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Prospective Study

Normal values of shear wave velocity in liver tissue of healthy children measured using the latest acoustic radiation force impulse technology

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Abstract

BACKGROUND

Several studies have demonstrated the feasibility and effectiveness of using ultrasound elastography to assess liver tissue stiffness. Virtual touch imaging quantification (VTIQ) based on acoustic radiation force impulse imaging has been developed as a latest and noninvasive method for assessing liver stiffness in children.

AIM

To determine the standard value in healthy children, and to identify possible factors that might influence the VTIQ measurement.

METHODS

With the ethical approval, 202 children between 1 month and 15 years old were included in this study. None of them had any liver or systematic diseases. All children had a normal ultrasound scan and normal body mass index (BMI) range. The subjects were divided into four age and BMI groups. The effects of gender, age, liver lobe, measurement depth, and BMI on liver elasticity were investigated.

RESULTS

A significant correlation was found between age and shear wave velocity (SWV) value. At measurement depths of 1.5 cm and 2.0 cm in the left lobe, there were significant differences among the age groups. SWV values were significantly

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negatively correlated with the measurement depth. Gender, liver lobe, and BMI showed no significant effect on the SWV values. Age and BMI may influence the quality of the elastogram.

CONCLUSION

VTIQ is a noninvasive technique that is feasible to measure liver stiffness in children. The afore-mentioned velocity value obtained utilizing VTIQ method could be used as reference value for normal liver stiffness in children.

Key words: Acoustic radiation force impulse; Virtual touch imaging quantification; Liver stiffness; Shear wave velocity

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Core tip: Virtual touch imaging quantification (VTIQ) is the latest elastic technology based on acoustic radiation force impulse imaging. Previously, the high-frequency linear probe (9L4) with VTIQ technology was used for the evaluation of breast and thyroid lesions. We found that this probe might also be suitable for the abdominal organs in children. This study analyzed the normal liver stiffness measured by VTIQ method and assessed the potential influencing factors of VTIQ value and factors affecting the quality of the elastogram. This study suggested that VTIQ is a feasible technique to measure liver stiffness in children.

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INTRODUCTION

Children with chronic liver disease may be complicated by liver fibrosis due to repetitive hepatocyte injury, which leads to cirrhosis ultimately^[1-3]. Therefore, it is of paramount significance to stage liver fibrosis to make early diagnosis and improve prognosis^[4]. Although liver biopsy remains the gold standard for the diagnosis of fibrosis, it is invasive with risks of several complications^[5,6]. Hence, an alternative method for assessing liver fibrosis is increasingly necessary. In the past few years, numerous studies have demonstrated the feasibility and effectiveness of using ultrasound elastography to assess liver tissue stiffness^[7-11]. Virtual touch tissue quantification (VTQ) of acoustic radiation force impulse (ARFI) is a new ultrasound elasticity technology that could assess tissue hardness quantitatively and the results are shown as shear wave velocity (SWV) values. The stiffer the tissue, the higher the SWV value. Some studies have confirmed the value of VTQ for the evaluation of liver stiffness and the staging for liver fibrosis^[12-14]. However, a fixed size of region of interest (ROI) of VTQ makes it not very suitable for the application in children liver. The ROI is too big for children liver to completely avoid blood vessels or biliary ducts; and for children who could not control their breath very well, the results may be affected by breath movement.

Virtual touch imaging quantification (VTIQ) is the latest elastic technology. Using the VTIQ method, the examiner can use a moveable Q box quantification tool to select a defined ROI. Different from VTQ which only provides the velocity value of a single point, the VTIQ technology instantly acquires comprehensive information in the ROI, which is displayed as a two-dimensional color-coded image of SWV^[15,16]. The high-frequency linear probe (9L4) with VTIQ technology was used in evaluating the stiffness of breast and thyroid lesions. And this probe may also be suitable for the abdominal organs in children, with a better identification of vessels and biliary structures that should not be included in the ROI^[10].

