

# Role of ultrasound in diagnosis and differential diagnosis of deep infantile hemangioma and venous malformation



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## ABSTRACT

**Objective:** For vascular anomalies, when clinical findings are not sufficient, auxiliary examination is essential. In this study, we characterize and differentiate the ultrasound (US) findings of deep infantile hemangioma (DIH) and venous malformation (VM).

**Methods:** A total of 135 patients (140 lesions) with clinically proven DIH and VM were analyzed. The following US characteristics were assessed: size, shape, border, echogenicity, echotexture, vascularity, and lesion softness. One-way analysis of variance, nonparametric test,  $\chi^2$  test, Fisher exact test, and paired sample *t*-test were used to analyze the US results.

**Results:** On gray-scale US images, DIH and VM were more common in subcutaneous soft tissue, but VM could invade the muscle. Most DIHs were expressed as hyperechoic structures (47.0%), had a well-defined border (74.2%), and were homogeneous (53%), whereas the majority of VMs showed mixed echoic with anechoic structures (87.8%), had an ill-defined border (58.1%), and were heterogeneous (100%). On color Doppler US, most DIHs (90.9%) showed high vascular density, whereas only a few blood flow signals were found in most VMs (98.6%). On elastic US, VM was softer than DIH ( $2.9 \pm 0.8$  vs  $2.6 \pm 0.5$ ;  $P = .048$ ). After DIH involution, the distance from the body surface increased ( $P = .015$ ); the lesion's vertical diameter, peak arterial systolic velocity, and Vmax were significantly decreased ( $P = .006$ ,  $P = .047$ , and  $P = .026$ , respectively). Also, early VM (<18 months) has the typical US performance of VM. Compared with elastic US, gray-scale and Doppler US provided stronger evidence for differential diagnosis.

**Conclusions:** DIH and VM have different US manifestations that can provide evidence for diagnosis and differential diagnosis of DIH and early VM. (J Vasc Surg: Venous and Lym Dis 2019;7:715-23.)

**Keywords:** Infantile hemangiomas; Venous malformations; Ultrasound

In 1982, John B. Mulliken first proposed a classification method based on the biologic characteristics of vascular endothelial cells. The International Society for the Study of Vascular Anomalies categorizes the previously traditional "vascular anomalies" as vascular tumors and vascular malformations.<sup>1</sup> Vascular tumors are true neoplasms that originate from the cellular proliferation of endothelial cells; the origin of vascular malformations is an abnormal embryonic development of the vascular buildup after the endothelial stage.<sup>1</sup>

Infantile hemangioma (IH), the most common benign tumor in infants, affects about 1.2% to 12% of infants younger than 1 year.<sup>2</sup> It has a characteristic natural history of occurrence within a week or a month after birth, rapid

proliferation, and spontaneous regression after 1 year of age. During the proliferative phase, IHs can be classified on the basis of their depth: superficial IH, deep IH (DIH), and combined IH.<sup>3</sup> Typical IH is manifested as a red strawberry-like lesion. Vascular malformations occur in approximately 0.3% to 0.5% of the population.<sup>4,5</sup> Venous malformations (VMs) are the most common type. VM exists at the time of birth, but sometimes it is not obvious. VMs grow proportionally with the human body and do not spontaneously involute. The typical VM is manifested as an ectatic superficial vein, purple vein bubbles, or blue tones involving the skin.

The two abnormal vascular conditions are fundamentally different, not only in their anatomic, histologic, and pathophysiologic characteristics but also in their clinical manifestations. In most cases, a careful history and physical examination provide enough data to clinically distinguish VM and IH.<sup>6</sup> However, in some cases, the medical history and clinical presentation can be confusing, especially for infants and young children.

When clinical findings are not sufficient, distinction between the two diagnoses is often made by additional noninvasive methods.<sup>7</sup> Ultrasound (US) is the first-line modality for evaluating cutaneous and subcutaneous mass lesions, and it plays a major role in the evaluation of vascular anomalies by providing valuable information for diagnosis, assessment of lesion extent, and monitoring of response to therapy. This is particularly useful in the management of

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lesions present in deep soft tissues that can be difficult to assess clinically. In this study, we present the US image findings of DIHs and VMs and their utility in differential diagnosis.

## METHODS

**Patients.** In this study, we retrospectively reviewed the data of 135 patients (140 masses) who were treated at our hospital between January 2014 and December 2016. The data were obtained from the Department of Ultrasound, Shanghai Ninth People's Hospital, School of Medicine, Shanghai Jiao Tong University (Shanghai, PR China). All patients had not been treated earlier and were clinically difficult to diagnose without auxiliary examination. Institutional Review Board approval was also obtained for the retrospective review of patients' medical data.

**Imaging methods.** Certified sonologists (who had together performed >2000 examinations every year) performed US on patients with DIH or VM with a linear 7-11 MHz multifrequency transducer (GE Voluson E8; GE Healthcare, Zipf, Austria) and 10 MHz transducer (MyLab Twice; Esaote, Genova, Italy). The whole affected body region was examined. The lesions were evaluated using gray-scale, color Doppler, and elastic US.

Because certain VMs have a wide range of lesions and US cannot accurately measure the size of the mass, the lesion's size was represented by its vertical diameter. The distance from the body surface means the distance from skin surface to the most superficial border of the lesion.

On color Doppler US, the degree of vascularity can be estimated by counting the number of vessels (color pixels) per square centimeter in a region of interest within the area of greatest intralésional vascularity. Dubois et al<sup>8</sup> categorized the vascular density of lesions: high vascular density, if more than five vessels are present per square centimeter; moderate vascular density, if two to four vessels are present per square centimeter; and low vascular density, if fewer than two vessels are present per square centimeter.

According to Teusch et al,<sup>9</sup> the masses were assessed for the ratio of soft tissue and stiff tissue and categorized into five grades (Table I). The grade level increased with increasing tissue stiffness. The highest grade had the highest level of tissue stiffness, whereas the lowest grade had the highest percentage of soft tissue.

