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## The influence of load on tendons and tendinopathy

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*Document Version*

Publisher's PDF, also known as Version of record

*Publication date:*

2019

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Maciel Rabello, L. (2019). *The influence of load on tendons and tendinopathy: Studying Achilles and patellar tendons using UTC*. [Thesis fully internal (DIV), University of Groningen]. Rijksuniversiteit Groningen.

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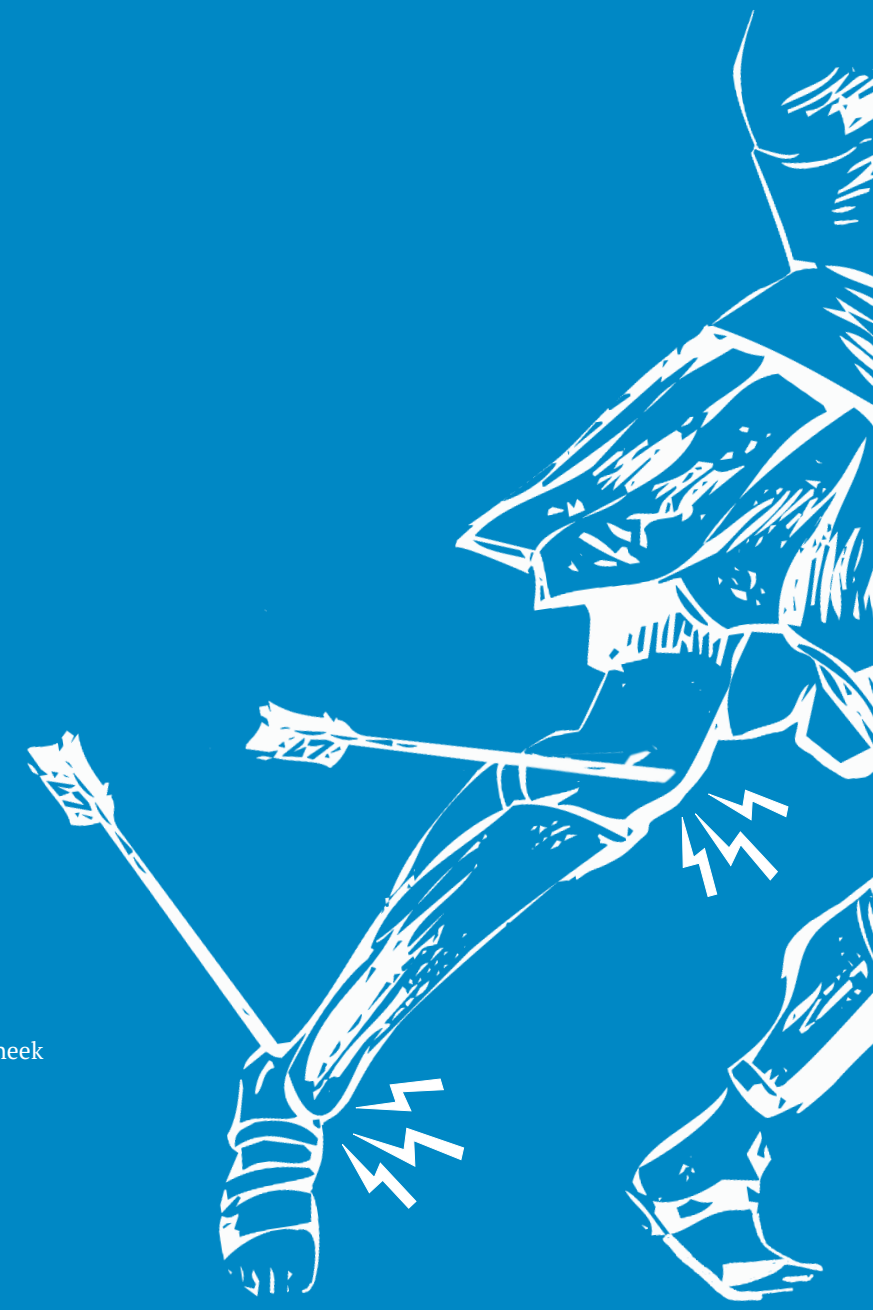
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# Chapter 9

**Pain, function and tendon structure – a prospective cohort study into their association in patients with Achilles or patellar tendinopathy**

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Submitted



## Abstract

**Purpose:** To investigate the association between clinical examination (pain and function) and tendon structure (ultrasound tissue characterisation [UTC] echo types) after conservative treatment of patients diagnosed with chronic Achilles tendinopathy (AT) or patellar tendinopathy (PT).

