and

when associated syndromic structural abnormalities are suspected.[6,7,14] Children with hepatic IHs or large cutaneous lesions are at increased risk to develop high-output cardiac failure and/or hypothyroidism.[6,7,14,19] Segmental hemangiomas with a diameter ≥ 5 cm of the scalp, face, or neck are frequently associated with cerebrovascular and cardiac anomalies and should be screened by MRI angiography of the head and neck and by echocardiography.[7,19] Some of these children may have segmental IHs of the upper chest, shoulder, or arm, without facial involvement.[6] Segmental lumbosacral, perineal, gluteal cleft or pelvic hemangiomas may be associated with anogenital, renal, or spinal abnormalities, and should be screened by spine MRI and renal ultrasound.[7,14]

Complications

Ulceration is the most common complication, affecting up to 10% of IHs, especially large and segmental superficial hemangiomas of the neck, axillary, or anogenital regions.[19] Ulceration occurs during the proliferation phase and may cause pain with or without bleeding, infection, and/or scarring.[19] Periocular hemangiomas with a diameter > 1 cm can cause amblyopia, astigmatism, or strabismus.[7,19] Nasal hemangiomas can impair breathing,[19] while hemangiomas involving the lip or oral cavity may impair oral feeding.[7,19] Bulky neck hemangiomas can lead to positional torticollis,[19] and those of the beard area to subglottic obstruction.[7,19] Hemangiomas located at the central areas of the face and scalp, ears, and peri-mammary area may cause disfigurement.[7,19] Breast hemangiomas can cause breast asymmetry or distortion of the shape of the nipple.[7] Hemangiomas of lips, nose, cheeks, ears, or those of diameter >2 cm of neck, trunk, and extremity, can leave permanent changes including deformity, scarring, atrophy, telangiectasia, and redundant skin with a significant risk of psychological impact.[7,14] Nasal and lip hemangiomas are known to exhibit incomplete regression.[19] Scalp IHs > 2 cm can cause bleeding and/or permanent alopecia.[7] After identifying an IH as of high risk, clinicians should request specialist involvement as soon as possible.[7]

HEMANGIOMA SCORING TOOLS

Clinical observation and recommendations are helpful, but their impact on individual case management is challenging and biased by disease heterogeneity (age, growth, color, size, site, and depth), parental preference, and clinician's experience. Most physicians still use subjective visual clinical changes in size and color to predict their evolution, with questionable objectivity, reliability, and effectiveness. There are clinicians who take into consideration the parents' perceptions on the variations of the lesions, as a rough assessment. Validated reliable instruments to measure disease severity are essential for definitive diagnosis and appropriate treatment in clinical practice.

Researchers created scoring systems as triage tools to assess severity, and to help medical professionals who do not possess highly specialized knowledge to assess which IHs required expertise examination, and management. Janmohamed et al.[29] developed the Hemangioma Activity Score (HAS) system aiming to evaluate the proliferative activity of IHs. The Hemangioma Investigator Group Research Core proposed the Hemangioma Severity Scale (HSS) and the Hemangioma Dynamic Complication Scale for longitudinal use in time.[30] Based on the HAS and the HSS,[31] Semkova et al.[32] designed the Hemangioma Activity and Severity Index scoring index (HASI) for the clinical evaluation of IHs. Recently, the Infantile Hemangioma Referral Score (IHReS) tool was developed by the Infantile Hemangioma European Task Force.[22]

These systems predict the risk of complications and the need for systemic intervention. They can also evaluate the effectiveness of the treatment. In simpler versions, they could be useful as screening referral tools for non-expert health care providers.

