

# Patellar tendon ultrasonographic properties and lower limb function in rheumatoid arthritis patients

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## Aim of work

The aim of this work was to investigate patellar tendon (PT) biomechanical properties in rheumatoid arthritis (RA) patients through changes in ultrasonographic tendon properties and its effect on lower limb function.

## Patients and methods

Forty RA patients and 20 healthy participants were included in this study. The physical function was assessed by Health Assessment Questionnaire, the activity of RA by disease activity score 28 and range of motion for all knees by a manual goniometer. RA patients were divided into the following groups: group I comprised patients with low disease activity score 28, who were further subdivided according to the presence of knee flexion deformity into two subgroups (GIA and GIB) and group II patients in the remission stage. Ultrasonography was used for measuring PT elongation and cross-sectional area and quadriceps' muscle strength was measured. The lower limb function was assessed clinically by 50-foot walk test and smart balance master system through unilateral stance test, step up and over and sit to stand tests.

## Results

There was an increased elongation of PT of all RA groups relative to the control group ( $P=0.001$ ); no significant difference was found in the PT (cross-sectional area). RA patients showed quadriceps' muscle strength reduction ( $P=0.001$ ) and delayed walking time of the 50-foot walk test ( $P=0.05$ ). Unilateral stance test showed increased center of gravity sway velocity during either eye open or eye closed conditions in RA groups and deterioration in all parameters of step up and over and sit to stand tests ( $P=0.05-0.001$ ). All physical function evaluation of RA patients showed impairment associated with a reduction of PT stiffness and quadriceps' strength.

## Conclusion

Inflammation of the PT and peritendinous tissues in RA alters its biomechanical properties; this impairs RA patients' physical and lower limb functions.

## Keywords:

lower limb function and performance, patellar tendon properties, physical function, rheumatoid arthritis

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## Introduction

Rheumatoid arthritis (RA) is a chronic, systemic, and inflammatory disease that primarily affects the synovial joints and leads to bone and cartilage destruction, as well as shows extra-articular manifestations [1]. Inflammation also affects other musculoskeletal structures including the tendons and their insertions into the bone (entheses) and is accompanied by impaired physical function. But whether this leads to chronic alterations in the biomechanical function of the tendon–muscle complex is unknown [2].

The tendon is responsible for the transmission of contractile forces from muscle to bone, allowing movement to occur [3].

The function of a tendon is determined by its stiffness, that is, its elastic properties, which in turn influence skeletal muscle force output and function. The tendon, however, is not an inextensible tissue, but it deforms in response to the applied load in a manner dependent upon its mechanical properties. When the force of the contracting muscle is transmitted via the tendon, the resulting elongation of the tendon attenuates the impact of the contraction on the connected bone [2].

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Local diffusion of inflammatory cells and molecules from the synovium is thought to be responsible for inflammatory changes seen in and around adjacent tendons in RA. The close proximity of the patellar tendon (PT) to the synovial spaces of the knee joint facilitates its direct exposure to the local inflammatory process [4].

The reduction in PT stiffness in RA is likely due to local and systemic effects of cytokines on the tendon, as proinflammatory cytokines are known to alter tendon structural characteristics in inflammatory arthropathies. The main drivers of the local inflammatory process are tumor necrosis factor- $\alpha$ , interleukin-1 and interleukin-6, which produce proteolytic enzymes such as matrix metalloproteinases that lead to collagen destruction, and the proangiogenic vascular endothelial growth factor, which evokes synovial hyperplasia and infiltration of macrophages and T cells into the synovium. Systemically circulating cytokines could have an additional detrimental effect on the tendon in RA [2,5].

Ultrasound is used to investigate the biomechanical properties of healthy tendons (especially the load-bearing patellar and Achilles tendons) and how they adapt to high-intensity exercise, immobilization, and changes with ageing [6]. Ultrasound is one of the best imaging modalities for assessing tendons due to its high image resolution. When diseased, tendons may become hypoechogenic, with loss of their fine fibrillar pattern, and thicker (diffusely or focally); they have internal Doppler signals and a thickened surrounding tendon sheath, which may exhibit Doppler signals [7].

Tendon properties influence joint stability and the ability to make postural adjustments and thus play a major role to maintain balance and prevent falls [2].

This study aimed to investigate the biomechanical properties of the PT in RA patients and to assess the effect of the changes in tendon ultrasonographic properties (tendon stiffness) on lower limb function and performance.

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### **Patients and methods**

The present study was conducted on 40 RA patients (80 knees), who were diagnosed according to the 2010 ACR/EULAR classification criteria for RA, and 20 healthy participants as a control group (40 knees).

An approval from the medical ethics committee of Al Azhar University was obtained and conforms to the Helsinki declaration, and all participants included in this study were informed about the study design and a written consent was obtained from them.

Selection of the RA patients was from both sexes; there were 33 (82.5%) female patients and seven (17.5%) male patients. Their ages ranged between 29 and 64 years with a mean age of 47 years; their disease duration ranged from 3 to 23 years with a mean duration of  $11 \pm 6.63$  years.

The activity of RA was assessed using the 28-joint disease activity score (DAS-28) and pain was evaluated using the visual analogue pain scale.

