

Treatment patterns and outcomes in children with infantile hemangiomas: A retrospective observational analysis

SAGE Open Medicine

Volume 9: 1–8

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DOI: 10.1177/20503121211056844

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Abstract

Objective: This study aimed to make use of real-world medical records to explore the clinical characteristics, treatments, and outcomes of infantile hemangiomas in southeastern China.

Methods: This study applied a retrospective observational method using real-world data derived from the electronic medical records of the Foshan Women and Children Hospital, southeastern China dated between June 2014 and June 2019.

Results: A total of 2427 patients with infantile hemangiomas were recruited in this study, including 942 (38.8%) males and 1485 (61.2%) females. Among the participants, 620 (25.5%) were high-risk infantile hemangioma, 449 (18.5%) were medium risk, and 1358 (56.0%) were low risk. A total of 14 treatment patterns in clinical practice were identified. The top 3 treatment patterns in each group of risk levels were the same: laser therapy, a combination of laser therapy and topical timolol maleate, and topical timolol maleate. The outcomes of the top 3 treatment patterns were significantly ($P < 0.05$) different in each risk group.

Conclusion: Among the top 3 treatment patterns, laser therapy or a combination of laser therapy and topical timolol maleate were more likely to have an “Excellent” outcome.

Keywords

Infantile hemangioma, clinical characteristics, treatment, outcomes, real-world data, China, retrospective

Date received: 17 June 2021; accepted: 13 October 2021

Introduction

Infantile hemangioma is one of the most common benign tumors of infancy.¹ It is a true tumor that occurs in the vascular endothelium and is characterized by abnormal proliferation of vascular endothelial cells and abnormalities in the vascular architecture.^{2,3} Differing from abnormalities in the vascular architecture of congenital vascular malformation, infantile hemangioma usually does not appear until a few weeks after birth. Its prodromal symptoms may exist when the baby is born, and there is a proliferative period after birth, which means that infantile hemangioma develops rapidly after birth.^{4–9} Most clinically common infantile hemangiomas are small and generally are not life-threatening to the patients. However, the location of some hemangiomas in some special areas may cause functional impairment, such as a permanent facial scar, disfigurement, and ulcers. If hemangiomas appear in key sites, such as liver, thyroid, and airway, it may lead to life-threatening lesions including airway obstruction, heart failure, and hypothyroidism.^{10,11}

It is generally observed that there is a racial difference in the incidence of infantile hemangiomas, and the occurrence of the disease may also be related to genetic factors.¹² Some

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countries and regions have previously performed descriptive studies on the epidemiological characteristics of infantile hemangiomas. A prospective study in the United States included 594 infants and found that the incidence of hemangiomas was 4.5% when the infants were at 3 months of age.¹³ In a survey study with women in Australian hospitals, it was found that the incidence of infantile hemangioma in Australian newborns at 6 weeks was 2.6% after analyzing 1034 valid questionnaires.¹⁴ In a retrospective study of 6-year-old children in Tyrol, Austria, the results showed that approximately 3% of mature newborns in these children had hemangiomas, and the prevalence of hemangiomas in preterm infants was as high as 12.5%.¹⁵ By analyzing the medical data of patients with medical insurance in Germany, it was found that the incidence of infantile hemangiomas in the country from 2007 to 2012 was 2.0%–3.2%.¹⁶ A research in Taiwan included infantile hemangiomas in pigmented birthmarks and studied 500 newborns and found that the incidence of infantile hemangiomas was 0.2%.¹⁷

In China, some researchers explore the epidemiological characteristic of infantile hemangioma by survey method. For instance, Yao selected multiple community service centers in multiple provinces to conduct a survey study to explore the epidemiological of infantile hemangiomas in China.¹⁸ In this study, the incidence of infantile hemangiomas was 2.51% and, unlike previous studies showing that the most affected area was the head in western countries, the infantile hemangiomas in China mostly occurred in the trunks and limbs. Furthermore, Yao's study showed that the incidence of infantile hemangiomas was related to such factors as the mother's health state, birth weight of baby, and whether or not the baby was full-term. However, the research about the clinical characteristics and treatment of infantile hemangioma based on the real-world data in China is scarce.

