Number of active joints, not diagnosis, is the primary determinant of function and performance in early synovitis

L.H. Gerber, G. Furst, C. Yarboro, H. El-Gabalawy

Lynn H. Gerber, MD; Gloria Furst, OTR, MPH; Cheryl Yarboro, RN; Hani El-Gabalawy, MD.

Please address correspondence and reprint requests to: Lynn H. Gerber, MD, Chief, Rehabilitation Medicine Department, Department of Health & Human Services, National Institutes of Health, Warren G. Magnuson Clinical Center, Building 10, Room 6S235, MSC 1604, Bethesda, Maryland, 20892-1604, USA.
E-mail: lynn_gerber@nih.gov

Clin Exp Rheumatol 2003; 21 (Suppl. 31): S65-S70.

Key words: Arthritis, function.

ABSTRACT

Objective. *A substudy within a larger study of patients with inflammatory arthritis of less than one year, to analyze baseline measures or joint counts, laboratory values, patient questionnaires and ARA diagnostic criteria for rheumatoid arthritis, as predictors of one year performance and functional status.*

Methods. *229 patients with synovitis of less than one year were enrolled and evaluated at baseline and one year. Measures included the number of swollen or tender joints [active joint counts]; biological indices of inflammation [erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)]; and patient questionnaire measures of pain [Wisconsin Brief Pain Inventory], fatigue [multi-dimensional assessment of fatigue], depression [Center for Epidemiologic Studies – Depression Scale], sleep [Sleep Quality Index], performance [Human Activity Profile], and function [Sickness Impact Profile ambulation subscale and Health Assessment Questionnaire]. Correlations between these measures were evaluated using the Spearman rank order correlation. Patients were classified according to whether they met ARA criteria for RA, had high (>7) or low (≤ 7) numbers of affected joints; and high, intermediate, or low levels of performance; and were compared using the Kruskal-Wallis test.*

Results. *At baseline, an active joint count of > 7 versus ≤ 7 was associated significantly with higher age, rheumatoid factor positivity, a diagnosis of rheumatoid arthritis versus spondyloarthropathy or undifferentiated arthritis, and receiving a disease modifying antirheumatic drug (DMARD), but not with sex, race, erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), or receiving prednisone. Furthermore, high baseline active joint counts were associated significantly with patient questionnaire scores for maximum activity, fatigue and depression, but differences were not significant for sleep, ambulation and pain scores. A comparison of patients who met or did not meet criteria for RA indicated significant differences only according to the fatigue scores, but none of the other questionnaire measures. Correlations of baseline measures with one-year performance were highest for the baseline active joint count compared to laboratory and questionnaire variables. The maximum activity score at one year was predicted significantly by the baseline maximum activity score, active joint count, and age, but not by laboratory tests or whether the patient met criteria for RA.*

Conclusion. *The active joint count predicts subsequent performance and function for patients with recent onset, inflammatory synovitis more effectively than whether patients met ARA criteria for RA.*

Introduction

Disability is the result of biological, psychological, and sociological factors, resulting from anatomical or physiological abnormalities, which are called impairments in the rehabilitation model, and functional limitations (1). Most reports which have analyzed risks to develop disability in patients with rheumatoid arthritis (RA) are retrospective and based on patients with established disease, many of whom have fixed structural damage (2-6). Reports of prospective data on recently diagnosed patients with arthritis have traditionally emphasized clinical, laboratory and radiographic measures (7), but not data concerning functional limitation and disability. Furthermore, few studies have investigated whether performance is impaired in early arthritis.

Performance is a term that refers to an

individual's ability to accomplish a variety of daily activities, including work and personal needs, often measured by stamina or oxygen consumption and measures of aerobic capacity. In this study, performance measures are correlated with patient questionnaire measures such as the Health Assessment Questionnaire (HAQ) (8).

We had an opportunity to perform a sub-study in subjects enrolled in a NIH study of early synovitis (NIH protocol 94-AR-0194) involving patients with one or more swollen joints for 3-12 months, recruited from the community. We analyzed demographic, clinical, laboratory variables, as well as performance, sleep, fatigue, depression, and functional status both at initial presentation and one year later. Our data suggest that the number of active (either swollen and/or painful) joints is the most important predictor of poor performance and functional loss, irrespective of whether or not patients meet criteria for RA, as summarized in this report.

Methods

Participants were subjects enrolled in a NIH study of early synovitis (NIH protocol 94-AR-0194). Inclusion criteria were one or more swollen peripheral joints for more than 3 months but less than 12 months in duration. Patients were recruited by referral from community rheumatologists and primary care physicians. In many cases, the patients were evaluated initially prior to starting of disease modifying antirheumatic therapy (DMARD). After the baseline evaluation, the patients were treated by their referring physicians and were then re-evaluated one year later.

At the baseline and one-year evaluations, a comprehensive clinical evaluation was performed, which included several types of measures: articular [the number of painful, tender or swollen joints - active joint count (AJC) (9)]; laboratory [rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), hemoglobin (hgb), and platelet count (plts)]; self report questionnaires to assess pain [Wisconsin Brief Pain Questionnaire (WSC) (10)], fatigue [Multidimensional Assessment of Fatigue (MAF) (11)], depression [CES-D (12)]; sleep [Sleep Quality Index (SLP)]; and functional status [the Sickness Impact Profile (SIP) ambulation sub-scale (13), Health Assessment Questionnaire (HAQ) (8)], and performance [Human Activity Profile (14)].