Before proceeding to the presentation and analysis of the scoring systems, it is of note to discuss the guidelines of the American Academy of Pediatrics (AAP), which are multidisciplinary and evidence-based.[6,7] Though information from this source has been included and quoted in the previous paragraphs, we suggest a meticulous study of the text, especially the tables, charts, figures, flow sheets, and supplemental material, all being open access. For example, there are drawings where the clinician can depict in detail the geography and extension of the lesions, creating a measure for the follow-up period. The AAP guidelines provide statements on the benefits, the risks, the harm, the cost, a benefit-harm assessment, a possible intentional vagueness, the role of the patient's preferences, and a hint of any exclusion parameters. There is an estimation of the strength of every recommendation and, finally, a citation of the relevant literature references.[6,7]

Hemangioma activity score

HAS was an easy, simple, and non-time-consuming way to assess the proliferative activity of the IH lesions.[29] It is an objective evaluation method that allows observation of the lesions and comparison of their score changes between visits, before and after their treatment. It does not intend to compare different lesions of the same patient or different patients. It uses the color of the hemangiomas (very red in the growing phase, purplish red in the stabilization phase, grey to skin-colored in the regression phase) and the degree of deep swelling as the preliminary main scoring items, and

ulceration as an additional item.[29] It is possible to have more than one different color score item if they apply to different parts of the same lesion. Swelling means that the lesion is larger than the portion that is visible on the outside. The total score ranges from 0 to 8.

To validate the HAS system, the creators conducted a comparative study of case photos.[29] A total of 177 photographs of 78 pediatric hemangiomas were evaluated and scored independently at two time points by three separate observers. There was good agreement with no significant statistical difference between the scores achieved by the three researchers at the two time points. The estimation of swelling reduction rate and the fact that the size of the ulcer with photographs is evaluated in a growing child are limitations of this scoring system.[29] A major additional disadvantage is to estimate whether a deep infantile hemangioma has shrunk by more or less than half its initial size in depth.[33]

Hemangioma severity scale

A multi-institutional research group from nine academic medical centers developed the HSS by comparing the severity scores of a wide variety of hemangiomas with already-known outcomes.[30] The score contains both subjective (pain, risk of disfigurement), and objective (size, location, presence of risk factors for structural and/or functional complications) clinical variables. For the scale, two distinct size classification schemes distinguish the severity of a lesion located on the head and neck against similar-sized hemangiomas elsewhere on the body.[30] The validation study included twenty heterogeneous clinical cases, evaluated twice by 13 raters for estimation of inter-rater and intra-rater reliability. Both exceeded 99% for objective, subjective, and total severity ratings.[30]

Mull et al.[34] evaluated the clinical ability and utility of HSS as a tool for primary care providers to predict the need for referral and treatment of high-risk IHs. This retrospective study included 106 patients. Medical records and clinical photographs from the patients' initial visit were used. The percentages of children requiring intervention and children experiencing at least one hemangioma-related complication correlated significantly with the score outcomes.[34] Higher scores suggested greater risks of associated underlying structural anomalies and/or disfigurement. According to the authors, the exploratory items of the HSS are objective, and the scale is suitable for pediatricians and general dermatologists with a wide range of experience in evaluating IHs, but they would like to further explore the HSS's utility as a tool for primary care providers.[34] In conclusion, they recommended that the easy-to-accomplish-in-a-few-minutes scale may be a useful tool for primary care physicians to identify high-risk hemangiomas, and stated that a child with a total score ≥ 6 should be referred for evaluation by a specialist.[34]

A study on 657 patients compared the scores between patients with IHs for whom propranolol treatment was indicated at their first visit and those who were not treated.[35] HSS score ≤ 6, used as a marker of withhold, resulted in 94% sensitivity.[35] The outcome was that propranolol treatment should not be indicated in patients with an HSS score ≤ 6, while patients with a score ≥ 11 (specificity 89%) should receive treatment. Furthermore, the study concluded that the use of an HSS score ≥ 11 as a triage tool for referral, may help less experienced physicians to decide whether a child with an IH should be referred to an expertise center.[35]

Hemangioma activity and severity index

HASI is a unified scoring system, that assesses both activity and severity of IHs. The activity section monitors morphological changes, while the severity section aims to help predict complications.[32] The separation of the two sections aimed to highlight the fact that an active lesion is not necessarily severe, and a severe one may be in a stage of involution.[32]

The activity section evaluates the color, the gray-blue areas of regression, the flattening, the consistency, the ulceration size and depth, and the consistency and reduction of the deep tissue component. The severity section evaluates the number, size, type (morphologic subtype and depth of involvement), localization, the involvement of other organs, and functional impairment in vision, breathing, and feeding.[32] The findings on each subscale (activity and severity) must be assessed separately. The activity score ranges from 0 to 17.5 while the severity score is from 0 to 13.