**Data analysis.** Statistical analyses were performed using SPSS 19.0 Statistics for Windows software (IBM Corp, Armonk, NY). One-way analysis of variance (ANOVA), nonparametric test,  $\chi^2$  test, Fisher exact test, and paired sample *t*-test were used to analyze the US findings of DIHs and VMs;  $P < .05$  was defined as being statistically significant.

## RESULTS

In this study, we defined multiple separate masses in a patient as multiple lesions. Five patients in the DIH group had two lesions. Of 140 lesions, we identified 66 DIH and 74 VM lesions.

## ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center retrospective case-control study
- **Key Findings:** In 135 patients (140 lesions), deep infantile hemangioma (DIH) and venous malformation (VM) had different ultrasound (US) manifestations. On gray-scale US, DIHs were hyperechoic structures (47.0%), had a well-defined border (74.2%), and were homogeneous (53%); VMs showed mixed echoic with anechoic structures (87.8%), had an ill-defined border (58.1%), and were heterogeneous (100%). On color Doppler US, DIHs (90.9%) showed high vascular density, whereas only a few blood flow signals were found in VMs (98.6%). On elastic US, VM was softer than DIH ( $2.9 \pm 0.8$  vs  $2.6 \pm 0.5$ ;  $P = .048$ ).
- **Take Home Message:** US is suitable for differential diagnosis between DIH and VM and is able to confirm the diagnosis of each.

**Clinical findings.** We noted the relevant clinical findings, such as age, sex, and lesion site (Table II). Ten patients in the DIH group had multiple IHs, of whom five had combined IH and DIH (only DIH is included in this study) and five had multiple DIHs. In this study, we did not include cases with combined DIH and VM.

With respect to anatomic site, the incidence of lesions in the DIH group was highest in the head and neck (39/66 [59.1%]), followed by the trunk (24/66 [36.4%]); there were only three cases (4.5%) of DIH in the extremities. The majority of VMs were present in the head and neck (33/74 [44.6%]) or extremities (33/74 [44.6%]); only eight cases (10.8%) were present in the trunk. There was a significant difference in the tumor site of DIH and VM (Fisher exact test,  $P = .000$ ).

**Gray-scale US characteristics.** Table III summarizes the gray-scale US findings. For DIHs, the average ( $\pm$  standard deviation [SD]) distance from the body surface was  $2.7 \pm 1.4$  mm (Fig 1, A). For VMs, we also observed anechoic structures under gray-scale US (Fig 2, A). The average ( $\pm$  SD) diameter of anechoic structures was  $3.2 \pm 1.6$  mm. The vertical diameter of the DIH group was smaller than that of the VM group, and this difference was statistically significant (ANOVA,  $P = .032$ ). Furthermore, there were significant differences between DIH and VM lesions in regard to involved tissue (Fisher exact test,  $P = .000$ ), shape ( $\chi^2$  test,  $P = .000$ ), border ( $\chi^2$  test,  $P = .009$ ), echogenicity (Fisher exact test,  $P = .000$ ), echotexture (Fisher exact test,  $P = .000$ ), and phleboliths (Fisher exact test,  $P = .000$ ).

**Doppler US features.** We observed high vascular density (60/66 [90.9%]) in most of the DIHs (Fig 1, B). On the contrary, only a small amount of blood flow was found in most VMs (73/74 [98.6%]; Fig 2, C). More

**Table I.** Elasticity score

Grade	Soft tissue in the lesion, %	Stiff tissue in the lesion, %
1	100	0
2	75	25
3	50	50
4	25	75
5	0	100

important, there was an increase in blood flow signal after compression in VMs (Fig 2, C and D). In some VM lesions (20/74 [27.0%]), flow was discernible only during compression and release of the lesion.

Spectral Doppler US showed that arterial and venous spectra can be measured in the DIH group (Fig 1, C and D). The average ( $\pm$  SD) peak arterial systolic velocity (PASV) was  $36.2 \pm 25.6$  cm/s, the average ( $\pm$  SD) resistance index (RI) was  $0.6 \pm 0.1$ , and the average ( $\pm$  SD) maximum venous velocity (Vmax) was  $11.6 \pm 7.6$  cm/s. Furthermore, we found supply arteries in 21 lesions in the DIH group. Only the venous spectrum can be measured in the VM anechoic structures (Fig 2, A and B). The Vmax was  $6.8 \pm 4.6$  cm/s. Only a small amount of the arterial spectrum could be measured in VMs (2/74 [2.7%]). The average PASV was 12.5 cm/s; the average RI was 0.62. Vmax was significantly different between DIH and VM (ANOVA,  $P = .000$ ).

**Elastic US findings.** Forty patients with DIH and 43 patients with VM underwent elastic US. All patients in the DIH group had scores of 2, 3, or 4 points (Fig 3); all VM patients had scores of 2 or 3 points (Fig 4). The mean ( $\pm$  SD) elasticity values were  $2.9 \pm 0.8$  and  $2.6 \pm 0.5$  for DIH and VM, respectively. The elasticity value of the DIH group was slightly higher than that of the VM group, and this difference was statistically significant (ANOVA,  $P = .048$ ).

**Table II.** Clinical characteristics of deep infantile hemangioma (DIH) and venous malformation (VM)

Variables	DIH	VM
No.	61	74
Sex		
Male	22 (36.1)	34 (45.9)
Female	39 (63.9)	40 (54.1)
Age		
Average	5.6 months	15 years
Median	7 months	10 years
Range	1-23 months	0-55 years
Region		
Head and neck	39 (59.1)	33 (44.6)
Trunk	24 (36.4)	8 (10.8)
Extremities	3 (4.5)	33 (44.6)
Categorical variables are presented as number (%).		

