

# Diagnostic value of real-time shear wave elastography in children with chronic kidney disease

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## Research

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# Abstract

**Objective** To investigate the diagnostic value of real-time shear wave elastography (SWE) in children with chronic kidney disease (CKD).

**Methods** Children with CKD diagnosed by the ultrasound-guided biopsy between January 2018 and May 2019 were enrolled as the case group. Age- and sex- matched healthy children were selected as the control group. The Young's Modulus (YM) of the renal cortex was measured by SWE after the traditional ultrasound examination. Variance analysis was performed to compare the values of YM between the two groups. Receiver operating characteristic curve (ROC) analysis was used to compare the values of YM, and explore the cut-offs of the YM.

**Results** In the case group (n=60, 45% male, mean age of 9.2 years), the kidney YM modulus on the left side ( $16.8 \pm 4.8$  Kpa vs.  $8.3 \pm 2.1$  Kpa) and the right side ( $16.0 \pm 4.7$  Kpa vs.  $8.3 \pm 2.4$  Kpa) were both higher than the control group (all  $P$  values  $< 0.001$ ). With the progress of CKD, the YM value of the left and right kidneys gradually increased. ROC analysis showed that when the left and right kidney YM value was 11.7 KPa and 11.0 Kpa, the diagnostic sensitivity and specificity were the highest (left: respectively 93.3% and 95.0%; right: respectively 93.3 % and 91.7%).

**Conclusion** The increase of YM in CKD is related to the progression of renal dysfunction which may provide a new method for early diagnosis of CKD, dynamic monitoring of disease progression, and evaluation of curative effect and prognosis.

## Introduction

Chronic kidney disease (CKD) has become an important public health problem in China<sup>1</sup>. The primary cause of CKD in children is complex, but when it develops to a certain stage, its pathological changes tend to be the same, such as glomerulosclerosis, interstitial fibrosis, vascular atrophy and collapse, etc. The gross anatomy of these pathological changes mainly shows that the tissue becomes hard. Renal biopsy is the gold standard for the diagnosis of CKD in the traditional examination, however, it is difficult to be widely used as a clinical general survey or routine means due to its invasive and difficulty to be reused. However, traditional ultrasound technologies can only show positive results when the renal function is obviously damaged. Real-time shear wave elastography (SWE) is a kind of safe, effective and reproducible ultrasound technology that does not rely on shear wave generated by external force to measure tissue elasticity. At present, its diagnostic value has been widely confirmed in thyroid nodule<sup>2</sup>, liver<sup>3</sup>, breast<sup>4</sup> and other tissues. The purpose of this study was to explore the diagnostic value of SWE in children with CKD.

## Methods

### *Participants*

From January 2018 to May 2019, 60 children with chronic kidney disease (CKD) were selected as the case group. According to 1:1 sex- and age-specific matching, normal children (without liver and kidney disease and with normal blood, urine routine and renal function, and normal renal ultrasound) who were examined in the health care department at the same time were selected as the control group. Informed consent was obtained from their parents. Ethical approval was obtained from the Ethics Committees of Capital Institute of Pediatrics, Beijing, China

### *Testing*

The SC6-1 convex array probe with 1-6 MHz frequency and renal condition were used. When the patient is in a quiet state, take a prone position, lift both upper limbs up, hold breath after inhalation, the sound beam is perpendicular to the renal capsule, start SWE after the image is stable: the elastic imaging sampling frame is placed in the renal cortex of the lower pole of the kidney, and the image color is required to fill the sampling frame more than 90% during SWE imaging. In the imaging area, the circular area with a diameter of 15-20 mm of Q-box was selected for quantitative detection (Figure 1). The mean value of the elastic modulus of the kidney in the detection area was displayed and recorded. Each child was tested five times at the same site, and the mean value was used for analysis. The Young's Modulus (YM) of the lower polar cortex of both kidneys was measured respectively.