**Methods:** Fifteen patients diagnosed with AT and twenty with PT were recruited. All patients underwent conservative treatment based on pain and load management, loading exercise, patient education and/or extracorporeal shockwave therapy (ESWT). Pain, function and tendon structure measures were taken at baseline and at short-term follow-up (within six months). To measure pain and function, the Victorian Institute of Sport Assessment (VISA) questionnaire was used. Tendon structure was assessed using the UTC with percentage of echo types I-IV as outcomes.

**Results:** For both AT and PT, VISA score improved (significantly in the AT group) and percentages of echo types showed no significant changes after treatment. It was observed that a higher VISA-A score was moderately associated with a decrease in percentage of echo type II ( $p = 0.01$ ). No other significant associations were observed in either group. Individual analysis showed high agreement between changes in VISA score and changes in echo types I and III for the AT group and echo types I and IV for the PT group.

**Conclusion:** Analysing the association between pain and function and tendon structure based on group or individuals analyses provide different results. The individual analyses were in line with the expected changes after treatment; patients that improved clinically showed an increase of the aligned fibrillar matrix (echo type I) and a reduction in the disorganised structure (echo types III or IV). However, this agreement was not observed in all patients (approximately 50%), which stresses the importance of performing both clinical and imaging examinations.

**Key words:** questionnaire, tendon structure, Achilles tendinopathy, jumper's knee

## Introduction

Achilles and patellar tendinopathy are commonly observed in the clinical practice of doctors and physiotherapists. Most patients with Achilles tendinopathy (AT) are from an athletic population; incidence is high among runners,<sup>1</sup> but sedentary people can also be affected.<sup>2</sup> Patellar tendinopathy (PT) is mainly observed among recreational or elite athletes, with a high incidence in sports that require explosive extension of the knee or eccentric flexion, like volleyball and basketball.<sup>3,4</sup> Usually the first choice of treatment for patients diagnosed with AT<sup>5-7</sup> or PT<sup>8</sup> is conservative treatment. This generally leads to pain reduction and improvement in function in patients diagnosed with AT,<sup>9,10</sup> but results for patients with PT are not consistent.<sup>8,11-15</sup>

To monitor and evaluate the clinical effect of treatment clinicians can use the Victorian Institute of Sport Assessment (VISA) questionnaire, which assesses changes in the pain, function and sport domains. This instrument is considered a valid and reliable index of the severity of Achilles or patellar tendinopathy.<sup>14,15</sup>

Clinicians might also be interested in potential changes in tendon structure. Conventional imaging tools like ultrasound (US) and magnetic resonance imaging (MRI) can be used to assess these changes. Interpretation of the outcomes obtained by these imaging methods is based on measurements of tendon dimensions.<sup>16</sup> To objectively quantify tendon structure, ultrasound tissue characterisation (UTC) is available.<sup>17</sup> UTC describes the investigated tendon through four different echo types (I-IV), where echo type I is the most stable echo pattern and echo type IV the least stable.

Results of studies using conventional imaging tools show that patients who report an improvement in pain and function after treatment do not necessarily show improvement in tendon structure at short-term follow-up.<sup>18,19</sup> For UTC, there is a paucity of studies investigating the association between clinical outcomes and tendon structure. To the best of our knowledge, only three studies have been conducted: two investigating patients with midportion AT who performed eccentric exercise therapy combined (or not) with injections,<sup>20,21</sup> and one study that included patients diagnosed with PT who followed an isometric or isotonic exercise programme.<sup>22</sup> All three studies found a poor association between clinical outcomes and UTC echo types (I-IV). Different factors, such as tendinopathy location, follow-up period and treatment regimen could influence this association, which urges more research in the field.<sup>19</sup> The aim of this study was therefore to investigate the association between clinical and imaging outcomes using UTC after conservative treatment of patients diagnosed with chronic AT or PT.