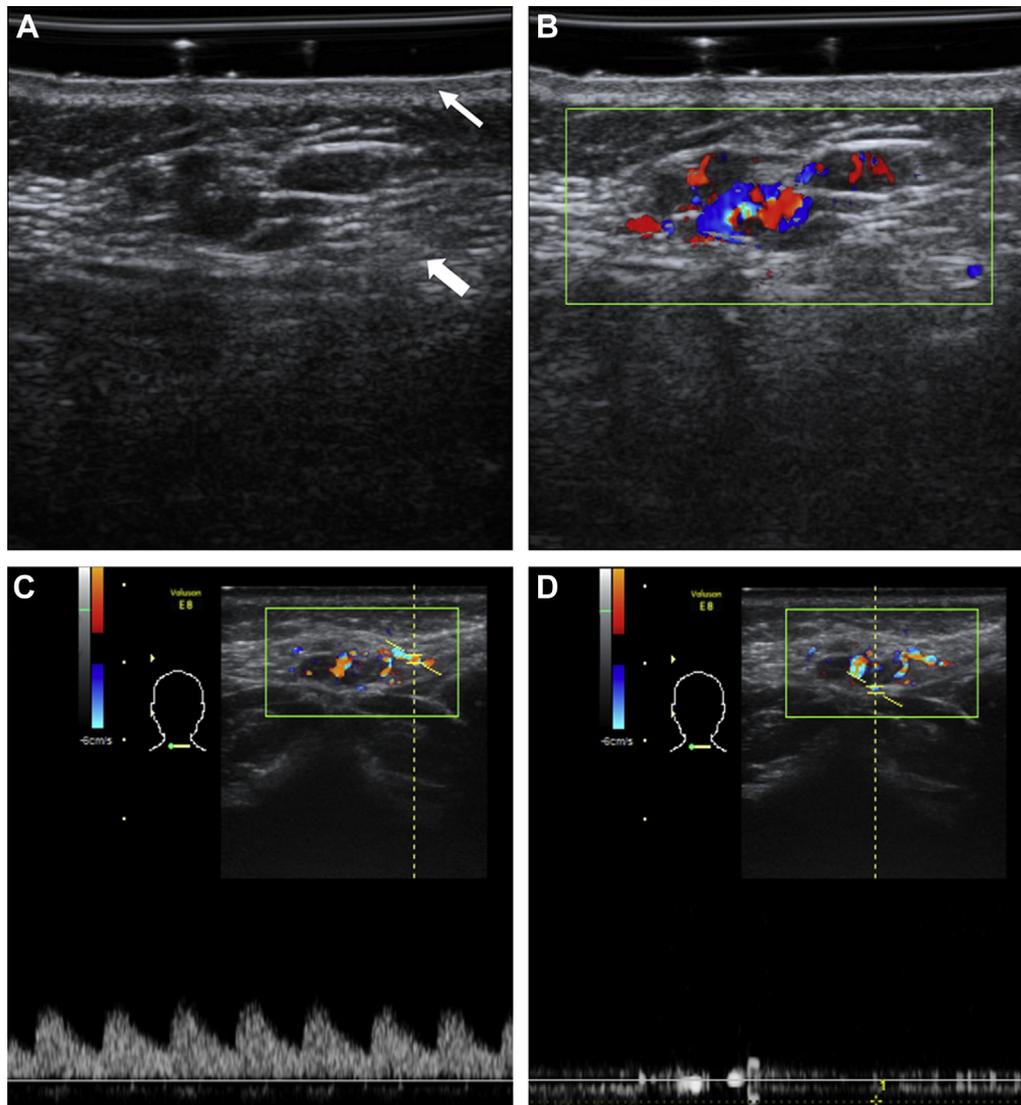
**Table III.** Summary of gray-scale ultrasound (US) characteristics of deep infantile hemangioma (DIH) and venous malformation (VM)

Variables	DIH	VM
No.	66	74
Depth, mm	$10.1 \pm 5.5$	$13.2 \pm 8.1$
Involved tissue		
Subcutaneous soft tissue	59 (89.4)	61 (82.4)
Muscle	0 (0)	7 (9.5)
Subcutaneous soft tissue and muscle	0 (0)	6 (8.1)
Between subcutaneous soft tissue and muscle	7 (10.6)	0 (0)
Shape		
Regular	60 (90.9)	26 (35.1)
Irregular	6 (9.1)	48 (64.9)
Border		
Well-defined	49 (74.2)	31 (41.9)
Ill-defined	17 (25.8)	43 (58.1)
Echogenicity		
Hyperechoic	31 (47.0)	0 (0)
Hypoechoic	25 (37.9)	6 (8.1)
Mixed echoic	10 (15.2)	65 (87.8)
Anechoic tubular structures only	0 (0)	3 (4.1)
Echotexture		
Homogeneous	35 (53.0)	0 (0)
Heterogeneous	31 (47.0)	74 (100)
Phleboliths		
Present	0 (0)	15 (20.3)
Categorical variables are presented as number (%). Continuous variables are presented as mean $\pm$ standard deviation.		

**Comparison of VMs in different age groups.** Because VM patients have a large age span, we divided them into two groups according to age (Table IV): pediatric (<18 years old) and adult ( $\geq 18$  years old). There was no statistically significant difference in the vertical diameter ( $11.6 \pm 7.1$  mm vs  $14.8 \pm 8.9$  mm) and anechoic structure diameter ( $2.9 \pm 1.5$  mm vs  $3.4 \pm 1.8$  mm) between the two groups (ANOVA,  $P = .112$ ,  $P = .250$ ). Vmax was greater in the adult group than in the pediatric group ( $5.8 \pm 2.8$  cm/s vs  $8.0 \pm 6.1$  cm/s; ANOVA,  $P = .043$ ).

**Comparison of focal VMs (F-VMs) and diffuse VMs (D-VMs).** VMs can be classified into focal and diffuse lesions<sup>10</sup> on the basis of the lesion's margins. The F-VM had a well-defined or circumscribed margin with a sharp abrupt transition from the surrounding tissue and remained confined to its tissue and fascial planes ( $n = 31$ ). The D-VM had an ill-defined margin and irregular interface with the surrounding tissue, and it appeared to cross tissue and fascial planes ( $n = 43$ ).

