Hand dominance in early and established rheumatoid arthritis: evaluation by dynamometer, Ritchie index and musculoskeletal ultrasound: a cross sectional study

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SUMMARY

Rheumatoid arthritis (RA) usually occurs as a symmetrical disease, which mainly affects the small joints of the hands and feet. The correlation of handedness with radiological changes shows significantly greater radiological changes in the dominant hand than in the non-dominant one. Additionally, the dominant hand is more severely affected in terms of strength, function and deformity. Our objective is to evaluate the influence of handedness on musculoskeletal ultrasound (US), Ritchie articular index (RAI) and digital dynamometer findings in patients with active RA (early, group B, vs. established, group A). A total number of 113 patients with established RA and 44 patients with early RA with active disease (DAS28-ESR >3.2) were included in the study. US assessments of both hands were performed to assess synovitis, tenosynovitis, and erosions. RAI was used to evaluate three joint groups in each hand. Handgrip strength was measured with a digital dynamometer. The US5 score showed that the dominant hand was more affected than the non-dominant one. This was significant in group A for the synovitis Power Doppler (PD) mode (p=0.032) and tenosynovitis PD (p=0.005) scores, and in group B for synovitis Grey Scale (GS) mode (p<0.001), synovitis PD (p=0.037) and erosions (p=0.027) scores. RAI was significantly higher in the dominant hand (p=0.013) in group A and even greater in group B (p=0.011). The dominant hand was stronger than the non-dominant hand in both groups. The dominant hand is generally affected in early RA. Subsequently, the disease tends to become more symmetrical with disease progression.

Key words: Rheumatoid arthritis; early, established; hand dominance; ultrasound.

■ INTRODUCTION

Rheumatoid arthritis (RA) is a common autoimmune disease. It affects about 1% of the population worldwide (1). It is a chronic inflammatory symmetrical disease which affects mainly small joints, especially at its onset (2).

Several previous studies have addressed the effect of handedness on RA progression. Most of them compared both hands in terms of radiological score, hand deformity, handgrip strength and Ritchie articular index (RAI) (3-5). These studies concluded that

hand dominance has an impact on the disease course, and hypothesized that mechanical stress increase the disease plateau (3, 4), which is mainly seen in early RA (5, 6).

In many studies, RA disease activity and outcome were evaluated by ultrasound (US), which is a useful, noninvasive, rapid, painless bedside method preferred by most patients and physicians. It can detect early changes in bone (such as erosions) and soft tissues (such as synovitis and tenosynovitis) with high sensitivity. The 'US5 score' was proposed as a modification of the US7 score for hand evaluation in RA (7-12).

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RAI is a summation of tenderness scores for joints calculated by applying pressure on the articular margins. This score is widely used for evaluation of RA activity (13). RAI is considered a standard method for comparing the dominant and non-dominant hands in RA (5).

The handgrip is usually affected by the activity of RA and its evaluation reflects to a great extent functional impairment in RA patients (14). Weakness is usually the result of muscle atrophy, joint pain, and stiffness. Hydraulic, pneumatic, and digital dynamometers are generally used for handgrip measurement (15).

In this study, we aimed to answer the following questions: i) how does disease symmetry change with disease progression? ii) does hand dominance constitute an important aspect of the clinical manifestations of RA, and does it influence disease progression? iii) should both hands be included in imaging scores (*i.e.* US) or is it sufficient to examine one hand?

■ MATERIALS AND METHODS

Permission of publishing data related to the study participants was obtained. Personal and medical information was kept confidential and not made available to third parties. Patients with RA diagnosed on the basis of 2010 ACR/EULAR criteria (16) were recruited from the outpatient clinic of the rheumatology department, all of whom aged 18 or more. ESR was determined to calculate the DAS28, and patients with active disease (defined as DAS28-ESR >3.2) were included in the study (17). Patients with overlapping syndromes were excluded.

Patients were divided into two groups according to disease duration. Group A with established RA (disease duration ≥6 months) and group B with early RA (disease duration <6 months) (18). The two groups were age- and sex-matched.

A descriptive cross-sectional study was carried out on 226 hands of 113 patients (six of them were left-handed) including 30 males and 83 females with established RA (group A), and 88 hands of 44 patients

(2 of them were left-handed) with early RA (group B) including 16 males and 28 females. All patients in both groups were naïve for biologic therapies.

The dominant hand was defined as the hand that is used for handwriting or scissoring or daily activity (5, 6). Hand dominance in both groups was evaluated by US, RAI, and a dynamometer.

Musculoskeletal US was performed using a 7-12 MHz (General Electric Logic E, China) linear probe. Five joints [wrist, metacarpophalangeal joints (MCP) 2,3, proximal interphalangeal joints (PIP) 2,3] on both hands (bilateral 'US5 score'), which are part of the German US7 score, were assessed to evaluate synovitis, tenosynovitis and erosions in each hand (12). The US assessment included evaluation of synovitis, tenosynovitis, and erosions by grey scale (GS) and power Doppler (PD) mode (19). Synovitis and synovial/ tenosynovial vascularity were scored on a semiquantitative scale (grade 0-3) by power Doppler ultrasound (PDUS) (20). Synovitis (effusion and or synovial hypertrophy) was considered semi-quantitatively (0-3) by gray scale ultrasound (GSUS) (21). Tenosynovitis and erosions in GSUS were evaluated as being 0, when absent, or 1, when present (12). All the joints included were examined from the palmar side, the dorsal side, and also the radial side of MCP II (only for erosion) (Figure 1). The 1st and 3rd author performed the US examination and both were blinded for clinical data. The 1st author has 8 years of experience in the field of musculoskeletal US and performs 6 US examinations daily on average. The 3rd author has 6 years of experience in the same field and carries out 6 US examinations daily on average. The interobserver Cohen's Kappa value was 0.73, which means a good to excellent agreement between the two observers.