## Methods

### Participants

Patients included in this cohort study visited the Tendinopathy Clinic at the Sports Medicine Center of University Medical Center Groningen (UMCG) in the Netherlands. Patients were referred to the clinic by a general practitioner or a specialist. The diagnosis of midportion AT or PT was made by an expert sports physician, based on clinical examination. Imaging examination (MRI or ultrasound) was performed to exclude other diagnoses such as tears, but the results of those tests are not reported in this study. The study was approved by the medical ethical committee of the University of Groningen, and patients signed an informed consent.

### Procedure

After being diagnosed with AT or PT, all patients included in this study underwent conservative treatment based on a combination of: a) education about their tendon problem, pain and load management, b) therapeutic loading exercises, and/or c) extracorporeal shockwave therapy (ESWT). Patients treated with injections or surgery were excluded. Clinical and imaging outcomes were measured at baseline and at short-term follow-up (within six months after the baseline visit).

### Measurements

VISA questionnaire

Patients completed the VISA questionnaire at both baseline and follow-up visits. This is a self-reported outcome measure that includes questions about pain, function and sports activity, and is considered a valid and reliable index of the severity of Achilles or patellar tendinopathy.<sup>14,15</sup> A lower score indicates more symptoms and greater limitation of function and activity. The Dutch versions of the VISA-A<sup>23</sup> and VISA-P<sup>24</sup> questionnaire were used.

### UTC examination

UTC was used to assess the changes in tendon structure between baseline and follow-up visits. The scans were performed by a single experienced examiner (LMR). Images were acquired using a 7 MHz to 10 MHz linear ultrasound transducer (SmartProbe 12L5-V, Terason 2000+; Teratech; Burlington, MD, USA) positioned in a tracking device (UTC Tracker, UTC Imaging, Stein, The Netherlands) that moved automatically along the tendon long axis over a distance of 12 cm recording regular images at intervals of 0.2 mm. Transducer tilt, angle, gain, focus and depth were standardised by the tracking device. Images from the sagittal, coronal and transverse planes were compiled to create a 3D view of the tendon.

A standardised protocol was used to perform the UTC scan of the Achilles and patellar tendons. The Achilles tendon was scanned with the patient lying prone on the examination table with feet hanging over the edge and the ankle in maximal passive dorsiflexion.<sup>25</sup> The patellar tendon was scanned with the patient lying supine on the examination table and the knee positioned in an angle of approximately 100° flexion. The tracking device was placed perpendicular to the long axis of the tendon (Achilles or patellar), ensuring that the calcaneus or the inferior pole of the patella was observed on the image. This bony landmark also served as reference point for the analysis. The Achilles and patellar tendons