Thus, this study aimed to use real-world medical records to explore the clinical characteristics, treatments, and outcomes of infantile hemangiomas in southeastern China. It is expected that the findings can contribute to the understanding of the incidence and treatment of infantile hemangiomas in China and provide evidence for improving clinical diagnosis and treatment guidelines in the country and abroad.

Methods

Research design

This study used a retrospective observational study design. The study design was reviewed and approved by the Ethics Committee at the Foshan Women and Children's Hospital (FSFY-MEC-2018-061). Informed consent was waived by the Ethics Committee at the Foshan Women and Children Hospital because this study only used retrospective data set that only included anonymous data and the individual patients could not be identified.

Research setting

The study was carried out at the Foshan Maternity & Child Healthcare Hospital, which was the leading medical specialty institution for women and children in Foshan City, southeastern China. The Foshan Maternity & Child Healthcare Hospital is a public non-profit tertiary specialty hospital specializing in maternal and child health. Considering the population and economic status, the findings of the patients in Foshan City can be used to reflect the disease characteristics in the developed regions of southeastern China with sound generalizability.

Data collection

The data were collected by extracting real-world data from the electronic medical records of all the children diagnosed with infantile hemangioma in the Department of Dermatology and Rheumatology of Foshan Maternity & Child Healthcare Hospital from June 2014 to June 2019. Information about the patients' gender, age, clinical characteristics, treatment, and outcomes were collected. The whole medical process of each patient was compiled into one data record. Identification information of patients was disguised before data extraction.

Inclusion and exclusion criteria

All the patients who had been diagnosed with infantile hemangioma were included. Regarding exclusion criteria, patients with one or more of the following conditions were not included: (1) erythematous nevus; (2) history of epilepsy; (3) abnormal liver and kidney function, hypoglycemia, and hypothyroidism; (4) sinus bradycardia, grade II or III AV Stagnation, marked heart failure, and cardiogenic shock; (5) bronchial asthma or with a history of bronchial asthma, severe chronic obstructive pulmonary disease; or (6) previous treatment of radiotherapy or oral hormone therapy.

Measurement of clinical characteristics

Clinical characteristics were measured by three aspects: clinical appearance, soft-tissue depth, and risk level. First, according to the clinical appearance of infantile hemangioma, the participants were divided into (1) head/neck hemangioma; (2) trunk hemangioma; (3) extremities hemangioma; and (4) multifocal hemangioma.

Second, based on the distribution in soft-tissue depth, infantile hemangioma in children were divided into (1) superficial, red with little or no evidence of a subcutaneous component (formerly called "strawberry hemangiomas"); (2) mixed, both superficial and deep components are present; and (3) deep, blue and located below the skin surface (formerly called "cavernous hemangiomas").¹⁹

Third, the risk level of the infantile hemangioma was categorized by the physicians in the original medical records according to the ISSVA Classification for Vascular Anomalies, including:

- High risk: facial segmental hemangiomas > 5 cm in diameter; lumbosacral, perineal segmental hemangiomas > 5 cm; non-segmental large-area hemangiomas; early white pigmented hemangiomas; middle-panel hemangiomas; eye area, perinasal, and perioral hemangioma; higher probability of causing devastating damage and functional damage; and the possibility of permanent scarring or disfiguring risk or accompanied by abnormal tissue structure, tissue deformation, or ulcer;
- Medium risk: infantile hemangiomas on the sides of the face, scalp, hands, and feet; hemangiomas in the body's wrinkles such as the neck, perineum, and underarms; segmental hemangiomas of the trunk and limbs > 5 cm in diameter; risk of disfigurement, lower probability of impaired function, a higher risk of ulcers, and leaving permanent residue on the skin.
- Low risk: infantile hemangiomas that are less pronounced on the trunk and limbs; having a lower risk of causing disfigurement damage and functional damage.^{20,21}

Measurement of treatments

Treatment options for infantile hemangiomas varied for different disease characteristics and included single treatment or different combinations of topical timolol maleate, oral propranolol, laser therapy, and triamcinolone injection.

