Purpose

Rheumatoid arthritis (RA) is a chronic progressive systemic disease affecting up to 1% of the global adult population, with an estimated annual incidence of 12.0-24.5 males and 23.9-54.0 females per 100,000, and a peak age of onset between 45 and 65 years [1]. The destructive action of RA originates from the synovium in the joints and tendon sheaths, and, during the course of the disease, adjacent structures such as the bone, tendons, capsule, and ligaments may become invaded by the synovial tissue [2]. Hand and wrist are the most frequently involved joints in patients with RA, with most of the structural damage occurring in these locations [3]. When this damage is advanced, wrist instability could represent a relevant problem [4]. The proper balance of the wrist is related not only to the integrity of bone articular surfaces, but also to that of the supporting capsular and ligamentous structures. Among them, extrinsic carpal ligaments play a relevant role [5]. Arising outside the carpus, they attach on the carpal bones during their course, thus providing both stability and flexibility.

Ultrasonography (US) performed with high-resolution linear probes is an excellent tool for the evaluation of superficial ligaments [6], owing to its high spatial resolution. In this setting, the ability of US in evaluating the normal anatomy of extrinsic carpal ligaments has already been demonstrated [7,8]. However, little is known on the status of these ligaments in patients affected by RA and on the role of US in their evaluation.

This work is concerned with an evaluation by US of extrinsic carpal ligaments in patients affected by RA compared to healthy volunteers matched for age and sex. Our findings were correlated with duration of disease and clinical and laboratory parameters.

Methods and Materials

Study population

Twenty-one consecutive patients affected by RA according to the 1987 ACR criteria (9), attending an outpatient clinic, were studied. Both wrists were imaged. Exclusion criteria included history of previous relevant trauma or surgery of the wrist. For such reasons, two wrists were excluded from our study group because of a previous arthrodesis in one patient and a joint prosthesis in a second one. As a result, 40 wrists from 21 patients were evaluable. Ethical Committee approval and patients’ informed consent were obtained. The control group was made of 42 wrists in 21 healthy volunteers matched for age and sex to the patients. No history of previous relevant trauma or previous surgery of the wrist was reported by controls. A flow chart of the study enrolment is shown in Figure 1.
Clinical and radiographic evaluation

Clinical parameters included disease duration, number of tender and swollen joints, 100 mm visual analogue scale of patient's general health, the health assessment questionnaire (HAQ), and the composite index disease activity score (DAS). Laboratory parameters included erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), IgM rheumatoid factor (RF), and anti cyclic citrullinate peptides (anti CCP) antibodies. In addition, an antero-posterior radiograph of the hands taken within 6 months from US examination was evaluated. The presence of, at least, one radiological erosion was searched in order to classify RA as erosive or non-erosive, as a dychotomic variable.

US evaluation

A Philips iU22 system (Koninklijke Philips Electronics, Eindhoven, the Netherlands) equipped with a high-frequency probe (5-17 MHz) was used. Both wrists of patients and controls were imaged according to previously described scanning guidelines [7,8], on the palmar and dorsal sides. US scans were performed by a radiologist with 5 years of experience in musculoskeletal ultrasound, who was not aware of the diagnosis.

Seven extrinsic carpal ligaments were included in our analysis: radio-scapho-capitate (RSC), radio-luno-triquetral (RLT), palmar ulno-lunate (pUL), palmar ulno-triquetral (pUT), dorsal radio-triquetral (dRT), dorsal ulno-triquetral (dUT), and radial collateral ligament (RC). The radio-scapho-lunate and ulnar collateral ligaments were not included in our study, as they have been demonstrated to be undetectable on US [7,8]. The normal location and anatomy of the studied ligaments is shown in Figure 2 on page 4. We noted whether each single ligament was detectable or not and, if yes, we measured its maximum thickness.