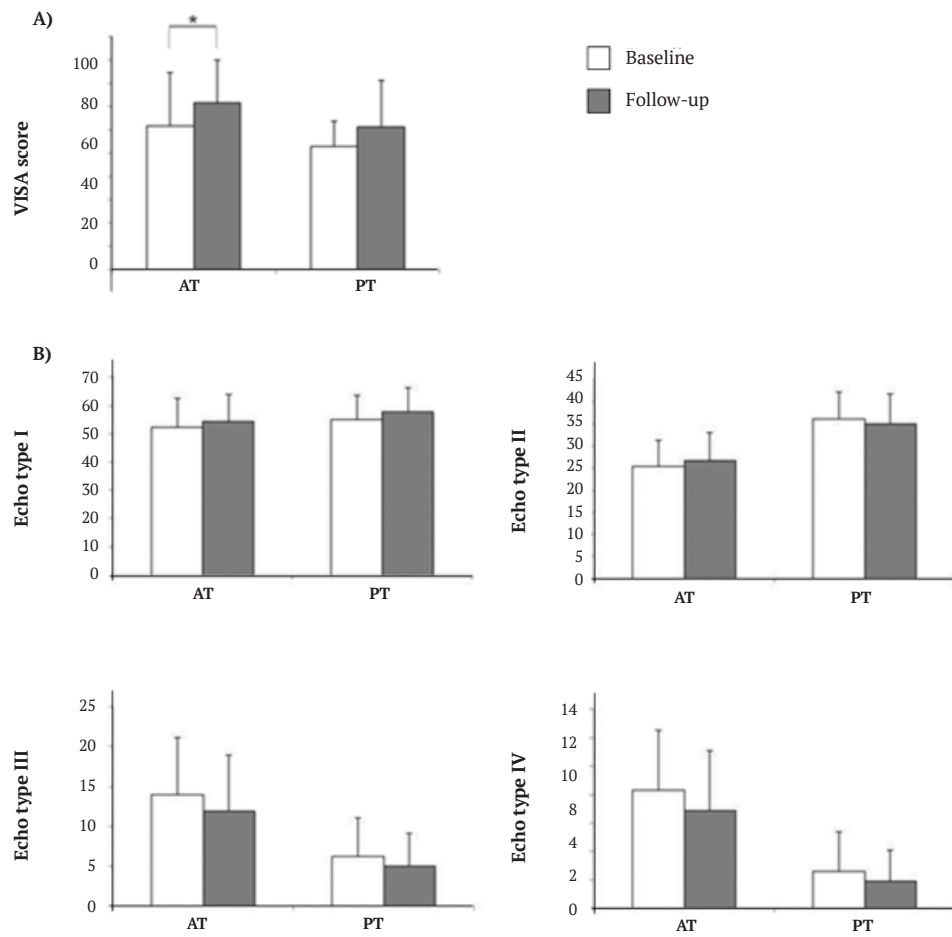
were scanned from distal to proximal and from proximal to distal. Coupling gel between transducer, standoff pad, and skin was applied to ensure maximum contact. The recorded images were stored via the UTC software (UTC v1.05, UTC Imaging). The UTC algorithm quantified echo types across a rolling window of 17 continuous images.

Tendon structure was quantified from a region of interest (ROI) that was selected around the border of the tendon in the sagittal plane. For both Achilles and patellar tendons, ROIs were contoured at intervals of 5 mm. For patients diagnosed with midportion tendinopathy, nine ROIs were contoured from 2 cm above the calcaneus to 6 cm proximally. For patients diagnosed with patellar tendinopathy five ROIs were contoured from the apex of the patella to 2 cm distally.

The outcomes obtained from the UTC analysis are four valid echo types: echo type I: intact and aligned tendon bundles; echo type II: less integer and waving tendon bundles; echo type III: mainly fibrillar tissue; echo type IV: a mainly amorphous matrix with loose fibrils, cells or fluid.<sup>17</sup>

### Statistical analysis

Descriptive statistics with means and standard deviations (SD) were used. Non-parametric tests were used since the data were not normally distributed. The related-samples Wilcoxon signed rank test was used to compare baseline and follow-up data for all echo types (I-IV). A Bonferroni correction was applied to adjust for multiple testing; the alpha level was set at 0.01. Correlations between VISA score and echo types were analysed using Spearman's correlation coefficients. Correlation coefficients were defined as: poor (0.00 to 0.30), low (0.30 to 0.50), moderate (0.50 to 0.70), high (0.70 to 0.90) and very high (0.90 to 1.00).<sup>26</sup> For an individual analysis of the correlations, lines demonstrating the minimum clinically important change (MCID) for the VISA score and lines demonstrating the minimal detectable changes (MDCs) for each echo type were drawn. For the VISA-A and VISA-P scores, a change of 12 points<sup>27</sup> and 13 points<sup>28</sup> respectively is considered as an MCID. For the UTC of midportion Achilles tendons the minimal detectable changes (MDCs) were 2.4%, 2.1%, 1.3% and 0.8% for echo types I-IV, respectively. For the patellar tendons the MDCs were 4.0%, 3.4%, 1.2% and 0.4% for the four echo types, respectively. To determine the individual percentages of agreement between changes in VISA score and changes in echo types (percentages), three different areas in the correlation charts were highlighted, together called the 'agreement zones': 1. Improvement zone: area referring to an improved VISA score above the MCID, an increase of echo types I and II, and a decrease of echo types III and IV (above the MDC); 2. No-change zone: area referring to the changes in VISA score and echo types below the MCID and MDC, respectively; and 3. Worsening zone: area referring to a lower VISA score (above the MCID), a decrease of echo types I and II, and an increase of echo types III and IV (above the MDC). Patients who improve clinically above the MDC are expected to increase above the MCID in percentage of echo types I and II and decrease above the MCID in percentage of echo types III and IV. On the other hand, patients who got worse clinically (above the MDC) were expected to decrease in percentage of echo types I and II and increase in percentage of echo types III and IV (above the MCID). Those patients who show no changes in clinical outcomes above the MDC are expected to show no changes in tendon structure above the MCID. The percentage of patients in the agreement zones represents those who reported changes as described above. For example, if 10 patients improve their VISA score above the MCID and four of those patients increase in percentage of echo type I above the MDC, 40% of the patients are in the Improvement zone.