- Topical timolol maleate: timolol maleate eye drop distributed evenly on a cotton sheet and applied to the skin lesions followed by wrapping with cling film.
- Oral propranolol: punelol hydrochloride tablet was prescribed. The total daily dose was divided into two doses, once every 12 h. About 0.5 mg/kg per day on days 1 and 2; 1.0 mg/kg per day on days 3 and 4; 1.5 mg/kg per day on days 5–7; and 2.0 mg/kg per day in week 2; treatment is continued until the established dose-reduction requirements were fulfilled then the dose was gradually reduced to 1.5 mg/kg per day on days 1–7; 1.0 mg/kg per day on days 8–14; 0.5 mg/kg per day on days 15–12 until treatment was ceased on day 22.
- Laser therapy: the laser instrument uses a long-pulsed Nd:YAG laser. The wavelength of the laser is a long pulse width of 1064 nm (LP1064 nm). Laser treatment is applied according to the characteristics of the skin lesions, age, risk level, and the effect of pretreatment. The power of laser therapy was determined according

to the patient's month age, skin lesion color, and thickness ranging between 30 and 90 J/cm² to a maximum of 100 J/cm², at an incremental increase of 10 J/cm² and a pulse width of 12–15 ms.

- Triamcinolone injection: topical injection of triamcinolone.

Measurement of outcomes

Children were followed up once a month after treatment. The final treatment outcome was evaluated at the end of the sixth month. The final treatment outcome was evaluated based on the degree of change in the size and color of the hemangiomas area before and after treatment as proposed by Achauer et al.²² The evaluation criteria for outcomes were divided into four levels:

- Excellent (level IV): hemangiomas area is reduced by more than 75%.
- Good (grade III): hemangiomas area is reduced by 51%–75%.
- Normal (grade II): hemangiomas area is reduced by 26%–50%, skin lesions stop growing, and hemangiomas body became lighter in color.
- Poor (grade I): hemangiomas area is reduced by less than 25%, and the skin damage changes are not obvious or continue to grow.

Statistical analysis

For data analysis, descriptive analysis was conducted to describe the clinical characteristics and treatments for the whole sample. Then, a chi-square test was performed to compare the clinical characteristics among three risk levels. Chi-square test was also used to compare the outcomes of main treatment in three risk-level groups, respectively. *P*-value of <0.05 was considered statistically significant. All the statistical analysis was performed using the SPSS software package (IBM SPSS 25.0).

Results

Clinical characteristics analysis of patients

As shown in Table 1, a total of 2427 patients with infantile hemangiomas were included in the final sample, including 942 (38.8%) males and 1485 (61.2%) females. Among them, 1191 (49.1%) hemangiomas developed within 3 months of birth; 895 (36.9%) within 3–9 months of birth; and 341 (14%) after 9 months of birth.

For the clinical appearance of infantile hemangioma, there were 845 (34.8%) at head/neck, 835 (34.4%) at the trunk, 578 (23.8%) at extremities, and 169 (7.0%) at multifocal. Regarding the depth of soft-tissue affected, 86.5% of infantile hemangiomas were superficial and only 1.5% were deep.

Table 1. Clinical characteristics of patients with infantile hemangioma.

Item	n (%)
Gender	
Male	942 (38.8)
Female	1485 (61.2)
Age	
>12 months	69 (2.8)
9–11 months	272 (11.2)
3–8 months	895 (36.9)
<3 months	1191 (49.1)
Soft-tissue depth	
Superficial	2099 (86.5)
Mixed	290 (12.0)
Deep	37 (1.5)
Anatomic appearance	
Head/neck	845 (34.8)
Trunk	835 (34.4)
Extremities	578 (23.8)
Multifocal	169 (7.0)

Risk-level analysis

As shown in Table 2, there were 620 (25.5%) cases of high-risk infantile hemangioma, 449 (18.5%) of medium risk, and 1358 (56.0%) of low risk. Gender, age, clinical appearance, soft-tissue depth, and outcome were significantly different among the three risk groups as examined by the chi-square test ($P < 0.05$).