Statistical analysis

Differences of the means were analyzed by the Mann Whitney $U$ test. Percentages were compared using the $\chi^2$ test. Ligament lesions were associated with clinical and laboratory parameters in two different ways: a) by determining the correlation coefficient for parametrical and non-parametrical (Spearman's rho) tests; b) by dividing the sample in two subgroups, with values for each single ligament higher or lower than that of the mean plus two standard deviations, and comparing them by ANOVA or Kruskall-Wallis test. A $p$ value of $<0.05$ was considered statistically significant. The MedCalc® statistical software version 9.2.0.1 (Belgium) was used.

Images for this section:
Fig. 1: Figure 1. Flow chart of the study investigating ultrasound evaluation of extrinsic carpal ligaments in patients affected by rheumatoid arthritis and controls: total subjects enrolled, excluded patients, and eligible patients.
Fig. 2: Figure 2. Normal location and anatomy of dorsal (a) and palmar (b) extrinsic carpal ligaments.
Results

Of the 21 patients, 12 were men and 9 women with mean age 57±14.6. The controls were 12 men and 9 women with mean age 54±12.1 years. No statistical difference between patients and controls was found for age (p=0.69) and sex (p=1) distribution. Median disease duration was 60 months (range 2-408 months). Nine out of 21 patients (42.9%) were RF positive and 7 (33.3%) anti CCP positive, 10 (47.6%) had erosive arthritis at radiological examination. Mean DAS was 4.76±1.98, median HAQ was 0.85 (0-3), and mean ESR and CRP were 62.9±42.3 mm/h and 31.7±36.6 mg/dL, respectively.

 Altogether, 273 and 294 ligaments were studied in patients and controls, respectively. The overall number of ligaments detected by US in patients was significantly lower than that detected in controls (258/273 vs. 290/294; p=0.005). In particular, the number of pUL and pUT ligaments detected by US in patients was significantly lower than that detected in controls (p=0.031 and p= 0.037, respectively) (table 1). Conversely, no statistical difference was found between the number of RSC, pRLT, dRLT, dUT, RC ligaments between groups.

 All the ligaments were significantly thinner in patients than in controls (p<0.001) (Table 1 on page 10 and Figures 3a on page 6b on page 7, 4a on page 7b on page 7, 5a on page 8b on page 10, 6a on page 9b on page 9, 7a on page 9b on page 8, 8a on page 8b on page 10)

 No correlation was found between ligament thickness, calculated in the two different ways cited above, and clinical, laboratory, and radiographic parameters (data not shown). Similarly, also the presence of undetectable ligaments was not associated with clinical, laboratory, and radiographic parameters.

Images for this section:
Fig. 1: Figure 3a. Radial Collateral ligament missing in a patient affected by rheumatoid arthritis.

Fig. 2: Figure 3b. Radial Collateral Ligament in a healthy volunteer.

Fig. 3: Figure 4a. Radial Lunar Triquetral ligament in a patient affected by rheumatoid arthritis.
Fig. 4: Figure 4b. Radial Lunar Triquetral ligament in a healthy volunteer.

Fig. 5: Figure 5a. Palmar Radial Lunar Triquetral ligament in a patient affected by rheumatoid arthritis.

Fig. 6: Figure 8a. Dorsal Ulnar Triquetral ligament in a patient affected by rheumatoid arthritis.
Fig. 7: Figure 7b. Palmar Ulnar Lunate ligament in a healthy volunteer.

Fig. 8: Figure 7a. Palmar Ulnar Lunate ligament in a patient affected by rheumatoid arthritis.

Fig. 9: Figure 6b. Palmar Radial Scaphoid Capitate ligament in a healthy volunteer.
**Fig. 10:** Figure 6a. Palmar Radial Scaphoid Capitate ligament in a patient affected by rheumatoid arthritis.