Recently, a few studies have investigated the clinical application of this method in differentiating biliary atresia from other causes of neonatal/infantile liver diseases^[17], and assessing the degree of liver parenchymal fibrosis in children^[3,11]. Given the differences between infants and teenagers and the diversity of children, it seems

essential to establish a normal range of liver stiffness measurement in children to differentiate the normal liver from abnormalities^[4,6] so that the method could be employed correctly in evaluation of liver diseases of children.

Therefore, the objective of the present study was to determine the standard values of SWV in healthy children using VTIQ technology, to assess the potential effects of factors such as gender, age, body mass index (BMI), and the depth and position of the measurement, and to analyze factors affecting the quality of the elastogram.

MATERIALS AND METHODS

Study population

The study was approved by the institutional ethics committee of Shanghai Children's Medical Center; parental informed consent was obtained in all cases. This study was carried out between July and December 2018 and included 220 healthy children between 1 mo and 15 year of age, all without known hepatic or systematic disease, altered liver tests, or chromosomal abnormality. Children who could not cooperate, with a bad quality of elastogram, or with abnormal findings upon abdominal ultrasound examination were excluded. BMI had to be between the 3rd and 97th percentiles. BMI was calculated according to the World Health Organization (WHO) Anthropometric Program (WHO Anthro, version 3.2.2, Jan 2011) for children younger than 5 years or according to WHO BMI-for-age percentile reference table for children older than 5 years.

Elastographic measurements

In all subjects, shear wave elastography (SWE) was performed by a senior pediatric radiologist with more than 1 year of experience in this technology using an Acuson Oxana2 system with a 9L4 (4.0-9.0 MHz) liner transducer (Siemens Medical Solutions, Mountain View, CA, United States). All children were placed in a spine position with free breathing. SWE was performed using the VTIQ method to measure SWV in several ROIs within the liver parenchyma while avoiding the identifiable biliary and vascular structures. SWE was conducted in both lobes (segment IV and V, respectively); an intercostal approach was employed to make the measurements for the right liver lobe, while in the left lobe, measurements were performed by placing the transducer under the xiphoid of the sternum. Three valid measurements of SWV were performed and the average value was calculated at each depth of 1.5, 2.0, 2.5 cm, and 3.0 cm beneath the skin surface. The results are expressed in meter per second (m/s). The quality of the elastogram was evaluated upon the quality mode of VTIQ; the elastogram box with a uniform green color fill-in was referred to as "superior" (Figure 1), while the elastogram box with > 80% green color fill-in was referred to as "good" quality (Figure 2).

Statistical analysis

Continuous variables are presented as the mean \pm SD, range, or 95% confidence interval (CI), while categorical data are summarized as counts and percentages (%). Differences between two groups were determined by the Student's *t*-test or Mann-Whitney *U* test when data were not normally distributed. For comparison among more than two groups, Kruskal-Wallis test or analysis of variance (ANOVA) was used as appropriate; when the differences were significant, the post hoc test was performed using the Bonferroni's adjustment or Bonferroni method accordingly. The relationship between SWV and continuous variables was investigated using Pearson liner correlation analysis. The chi-square test or Fisher's exact test was used for comparing the categorical data. All statistical analyses were performed using SPSS software for Mac, Version 23.0. A two-tailed *P*-value less than 0.05 was considered to indicate a significant difference.

RESULTS

Eighteen children were excluded, fifteen because of bad quality of elastogram or lack of cooperation, and three because of hepatic calcifications observed on gray-scale ultrasound. After exclusion, a collective of 202 subjects (116 girls and 86 boys) were enrolled in this study. The study group was divided into four age groups: Group 1 (≤ 2 years old, $n = 28$), group 2 (> 2 but ≤ 6 years old, $n = 68$), group 3 (> 6 but ≤ 10 years old, $n = 58$), and group 4 (> 10 years old, $n = 48$). The participants were also divided into four BMI groups: Group 1 ($\text{BMI} \leq 15$, $n = 23$), group 2 ($15 < \text{BMI} \leq 16$, $n = 65$), group 3 ($16 < \text{BMI} \leq 17$, $n = 54$), and group 4 ($\text{BMI} > 17$, $n = 60$). Table 1 shows the gender, age,