Regarding the soft-tissue depth, 1304 (96.0%) of low-risk infantile hemangioma were superficial, compared with 446 (71.9%) of high risk and 350 (78.0%) of medium risk. For mixed soft-tissue depth of infantile hemangioma, there were 158 (25.5%) of high risk, 93 (20.7%) of medium risk, much higher than the 39 (2.9%) of low risk.

In terms of the clinical appearance of infantile hemangioma on the head/neck, there were 249 (40.2%) of high risk and 242 (53.9%) of medium risk, much higher than 354 (26.1%) of low risk. Comparatively, 145 (23.4%) of high risk and 89 (19.8%) of medium risk appeared on the trunk of children, much lower than the 601 (44.3%) of low risk.

Treatment patterns of the three risk groups

As shown in Table 3, there were a total of 14 treatment patterns in clinical practice. The top 3 treatment patterns in each group of risk levels were the same: laser therapy, a combination of laser therapy and topical timolol maleate, and topical timolol maleate.

For the high-risk patients, 132 (21.3%) patients were treated with laser therapy; 73 (11.8%) patients treated with topical timolol maleate; 72 (11.6%) patients treated with a combination of topical timolol maleate and laser therapy, and 67 (10.8%) patients took propranolol orally. In addition,

Table 2. Clinical characteristics of patients with infantile hemangioma at different risk levels.

	No. (%) of patients			P value
	High risk (n = 620)	Medium risk (n = 449)	Low risk (n = 1,358)	
Gender				0.017
Male	211 (34.0)	178 (39.6)	553 (40.7)	
Female	409 (66.0)	271 (60.4)	805 (59.3)	
Age				<0.01
>12 months	25 (4.0)	18 (4.0)	26 (1.9)	
9–11 months	75 (12.1)	65 (14.5)	131 (9.6)	
3–8 months	203 (32.8)	161 (35.9)	532 (39.2)	
<3 months	317 (51.1)	205 (45.6)	669 (49.3)	
Soft-tissue depth				<0.01
Superficial	446 (71.9)	350 (78.0)	1,304 (96.0)	
Mixed	158 (25.5)	93 (20.7)	39 (2.9)	
Deep	16 (2.6)	6 (1.3)	15 (1.1)	
Clinical appearance				<0.01
Head/neck	249 (40.2)	242 (53.9)	354 (26.1)	
Trunk	145 (23.4)	89 (19.8)	601 (44.3)	
Extremities	176 (28.4)	66 (14.7)	336 (24.7)	
Multifocal	50 (8.0)	52 (11.6)	67 (4.9)	
Outcome				<0.01
Excellent	230 (37.1)	176 (39.2)	563 (41.5)	
Good	127 (20.5)	87 (19.4)	334 (24.6)	
Fair	141 (22.7)	97 (21.6)	284 (20.9)	
Poor	122 (19.7)	89 (19.8)	177 (13.0)	

triple therapy (topical timolol maleate + laser therapy + oral propranolol) was used in 66 (10.6%) patients.

For the medium-risk patients, 142 (31.6%) patients in this group were treated with laser, followed by dual therapy (topical timolol maleate + laser therapy), which were used by 100 (22.3%) patients. Besides, 52 (11.6%) patients received topical timolol maleate.

For the low-risk patients, laser therapy was the most common treatment and was used to treat 674 (49.6%) patients; 263 (19.4%) patients were treated with topical timolol maleate combine laser, and 180 (13.3%) patients received topical timolol maleate.

Treatment outcomes within three groups of risk level

Table 4 showed that the outcomes of the top 3 treatment patterns were significantly different in each risk group ($P < 0.05$). For high-risk patients, single-laser therapy achieved “Excellent” outcome for 50% of the patients; combination treatment of topical timolol maleate and laser therapy achieved “Excellent” outcomes for 55% of the patients, but single treatment topical timolol maleate achieved

Table 3. Treatment of patients with infantile hemangiomas at different risk levels.

