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Ultrasonography shows increased cross-sectional area of the median nerve in patients with arthritis and carpal tunnel syndrome

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***Objectives*. To examine whether patients with arthritic diseases and carpal tunnel syndrome (CTS) have increased cross-sectional areas of the median nerves measured by ultrasonography (US). Enlarged cross-sectional areas have previously been found in non-arthritic patients with idiopathic CTS.**

***Methods*. During 1 yr, all 12 patients with rheumatoid arthritis (RA) or other arthritic diseases hospitalized in our department for surgery for CTS were included. Nine of the patients had bilateral CTS, giving a total of 21 pathological nerves. The median duration of CTS symptoms was 9.5 months. The controls were 30 randomly selected RA patients without symptoms of CTS and 30 healthy persons. Both CTS patients and controls were examined bilaterally by use of US at the entrance of the carpal tunnel, and the cross-sectional areas of the median nerves were calculated.**

***Results*. Cross-sectional areas of the median nerves were significantly higher in the CTS patients compared with the RA controls and healthy persons; median (range) areas were 15.7 mm^2 (11.1–21.8), 8.5 mm^2 (5.8–11.0) and 8.0 mm^2 (4.9–12.0), respectively ($P < 0.0001$). No significant differences in cross-sectional areas were observed between the two control groups, or between the right and left hand in the control groups.**

***Conclusions*. Higher cross-sectional areas were found in the arthritic patients with CTS than in RA patients and healthy persons without CTS. This supports previous studies of idiopathic CTS in which increased cross-sectional areas have been found. Thus, as in idiopathic CTS, arthritic patients may be examined by US of the median nerve when CTS is suspected.**

KEY WORDS: Rheumatoid arthritis, Ultrasonography, Carpal tunnel syndrome, Imaging.

Carpal tunnel syndrome (CTS) is caused by compression of the median nerve in the carpal tunnel beneath the flexor retinaculum and is relatively common in the general population. An even higher prevalence may be found in arthritic patients since they may have inflammatory changes in the wrists that decrease the space available for the median nerve [1]. Ultrasonography (US) has been found to be a precise method to display the anatomy of the median nerve [2], and several studies have shown US to have high sensitivity and specificity for the diagnosis of idiopathic CTS [3–10].

A variety of US measurements may be used to diagnose CTS, e.g. the cross-sectional area of the nerve at the entrance of the carpal tunnel (at the level of the pisiform bone), the flattening ratio (defined as the ratio of the major axis of the median nerve to its minor axis), the increased palmar bowing of the flexor retinaculum and the cross-sectional area of the nerve at the outlet of the tunnel. Among these assessments, the cross-sectional area at the entrance of the carpal tunnel seems to have the highest sensitivity and specificity for CTS [3–7, 9]. Examination at this level may also be performed most reliably by untrained US users.

There is no diagnostic gold standard for CTS, but nerve conduction studies are usually performed when CTS is suspected. Arthritic patients may have pain in the hands and wrists caused by several conditions, such as arthritis, tenosynovitis, sequelae from arthritis, or neuropathy of different aetiologies, where entrapment of the median nerve may be an important cause. Thus, US may be a feasible tool for the differentiation of the various causes of pain in the clinical setting [11–13]. Previous US studies have found significantly increased cross-sectional areas of the median nerves in non-arthritic patients with idiopathic CTS. Our hypothesis was that similar findings would be present in CTS patients with arthritis. To our knowledge, this hypothesis has not been explored by previous controlled studies. Since it was not known whether arthritic patients have a cross-sectional area that differs from that of healthy persons, we used RA patients without CTS symptoms as well as healthy individuals as controls.

Methods

Patients with arthritis and CTS

During 1 yr, a total of 12 patients with arthritic diseases (seropositive RA, $n = 4$; seronegative RA, $n = 3$; psoriatic arthritis, $n = 2$; ankylosing spondylitis, $n = 1$; Sjögren syndrome, $n = 1$; unspecified polyarthritis, $n = 1$) and typical CTS symptoms were referred to our department for surgical treatment. All the patients gave written consent according to the Declaration of Helsinki, and the study was approved by the local ethics committee. The median (range) age of the CTS patients was 65 (39–83) yr, seven were females, and the median (range) duration of arthritis was 8 (0.3–18) yr. Seven of the patients were current users of

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prednisolone, on a dosage ranging from 5 to 27.5 mg per day (median 7.5), two were on methotrexate, one used sulphasalazine and eight used non-steroidal anti-inflammatory drugs. The median (range) erythrocyte sedimentation rate was 18 (3–36) mm/h and C-reactive protein was 6 (1–10) mg/l. Nine of the patients had CTS in both hands, a total of 21 pathological median nerves were examined, and the median (range) duration of CTS symptoms was 9.5 (1–60) months. Of the patients with relevant concomitant diseases, two had diabetes mellitus and one had hypothyroidism.

