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Research Article

Impact of Morning Stiffness Duration in Rheumatoid Arthritis Activity's Evaluation/study data quest-Ra Morocco

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Abstract

Objective: To evaluate the impact of morning stiffness duration reported by the patient on the evaluation of rheumatoid arthritis activity.

Materials and Methods: A multi-national cross-sectional study that included 1129 patients with rheumatoid arthritis according to the 1987 ACR criteria. The Quest-RA (Quantitative Standard monitoring of patients with Rheumatoid Arthritis)" Morocco study was inspired from the Finnish study, including public and private rheumatologists over a period from January 2008 to December 2010. A pre- questionnaire with Socio- demographic, clinical and paraclinical was completed by all patients. The duration of the Morning Stiffness (MS) was evaluated from the time of awakening patients until the maximum improvement in pain. Four groups were established according to the disease activity (DAS28 values in and MS). We conducted correlation analysis to establish the relationship between MS and disease activity based on DAS28. Linear regression analysis was used to identify the determinants of this relationship. The ROC curve was used to differentiate between active and inactive forms in the MS and the DAS28.

Results: The average age of our patients was 48.82±12.72 years with a female predominance (87.3 %). The median disease duration was 6 years (3-12). The mean DAS28 was 4.93±1.68, the length of the MS averaged 29.9±19.16 min. A significant correlation was noted between the DAS28 ($r = 0.318$) VAS tired ($r = 0.343$) overall VAS ($r = 0.315$) ESR ($r = 0.144$) and the duration of the MS (all $p < 0.05$). More than half of our patients were severe activity DAS28 (54%). Among this group, 71.5 % had a sup MS 30 minutes (16 - 59min). The duration of MS in patients with severe activity was different from subjects in the other groups ($p< 0.0001$). In univariate and multivariate analysis and adjusting for confounding factors, the DAS28 increased 8.6 10-2 when the duration of the MS increases a minute. The Roc curve is a threshold value of 16.50 with Specificity = 0.57 and Sensibility = 0.77.

Conclusion: Our study suggests that the MS reported by patients influences the disease activity assessed by the DAS28.

Keywords: DAS28; Disease Activity; Morning Stiffness; Rheumatoid Arthritis

Introduction

Rheumatoid arthritis (RA) is the most common chronic inflammatory rheumatic autoimmune disease and the most destructive. Early diagnosis and initiation of treatment are very important for the optimal management of this disease [1,3]. The diagnosis is based on the ACR / EULAR 1987 amended in 2009 and morning stiffness is one of the components of these criteria to assess disease activity [2]. The initial manifestations are characterized by joint pain associated with morning stiffness and joint swelling (Synovitis). There is typically an inflammatory syndrome, joint damage (erosions, joint destruction exceptionally) and inconstant extra-particular manifestations such as rheumatoid nodules [1]. Stiffness in the joints after periods of rest is commonly experienced by patients with RA and is assessed clinically by Morning Stiffness (MS). It is listed in classification criteria [4] and is a component

of American College of Rheumatology (ACR) remission criteria for RA [5]. Recognition of MS as a common symptom of RA led to suggestion that MS might be useful for differentiating RA from non-inflammatory joint diseases [6]. Though recent clinical trials of RA don't include MS as an outcome measure it is still commonly used as eligibility criteria for participation [7]. The 2002 ACR guidelines for the management of RA recommend assessment of MS duration as one of the parameters for evaluation of the disease activity [8]. MS duration was found to be the second strongest predictive factor for change of disease modifying anti-rheumatic drug therapy in routine clinical care of RA patients in a tertiary care center [9]. The evolution of this disease is in spurts and in the absence of support, resulting in a disability [1]. Treatment goals are to control disease activity and obtain Remission stop joint destruction and protect or restore joint function, giving patients a better quality of private and social work [1]. Several tools are used to assess disease activity but DAS 28 is the time used in practice. It concerns 28 joints. The formula for calculating the DAS28 is as follows: DAS28 = 0.56 x square root (AG/28) + 0.28 x square root (AG/28) + 0.70 x In (VS) + 0.014 x Score VAS General (sqrt = square root ln = natural log , IR = Ritchie articular index , VAS = visual analogue scale (0-10 cm) , AG = swollen joints , painful joints = AD) [1,3]. Four groups were established according to the disease activity (High activity if DAS28 > 5.1; Moderate activity if 3.2 > DAS28 ≤ 5.1; Low activity if DAS28 ≤ 3.2; remission if DAS28 <2.6) [1,3,10].

