Point shear wave elastography (pSWE) using Acoustic Radiation Force Impulse (ARFI) imaging: a feasibility study and norm values for renal parenchymal stiffness in healthy children and adolescents

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Abstract

Aims: To evaluate the applicability of point shear wave elastography (pSWE) for measuring renal parenchymal stiffness in healthy children and adolescents and to establish norm values for shear wave speed (SWS) using two ARFI methods and ultrasound probes. **Material and methods:** We prospectively investigated 264 children (43.9% males). pSWE (Virtual Touch™ Quantification and Virtual Touch™ Imaging Quantification (VTQ and VTIQ; Siemens, Germany)) was performed in the renal cortex of 528 healthy kidneys using a 1-6 MHz convex and a 4-9 MHz linear ultrasound probe in ventrolateral and dorsal examinations. Feasibility and reproducibility of pSWE measurements were evaluated. SWS values were analysed with regard to age, body dimensions, kidney volume and measuring depth. **Results:** pSWE measurements were successful in >95% of subjects using the low and in <60% using the high-frequency probe. Mean SWS values (m/s) differed by method and probe: 2.10±0.43 (VTQ1-6MHz, convex, ventrolateral), 2.30±0.37 (VTQ1-6MHz, convex, dorsal), 1.58±0.44 (VTQ4-9MHz, linear, dorsal) and 1.96±0.27 (VTIQ4-9MHz, linear, dorsal). SWS was positively correlated with age, weight and body height, but independent of sex, BMI, or kidney volume and depth. **Conclusions:** pSWE (VTQ) is a feasible method to evaluate renal parenchymal stiffness in children of all ages. SWS values are age and weight dependent and differ significantly between high- and low-frequency probes. High-frequency probes and VTIQ should only be used in children <10 years.

Keywords: acoustic radiation force impulse; children; shear wave velocity; normal values; kidney

Introduction

The prevalence of chronic kidney disease (CKD) in adults and children is increasing worldwide [1]. Renal hypoplasia, dysplasia and vesicoureteral reflux are the most frequent causes of CKD in children [2].

Ultrasound can be seen as an ideal diagnostic tool for diagnosis of renal pathologies in pediatric patients. It is non-invasive, patients are not exposed to radiation, no patient preconditioning is needed and a fast and easy repetition rate is possible [3]. Meanwhile, conventional ultrasound has a good sensitivity and specificity for the diagnosis of inborn kidney diseases, such as renal cystic diseases [3]. However, the sensitivity and specificity for the detection of acquired renal parenchymal damage, as renal parenchymal fibrosis or sclerosis, is low. Invasive diagnostic methods, such as renal biopsy or renal scintigraphy [4,5], remain the gold standard.

A new promising method called point shear wave elastography (pSWE), integrated into the conventional ultrasound system, enables the evaluation of tissue elas-

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ticity while ultrasound investigation. By placing the region of interest (ROI) in the real-time B-mode, the measured region can be chosen precisely. A short-duration acoustic push pulse leads to localized displacements and shear waves are generated. The velocity of transverse shear waves is directly correlated with the tissue elasticity: the higher the shear wave speed (SWS), the higher tissue stiffness [6-8].

Several studies have evaluated pSWE for the detection of liver fibrosis and cirrhosis. A positive correlation of SWS and liver tissue stiffness was shown [9-11]. pSWE may also be useful for evaluating renal histological fibrosis in CKD. Guo et al reported a significant correlation of SWS and the serum creatinine, estimated glomerular filtration rate (eGFR), and urea nitrogen in CKD patients [12]. Furthermore, histological studies revealed a correlation between SWS and the pathologic degree of renal fibrosis [13,14]. pSWE might also be an effective tool in the detection of renal transplant fibrosis. Renal transplant failure is often caused by chronic allograft nephropathy, which can lead to interstitial fibrosis [15] and Stock et al. showed that SWS was significantly correlated with renal allograft fibrosis [16].

Recently, a limited number of studies applied pSWE in the evaluation of renal parenchymal stiffness in children with vesicoureteral reflux (VUR) [17-19], ureteropelvic junction obstruction [20] and in healthy children [21].