Clinical evaluation and nerve conduction studies were performed bilaterally on all patients by one investigator (I.A.H.H.) 1 day prior to surgery. A diagnosis of CTS was made according to the laboratory's routinely used standards, i.e. palm-to-wrist median sensory nerve action potential (SNAP) onset latency >2.0 ms (distance 7 cm), or absence of SNAP and median distal motor latency >4.9 ms (stimulus at the proximal wrist crease). CTS was confirmed in all the symptomatic hands.

RA controls (RA patients without CTS)

Thirty randomly selected RA patients with no symptoms of CTS, participating in a different study, agreed to have their median nerves bilaterally examined by US. They had a median (range) age of 59 (42–81) yr, 21 were females and the median (range) RA disease duration was 7 (0.5–49) yr. Eighteen of these patients used prednisolone in doses from 2.5 to 20 mg (median 5 mg), nine were on anti-TNF-α medication and methotrexate, 16 used only methotrexate, one used leflunomide, one used hydroxychloroquine and 18 were on non-steroidal anti-inflammatory drugs. One of the RA patients had diabetes mellitus and two had hypothyroidism.

Healthy controls

Thirty healthy persons randomly selected among workers in our department [median age 43 yr (range 22–66), 26 females] without any symptoms of CTS agreed to undergo US examination of their median nerves.

US measurements

All the US investigations were performed by one person (H.B.H.). The CTS patients were examined by US 1 day prior to surgery. Both patients and controls were sitting with their forearm in a supinated resting position on a small table. The US probe (an 8–16 MHz linear array transducer; Diasus, Dynamic Imaging, UK) was held as lightly as possible so as not to disturb the anatomy. The median nerve was examined at the entrance of the carpal tunnel, between the pisiform bone and tubercle of the navicular, for which the distal volar crease is an external landmark. The software of the US machine calculated the cross-sectional area of the median nerve directly when a continuous trace was made just within the hyperechogenic boundary of the nerve. Each median nerve was examined three times, and the mean value was used in further calculations. Only controls in whom the median nerve was not divided at the entrance of the carpal tunnel were included. Seven of the CTS patients had a US measurement of their median nerves at a median (range) of 5 (1–9) months after surgery.

Statistics

The difference in cross-sectional area between CTS patients and controls was analysed with the Kruskal–Wallis test (three samples) or the Mann–Whitney test (two samples). Correlation coefficients were calculated by the use of Spearman's rank correlation analysis with a two-tailed test of significance. Comparisons between cross-sectional areas of the median nerves of the right and left hands as well as the pre- and postoperative areas were performed with the Wilcoxon signed rank test. All statistics were performed by using the Statistical Package for the Social Sciences for Windows (SPSS) version 11 (SPSS, Chicago, IL, USA), and $P<0.05$ was considered significant.

Results

The cross-sectional areas of the median nerves at the entrance of the carpal tunnel differed between the three groups, with significantly higher values in the CTS patients than in the two control groups ($P<0.001$). The median (range) value in the CTS patients was 15.7 mm^2 (11.1–21.8), in the RA controls it was 8.5 mm^2 (5.8–11.0) ($P<0.001$) and in the healthy controls it was 8.0 mm^2 (4.9–12.0) ($P<0.001$) (Figs. 1 and 2).

Only one of the CTS patients had a cross-sectional area that was lower than the highest value in any of the controls. The three CTS patients with unilateral symptoms had cross-sectional areas between 11.1 and 16.4 mm^2 on the symptomatic side and between 9.0 and 12.8 mm^2 on the asymptomatic side.

The clinical evaluation of the CTS patients showed thenar atrophy in eight hands, reduced pinprick and/or tactile sensibility in 14 hands, a positive Tinel sign in seven hands and a positive Phalen sign in eight hands. Patients with a positive Tinel and/or Phalen test had a slightly higher cross-sectional area of the median nerve ($P=0.05$), while the other clinical tests showed no covariation with the area of the median nerve.