Many studies have been conducted within the framework of the establishment of a link between the activity and morning stiffness of rheumatoid arthritis. Several of these studies showed that there was a good correlation between the assessment of disease activity and morning stiffness [11-15]. But all these studies were conducted in other countries. Since Morocco is a country or rheumatoid arthritis is considered the most common rheumatic disease and most destructive our study is assigned a goal to evaluate the influence of morning stiffness reported by RA patients Moroccan assessment of the activity of rheumatoid arthritis.

Materials and Methods

QUEST-RA is a multi- national cross-sectional study conducted by the public and private rheumatologists in Morocco. The database was started in January 2008 to December 2010. It was included 1129 patients with rheumatoid arthritis according to the 1987 ACR criteria.

Socio-demographic

All patients was completed a pre-established with clinical and paraclinical socio-demographic questionnaires. The MS duration was evaluated from the time of awakening patients until the maximum improvement in pain. Morning stiffness duration was classified into three groups: mild (1 -15minutes), moderate (16-59) and severe (≥ 60 minutes). HAQ (Health Assessment Questionnaire) was used to assess the functional consequences (0-3). Visual analog scale (VAS) of pain according to the patient and the doctor, VAS fatigue and gene reported by the patient and VAS overall were evaluated from 0-100%. The disease evolution duration expressed in years extending from diagnosis of the disease at the time of recording of patient data [16-20]. The presence or absence of pain and joint swelling was noted. The results of biological tests with the inflammatory balance: ESR and CRP, the dosage of anti-CCP and rheumatoid factor were taken.

The disease activity was assessed by DAS28 (Disease Activity Score) obtained using a calculator and using the following formula: 0.56* sqrt (28 tender) + sqrt (28swollen) 0", 70* ln (ESR) 0, 014* VAS General. The DAS28 was categorized by four groups established according the disease activity as remission (DAS28 < 2.6), low activity (2.6 > DAS28 ≤ 3.2), moderate activity (3.2 > DAS28 ≤ 5.1) and severe (DAS28 > 5.1).

Statistical Analysis

Our data was analysed by spas version 18. We conducted correlation analysis to establish the relationship between MR and disease activity based on DAS28. The relationship between the duration of the RM and the socio demographic variables such as age, DAS28 was established with the Pearson correlation coefficient while for HAQ variables EVAG, ESR, CRP, fatigue and the number of swollen joint the Spearman correlation coefficient. Analysis by univariate and multivariate regression was used to identify the determinants of this relationship. The ROC curve was used to differentiate between active and inactive forms in the MS and the DAS28 and check the sensitivity and specificity of the study [21].

Results

Demographic analysis shown in Table 1 showed that the average age of our patients was 48.8 years ±12.7, and the female was the most represented is 87.3 %, 788 patients were 73.5 % had FR + and the activity of disease expressed by the mean DAS28 was 4.9 ±1.6, duration of morning stiffness was on average 29.9 ±19.1 min , and the median disease duration was 6 years (6 to 12), the median HAQ was 1 (0.3-1.6), the median VAS pain score was 37 (17-60), median VAS fatigue was 44 (20-65), the median ESR was 44mm / h (20-65), median CRP of 15mg / h (8-28.5) NAG was present in 1057 were 94.7 % of patients [22].

Characteristics	Soci Demographic
Age (année) [1]	48.82+/-12.72
DD[2]	6(3-12)
HAQ[2]	1(0.3-1.6)
EGA[2]	37.0 (17-60)

Sex(f) [3]	895(87.3%)
RF(+) [3]	788(73.5%)
NAG[3]	1057(94.7%)
tired[2]	44(20-65)
ESR (mm/h)[2]	44(20-65)
CRP (mg/l)[2]	15(8-28.5)
DAS28[1]	4.93(+/-1.68)
MS[1]	29.95(+/-19.16)

Abbreviations:

1 : Mean and standard deviation
2 : Median and Quartile
3 : Number and Percentage
DD : Duration of Disease
RF (+) : Positive Rheumatoid Factor
HAQ : Health Assessment Questionnaire
EGA : Evaluator's Assessment of Global Disease Activity
NAD : Number' Swollen Joints
ESR : Erythrocyte Sedimentation
CRP : C- reactive protein
DAS28 : Disease Activity Score
MS : Morning Stiffness

Table1: Characteristics Soci Demographic.

