Assessment of tendon involvement in chronic hemodialysis patients: an ultrasonographic study

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Aim of the work
The aim of this study was to detect changes occurring in some tendons, for example, Achilles, quadriceps, and supraspinatus tendons, using musculoskeletal ultrasound (MSUS) imaging in patients with chronic kidney disease (CKD) on regular hemodialysis and to evaluate associations of these changes with patients' clinical status, parathyroid hormone (PTH) level as well as other laboratory parameters.

Patients and methods
This study was carried out on 35 patients and a group of 25 age-matched and sex-matched apparently healthy participants as a control group. All patients underwent history taking; clinical examination; and shoulder, knee, and ankle plain radiography. Laboratory investigations including PTH level were done. MSUS was performed on the selected tendons for all patients and controls.

Results
The ankle was the most clinically affected joint. US abnormalities most commonly affected the Achilles tendon (15.2%) having calcific deposits, abnormal peritendon tissue, increased thickness, and abnormal structure, followed by the quadriceps tendon (2.9%), whereas the supraspinatus tendon was the least affected (2.3%). There were highly statistically significant differences between patients with CKD and controls regarding mean tendon thickness, with the quadriceps tendon and supraspinatus tendons being thicker in the study group ($P<0.001$). Significant positive correlations of PTH level with age, the duration of dialysis, and PO_4 level were observed.

Conclusion
There were significant tendon involvements among patients with CKD with the Achilles tendon mostly involved having calcific deposits, abnormal peritendon tissue, increased thickness, and abnormal structure. Tendon abnormalities occurred mainly in older patients with longer durations of dialysis, hypercalcemia (Ca), hyperphosphatemia (PO_4), and a higher Ca×PO_4 product. MSUS is a simple, noninvasive, and a substantial tool in the diagnosis and follow-up of tendon involvement among patients with CKD.

Keywords:
Achilles tendon, chronic kidney disease, musculoskeletal ultrasound, parathyroid hormone

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Introduction

Chronic kidney disease (CKD) is a worldwide public health problem, with increasing prevalence and adverse outcome, including progressive loss of kidney function, extraskeletal calcification, cardiovascular disease, and premature death [1]. Disturbances in mineral and bone metabolism are prevalent in CKD. Musculoskeletal problems are still one of the important determinants of the quality of life in patients with chronic renal failure, especially in patients under hemodialysis (HD) [2].

Renal osteodystrophy is the term used to describe abnormalities in bone morphology developing in CKD. It appears when the glomerular filtration rate falls below 60 ml/min [3]. Its most common forms are largely attributable to variations in the plasma levels of parathyroid hormone (PTH). As such, circulating PTH levels have been used as a surrogate indicator of bone turnover, which are used together with measurements of serum calcium, phosphorus, and alkaline phosphatase levels to evaluate, diagnose, and guide the treatment of renal osteodystrophy. However, the specificity of PTH as an indicator of bone turnover has been questioned [4].

In addition to bone histology and serum biomarkers, imaging has been an important component of evaluating bone disease. Musculoskeletal ultrasonography (MSUS)

is considered to be a valid and probably the most suitable method when it comes to investigating superficially located structures such as tendons [5]. It is known that, with modern high-frequency transducers (10–15 MHz), US can achieve a higher spatial resolution than the routine MRI. Fine structures, like fiber bundles of a tendon, can be depicted with US but not with the routine MRI [6].

Aim of the work

The aim of this study was to detect changes occurring in some tendons, for example, Achilles, quadriceps, and supraspinatus tendons, using MSUS imaging in patients with CKD on regular HD and to evaluate associations of these changes with patients' clinical status, PTH level as well as other laboratory parameters.

Patients and methods

This study was carried out on 35 patients who fulfilled the criteria for the diagnosis of CKD [7].

Patients were recruited from the attendants to the dialysis unit in the Internal Medicine Department of Benha University Hospitals. These patients were receiving a 4-h dialysis session three times weekly. A group of 25 age-matched and sex-matched apparently healthy participants was recruited to serve as a control group.