During surgery, nine of the patients were described as having flexor tenosynovitis, some quite extensively. The patient with Sjögren syndrome had no tenosynovitis; however, like most of the others, she was described as having a typical hourglass shape of the nerve.

Eleven median nerves (from seven CTS patients) examined before and after surgery had a median (range) cross-sectional area of 15.9 (11.1–21.8) mm^2 before and 16.2 (10.1–21.4) mm^2 after surgery ($P=0.59$). Nine patients (13 symptomatic nerves) had nerve conduction studies performed 3–10 months after surgery; this showed unchanged pathology in three nerves, improvement in nine nerves and normalization in only one nerve.

No significant difference was found between the RA and healthy control groups regarding the cross-sectional area of the median nerve. Neither was there any significant difference between the right and left hands in the two control groups. Healthy controls had significant correlations between the cross-sectional area of the median nerve and height ($r=0.60$, $P<0.001$) and weight ($r=0.43$, $P=0.001$), whereas no significant correlations were found in the RA group ($r=0.10$ and $r=0.25$, respectively).

During the inclusion of RA and healthy control persons in this study, between 10 and 15% were excluded because of division of their median nerve at the entrance of the carpal tunnel. Typically, the median nerve was divided into two parts, but division into three parts was also seen. The parts often had quite different cross-sectional areas. When the cross-sectional areas of the parts were summed and compared with the areas of the controls who were included, no significant difference was found.

Discussion

Arthritic patients with CTS had significantly increased cross-sectional areas of the median nerves at the entrance of the carpal tunnel. This finding is in accordance with several previous studies of patients with idiopathic CTS [3–10]. Many rheumatologists are using US as an important diagnostic tool in their routine practice. The results of this study support the value of using US