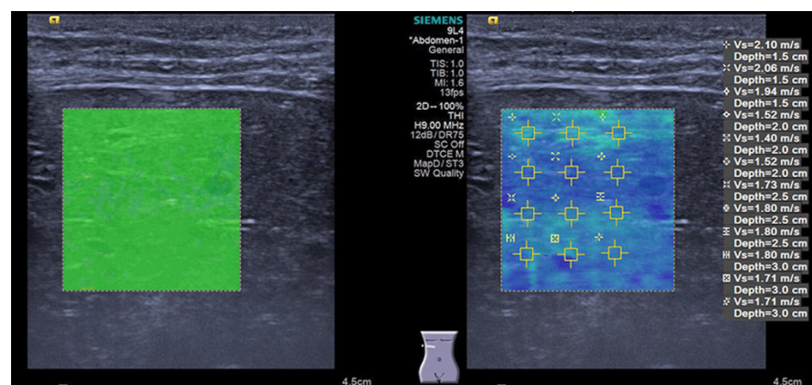


Figure 1 Virtual touch imaging quantification measurements in the right liver lobe of a 3-year-old boy at depths of 1.5 cm, 2.0 cm, 2.5 cm, 3.0 cm from the skin surface, respectively, with a superior quality of the elastic image.

and the BMI information of the subjects. No significant differences were identified in age or BMI between the gender groups.

SWV and gender

There was no significant difference in SWV values measured in the same lobe and at the same depth between the gender groups (Table 2).

SWV and age

Significant correlations were identified between age and SWV values in the left lobe at all measurement depths, and in the right lobe at depths of 1.5 cm, 2.0 cm, and 3.0 cm ($P < 0.05$). The correlation between age and SWV value in the right lobe at a depth of 2.5 cm was marginally significant ($P = 0.09$). After grouping the age into four classes, only in cases of measurement at a depth of 1.5 cm and 2.0 cm in the left lobe were there significant differences among the age groups ($P < 0.05$, Table 3). There was significant difference in SWV values at a depth of 1.5 cm between groups 1 and 3. And SWV values at a depth of 2.0 cm in groups 3 and 4 were significantly higher than those in group 1 (Table 3).

SWV, liver lobe, and measurement depth

SWV values were significantly negatively correlated with the measurement depth in each lobe ($P < 0.001$). The deeper the depth, the lower the SWV values. And there were significant differences in the SWV value between any two of the measurement depths ($P < 0.05$, Figure 3). The SWV values at a depth of 3.0 cm had the lowest variance ($P < 0.05$). There was no significant difference in SWV values between the left and right lobes at the same depth (Figure 3), and there was no significant difference in SWV value variance between the left and right lobes.

SWV and BMI

No statistically significant correlations were found between BMI and the SWV in either lobe at each depth in our study group. After categorizing BMI into four groups, no significant differences were detected among the four groups at each measurement depth in either lobe (Table 4).

Factors influencing the quality of elastic images

Lastly, we investigated the potential factors which might influence the quality of elastic images (Table 5). The gender did not have any effect on the image quality (Table 5). A significant association was found between age and the quality of the elastic image; subjects with a relatively younger age tended to have a superior image quality in each liver lobe ($P < 0.001$). BMI also had an impact on the image quality, and it was significantly associated with the elastic image quality of the left lobe; subjects with a lower BMI tended to have a superior image quality ($P < 0.001$). However, the significant association could not be identified between BMI and the image quality of the right lobe ($P = 0.075$).