### *Statistical analysis*

SPSS21.0 was used for statistical analysis, mean  $\pm$  standard deviation was used for continuous data, and n (%) was used for classified data. T-test was used to compare the continuity data. The receiver operating characteristic curve (ROC) analysis was used to compare the YM value of children's kidney in the two groups. A two side value of  $P < 0.05$  was considered to be statistically significant.

## **Results**

As shown in Table 1, 60 children with CKD ( $9.2 \pm 2.7$  years) and 60 healthy children ( $9.1 \pm 2.7$  years) were included. YM value of the left and right kidneys of CKD children is significantly higher than that of normal children (left kidney: 16.8 vs. 8.3 Kpa; right kidney: 16.0 vs. 8.3 Kpa,  $P < 0.05$ ), and the thickness is also significantly higher than that of normal children (left kidney: 3.9 vs. 3.6 cm; right kidney: 3.8 vs. 3.6 cm,  $P < 0.05$ ).

Table 2 shows that there are differences in YM values among different pathological types of the case group. In the case group, 23 patients with IgA nephropathy were found (38.3%) with following Lee classification: grade  $\geq$  12 cases (20%), grade  $\geq$  7 cases (11.7%), and grade  $\geq$  4 cases (6.7%). With the increase of IgA nephropathy grade, YM values of both left and right kidneys showed an increasing trend ( $P < 0.001$ ); The 14 cases (23.3%) of Henoch Schonlein purpura nephritis were classified by International Study of Kidney Disease in Children (ISKDC), including 3  $\geq$ B cases (5%), 10  $\geq$ B cases (16.7%), and 1  $\geq$ B case (6.7%). With the increase of Henoch Schonlein purpura nephritis grading, YM values of left and right kidneys showed an increasing trend ( $P < 0.01$ ).

Table 3 shows that with the increase of CKD level, the YM values of the left kidney (from 14.6 Kpa to 40.7 kpa) and right kidney (increasing from 14.4 kpa to 39.5 Kpa) of the children show an increasing trend.

Figure 2 shows that YM values of left and right kidneys have high sensitivity and specificity in the diagnosis of CKD. Among them, when the YM value of the left kidney is 11.7 Kpa, the sensitivity and specificity are the best (93.3% and 95.0% respectively) and the positive predictive value and negative predictive values were 94.9% and 93.4% respectively. When the YM value of the right kidney is 11.0 Kpa, the sensitivity and specificity are the best (93.3% and 91.7% respectively) and the positive predictive value and negative predictive values were 91.8% and 93.2% respectively.

## Discussion

In this study, we found that the hardness of CKD children's kidney was higher than that of normal children, and the YM value of CKD children was related to the progression of renal dysfunction. When the YM values of left and right kidneys were 11.7 Kpa and 11.0 Kpa respectively, the diagnosis of CKD children had the best sensitivity and specificity.

Previous studies have shown that SWE technology can objectively measure the YM value of normal kidney<sup>5</sup> with a good repeatability<sup>6</sup>. Consistent with our findings, a study of 25 CKD patients aged 61(56, 70) years found that the YM values using SWE technology were significantly higher than those of normal healthy people, and with the aggravation of CKD, the YM values of renal cortex also showed an increasing trend<sup>7</sup>. Another study on 32 CKD patients also showed that YM value of renal parenchyma in CKD patients was higher than that in healthy people<sup>8</sup>.

A study on the effectiveness of using SWE technology to measure the shear wave velocity of cortex, medulla and renal sinus in the diagnosis of diffuse renal diseases found that the sensitivity range is 75.3-97.5%, and the specificity range is 65%-95%<sup>9</sup>. Hou et al. found that the sensitivity and specificity of YM in the diagnosis of CKD of 105 CKD patients aged 17-84 years were 89.9% and 91.4% respectively when YM got the optimal value<sup>10</sup>. In this study, we found the best cut-off value of left and right kidney FM value in diagnosing CKD in children using ROC curve with both sensitivity and specificity higher than 90%.