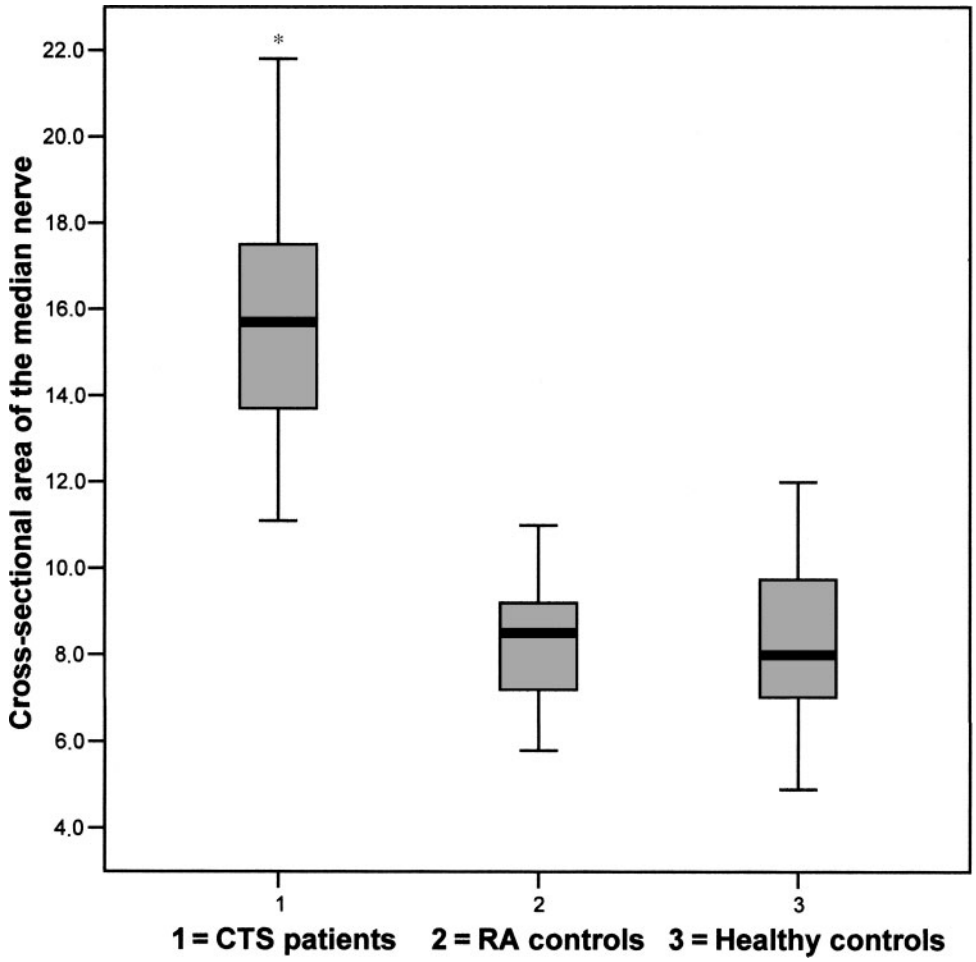

FIG. 1. Cross-sectional areas (mm^2) of the median nerves from arthritic patients with CTS (21 nerves), RA controls (60 nerves) and healthy controls (60 nerves). Each box shows the median, the quartiles and the extreme values. $*P<0.001$, Mann–Whitney test comparing the CTS patients and the two control groups.

as a diagnostic tool in arthritic patients in daily clinical practice when CTS is suspected.

RA is a systemic disease, and inflammatory-mediated changes in nerves may be found. The present study did not show any significant difference between the cross-sectional areas of the median nerves in RA patients without CTS and healthy controls, supporting the idea that these groups have similar normal values. However, we are now performing a larger study of the cross-sectional area of the median nerve in RA patients without CTS, to look for the cut-off value in this patient group, as there are already several studies of the cut-off value in healthy individuals.

In several studies, the cross-sectional area is calculated by the use of a formula for an ellipse after measurement of the height and the width of the nerve [3, 10, 14–16]. The median nerves in the present study had quite different configurations, suggesting that calculation using a continuous boundary trace of the nerves may give the most correct cross-sectional area.

Increasing CTS symptoms seem to correspond with increasing cross-sectional areas [17, 18]. In the study by El Miedany *et al.* [18], a cross-sectional area of 10.0–13.0 mm^2 was found in mild CTS, while areas of 13.0–15.0 mm^2 represented moderate CTS symptoms, and areas greater than 15.0 mm^2 were found in severe CTS. We did not analyse the severity of the symptoms. A median area of 15.7 mm^2 may, however, indicate severe CTS in a majority of the patients in this study. Since some of these CTS patients also had arthritis in finger joints and wrists, the CTS symptoms may have been underestimated and the diagnosis delayed in some patients.

We did not find any significant difference between the cross-sectional areas of the median nerves on the right and left sides in the control groups. This finding was expected, but supports the idea that a significant difference between the two areas strengthens the suspicion of CTS in an RA patient with asymmetrical symptoms.

After the completion of this study, one of the CTS patients with unilateral symptoms experienced CTS symptoms in the contralateral hand. The cross-sectional area of the previously asymptomatic median nerve was reached 12.8 mm^2 during the study, i.e. higher than in any of the controls. This observation suggests that a pathologically increased cross-sectional area may predict subsequent CTS symptoms.

A relationship between the cross-sectional areas of the median nerves and height and weight was found in healthy controls, but not in RA controls. The reasons for this discrepancy are not known. This finding implies that neither height nor weight should be considered to have a major impact on the evaluation of the measured area of the median nerve in an RA patient.

None of the CTS patients had been treated by introducing local steroids into the carpal tunnel before surgery. Girlanda *et al.* [19] have reported that such treatment may have a transient effect, and a good short-term response has been found after steroid injections when US was used to support the anatomical placement of steroids into the area of inflammation [20].