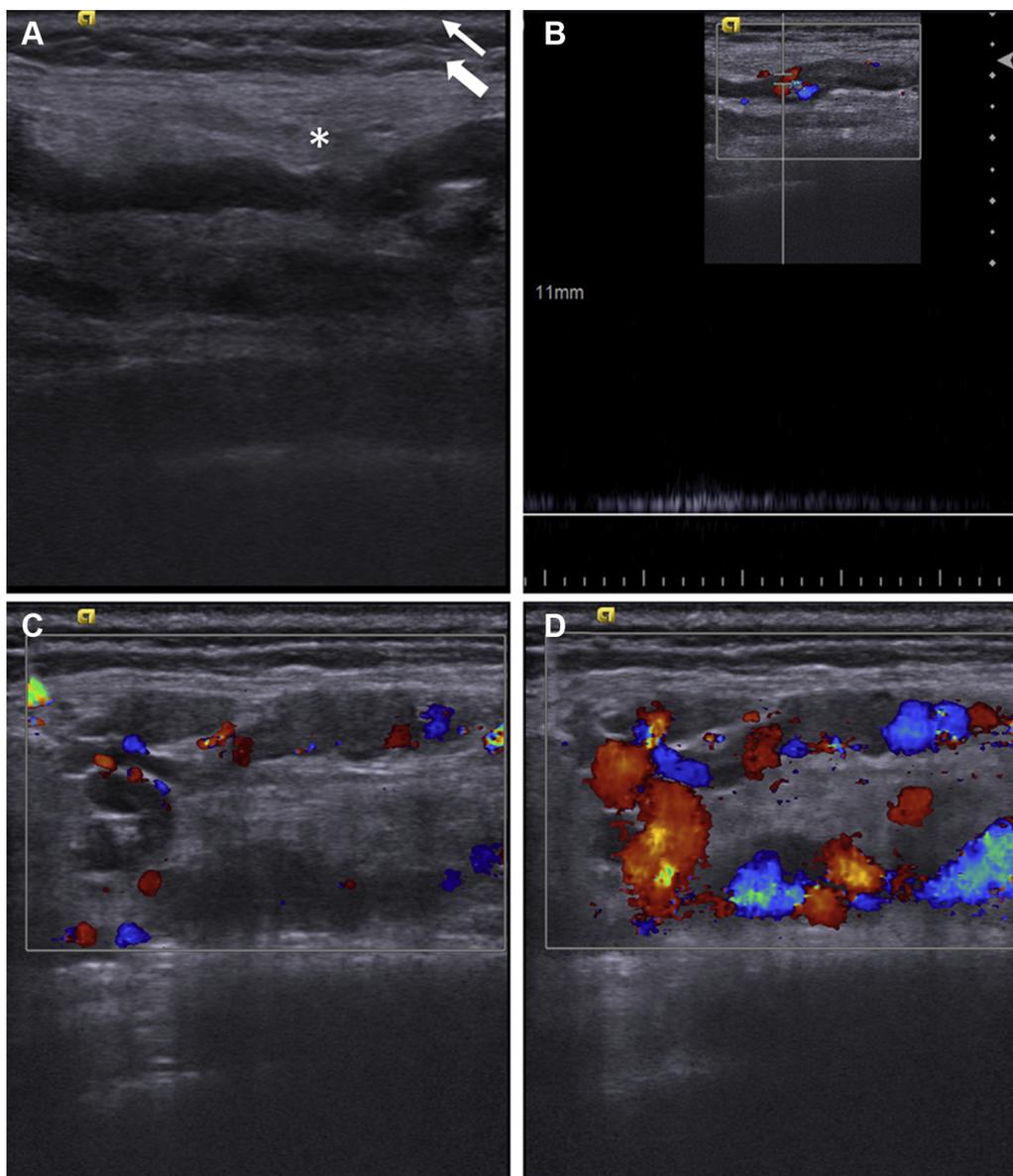
According to the classification criteria, F-VMs are confined to subcutaneous soft tissue or muscle, whereas



**Fig 1.** Deep infantile hemangioma (DIH) in a 5-month-old boy who presented with a small nodule in the neck that was noticed 2 weeks after birth. **A**, Transverse gray-scale ultrasound (US) shows a well-defined hypoechoic nodule confined to the subcutaneous soft tissues. **B**, Transverse color Doppler US shows high vascular density. **C**, Transverse spectral Doppler US shows arterial spectrum. **D**, Transverse spectral Doppler US shows venous spectrum. The *thin arrow* indicates skin; the *thick arrow* indicates subcutaneous soft tissue.

D-VMs can simultaneously invade the subcutaneous soft tissue and muscle layer. We compared the differences in vertical diameter, anechoic tubular diameter, Vmax, and elastic score. We found that the vertical diameter of the lesion ( $10.8 \pm 6.3$  mm vs  $14.9 \pm 8.8$  mm) and anechoic tubular diameter ( $2.4 \pm 1.2$  mm vs  $3.7 \pm 1.7$  mm) of F-VMs were less than those of D-VMs (ANOVA,  $P = .026$ ,  $P = .001$ , respectively). There was no significant difference in the elasticity score and Vmax ( $6.3 \pm 4.6$  cm/s vs  $7.1 \pm 4.7$  cm/s) between the two groups (nonparametric test,  $P = .578$ ,  $P = .119$ , respectively). In addition, phleboliths were found in nine cases of F-VM and seven cases of D-VM. The proportion of phleboliths in F-VMs was slightly higher than that in D-VMs. This could be related to the wide range of D-VMs, and US cannot be fully explored.

**DIH involution.** We performed secondary examination of nine patients with DIH. The first US examination was conducted at the age of  $8.3 \pm 3.1$  months, and the average follow-up time was  $5.1 \pm 2.9$  months. The findings of the second examination were compared with those of the first examination. Although the RI was increased ( $0.57 \pm 0.05$  vs  $0.62 \pm 0.06$  [ $n = 8$ ]), the difference was not statistically significant (paired sample  $t$ -test,  $P = .886$ ). The distance from the body surface increased ( $2.5 \pm 0.6$  mm vs  $2.8 \pm 0.7$  mm [ $n = 9$ ]), whereas the vertical diameter ( $10.7 \pm 5.5$  mm vs  $7.7 \pm 4.0$  mm [ $n = 9$ ]), PASV ( $58.6 \pm 36.4$  cm/s vs  $30.6 \pm 12.3$  cm/s [ $n = 8$ ]), and Vmax ( $13.7 \pm 8.7$  cm/s vs  $7.2 \pm 4.5$  cm/s [ $n = 9$ ]) significantly decreased (paired sample  $t$ -test,  $P = .015$ ,  $P = .006$ ,  $P = .047$ ,  $P = .026$ , respectively).