Patients were included in this study if their disease duration was at least 3 years and if they had a stable disease activity (no flare or change in medication for the past 3 months) to ensure that all the patients were able to stand on the balance platform and to withstand posturographic evaluation with tolerable pain. They were excluded if they had any other autoimmune or neurological diseases, were under high-dose steroid therapy ( $>10$  mg prednisolone/day), had a recent knee steroid injection, had a joint replacement or current severe knee pain or effusion.

The patients were divided according to their DAS-28 [8] into two groups: group I comprised patients in a stage of low disease activity; there were a total of 20 patients (40 knees). Group II comprised patients in a stage of remission; there were a total of 20 patients (40 knees). Group I patients were subdivided according to the presence of knee flexion deformity into GIA, which comprised nine patients with knee flexion deformity, and GIB, which comprised 11 patients without knee flexion deformity.

All participants were subjected to the following assessments:

- (1) Full history taking.
- (2) Clinical examination and routine laboratory investigation.
- (3) Health Assessment Questionnaire (HAQ), using its final version. It includes 20 questions in eight subdimensions: dressing and grooming, getting up, eating, walking, hygiene, reach, grip, and common daily activities (0–1 represent mild to moderate impairment, 1–2 moderate to severe impairment, and 2–3 severe to very severe impairment) [9].

(4) Biomechanical properties of the PT have been evaluated by the following tests:

(a) Ultrasonography for PT measurements: PT length, elongation and cross-sectional area (CSA) were assessed using Xario 200, Toshiba ultrasound machine (Toshiba, Toshiba medical systems corporation, Tochigi, Japan), using multifrequency linear probe with frequency 11 Mega Hertz in B-mode. PT length is the distance between the inferior pole of the patella and the superior aspect of the tibial tuberosity visualized on sagittal plane. Participants sat upright; the knee joint angle was fixed at 90 from full leg extension and the hip angle at 90. After a set protocol of warm-up contractions, participants performed maximal voluntary isometric knee extension contractions, building up to maximum force [10]. Ultrasound images were recorded at full knee extension and with the knee joint at 90°.

The CSA of PT was measured as three ultrasound images taken in the axial plane at 25, 50, and 75% of the PT length. The mean CSA was calculated using the following three measurements.

(b) Quadriceps muscle power by manual push-pull dynamometry expressed in kilograms.

(5) Physical function performance of the lower limb was assessed by the following tests:

(a) Clinically by estimating walking time by 50-foot walk test (FWT). The protocol has been described by Gill and McBurney [11] as the 50 FWT that has been completed by walking 25 feet, turning around 180° and walking 25 feet back to the starting position. Participants were advised to 'go as fast as you can safely walk.' The time taken was assessed with a hand-held stopwatch and recorded in seconds.

(b) Computerized dynamic posturography (Balance Master System, version 8), Neurocom International Incorporation manual [12]:

Balance Master System compares test results to normative data (on the software of the apparatus) relative to corresponding age, sex, and height.

(i) Unilateral stance test (UST): The US quantifies postural sway velocity with the patient standing on either the right or left foot on the force plate, with eyes open and with eyes closed. There were three trials for each condition; the length of each trial was ten seconds. The center of gravity (COG) sway velocity scores indicate how well the

patient accomplished this objective. Small scores reflect little movement and are good.

(ii) Step up and over (SUO) test: the patient is instructed to step up onto a curb using a 20 cm wooden step placed in the center of the platform; on command, the patient will step with one foot, swing the other foot over the curb while lifting the body through an erect standing position as quickly as possible, and then lower the body weight to land the swing leg as gently as possible. The SUO measures, for each leg, the strength of the rise (lift up index), which was recorded by the percentage of body weight exerted to lift the leading leg to the wooden step, the movement time, and the impact of the swing leg landing (impact index), which was expressed as the percentage of body weight used to step down onto the force plate.

(iii) Sit to stand (STS) test: the participants were instructed to stand up as quickly as possible, but they were not allowed to use arms or hands to push off their legs or the seat surface. They were also instructed to stand as still as possible for 5 s following the STS movement as part of the COG sway measurement. The STS procedure was repeated three times.

The measured parameters were weight transfer time, rising index, and sway velocity during the rising phase. Weight transfer time expressed in seconds is the time required to voluntarily shift COG forward, beginning in the seated position and ending with full weight bearing on the feet. Rising index is the amount of force exerted by the legs during the rising phase. The force is expressed as a percentage of the patient's body weight. COG sway velocity documents control of the COG over the base of support during the rising phase and for 5 s thereafter. Sway is expressed in degrees per second.

#### Statistical analysis

Data were analyzed using statistical program for the social science (IBM Inc., NY city, NY, USA), version 20.0. Quantitative data were expressed as mean±SD. Qualitative data were expressed as frequency and percentage. The following tests were carried out:

- (1) Independent samples *t* test of significance was used when comparing between two means.
- (2)  $\chi^2$  test of significance was used in order to compare proportions between two qualitative parameters.

- (3) Pearson's correlation coefficient ( $r$ ) test was used for correlating data.
- (4)  $P$  value less than 0.05 was considered significant.

## Results

The present study was conducted on 40 RA patients (80 knees), and 20 healthy participants (40 knees) as a control group. The patients' characteristics are presented in Table 1.

The patients were divided according to disease activity score DAS-28 into two groups.