Criteria for exclusion

Patients were excluded from the study if they had systemic inflammatory diseases such as rheumatoid arthritis or systemic lupus erythematosus as a cause of renal failure, a previous trauma or bone fracture at target sites, tuberculosis, osteoarthritis, endocrinal, metabolic disorders, and acute renal failure.

Ethical considerations

A written consent was taken from all patients and controls before participation in the study, which was approved by the ethical committee of Benha Faculty of Medicine, Benha University, Egypt.

All patients were subjected to the following:

(1) A complete history taking and clinical examination, which included extension knee test, empty/full can test, and Thompson test.
(2) Assessment of tendinopathy and/or enthesopathy with clinical tests for the selected tendons (Achilles, quadriceps, and supraspinatus tendons).
(3) Laboratory investigations, including the erythrocyte sedimentation rate, C-reactive protein, complete blood count, serum creatinine, blood urea and serum uric acid, urine analysis, serum calcium (Ca), serum phosphorus, and Ca×PO_4 product. The PTH was measured using the enzyme-linked immunosorbent assay [8].
(4) Imaging:
    (a) Plain radiography on both shoulders (AP view), knees (AP and lateral views), ankles (AP and lateral views).
    (b) MSUS.

All patients with CKD and the healthy controls underwent MSUS assessment performed by a rheumatologist experienced in MSUS, using a GE Logiqe 9 scanner (General Electric Medical Systems, Milwaukee, Wisconsin, USA) with a multifrequency linear array transducer (8–13 MHz) according to the European League Against Rheumatism guidelines in both longitudinal and transverse views. A systematic multiplanar gray-scale and power Doppler examination of selected tendons were done. It was important not to place too much pressure on the transducer, thereby missing some of the present changes.

The study was restricted to bilateral Achilles tendons, quadriceps tendons, and supraspinatus tendons because of their easy accessibility, providing the most appropriate model for ultrasonographic analysis as a result of their superficial position and large size [9].

Statistical analysis

The collected data were summarized in terms of mean ±SD and range for quantitative data and frequency and percentage for qualitative data. Comparisons between the different study groups were carried out using the Fisher exact test to compare proportions. The Student *t* test was used to compare means of two parametric data. Pearson's correlation coefficient (*r*) was used to test for the correlation between PTH and other parameters.

After the calculation of each of the test statistics, the corresponding distribution tables were consulted to get the *P* value. Statistical significance (S) was accepted at *P* value less than 0.05. A *P* value less than 0.001 was considered highly significant (HS), whereas a *P* value more than 0.05 was considered nonsignificant.

The statistical analysis was conducted using version 11.2, STATA/SE for Windows (STATA Corporation, College Station, Texas, USA).

Results

This study included 35 patients with CKD [14 (40%) males and 21 (60%) females] on regular HD (three times/week). Their ages ranged between 29 and 70

years, with a mean±SD of 51.5±10.7 years. A group of 25 age-matched and sex-matched apparently healthy participants was also included as a control group. Their ages ranged between 28 and 62 years with a mean±SD 46.6±11.0 years. There were 14 (56%) females and 11 (44%) males, with no statistically significant differences between both groups ($P<0.05$).

Patients in the study were on dialysis for a duration ranging from 1 to 15 years, with a mean±SD 7.5±4.6 years, and a disease duration from 1 to 25 years.

The most common causes of dialysis were hypertension in 14/35 (40%) patients, diabetes mellitus in 8/35 (22.9%) patients, renal obstruction in 7/35 (20.02%) patients, chronic pyelonephritis and analgesic abuse in 3/35 (8.6% each) patients, and chronic glomerulonephritis in 2/35 (5.7%). Unknown causes as well as diabetes mellitus with hypertension affected two (5.7% each) patients. Autosomal dominant polycystic kidney disease was the least cause found, affecting one (2.9%) patient only.

Symptoms and clinical examination in patients with CKD revealed that the ankle joint was the most clinically affected joint showing all physical signs of articular disease affection, including tenderness, swelling, range of motion (ROM) limitation, and muscle atrophy around the joint.