The aim of our study was to constitute reference values for renal SWS in healthy children of all ages. SWS values were compared with respect to the use of different ultrasound probes (high and low frequency), pSWE measuring methods (Virtual Touch™ Quantification (VTQ) vs. Virtual Touch™ Imaging Quantification (VTIQ)) and measuring positions (ventrolateral vs. dorsal). The study evaluated the feasibility of SWS measurements and tried to identify possible influencing factors on measured SWS values and measurement success rate.

Materials and methods

Patients

This prospective single-center study was conducted at the Center for Pediatrics and Adolescent Medicine in Heidelberg, Germany, from December 2015 to September 2016; 116 males (43.9%) and 148 females (56.1%) were recruited with a median age of 9 years (range: 0.0 – 20.0 years). Subjects' clinical characteristics are summarized in Table I. The study was approved by the Ethical Review Board of the University of Heidelberg and was conducted according to GCP and the Declaration of Helsinki in its present version. All subjects and their parents gave informed consent prior to inclusion in the study.

Table I. Demographic data

Variable	Mean ± SD
N	264
Male (%)	43.9
Age (years)	8.8 ± 5.4
Weight (kg)	36.3 ± 22.1
Height (cm)	133.2 ± 33.8
BMI (kg/m ²)	18.2 ± 4.03
Kidney volume (ml)	71.4 ± 36.7
Age-adjusted kidney volume (Percentile)	38.6 ± 22.5

SD – standard deviation

We prospectively investigated 528 healthy kidneys of 264 children. All subjects had no evidence of renal disease in clinical records and blood or urine analysis (normal renal function test, i.e. serum creatinine, serum urea nitrogen, urinary protein excretion) and no pathologic findings by conventional ultrasound. Subjects with pathological findings (e.g. cysts, masses, hydronephrosis, or kidney stones) were excluded.

Conventional ultrasound evaluation

A conventional ultrasound was performed in all subjects using a Siemens Acuson S3000 HELX™ Evolution ultrasound system (Siemens AG, Erlangen, Germany) with a 1-6 MHz convex probe (6C1). Kidneys were investigated assessing tissue echogenicity and absolute kidney volume as well as kidney volume percentile according to Dinkel et al [22].

Point Shear wave elastography (pSWE) of renal cortex

pSWE measurements were performed during the conventional ultrasound session. VTQ measurements were operated as follows: in each subject, five SWS measurements were performed on each kidney with the subject lying in the supine position placing the 1-6 MHz convex probe (6C1) ventrolateral. Another five SWS measurements were done placing the 6C1 probe dorsal in prone position. Using the 4-9 MHz linear probe (9L4), five SWS measurements were performed on each kidney with a dorsal approach with the subject lying in prone position. Finally, 10 VTIQ measurements per kidney were completed using the 9L4 probe with a dorsal approach (fig 1, fig 2).

VTQ measurements were done after placing the ROI (region of interest: 1.0 x 0.5 cm for the convex probe; 0.5 x 0.6 cm for the linear probe) in the renal cortex during the real-time conventional ultrasound, excluding the renal pelvis, capsule and vessels. For VTIQ, which combines qualitative and quantitative measurements, the ROI was additionally positioned in the outer renal cortex. After obtaining a unique quality map of shear waves, several measurements were operated by choosing the measuring sites precisely.

Fig 1. Shear wave speed measurements with a 9L4 linear probe. Point shear wave elastography (pSWE) in a healthy kidney using Acoustic Radiation Force Impulse Imaging (ARFI) (a) Virtual Touch Imaging Quantification (VTIQ) method and (b) Virtual Touch Quantification (VTQ) method.

If possible, measurements were made during breath holding with a minimal pressure of the transducer on the tissue. pSWE measurements were terminated if the child was unable to tolerate the measuring procedure. Invalid measurements were reported. Mean SWS values were calculated for each location and ultrasound probe and used for further statistical analysis.

