Original Article

Diagnostic Utility of Strain Elastography in Assessing Median Nerve Changes among Rheumatoid Arthritis Patients without Symptoms of Carpal Tunnel Syndrome: An Analytical Observational Study

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Abstract

Background: The elastography measurements in rheumatoid arthritis (RA) without carpal tunnel syndrome (CTS) are the least studied. Hence, the present study assessed the role of elastography in detecting the median nerve changes before the development of CTS in subjects with RA.

Methodology: A prospective observational study was conducted from January 2020 to July 2021 among 112 patients with and without RA. They were divided into Group A cases and Group B controls of 56 each. The patients underwent ultrasonography and strain elastography. Changes in median nerve stiffness were the primary outcome variable. $P < 0.05$ was considered significant and was analyzed using CoGuide software.

Results: The mean age of the patients was 48.5 ± 13.31 years, and most of them were females (64.29%) in both groups. The cross-sectional area (CSA) of median nerve at carpal tunnel inlet in cases and controls was 0.110 (0.105–0.116 cm^2) and 0.090 (0.083–0.095 cm^2) in right hands, respectively, and 0.109 (0.104–0.116 cm^2) and 0.089 (0.082–0.093 cm^2) in left hands, respectively. The mean strain ratio (SR) of the median nerve in cases and controls was 2.84 (2.41–2.98) and 1.65 (1.41–1.94) in right hands, respectively, and 2.76 (2.45–3.04) and 1.66 (1.43–1.93) in left hands, respectively. The difference in means of CSA and SR was significant across the groups ($P < 0.001$).

Conclusion: The use of elastography in evaluating the median nerve changes in RA subjects without CTS was useful as changes in the CSA and SR were significant in cases compared to controls.

Key Words: *Carpal tunnel syndrome, elastography, median nerve, rheumatoid arthritis, strain ratio*

Introduction

Rheumatoid arthritis (RA) presents with persistent pain, stiffness, progressive joint destruction, functional disability, and progressive morbidity and mortality, and is a chronic systemic autoimmune disease.[1] RA is the most common cause of inflammatory arthritis, affecting around 1% of the population of India. Globally, the incidence of RA is three times more in women than men. The standardized prevalence of rheumatic diseases in the Community-Oriented Program for Control of Rheumatic Diseases (COPCORD) Bhigwan was 0.67, n ¼ 4092 and in Bone and Joint Decade India COPCORD, it was 0.34, n ¼ 56,541 surveys. The burden of RA was high, with a point prevalence of 0.7%. These survey data on RA and osteoarthritis knees were used by the WHO to project the likely burden in South East Asia.[2] The cause of RA remains unknown, but the pathological mechanism of synovial inflammation may result due to the complex interplay of genetic immunology and environmental factors.[3]

Early diagnosis is fundamental to prevent the permanent sequel of RA. Recent advances in diagnostic imaging in rheumatology have benefited patients clinically and also provided information related to the pathophysiology of diseases like arthritis. Ultrasound (US) and magnetic

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resonance imaging were most commonly used in diagnosing and monitoring RA progression in joints and related joint structures.[4]

Musculoskeletal imaging is currently being used to study muscles, tendons, nerves, ligaments, and various tumors.[5] US elastography measures tissue elasticity using high-frequency sound waves to assess tissue's static or dynamic deformation behavior after a stimulus is applied. This technique has been described most commonly in the context of isotropic tissues, such as the liver and neoplastic diseases, but is now becoming of more interest in anisotropic tissues, such as those in the musculoskeletal system.[6] Intrinsic tissue properties can be assessed by quantitatively measuring tissue elasticity when abnormalities are not depicted by conventional US and tissue healing methods. Furthermore, techniques may help predict impending tendon failure, which may help the clinician decide on early treatment initiation.[7]

There are primarily two elastographic methods, as follows: strain elastography (SE) and shear wave elastography (SWE). In SWE, shear waves are produced by the transducer, and their speed is measured, and SE visualizes tissue deformation with compression applied by the examiner.[8] Many previous studies have examined the utility of shear wave elastography.[9-11] However, changes in the cross-sectional area (CSA) and stiffness of the median nerve in patients with RA due to compression are limited. A study by Burulday *et al*.[12] found increased stiffness and CSA of the median nerve in acromegaly patients using SE.