In this study, we first analyzed the diagnostic value of SWE for CKD in children and found the optimal cut-off value of YM on the left and right sides. The limitation of this study is that the sample size is relatively small, which limits the statistical efficiency of each subgroup and the extrapolation of the results.

## Conclusions

To sum up, the YM value of CKD children's kidney increased and it is related to the progress of renal dysfunction, which may provide a new method for early diagnosis of CKD, dynamic monitoring of disease progress, and evaluation of curative effect and prognosis.

# Declarations

## Ethics approval and consent to participate

Ethical approval was obtained from the Ethics Committees of Capital Institute of Pediatrics, Beijing, China. Informed consent was obtained from children's parents.

## Consent for publication

Not applicable.

## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Competing interests

The authors declared no conflicts of interest.

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## Author's contributors

QL and ZW contributed to the design of the study and writing of the manuscript. QL collated and analyzed the data.

## Acknowledgements

Not applicable.

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## Tables

Table 1 Characteristics of study participants

	Control group	Case group	<i>t</i>	<i>P</i> -value
Age, year	9.1±2.7	9.2±2.7	-1.619	0.111
Boys, n (%)	27 (45.0)	27 (45.0)	—	—
Left kidney				
YM, Kpa	8.3±2.1	16.8±4.8	-13.183	<0.001
Length, cm	9.3±1.2	9.3±1.3	-0.376	0.708
Width, cm	4.6±0.8	4.6±0.8	0.246	0.806
Height, cm	3.6±0.7	3.9±0.9	-3.827	<0.001
Volume, cm <sup>3</sup>	85.3±42.2	92.7±58.4	-1.797	0.077
Right kidney				
YM, Kpa	8.3±2.4	16.0±4.7	-11.47	<0.001
Length, cm	9.0±1.3	9.3±1.3	-2.163	0.035
Width, cm	4.5±0.8	4.4±0.7	0.863	0.392
Height, cm	3.6±0.6	3.8±0.7	-3.3	0.002
Volume, cm <sup>3</sup>	80.2±38.7	85.6±40.6	-1.665	0.101

Data are presented as mean±SD for continuous variables and n (%) for categorical variables;

YM: Young's Modulus.

Table 2 Comparison of YM values among different pathological types in case group (, Kpa)

	N (%)	YM <sub>LK</sub>	YM <sub>RK</sub>
IgA nephropathy <sup>a</sup>	23(38.3)	—	—
Grade I	12(20)	12.4±1.8	12.3±2.2
Grade II	7(11.7)	14.6±0.8	14.9±1.4
Grade III	4(6.7)	20.9±2.3	20.3±2.8
<i>P</i> for trend		<0.001	<0.001
HSPN <sup>b</sup>	14(23.3)	—	—
Type I	3(5.0)	14.3±0.8	13.3±1.8
Type II	10(16.7)	16.5±1.5	16.3±1.5
Type III	1(1.7)	40.7	39.5
<i>P</i> for trend		0.005	0.003

a: according to Lee; b: according to the International Study of Kidney Disease in Children; HSPN: Henoch Schonlein purpura nephritis; YM<sub>LK</sub>: Young's Modulus of left kidney; YM<sub>RK</sub>: Young's Modulus of right kidney.

Table 3 Comparison of YM values in children with CKD at different clinical stages (, Kpa)

stage	N	YM <sub>LK</sub>	YM <sub>RK</sub>
1	42	14.6±2.0	14.4±2.6
2	14	20.1±2.5	17.7±4.5
3	3	23.3±5.7	20.5±5.2
4	1	40.7	39.5
<i>P</i> for trend	—	<0.001	<0.001