The pilot validation study included 59 patients in the proliferative phase, 40 of which had superficial and 19 had mixed hemangiomas, who were scored seven different times in a period of six months by two main investigators separately.[32] The intra-rater and inter-rater reliability of the scoring system was high, with a mean time of 2.5 min required for completion.[32] HASI has good clinical applicability and utility, and the decision to start treatment was suggested by the authors to be made when the activity scale is ≥ 15, and the severity scale ≥ 4.[32]

Critical evaluation of the three scoring systems

HSS appears to be the most accessible among the three scoring systems as a referral tool,[36] although studies on the correlation between them are limited.[33] An HSS score ≥ 11 is highly recommended as a triage tool which may help less experienced physicians to decide whether a child

with IH should be referred to an expertise center.[35] There is a critical differentiation between the HSS objective clinical features (including the already presented complications) and the subjective physician-rated findings, which questions the usefulness of HSS as a clinical predictor tool for referral to an expert individual or center. Further studies are needed to determine a referral score of the separated HSS objective score.

Compared with the other three tools, the HASI score seems to be more subjective and complicated as well as time-consuming, as some of the items examined are harder to be assessed on photographs.[31] Moreover, it consists of more subjective items than HAS, and some items cannot be assessed on photographs.[31] HASI is rather a treatment-initiation decision tool for expert doctors than a referral tool for inexperienced healthcare providers. Further studies are needed to determine a critical score, which may help less experienced physicians to decide whether a child with IH should be referred to a specialist.

HAS emphasizes the activity rather than the severity of IHs, in contrast with the HSS. It may be applied both in patients and in photographs when photographic information for HSS scoring is missing.[33] Completion of HAS score takes less than 1 min compared to 2 min for the HSS.[33] HSS consists of more subjective items than HAS. Though HAS is faster to apply, it includes the subjective estimation of whether the swelling of a deep lesion has shrunk by more or less than half.[33] Maybe the isolated use of preliminary HAS score could be useful for general physicians to estimate the need for expertise referral according to the IH severity because they should anyway classify an IH as high-risk and referable if there is ulceration. A referral preliminary HAS score should be determined.

Infantile hemangioma referral score

The recently constructed IHReS aims to help general practitioners, pediatricians, and other medical professionals not possessing the highly specialized knowledge required to assess which IHs require further examination and potential treatment.[22]

IHReS consists of 12 questions and a two-part algorithm. The first part consists of six questions. If the answer to at least one of these questions is positive, then referral to a specialist is mandatory. If neither of the first six questions is positive, then the user moves on to the second part, which consists of another set of six questions. If the sum of the points accumulated in the second part is equal to or greater than four, then referral to a specialist is mandatory. If the sum is lower than four, then referral is not necessary and watchful monitoring is recommended by the creators of the tool. The diagnostic test should take place at every visit. If there are multiple hemangiomas, the test should be done separately for each one separately.[22]

For the creation of the IHReS, a multicenter, cross-sectional, observational study, consisting of three stages, was conducted.[22] In stage one, the Infantile Hemangioma European Task Force developed the instrument and prepared a set of 42 cases (each case included an image and some basic medical history information). In stage two, a separate committee of experts examined these cases, and their decisions, on whether each patient needed to be referred to a specialist or actively monitored were used to define the gold standard. In the third stage, the IHReS tool was used for the evaluation of the study group by an expert committee (each member on their own), as well as a group of 60 non-expert primary physicians from seven European countries. The participants (both expert and non-expert) had to make two separate decisions, firstly without the use of the tool and then two times (the second time being a retesting, to establish intra-rater reliability) with its use. The tool presented a sensitivity (ability to correctly classify a case as needing referral to an expert) of approximately 97% and a specificity of 55% (ability to classify a case as needing active monitoring).[22]