### Group I (in a stage of low disease activity)

There were 20 patients (40 knees), and they were subdivided into the following subgroups: Subgroup IA: This subgroup comprised nine patients (18 knees) with knee flexion deformity, seven female patients and two male patients, with ages ranging between 45 and 57 years with a mean age of  $52.44 \pm 3.54$  years; their disease duration ranged from 5 to 23 years with a mean duration of  $13.44 \pm 5.85$  years, and their flexion deformity ranged from 10 to  $30^\circ$  with mean flexion deformity of  $15^\circ$ .

Subgroup IB: this subgroup comprised 11 patients (22 knees) without knee flexion deformity, nine female patients and two male patients, with their ages ranging between 32 and 64 years with a mean age of  $47.64 \pm 10.25$  years; their disease duration ranged from 3 to 22 years with a mean duration of  $8.8 \pm 6$  years.

**Table 1 Rheumatoid arthritis patients' characteristics**

| Variables                                 | RA patients (N=40)   |
|---|----------------------|
| Age [range (mean)] (years)                | 29–64 (47±10.01)     |
| Disease duration (years)                  | 3–23 (11±6.63)       |
| Sex [n (%)]                               |                      |
| Female patients                           | 33 (82.5)            |
| Male patients                             | 7 (17.5)             |
| RF positive [n (%)]                       | 25 (62.5)            |
| Anti-CCP positive [n (%)]                 | 28 (70)              |
| ESR [range (mean)] (mm/h)                 | 11–45 (28.38±10.34)  |
| Medical treatment (last 6 months) [n (%)] |                      |
| Methotrexate                              | 23 (57.5)            |
| Antimalarial                              | 37 (92.5)            |
| Leflunamide                               | 21 (52.5)            |
| NSAIDs                                    | 40 (100)             |
| Pain according to VAS [n (%)]             |                      |
| Mild (<OR=5)                              | 21 (52.5)            |
| Moderate (6–7)                            | 19 (47.5)            |
| DAS-28 [range (mean)]                     | 1.5–3.19 (2.37±0.52) |

DAS-28, 28-joint disease activity score; CCP, cyclic citrullinated peptide; ESR, erythrocyte sedimentation rate; RA, rheumatoid arthritis; VAS, visual analogue scale.

### Group II (in a stage of remission)

There were 20 patients (40 knees) in this group, all without knee flexion deformity; there were 17 female patients and three male patients, with their ages ranging between 27 and 61 years, with a mean age of  $41.95 \pm 9.76$  years, and their disease duration ranged from 3 to 22 years, with a mean duration of  $7.8 \pm 6.05$  years.

### The control group

The control group comprised 20 apparently healthy participants (40 knees), 16 (80%) female patients and four (20%) male patients; their ages ranged between 29 and 56 years) with a mean age of  $43.15 \pm 7.86$  years, matching in age with RA patients. Table 2 shows their PT properties, quadriceps muscle power and 50 FWT results. The control participants' PT elongation was considered as the standard for evaluation; the mean was  $2.81 \pm 0.41$  mm (100%).

On comparing the biomechanical properties of the PT between patient groups and the control group, with regard to subgroup IA, there was increased elongation of PT by 31.3%, with a mean of  $4.09 \pm 0.69$  mm, which indicates reduction of PT stiffness, with high significant difference between subgroup IA and the control group ( $P < 0.001$ ). However, subgroup IB showed increased elongation of PT by 20.9%, with a mean of  $3.54 \pm 0.57$  mm, with a significant difference between subgroup IB and the control group. Moreover, there was increased elongation of PT in group II by 15.66%, with a mean of  $3.32 \pm 0.49$  mm, with a significant difference between group II and the control group (Figs 1–3).

As regards PT CSA, there was no significant difference between the RA patient groups and the control group ( $P > 0.05$ ). The mean CSA of the control group was  $90.62 \pm 3.00$  mm<sup>2</sup>, subgroup IA was  $90.28 \pm 3.31$  mm<sup>2</sup>, while the mean of subgroup IB was  $89.70 \pm 5.78$  mm<sup>2</sup>, and the mean of group II was  $90.11 \pm 5.52$  mm<sup>2</sup>.

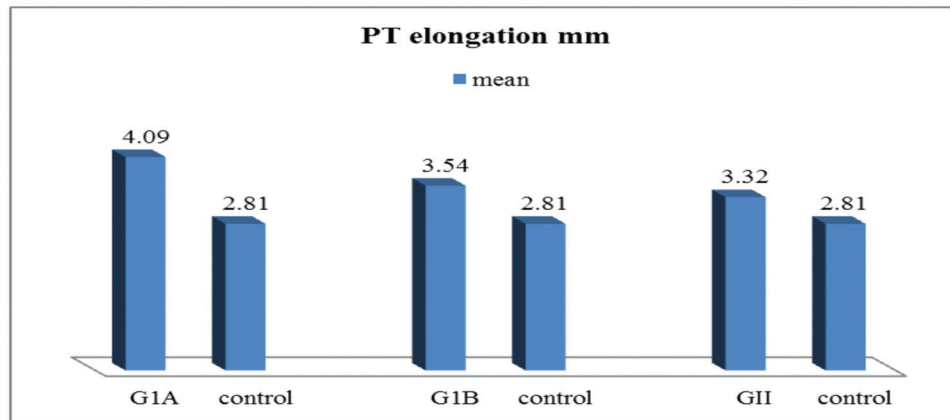
**Table 2 Quadriceps' muscle strength, patellar tendon elongation, patellar tendon cross-sectional area, and 50-foot walk test of the control participants**

|                           | Minimum | Maximum | Mean  | SD   |
|---------------------------|---------|---------|-------|------|
| Quadriceps strength (kg)  | 32      | 38      | 35.40 | 1.26 |
| PT elongation (mm)        | 1.8     | 3.6     | 2.81  | 0.41 |
| PT CSA (mm <sup>2</sup> ) | 84.1    | 99.8    | 90.62 | 3.00 |
| 50 FWT (s)                | 9       | 18.2    | 13.83 | 2.69 |