DISCUSSION

In recent years, a variety of non-invasive ultrasound-based methods have been

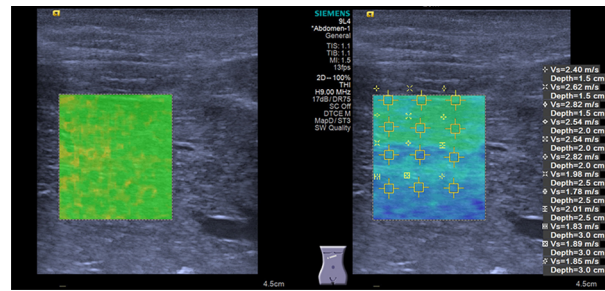


Figure 2 Virtual touch imaging quantification measurements in the left liver lobe of a 10-year-old girl at depths of 1.5 cm, 2.0 cm, 2.5 cm, and 3.0 cm from skin surface, respectively, with a good quality of the elastic image.

developed with the hope of eliminating the necessity for traditional liver biopsy in as many individuals as possible^[18]. SWE is one of the latest methods, and offers a non-invasive, non-ionizing, low-cost, and well-tolerated approach to quantify liver stiffness and presumably liver fibrosis. Up to date, several studies^[6,19,20] have assessed the usefulness of SWE techniques of ARFI for detecting liver fibrosis in children. Hence, a normal range of liver stiffness in children is expected to be established, to discriminate between normal and abnormal livers. To the best of our knowledge, this is the first study to define the normal SWV values in healthy children using the newest VTIQ mode of ARFI technology.

A few published articles about liver stiffness using VTQ technique had some contradictory results. The study of Eiler *et al*^[5] showed that there was a significant effect of gender on the SWV value, and girls had lower SWV values. The explanation might be that estrogen in females might have an anti-fibrosis effect and there could be an intrinsic difference between genders in elasticity. Whereas, other researchers^[4,6] had different results, which showed no significant differences in SWV values of the liver in children with different sex. Furthermore, the studies of Rifai *et al*^[21] and Fontanilla *et al*^[4] demonstrated that aging process might contribute to the increase of liver elasticity. Other researchers^[5,6], however, reported that age showed no significant effect on SWV value. Similar contradictory results were shown about the effects of the location of ARFI measurements and the impact of BMI on SWV^[22-30]. One important reason for all the discrepancies could be that VTQ technique with fixed and big ROI may not be a very repetitive method for children's liver.

In our study, we used VTIQ to measure the stiffness of normal children liver and the results showed that no significant difference in SWV value was observed between boys and girls at each measurement depth in either lobe. Our results on the effects of age on SWV revealed a tendency toward higher SWV values in the relatively elder children. This did not reach statistical significance when the measurements were made in the right lobe, yet some significant differences were noted between measurements in different age groups in the left lobe (at depths of 1.5 and 2.0 cm, with higher SWV value in group 4). Also, our results indicated a significant correlation between SWV value and measurement depth. There was a significant difference in SWV among the measurement depths, with lower SWV values and lower variance at a deeper measurement depth. And these differences were observed in both hepatic lobes. Therefore, we recommend that the VTIQ measurement be conducted at the deep region of the liver parenchyma where the elasticity box with a homogeneous green color filling can be chosen.

With respect to the location of TVIQ measurements, no significant inter-lobe difference in SWV values at each measurement depth was found in our study. When we performed the elastography examination, the elastogram box in each lobe was only confined within the segments IV and V to minimize the measurement error. Despite that there is no significant inter-lobe difference, the elastography examination is recommended to perform in the right lobe, because the biopsy procedure for evaluating the liver fibrosis was performed on the right lobe, so was the elastic measurement. Moreover, the right lobe is larger, making it easier to place ROI in various regions and avoid vessels.

Data from the present study failed to demonstrate either a significant correlation between SWV and BMI, or the significant differences in SWV across the individual BMI classes. This result indicated that SWV values were reliable for people regardless of their BWI.

Lastly, we analyzed the factors which might influence the quality of the elastogram. Interestingly, the superior image quality in each lobe could frequently be found in

Table 1 Description of the subjects

	Female (%)	Male (%)	All	P value
Age	116 (42.6)	86 (57.4)	202	
Mean \pm SD (yr)	7.2 \pm 3.4	6.3 \pm 4.0	6.8 \pm 3.7	0.081
Range	0.1-15	0.1-15	0.1-15	
BMI				
Mean \pm SD (kg/m ²)	16.7 \pm 2.6	16.4 \pm 1.6	16.6 \pm 2.1	0.335
Range	13.8-25.5	13.2-24.2	13.2-25.5	

SD: Standard deviation; BMI: Body mass index.

relatively younger subjects, and BMI of the subjects might have a greater influence on the image quality in the left lobe. Therefore, as mentioned above, the right lobe of the liver may be a better choice for elastography measurement.