**Figure 1.** A) VISA score (VISA-Achilles and VISA-Patellar) at baseline and follow-up. B) Echo types (I-IV) percentage measured with UTC, at baseline and follow-up. NOTE: Y axis differs per echo type.

**Results**

A total of 35 patients were included in this study. Fifteen patients (nine males and six females) were included in the AT group, with a mean age of 47.5 (10.8) years and a mean follow-up period of 3.3 (0.80) months. For the PT group, a total of 20 subjects were included (17 males and three females) with a mean age of 28.3 (9.2) years and a mean follow-up period of 3.5 (1.3) months.

**VISA score**

Patients diagnosed with AT showed significant improvement in VISA-A score between baseline and follow-up ( $p = 0.008$ ). In the group of patients diagnosed with PT, no significant changes were observed between baseline and follow-up in VISA-P score ( $p = 0.108$ ). In both the AT and PT groups the mean improvement observed was lower than the MCID. Changes in VISA score are shown in Figure 1A.

**Tendon structure**

Investigating the changes in percentage of echo types (I-IV) over the follow-up period, no significant changes were observed for either group. The echo type percentages are shown in Figure 1B.

**Relation between tendon structure and VISA score**

For both groups, AT and PT patients, the associations between changes in VISA score and changes in percentages of echo types (I-IV) are shown in Figures 2 and 3. For patients diagnosed with AT, VISA-A showed a poor/low positive association with echo types I ( $r = 0.21$ ;  $p = 0.45$ ), III ( $r = 0.10$ ;  $p = 0.71$ ) and IV ( $r = 0.45$ ;  $p = 0.09$ ). A moderately negative association was observed between changes in VISA-A score and echo type II ( $r = -0.61$ ;  $p = 0.015$ ). For the PT group, a poor negative association was observed between changes in VISA-P score and changes in echo types II ( $r = -0.14$ ;  $p = 0.65$ ), III ( $r = -0.28$ ;  $p = 0.22$ ) and IV ( $r = -0.26$ ;  $p = 0.26$ ). Change in VISA-P score had a poor positive association with change in echo type I ( $r = 0.26$ ;  $p = 0.28$ ).

**Individual analysis of the association between changes in VISA score and changes in echo type percentage**

The results of the agreement zone and the individual percentages of the specific zones (Improvement zone, No-change zone and Worsening zone) are shown in Table 1.

**Table 1.** Agreement zones between changes in VISA score and changes in percentage of echo types (I-IV) in patients diagnosed with AT or PT.