RAI is a score that is used for the assessment of degrees of joint tenderness in RA. It gives three grades for joint tenderness: grade 0 means no tenderness, grade 1 means that the patient complains of pain, grade 2 means that the patient complains of pain and winces, and grade 3 means

that the patient complains of pain, winces and withdraws his or her hands. The joints evaluated by this score in our study included the wrist, MCP 1-5 joints (considered as one joint group), PIP 2-5 joints and interphalangeal (IP) joints (IP and PIP were considered as one joint group) in each hand (22). A minimum score of 0 and a maxi-
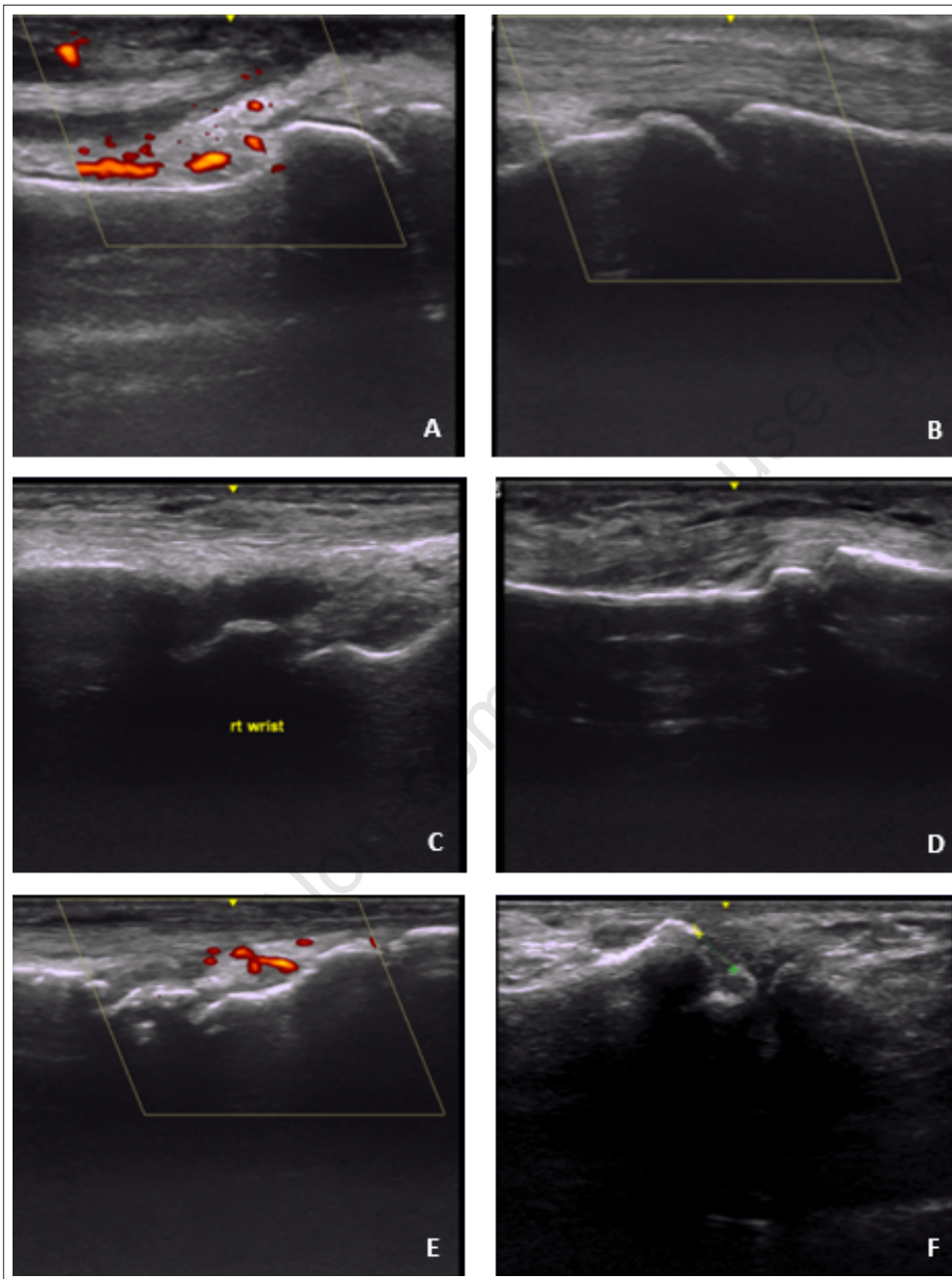

Figure 1 - Different features of the US5 score. A) MCP palmar sagittal scan with flexor tenosynovitis grade 2 by PDUS; B) MCP palmar sagital scan with grade 1 synovitis on GS and 0 on PDUS for synovitis and tenosynovitis; C) wrist palmar sagittal scan with grade 3 synovitis on GS; D) PIP palmar sagittal scan with synovitis grade 1 and tenosynovitis by GS; E) Wrist palmar longitudinal scan with grade 2 synovitis by PDUS; F) MCP palmar sagittal scan showing erosion.

mum score of 9 for each hand was considered. Firm pressure was applied to the joint margin (enough to blanch the examiner's nail bed) (23).

Handgrip was measured using a baseline digital dynamometer (produced by Pro-health Care Company, New York; USA). During handgrip examination, the patient was standing with his back straight, shoulder slightly abducted, elbow fully extended and wrist extended. The display screen was facing the examiner. The physician requested the patient to squeeze as much as possible and then the examiner asked to compress harder and harder (24). The highest of three measures within a 2-minute interval (in order to avoid fatigue) was considered (15, 25). The dominant hand was tested first.