Clinical tests showed a positive extension knee test for the quadriceps tendon suggestive of rupture in one (2.9%) patient and a positive empty/full can test for the supraspinatus tendinopathy in six (17.1%) patients; however, the Thompson test for the Achilles tendon rupture was negative in all patients.

A total of 210 tendons of all patients (6×35) as well as 150 tendons of controls (6×25) were examined clinically by palpation for tenderness. For each tendon entity, results for 70 patients' tendons (2×35) and 50 controls' tendons (2×25) were recorded.

Tenderness on palpation was detected in 51/210 (24.3%) tendons. Bilateral affection was encountered in 18/35 (51.4%) patients, whereas 15/35 (42.8%) patients had unilateral affection, with the right side more affected. The Achilles tendons showed the highest percentage of involvement compared with the quadriceps and supraspinatus tendons (45.7 vs. 8.5% and 7.1%, respectively).

Tenderness on probing occurred in 43/210 (20.5%) of all tendons. Tendons tender on probing represented 43/51 (84.3%) of tendons tender on palpation. All patients who complained of tenderness on probing had tenderness on palpation but not the reverse, with a statistically insignificant difference ($P=0.1$). This may be explained by the deep pressure applied on clinical examination, whereas on performing MSUS only gentile pressure is used.

Using MSUS, abnormalities were detected in 43/210 (20.5%) tendons. This involved 23/35 (65%) patients. Bilateral affection was encountered in 16/35 (45.7%) patients, whereas 11/35 (31.4%) patients had unilateral affection, with the right side more affected.

US abnormalities most commonly affected the Achilles tendon in 32/210 (15.2%), followed by the quadriceps tendon in 6/210 (2.9%), whereas the supraspinatus tendon was the least affected in 5/210 (2.3%).

MSUS findings included calcific deposits seen in 24/210 (11.4%) tendons, abnormal peritendon tissue in 19/210 (9.0%) tendons, AP distal 1/3 tendo-Achilles thickness (>6 mm) in 10/210 (4.8%) tendons, AP middle 1/3 tendo-Achilles thickness (>6 mm) in 24/210 (11.4%) tendons, abnormal tendon structure in 6/210 (2.9%) tendons, and tendon tear in 1/210 (0.4%) tendons (Tables 1, 2 and Figs 1–5).

Comparative studies of US changes of affected tendons regarding patients' data and laboratory parameters were

Table 1 Musculoskeletal ultrasound findings of the Achilles, quadriceps, and supraspinatus tendons

Tendons (*N*=70)	*n* (%)
Calcific deposits	
Achilles tendon	18 (25.7)
Quadriceps tendon	4 (5.7)
Supraspinatus tendon	2 (2.8)
Total	24 (34.3)
Abnormal peritendon tissue	
Achilles tendon	13 (18.6)
Quadriceps tendon	3 (4.2)
Supraspinatus tendon	3 (4.2)
Total	19 (27.1)
A-P distal 1/3 thickness (>6 mm)	
Achilles tendon	10 (14.3)
AP middle 1/3 thickness (>6 mm)	
Achilles tendon	20 (28.5)
Abnormal tendon structure	
Achilles tendon	6 (8.6)
Quadriceps tendon	2 (2.8)
Supraspinatus tendon	2 (2.8)
Tendon tear	
Supraspinatus tendon	1 (1.4)

Thickness of the Achilles tendons was presented separately as abnormal if more than 6 mm at any point along its length. AP, anteroposterior.

done. Abnormalities were considered per patient for the most affected side. Very low number not legible for statistical comparisons were not reported.