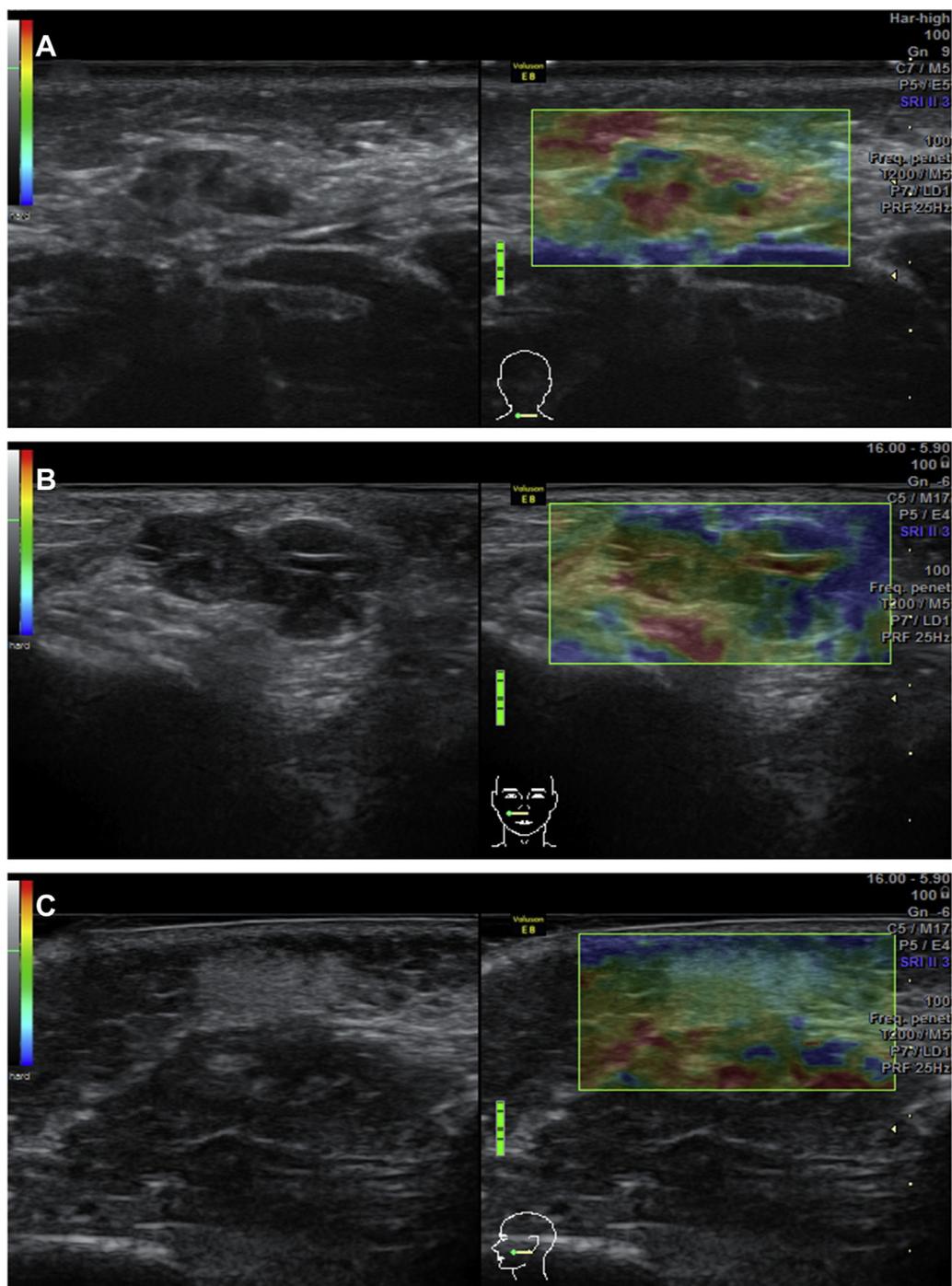


**Fig 2.** Venous malformation (VM) in a 52-year-old woman who presented with a 3-month history of back mass. **A**, Transverse sonogram shows an ill-defined intramuscular mass. **B**, Transverse spectral Doppler ultrasound (US) shows that venous spectrum can be measured. **C**, Transverse color Doppler US shows low vascular density. **D**, Transverse color Doppler US shows an increase in blood flow signals after compression. The *thin arrow* indicates skin; the *thick arrow* indicates subcutaneous soft tissue. The *asterisk* indicates muscle.

#### Differential diagnosis of early VM (E-VM) and DIH.

E-VM (<18 months [n = 18]) and DIH can be expressed as bluish nodules under normal skin, which may result in diagnosis confusion. We compared the differences between E-VM and DIH and found that E-VM also has the typical US performance of VM. The E-VM was located in the head and neck (6/18 [33.3%]), extremities (9/18 [50%]), and trunk (3/18 [16.7%]) and was mostly confined to the subcutaneous soft tissue (15/18 [83.3%]), muscle (1/18 [5.6%]), or both muscle and subcutaneous soft tissue layers (2/18 [11.1%]). E-VM showed mixed echo structures

(14/18 [77.8%]), hypoechoic structures (2/18 [11.1%]), or only multiple anechoic structures (2/18 [11.1%]) on gray-scale US. Color Doppler showed a few blood flow signals (16/18 [88.9%]). We compared E-VM with DIH and found significant differences in Vmax ( $6.3 \pm 3.3$  cm/s vs  $11.6 \pm 7.6$  cm/s; ANOVA,  $P = .002$ ). Although the elasticity score was lower ( $2.7 \pm 0.5$  vs  $2.9 \pm 0.8$ ) and the tumor vertical diameter was larger compared with DIH ( $12.4 \pm 8.2$  mm vs  $10.1 \pm 5.5$  mm), the differences were not statistically significant (nonparametric test,  $P = .397$ ; ANOVA,  $P = .769$ ).