To assess the inter-operator reproducibility, 21 subjects were investigated by two different operators within one day. Operators were blinded to the results.

Statistical analysis

The statistical analysis was performed using the statistical package SAS for Windows Version 9.4 (SAS Institute Inc., North Carolina). Demographic and kidney information was analysed descriptively. pSWE measurements were analysed descriptively using summary statistics separately for kidney side (left/right) and the four different examination methods. Between-group differences were analysed using paired t-test or if normality could not be assumed by Wilcoxon signed-rank test. Correlations of the pSWE measurements with relevant factors (age, sex, weight, height, BMI and kidney volume, percentile and depth) were analysed using Spearman's rank correlation coefficient. Standard deviation scores for height and BMI were calculated [23,24]. Normal BMI was defined as a standard deviation of BMI related to age lower than 1 SDS. Overweight/obesity was defined as BMI-SDS >1.

Feasibility of pSWE measurement was analysed by calculating frequencies and percentages for successful measurements. The influence of the age, body weight,

Fig 2. Point shear wave (pSWE) measurement in (a) ventrolateral and (b) dorsal position with a 6C1 probe using the VTQ method.

body height, BMI and the depth of measurement on the success rate was analyzed using logistic regression model.

Agreement between both raters was assessed by Bland-Altman plots and estimation of the 95% limits of agreement. Additionally, the interclass coefficient of correlation for VTQ-6C1 was calculated.

Age-specific reference values were established using the LMS method of Cole and Green [25]. The LMS method describes the distribution of a measurement Y by its median (M), the coefficient of variation (S), and a measure of skewness (L) required to transform the data to normality. Estimates for these parameters are obtained by applying a maximum-likelihood curve-fitting algorithm to the original data plotted over the independent variable of interest, in this case, age. Percentile curves were constructed.

Results

Point shear wave elastography (pSWE)

The mean SWS values for the different pSWE methods and probes are given in Table II and figure 3, the corresponding LMS percentile curves in figure 4.

No significant difference of median SWS was observed between left and right kidney for VTQ-6C1-ventrolateral, VTQ-9L4-dorsal, and VTIQ-9L4-dorsal, but for VTQ-6C1-dorsal. Mean SWS value in the left kidney was slightly, but significantly higher than in the right kidney (2.36 ± 0.41 m/s vs. 2.24 ± 0.44 m/s ($p < 0.001$)). Therefore, for the following analyses, mean values of

Table II. Mean shear wave speed [m/s] by pSWE for left and right kidneys.

	Overall	Left Kidney	Right Kidney	p*
VTQ 6C1 ventrolateral	2.10 ± 0.43	2.07 ± 0.54	2.14 ± 0.48	0.08
VTQ 6C1 dorsal	2.30 ± 0.37	2.36 ± 0.41	2.24 ± 0.44	<0.001
VTQ 9L4 dorsal	1.58 ± 0.44	1.56 ± 0.48	1.60 ± 0.47	0.13
VTIQ 9L4 dorsal	1.96 ± 0.27	1.94 ± 0.31	1.97 ± 0.28	0.66

The results are expressed in mean $\pm$ standard deviation; *significance level of difference between left and right kidney; paired t-test

Fig 3. Shear wave speed values by ARFI method (VTQ or VTIQ), probe, dorsal vs. ventrolateral measurement, and by right and left kidney. Boxplots represent 25th, 50th, and 75th percentiles; whiskers 5th and 95th percentiles; open circles outliers.

the measurements in the left and right kidney were used except for the VTQ-6C1-dorsal measurements in which SWS values for left and right kidneys were considered separate.