(1) There were statistically significant differences of mean patients' ages regarding tenderness during probing, calcific deposits, and AP middle 1/3 thickness of Achilles tendon (>6 mm). Abnormalities occurred with older ages.
(2) There were highly statistically significant ($P<0.001$) differences of mean durations of dialysis regarding tenderness during probing and calcific deposits of Achilles tendon and a statistically significant difference regarding abnormal peritendon tissue of Achilles ($P=0.006$) tendons ($P=0.005$). Abnormalities associated longer durations.
(3) There were highly statistically significant differences ($P= 0.001$) of mean serum Ca levels, mean serum phosphate levels, and mean Ca×PO_4 product regarding tenderness during probing and calcific deposits of Achilles tendons, and a statistically significant difference ($P=0.01$) regarding abnormal peritendon tissue of Achilles tendons. Abnormalities occurred with a higher Ca, PO_4, and Ca×PO_4 product levels.
(4) There were insignificant differences ($P>0.05$) of mean serum creatinine levels and mean blood urea nitrogen regarding MSUS findings.

Table 2 Correlations between parathyroid hormone level and laboratory parameters among patients with chronic kidney disease

Variable (N=35)	Pearson's correlation coefficient (r)	P value
Age (years)	0.36	0.03*
Duration of dialysis (years)	0.97	<0.001**
Ca (mg/dl)	–0.042	0.619
PO_4 (mg/dl)	0.94	<0.001**
Ca×PO_4 product (mg/dl)	–0.12	0.35
Creatinine (mg/dl)	0.11	0.51
BUN (mg/dl)	–0.12	0.49
Hb (g/dl)	0.03	0.88

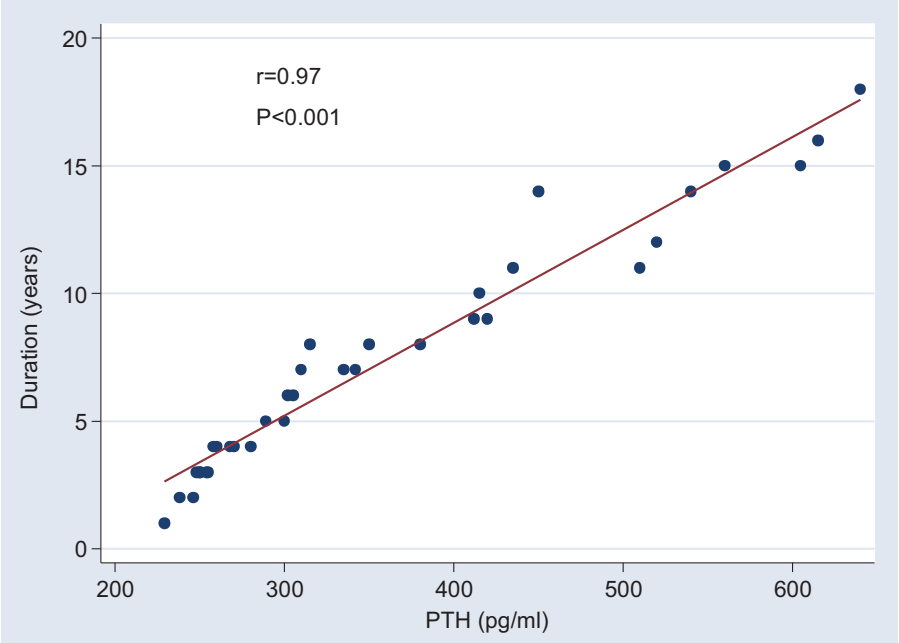
BUN, blood urea nitrogen; Hb, hemoglobin. P value less than 0.001, highly significant; P value less than 0.05, significant; P value more than 0.05, insignificant. *significant. **highly significant.

There were statistically insignificant differences ($P>0.05$) of PTH level with both quadriceps and supraspinatus tendons thickness (mm) bilaterally.