	No. (%) of patients		
	High risk (n = 620)	Medium risk (n = 449)	Low risk (n = 1358)
Interventions			
TTM	73 (11.8)	52 (11.6)	180 (13.3)
LT	132 (21.3)	142 (31.6)	674 (49.6)
OP	67 (10.8)	14 (3.1)	4 (0.3)
Surgery	0 (0.0)	1 (0.2)	2 (0.1)
TTM + LT	72 (11.6)	100 (22.3)	263 (19.4)
TTM + OP	39 (6.3)	7 (1.6)	7 (0.5)
TI + LT	1 (0.2)	1 (0.2)	1 (0.1)
TI + OP	4 (0.6)	0 (0.0)	0 (0.0)
LT + OP	47 (7.6)	15 (3.3)	7 (0.5)
TTM + TI + LT	1 (0.2)	3 (0.7)	2 (0.1)
TTM + TI + OP	1 (0.2)	0 (0.0)	0 (0.0)
TTM + LT + OP	66 (10.6)	34 (7.6)	8 (0.6)
TI + LT + OP	3 (0.5)	1 (0.2)	0 (0.0)
OP + TTM + LT + TI	4 (0.6)	2 (0.4)	2 (0.1)
Follow-up	110 (17.7)	77 (17.1)	208 (15.3)
Total	620 (100.0)	449 (100.0)	1358 (100.0)

TTM: topical timolol maleate; LT: laser therapy; OP: oral propranolol; TI: triamcinolone injection.

Table 4. Outcomes of the top three treatment patterns in each risk group.

	Excellent	Good	Fair	Poor	Total	P value
High-risk group						
LT	71 (50.0)	31 (21.8)	30 (21.1)	10 (7.0)	142 (100.0)	<0.01
TTM + LT	55 (55.0)	8 (8.0)	36 (36.0)	1 (1.0)	100 (100.0)	
TTM	1 (1.9)	29 (55.8)	13 (25.0)	9 (17.3)	52 (100.0)	
Medium-risk group						
LT	55 (41.7)	43 (32.6)	31 (23.5)	3 (2.3)	132 (100.0)	<0.01
TTM + LT	40 (55.6)	10 (13.9)	22 (30.6)	0 (0.0)	72 (100.0)	
TTM	2 (2.7)	44 (60.3)	12 (16.4)	15 (20.5)	73 (100.0)	
Low-risk group						
LT	368 (54.6)	130 (19.3)	171 (25.4)	5 (0.7)	674 (100.0)	<0.01
TTM + LT	173 (65.8)	25 (9.5)	65 (24.7)	0 (0.0)	263 (100.0)	
TTM	13 (7.2)	107 (59.4)	34 (18.9)	26 (14.4)	180 (100.0)	

LT: laser therapy; TTM: topical timolol maleate.

“Excellent” outcomes for only 1.9% of the patients. Besides, single treatment topical timolol maleate also resulted in “Poor” outcome for 17.3% of the patients, as compared to 7.0% when laser therapy was used and 1.0% when a combination of topical timolol maleate and laser therapy was used. Similar relationships between the top three treatment patterns and their outcomes were also observed in the other two risk groups.

In addition to the top three most-used regimens, we also found potentially significant outcomes associated with OP and LT treatment. Nearly half of high-risk patients use OP to cure IH (47.8%). As these patients are the main population using this method, high-risk patients usually combine OP with other therapy. According to the results of monotherapy

and combination therapy in the high-risk population, we found that OP brought a higher cure rate than TI. However, when combined with TTM, the outcome was inconsistent (LT vs OP: 41.7% vs 47.8%; TTM + LT vs TTM + OP: 55.6% vs 46.2%). We also found that the outcome of LT may be better than TTM. The results in high-risk patients and all patients are consistent (high risk: LT vs TTM: 41.7% vs 2.7%; LT + OP vs TTM + OP: 66.0% vs 46.2%; all: LT vs TTM: 52.1% vs 5.2%; LT + OP vs TTM + OP: 60.9% vs 37.7%). TTM + LT + OP is a treatment for high-risk patients, the “Excellent” outcome rate of all patients is 67.9%, which is higher than that of LT + OP (60.9%). The treatment outcome of high-risk patients was similar (TTM + LT + OP vs LT + OP: 69.7% vs 66.0%). Maybe combination therapy can

shorten the course of treatment, reduce side effects, shorten the course of the disease, and improve the benefit of the treatment outcome (Supplemental Appendix Tables 1–4).