The high sensitivity of the screening tool makes it an appropriate tool for screening purposes.[22,36] A new study evaluated the reliability of the IHReS tool, using selected clinical cases, which were to be examined by general practitioners, pediatricians, and pediatric dermatologists.[36] The study found that the difficulty in decision-making, as far as IHs are concerned, was higher in non-expert medical professionals with the usual assessment procedure and without the assisting instruments.[36] The IHReS however helped physicians in deciding, and furthermore, there was higher agreement among non-experts as well as experts in IHs.[36] Another advantage of the IHReS was the short duration of 13 s needed to be completed. Finally, the satisfaction survey sent after the completion of the IHReS revealed that most physicians (73.5%) would use the IHReS again in the future to make decisions to refer patients with IHs to specialists.[36]

It becomes clear that the IHReS is a useful and easy-to-use tool, that can aid non-experts as well as experts, in making decisions when faced with an infant patient with a hemangioma.[36] It can also increase awareness among general practitioners regarding the need to monitor the IHs regularly, and not adopt a passive attitude that can harm the patient, since the IHs can evolve unpredictably and rapidly.[22] This tool is free to use and is available to be downloaded from www.ihscoring.com.[36]

CONCLUSIONS

Primary care physicians often face difficulties in clinical judgments regarding which IHs require referrals to expert centers. Occasionally, hesitance and misjudgment may lead to the loss of the optimal time window during which intervention might be effective in the treatment. Therefore, four mail-validated questionnaires have been employed in this quest, each one contributing to the scope of a subjective, timely, and precise evaluation of IHs. Among them, the latest, IHReS, seems to be able to improve clinical outcomes by identifying which child needs early referral and possible intervention to minimize possible complications. Data obtained from large clinical studies will produce stronger recommendations.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Steele L, Zbeidy S, Thomson J, Flohr C. How is the term haemangioma used in the literature? An evaluation against the revised ISSVA classification. *Pediatr Dermatol.* 2019;36:628-633. DOI: 10.1111/pde.13885
2. Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. *Plast Reconstr Surg.* 1982;69:412-422. DOI: 10.1097/00006534-198203000-00002
3. Wang MX, Kamel S, Elsayes KM, Guillerman RP, Habiba A, Heng L, et al. Vascular anomaly syndromes in the ISSVA classification system: Imaging findings and role of interventional radiology in management. *Radiographics.* 2022;42:1598-1620. DOI: 10.1148/rg.210234
4. Steiner JE, Drolet BA. Classification of vascular anomalies: An update. *Semin Intervent Radiol.* 2017;34:225-232. DOI: 10.1055/s-0037-1604295
5. Lee KC, Bercovitch L. Update on infantile hemangiomas. *Semin Perinatol.* 2013;37:49-58. DOI: 10.1053/j.semperi.2012.11.003
6. Darrow DH, Greene AK, Mancini AJ, Nopper AJ, Section on Dermatology, Section on Otolaryngology–Head and Neck Surgery, Section on Plastic Surgery. Diagnosis and management of infantile hemangioma. *Pediatrics.* 2015;136:e1060-e1104. DOI: 10.1542/peds.2015-2485
7. Krowchuk DP, Frieden IJ, Mancini AJ, Darrow DH, Blei F, Greene AK, et al. Clinical practice guideline for the management of infantile hemangiomas. *Pediatrics.* 2019;143. DOI: 10.1542/peds.2018-3475