Discussion

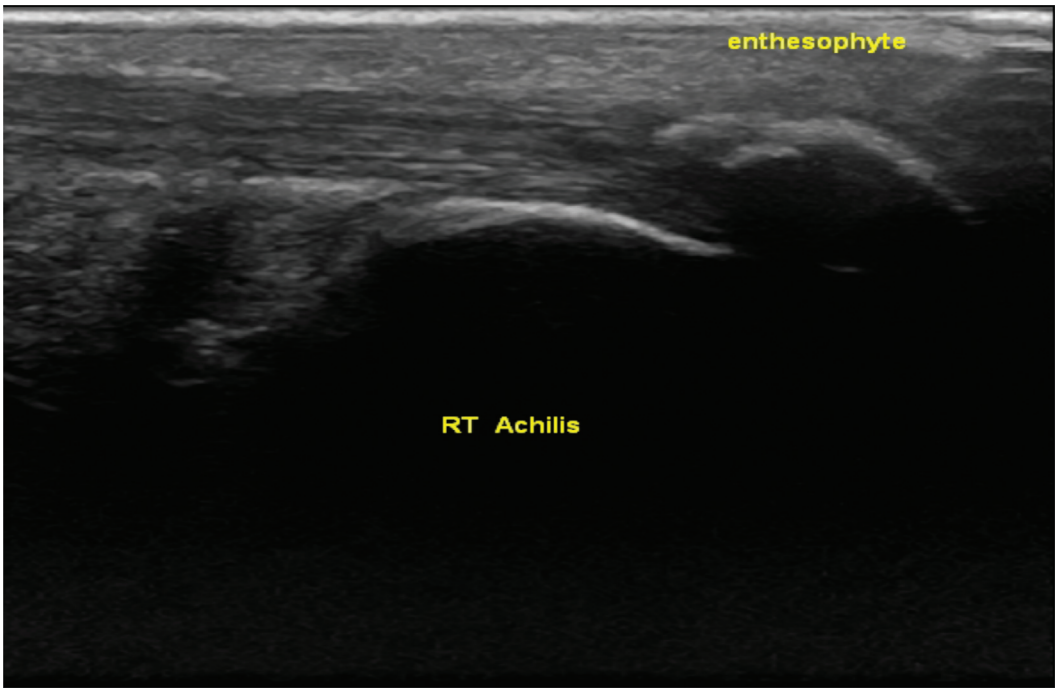
In our study, the ankle joint was the most clinically affected joint (8.6%) showing all physical signs of articular disease affection. This was in agreement with Hussein *et al.* [10], whereas the results reported by

Figure 1



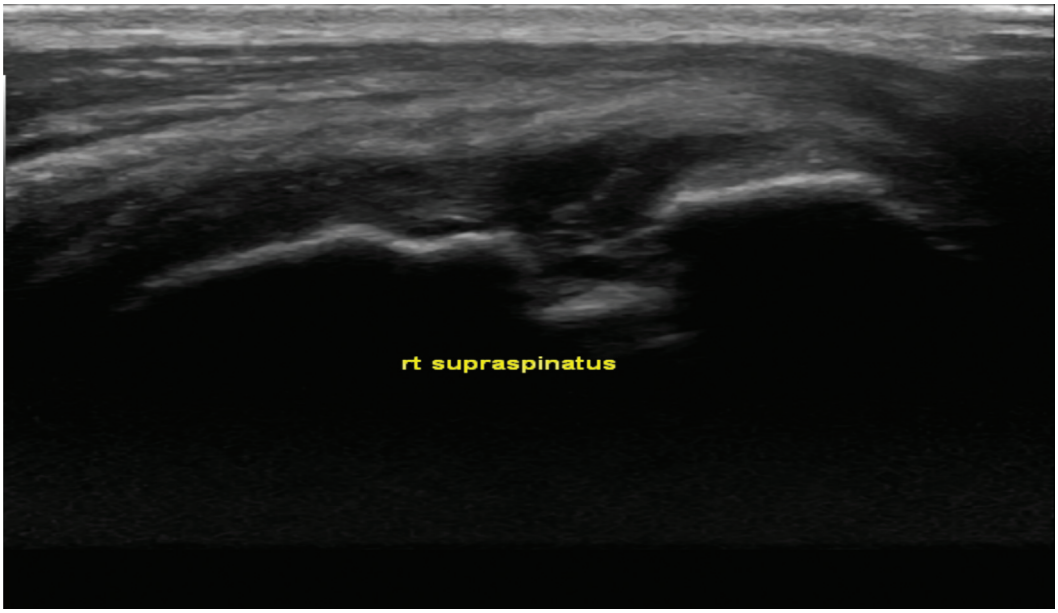
Correlation between PTH level and duration of dialysis in patients with CKD. Hyperparathyroidism was observed in all patients with CKD (100%) – with a highly significant mean difference ($P<0.001$) compared with the control group (361.6 vs. 55.07 ng/l) – accompanied with hyperphosphatemia and increased serum creatinine with a hypocalcemic status where other laboratory findings were normal. Correlations between PTH level, patients' data, and laboratory parameters among patients with CKD are shown in Table 2 and Fig. 1. CKD, chronic kidney disease; PTH, parathyroid hormone.