50 FWT, 50-foot walk test; CSA, cross-sectional area; PT, patellar tendon.

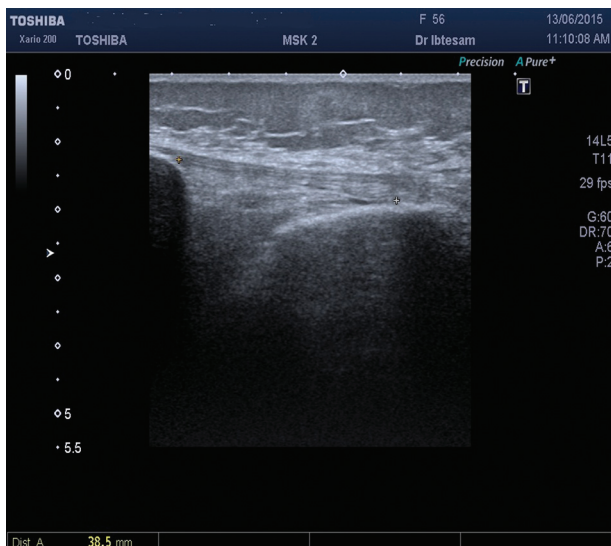


Figure 1



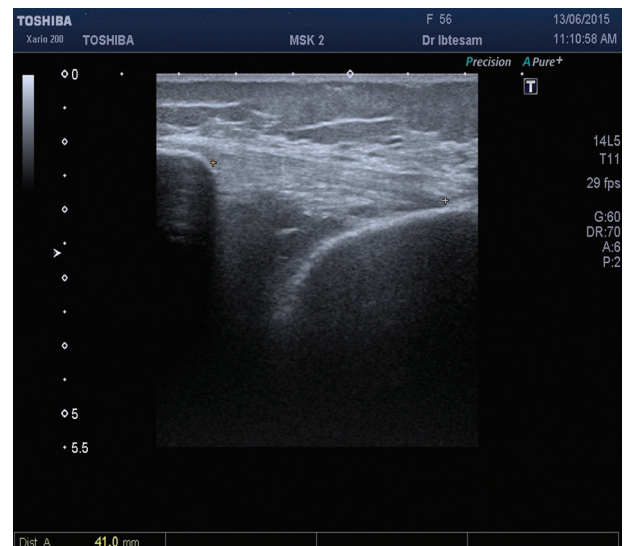
Shows the mean PT elongation (difference in length in mm after MVC) of subgroup IA, subgroup IB, and group II relative to the control group. MVC, maximal voluntary isometric knee extension contractions; PT, patellar tendon

Figure 2



Ultrasound of the PT at rest (measured from the lower pole of the patella to the tibial tuberosity). PT, patellar tendon.

Figure 3



PT deformation during maximum voluntary MVC. MVC, maximal voluntary isometric knee extension contractions; PT, patellar tendon.

The HAQ of subgroup IA ranged from 1 to 1.9, with a mean of  $1.31 \pm 0.30$ , which is severely impaired, while HAQ of subgroup IB ranged from 0.3 to 1), with a mean of  $0.61 \pm 0.27$ , which is impaired, and, for group II, it ranged from 0 to 0.9, with a mean of  $0.36 \pm 0.3$ , which is impaired (Table 3).

On comparing the quadriceps muscle strength between the RA patient groups and the control group, all patient groups showed a reduction of quadriceps' muscle strength with a significant to highly significant difference between them and the control group (Fig. 4).

Concerning the physical performance of the lower limbs, all patient groups showed a delay in walking

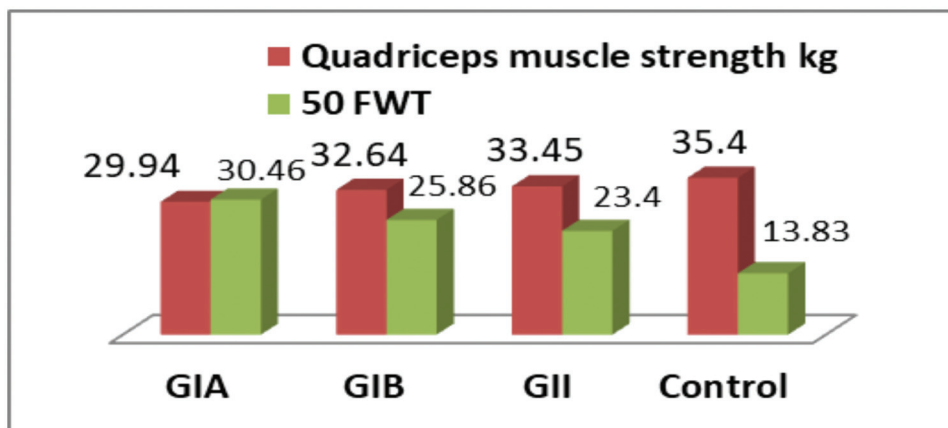
**Table 3 Health Assessment Questionnaire of all rheumatoid arthritis patient groups**

|             | Mean $\pm$ SD   |                   | Range |
|-------------|-----------------|-------------------|-------|
| Subgroup IA | $1.31 \pm 0.30$ | Severely impaired | 1–1.9 |
| Subgroup IB | $0.61 \pm 0.27$ | Impaired          | 0.3–1 |
| Group II    | $0.36 \pm 0.3$  | Impaired          | 0–0.9 |

time in the 50 FWT time by 54.6% for subgroup IA, 46.5% for subgroup IB and 40.9% for group II, as compared with the control group, with highly significant difference between all patient groups and the control group (Fig. 4).