		AT group	PT group
<b>VISA score vs echo type I (%)</b>	Agreement zone	9 (65%)	10 (50%)
	Improvement zone	4 (80%)	6 (67%)
	No-change zone	5 (50%)	3 (33%)
	Worsening zone	0 (100%)	1 (50%)
<b>VISA score vs echo type II (%)</b>	Agreement zone	4 (27%)	7 (35%)
	Improvement zone	1 (20%)	2 (22%)
	No-change zone	3 (30%)	4 (44%)
	Worsening zone	0 (100%)	1 (50%)
<b>VISA score vs echo type III (%)</b>	Agreement zone	7 (47%)	8 (40%)
	Improvement zone	3 (60%)	5 (55%)
	No-change zone	4 (40%)	3 (33%)
	Worsening zone	0 (100%)	0 (0%)
<b>VISA score vs echo type IV (%)</b>	Agreement zone	3 (20%)	10 (50%)
	Improvement zone	1 (20%)	5 (55%)
	No-change zone	2 (20%)	5 (55%)
	Worsening zone	0 (100%)	0 (0%)

Individual analysis of changes in the VISA score (above the MCID) showed that five (33%) of the 15 patients in the AT group and nine (45%) of the 20 patients in the PT group improved. With respect to changes in echo type percentage, in the AT group seven patients showed an increased percentage of echo types I and II and eight patients a decreased percentage of echo types III and IV above the MDC. For the PT group, ten patients showed an increased percentage of echo type I, six patients an increased percentage of echo type II, nine patients a decreased percentage of echo type III and ten patients a decreased percentage of echo type IV.

In the PT group there was one patient who got clinically worse (above the MCID). Remarkably, the patellar tendon structure of this patient showed an increased percentage of echo type I (above the MCD) and a decreased percentage of echo types II, III and IV (above the MCD).

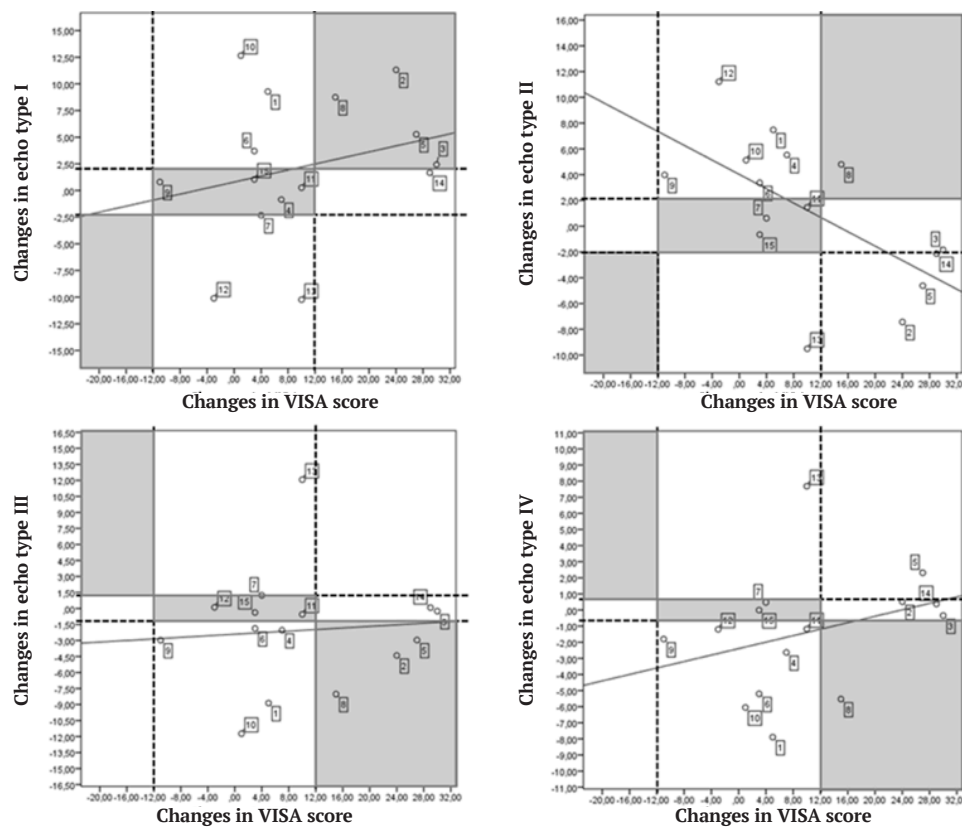


Figure 2. Association between changes in VISA-A score and changes in echo type percentages in patients diagnosed with Achilles tendinopathy.