Discussion

At present, there is no unified guideline for the diagnosis and treatment of infantile hemangioma in China. Researchers' knowledge about the diagnosis of infantile hemangiomas in China is still in the exploratory stage. Therefore, it is believed that the findings of this study can contribute to the field of infantile hemangioma. The main findings are worth further discussion in the following.

In this study, the overall incidence of infantile hemangiomas was characterized by the age of onset within 8 months after birth, with the majority being female, which is consistent with the findings in other literature.^{19,23,24} Regarding the depth of soft tissue affected, the majority of patients were with superficial hemangioma. This result is also consistent with the pathological characteristics of existing studies.^{25–29}

Regarding the clinical appearance of infantile hemangioma, this study found that there was a high incidence of hemangioma at the head/neck, trunk, and extremities. These findings were different from Yao's study which concluded that the high incidence of infantile hemangioma in China occurred in the trunk and extremities, but not the head/neck.¹⁸ However, the findings of this study were similar to the results in other countries and regions, such as the United States, Australia, Austria, Germany, Japan, and Taiwan.^{30–32} As the location of infantile hemangioma is directly related to the choice of treatment options, the clinical appearance of infantile hemangioma in China needs further investigation.

For three groups of risk levels, it was found that there were significant differences in terms of gender, age, clinical appearance, soft-tissue depth, and outcomes. Female patients were more than males. The incidence of high risk was associated with younger age. Within high-risk and medium-risk groups, there was more clinical appearance on the head/neck, while the trunk was the highest incidence area in the low-risk group. In addition, the superficial soft-tissue depth was more common in low risk than high risk and medium risk. Moreover, fewer high-risk children had "Excellent" or "Good" outcomes after treatment, compared to low-risk children. All of these findings imply that special alerts should be given to the infantile hemangioma that develops rapidly at the head/neck of children less than 8 months old.

Regarding treatment for infantile hemangiomas, this study found that there were 14 treatment patterns for children with hemangiomas, and different treatment patterns were adopted for children with different risk levels. Among the treatment pattern adopted by the three groups of risk levels, the top three patterns were laser therapy, a combination of laser therapy and topical timolol maleate, and topical timolol maleate. These three treatment patterns were significantly associated with outcomes ($P < 0.05$). To date, the pathogenesis of IH has not been clarified, one of which is supposed to be the role of

the renin-angiotensin system (RAS) in endothelial cell proliferation. Using β -receptor blockers can inhibit the production of renin in the kidney, ultimately reduce the level of angiotensin II (ATII), and control the progress of IH.³³ In this study, topical timolol maleate had a satisfying therapeutic effect, which supported the pathogenesis of the RAS system to a certain extent. This finding is similar to the result of an earlier meta-analysis which found that treatment with topical timolol alone was effective and resulted in few adverse events.³⁴

In the literature, it has been suggested that children with low-risk hemangiomas can be treated with topical timolol maleate to achieve good therapeutic efficacy.³⁵ In particular, for children with superficial hemangiomas, topical timolol maleate is preferred when the disease condition is not very severe, which is not likely to cause disfigurement or visual threat.³⁶ Compared with oral propranolol, it has been suggested that topical timolol maleate has objective clinical benefits and is well tolerated by newborns.^{37,38} Nevertheless, this study found that laser therapy or a combination of laser therapy and topical timolol maleate were associated with "Excellent" outcomes more often. While topical timolol maleate was highly associated with a "Good" outcome (59.4%), this treatment also resulted in a "Poor" outcome for 14.4% of the patients. It implies that laser therapy or a combination of laser therapy and topical timolol maleate, rather than single therapy of topical timolol maleate, should be considered as the first choice of treatment for low-risk infantile hemangiomas.