Many studies are published on the diagnostic utility of real-time tissue elastography (RTE) in carpal tunnel syndromes (CTSs). However, the data on the diagnostic utility of elastography in assessing median nerve changes among RA patients are limited, especially in developing countries like India.

Therefore, developing this noninvasive method to show the changes in the median nerve in RA patients may be helpful in evaluating treatment effectiveness. With this background, the present study aimed to determine if SE can help detect median nerve changes in RA so that early intervention can be started to prevent the progression of CTS.

Aims and objectives

To assess the role of ultrasonography and SE in detecting the median nerve changes before progression to CTS in patients with RA.

Methodology

Study design

A hospital-based analytical observational study was conducted for a period of 18 months, from January 2020 to July 2021, among 112 RA patients who were referred to the department of radio-diagnosis at a tertiary care center in South India. Ethical clearance was obtained from the institutional review board, and a written informed consent was taken from the participants.

Sample size calculation

Sample size was estimated by using the proportion of patients with RA without symptoms of CTS and patients without RA assessed by son-elastography from the study by Anno *et al*.[13]

Standard deviation in Group I = 1.3

Standard deviation in Group II = 0.8

Mean difference = 0.6

Effect size = 0.571428571428571

Alpha error (%) = 5

Power (%) = 80

Sided = 2

Minimum required sample size per group = 51; in our study, 56 subjects were included per group.

Sample size

A total of 112 cases were selected using a convenience sampling method and were divided into two groups.

Group A (56 cases): Cases with RA and those without CTS.

Group B (56 controls): Age- and sex-matched cases without RA undergoing US for causes unrelated to RA or CTS.

Inclusion criteria

Cases – All patients diagnosed with RA and ruling out CTS by clinical evaluation that included Phalen's test, a manual muscle test of the abductor's muscle, and a search for Tinel-like signs and thenar muscle atrophy.

Controls – Age- and sex-matched cases without RA undergoing US for causes unrelated to RA or CTS.

The criteria for RA were adopted from The American Rheumatism Association (1987) for the classification of RA.[14]

In the new criteria set, classification as "definite RA" is based on the confirmed presence of synovitis in at least 1 joint, absence of an alternative diagnosis that better explains the synovitis, and achievement of a total score of 6 or greater (of a possible 10) from the individual scores in the following four domains: number and site of involved joints (score range 0–5), serologic abnormality (score range 0–3), elevated acute-phase response (score range 0–1), and symptom duration (2 levels; range 0–1).

Exclusion criteria

- History of a condition other than RA that could cause CTS (e.g., diabetes mellitus, acute trauma, pregnancy,

hypothyroidism, hyperthyroidism, connective tissue disease)
- History of surgery for a wrist or hand fracture
- History of other systemic neurological disorders or radiculopathy
- Bifid median nerve or any mass lesion identified on US examination
- Pregnant patients were excluded
- All participants underwent a clinical evaluation that included Phalen's test, a manual muscle test of the abductor pollicis brevis muscle, and a search for Tinel-like signs and thenar muscle atrophy. In addition, if a participant exhibited CTS symptoms, he or she was excluded from the study.

Data collection

Each case was asked to lie on the examination bed with their elbow extended and their hand supinated. Fingers were kept relaxed, and slight flexion of the wrist was maintained during the measurements. B mode ultrasonography was done first, followed by elastography using a 5–12 MHz linear array transducer (PHILIPS EPIQ 5G US machine). Elastography values were calculated between any two areas as the index of elasticity. The region of interest box was placed over the whole CSA of the median nerve (average strain represented as A). The adjacent tissue at the acoustic coupler (moderate strain represented as B) is used as the reference. The elasticity of the median nerve is assessed as the B/A strain ratio (SR) in a transverse plane at the exact point with B-mode imaging. The median nerve SR in a transverse plane at the carpal tunnel inlet in the RA group without symptoms of CTS was compared with the non-RA group. Three SR readings were taken at the different areas of the nerve at the same level, and then the average value was taken for final data and RTE was performed, and the color code, which ranged from red (soft) to blue (hard), which indicated the relative stiffness of tissues within the region of interest (green and yellow indicates medium elasticity) was recorded.

Study variables

Changes in median nerve were considered as a primary outcome variable.