Potential influencing factors

Potential correlations of pSWE SWS values with sex, age, body weight, body height, BMI, depth of kidney, and absolute kidney volume or volume percentile were analyzed. No significant difference of SWS was found between males and females. Age and SWS correlated significantly for SWS measured by VTQ-6C1-ventrolateral ($r=0.28$, $p<0.001$) and VTIQ-9L4-dorsal ($r=0.32$, $p<0.001$), but not by VTQ-6C1-dorsal and VTQ-9L4-dorsal. In addition, quantile regression was performed to examine the dependency of the 2.5% and 97.5% percentiles on age. As shown in figure 4, the range of SWS increases with age. For all methods except VTQ-9L4-dorsal, the upper bound increases observably with age. Body weight was correlated significantly with SWS measured by VTQ-6C1-ventrolateral ($r=0.26$, $p<0.001$), VTQ-6C1-dorsal of the right kidney ($r=0.22$, $p<0.001$) and VTIQ-9L4-dorsal ($r=0.29$, $p<0.001$), but not with VTQ-6C1-dorsal in the left kidney and VTQ-9L4-dorsal.

The correlation analysis showed a significant correlation between body height and SWS measured with VTQ-6C1-ventrolateral ($r=0.25$, $p<0.001$) and VTIQ-9L4-dorsal ($r=0.30$, $p<0.001$), but not with VTQ-6C1-dorsal and VTQ-9L4-dorsal. A significant correlation ($p<0.001$) between kidney volume and SWS was only found for measurements with VTQ-6C1-ventrolateral, but not with VTQ-6C1-dorsal, VTQ-9L4-dorsal and VTIQ-9L4-dorsal.

Fig 4. Percentile curves for shear wave speed by ARFI method and probe over age for a) VTQ-6C1-ventrolateral; b) VTQ-6C1-dorsal – right kidney; c) VTQ-6C1-dorsal – left kidney; d) VTQ-9L4-dorsal; e) VTIQ-9L4-dorsal. For each plot the 3rd to 97th percentiles are given.

No correlation was found between pSWE measurements and BMI, depth of measurement and percentile of kidney volume.

Feasibility of measurements

The highest measurement success rates were observed for VTQ-6C1-dorsal (96.6%) and VTQ-6C1-ventrolateral (96.2%). Success rates for VTQ-9L4-dorsal (51.1%) and VTIQ 9L4 dorsal (59.5%) were considerably lower.

The influence of age, weight, height and measuring depth on the success rate was analysed. The analysis revealed that BMI was the only significant variable for successful VTQ-6C1-dorsal measurements in the adjusted model. Correcting for age, body weight, body height and depth of measurement, each one unit increase in BMI was associated with a 52% lower probability of having a successful pSWE measurement (table III).

Additionally, success rates were calculated separately for subjects with normal BMI and overweight or obese subjects. Success rates of overweight subjects were lower for all ARFI measuring methods. The biggest difference of success rates between overweight and non-overweight subjects was found for the 9L4 probe (table IV).

Furthermore, success rates were calculated for four different age classes, defined empirically by the 25%, the 50% and the 75% distribution quartile of age (table V). Overall, pSWE measurements had the highest success rate in subjects aged 5-9 years followed by infants aged

Table III. Potential explanatory variables on success rate

	OR [95%-CI] unadjusted	OR [95%-CI] adjusted*
VTQ 6C1 ventrolateral		
age	0.99 [0.88; 1.11]	0.72 [0.46; 1.14]
weight	0.97 [0.95; 1.00]	1.11 [0.90; 1.37]
height	1.00 [0.98; 1.02]	1.05 [0.94; 1.17]
BMI	0.80 [0.70; 0.90]	0.57 [0.31; 1.07]
depth	0.35 [0.19; 0.64]	0.38 [0.11; 1.31]
VTQ 6C1 dorsal		
age	0.91 [0.80; 1.03]	0.87 [0.57; 1.33]
weight	0.95 [0.92; 0.98]	1.02 [0.85; 1.22]
height	0.98 [0.95; 1.00]	1.02 [0.92; 1.13]
BMI	0.71 [0.61; 0.83]	0.48 [0.27; 0.86]
depth	0.42 [0.22; 0.77]	5.04 [0.72; 35.22]
VTQ 9L4 dorsal		
age	0.77 [0.72; 0.82]	0.75 [0.58; 0.97]
weight	0.91 [0.90; 0.93]	0.88 [0.78; 1.00]
height	0.96 [0.94; 0.97]	1.08 [1.02; 1.15]
BMI	0.60 [0.53; 0.68]	1.04 [0.75; 1.44]
depth	0.15 [0.08; 0.25]	0.39 [0.12; 1.22]
VTIQ 9L4 dorsal		
age	0.71 [0.66; 0.77]	1.26 [0.65; 2.41]
weight	0.89 [0.87; 0.91]	1.73 [0.74; 4.08]
height	0.93 [0.92; 0.95]	0.68 [0.42; 1.09]
BMI	0.60 [0.53; 0.68]	0.24 [0.04; 1.59]
depth	0.10 [0.02; 0.49]	0.62 [0.07; 5.56]