Comparing the duration of morning stiffness between the different stages of disease activity (Table 2) was found in our study there were 27 patients in remission and 16 of them are 59.3 % had morning stiffness between 1 to 15min and 11 are 40.7 % had a duration of stiffness Matinale between 16-59 'but none had more than 60 minutes duration of morning stiffness. 20 patients were low and the majority of them had a duration of morning stiffness between 1 to 15 minutes for 11 (55.0 %). 123 patients were in moderate activity among them and duration of morning stiffness 16 to 59 min was the most observed in 70% of cases were 86 patients. 199 patients were in severe activity and 71.9% were 143 patients had a duration of morning stiffness between 16-59 min [23-25].

	Corrélation of Coeff	P
Age	-0.22	0.681
HAQ	0.331	0.001
DAS28	0.318	0.001
EGA	0.315	0.001
EVAt	0.343	0.001
DD	0.051	0.336
ESR	0.144	0.05
CRP	0.114	0.72

Abbreviations:

HAQ : Health Assessment Questionnaire
EGA : Evaluator's Global Assessment of Disease Activity
DAS28 : Disease Activity Score
EVAt : Visual Assessment and Analog Tired
DD : Duration of Disease
ESR : Sedimentation Rate
CRP : C- reactive protein

Table 2: Existing relationship between the duration of morning stiffness and other variables of disease.

The analysis of the relationship between the duration of morning stiffness and the activity of rheumatoid arthritis **(**Table 3**)** showed that he was a moderate correlation between the DAS28 (r = 0.318) (p < 0.001) , EVAF (r = 0.343) (p < 0.001), EGA (r = 0.315 , p <0.001) , ESR (r = 0.144 , p <0.001) and the duration of morning stiffness [26].

SL. No.	RA activity by DAS28	N	2(1-15')	3(16-59')	4(60')
1	n (%)	27	16(59.3)	11(40.7)	
2	n (%)	20	11(55.0)	11(55.0)	1(5.0)
3	n(%)	123	35(28.5)	86(69.9)	2(1.6)
4	n (%)	199	38(19.1)	143(71.9)	18(9.0)
TOTAL n (%)					

Abbreviations:

1 : Remission
2 : Low activity
3 : Moderate activity
4 : Severe activity

Table 3: The distribution of the duration of morning stiffness depending on the severity of RA assessed by DAS28.

There was no relationship between age, duration of disease progression with respective correlation coefficients (r = -0.22, p = 0.681) and (r = 0.051, p = 0.336) and morning stiffness. To predict the impact of morning stiffness duration of the activity of RA **(**Table 4**)** was used to test statistical analysis of variance ANOVA for independent variables and found that there was a statistically significant difference between four groups with p <0.001 and then defined the groups behind this difference post hoc test of Bonfferoni it came out that the duration of greater than 60 min subjects in remission morning stiffness was different subjects low, moderate, and severe activity by cons there was no difference in the duration of morning stiffness between 1-15 min and 15-59 min between subjects in remission and low and moderate activity and a

significant difference the duration of morning stiffness in severe about the group activity and other groups [27-28].

RA activity By DAS28	score	Mean difference	P	IC95%
Remission	2	-1.36	1.000	-15.90 13.18
	3	-7.25	0.403	-17.72 3.22
	4	-16.28	0.001	-26.39 -6.18
Low	1	1.36	1.000	-13.18 15.90
	3	-5.89	1.000	-17.77 5.99
	4	-14.92	0.004	26.48 -3.36
Moderate	1	7.25	0.403	-3.22 17.72
	2	5.89	1.000	-5.99 17.77
	4	-9.03	0.001	14.68 -3.38
High	1	16.28	0.001	6.18 26.39
	2	14.92	0.004	3.36 26.48
	3	9.03	0.001	3.88 14.68

Abbreviation:

a : Mean difference in morning stiffness duration (in minute)

1 : 0 à 1 min

2 : 1 à 15 min

3 : 16 à 59 min

4 : sup ou égal à 60 min

Table 4: Comparison of the duration of morning stiffness compared to disease activity.