**Fig. 11:** Figure 5b. Palmar Radial Lunar Triquetral ligament in a healthy volunteer.

**Fig. 12:** Figure 8a. Dorsal Ulnar Triquetral ligament in a healthy volunteer.
<table>
<thead>
<tr>
<th>Ligament</th>
<th>Number of ligaments</th>
<th>Thickness (mm)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients</td>
<td>Controls</td>
<td></td>
</tr>
<tr>
<td>Radio-scapho-capitate</td>
<td>39/39 (100%)</td>
<td>42/42 (100%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Palmar radio-luno-triquetral</td>
<td>39/39 (100%)</td>
<td>42/42 (100%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Palmar ulno-lunate</td>
<td>31/39 (79%)</td>
<td>40/42 (95%)</td>
<td>0.031</td>
</tr>
<tr>
<td>Palmar ulno-triquetral</td>
<td>34/39 (87%)</td>
<td>41/42 (98%)</td>
<td>0.037</td>
</tr>
<tr>
<td>Dorsal radio-luno-triquetral</td>
<td>38/39 (97%)</td>
<td>42/42 (100%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Dorsal ulno-triquetral</td>
<td>38/39 (97%)</td>
<td>41/42 (98%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Radial collateral</td>
<td>37/39 (95%)</td>
<td>42/42 (100%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Total</td>
<td>258/273 (94.5%)</td>
<td>290/294 (98.6%)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

**Fig. 13:** Table 1. Detection rate and ligament thickness of seven extrinsic carpal ligaments evaluated by ultrasound in 39 wrists of 20 RA patients and in 42 wrists of 21 controls. (Ligament thickness is given as mean±standard deviation and median. ^chi-square test; §U Mann-Whitney test).
Conclusion

Our results demonstrate that carpal ligaments are thinner and less visible by US in patients affected by RA compared to healthy volunteers. Considering the single ligaments, only pUL and pUT were seen in less patients than controls. The explanation for this observation is not clear, because these ligaments are easily detectable in normal subjects. It is possible that these ligaments were ruptured in some patients, although there is no proof of it because surgical inspection was not performed.

Ligament thickness measured in our control group is comparable to what reported by Lacelli et al in normal volunteers (8). In patients, all ligaments were significantly thinner than in controls. These results confirm the view that RA synovitis can damage also extrinsic ligaments. We found no correlation between disease characteristics and ligaments’ damage. In particular, there was no association with disease activity, nor with disease duration. We would have expected that the longer and severe the disease, the more damaged the ligaments. The lack of correlation between ligament damage and disease duration may be explained by the fact that the destructive potential of RA is exerted at the beginning of the disease and is usually later attenuated by treatment. We can speculate that the largest part of damage of extrinsic carpal ligaments occurs in the early phases of the disease. A similar finding has been observed for erosions that tend to increase in frequency in the initial years of RA and later reach a plateau (10). Alternatively, the relatively low number of patients may explain the lack of correlation.

In a paper published in 2004, Muramatsu et al. (4) described an increased frequency of volar intercalated segment instability and scapho-lunate dissociation in a series of 100 plain films of wrists of RA patients. This finding is surprising, because the scapho-lunate instability pattern is usually more frequently associated to dorsal intercalated segment instability (11,12). The fact that some ligaments could be ruptured in RA is a possible explanation of this different instability pattern. In addition, thinner ligaments could also be laxer, possibly contributing to carpal instability.

In our study, several limitations should be taken into account. Firstly, US scans were performed by a single observer. However, the same experienced radiologist, who received intensive training about anatomy of extrinsic carpal ligaments, examined both patients and controls, making the comparison reliable. We cannot exclude that operators with different training could obtain dissimilar results. In addition, a good reproducibility of US in detecting extrinsic carpal ligaments has already been demonstrated (8). Second, a gold standard for the integrity of extrinsic ligaments of the wrist is lacking. Surgical inspection could represent the reference method but is impossible to apply to unselected RA patients. Alternatively, MR arthrography could demonstrate the presence and integrity of the ligaments assessed by US (13). Finally, we did not perform a power
Doppler evaluation of the ligaments and of the adjoining synovial tissue. This could have represented a further parameter to correlate with ligaments detection rate and thickness.

In conclusion, our data demonstrated for the first time that extrinsic carpal ligaments are globally less detectable and thinner in patients affected by RA, compared to healthy volunteers matched for age and sex. In our series ligament thinning was not directly correlated to RA duration and clinical parameters.

References


Personal Information