*adjusted for age, weight, height, BMI and depth

Table IV. Success rate of pSWE measurement in subjects with normal BMI or in overweight or obese subjects.

	Number of subjects	Success rate (%)
VTQ 6C1 ventrolateral		
Normal	209	97.1%
Overweight / obese	55	92.7%
VTQ 6C1 dorsal		
Normal	209	99.5%
Overweight / obese	55	85.5%
VTQ 9L4 dorsal		
Normal	209	57.4%
Overweight / obese	55	27.3%
VTIQ 9L4 dorsal		
Normal	209	65.1%
Overweight / obese	55	38.2%

0-4 years, VTQ-6C1-ventrolateral showed a success rate >92% for all age groups, as well as VTQ-6C1-dorsal. The 9L4 probe had significantly lower success rates in adolescents compared to children: VTQ-9L4-dorsal measurements were successful in 76.4% of infants, 79.7% of school children, 40% of children aged 10-13 years but only in 6.7% of adolescents (14-20 years). VTIQ-9L4-dorsal revealed success rates with increasing age class of 87.3%, 90.5%, 45.3%, and 13.3%, respectively.

Table V. Success rate of pSWE measurements for different age classes

	Number of sub- jects	Success rate (%)	95%-CI
VTQ 6C1 ventrolateral			
age ≤ 4 years	55	92.7%	[82.4%-98.0%]
age 5 to 8 years	74	100%	
age 9 to 12 years	75	96.0%	[88.8%-99.2%]
age ≥ 13 years	60	95.0%	[86.1%-99.0%]
VTQ 6C1 dorsal			
age ≤ 4 years	55	96.4%	[87.5%-99.6%]
age 5 to 8 years	74	100%	
age 9 to 12 years	75	96.0%	[88.8%-99.2%]
age ≥ 13 years	60	93.3%	[83.8%-98.2%]
VTQ 9L4 dorsal			
age ≤ 4 years	55	76.4%	[63.0%-86.8%]
age 5 to 8 years	74	79.7%	[68.8%-88.2%]
age 9 to 12 years	75	40.0%	[28.9%-52.0%]
age ≥ 13 years	60	6.7%	[1.9%-16.2%]
VTIQ 9L4 dorsal			
age ≤ 4 years	55	87.3%	[75.5%-94.7%]
age 5 to 8 years	74	90.5%	[81.5%-96.1%]
age 9 to 12 years	75	45.3%	[33.8%-57.3%]
age ≥ 13 years	60	13.3%	[5.9%-24.6%]

Inter-observer reliability

The mean difference between the two observers differed only marginally for VTQ-6C1 and VTIQ-9L4. The smallest 95% limit of agreement was obtained for VTIQ-9L4 with a mean difference of -0.02 m/s (95% limit of agreement -0.18 to 0.13 m/s). The mean difference for VTQ-9L4 was -0.07 m/s (95% limit of agreement -0.44 to 0.31 m/s) and -0.01 m/s for VTQ-6C1 (95% limit of agreement -0.29 to 0.28 m/s).

The interclass correlation coefficient (ICC) for VTQ-6C1 measurements was 0.81.

Discussions

While pSWE has been increasingly recognized as a potential tool for measuring renal parenchymal stiffness in adult kidney patients, only a very few studies have evaluated the applicability and feasibility of pSWE in children with and without kidney disease [17-21]. In contrast to previous studies, where only VTQ had been used, this is the first study to provide also data on the use of VTIQ in healthy children.