The present study has several limitations. First, since all repeated measurements were made by a single examiner, the inter-observer reproducibility could not be evaluated. Second, the choice of healthy children was based solely on normal laboratory liver tests, medical history, and normal appearance of the abdominal ultrasound examination. No liver biopsy was performed to exclude the liver diseases; however, its application in healthy population is not justified. Third, the sample volume in our study was not large enough. The results of this study need to be testified by further studies with more subjects.

In conclusion, our study suggested that VTIQ is a feasible technique to measure liver stiffness in children, and reported the normal liver stiffness measured by the VTIQ method. The lower SWV values are expected in younger children, and at a deeper measurement depth. Liver elasticity is not affected by gender, BMI, and the location of measurement. When available, the VTIQ measurement in the right lobe at deep regions is preferably suggested.

Table 2 Shear wave velocity measured by virtual touch imaging quantification in patients of different gender

Liver lobe/depth	Male		Female		P value
	Mean \pm SD	95%CI	Mean \pm SD	95%CI	
Left/1.5 cm	2.56 \pm 0.41	2.46-2.66	2.58 \pm 0.47	2.47-2.68	0.788
Left/2.0 cm	2.15 \pm 0.44	2.05-2.24	2.06 \pm 0.37	2.00-2.13	0.144
Left/2.5 cm	1.77 \pm 0.27	1.71-1.83	1.77 \pm 0.30	1.71-1.82	0.901
Left/3.0 cm	1.64 \pm 0.19	1.60-1.69	1.66 \pm 0.25	1.61-1.72	0.565
Right/1.5 cm	2.51 \pm 0.33	2.42-2.60	2.55 \pm 0.44	2.45-2.65	0.591
Right/2.0 cm	2.10 \pm 0.33	2.03-2.18	2.10 \pm 0.37	2.04-2.17	0.982
Right/2.5 cm	1.75 \pm 0.28	1.69-1.81	1.74 \pm 0.29	1.69-1.79	0.752
Right/3.0 cm	1.66 \pm 0.22	1.60-1.72	1.61 \pm 0.25	1.55-1.67	0.284

VTIQ: Virtual touch imaging quantification; SD: Standard deviation; CI: Confidence interval.

Table 3 Effect of age on shear wave velocity measured in different hepatic lobes and at different depths

Liver lobe/depth	Age group (yr)				P value	Comparison	P value
	Group 1 (n = 28)	Group 2 (n = 68)	Group 3 (n = 58)	Group 4 (n = 48)			
Left/1.5 cm					0.038		
Mean \pm SD	2.41 \pm 0.40	2.53 \pm 0.40	2.70 \pm 0.46	2.63 \pm 0.53		G1-G3	0.038
95%CI	2.25-2.56	2.43-2.63	2.56-2.85	2.34-2.92			
Left/2.0 cm					0.002		
Mean \pm SD	1.92 \pm 0.25	2.07 \pm 0.39	2.08 \pm 0.29	2.27 \pm 0.55		G1-G4	0.002
95%CI	1.82-2.02	1.97-2.16	2.01-2.16	2.11-2.43		G2-G4	0.042
Left/2.5 cm					0.116		
Mean \pm SD	1.69 \pm 0.23	1.75 \pm 0.28	1.76 \pm 0.26	1.84 \pm 0.33			
95%CI	1.60-1.78	1.69-1.82	1.69-1.83	1.75-1.94			
Left/3.0 cm					0.091		
Mean \pm SD	1.56 \pm 0.15	1.65 \pm 0.21	1.68 \pm 0.25	1.69 \pm 0.24			
95%CI	1.49-1.62	1.58-1.72	1.60-1.75	1.62-1.77			
Right/1.5 cm					0.160		
Mean \pm SD	2.37 \pm 0.29	2.53 \pm 0.41	2.61 \pm 0.44	2.57 \pm 0.38			
95%CI	2.25-2.50	2.41-2.65	2.46-2.75	2.41-2.72			
Right/2.0 cm					0.131		
Mean \pm SD	1.98 \pm 0.22	2.09 \pm 0.36	2.12 \pm 0.30	2.18 \pm 0.43			
95%CI	1.90-2.07	2.00-2.18	2.04-2.20	2.05-2.30			
Right/2.5 cm					0.419		
Mean \pm SD	1.69 \pm 0.23	1.75 \pm 0.29	1.73 \pm 0.23	1.79 \pm 0.35			
95%CI	1.60-1.77	1.68-1.82	1.67-1.79	1.69-1.90			
Right/3.0 cm					0.061		
Mean \pm SD	1.53 \pm 0.24	1.65 \pm 0.32	1.59 \pm 0.18	1.70 \pm 0.22			
95%CI	1.42-1.65	1.52-1.78	1.53-1.66	1.63-1.76			