The US examination was done first, followed by the handgrip test and finally RAI. RAI was postponed to the last step in order not to affect the other two examinations. All three examinations were done on the same day.

A DAS28-ESR >3.2 was used as cut-off for the inclusion of RA patients with active disease. We excluded patients in remission or with low disease activity. RAI, hand grip and DAS28-ESR all were carried out by the second author, who was blinded for the US examination.

Data is presented as an arithmetic mean±SD as all of the quantitative data were normally distributed (Kolmogorov-Smirnov test). Student's t-test was used to compare means between two independent groups and the paired t-test was used to compare means of the same patient group between dominant and non-dominant hands. Comparisons of percentage qualitative data were tested using the Chi-square test or Fisher's exact test. Instead, for comparing percentages between the two hands in the same group, the McNemar Chi-square test was used. Correlations between two quantitative data were assessed using Pearson's correlation test. The Statistical Package for the Social Sciences (SPSS) software (version 22.0, SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. A p value <0.05 was considered significant.

RESULTS

The mean age of the patients was 39.73±10.11 years in group A and 37.59±6.29 years in group B. The male-to-female ratio was around 1:3 in group A and 1:2 in group B. The mean disease duration was 36.73±17.03 months in group A and was 3.53±1.44 months in group B (Table I).

Musculoskeletal ultrasound
Regarding the US5 score, the mean scores of GS-US5 synovitis score, PD-US5 synovitis score, GS-US5 tenosynovitis score, PD-US5 tenosynovitis score and erosion sum score of 5 joints were 27.24±7.68, 2.06±2.78, 1.75±1.53, 0.63±0.97 and 1.94±2.07 respectively in group A, compared to 22.09±6.41, 1.64±1.88, 1.32±1.23, 0.55±0.70 and 0.93±1.19 respectively in group B. The erosion and synovitis (GS only) scores were significantly higher in group A (p=0.006 and <0.001, respectively). No significant differences between the two groups were detected for the other components of the US5 score (Table I).

Among group A, synovitis was the most common finding (found in 100% of cases, with different degrees) followed by tenosynovitis (found in more than 60% of cases), and lastly erosions (found in 58% of patients) (Tables II-IV). In group B, synovitis was also the most common finding (found in 100% of cases, with different degrees) followed by tenosynovitis (found in 50% of cases) and lastly erosions (found in around 45% of patients) (Tables II, III, V).

The comparison between the dominant and non-dominant hands regarding the US5 score in group A showed that the dominant hand was significantly more affected in the synovitis PD (p=0.032) and tenosynovitis PD (p=0.003). In group B, the US5 score showed that the dominant hand was significantly more affected for synovitis GS (p<0.001), synovitis PD (p=0.037), and erosions (p=0.027) (Table VI).

Seropositive patients were more symmetrical, especially in group A. In group A, the US5 score showed non-significant differences between both hands among RF-

Table I - Demographics, and clinical and sonographic comparison between the two study groups.

		Group A (Established RA) (N=113)	Group B (Early RA) (N=44)	P value
Sex	Male	30 (26.5%)	16 (36.4%)	0.225
	Female	83 (73.5%)	28 (63.6%)	
Age	Mean (SD)	39.73 (10.11)	37.59 (6.29)	0.113**
	Median (range)	37 (25-62)	36 (25-53)	
Disease duration (in months)	Mean (SD)	36.73 (17.03)	3.53 (1.44)	**<0.001****
	Median (range)	34 (9-80)	3.5 (1.5-6)	
RF	Positive	95 (84.1%)	25 (56.8%)	**<0.001**
Dominant hand	Right	107 (94.7%)	42 (95.5%)	1.000*
	Left	6 (5.3%)	2 (4.5%)	
DAS28	Mean (SD)	4.81 (1.21)	4.60 (1.06)	0.295**
	Moderate disease activity	76 (67.3%)	31 (70.5%)	0.699
	High disease activity	37 (32.7%)	13 (29.5%)	
Ritchie, mean (SD)	Dominant hand	4.98 (1.65)	4.77 (1.82)	0.488**
	Non dominant hand	4.55 (1.63)	3.93 (1.56)	**0.032****
	Total Richie	9.53 (2.71)	8.70 (2.66)	0.087**
Hand grip, mean (SD)	Dominant hand	14.30 (3.44)	14.50 (4.16)	0.760**
	Non dominant hand	14.05 (3.79)	13.30 (3.61)	0.256**
US5 score items				
Synovitis, B mode, mean (SD)	Dominant hand	13.90 (4.64)	12.32 (3.81)	**0.046****
	Non dominant hand	13.34 (4.24)	9.77 (3.50)	**<0.001****
	Both hands	27.24 (7.68)	22.09 (6.41)	**<0.001****
Synovitis, PD, mean (SD)	Dominant hand	1.27 (2.44)	1.09 (1.67)	0.861+
	Non dominant hand	0.79 (0.87)	0.55 (0.63)	0.181+
	Both hands	2.06 (2.78)	1.64 (1.88)	0.566+
Tenosynovitis, B mode, mean (SD)	Dominant hand	0.78 (0.86)	0.61 (0.72)	0.359+
	Non dominant hand	0.97 (1.03)	0.70 (0.88)	0.136+
	Both hands	1.75 (1.53)	1.32 (1.23)	0.135+
Tenosynovitis, PD, mean (SD)	Dominant hand	0.17 (0.42)	0.25 (0.53)	0.388+
	Non dominant hand	0.46 (0.91)	0.30 (0.55)	0.547+
	Both hands	0.63 (0.97)	0.55 (0.70)	0.876+
Erosions, mean (SD)	Dominant hand	0.98 (1.36)	0.64 (0.94)	0.226+
	Non dominant hand	0.96 (1.09)	0.30 (0.55)	**<0.001**+
	Both hands	1.94 (2.07)	0.93 (1.19)	**0.006**+
Treatment	NSAIDs	56 (42.11%)	21 (47.73%)	0.514
	Steroids	26 (19.55%)	13 (29.55%	0.166
	MTX alone	33 (24.81%)	18 (40.91%)	**0.040**
	HCQ alone	1 (0.75%)	5 (11.36%)	**0.004***
	LEF alone	14 (10.53%)	9 (20.45%)	0.089
	HCQ + SSZ	5 (3.76%)	6 (13.64%)	**0.046**
	MTX + HCQ	22 (16.54%)	5 (11.36%)	0.407
	MTX + HCQ + SSZ	12 (9.02%)	0	0.086*
	MTX + LEF	46 (34.59%)	1 (2.27%)	**<0.001**