Information regarding the impact of the quantity of measurements, measuring depth, measuring position and type of ultrasound probe on SWS values are lacking so far.

For this reason, we have provided reference data for pSWE elasticity of renal tissue in healthy children and adolescents comparing SWS values for high frequency (4-9 MHz) vs. low frequency (1-6 MHz) ultrasound probes, the VTQ vs. the VTIQ method and a dorsal vs. a ventrolateral approach.

Comparing mean SWS values of measurements in left and right kidneys, we found no significant difference except for the VTQ method, using the 1-6 MHz ultrasound probe with a dorsal approach. This is in concordance with previous studies in adult kidneys, which also did not show a difference between the left and right kidney [26,27]. However, data in pediatric studies are not consistent. While one study reported a difference of SWS values between right and left kidneys [21], others showed no significant difference [18,19].

The evaluation of SWS using the ARFI elastography VTQ method in 264 children resulted in mean values ranging from 1.58 m/s (9L4-dorsal) to 2.30 m/s (6C1-dorsal) and in mean VTIQ SWS values of 1.96 m/s (9L4-dorsal). Recently published mean SWS values of healthy kidneys in children by the use of VTQ ranged from 1.75 – 3.13 m/s [17-21]. Lee et al published a mean SWS value of 2.10 m/s for the right kidney and 2.33 m/s for the left kidney by investigating 202 children. They used a 4-9 MHz linear ultrasound probe for children younger than five years and a 1-4 MHz convex probe for children older than four years. Measurements were done with the child lying in supine position [21]. Goya et al reported a mean renal SWS value of 2.4 m/s based on 98 subjects with healthy kidneys. A 1-4.5 MHz convex probe had been used with the patient lying in lateral decubitus [19]. The other studies on pSWE of healthy kidneys in children are not fully comparable because of study populations of less than 20 healthy children or a limited age range [17-20]. For example, Sohn et al enrolled 19 healthy children under the age of 24 months and reported a mean SWS of 1.75 m/s [18].

With regard to mean SWS values in healthy adult kidneys our results in pediatric patients show lower mean values: Hu et al reported a SWS of 2.81 m/s with a 4C1 ultrasound probe [14], whereas Bota et al found SWS values in adult kidneys with a mean of 2.49 m/s for the right and 2.36 m/s for the left kidney using a 9L4 ultrasound probe [28].

Compared to mean SWS values by VTQ measurements from various studies on liver elasticity in healthy children, ranging from 1.12-1.19 m/s [29-31], renal tissue SWS values are higher.

This is the first study to report significant differences in SWS values of the renal parenchyma for different ultrasound probes in children and adolescents. So far, studies on the comparison of high and low-frequency probes have been restricted to the liver. Pfeifer et al compared a

1-6 MHz US probe and a 1-4 MHz ultrasound probe by measuring the liver stiffness of healthy patients, cirrhotic patients and in an elasticity phantom model. No difference was found in healthy patients; however, a slightly but significantly higher SWS mean value was measured with the 1-6 MHz probe in cirrhotic patients as well as in the phantom model. The authors assume that these differences might be caused by various numbers of elements and channels in the ultrasound probe and a different beam profile [29]. Fontanilla et al. compared a 4-9 MHz probe and a 1-4 MHz probe by measuring the liver tissue of healthy children. Results showed lower mean SWS values and less measurement variability by using the 4-9 MHz ultrasound probe [32]. A better feasibility of the 4-9 MHz transducer in smaller children was observed due to a smaller ROI [33]. Canas et al compared a 1-4 MHz probe and a 4-9 MHz probe by measuring the tissue elasticity of spleens in healthy children. No significant difference could be found [30]. In summary, so far no relevant difference between different ultrasound probes could be found in the liver and spleen, in contrast to measurements in kidneys. Our results indicate that renal SWS measured with high and low-frequency probes may differ significantly.