The analysis of (Tables 5 A&B) was found: In univariate analysis the DAS28, HAQ, EVA fatigue, EGA are predictors of longer duration of morning stiffness confused with all $p < 0.0001$. In multivariate analysis [29-30], we find that adjusting for other factors predictive of disease activity only DAS28, HAQ varied according to the morning time with respectively OR 0.16 and 0.14 and all $p < 0.05$.

Model	R	R2	ESE	R2 adjusted	F	Ddl	df2	P
1	0.487a	0.237	0.41	0.236	326	1	-	0.001
2	0.486b	0.236	0.41	0.235	341	1	-	0.001
3	0.277c	0.077	0.45	0.45	91.6	1	-	0.001
4	0.551d	0.304	0.39	0.302	228.2	1	-	0.001
5	0.513e	0.263	0.4	0.262	186.4	1	-	0.001
6	0.56f	0.313	0.39	0.311	157.9	1	-	0.001

Abbreviations:

a **:** Predicted value: DAS28

b **:** Predicted values

c **:** HAQ predicted values : global assessment of health

d **:** Predictive values: DAS28, HAQ

e **:** Predictive values: DAS28, overall health assessment

d **:** Predictive values : DAS28, HAQ assessment

Table 5A: Evaluation of the prediction of DAS28 with the duration and other variables / regression.

Characteristics	Unified analysis			Multi varied analysis		
	B	P	IC95%	OR	P	IC95%
Age	-3,12E-02	0,68	-0.180 0,012	-	-	-
EVAt	0,226	0,0001	0,146 0;30	0,074	0,270	-0,048 0,172
EGA	0,247	0,0001	0,158 0,337	0,079	0,264	-0,054 0,195
CRP	0,114	0,073	-0,011 0,239	-	-	-
ESR	5.26E-01	0,198	-0,028 0,133	-	-	-
MS	0,136	0,336	-0,142 0,415	-	-	-
HAQ	7,224	0,0001	4,583 9,866	0,143	0,021	0,608 7,247
DAS28	4,050	0,0001	2,819 5,282	0,166	0,010	0,510 3,659

Abbreviation:

HAQ : Health Assessment Questionnaire

EGA : Evaluator's Global Assessment Of Disease Activity

DAS28 : Disease Activity Score

MS : Morning Stiffness

EVAt : Visual Analog and Tired Evaluation

ESR : Sedimentation rate

CRP : C-reactive protein

Table 5B: Evaluation of the prediction of DAS28 with the duration and other variables / regression.

Discussion

Our study found a moderate correlation between the duration of morning stiffness with the degree of activity of rheumatoid arthritis, functional impairment (HAQ) , global assessment of disease activity reported by the patient and fatigue this consistent with results reported by Khan et al in 2009 who found (r = 0.41-0.48) as well as in many other studies [31]. Contrary to the results of Yazici et al who reported in 2004 a strong correlation between stiffness and functional impairment [32-34]. We found that the DAS28, HAQ, VAS fatigue, EGA are predictors of longer duration of morning stiffness confused with all p <0.0001. But we find that adjusting for other predictors of disease activity only DAS28, HAQ varied according to the morning time with respectively OR 0.16 and 0.14 and all p <0, 05. The area under the curve Roc had reported a significant sensitivity and specificity in our series which is very important to the credibility and relevance of our study. This result corresponds to that reported by Khan et al [35-36].

Conclusion

The duration of morning stiffness has only a moderate correlation with the activity of rheumatoid arthritis in our study and is a predictor of disease flare.

Summary

RA : Rheumatoid Arthritis

RF (+) : Positive Rheumatoid Factor

HAQ : Health Assessment Questionnaire

EGA : Evaluator's Global Assessment of Disease Activity

NAD : Number of Swollen Joints

ESR : Erythrocyte Sedimentation

CRP : C- reactive protein

DAS28 : Disease Activity Score

MS : Morning Stiffness

EVAt : Visual Analog and Tired Assessment

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