Statistical methods

Descriptive statistics were presented for age, gender, CSA, and SR. Data were also represented using appropriate diagrams like box plots. A normality check was done for quantitative variables. Continuous variables were expressed as mean and standard deviation. Independent-samples *t*-tests and Chi-square test were used to check the changes between variables. For nonnormally distributed quantitative parameters, medians and interquartile range were compared between study groups using Mann–Whitney U test (two groups). Significance was set at $P < 0.05$. CoGuide (Company BDSS, Bangalore, Karnataka, India) was used for statistical analysis.[15]

Results

One hundred and twelve subjects (56 [50%] cases and 56 [50%] controls) were analyzed finally.

The mean age of the study population in both groups was 48.5 ± 13.31 years, and most of them were females 36 (64.29%) in both groups. The difference in CSA of the median nerve at the carpal tunnel inlet in the right and left hands of cases and controls was statistically significant ($P < 0.001$). The difference in mean SR of the median nerve in the right and left hands of cases and controls was statistically significant ($P < 0.001$) [Table 1 and Figure 1].

Figure 2 showing various deformities associated with rheumatoid arthritis.

• Swan neck deformity is characterized by proximal interphalangeal joint hyperextension and the distal interphalangeal joint flexion.

• Boutonniere deformity is a deformity of the fingers in which the proximal interphalangeal joint is flexed and the distal interphalangeal joint is hyperextended.

• Hitchhiker thumb deformity refers to flexion of the metacarpophalangeal joint hyperextension of the interphalangeal joint.

Figure 3 showing Ultrasound grey scale image showing cross-sectional area of mention nerve in case and controls at the level of carpal tunnel inlet. Elastography image showing calculation of strain ratio in case and controls [Figure 4].

Table 1: Comparison of baseline parameter between study group (*n*=112)

Parameter	Study group		*P*
	Cases (*n*=56)	Controls (*n*=56)	
Age	48.5±13.31	48.02±13.41	0.849*
Gender, *n* (%)			
Male	20 (35.71)	20 (35.71)	1.000†
Female	36 (64.29)	36 (64.29)	
Right side			
Cross-sectional area (cm^2)	0.110 (0.105-0.116)	0.090 (0.083-0.095)	<0.001‡
Strain ratio	2.84 (2.41-2.98)	1.65 (1.41-1.94)	<0.001‡
Left side			
Cross-sectional area (cm^2)	0.109 (0.104-0.116)	0.089 (0.082-0.093)	<0.001‡
Strain ratio	2.76 (2.45-3.04)	1.66 (1.43-1.93)	<0.001‡
Rheumatoid arthritis factor, *n* (%)			
Positive	56 (100)	0	§
Negative	0	56 (100)	

*Independent sample *t*-test, †Chi-square test, ‡Maan-Whitney test, §No statistical test was applied-due to 0 subjects in the cells