Figure 2



A longitudinal sonographic view of the right Achilles tendon showing an enthesophyte in a patient with CKD. CKD, chronic kidney disease.

Figure 3



A longitudinal sonographic view of the right shoulder joint showing step-down erosion of the humeral head, hypoechogenicity, and loss of the normal fibrillar pattern in the right supraspinatus tendon structure and a partial tendon tear in a patient with CKD. CKD, chronic kidney disease.

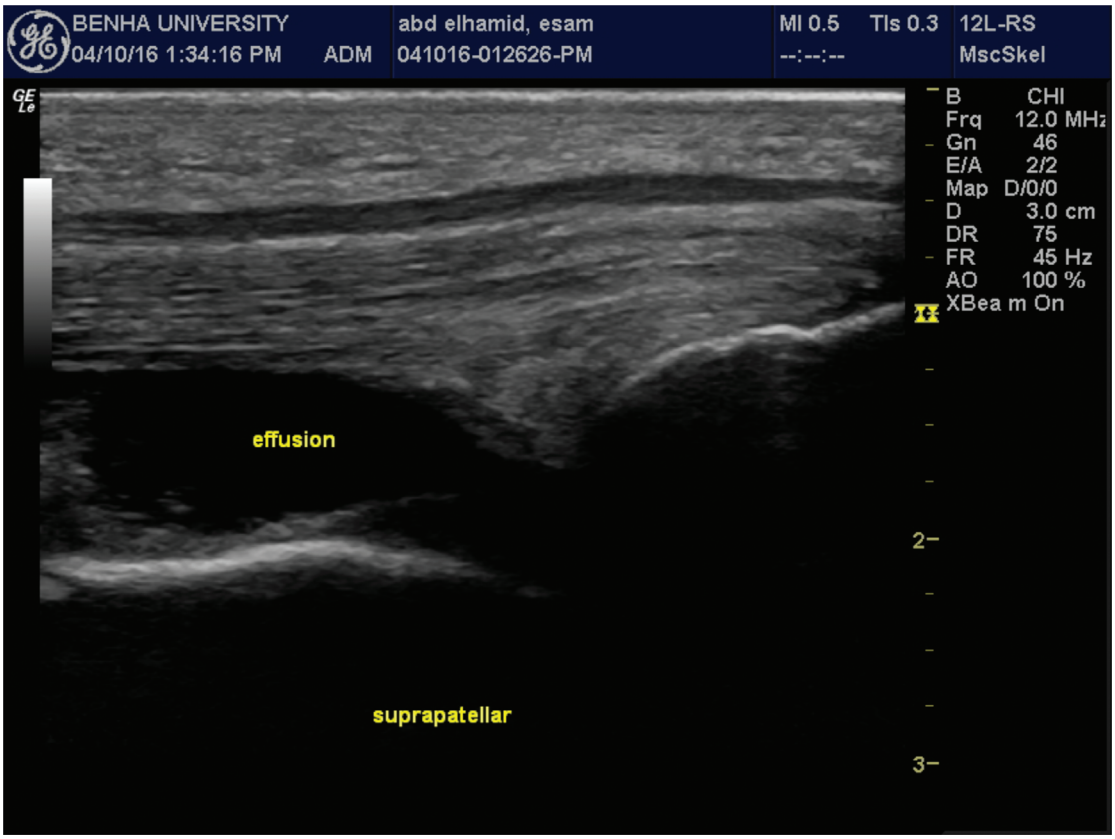
Maxime and Dougados [11] and Magee [12] were incongruent. None of these studies gave an explanation about the factors controlling this pattern of involvement.