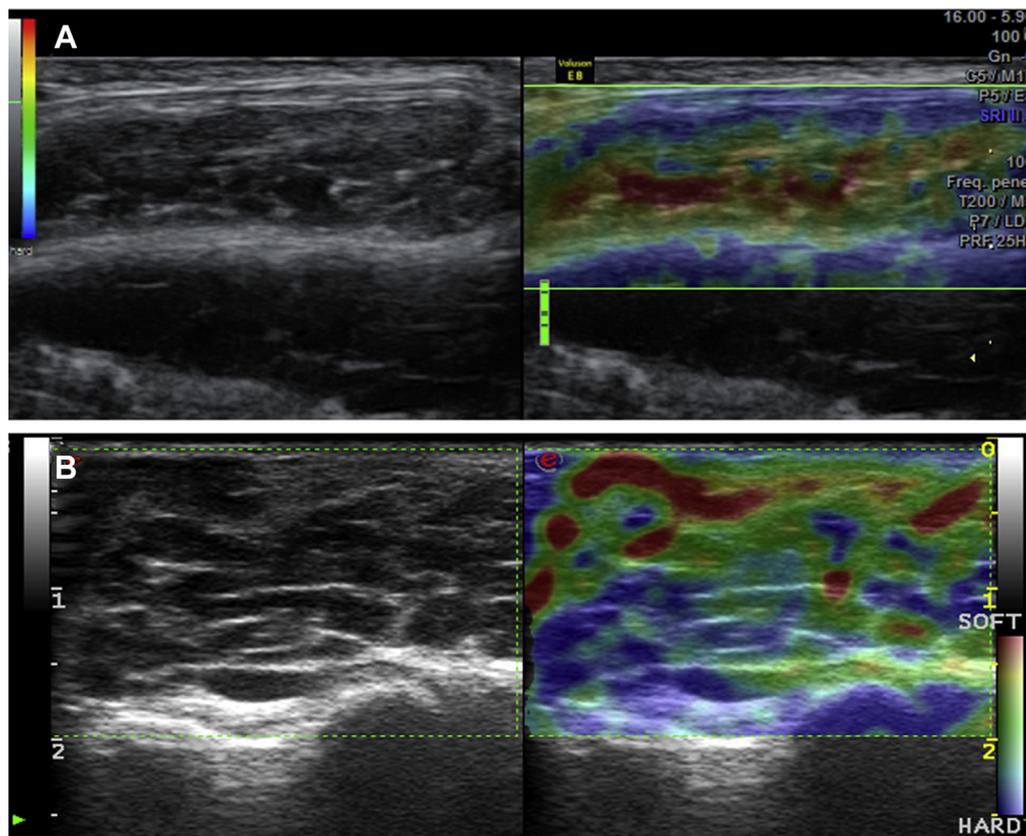


**Fig 3.** Elastic scoring images of deep infantile hemangioma (DIH). **A**, Mixed picture with mainly soft (red) and intermediate (green) colors, which is scored 2 points. **B**, Mixed picture with mainly soft (red) and stiff (blue) colors, which is scored 3 points. **C**, Mixed picture with mainly stiff (blue), intermediate (green), and less soft (red) colors, which is scored 4 points.

## DISCUSSION

Most common vascular anomalies can be identified by their typical or unique clinical features.<sup>6</sup> However, additional noninvasive laboratory studies are required to identify deeply seated IH mimicking VM. US is the first-line modality for evaluation of soft tissue vascular anomalies. Sonographic technique includes a combination of gray-

scale, Doppler, and elastic techniques. In terms of vascular anomalies, in addition to routine diagnosis, US can also be used to assess flow characteristics and signs of superficial or deep venous thrombosis or residual thrombosis in the VM,<sup>11</sup> to detect changes in softness and hardness of lesions after sclerotherapy within VM,<sup>9</sup> and to help in selection of the optimal treatment modality for IH.<sup>12</sup>



**Fig 4.** Elastic scoring images of venous malformation (VM). **A**, Mixed picture with mainly soft (red) and less stiff (blue) colors, which is scored 2 points. **B**, Mixed picture with soft (red), intermediate (green), and stiff (blue) colors, which is scored 3 points.

In this study, we studied the role of US in diagnosis and differential diagnosis of DIH and VM. We found that the two diseases have significant differences in anatomic site, level of invasiveness, and US characteristics, including gray-scale, Doppler, and elastic US. Apart from exploring the role of US in the natural resolution of DIH, we also compared the US performance of VMs of different ages, F-VMs and D-VMs, and E-VM and DIH.

IH and VM are distributed differentially in the different anatomic regions. IHs are found on the head and neck in 60% of cases, whereas 25% are found on the trunk and 15% on the extremities<sup>10</sup>; 40% of VM lesions are localized to the extremities, 20% are found on the trunk, and 40% are found on the head and neck.<sup>13</sup> These numbers are consistent with our findings (Table II). Therefore, in the differential diagnosis of the two lesions, the probability of VM is greater than that of DIH for lesions occurring in the extremities; for lesions occurring in the trunk, the probability of DIH is greater than that of VM. As shown in Table III, on gray-scale US, there were significant differences between DIH and VM lesions in regard to involved tissue, shape, border, echogenicity, echotexture, and phleboliths. Moreover, 31 (47%) DIH lesions were hyperechoic and 35 (53%) exhibited homogeneous texture, whereas no VM was hyperechoic or homogeneous.

According to the basic data and statistical analysis, we can conclude that when a lesion is hyperechoic or homogeneous on US, it is most likely DIH. Similarly, when the lesion invades the muscle layer or phleboliths are observed, it is also conclusive that the lesion is most likely VM according to our study. However, there is a sample size limitation in our research. Large-scale studies are needed in the near future to verify our conclusion.