The human acitivity profile was the primary measure used to assess performance. This instrument has been employed extensively in evaluating patients with cardiovascular disease and is an activity-based questionnaire to assess performance that is ranked in order of metabolic requirements needed to perform the activity in question, e.g. walking, climbing stairs and running/jogging three miles. The human acitivity profile includes 94 self-report items of common activities requiring a known amount of average energy expenditure. The higher the number for the activity, the greater the MET value for that activity. The activities cover a range from 1 MET (getting out of a chair) to 10 METS (jogging three miles in 30 minutes). Each activity is identified as "Still Doing this Activity", "Stopped Doing this Activity", or "Never Did this Activity". Two scores were used for this study: 1) the Maximum Activity Score, which corresponds to the highest number assigned to the activity the patient is "still doing" and reflects the highest oxygen requirement needed to perform the task, and 2) the Adjusted Activity Score which results from subtracting the total number of activities "no longer doing", that is a lower number than the maximum activity score. The total number of activities that meet this criterion is subtracted from the maximum activity score. For example, if the individual can swim 25 yards (item #77), but cannot walk three miles without stopping (item #76) or shovel for five minutes (item #73), the adjusted activity score would be 75 (maximum activity score of 77 minus the two activities "no longer doing"). The adjusted activity score represents the best estimate of the effort needed for "usual daily activity" for that individual. The adjusted activity score "adjusts for sudden bursts of activities that individuals might perform when absolutely necessary, but which might provide unrealistically high estimates of their normal energy expenditures" (14).

Data analysis

All clinical assessments and self-report instruments have been standardized and validated. Overall correlation between continuous variables was evaluated using the Spearman rank order correlation coefficient. The patients were grouped in two ways: low (≤ 7) versus high (>7) number of affected joints; and RA (met ACR criteria on initial visit) versus non-RA (did not meet ACR criteria on initial visit). A number of analyses were undertaken (as described below) to determine the optimum cut-off point for the total number of affected joints. Ultimately, 7 affected joints were shown to achieve the best discrimination between groups in terms of the performance measures. Patient groups were compared using the Kruskal-Wallis test, T-test or chi-square test as appropriate.

The maximum activity score score of the human activity profile instrument was used to classify patients regarding performance. We reasoned that patients who had essentially normal function should be compared with those who had significant disability. We thus evaluated a high performing group and a low performing group at the initial and one-year time points. The maximum activity score was used to define a high performing group and a low performing group. The high performing group was defined as those whose scores were greater than 81, those in the middle had maximum activity score scores from 73-81, and those whose scores were < 73 were the low performing group. The association between individual clinical parameters and the performance groups was determined using univariate analyses, including the T-test, Kruskal-Wallis test, and chi-square test, as appropriate.

Logistic regression models were generated to identify initial factors that were independently associated with either high or low performance at one year. The variables at the initial visit includ-

ed the active joint count, CRP, ESR, age, sex and treatment with DMARD and/or prednisone any time during the year.

Results

Baseline assessments

The cohort included 229 patients. Demographic data, clinical features, number meeting criteria for RA, and therapies are presented in Table I for patients classified as having > 7 or ≤ 7 affected joints. Patients with a high level of affected joints were more likely to be older, be positive for rheumatoid factor, meet criteria for RA, not have a spondyloarthropathy or undifferentiated arthritis, and use a DMARD. No significant differences were seen for sex, race, ESR, CRP, or use of prednisone.

Measures of performance and other self-report questionnaire measures were also compared for patients classified as having >7 or ≤ 7 affected joints and according to whether patients met the criteria for RA or not (Table II). Differences according to higher active joint counts were statistically significant for a lower maximum activity score and higher scores for fatigue and depression, but were not significant for sleep, ambulation and pain. When patients were analyzed according to whether or not they met the criteria for RA, the only significant differences were that fatigue scores were higher in patients who did not meet criteria for RA. There were no statistically significant differences between the two diagnostic groups for the maximum activity score, sleep, depression, ambulation, and pain.

Table I. Patient characteristics.

	Active joint count ≤ 7 (n = 125)	Active joint count > 7 (n = 104)	P value
Demographics			
Age	42 ± 13	46 ± 13	0.05
Females	63%	69%	ns
Caucasian	84%	82%	ns
Clinical features			
Active joint count (AJC)	2.5 ± 2.3	20 ± 12	< 0.01
ESR (mm/hr)	27 ± 25	37 ± 28	ns
C-reactive protein (CRP) (mg/dl)	1.2 ± 1.6	1.6 ± 1.6	ns
Rheumatoid factor+ (> 19 IU)	26%	50%	< 0.01
Diagnosis			
Meet criteria for RA*	35%	76%	< 0.01
Spondyloarthropathy**	12%	4%	< 0.05
Undifferentiated arthritis (UA)***	52%	20%	< 0.05
Anti-rheumatic therapy			
Using DMARD****	13%	25%	< 0.05
Using prednisone	16%	22%	ns