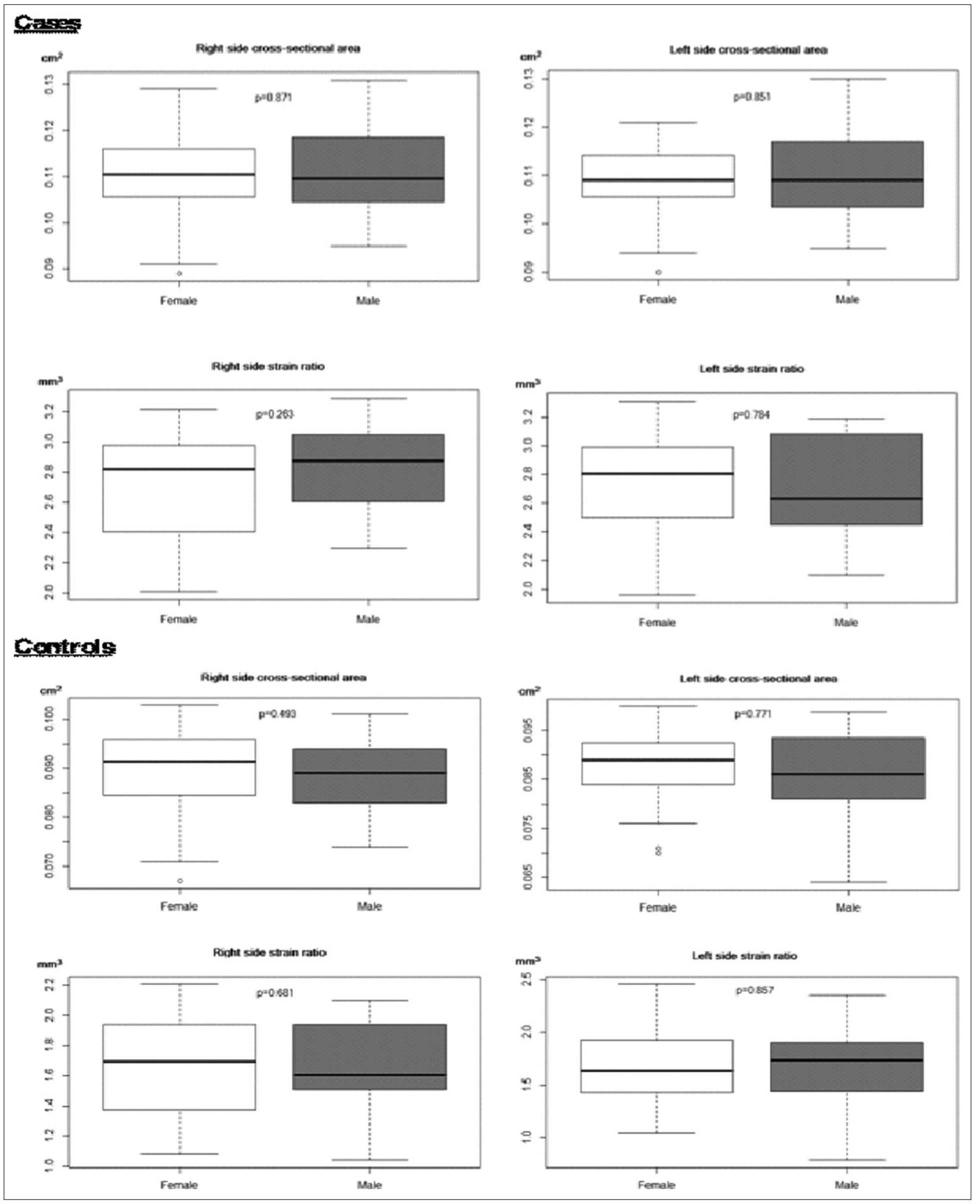

Figure 1: Box plots showing a comparison of right and left side cross-sectional area and strain ratio with gender in cases and controls (N = 56)

Discussion

The existing literature already reported the benefits of SWE over ultrasonography in patients with various musculoskeletal disorders. The authors of the present study assessed the diagnostic utility of SE in assessing median nerve changes among RA patients without symptoms of CTS, who were referred to the department of radio-diagnosis at a tertiary care center in South India. Published data pertaining to the diagnostic performance of SE in the same patients (RA patients without symptoms of CTS) are limited. Therefore, we compared the findings of our study with studies that used median nerve SE for diagnosing CTS and other diseases.

Dilip *et al*.[16] found the combined use of compression elastography (SE) and B-mode had 100% sensitivity, 90.91% specificity, and 93.1% diagnostic accuracy, respectively, in diagnosing diffuse pathologies of muscles, nerves, and tendons and also in differentiating benign and malignant masses. In the present study, the mean age of the study population in both groups (with and without RA) was 48.5 ± 13.31 years, and most of them were females 36 (64.29%). Similarly, Martin *et al*.[17] in his, a pilot study found the SE method a reliable tool to diagnose median nerve changes in CTS. The mean age was 45 ± 8.4 years in controls and 57 ± 10 years in CTS patients. Most of them were females in both groups.

In this study, the mean CSA of the median nerve in RA patients without CTS symptoms was within the normal range, and the difference was significant between the RA and non-RA groups. In contrast, Anno *et al*.[13] found no

Figure 2: Images showing various deformities associated with rheumatoid arthritis-Swan neck deformity, boutonniere's deformity & Hitchhiker's thumb

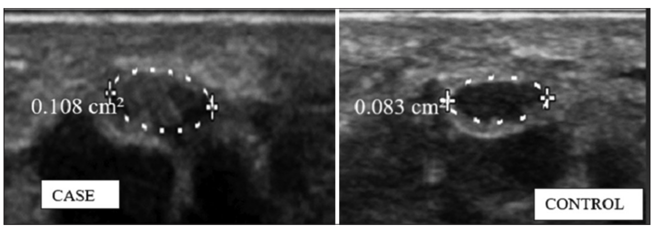

Figure 3: Cross sectional area (cm2) of the median nerve at the level of carpal tunnel inlet