Posturographic evaluation, as a part of lower limb functional evaluation showed that, with regard to

Figure 4



Comparison between group IA, group IB, group II, and control group with regard to mean of quadriceps' muscle strength in kg and 50 FWT in seconds. 50 FWT, 50-foot walk test.

**Table 4 Comparison between rheumatoid arthritis patients' subgroup IA, subgroup IB, and group II relative to the control group with regard to the posturographic evaluation using smart balance master system tests (unilateral stance test, step up over test, and sit to stand test)**

| Test                   | Test parameters            | Control group (mean±SD) | Subgroup IA (mean±SD) | Subgroup IB (mean±SD) | Group II (mean±SD) | P value of GIA and C | P value of GIB and C | P value of GII and C |
|------------------------|----------------------------|-------------------------|-----------------------|-----------------------|--------------------|----------------------|----------------------|----------------------|
| Unilateral stance test | REO (deg./s)               | 0.9±0.3                 | 3.21±0.45             | 2.59±0.66             | 1.69±0.28          | <0.001 HS            | <0.001 HS            | <0.001 HS            |
|                        | LEO (deg./s)               | 0.9±0.2                 | 3.59±0.56             | 2.12±0.75             | 1.72±0.49          | <0.001 HS            | <0.001 HS            | <0.001 HS            |
|                        | REC (deg./s)               | 2.1±1.1                 | 4.06±0.47             | 3.52±0.70             | 2.90±0.54          | <0.001 HS            | <0.001 HS            | <0.05 S              |
|                        | LEC (deg./s)               | 2.4±1.1                 | 4.26±0.67             | 3.24±0.72             | 2.97±0.40          | <0.001 HS            | <0.001 HS            | <0.05 S              |
| SUO test               | Lift up index (%)          | 43.38±4.86              | 24.31±2.19            | 32.26±7.64            | 32.90±6.85         | <0.001 HS            | <0.001 HS            | <0.001 HS            |
|                        | Movement time (s)          | 1.39±0.31               | 3.71±0.71             | 1.97±0.49             | 1.88±0.62          | <0.001 HS            | <0.05 S              | <0.05 S              |
|                        | Impact index (%)           | 48.13±2.88              | 32.63±5.73            | 38.05±9.92            | 42.44±9.47         | <0.001 HS            | <0.05 S              | <0.05 S              |
| Sit to stand test      | Weight transfer (s)        | 0.37±0.12               | 1.96±0.29             | 0.67±0.45             | 0.50±0.50          | <0.001 HS            | <0.001 HS            | <0.001 HS            |
|                        | Rising index (%)           | 29.50±5.73              | 12.98±4.13            | 13.14±4.24            | 14.28±3.91         | <0.001 HS            | <0.001 HS            | <0.001 HS            |
|                        | COG sway velocity (deg./s) | 3.73±1.17               | 7.97±1.39             | 5.56±0.83             | 5.47±0.56          | <0.001 HS            | <0.001 HS            | <0.001 HS            |

COG, center of gravity; LEC, left eye closed; LEO, left eye open; REC, right eye closed; REO, right eye open.