The color Doppler US performance of DIH and VM is different and can also provide strong evidence for clinical differential diagnosis. In DIH, color Doppler US typically demonstrates high-flow vessels in and adjacent to the mass, and the arterial feeder is recognized by its increased color flow, high Doppler shift, and low resistance. In this study, we found supply arteries in 21 lesions. In the VM group, Doppler interrogation shows low vascular density. The detection of flow can be enhanced by applying compression or performing the Valsalva maneuver.<sup>14</sup> The compression test is an important method to detect blood flow in VMs, and in 27.0% of lesions, flow is discernible only during compression and release of the lesion.

Elastography is a new but established US technique. It relies on diverging plasticity and deformability of different types of tissue. The elastic imaging method

**Table IV.** Comparison of venous malformations (VMs) in different age groups

Variables	Pediatric (<18 years)	Adult (≥18 years)
No.	42	32
Age, years	5.2 ± 4.1	27.9 ± 8.9
Location		
Head and neck	16 (38.1)	17 (53.1)
Trunk	7 (16.7)	2 (6.3)
Extremities	19 (45.2)	13 (40.6)
Depth, mm	11.6 ± 7.1	14.8 ± 8.9
Involved tissue		
Subcutaneous soft tissue	34 (81.0)	27 (84.4)
Muscle	4 (9.5)	3 (9.4)
Subcutaneous soft tissue and muscle	4 (9.5)	2 (6.3)
Echogenicity		
Mixed echoic	35 (83.3)	29 (90.6)
Hypoechoic	5 (11.9)	2 (6.3)
Anechoic tubular structures	2 (4.8)	1 (3.1)
Anechoic tubular structures		
Present	37 (88.1)	30 (93.8)
None	5 (11.9)	2 (6.3)
Diameter, mm	2.9 ± 1.5	3.4 ± 1.8
Vmax, cm/s	5.8 ± 2.8	8.0 ± 6.1
Elasticity score	2.6 ± 0.5	2.6 ± 0.6
Categorical variables are presented as number (%). Continuous variables are presented as mean ± standard deviation.		

used in this study is strain elastography, which is a qualitative method based on compression from an external source (US transducer).<sup>15</sup> After mechanical stress, tissue moves in the direction of the US beam, and displacement of the tissue is detected. The tissue displacement is calculated in relation to the surrounding area; the software displays the different tissue types in color codes.<sup>16</sup> Elastograms visualizing hard tissue in blue, intermediate tissue in green, and soft tissue in red were evaluated; therefore, they may contribute to discrimination of different tissue types.<sup>17,18</sup> Although VMs are usually very soft and compressible, there has not been much research on DIH elasticity. We qualitatively analyzed the softness of VM and DIH and found that VMs are softer than DIHs, consistent with the observation that DIH is mostly present as solid lumps but VMs appear to be spongiform changes on gray-scale US. In the follow-up study, we plan to quantify the degree of elasticity for more intuitive comparison.

VMs are classified into focal and diffuse lesions to aid in treatment planning and to determine prognosis. Unlike F-VMs, D-VMs communicate with main conducting veins, increasing the risk of systemic toxicity after treatment.<sup>10</sup> Whereas F-VMs are

effectively treated with sclerotherapy, D-VMs require multiple treatment sessions and are more likely to recur.<sup>10</sup> We compared the F-VM and D-VM differences on US examination and found that the vertical diameter and echoless lumen diameter of F-VMs were lower than those of D-VMs, which may explain the therapeutic differences.

Intramuscular VMs are rare,<sup>19</sup> and they have the potential to be missed because their involved sites are invisible to the eye. Moreover, the symptoms of intramuscular VM overlap with those of myofascial pain syndrome or muscle strain.<sup>20</sup> According to a study by Hein et al,<sup>21</sup> two-thirds of intramuscular VMs were noted at birth and the remainder manifested during childhood and adolescence. In this study, a total of seven cases of VMs (in patients aged 1-40 years) were located in the muscle layer, mostly on the limbs.

VMs are present at the time of birth and grow proportionally with the human body. However, we compared the US findings of VMs at different ages and found no significant differences in the lesion's vertical diameter, blood flow signal, and anechoic lumen diameter. US has a limited ability to display the full extent of large lesions and to demonstrate an intraosseous component.<sup>22,23</sup> We therefore use the lesion's vertical diameter only to indicate the size of the lesion, which is one of the limitations of our study. Therefore, for VMs with a large lesion range, US has a deficiency in the evaluation of overall lesion progression, and computed tomography or magnetic resonance imaging may be more useful. The superficial IHs or adult VMs can be diagnosed on the basis of typical appearance and growth pattern. However, the characteristics of DIH and E-VM (<18 months) have several similarities that may lead to error in diagnosis. Comparing DIH with the E-VM, we found that infants also had typical VM findings, and color Doppler US provided stronger evidence for the differential diagnosis than elastic US did. In addition, the detection of intralesional calcifications representing phleboliths is helpful for diagnosis of VMs because these are rare in other pediatric soft tissue masses. However, its practical utility is often overstated because phleboliths are not common in pediatric VMs. Trop et al<sup>24</sup> recognized phleboliths in only 16% of cases, and Paltiel et al<sup>25</sup> detected them in only 9% of cases. We found phleboliths in three E-VMs (3/18 [16.7%]).

Most IHs begin involution by the age of 1 year. DIHs tend to appear later and to grow somewhat longer.<sup>3</sup> In this study, we found reduced tumor vertical diameter after DIH involution. Peng et al<sup>26</sup> reported low-flow velocity and high-resistance spectrum in arteries of regressive hemangiomas. After the follow-up, we found PASV and Vmax to be decreased, indicating spontaneous regression of IH. Although RI was increased, the difference was not statistically significant. This may be related to our small number of cases and short follow-up. In one

patient, the age at the first examination was 5 months, and the second examination was performed 1 year later. We measured the signal of blood flow in the lesion, which was significantly reduced, and only the venous spectrum was measured. The vertical diameter of the lesion was also decreased.

## CONCLUSIONS

DIH and VM have completely different US manifestations on gray-scale, color Doppler, and elastic US. Even in the early stages of VM, when clinical findings are not sufficient, US can provide powerful information for both definitive diagnosis and differential diagnosis between the two.