For children with medium risk of hemangiomas, similar outcomes of the top three treatment patterns were found in this study. It is thus suggested that patients with medium-risk hemangioma may benefit more from laser therapy or laser therapy with topical timolol maleate. If laser treatment cannot control hemangioma growth, and there is a high-risk development trend (rapid growth exceeds the child's growth and development speed), or when the surface appears pale, a switch to oral medication may be considered.

For children with a high risk of hemangiomas, except for the similar effect of laser therapy or a combination of laser therapy and topical timolol maleate described above, oral propranolol may be worth considering when infantile hemangiomas may potentially lead to destructive facial damage or functional impairment. In 2008, Léauté-Labrèze applied propranolol to nine children with infantile hemangiomas and obtained good clinical outcome.³⁰ Since then, propranolol has become a new generation of first-line treatment following glucocorticoids.^{39–42} For severe infantile hemangioma, a combination of oral propranolol, laser therapy, and topical timolol maleate may be considered. The findings of this study suggested that if the growth trend of the hemangioma is controlled after oral propranolol, but the skin surface color does not improve significantly, laser therapy may be applied. After the laser treatment, if the skin is still reddish, topical timolol maleate can be added. The purpose of the combination therapy is to reduce the course of medication and the side effects brought by the medication while shortening the whole course of the disease. A recent

systematic review also confirmed the effectiveness of a combination of β -receptor blockers and laser therapy as the first-line treatment of infantile hemangioma.⁴³ Nevertheless, especially for the high-risk patients, more attention is needed because these patients have poor treatment results, and the treatment plan needs to be adjusted in time according to the outcome of the disease during the treatment process, to improve the quality of life of children and obtain better treatment outcomes.

According to our knowledge, this is the first study that uses real-world data derived from electronic medical records to analyze the clinical characteristics and treatment of infantile hemangioma in southeastern China. Nevertheless, this study has some limitations that could be addressed in future research. First, this study included all the patients diagnosed with infantile hemangioma at the Foshan Maternity & Child Healthcare Hospital from June 2014 to June 2019. Thus, we did not conduct power analysis for sample size calculation. Second, this study was a single-center study in southeastern China. A multi-center study in other regions of China is needed to verify the generalizability of the findings of this study. Third, this study did not clarify the relationship between infantile hemangioma and its risk factors. To address this shortcoming, a prospective study on parents' health status and incidence of infantile hemangioma can be conducted in the future to enrich the understanding of risk factors for infantile hemangioma. Fourth, this study did not consider the costs of different treatment patterns under analysis. As costs, especially reimbursement arrangements, may affect physicians' and patients' choices about treatment, future studies should also evaluate the cost-effectiveness of different treatment patterns to support health decisions about infantile hemangioma.

Conclusion

This study found that the clinical characteristics of infantile hemangiomas in southeastern China were similar to those in other countries. High-risk hemangioma may lead to certain adverse outcomes and requires special attention. In the three groups of risk levels, the top three treatment patterns were laser therapy, a combination of laser therapy and topical timolol maleate, and topical timolol maleate. From the perspective of the treatment outcomes, laser therapy or a combination of laser therapy was more likely to achieve an "Excellent" outcome. Oral propranolol may need to be added for high-risk children with severe hemangiomas.

Acknowledgements

The authors would like to thank the colleagues at the Foshan Women and Children's Hospital and the University of Macau for their comments on the early vision of this work.

Author contributions

Y.C., C.X., and H.H. conceived the study. Y.C., F.L., and C.X. collected the data. Y.G., C.O.L.U., J.W., and H.H. conducted data

analysis. Y.G., C.O.L.U., C.X., and H.H. drafted the manuscript. All the authors reviewed and approved the manuscript. Y.C. and Y.G. contributed equally.

Data availability statement

The raw data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest for the research, authorship, and/or publication of this article.

Ethical approval

This study was reviewed and approved by the Ethics Committee at the Foshan Women and Children's Hospital (FSFY-MEC-2018-061).

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was supported by funding from the Guangdong Medicine Science Project (grant no. A2019009).

Informed consent

Informed consent was waived by the Ethics Committee at the Foshan Women and Children Hospital because this study uses retrospective data set that only includes anonymous data that cannot identify any individual.

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Supplemental material

Supplemental material for this article is available online.

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