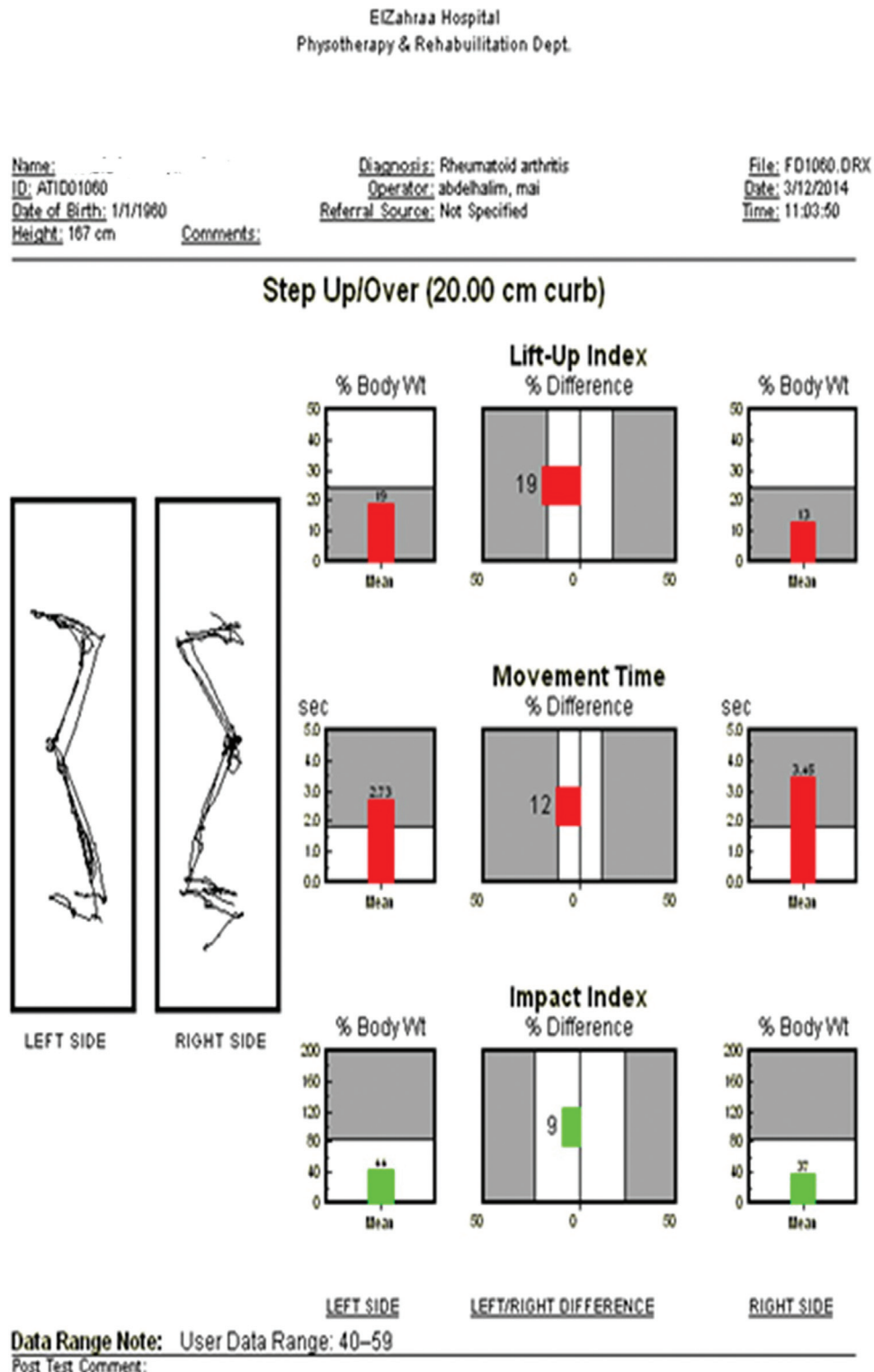
the UST, all patient groups showed increased COG sway velocity in right eye open (EO), right eye closed (EC), left EO, and left EC conditions in comparison with the healthy control group, with significant to highly significant difference between all the patient groups and the control group (Table 4).

Subgroup IA patients showed more increase of sway velocity by 74.2% and 78.3% with regard to right EO and left EO conditions, respectively, while it increased by 51.2 and (50.9%) with regard to right EC and left EC, respectively, due to improper alignment of the lower limb joints and lag of knee extension (Table 4).

As regards the SUO test, the mean lift up index of subgroup IA was 24.31±2.19%, and decreased by 36.8% relative to the control group; the mean for subgroup IB was 32.26±7.64%, and it decreased by 23.4% relative to the control group; the mean for group II was 32.90±6.85%, and it decreased by 23.2% relative to the control group.

While the mean movement time for subgroup IA was 3.71±0.71 s and increased relative to the control group by 56.9%, the mean for subgroup IB was 1.97±0.49 s, and it increased relative to the standard evaluation by 29.3%; the mean for group II was 1.88±0.62 s, and it increased by 26.6% relative to the control group.

Figure 5



Step up and over test report of an RA patient showing impaired lift up index and delayed movement time. RA, rheumatoid arthritis.

The mean impact index of subgroup IA was  $32.63 \pm 5.73\%$ , and it decreased relative to the control group by 32.6%; the mean for subgroup IB was  $32.63 \pm 5.73\%$ , and it decreased relative to the standard evaluation by 32.6%; the mean for group II was  $42.44 \pm 9.47\%$ , and it decreased relative to the control. Significant to highly significant difference was found between all patient

groups and the control group in all of the evaluated parameters of the SUO test (Table 4 and Fig. 5).

Concerning the STS test, subgroup IA showed prolongation of the time to transfer weight, with a mean of  $1.96 \pm 0.29$  s, and it increased by 81.1%, relative to the control group; for subgroup IB, it was 0.67

$\pm 0.45$  s, and it increased by 44.8% relative to the controls; for group II, it was  $0.50 \pm 0.50$  s, and the time increased relative to the controls by 26%.

The mean rising index of subgroup IA was  $12.98 \pm 4.13\%$ , and it decreased by 56% relative to the controls; for subgroup IB, it was  $13.14 \pm 4.24\%$ , and it decreased by 55.5% relative to the control group; for group II it was  $14.28 \pm 3.91\%$ , and it decreased by 51.6% relative to the control group. The mean COG sway velocity of subgroup A was  $7.97 \pm 1.39^\circ/\text{s}$ , and it increased by 53.2% in comparison with the control; for subgroup IB, it was  $5.56 \pm 0.83^\circ/\text{s}$ , and it increased by 31.8% in comparison with the controls; for group II, it was  $5.47 \pm 0.56^\circ/\text{s}$ , and it increased relative to the standard evaluation by 32.9% (Table 4). A linear positive correlation was found between PT elongation and 50 FWT, STS test parameters (weight transfer, COG sway), movement time of the SUO test, and UST parameters (sway velocity during EO and EC conditions) in RA patients.

