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Virtual Touch Tissue Imaging and Quantification Elastography in Determining the Effects of Chronic Kidney Disease on Tendons in Pediatric Patients

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Abstract

The aim of this study is to determine the possible elasticity changes of the quadriceps, patellar, and Achilles tendons using the Virtual Touch Tissue Imaging and Quantification (VTIQ) Elastography method in children with chronic kidney disease. VTIQ elastography measurements of the quadriceps, patellar, and Achilles tendons were performed in children with end-stage renal disease and the healthy control group. Tendon stiffness values of the patient and the control group were compared. Twenty children with end-stage renal disease and 13 healthy children were included in the study. The mean age was 13.05±3.3 years, 12.31±3.2 in the patient group and healthy control group, respectively. Age did not show a statistically significant difference between the patient and control group. The median duration of dialysis was 2.0 (1-9) years. Duration of the dialysis showed a positive correlation with shear wave velocity (SWV) of the musculotendinous junction (MTJ) of the right Achilles tendon (r=0.81 and p=0.001). Parathormone levels showed a positive correlation with SWV of MTJ of the right Achilles tendon (r=0.62 and p=0.03). There was no statistically significant difference in tendon stiffness values of right quadriceps, patellar tendons, Achilles MTJ, Achilles midtendinous (MIDT) area, left quadriceps, patellar tendons, Achilles MTJ, Achilles MIDT area between the patient and control group (p=0.93, p=0.42, p=0.21, p=0.67, p=0.55, p=0.19, p=0.08, p=0.89, respectively). Tendon stiffness values did not differ in children with CKD compared to healthy children. Nevertheless, further long-time follow-up studies are needed to reveal the relation between tendon stiffness and chronic kidney disease.

Keywords: Child; chronic kidney diseases; elastography; tendons; ultrasonography

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Introduction

Chronic kidney disease (CKD) means progressive loss of kidney function in course of time. It is related to significant health complications, growth impairment, and decreased life expectancy in childhood.[1,2] Spontaneous tendon rupture is one of the complications of chronic renal failure.[3,4] Secondary hyperparathyroidism, corticosteroid use, fluoroquinolone use, amyloidosis, chronic acidosis, chronic inflammation, and malnutrition are the predisposing factors for this complication.[5] The quadriceps, patellar, and Achilles tendons are mostly affected.[3,6] If not treated or missed, this complication may result in disability. To reduce the morbidity and the economic load on the healthcare expenditure, early detection, and early medical management are essential.

Ultrasonography (US) is more helpful in diagnosing tendon diseases than clinical examination.[7] Low cost, no radiation exposure, accessibility, portability, ease of use, and real-time capability are the advantages of the US. However, conventional US is not sufficient to evaluate biomechanical characteristics of the tendons. Ultrasound elastography (UE) is a method that helps to recognize pathologic conditions via determining tissue elasticity.[8] It has been used in the musculoskeletal system to evaluate muscle elasticity, shoulder bursitis, lateral epicondylitis, spondyloarthritis, and rotator cuff disease.[9]

The two UE methods are real-time elastography and shear wave elastography (SWE). Manual compression is used in real-time elastography whereas an acoustic beam is used in SWE. Virtual Touch Imaging Quantification (VTIQ) and Virtual Touch Quantification (VTQ) are the SWE techniques that directly measure tissue stiffness. VTIQ has a superior diagnostic performance compared to VTQ with a smaller region of interest (ROI) and multiple-point measurement.[10]

The goal of this study was to determine the possible elasticity changes of the quadriceps, patellar, and Achilles tendons using the VTIQ method in children with CKD.

Highlights

- Tendon stiffness values did not differ in children with CKD compared to healthy children
- Duration of the dialysis and PTH levels showed a positive correlation with shear wave velocity (SWV) of the musculotendinous junction (MTJ) of the right Achilles tendon
- Further long-time follow-up studies are needed to reveal the relation between tendon stiffness and chronic kidney disease.