*Fisher's Exact test is used instead of Pearson Chi square.
**Student's t test was done to compare means between the two groups.
+Mann Whitney test was used in non-parametric data instead of Student's t test.
MTX: Methotrexate, HCQ: Hydroxychloroquine, SSZ: Sulfasalazine, LEF: Leflunomide.

Table II - Comparison between dominant and non-dominant hand regarding Ritchie's index, hand grip and US5.

		Dominant hand	Non-dominant hand	P value
Ritchie, mean (SD)	Group A (established RA)	4.98 (1.65)	4.55 (1.63)	**0.013**
	Group B (Early RA)	4.77 (1.82)	3.93 (1.56)	**0.011**
	All patients	4.92 (1.69)	4.38 (1.63)	**<0.001**
Hand grip, mean (SD)	Group A (established RA)	14.30 (3.44)	14.05 (3.79)	0.486
	Group B (Early RA)	14.50 (4.16)	13.30 (3.61)	**0.045**
	All patients	14.36 (3.64)	13.84 (3.74)	0.092
US5 score items				
Synovitis (B mode) (score 0-33)	Group (A) established RA	13.90 (4.64)	13.34 (4.24)	0.181
	Group (B) early RA	12.32 (3.81)	9.77 (3.50)	**<0.001**
	Both groups	13.46 (4.47)	12.34 (4.34)	**0.001**
Synovitis (Power Doppler) (score 0-33)	Group (A) established RA	1.27 (2.44)	0.79 (0.87)	**0.032**
	Group (B) early RA	1.09 (1.67)	0.55 (0.63)	**0.037**
	Both groups	1.22 (2.24)	0.72 (0.82)	**0.005**
Tenosynovitis (B mode) (Score 0-5)	Group (A) established RA	0.78 (0.86)	0.97 (1.03)	0.070
	Group (B) early RA	0.61 (0.72)	0.70 (0.88)	0.561
	Both groups	0.73 (0.83)	0.90 (0.99)	0.062
Tenosynovitis (Power Doppler) (score 0-15)	Group (A) established RA	0.17 (0.42)	0.46 (0.91)	**0.003**
	Group (B) early RA	0.25 (0.53)	0.30 (0.55)	0.719
	Both groups	0.190 (0.45)	0.41 (0.82)	**0.005**
Erosions (score 0-9)	Group (A) established RA	0.98 (1.36)	0.96 (1.09)	0.833
	Group (B) early RA	0.63 (0.94)	0.30 (0.55)	**0.027**
	Both groups	0.89 (1.27)	0.77 (1.01)	0.254

Paired t test was used in all of the above comparisons.

positive patients. A significant difference among RF-negative patients was seen only for PD tenosynovitis US5 score (p=0.014). In group B, the US5 score showed a significant difference between both hands among RF positive patients for the synovitis GS score (p=0.006). Furthermore, a significant difference was present in RF-negative patients for synovitis (only GS) (p=0.001), tenosynovitis (only GS) (p=0.031), and erosion US5 scores (p=0.049). Asymmetry was more often found in the wrist followed by MCP and PIP joints in group A. Symmetry was measured qualitatively by comparing joints affected in both hands, and quantitatively by comparing the US5 score between both hands.

The DAS28 correlated with the compo-

nents of the US5 score, but there was no significant difference between the two groups. Only the erosion score in group B was significantly higher in patients with a high DAS28 (compared to moderate DAS28) (p=0.012).

RAI

In group A, the RAI was significantly higher in the dominant hand compared to the non-dominant hand (p=0.013), and in group B, the difference was even more significant (p=0.011). As to the comparison of RAI between the established and early RA groups, it was higher in group A. However, the difference between both groups was significant in the non-dominant hand and not significant in the dominant hand (Table VI).

Table III - Frequency of positive findings by US5 score in the dominant hand according to disease duration and joint.