A linear negative correlation was found between PT elongation and lift up index and impact index parameters of the SUO test.

A linear negative correlation was found between quadriceps' muscle strength and 50 FWT, parameters of the STS test (weight transfer and COG sway), parameters of the UST (sway velocity during EO and EC conditions), and movement time of the SUO test in RA patients. While a linear positive correlation was found between quadriceps' muscle power and SUO test parameters (lift up and impact index) and STS test parameter (rising index) in RA.

## Discussion

Tendons are extensible structures that reversibly deform when a mechanical load is applied [10]. Tendon properties influence motor control, joint stability, and the ability to make postural adjustments and, consequently, play a major role in maintaining balance and preventing falls [2,6,13]. The mechanical properties of tendons are essential for proprioception and for the reflex responses involved in the rapid adjustment of muscle tension to positional changes, as well as the stored elastic strain energy, which is key to efficient locomotion [6].

This can be explained by the fact that the reduced stiffness of the tendon reduces muscle fascicle length changes in response to passive joint movements and

thereby impairs recognition of small movements by the muscle spindle [14].

The extent of elongation of a tendon to loading, that is, the tendon stiffness influences the performance of the attached muscle, and thereby determines the magnitude and speed with which the force is transmitted from the muscle to the bone. Therefore, stiffer tendons result in increased and faster force production, whereas the opposite effect is seen in more compliant tendons, as increased elongation of the tendon requires further shortening of the muscle fibers, causing electromechanical delay [3]. This reduction of the tendon stiffness was correlated with decreased neuromuscular performance, either static as postural stability or dynamic as walking [15].

RA is a chronic autoimmune arthritis characterized by joint inflammation and progressive joint destruction and is accompanied by impaired physical function. Inflammation also affects other musculoskeletal structures including tendons; this leads to chronic alterations in the biomechanical function of the tendon–muscle complex [2].

The aim of this study was to investigate the biomechanical properties of the human PT in RA patients and, consequently, to assess the effect of the changes in PT properties (tendon stiffness) on lower limb function and performance, as compared with healthy age-matched and sex-matched control participants, by using ultrasonography to determine PT elongation and CSA, and measure knee extensor strength. However, the assessment of lower limb functional performance was carried out clinically by 50 FWT and by using smart balance master system, through UST, STS, and SUO tests.

With regard to PT elongation, all the RA patients (80 knees) showed increased PT elongation more than the control group. This increased PT elongation of all groups of RA patients indicates a reduction of PT stiffness relative to the control group. In a previous research, they studied the changes of Achilles tendon stiffness in patients with Achilles tendinopathy; they found that tendinopathy weakens the mechanical and material properties of the tendon. Tendinopathic tendons had more increased elongation and lower tendon stiffness relative to the control group [16].

The reduction of tendon stiffness in RA patients is the result of destruction of the tendon and the tenosynovium by proinflammatory cytokines, supported by a research study that studied the role of proinflammatory cytokines,



VEGF and MMPs on the destruction of tendons of RA, by cultured specimens of RA synovium (joint synovium, invasive tenosynovium, and encapsulated tenosynovium) *in vitro*; they found a high level of proinflammatory cytokines and proteolytic enzymes in the tenosynovium of RA similar to joint synovium, and that the proteolytic enzymes are produced in higher amounts by invasive tenosynovium compared with encapsulating tenosynovium, which explained the worse prognosis and increased rupture rate associated with invasive tenosynovitis in RA [5]. Another study added that RA tenosynovitis and joint synovitis exhibit indistinguishable histological features, including hyperplasia of the synovial lining layers and infiltration of leukocytes, largely CD4+ T cells and CD68+ macrophages [17].

A previous study found that all RA patients in their study had stable low DAS-28, and showed increased PT elongation at maximal voluntary isometric knee extension contractions, which indicates the reduction of PT stiffness relative to the control group in agreement with our results [2]. In another study, despite the stabilization of disease activity, there was no recovery of the PT biomechanics, wherein tendon stiffness is reduced, although there was a resolution of disease activity, which is likely due to local and systemic effects of cytokines on the tendon [18].

The current study showed an insignificant difference in PT CSA between the RA patient groups and the control group. This is in agreement with previous studies, which found that PT CSA of RA patients was  $91.4 \pm 4.5 \text{ mm}^2$ , and, of the healthy control group, it was  $91.3 \pm 2.6 \text{ mm}^2$ , with no significant difference between the two groups [2,18]. When they compared CSA of PT between ankylosing spondylitis patients and RA patients, they reported increased PT CSA of ankylosing patients more than that of RA patients, and they explained that it was due to the different pathology of both diseases, which was characteristic enthesal inflammatory changes of perienthesal swelling and edema and bone marrow edema associated with knee synovitis in spondyloarthropathies. These changes are not seen in RA [2].

A former research studied the relation between the mechanical properties of PT and quadriceps muscle strength in humans; they found that there is a positive correlation between both of them [19].

With regard to quadriceps muscle strength, our results showed that there was a reduction of quadriceps muscle

strength of all RA patient groups relative to the control group. Group IA showed the greatest reduction of strength. These results were supported by two studies, which stated that RA quadriceps muscle strength was weaker than that of healthy participants. They suggested that there is abnormal afferent information from articular mechanoreceptors, occurring as a result of joint damage, effusion, pain, and/or psychological factors, which decreases quadriceps motor neuron excitability via neurophysiological pathway in the spinal cord and supraspinal centers, and that this impairs voluntary activation, which is manifested as quadriceps' weakness [20,21].