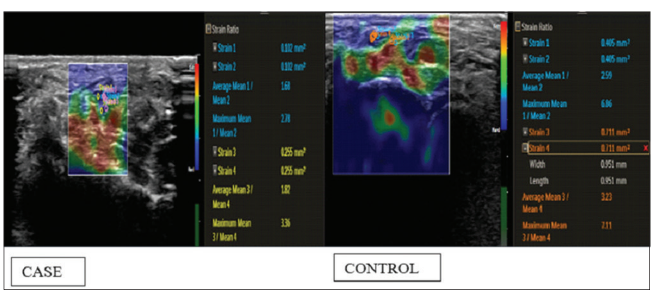

Figure 4: Strain ratio of the median nerve at the level of carpal tunnel inlet

significant differences in the circumference and CSA of the median nerve between the two groups. In the present study, the difference in mean SR of the median nerve in the right and left hands of cases and controls was statistically significant (P < 0.001). Anno *et al*.[13] found the SR of the median nerve significantly higher in RA group than in the nonRA group only at the inlet of the carpal tunnel level. In contrast, Martin *et al*.[17] found no significant difference in SR between those with CTS and controls (cross-sectional image P = 0.32; longitudinal image P = 0.20). SR did not correlate significantly with traditional US measures of CTS (lowest P = 0.26) but did correlate significantly with body mass index if obtained from cross-sectional images (r = 0.346; P = 0.02).

There was a significant increase in the median nerve strain. In the present study, there was a significant increase in the median nerve strain, cross-sectional area (CSA) of the median nerve at the carpal tunnel inlet in both cases and controls. The difference was statistically significant across the groups (P < 0.001). Yoshii *et al*.[18] his case control study reported that after releasing carpal tunnel, a significant increase was seen in the median nerve strain and CSA, and there was a significant decrease in the ratio of pressure strain (P < 0.001). In another comparative study by Park *et al*.[19] in Korea, the diagnostic performance of SE and SWE for diagnosing CTS was assessed. A significant intergroup difference (P < 0.001, P < 0.001, and P = 0.002, respectively) was noted with CSA, elasticity, and shear wave velocity. The SR showed no significant intergroup difference (P = 0.639), in contrast to the present study.

In the present study, median nerve strain at the inlet of the carpal tunnel level was significantly higher in the RA group than in the non-RA group, suggesting that SE was highly sensitive to reflecting median nerve degeneration. This finding was similar to a study by Miyamoto *et al*.[20] reported that the median nerve in patients with CTS was stiffer than that in healthy subjects, indicating that RTE provides significant improvement in the diagnostic accuracy of US assessment of CTS. In another study in the United Kingdom by Schneebeli *et al*.[21] used both strain and shear wave sonoelastography to detect changes in the Achilles tendon and found that SE, when used with reference material, was able to detect elasticity changes under load when compared to SWE which was less able to detect changes.

Quantifying mechanical and elastic tissue properties has become easy with this exciting and rapidly evolving strain wave elastography/tension elastography technique. It can complement the conventional US in the initial characterization and posttreatment follow-up of the musculoskeletal system's various traumatic and pathologic conditions. When an abnormal musculoskeletal soft tissue is difficult to detect with conventional US methods, strain wave elastography/tension elastography can be helpful in early disease diagnosis and management. It may also help stage chronic diseases, determine therapeutic responses, and monitor age-related changes, including carpel tunnel syndrome.

Limitations

Elastography and ultrasonography are operator dependent and can be affected by subjective changes in the degree of pressure applied, leading to information bias. Secondly, the study included only patients with and without RA and hence cannot be generalized. The sample size was also small, and it was a single-center study which can affect the findings and associations. Many covariates like comorbidities, family history, treatment outcome, and pre and postimages were not observed in the present study, which can influence the results. Another limitation of the study was using the 1987 classification criteria instead of the more recent 2010 classification criteria.

Conclusion

In conclusion, the median nerve stiffness measured by SE in patients with RA without CTS symptoms was significantly higher in non-RA individuals. This result suggested that subclinical, mild inflammation of the flexor tendon and wrist joint may cause fibrotic changes in the median nerve in RA patients. In particular, this can discriminate the severe group from the other groups. Hence, SE could help evaluate these changes in the median nerve. The findings may be helpful in assessing the therapeutic effect during the process of CTS treatment.

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Conflicts of interest

There are no conflicts of interest.

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