Material and Method

Study Population

This is a cross-sectional study consisting of thirty-three volunteers. Twenty patients with end-stage chronic renal disease who were on dialysis and thirteen control subjects admitted to our institution between January 2020 and March 2021 were included. The control group was formed from randomly selected healthy children who presented to the ultrasonography unit. The exclusion criteria for patient and control groups were as follows: previous trauma or surgery of lower extremity and history of systemic inflammatory diseases. Shear wave velocity (SWV) of bilateral quadriceps, patellar, and Achilles tendons were examined in all volunteers. Duration time of dialysis and parathormone levels were noted for the patients. This study was approved by Erciyes University ethics committee (date:22.05.2019, decision no: 308). Written informed consent was obtained from the parents of all individuals.

Examination Technique

Ultrasound elastography examinations were performed using a Siemens S 3000 (Siemens Healthcare, Erlangen, Germany) ultrasound device. A 9L4 probe and VTIQ technique is used. A single pediatric radiologist with 15 years of experience in ultrasonography and 3 years of experience in elastography performed the sonographic examinations.

Quadriceps tendons and patellar tendons were evaluated in a supine position while the knees were in flexion at approximately 45°, keeping the foot on the floor. The measurements of quadriceps and patellar tendons were obtained from the midtendinous (MIDT) area. Evaluation of the Achilles tendons were performed in prone position while hanging the feet down the end of the table. The measurements of Achilles tendons were obtained from the musculotendinous junction (MTJ) and midtendinous (MIDT) area. All tendons were evaluated in the longitudinal plane. Compared to the axial plane, the longitudinal plane was more appropriate to evaluate a larger area. The size of ROI specified by the manufacturer was 1.5×1.5 mm. Conventional B-mode ultrasound guided the positioning of the ROI. Four valid measurements were performed for each localization (**Figure 1, 2**). Then, a mean value of the SWV (expressed in m/s) was obtained.

Statistical Analysis

Statistical analyses were performed by SPSS IBM Statistics Version 22.0 (SPSS Inc, Chicago, IL, USA). Shapiro–Wilk test was used for testing normality. Variables were presented as mean±SD or median (range). The comparison of two groups distributed normally and the comparison of two groups not distributed normally, were performed by independent samples t-test and Mann–Whitney U test, respectively. Chi-square test was used to compare categorical variables. Pearson correlation was used for normally distributed data whereas Spearman correlation was used for non-normally distributed data. Reliability measurements which are expressed as intraclass correlation coefficient (ICC) were performed for the elastography measurements of each localization. Differences were regarded as significant at $p<0.05$.

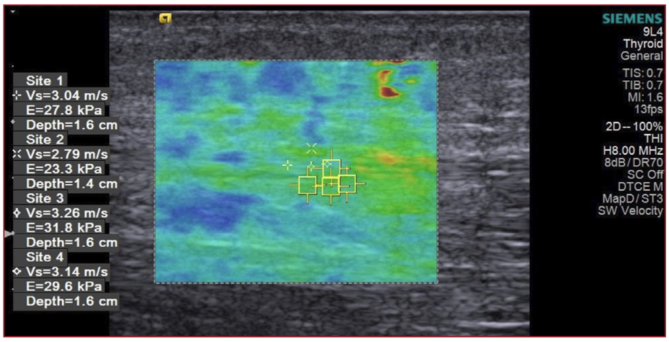

Figure 1. VTIQ measurements of MTJ of Achilles tendon in a 16 years old boy with CKD.