		Group A	Group B	P value
Synovitis (B mode)	Wrist dorso-median	103 (91.2%)	38 (86.4%)	0.268*
	Wrist dorso-ulnar	83 (73.5%)	30 (68.2%)	0.509
	2nd MCP dorsal	84 (74.3%)	31 (70.5%)	0.622
	3rd MCP dorsal	79 (69.9%)	29 (65.9%)	0.627
	2nd PIP dorsal	93 (82.3%)	36 (81.8%)	0.943
	3rd PIP dorsal	91 (80.5%)	37 (84.1%)	0.606
	Wrist palmo-median	87 (77%)	32 (72.7%)	0.575
	2nd MCP palmar	73 (64.6%)	28 (63.6%)	0.910
	3rd MCP palmar	72 (63.7%)	26 (59.1%)	0.591
	2nd PIP palmar	81 (71.7%)	30 (68.2%)	0.665
	3rd PIP palmar	77 (68.1%)	30 (68.2%)	0.996
	All	113 (100%)	44 (100%)	-
Synovitis (Power Doppler)	Wrist dorso-median	42 (37.1%)	13 (29.6%)	0.369
	Wrist dorso-ulnar	8 (7.1%)	4 (9.1%)	0.740*
	2nd MCP dorsal	6 (5.3%)	4 (9.1%)	0.468*
	3rd MCP dorsal	4 (3.5%)	1 (2.3%)	1.000*
	2nd PIP dorsal	14 (12.4%)	4 (9.1%)	0.560
	3rd PIP dorsal	4 (3.5%)	2 (4.5%)	0.673*
	Wrist palmo-median	7 (6.3%)	4 (9.1%)	0.503*
	2nd MCP palmar	6 (5.3%)	3 (6.8%)	0.711*
	3rd MCP palmar	4 (3.5%)	2 (4.5%)	0.673*
	2nd PIP palmar	10 (8.8%)	4 (9.1%)	1.000*
	3rd PIP palmar	2 (1.8%)	0	1.000*
	All	60 (53.1%)	24 (54.5%)	0.870
Tenosynovitis (B mode)	Wrist dorso-median	20 (17.7%)	6 (13.6%)	0.539
	Wrist dorso-ulnar	44 (38.9%)	10 (22.7%)	0.055
	Wrist palmo-median	8 (7.1%)	4 (9.1%)	0.740*
	2nd MCP palmar	6 (5.3%)	2 (4.5%)	1.000*
	3rd MCP palmar	10 (8.8%)	5 (11.4%)	0.763*
	All	59 (52.2%)	22 (50%)	0.803
Tenosynovitis (Power Doppler)	Wrist dorso-median	7 (6.2%)	3 (6.8%)	1.000*
	Wrist dorso-ulnar	8 (7.1%)	4 (9.1%)	0.740*
	Wrist palmo-median	2 (1.8%)	2 (4.5%)	0.313*
	2nd MCP palmar	0	1 (2.3%)	0.280*
	3rd MCP palmar	0	0	-
	All	17 (15%)	9 (20.5%)	0.413
Erosions	2nd MCP dorsal	26 (23%)	9 (20.5%)	0.730
	2nd MCP radial	49 (43.4%)	7 (15.9%)	**0.001**
	3rd MCP dorsal	8 (7.1%)	2 (4.5%)	0.727*
	2nd PIP dorsal	6 (5.3%)	3 (6.8%)	0.711*
	3rd PIP dorsal	4 (3.5%)	2 (4.5%)	0.673*
	2nd MCP palmar	7 (6.2%)	2 (4.5%)	1.000*
	3rd MCP palmar	4 (3.5%)	1 (2.3%)	1.000*
	2nd PIP palmar	4 (3.5%)	1 (2.3%)	1.000*
	3rd PIP palmar	3 (2.7%)	1 (2.3%)	1.000*
	All	56 (49.6%)	20 (45.5%)	0.644

*Fisher exact test was used instead of Pearson chi square.

Table IV - Frequency of positive findings by US5 score in group A according to the involved joint.

		Dominant hand	Non dominant hand	P value
Synovitis (B mode)	Wrist dorso-median	103 (91.2%)	103 (91.2%)	1.000
	Wrist dorso-ulnar	83 (73.5%)	84 (74.3%)	0.879
	2nd MCP dorsal	84 (74.3%)	71 (62.8%)	0.062
	3rd MCP dorsal	79 (69.9%)	83 (73.5%)	0.555
	2nd PIP dorsal	93 (82.3%)	99 (87.6%)	0.264
	3rd PIP dorsal	91 (80.5%)	96 (85%)	0.379
	Wrist palmo-median	87 (77%)	92 (81.4%)	0.412
	2nd MCP palmar	73 (64.6%)	78 (69%)	0.480
	3rd MCP palmar	72 (63.7%)	66 (58.4%)	0.413
	2nd PIP palmar	81 (71.7%)	86 (76.1%)	0.449
	3rd PIP palmar	77 (68.1%)	68 (60.2%)	0.212
	All	113 (100%)	113 (100%)	1.000
Synovitis (Power Doppler)	Wrist dorso-median	42 (37.1%)	50 (44.2%)	0.279
	Wrist dorso-ulnar	8 (7.1%)	10 (8.8%)	0.623
	2nd MCP dorsal	6 (5.3%)	0	**0.013**
	3rd MCP dorsal	4 (3.5%)	0	**0.044**
	2nd PIP dorsal	14 (12.4%)	6 (5.3%)	0.061
	3rd PIP dorsal	4 (3.5%)	0	**0.044**
	Wrist palmo-median	7 (6.3%)	3 (2.7%)	0.196
	2nd MCP palmar	6 (5.3%)	3 (2.7%)	0.308
	3rd MCP palmar	4 (3.5%)	3 (2.7%)	0.701
	2nd PIP palmar	10 (8.8%)	0	**0.001**
	3rd PIP palmar	2 (1.8%)	0	0.155
	All	60 (53.1%)	62 (54.9%)	0.790
Tenosynovitis (B mode)	Wrist dorso-median	20 (17.7%)	26 (23%)	0.321
	Wrist dorso-ulnar	44 (38.9%)	40 (35.4%)	0.582
	Wrist palmo-median	8 (7.1%)	15 (13.3%)	0.123
	2nd MCP palmar	6 (5.3%)	17 (15%)	**0.016**
	3rd MCP palmar	10 (8.8%)	0	**0.001**
	All	59 (52.2%)	69 (61.1%)	0.179
Tenosynovitis (Power Doppler)	Wrist dorso-median	7 (6.2%)	14 (12.4%)	0.109
	Wrist dorso-ulnar	8 (7.1%)	14 (12.4%)	0.178
	Wrist palmo-median	2 (1.8%)	5 (4.4%)	0.249
	2nd MCP palmar	0	5 (4.4%)	**0.024**
	3rd MCP palmar	0	0	1.000
	All	17 (15%)	32 (28.3%)	**0.015**
Erosions	2nd MCP dorsal	26 (23%)	20 (17.7%)	0.321
	2nd MCP radial	49 (43.4%)	47 (41.6%)	0.788
	3rd MCP dorsal	8 (7.1%)	3 (2.7%)	0.122
	2nd PIP dorsal	6 (5.3%)	6 (5.3%)	1.000
	3rd PIP dorsal	4 (3.5%)	4 (3.5%)	1.000
	2nd MCP palmar	7 (6.2%)	13 (11.5%)	0.160
	3rd MCP palmar	4 (3.5%)	7 (6.2%)	0.354
	2nd PIP palmar	4 (3.5%)	0	**0.044**
	3rd PIP palmar	3 (2.7%)	8 (7.1%)	0.122
	All	56 (49.6%)	66 (58.4%)	0.182