We also tried to determine possible influencing factors on renal tissue elasticity in pediatric patients. No significant difference was found between males and females. SWS values did not correlate with BMI, depth of kidney and percentile of kidney volume. A positive correlation between age and SWS value, as well as a positive correlation between weight and SWS value and a positive correlation between body height and SWS value, was found for VTQ-6C1-ventrolateral and VTIQ-9L4-dorsal. This is in concordance with two studies, which investigated a possible correlation between SWS values and age in children [20,21]. Only one study was published analyzing correlations between SWS values and sex, height, weight, BMI and kidney length. But no correlation between SWS values and sex, anthropometrical and renal characteristics has been described so far. However, it has to be mentioned, that these results are referring to a small study population of 15 patients with ureteropelvic junction obstruction (UPJO) and 16 healthy children. Furthermore, no correlation of SWS value and age could be found in this study [20]. In contrast, Lee et al reported a positive correlation between age and SWS value, measuring kidneys of 202 healthy children. It was shown, that SWS was age-related for all children, most notably for children younger than five years [21]. Concordant with our results, no correlation between SWS and depth of measurement was reported for adult studies in kidney, liver and spleen [31,34].

This is also the first study to compare measurement success rates of VTQ and VTIQ, using different ultra-

sound probes and operating with two measuring positions. VTQ is feasible for children of all ages. The use of a high-frequency probe should only be considered for children younger than 10 years. VTIQ, which is a component of the high-frequency probe only, is therefore not feasible for older children. In addition, pSWE shows lower success rates for overweight patients and is therefore not feasible for obese children.

Regarding the routine use of pSWE, it is important to evaluate the reproducibility of the SWS results. Because there are no published studies on the inter-observer agreement of renal pSWE measurements in children, we evaluated the inter-observer agreement of SWS values in 21 healthy subjects. The inter-observer agreement analysis showed high consistency; mean differences between the two operators were 0.01 to 0.07 m/s. To compare our findings with published data, we calculated the intra-class correlation coefficient (ICC) for VTQ-6C1. The ICC was 0.81. A study in adult kidneys with and without pathology revealed an inter-observer agreement assessed by ICC of 0.68 for healthy and 0.75 for pathologic kidneys [33]. Likewise, Hu et al reported a good inter-observer agreement for adult kidneys with chronic kidney disease of 0.63 [14]. A considerably lower inter-observer agreement was reported by Syversveen et al. Their inter-observer variability between kidney tissues of renal allografts of adults revealed an ICC of 0.31 [35]. A higher inter-observer agreement was obtained for pSWE measurements of liver tissue. Bota et al reported an ICC of 0.81 in both healthy and pathologic liver tissue [36] and Guzmán-Aroca et al revealed an ICC of 0.86 in healthy adult livers [37].

This study has several limitations. An optimal pSWE measurement is performed in children while breath holding and lying still. Particularly in young infants, this is not possible. Therefore, babies and younger children were breathing freely, and movement artifacts may have influenced the SWS values and the variability of SWS measurements. The second limitation is based on operator-dependent factors, such as applied transducer pressure. Syversveen et al demonstrated that the applied transducer force affects pSWE results in kidney transplants [38]. Since no technique exists for controlling the applied handheld transducer force, we tried to minimize the transducer pressure on the tissue. The third limitation is the variability of measuring sites in the kidney. pSWE measurements should be performed on multiple sites of the kidney to represent the whole organ. Thus the ROI was placed in the upper, mid- and lower pole, if possible. Especially in young children, it is difficult to place the ROI while excluding the medulla or the kidney capsule. Therefore, in some younger subjects, pSWE measurements were only possible in limited areas of the kidney.

Conclusions

VTQ, a quantitative method of pSWE, is a feasible method to measure renal parenchymal stiffness in children of all ages. The SWS percentile and LMS values provided may be used as norm values for renal parenchymal elasticity. The implementation of separate reference values for different ultrasound probes should be considered. Virtual Touch Imaging Quantification (VTIQ), which is only available for the linear probe, has a low success rate for children older than ten years and is recommended only in newborns and infants. High frequency probes with VTQ should only be used for children younger than ten years.

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