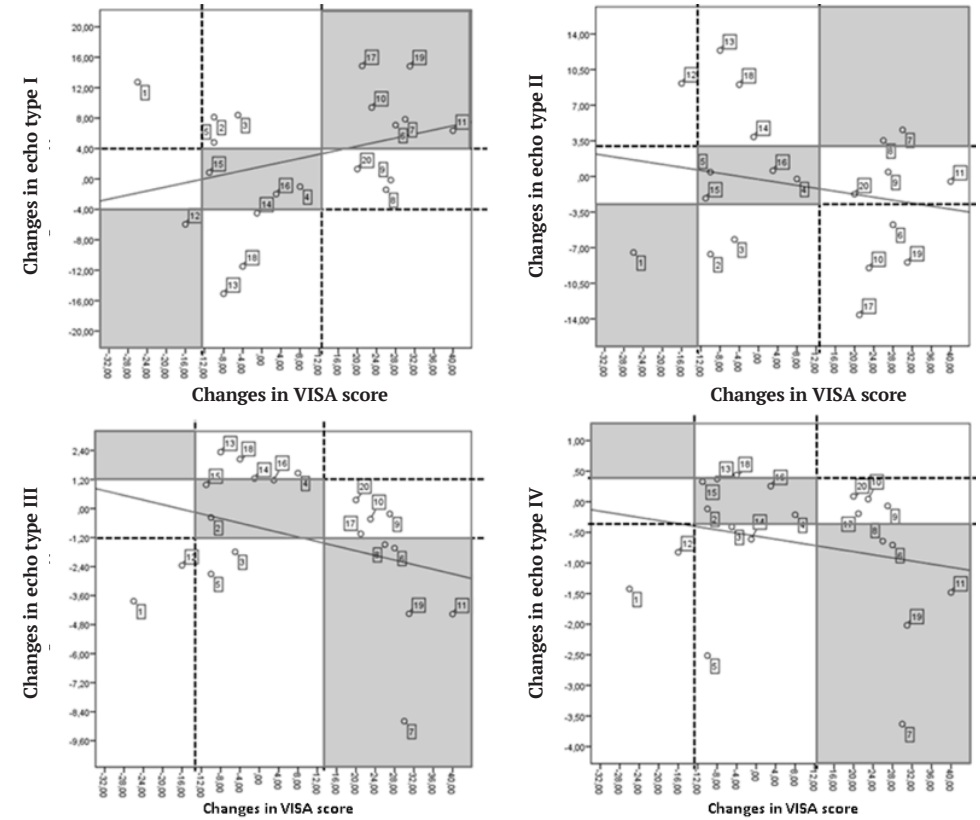


Figure 3. Association between changes in VISA-P score and changes in echo types in patients diagnosed with patellar tendinopathy

### Discussion

This study aimed to investigate the association between changes in clinical status and changes in tendon structure after conservative treatment in patients diagnosed with AT or PT. Different results were observed for group and individual analyses. For the group analysis we found that a higher VISA-A score (AT group) was moderately associated with a decreased percentage of echo type II. The individual analysis showed that higher percentages in the agreement zones were observed between VISA score and echo types I and III in those patients diagnosed with AT, and between VISA score and echo types I and IV in patients diagnosed with PT.

This is the first study to show that a patient-reported improvement of pain and function in patients with AT is associated (moderately) with a decrease in percentage of less integer and waving tendon bundles (echo type II) after treatment. Previous studies that used UTC to assess tendon structure did not find significant associations, but this

could be the result of different methodology. De Vos et al. (2012) performed the UTC examination manually, which might cause variations in distribution of echo types.<sup>20,21</sup> Additionally, each study used a different probe and the percentages of echo types I and II were investigated in combination (echo type I + echo type II).<sup>20,21</sup> In our study we used a probe with higher resolution and the percentages of echo types were analysed separately, which might have led to different findings.