McNemar chi square test was used.

Table V - Frequency of positive findings by US5 score in group B according to the involved joint.

		Dominant hand	Non dominant hand	P value
Synovitis (B mode)	Wrist dorso-median	38 (86.4%)	35 (79.5%)	0.395
	Wrist dorso-ulnar	30 (68.2%)	18 (40.9%)	**0.010**
	2nd MCP dorsal	31 (70.5%)	20 (45.5%)	**0.018**
	3rd MCP dorsal	29 (65.9%)	28 (63.6%)	0.823
	2nd PIP dorsal	36 (81.8%)	34 (77.3%)	0.597
	3rd PIP dorsal	37 (84.1%)	35 (79.5%)	0.580
	Wrist palmo-median	32 (72.7%)	24 (54.5%)	0.076
	2nd MCP palmar	28 (63.6%)	26 (59.1%)	0.661
	3rd MCP palmar	26 (59.1%)	24 (54.5%)	0.667
	2nd PIP palmar	30 (68.2%)	31 (70.5%)	0.818
	3rd PIP palmar	30 (68.2%)	28 (63.6%)	0.653
	All	44 (100%)	44 (100%)	1.000
Synovitis (Power Doppler)	Wrist dorso-median	13 (29.6%)	16 (35.4%)	0.496
	Wrist dorso-ulnar	4 (9.1%)	1 (2.3%)	0.167
	2nd MCP dorsal	4 (9.1%)	1 (2.3%)	0.167
	3rd MCP dorsal	1 (2.3%)	0	0.315
	2nd PIP dorsal	4 (9.1%)	2 (4.5%)	0.398
	3rd PIP dorsal	2 (4.5%)	0	0.153
	Wrist palmo-median	4 (9.1%)	1 (2.3%)	0.167
	2nd MCP palmar	3 (6.8%)	1 (2.3%)	0.167
	3rd MCP palmar	2 (4.5%)	0	0.153
	2nd PIP palmar	4 (9.1%)	0	**0.041**
	3rd PIP palmar	0	1 (2.3%)	0.315
	All	24 (54.5%)	21 (47.7%)	0.522
Tenosynovitis (B mode)	Wrist dorso-median	6 (13.6%)	9 (20.5%)	0.395
	Wrist dorso-ulnar	10 (22.7%)	11 (25%)	0.802
	Wrist palmo-median	4 (9.1%)	2 (4.5%)	0.398
	2nd MCP palmar	2 (4.5%)	7 (15.9%)	0.079
	3rd MCP palmar	5 (11.4%)	0	**0.021**
	All	22 (50%)	21 (47.7%)	0.832
Tenosynovitis (Power Doppler)	Wrist dorso-median	3 (6.8%)	3 (6.8%)	1.000
	Wrist dorso-ulnar	4 (9.1%)	7 (15.9%)	0.336
	Wrist palmo-median	2 (4.5%)	2 (4.5%)	1.000
	2nd MCP palmar	1 (2.3%)	1 (2.3%)	1.000
	3rd MCP palmar	0	0	1.000
	All	9 (20.5%)	11 (25%)	0.611
Erosions	2nd MCP dorsal	9 (20.5%)	2 (4.5%)	**0.024**
	2nd MCP radial	7 (15.9%)	6 (13.6%)	0.764
	3rd MCP dorsal	2 (4.5%)	1 (2.3%)	0.557
	2nd PIP dorsal	3 (6.8%)	1 (2.3%)	0.306
	3rd PIP dorsal	2 (4.5%)	0	0.153
	2nd MCP palmar	2 (4.5%)	1 (2.3%)	0.557
	3rd MCP palmar	1 (2.3%)	1 (2.3%)	1.000
	2nd PIP palmar	1 (2.3%)	0	0.315
	3rd PIP palmar	1 (2.3%)	1 (2.3%)	1.000
	All	20 (45.5%)	11 (25.0%)	**0.045**

McNemar chi square test was used.

Table VI - Frequency of positive findings by US5 score in the early RA group according to the involved joint.