G1-G4: Groups 1-4. Significant differences are highlighted in boldface.

Table 4 Effect of body mass index on shear wave velocity measured in different hepatic lobes and at different depths

Liver lobe/depth	BMI group (kg/m ²)				P value
	<15 (n = 23)	15-16 (n = 65)	16-17 (n = 54)	>17 (n = 60)	
Left/1.5 cm					0.599
Mean ± SD	2.44 ± 0.38	2.59 ± 0.42	2.59 ± 0.50	2.58 ± 0.43	
95%CI	2.27-2.62	2.48-2.70	2.44-2.75	2.40-2.77	
Left/2.0 cm					0.235
Mean ± SD	1.94 ± 0.29	2.01 ± 0.40	1.99 ± 0.27	2.06 ± 0.50	
95%CI	1.82-2.06	1.92-2.11	1.91-2.06	1.93-2.19	
Left/2.5 cm					0.363
Mean ± SD	1.72 ± 0.25	1.77 ± 0.29	1.73 ± 0.26	1.81 ± 0.31	
95%CI	1.62-1.82	1.70-1.84	1.66-1.80	1.73-1.90	
Left/3.0 cm					0.427
Mean ± SD	1.58 ± 0.19	1.69 ± 0.22	1.67 ± 0.26	1.64 ± 0.22	
95%CI	1.48-1.68	1.62-1.75	1.58-1.75	1.58-1.70	
Right/1.5 cm					0.218
Mean ± SD	2.48 ± 0.36	2.60 ± 0.41	2.43 ± 0.40	2.57 ± 0.39	
95%CI	2.29-2.26	2.48-2.72	2.30-2.56	2.42-2.71	
Right/2.0 cm					0.312
Mean ± SD	2.04 ± 0.26	2.11 ± 0.39	2.03 ± 0.27	2.18 ± 0.39	
95%CI	1.93-2.16	2.02-2.21	1.96-2.10	2.08-2.28	
Right/2.5 cm					0.064
Mean ± SD	1.65 ± 0.22	1.79 ± 0.29	1.69 ± 0.21	1.79 ± 0.34	
95%CI	1.56-1.75	1.71-1.86	1.63-1.75	1.70-1.87	
Right/3.0 cm					0.347
Mean ± SD	1.55 ± 0.26	1.65 ± 0.27	1.60 ± 0.19	1.65 ± 0.24	
95%CI	1.38-1.71	1.58-1.77	1.52-1.67	1.58-1.72	

BMI: Body mass index.