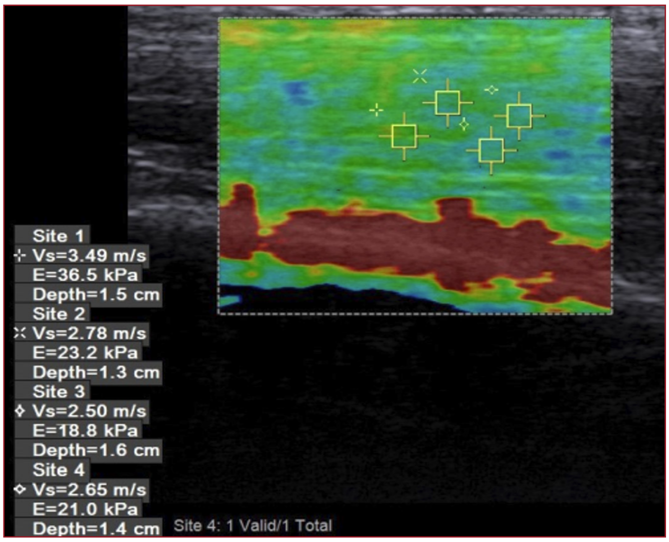

Figure 2. VTIQ measurements of MTJ of Achilles tendon in a 14 years old healthy boy.

Results

Demographic, clinical and laboratory characteristics of the volunteers were given in **Table 1.** There were 20 and 13 children in the patient group and control group, respectively. Age and gender did not show a statistically significant difference between the patient and control group (p=0.41 and p=0.52). Correlation analysis was performed for right and left sided tendons (**Table 2**). The duration of dialysis showed a high positive correlation with SWV of MTJ of the right Achilles tendon (r= 0.85 and p<0.001) but was not correlated with SWV of other locations. Parathormone levels showed a high positive correlation with SWV of MTJ of the right Achilles tendon (r=0.62 and p=0.03) but were not correlated with SWV of other locations. Shear wave elastography measurements of right and left, quadriceps MIDT, patellar MIDT, Achilles MTJ, Achilles MIDT for all volunteers was given in **Table 3.** The intraobserver agreement expressed as intraclass correlation coefficient (ICC) was perfect for each location. ICC values are shown in **Table 4**.

Table 1
Demographic, clinical and laboratory characteristics of patient and control groups

	Patient group N=20	Control group N=13	p
Age (years)	12 (6-17)	11 (9-18)	0.41
Gender (male/female)	7/6	13/7	0.52
Duration of dialysis (years)	2.0 (1-9)		-
PTH (pg/mL)	435±267	-	-

PTH; parathormone, The parameters are presented as median (range) for age and duration of dialysis and mean±SD for PTH levels

Table 2
Correlation analysis between SWV of tendons and age, duration of dialysis and PTH levels.

	Age	Duration of dialysis	PTH
SWVs of right Q MIDT	-0.346 0.057	0.192 0.445	-0.321 0.210
SWVs of right P MIDT	-0.146 0.424	-0.181 0.458	-0.266 0.285
SWVs of right A MTJ	0.060 0.779	0.812 0.001	0.616 0.033
SWVs of right A MIDT	0.171 0.357	-0.117 0.645	-0.117 0.656
SWVs of left Q MIDT	0.033 0.862	0.210 0.403	0.137 0.599
SWVs of left P MIDT	0.116 0.534	-0.124 0.623	-0.301 0.241
SWVs of left A MTJ	0.157 0.453	0.465 0.128	0.425 0.169
SWVs of left A MIDT	-0.214 0.248	0.242 0.333	0.151 0.562

The first line is r value, the second line is p value for all parameters. SWV, Shear wave velocity; PTH, parathormone

Table 3
Shear wave elastography measurements of right and left, Q MIDT, P MIDT, A MTJ, A MIDT

	Patient group	Control group	p
SWVs of right Q MIDT (m/s)	3.25±0.94	3.22±0.41	0.93
SWVs of right P MIDT (m/s)	3.12±1.01	3.40±0.85	0.42
SWVs of right A MTJ (m/s)	3.96±1.51	3.32±0.87	0.21
SWVs of right A MIDT (m/s)	4.75±1.15	4.91±0.80	0.67
SWVs of left Q MIDT (m/s)	3.22 (2.26-5.56)	3.05 (2.53-3.59)	0.55
SWVs of left P MIDT (m/s)	2.61±0.76	2.92±0.47	0.19
SWVs of left A MTJ (m/s)	4.19±1.26	3.47±0.69	0.08
SWVs of left A MIDT (m/s)	4.68±1.31	4.63±0.58	0.89