		Dominant hand	Non dominant hand	P value
Synovitis (B mode)	Wrist dorso-median	38 (86.4%)	35 (79.5%)	0.395
	Wrist dorso-ulnar	30 (68.2%)	18 (40.9%)	0.010
	2nd MCP dorsal	31 (70.5%)	20 (45.5%)	**0.018**
	3rd MCP dorsal	29 (65.9%)	28 (63.6%)	0.823
	2nd PIP dorsal	36 (81.8%)	34 (77.3%)	0.597
	3rd PIP dorsal	37 (84.1%)	35 (79.5%)	0.580
	Wrist palmo-median	32 (72.7%)	24 (54.5%)	0.076
	2nd MCP palmar	28 (63.6%)	26 (59.1%)	0.661
	3rd MCP palmar	26 (59.1%)	24 (54.5%)	0.667
	2nd PIP palmar	30 (68.2%)	31 (70.5%)	0.818
	3rd PIP palmar	30 (68.2%)	28 (63.6%)	0.653
	All	44 (100%)	44 (100%)	1.000
Synovitis (Power Doppler)	Wrist dorso-median	13 (29.6%)	16 (35.4%)	0.496
	Wrist dorso-ulnar	4 (9.1%)	1 (2.3%)	0.167
	2nd MCP dorsal	4 (9.1%)	1 (2.3%)	0.167
	3rd MCP dorsal	1 (2.3%)	0	0.315
	2nd PIP dorsal	4 (9.1%)	2 (4.5%)	0.398
	3rd PIP dorsal	2 (4.5%)	0	0.153
	Wrist palmo-median	4 (9.1%)	1 (2.3%)	0.167
	2nd MCP palmar	3 (6.8%)	1 (2.3%)	0.167
	3rd MCP palmar	2 (4.5%)	0	0.153
	2nd PIP palmar	4 (9.1%)	0	0.041
	3rd PIP palmar	0	1 (2.3%)	0.315
	All	24 (54.5%)	21 (47.7%)	0.522
Tenosynovitis (B mode)	Wrist dorso-median	6 (13.6%)	9 (20.5%)	0.395
	Wrist dorso-ulnar	10 (22.7%)	11 (25%)	0.802
	Wrist palmo-median	4 (9.1%)	2 (4.5%)	0.398
	2nd MCP palmar	2 (4.5%)	7 (15.9%)	0.079
	3rd MCP palmar	5 (11.4%)	0	**0.021**
	All	22 (50%)	21 (47.7%)	0.832
Tenosynovitis (Power Doppler)	Wrist dorso-median	3 (6.8%)	3 (6.8%)	1.000
	Wrist dorso-ulnar	4 (9.1%)	7 (15.9%)	0.336
	Wrist palmo-median	2 (4.5%)	2 (4.5%)	1.000
	2nd MCP palmar	1 (2.3%)	1 (2.3%)	1.000
	3rd MCP palmar	0	0	1.000
	All	9 (20.5%)	11 (25%)	0.611
Erosions	2nd MCP dorsal	9 (20.5%)	2 (4.5%)	**0.024**
	2nd MCP radial	7 (15.9%)	6 (13.6%)	0.764
	3rd MCP dorsal	2 (4.5%)	1 (2.3%)	0.557
	2nd PIP dorsal	3 (6.8%)	1 (2.3%)	0.306
	3rd PIP dorsal	2 (4.5%)	0	0.153
	2nd MCP palmar	2 (4.5%)	1 (2.3%)	0.557
	3rd MCP palmar	1 (2.3%)	1 (2.3%)	1.000
	2nd PIP palmar	1 (2.3%)	0	0.315
	3rd PIP palmar	1 (2.3%)	1 (2.3%)	1.000
	All	20 (45.5%)	11 (25.0%)	**0.045**

McNemar chi square test was used.

Handgrip

The dominant hand was always stronger than the non-dominant hand in both groups. However, the difference was not significant in the established RA group (p=0.486), but it was significant in the early RA group (p=0.045) (Table VI).

Comparison of the three modalities

Using Pearson Correlation statistics to estimate the correlation between the three modalities (US5, RAI and hand grip) in the dominant hand and the non-dominant hand, the following results were obtained.

1. The correlations between US5 and RAI in the dominant hand were significant in group A for synovitis GS (r=251, p=0.007) and tenosynovitis PD (r=0.262, p=0.005), while they were significant in group B for synovitis (GS) (r=0.616, p<0.001), tenosynovitis (PD) (r=0.324, p=0.032) and erosions (r=0.345, p=0.022). However, in the non-dominant hand, the correlations were non-significant in group A, whereas they were was significant in group B only for synovitis GS (r=0.312, p = 0.039).

2. The correlations between US5 and hand grip in the dominant hand were non-significant in group A with the exception of synovitis GS (r= –0.263, p=0.005) and synovitis PD (r= –0.342, p=0.001). In group B, the correlations were significant for synovitis GS (r= –0.295, p = 0.050), synovitis PD (r= –0.413, p=0.005), tenosynovitis PD (r= –0.267, p=0.049) and erosions (r= –0.297, p=0.039). In the non-dominant hand, all correlations were non-significant.

3. In group A, the correlations between RAI and handgrip were r= –334, (p=0.001) in the dominant hand and r= –0.374, (p<0.001) in the non-dominant hand, whereas in group B the correlations were r= –0.484, (p<0.001) in the dominant hand and r= –0.510 (p<0.001) in the non-dominant hand.

■ **DISCUSSION**

US is gaining increasing importance in the field of early diagnosis and follow-up

of disease activity in RA patients. Several scores have been developed for the assessment of RA activity by US (21, 26). Some scores included only one hand. Indeed, others included both hands, but the examination times recorded by this scores were too long, ranging from 20 to 70 minutes (27, 28) or they did not include a thorough examination of both hands (29).

There is no agreement in the literature on the effect of handedness on disease activity. Some state that the dominant hand is more affected; others maintain that the difference is not significant. This controversy could be attributed to the inclusion of patients with different disease durations (3, 4, 7, 8).

Some papers in the literature concluded that the difference is not significant and the disease is symmetrical in nature (7, 8) and even asymptomatic joints may have arthritis (9). In addition, one study in established RA showed no difference between the dominant hand and non-dominant hand in terms of joint space width (10).