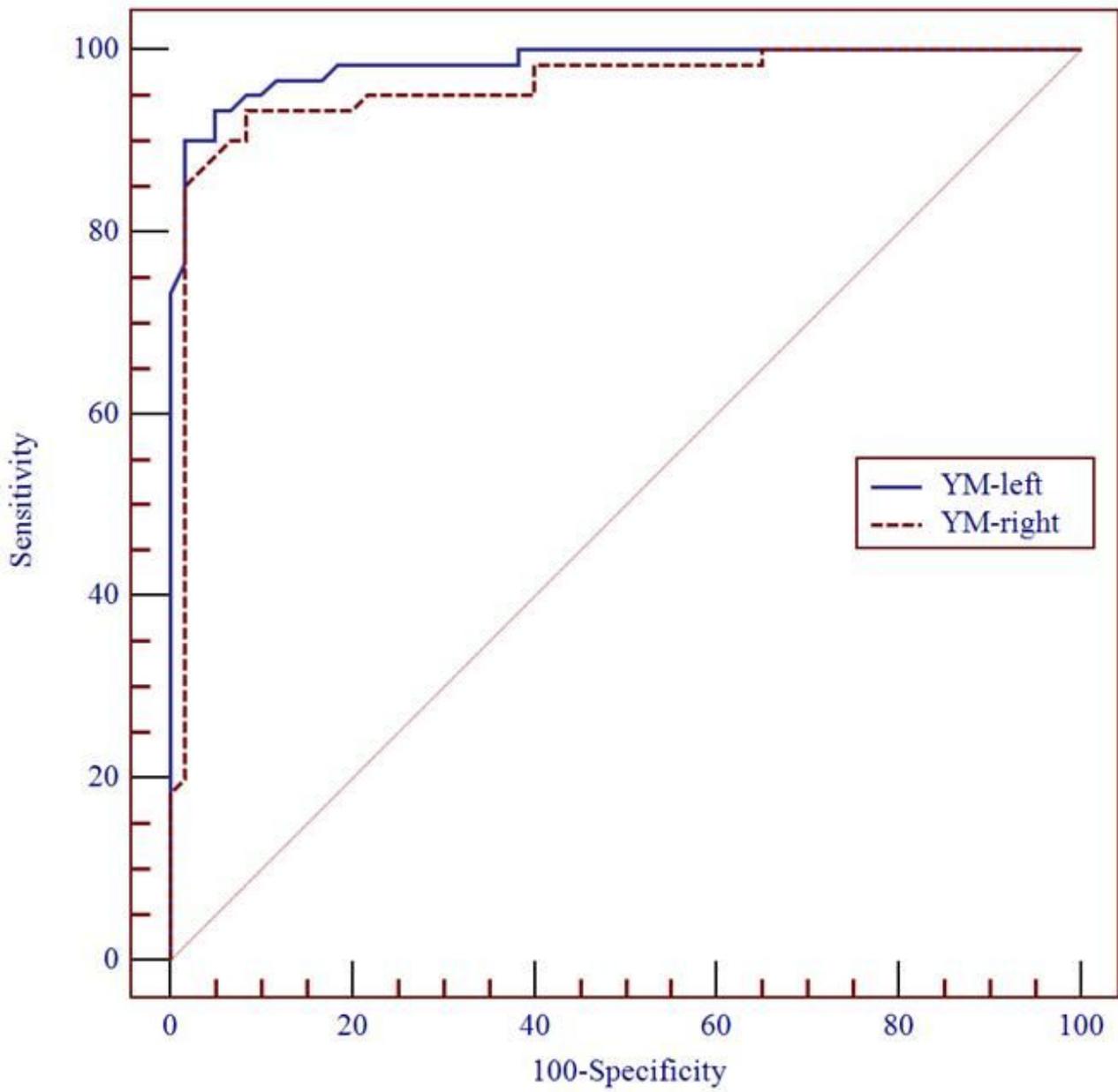
YM<sub>LK</sub>: Young's Modulus of left kidney; YM<sub>RK</sub>: Young's Modulus of right kidney.

## Figures



Figure 1

Ultrasound images of kidney SWE in CKD children (left) and control group (right)



**Figure 2**

ROC curve of Young's Modulus value in diagnosis of CKD