Clinically, 24.3% of our patients with CKD experienced tendon tenderness on palpation, with the Achilles tendons showing the highest percentage compared with the quadriceps and supraspinatus tendons.

Using MSUS, abnormalities were detected in 20.5% of tendons, where the Achilles tendon was the most frequently affected among the examined tendons.

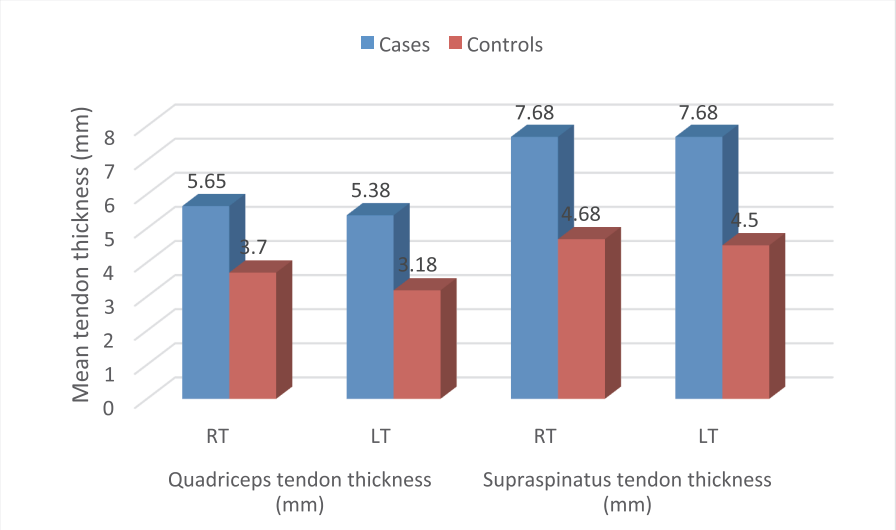
These results were in agreement with Hussein *et al.* [10] who reported 44% of tendons showed tenderness on palpation, whereas Brountzos *et al.* [9] encountered this in 11.9% of their patients.

Figure 4



A longitudinal sonographic view of the left knee joint showing effusion and abnormal diffuse hypoechogenicity of the left quadriceps tendon structure with loss of normal fibrillar pattern in a male patient with CKD, aged 65 years. CKD, chronic kidney disease.

Figure 5



Comparisons between mean tendon thickness of the quadriceps and supraspinatus tendon in the studied groups. There were highly statistically significant differences between patients with CKD and controls regarding mean thickness of the quadriceps and supraspinatus tendons, being thicker in the patient group ($P<0.001$). CKD, chronic kidney disease.

Rutten *et al.* [13] stated that supraspinatus tendon pain during probing is a predictor of partial tendon tear.

Langenhan *et al.* [14] explained that pain on palpating the quadriceps tendon may be related to bilateral injuries or injuries associated with trivial trauma

associated with the use of anabolic steroids or metabolic bone diseases.

In our study, abnormal US changes of the Achilles tendons included an abnormal AP middle 1/3 thickness; calcific deposition; an abnormal peritendon tissue in the form of patchy thickening, irregularities of tendon margins and fluid collection; an abnormal AP distal 1/3 thickness; and an abnormal tendon structure in the form of distorted tendon echo-structure as the least detected finding. These findings were in agreement with Brountzos *et al.* [9], Jukić *et al.* [15], and Hussein *et al.* [10].

Our results were comparable to those of Hussein *et al.* [10]; however, Brountzos *et al.* [9] reported that the most common finding in patients with CKD was abnormal Achilles tendon structure in 44.1%.

In this study, regarding the quadriceps tendons, calcific deposits were the most frequent finding followed by an abnormal peritendon tissue and an abnormal tendon structure. Clinical testing result suggesting tendon rupture which was negative with US. On the contrary, Brountzos *et al.* [9] and Hussein *et al.* [10] did not report any ultrasonographic abnormality of this tendon.