8. Lee SJ, Shin DJ, Kim HY, Lee WJ, Kim DW, Chung HY, et al. A fraction of deep vascular birthmarks are true deep hemangiomas of infancy. *Int J Dermatol.* 2009;48:817-821. DOI: 10.1111/j.1365-4632.2008.04035.x
9. Smith C, Friedlander SF, Guma M, Kavanaugh A, Chambers CD. Infantile hemangiomas: An updated review on risk factors, pathogenesis, and treatment. *Birth Defects Res.* 2017;109:809-815. DOI: 10.1002/bdr2.1023
10. Chang LC, Haggstrom AN, Drolet BA, Baselga E, Chamlin SL, Garzon MC, et al. Growth characteristics of infantile hemangiomas: implications for management. *Pediatrics.* 2008;122:360-367. DOI: 10.1542/peds.2007-2767
11. Tiemann L, Hein S. Infantile hemangioma: A review of current pharmacotherapy treatment and practice pearls. *J Pediatr Pharmacol Ther.* 2020;25:586-599. DOI: 10.5863/1551-6776-25.7.586
12. Suh KY, Frieden IJ. Infantile hemangiomas with minimal or arrested growth: a retrospective case series. *Arch Dermatol.* 2010;146:971-976. DOI: 10.1001/archdermatol.2010.197
13. Brandling-Bennett HA, Metry DW, Baselga E, Lucky AW, Adams DM, Cordisco MR, et al. Infantile hemangiomas with unusually prolonged growth phase: a case series. *Arch Dermatol.* 2008;144:1632-1637. DOI: 10.1001/archderm.144.12.1632
14. Smithson SL, Rademaker M, Adams S, Bade S, Bekhor P, Davidson S, et al. Consensus statement for the treatment of infantile haemangiomas with propranolol. *Australas J Dermatol.* 2017;58:155-159. DOI: 10.1111/ajd.12600
15. Léauté-Labrèze C, Harper JI, Hoeger PH. Infantile haemangioma. *Lancet.* 2017;390:85-94. DOI: 10.1016/S0140-6736(16)00645-0
16. Baselga E, Roe E, Coulie J, Muñoz FZ, Boon LM, McCuaig C, et al. Risk factors for degree and type of sequelae after involution of untreated hemangiomas of infancy. *JAMA Dermatol.* 2016;152:1239-1243. DOI: 10.1001/jamadermatol.2016.2905
17. Haggstrom AN, Drolet BA, Baselga E, Chamlin SL, Garzon MC, Horii KA, et al. Prospective study of infantile hemangiomas: clinical characteristics predicting complications and treatment. *Pediatrics.* 2006;118:882-887. DOI: 10.1542/peds.2006-0413
18. Chinnadurai S, Snyder K, Sathe N, Fonnesbeck C, Morad A, Likis FE, et al. Diagnosis and management of infantile hemangioma. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016. Accessed April 11, 2023 https://www.ncbi.nlm.nih.gov/books/NBK344065/
19. Hoeger PH, Harper JI, Baselga E, Bonnet D, Boon LM, Ciofi Degli Atti M, et al. Treatment of infantile haemangiomas: recommendations of a European expert group. *Eur J Pediatr.* 2015;174:855-865. DOI: 10.1007/s00431-015-2570-0
20. Maguiness SM, Frieden IJ. Management of difficult infantile haemangiomas. *Arch Dis Child.* 2012;97:266-271. DOI: 10.1136/archdischild-2011-300851
21. Onnis G, Dreyfus I, Mazereeuw-Hautier J. Factors associated with delayed referral for infantile hemangioma necessitating propranolol. *J Eur Acad Dermatol Venereol.* 2018;32:1584-1588. DOI: 10.1111/jdv.14842
22. Léauté-Labrèze C, Baselga Torres E, Weibel L, Boon LM, El Hachem M, van der Vleuten C, et al. The Infantile Hemangioma Referral Score: A validated tool for physicians. *Pediatrics.* 2020;145. DOI: 10.1542/peds.2019-1628
23. Colmenero M, Del Boz J, Bernabeu Wittel J, Roé E, Feito-Rodríguez M, Vicente-Villa MA, et al. Inter- and intra-observer variability in the selection of therapy for infantile hemangiomas among pediatric dermatologists in