Table 5 Factors influencing the quality of the elastic image, n (%)

Factor	Image quality		P value	Image quality		P value
	Superior	Good		Superior	Good	
Gender			0.875			0.423
Male	61 (70.9)	25 (29.1)		70 (81.4)	16 (18.6)	
Female	84 (72.4)	32 (27.6)		89 (76.7)	27 (23.3)	
Age group (yr)			<0.001			<0.001
<2	24 (85.7)	4 (14.3)		25 (89.3)	3 (10.7)	
3-6	58 (85.3)	10 (14.7)		57 (83.8)	11 (16.2)	
7-10	41 (70.7)	17 (29.3)		44 (75.9)	14 (24.1)	
>10	22 (45.8)	26 (54.2)		27 (56.3)	21 (43.8)	
BMI group (kg/m ²)			<0.001			0.075
<15	21 (91.3)	2 (8.7)		17 (73.9)	6 (26.1)	
15-16	60 (92.3)	5 (7.7)		56 (86.2)	9 (13.8)	
16-17	34 (63.0)	20 (37.0)		45 (83.3)	9 (16.7)	
>17	30 (50.0)	30 (50.0)		41 (68.3)	19 (31.7)	

BMI: Body mass index; LL: Left lobe; RL: Right lobe. Significant differences are highlighted in boldface.

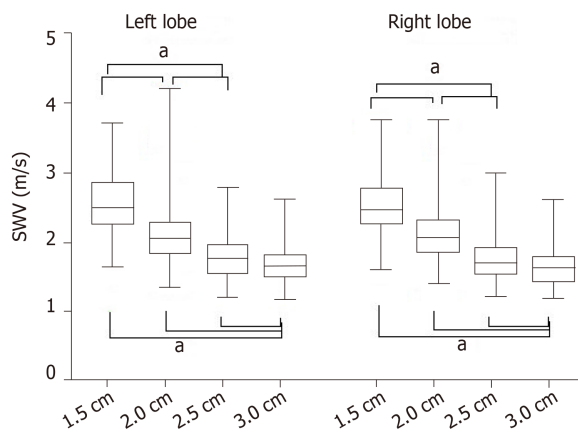


Figure 3 Box-and-whisker plot of the shear wave velocity value of the virtual touch imaging quantification measurement in each liver lobe at different measurement depths. Significant differences were found between any two measurement depths. Statistically significant by the Kruskal-Wallis test with Bonferroni's adjustment. ^a $P < 0.05$.

ARTICLE HIGHLIGHTS

Research background

Non-invasive assessment of liver stiffness in children with chronic liver disease plays a critical role in clinical evaluation of liver fibrosis. Virtual touch imaging quantification (VTIQ) based on acoustic radiation force impulse imaging has been developed as a latest and noninvasive method for assessing liver stiffness in children.

Research motivation

Given the diversity of children in all aspects, a normal range of liver stiffness measurements must be established in children to differentiate the normal liver from abnormalities.

Research objectives

To determine the standard shear wave velocity (SWV) values in healthy children, and to identify possible factors that might influence the VTIQ measurement.

Research methods

We conducted a prospective study. After exclusion, a total of 202 children between 1 mo and 15 years old were included in this study. None of them had any liver or systematic diseases. All children had a normal ultrasound scan and normal body mass index (BMI) range. The subjects were divided into four age and BMI groups. The effects of gender, age, liver lobe, measurement depth, and BMI on liver elasticity were investigated.

Research results

A significant correlation was found between age and SWV values. At measurement depths of 1.5 cm and 2.0 cm in the left lobe, there were significant differences among the four age groups. Negative correlations were found between the measurement depth and SWV values. Gender, liver lobe, and BMI showed no significant effect on the SWV values. Age and BMI may influence the quality of the elastogram.

Research conclusions

As a recently developed noninvasive technique, VTIQ is feasible for physicians to measure liver stiffness in children. Lower SWV values are expected in younger children, and at a deeper measurement depth. Liver elasticity is not affected by gender, BMI, and the location of measurement. Therefore, when available, the VTIQ measurement at deep regions in the right lobe of the liver is preferably suggested.

Research perspectives

The results of this study provide a range of normal reference values for measuring the liver elasticity in normal children. In the future, more subjects should be incorporated to further confirm the results of this study, and the consistency between observers needs to be evaluated so that VTIQ technology can be better applied to clinical practice. More importantly, with the reliable normal reference value, this noninvasive method can widely be used to detect and evaluate liver fibrosis in children.

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