A prior research work studied the physiological properties of the skeletal muscle in 23 stable RA patients, and they concluded that physiological muscle properties were preserved in patients with stable RA [22].

The current study assessed the functional performance of the lower limb in RA patients by the 50 FWT, UST, SUO test, and STS test.

On performing the 50 FWT, there was a highly significant difference between RA patient groups and the control group. Group IA showed the worst performance in 50 FWT than those with low disease activity or remission without knee flexion. GIA showed more delay in walking time, as flexion contracture has an adverse effect on function. Flexed knees require a considerable expenditure of energy by the quadriceps, with a consequent increase in the forces across the patellofemoral and tibiofemoral joints [23].

Our results are supported by an earlier study. It explained this delayed walking time by pain, stiffness, muscle weakness, and fear of falling in RA patients. This requires a great cognitive effort in these patients to maintain stability [24].

Our results are supported by several former studies [25–27] that reported that RA patients walk slower than healthy controls. Another study explained that the impairment of physical functional performance in 50 FWT was associated with quadriceps weakness and proprioception deficits in RA patients [20].

A prior research investigated the properties of skeletal muscles in RA patients and its effect on the physical performance of the patients; they found that there is a delay in walk time in RA patients relative to the control due to muscle weakness [22]. Later, they continued

their studies on muscle–tendon complex, especially PT, and they concluded that alterations of tendon properties play a role in this delay of walking time in RA patients [2,18].

We also found a negative correlation between the walking time of our RA patients and their quadriceps muscle strength and PT stiffness. This agrees with a former study that found that the knee extensor strength is negatively correlated with walking time [28].

UST (US-EO and US-EC) results in our study showed that there was an evident difference as regards COG sway in both EO and EC conditions for RA patient groups relative to the controls of the same age and sex. The presence of postural sway at US-EO reveals instability due to lower limb joints, tendon properties, and muscle weakness affection in RA. Moreover, the increased sway during US-EC denotes altered proprioception, which cannot be compensated when eyes are closed. Our results agreed with Rome *et al.* [24] who studied static postural stability in RA patients and reported that RA patients might be markedly dependent upon visual information to maintain anterior–posterior stability, as stability was compromised with visual deprivation.

Several studies documented that there was a poorer performance of RA patients for this task in comparison with healthy controls, which was linked to the changes of tendon–muscle complex mechanical properties [3,18,22]. Other authors documented a relationship between compromised postural stability and tendon stiffness: the muscle strength and the mechanical properties of the tendon had a significant association with postural sway in the UST [6].

RA patients in the current study showed significant deterioration in the lift up index, movement time, and impact index of the SUO test in comparison with the normal standard. The lift up and impact indices were more obviously reduced, and movement time was more prolonged in GIA; this is possibly secondary to joint movement delay and muscles' inco-ordination of the lower extremity, which affects joint trajectory of the lower limbs, in addition to the reduction of PT stiffness.

In the STS test, our RA patients showed significant deterioration in weight transfer, rising index and sway velocity of COG in relation to the normal standard, with more affection of GIA. This can be attributed to the presence of pain and fear of falling secondary to the adverse effect of RA on muscle–tendon mechanical

properties and affection of proprioception. A former study reported that the ambulatory impairments present in RA patients force them to modify activities due to fear of falling, resulting in increased time demands to perform STS and foot up and go tests [34]. Another study added that pain increased the weight transfer time of the STS, as patients transfer from a sitting to a standing position in a more cautious manner. Moreover, deficits in the lower limb proprioception and muscle strength of RA patients play a role in balance impairment [29].

RA patients with low disease activity in this study showed more tendon elongation, and they were the worst with regard to the quadriceps muscle strength; they showed the worst performance in all lower limb functional performance tests. This is in agreement with a previous study, which reported that disease activity and functional disability (HAQ) in patients with RA, correlated with worse performance in STS and foot up and go tests, due to pain during disease activity [30]. Other authors explained the reduction of objective physical function of RA patients by using STS and foot up and go tests in relation to the controls by RA effect on PT properties [2]. Thus, treatment of RA is directed to suppressing inflammation, with the aim of eliminating synovitis and establishing a state of remission. Remission is regarded as the ideal therapeutic target for patients with RA, because further joint damage and disability should be prevented and function and quality of life maintained [31].

In this study, RA patients with flexion deformity (GIA) showed the worst performance in all physical function tests, which is supported by a prior study that documented a relationship between the range of motion and the disability and found that the more the restriction of range of motion the more the disability [32]. In addition, articular damage may reduce quadriceps motoneuron excitability, which decreases voluntary quadriceps activation, thus contributing to quadriceps weakness, and diminishes proprioceptive acuity. The arthrogenic impairment in quadriceps sensorimotor function and decreased postural stability were associated with reduced functional performance [33].

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## Conclusion

As a consequence of the inflammation of the PT and peritendinous tissues in RA patients, affection of the biomechanical properties of the tendon becomes a common pathological lesion in patients with RA.

The present study revealed that the adverse changes in PT mechanical properties in RA patients may contribute to the impaired physical function. Knee flexion deformity also impairs functional performance in RA.

RA disease activity influences PT stiffness, which reflects the systemic effect of RA on the PT, and is related to worse functional performance.

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#### Conflicts of interest

There are no conflicts of interest.

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