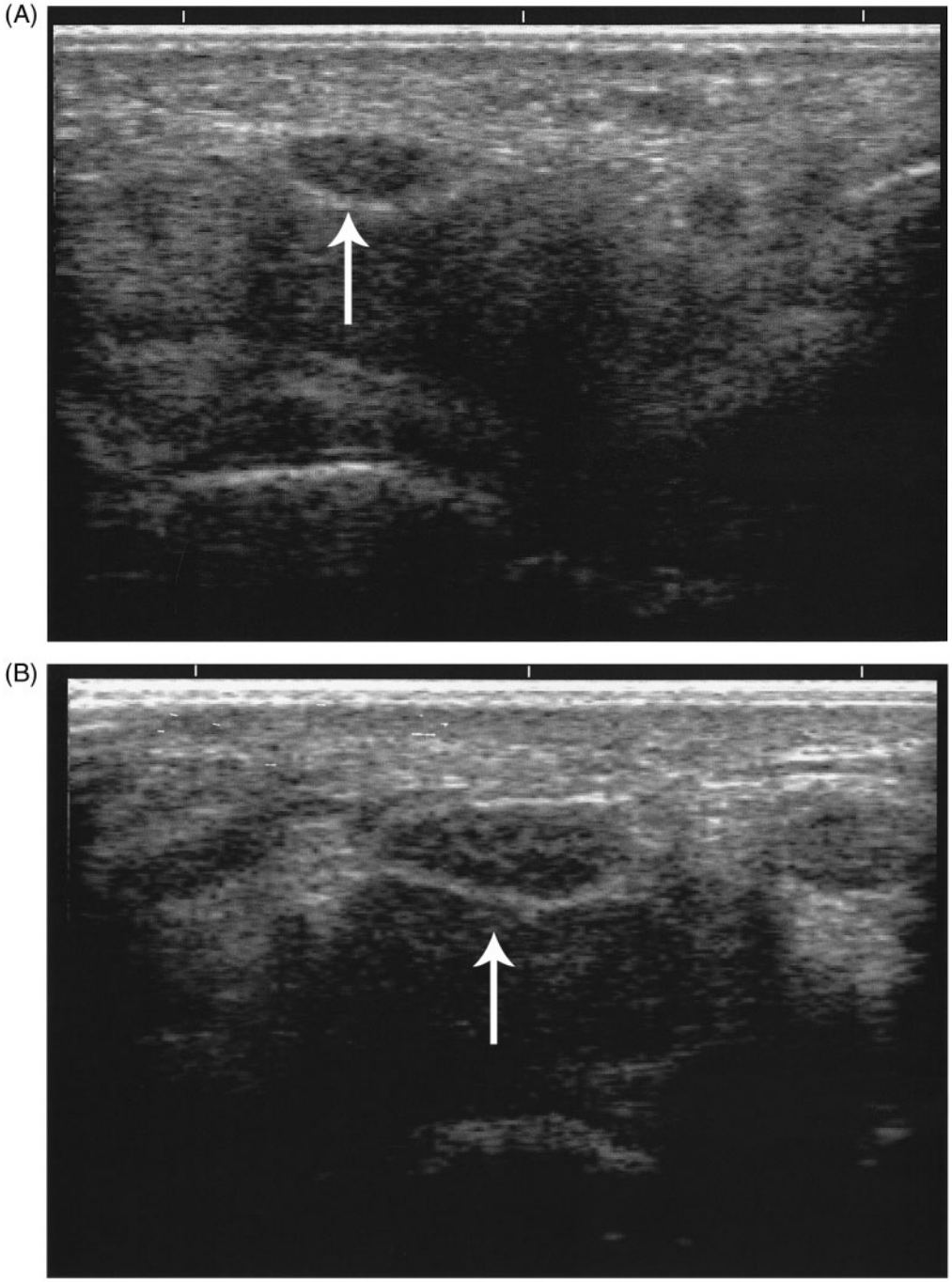

FIG. 2. Ultrasonographic pictures of a normal median nerve from an RA patient without CTS symptoms (**A**) and a pathological median nerve from a patient with RA and CTS (**B**). The arrows indicate the median nerves.

Preoperative US may detect the causes of CTS [21]. This was not a goal in the present study. However, it would have given additional information about the reasons for CTS, and thus given further insight into the pathological process in our arthritic patients with CTS. Future studies should include this issue.

The reasons for the enlargement of the median nerve are not known, but oedema has been mentioned as a possible explanation. Eleven of the pathological nerves in this study were examined a second time several months after the CTS operation. The area was not significantly changed, however, although the symptoms were alleviated. The reasons for the persistence of the increased area are not known, but it may have been caused by permanent internal changes in the nerves.

The findings in the present study may suggest that rheumatologists should expand their clinical diagnostic tools to include ultrasonographic assessment of the median nerve. Practical exercises in the use of US will rapidly give good skills [22], and the measurement of the cross-sectional area of the median nerve is easy. In addition, both tenosynovitis and other inflammatory causes of impingement of the median nerve in arthritic patients may be treated by the use of US-guided local depot steroids. Thus, the use of US should be encouraged to achieve an earlier diagnosis of CTS in arthritic patients.

Rheumatology	Key messages
	• The cross-sectional area of the median nerve was significantly higher in arthritic patients with CTS than in healthy controls and in RA patients without symptoms of CTS. • Healthy controls and RA patients without symptoms of CTS had no significant differences in their cross-sectional area of the median nerve.

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The authors have declared no conflicts of interest.

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