## AUTHOR CONTRIBUTIONS

Conception and design: AD, PX

Analysis and interpretation: AD, XG, PX

Data collection: AD, XG, JL

Writing the article: AD

Critical revision of the article: AD, XG, JL, PX

Final approval of the article: AD, XG, JL, PX

Statistical analysis: AD

Obtained funding: PX

Overall responsibility: PX

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## REFERENCES

1. International Society for the Study of Vascular Anomalies. ISSVA classification for vascular anomalies. Available at: <http://www.issva.org/UserFiles/file/Classifications-2014-Final.pdf>. Accessed April 12, 2017.
2. Gong H, Xu DP, Li YX, Cheng C, Li G, Wang XK. Evaluation of the efficacy and safety of propranolol, timolol maleate, and the combination of the two, in the treatment of superficial infantile haemangiomas. *Br J Oral Maxillofac Surg* 2015;53:836-40.
3. Darrow DH, Greene AK, Mancini AJ, Nopper AJ. Section on Dermatology, Section on Otolaryngology—Head and Neck Surgery, and Section on Plastic Surgery. Diagnosis and management of infantile hemangioma: executive summary. *Pediatrics* 2015;136:786-91.
4. Redondo P, Aguado L, Martinez-Cuesta A. Diagnosis and management of extensive vascular malformations of the lower limb: part I. Clinical diagnosis. *J Am Acad Dermatol* 2011;65:893-906. quiz: 907-8.
5. Berenguer B, Burrows PE, Zurakowski D, Mulliken JB. Sclerotherapy of craniofacial venous malformations: complications and results. *Plast Reconstr Surg* 1999;104:1-11; discussion: 12-5.
6. Chen H, Lin X, Jin Y, Fan X, Li W, Ma G, et al. Deep infantile hemangiomas and early venous malformations: differential diagnosis by 3D CT angiography. *Ann Plast Surg* 2010;64:755-8.
7. Lee BB. Venous malformation and haemangioma: differential diagnosis, diagnosis, natural history and consequences. *Phlebology* 2013;28(Suppl 1):176-87.
8. Dubois J, Patriquin HB, Garel L, Powell J, Filiatrault D, David M, et al. Soft-tissue hemangiomas in infants and children: diagnosis using Doppler sonography. *AJR Am J Roentgenol* 1998;171:247-52.
9. Teusch VI, Piehler AP, Uller W, Muller-Wille R, Prantl L, Stroszczyński C, et al. Value of different ultrasound elastography techniques in patients with venous malformations prior to and after sclerotherapy. *Clin Hemorheol Microcirc* 2017;66:347-55.
10. Mulligan PR, Prajapati HJ, Martin LG, Patel TH. Vascular anomalies: classification, imaging characteristics and implications for interventional radiology treatment approaches. *Br J Radiol* 2014;87:20130392.
11. van Es J, Kappelhof NA, Douma RA, Meijers JC, Gerdes VE, van der Horst C. Venous thrombosis and coagulation parameters in patients with pure venous malformations. *Neth J Med* 2017;75:328-34.
12. Li M, Liu J, Valeska M, Luo D, Zhou B. Clinical evaluation of color Doppler ultrasound in selecting the optimal treatment modality for infantile hemangioma. *Chin Med Sci J* 2017;32:100-6.
13. Loose DA. Surgical management of venous malformations. *Phlebology* 2007;22:276-82.
14. Dubois J, Alison M. Vascular anomalies: what a radiologist needs to know. *Pediatr Radiol* 2010;40:895-905.
15. Barr RC. Sonographic breast elastography: a primer. *J Ultrasound Med* 2012;31:773-83.
16. Goddi A, Bonardi M, Alessi S. Breast elastography: a literature review. *J Ultrasound* 2012;15:192-8.
17. Frulio N, Laumonier H, Carteret T, Laurent C, Maire F, Balabaud C, et al. Evaluation of liver tumors using acoustic radiation force impulse elastography and correlation with histologic data. *J Ultrasound Med* 2013;32:121-30.
18. Pu H, Zhao LX, Yao MH, Xu G, Liu H, Xu HX, et al. Conventional US combined with acoustic radiation force impulse (ARFI) elastography for prediction of triple-negative breast cancer and the risk of lymphatic metastasis. *Clin Hemorheol Microcirc* 2017;65:335-47.
19. Johnson CM, Navarro OM. Clinical and sonographic features of pediatric soft-tissue vascular anomalies part 2: vascular malformations. *Pediatr Radiol* 2017;47:1196-208.
20. Jung HC, Kim DH, Park BK, Park MK. Extensive intramuscular venous malformation in the lower extremity. *Ann Rehabil Med* 2012;36:893-6.
21. Hein KD, Mulliken JB, Kozakewich HP, Upton J, Burrows PE. Venous malformations of skeletal muscle. *Plast Reconstr Surg* 2002;110:1625-35.
22. Ziyeh S, Schumacher M, Strecker R, Rossler J, Hochmuth A, Klisch J. Head and neck vascular malformations: time-resolved MR projection angiography. *Neuroradiology* 2003;45:681-6.
23. Gorincour G, Kokta V, Rypens F, Garel L, Powell J, Dubois J. Imaging characteristics of two subtypes of congenital hemangiomas: rapidly involuting congenital hemangiomas and non-involuting congenital hemangiomas. *Pediatr Radiol* 2005;35:1178-85.
24. Trop I, Dubois J, Guibaud L, Grignon A, Patriquin H, McCuaig C, et al. Soft-tissue venous malformations in pediatric and young adult patients: diagnosis with Doppler US. *Radiology* 1999;212:841-5.
25. Paltiel HJ, Burrows PE, Kozakewich HP, Zurakowski D, Mulliken JB. Soft-tissue vascular anomalies: utility of US for diagnosis. *Radiology* 2000;214:747-54.
26. Peng GH, Yu S, Cao YZ, Tao WH. Study on color Doppler ultrasound differential diagnosis between proliferating hemangioma and involuting hemangioma in children. *Chin J Med Imaging Technol* 2007;23:1703-5.