On examining the supraspinatus tendons, an abnormal peritendon tissue was the most frequent finding followed by an abnormal tendon structure and calcific deposits, whereas a partial tendon tear was defined in one case.

CKD and HD sequelae are suggested to be the predisposing factors for rupture beside other concomitant factors. These predisposing factors include being on long-term HD, development of secondary hyper parathyroidism (SHPT), β-2 microglobulin-associated amyloidosis, fluoroquinolone use, corticosteroid use, malnutrition/chronic inflammation syndrome, and chronic acidosis [16].

Jukić *et al.* [15] found six patients with tendon rupture (three quadriceps, one Achilles, and one supraspinatus tendon rupture).

In the present study, with MSUS tendon examinations, there was a highly statistically significant difference between patients with CKD and the controls regarding the mean tendon thickness, with the quadriceps tendon and supraspinatus tendons being thicker in the patient group ($P<0.001$).

Jadoul *et al.* [17] and Slavotinek *et al.* [18] showed significant rotator cuff thickening present predominantly in the supraspinatus tendon. However, Botter *et al.* [19] reported no differences in tendon thickness, especially quadriceps and Achilles, between the studied groups of their patients with CKD.

Our study showed highly significant positive correlations ($P<0.001$) of PTH level with the duration of dialysis and PO_4 level, a statistically significant ($P<0.005$) positive correlation with patients' ages, and statistically insignificant differences ($P>0.05$) with other laboratory parameters.

This was in agreement with the studies of Nasri and Kheiri [20], and Isaka *et al.* [21].

Our study revealed that there were statistically significant differences in mean patient ages regarding tenderness during probing ($P=0.01$), calcific deposits ($P=0.007$), and AP middle 1/3 thickness of Achilles tendon (>6 mm), where abnormalities occurred with older ages.

This was explained to occur owing to degeneration of the tenocytes and collagen fibers, and accumulation of lipid, ground substance (glycosaminoglycans), and calcium deposits. These may occur separately or in combination and very often these changes occur with changes in the blood vessels of the tendon or its paratenon [22].

These results did not coincide with Hussein *et al.* [10] who found that there was no statistically significant correlation between abnormal peritendon tissue of the Achilles tendon and age, duration of dialysis, laboratory results, or any other US findings.

Our results showed that there were highly statistically significant differences ($P<0.001$) in mean durations of dialysis regarding tenderness during probing ($P<0.001$) and presence of Achilles tendon calcific deposits ($P<0.001$), and a statistically significant differences regarding abnormal peritendon tissue of Achilles tendon ($P=0.006$). These abnormalities were associated longer duration of dialysis.

This coincided with Hussein *et al.* [10] who reported that there was a highly significant positive correlation between the presence of calcific deposits and duration of dialysis. Moreover, Brountzos *et al.* [9] mentioned that tendon abnormalities were associated with the duration of end-stage renal disease, and all occurred

after a mean duration on HD of more than 6 years. In particular, the alterations of the peritenon and the calcifications developed after a mean HD duration of 6 years, and pain during palpation was identified later in the course of the disease, after a mean HD duration of 10 years. These findings are in accordance with previous reports, which are based on clinical observations speculated that musculoskeletal manifestations are more frequently seen in patients who have undergone long-term HD [23].

In the present work, there were highly statistical significant differences of mean serum Ca or PO_4 or their product levels regarding tenderness during probing and calcific deposits of Achilles tendons, and a statistical significant difference regarding abnormal Achilles peritendon tissue. Abnormalities occurred with higher Ca or PO_4 or Ca×PO_4 levels. This was in agreement with Brountzos *et al.* [9] and Hussein *et al.* [10].

Conclusion

There were significant tendon involvements among patients with CKD with the Achilles tendon mostly involved having calcific deposits, abnormal peritendon tissue, increased thickness and abnormal structure. Tendon abnormalities occurred mainly in older patients with longer durations of dialysis, hypercalcemia (Ca), hyperphosphatemia (PO_4), and a higher Ca×PO_4 product. MSUS is a simple, noninvasive and a substantial tool in the diagnosis and follow-up of tendon involvement among patients with CKD.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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