Looking especially into echo types I and II is important because the expectation after treatment is to observe changes in the aligned fibrillar matrix portion (echo types I and II) rather than in the degenerative area (echo types III and IV).<sup>29</sup> A positive adaptation of the tendon to the treatment would be represented by an increase in percentage of echo type I and a decrease in percentage of echo type II. This was seen in our study for both groups, although overall the associations with clinical status are poor. Future studies must verify if at long-term follow-up an improvement in clinical status is more strongly associated with an increase in echo type I percentage.

Some experts state that the treatment should not be focused on stimulating the healing process in the degenerative portion because this area shows limited reversibility.<sup>29</sup> Changes are thus expected to occur in the aligned fibrillar matrix portion,<sup>29</sup> and a poor association between clinical status and changes in percentage of echo types III and IV would be expected. Our results are in line with this model.

In contrast with the group analysis, the individual analysis performed in this study showed – not only for the AT patients but also for the PT patients – that for approximately 50% of the subjects the changes in VISA score were in agreement with the changes in echo types I (AT/PT) and III (AT)/IV (PT). This means that the percentage of subjects that improved clinically also showed a significant decrease in percentage of echo types III and IV. Although this is not in line with the model presented in the previous paragraph, the results do corroborate a previous study that investigated tendon structure using conventional US:<sup>30</sup> out of 26 patients treated, 19 showed normal tendon structure at follow-up. No previous studies using UTC found similar findings, although none of them performed an individual analysis. It would be interesting to investigate in future studies whether the high degree of individual variation results in the findings that change at the individual level indeed differs at the group level.

Personalised medicine is becoming increasingly important in different areas of the profession. This term can be described as the concept of delivering the right treatment to the right patient at the right time.<sup>31</sup> Personalised radiology might also play an important role in the assessment of therapeutic response.<sup>31</sup> In tendinopathy, a personalised imaging examination can not only help clinicians decide which treatment is the best for each individual patient, but can also be used to monitor changes in tendon structure. Based on a personalised examination, clinicians might be able to identify individual characteristics that influence changes in tendon structure after rehabilitation. More research is therefore needed that investigates individual tendon responses to treatment, relating them to the individual characteristics of the patients. This would contribute not only to better treatment outcome, but also to the communication of realistic expectations about rehabilitation and thus to patient satisfaction.

#### **Limitations**

This study contributes to our understanding of the association between pain and function and tendon structure (as measured with UTC) in patients diagnosed with AT and PT. The results should be interpreted with caution, as a limited number of subjects were included in this study. Additionally, since patients were part of a clinic specialised in tendon rehabilitation, a high number of patients had undergone conservative treatment previously without improvement. Other therapies were suggested to these patients, who were not included in the present study; this might hamper generalisability of results to this specific group of patients.

#### **Clinical implications**

This study provides insights on the use of clinical and imaging examination to monitor the effect of treatment in patients diagnosed with AT or PT. Assessing Achilles or patellar tendon structure using UTC, rather than conventional US, provides more information to clinicians on changes after treatment. Clinicians should be aware that the UTC outcomes (echo types) might be in agreement with the changes in clinical scores at short-term follow-up, especially for echo type I. However, this agreement is not observed in all patients, which confirms that performing both clinical and imaging examinations is still necessary.

#### **Conclusion**

This study has shown that, in patients diagnosed with AT (group analysis), changes in pain and function (VISA score) were moderately associated with a decrease in percentage of less integer and waving tendon bundles (echo type II). When subjects were investigated individually, we found high agreement between changes in pain and function and changes in echo types I and III/IV. Taken together, these results suggest that conducting a personalised imaging examination might provide additional information to patients and clinicians about changes in tendon structure after treatment. More research investigating the individual characteristics that influence changes in tendon structure needs to be conducted.

**Acknowledgements:** This work was supported by CNPq, National Council for Scientific and Technological Development – Brazil.

**Conflicts of Interest and Source of Funding:** LMR is currently receiving a grant (number 203668/2014-6) from CNPq, National Council for Scientific and Technological Development, Brazil. None were declared for the remaining authors.

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