The parameters are presented as mean±SD for SWVs of right and left tendons except for left Q MIDT of the patient and control group. SWV of the left Q MIDT of the patient and control group was presented as median (range). Q; quadriceps, P; patellar, A; Achilles, MTJ; musculotendinous junction, MIDT; midtendinous area

Table 4
Intraobserver reliability measurements

Localization	ICC	95% CI	p
Right Q MIDT	0.94	0.84-0.98	<0.001
Right P MIDT	0.95	0.87- 0.98	<0.001
Right A MTJ	0.95	0.88-0.99	<0.001
Right A MIDT	0.94	0.84-0.99	<0.001
Left QMTJ	0.94	0.86–0.98	<0.001
Left P MIDT	0.95	0.89-0.99	<0.001
Left A MTJ	0.93	0.83-0.98	<0.001
Left A MIDT	0.89	0.74-0.97	<0.001

Q; quadriceps, P; patellar, A; Achilles, MTJ; musculotendinous junction, MIDT; midtendinous area, ICC; interclass correlation coefficient

Discussion

In the current study, the tendon stiffness values of the children with end-stage renal disease and healthy children were evaluated. There was no statistically significant difference in tendon stiffness between the groups. Duration of dialysis and parathormone levels showed a positive correlation with SWV of right MTJ of Achilles tendons whereas no correlation was found with SWV of other tendons.

Elastographic studies on the tendons with different pathologic conditions reveal a wide variety of discrepancies in results. In some studies, it is reported that a tendon with pathologic changes is softer than the normal tendon.[11-15] Turan et al.[11] reported that the Achilles tendons of patients with ankylosing spondylitis were softer than the healthy group. De Zordo et al.[12] evaluated the stiffness of Achilles tendon in patients with chronic Achilles tendinopathy and reported evident softening. Dirrichs et al.[13] evaluated Achilles, patellar or epicondylar tendons in patients with chronic tendon pain and reported that SWVs was lower in symptomatic tendons compared to those in asymptomatic ones. Chen et al.[14] evaluated ruptured Achilles tendons and reported softening compared with the healthy tendons. In a study comparing quadriceps tendons of the patients with chronic hemodialysis and healthy individuals, softening and thinning are reported in the patient group.[15] On the other hand, opposed results are reported in some studies.[16-18] Mutlu et al.[16] evaluated the Achilles tendons and performed the measurements in proximal, middle, and distal thirds of the tendons in patients with CKD. They reported that there was an increased stiffness for all 3 parts in the patient group compared to healthy individuals. Caglar et al.[17] evaluated the Achilles tendon in patients with CKD in hemodialysis and healthy individuals, using VTIQ. They reported that tendon stiffness values were higher in the distal third of the Achilles in patients, compared to healthy controls. Zhang et al.[18] reported that the patellar tendons of the athletes with unilateral tendinopathy had higher stiffness measurements compared to both the controls and unaffected tendons of the athletes.

Using SWE, Coombes et al.[19] evaluated SWV of insertional Achilles tendons and patellar tendons in patients with tendinopathy and healthy individuals. They reported lower tendon stiffness in Achilles whereas higher tendon stiffness in patellar tendons in the patient group compared to healthy controls. Hekimoglu et al.[20] evaluated Achilles tendon elasticity in patients with CKD in hemodialysis and healthy individuals by using SWE. No statistically significant difference was reported between the groups in their study. In contribution with Hekimoglu et al.[20] there was no significant difference in SWE measurements between the patient and control groups in the current study. They performed the measurements only in the middle part of the tendon and stated that as a reason for the statistically insignificant difference. In the current study, the measurements of the Achilles tendons were performed in two localization (musculotendinous junction and midtendinous area). However, still, there was no statistically significant difference between groups. Hekimoğlu et al.[20] reported that there was no association between the duration of hemodialysis and mean stiffness values of Achilles tendons. Unlike their results, in the current study, the duration of the dialysis showed a very high positive correlation with SWV of the musculotendinous junction of the right Achilles tendon. Also, parathormone levels showed a high positive correlation with the SWV of right Achilles at the musculotendinous junction. Kural et al.[21] reported that the SWV measurements of the Achilles of the patients with chronic kidney disease on hemodialysis and the people with renal transplant showed significant differences when compared with healthy people. In their study the median duration of dialysis was 12 years (range, 5-20 y) for the patients with CKD and 8 years (range, 5-16 y) for transplant group. The median duration of dialysis was 2 years (range, 1-9 y) in the current study. Based on these findings, the relatively short duration of dialysis in our patient group may be responsible for the insignificant difference. If the duration time was longer, significant differences might be obvious in tendon stiffness between groups. Thus, further long-time follow-up studies are needed to reveal the relation between tendon stiffness and CKD.