Spain. *Pediatr Dermatol.* 2022;39:557-562. DOI: 10.1111/pde.15015
24. Barton MT, Latour E, Small A, Leitenberger S, Funk T. Measuring the impact of clinical practice guidelines on infantile hemangioma referrals. *Pediatr Dermatol.* 2021;38:1393-1395. DOI: 10.1111/pde.14783
25. Fogel I, Ollech A, Zvulunov A, Valdman-Greenshpon Y, Atar Snir V, Friedland R, et al. Safety profile during initiation of propranolol for treatment of infantile haemangiomas in an ambulatory day-care hospitalization setting. *J Eur Acad Dermatol Venereol.* 2018;32:2004-2009. DOI: 10.1111/jdv.14955
26. Léauté-Labrèze C, Hoeger P, Mazereeuw-Hautier J, Guibaud L, Baselga E, Posiunas G, et al. A randomized, controlled trial of oral propranolol in infantile hemangioma. *N Engl J Med.* 2015;372:735-746. DOI: 10.1056/NEJMoa1404710
27. Lee JC, Modiri O, England RW, Shawber CJ, Wu JK. Propranolol therapy in infantile hemangioma: It is not just about the beta. *Plast Reconstr Surg.* 2021;147:875-885. DOI: 10.1097/PRS.0000000000007699
28. Drolet BA, Frommelt PC, Chamlin SL, Haggstrom A, Bauman NM, Chiu YE, et al. Initiation and use of propranolol for infantile hemangioma: report of a consensus conference. *Pediatrics.* 2013;131:128-140. DOI: 10.1542/peds.2012-1691
29. Janmohamed SR, de Waard-van der Spek FB, Madern GC, de Laat PC, Hop WC, Oranje AP. Scoring the proliferative activity of haemangioma of infancy: the Haemangioma Activity Score (HAS). *Clin Exp Dermatol.* 2011;36:715-723. DOI: 10.1111/j.1365-2230.2011.04080.x
30. Haggstrom AN, Beaumont JL, Lai JS, Adams DM, Drolet BA, Frieden IJ, et al. Measuring the severity of infantile hemangiomas: instrument development and reliability. *Arch Dermatol.* 2012;148:197-202. DOI: 10.1001/archdermatol.2011.926
31. Janmohamed SR, Oranje AP. Scoring systems for infantile hemangioma: the Hemangioma Activity Score versus the Hemangioma Activity and Severity Index. *Int J Dermatol.* 2016;55:e416-417. DOI: 10.1111/ijd.13242
32. Semkova K, Kazandjieva J, Kadurina M, Tsankov N. Hemangioma Activity and Severity Index (HASI), an instrument for evaluating infantile hemangioma: development and preliminary validation. *Int J Dermatol.* 2015;54:494-498. DOI: 10.1111/ijd.12646
33. Janmohamed SR, van Oosterhout M, de Laat PC, van Rosmalen J, Madern GC, Oranje AP. Scoring the therapeutic effects of oral propranolol for infantile hemangioma: A prospective study comparing the Hemangioma Activity Score (HAS) with the Hemangioma Severity Scale (HSS). *J Am Acad Dermatol.* 2015;73:258-263. DOI: 10.1016/j.jaad.2015.05.012
34. Mull JL, Chamlin SL, Lai JS, Beaumont JL, Cella D, Rancour EA, et al. Utility of the Hemangioma Severity Scale as a triage tool and predictor of need for treatment. *Pediatr Dermatol.* 2017;34:78-83. DOI: 10.1111/pde.13032
35. Moyakine AV, Herwegen B, van der Vleuten C. Use of the Hemangioma Severity Scale to facilitate treatment decisions for infantile hemangiomas. *J Am Acad Dermatol.* 2017;77:868-873. DOI: 10.1016/j.jaad.2017.06.003
36. Chitpiromsak K, Techasatian L, Jetsrisuparb C. Utility of the Infantile Hemangioma Referral Score (IHReS) as a decision-making tool for referral to treatment. *BMJ Paediatr Open.* 2021;5:e001230. DOI: 10.1136/bmjpo-2021-001230

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