The disease duration varied widely among all these studies. Furthermore, many of them did not clearly define it. US scores used for follow-up examinations of RA patients consider only the examination of the clinically dominant hand (*i.e.* for tenderness and swelling) (11). Since controversy has been raised about hand dominance in RA, further research is needed in this field. Our study was designed to compare hand dominance by detailed US examinations using the US5 score of both hands assessing synovitis, tenosynovitis, and erosions, and comparing US findings to RAI and hand grip strength.

We found that the commonest sonographic finding was synovitis followed by tenosynovitis and erosions in both groups, as was also emphasized by Mendonça *et al* (30). The sample size in that study is relatively small (only 39 participants), because the target was early arthritis. Disease duration at the beginning of the study ranged between 3 months and 2 years. They considered ACR 1987 criteria for diagnosis and the presence of a single synovitis by US as an entry criterion for all participants. The

mean DAS was 4, which indicates inclusion of relatively active patients. The evaluation included conventional radiography and US assessment, by the modified US 7 score, measuring joint swelling and tenderness. The mean age of the participants was older than the mean age in our study. As to pain, the right wrist, MCP 2-5, PIP 3 and 5 had more pain, but the difference was not significant for most of these locations. For swelling, right wrist, MCP 2-4, and PIP 2, 3, and 5 were more affected. For GS, right MCP 2 and MCP 3 were more significantly involved than the left ones. The left wrist showed a higher PDUS score than the right one, with a significant difference. The main limitations in this study were that the dominant hand definition was not taken in consideration, and the lack of a total score summation in each hand, which could have facilitated comparison of both sides (30).

Comparing the US5 scores between the two hands, the dominant hand was found to be significantly more affected, in particular in early RA cases. Significantly higher scores were found in the dominant hand for synovitis (both GS and PD) and erosions in early RA cases, and in the dominant hand for synovitis and tenosynovitis (PD only for both) in established RA cases. Furthermore, we found a significant relation between symmetry and seropositivity on one side and symmetry and activity on the other side. Moreover, erosions was related to disease duration and progression. These findings were comparable to the results from Zangger et al. (7). Their study focused on radiological evaluation of hand and foot symmetry in RA patients by modified Larsen score. They followed 2 unequal groups of patients longitudinally, one from England and another from Canada. RA patients were diagnosed according to ARA criteria. They examined all the MCPs, interphalangeal joints of the thumb, the four PIPs and the wrist joint in addition to foot joints. The overall asymmetry was found in 13% of the 1st group and asymmetry was mainly in the MCPs and wrist joints. Progression to symmetry was detected in 58% in the English group. In the second group, it was identified in approximately 30% of patients. The au-

thors observed that the presence of RF did predict evolution to symmetry. Although the longitudinal pattern adds power to this study, it has some drawbacks. Two unequal groups of participants were considered, radiological evaluation was performed without US assessment, and finally there was no clinical evaluation for disease activity (31). Aga et al. studied two cohorts (32), the first including DMARD-naïve participants with early RA and disease duration <2 years; the second cohort had established RA with active disease. All were diagnosed according to the ACR/EULAR 2010 criteria. Both groups were subjected to US assessment of the hand, elbow and foot joints in addition to DAS28-ESR. The mean age in this study for both groups was around 50 (older than ours). Most of the participants in both groups had moderate disease activity. The aim of this study was to compare different US scores used for evaluation of RA patients. However, there was no clear indication about hand dominance and erosions, and the dominant hand was not compared with the non-dominant one. The conclusion of that study was that RA is not essentially a symmetrical disease, and that bilateral evaluation could provide additional information (32).

Backhaus et al. examined only the dominant hand with the US7 score (26). Furthermore, a 6-joint US assessment done by Perricone et al. (29) examined both hands, but included only the wrist and MCP 2 joints.

To our knowledge, our study is the first one to use US to evaluate the role of hand dominance in early and established RA.

RAI was always higher in the dominant hand in both groups, but this difference was more pronounced in group A in comparison to group B, which also emphasizes the tendency towards symmetry over time. Adams et al. compared dominant and non-dominant hands (5). In their study they included early RA patients, diagnosed by the ACR 1988 criteria, with a mean disease duration of 10 months. The mean age of the participants was 10 years older than that in our study. One advantage in this study is the clear definition and identifica-

tion of hand dominance. They considered the Ritchie score, joint swelling, wrist mobility, ulnar deviation and hand grip. Wrist mobility was significantly impaired in the dominant side. Hand grip strength was less in the dominant hand with a non-significant difference. Ritchie score, swollen joint count and ulnar deviation were higher in the dominant hand with a non-significant difference. The drawbacks of this study comprise the lack of a comparative group of established RA patients, the absence of the 6 month cut-off between early and established RA, of disease activity evaluation as an inclusion criterion, and of US assessment. In addition, the frequency of a left handedness in their study was about 17%, which differed greatly from patients in the present study.

Handgrip was stronger in the dominant hand in both groups. The difference was significant in group B and non-significant in group A. Björk et al. included in their study patients with a disease duration shorter than 1 year and followed them regularly for 5 years. They evaluated handgrip using the Grippit device. Their results showed that the dominant hand was always stronger, and, with disease progression, there was a manifest impairment of the handgrip (33). Their results were comparable to ours.

■ CONCLUSIONS

The dominant hand is more affected in early RA, and the disease becomes more symmetrical with its progression. This may suggest that an US evaluation of RA is performed on both hands in established RA, while in the early disease the examination of the dominant hand only may be satisfactory. In addition, protection of the dominant hand against mechanical stress in early RA might prevent disease progression in this side.

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