Age did not show a correlation with the SWV of the tendons in the current study, in contribution with Wakker et al.[22] and Fu et al.[23] who studied the normal SWV values of Achilles tendons in healthy individuals.

The discrepancy between the results of all these studies may be explained by several factors. One of them is the various ultrasound elastography methods and manufacturers used for measurements. For example, Turan et al.[11] and De Zordo et al.[12] used compression elastography while Dirrichs et al.[13], Chen et al.[14], Zhang et al.[18], Coombes et al.[19] used SWE. Trottmann et al.[24] in their study, used two different manufacturers for ultrasound elastography measurements and compared the values. They stated that the measurement values showed statistically significant differences. Another factor is the nonuniformity of examination protocols. Aubry et al.[25] compared the SWV of the Achilles tendons under variable tightness, they reported that the highest velocities were found in dorsiflexion of the ankle and maximum plantarflexion gave the lowest values. De wall et al.[26] evaluated the Achilles tendon in three positions; 15° plantar flexion, neutral, and 15° dorsiflexion. In several studies,[15-17,22] the Achilles tendon was evaluated in the prone position, with feet hanging down from the side of the table. In contribution with them, in the current study, the measurements of the Achilles were performed in the prone position, feet hanging down the end of the table. Breda et al.[27] evaluated the patellar tendons in passive extension. Dickson et al.[28] evaluated the quadriceps and patellar tendons in a supine lying or seated position in 30° flexion. Quadriceps and patellar tendons were evaluated in 45° flexion in the current study similar to the study of Dickson et al. SWV is affected by the plane of acquisition due to anisotropy. The tendons are anisotropic organs. Therefore, SWV values vary according to the angle at which the ultrasound elastography waves pass through the tendon fibers. The mean SWV was reported to be higher in the sagittal plane compared with the axial plane.[23]

The relation between secondary hyperparathyroidism and the tendon rupture mechanism is controversial. Shiota et al.[29], reported that the cause of the tendon rupture was osteolytic bone resorption at the tendon insertion site and tendon structure was not affected. Nevertheless, Terai et al.[30], reported that vascular calcification increased in CKD with secondary hyperparathyroidism. Kurtoglu et al.[31], reported intratendinous calcific nodules in Achilles tendons in a patient with hyperparathyroidism associated with parathyroid adenoma. Supporting Terai et al.30 and Kurtoglu et al.[31], parathormone levels correlated positively with tendon stiffness values of Achilles MTJ, in this study.

There are some limitations in the current study. One of them is the relatively small study population. Another one was that, we did not perform a histological analysis because it wasn't possible to achieve histologic samples as there was no indication. Another limitation was the duration of dialysis, which was relatively short to see the effects of hyperparathyroidism on tendon elastography properties.

However, this study is the first to evaluate the elastic properties of the tendons in the pediatric age group with CKD, to the best of our knowledge.

Conclusion

Tendon stiffness values were not statistically different in children with CKD compared to healthy children. A relatively short duration of the dialysis in the volunteers may be responsible for the result. Further long-time follow-up studies are needed to reveal the relation between tendon stiffness and CKD.

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Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Ethics Committee Approval: This study was approved by Erciyes University ethics committee (date:22.05.2019, decision no: 308).

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Informed Consent: All patients signed the free and informed consent form.

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