ESR: erythrocyte sedimentation rate; RA: rheumatoid arthritis.
*RA diagnosis by ACR criteria.
**Spondyloarthropathy diagnosis by ESSG criteria (n=15). Of the 15 patients,12 had reactive arthritis and 3 had psoriatic arthritis.
***UA diagnosis indicates that specific rheumatic diagnosis could not be made at the time of evaluation: study entry criteria were met.
****DMARD; disease modifying anti-rheumatic drugs, including methotrexate, sulfasalazine, and hydroxychloroquine.
ns = not significant

Comparison of baseline assessments and one year measures

Analysis of correlations between the baseline patient questionnaire, laboratory, and joint count measures with various performance variables, including the maximum activity score, adjusted activity score, sickness impact profile score, and health assessment questionnaire (HAQ) score at one year were computed (Table III). Correlations of baseline pain, fatigue, sleep, and depression scores as well as laboratory data with the one-year performance

Table II. Clinical and performance parameters at the initial evaluation. Patients were grouped by diagnosis and affected joint count.

	Meet criteria for RA n = 122 Median (range)	Do not meet criteria for RA n = 107 Median (range)	p	Active joint count ≤ 7 n = 125 Median (range)	Active joint count > 7 n = 104 Median (range)	p
Maximum activity score	72 (31-94)	76 (44-94)	ns	78 (45-94)	74.5 (31-94)	0.005
Fatigue (MAF)	31 (0-86)	35 (0-95)	0.02	26 (0-91)	31 (0-95)	0.0005
Sleep (SLP)	36 (5-84)	37 (2-79)	ns	32 (5-79)	37 (2-84)	ns
Depression (CESD)	19 (0-70)	21 (0-92)	ns	17 (0-92)	20 (0-70)	0.05
Ambulation (SIP)	12 (0-56)	9 (0-57)	ns	11 (0-57)	0 (0-50)	0.001
Pain (WSC)	39 (0-100)	42 (0-90)	ns	40 (0-100)	40 (0-80)	ns

Kruskal-Wallis for non-parametric data.
MAF: Multidimensional assessment of fatigue; SLP: Sleep quality index; CESD:Center for Epidemiologic Studies Depression Scale; SIP: Sickness impact profile; WSC: Wisconsin brief pain inventory; ns: not significant.

Table III. Correlation between baseline variables with 1 year performance variables*.

		1 year performance variables			
		Maximum activity score	Adjusted activity score	Sickness impact profile	HAQ
Patient questionnaire variables					
Pain (WSC)	r	-0.2	-0.22	0.2	0.17
	p	0.01	0.009	0.02	0.06
Fatigue (MAF)	r	-0.03	-0.12	0.17	0.15
	p	0.72	0.14	0.04	0.07
Sleep (SLP)	r	-0.1	-0.14	0.19	0.16
	p	0.2	0.08	0.02	0.05
Depression (CESD)	r	0.006	-0.05	0.11	0.11
	p	0.93	0.48	0.2	0.18
Laboratory variables					
ESR (mm/hr)	r	-0.18	-0.19	0.25	0.2
	p	0.02	0.02	0.002	0.01
C-reactive protein, mg/dl	r	-0.08	-0.08	0.17	0.1
	p	0.32	0.33	0.05	0.23
Physical exam variables					
Active joint count	r	-0.24	-0.28	0.3	0.39
	p	0.002	0.0004	0.0002	< 0.0001

*Spearman rank order correlation
HAQ: Health Assessment Questionnaire; ESR: erythrocyte sedimentation rate; WSC: Wisconsin brief pain inventory; MAF:Multidimensional assessment of fatigue; SLP:Sleep quality index; CESD:Center for Epidemiologic Studies Depression Scale.

Table IV. Performance after one year follow-up according to baseline measures*.

	Maximum activity score			
Variable	Low (< 73) performers	Moderate (73-81) performers	High (> 81) performers	P**
Number of patients	43	68	59	
Age	48.5 ± 14.6	43.3 ± 11.7	41.5 ± 13.3	0.04
Females	32/43 (74%)	49/68 (72%)	39/59 (66%)	ns
Meet criteria for RA	23 (53%)	39 (57%)	27 (46%)	ns
Do not meet criteria for RA	20 (46%)	29 (43%)	32 (54%)	ns
Baseline findings				
Maximum activity score	69.5 ± 11.9	74.0 ± 10.8	80.4 ± 9.2	< 0.0001
Active joint count	13.3 ± 13.0	10.8 ± 11.3	7.2 ± 9.5	0.008
ESR (mm/hr)	35.3 ± 26.9	33.3 ± 25.5	27.2 ± 25.3	ns
Rheumatoid factor +	17/43 (40%)	30/68 (44%)	19/59 (32%)	ns
Follow-up findings				
Active joint count	9.7 ± 18.7	9.0 ± 12.3	5.6 ± 8.1	ns
ESR (mm/hr)	26.8 ± 23.0	27.4 ± 20.4	19.9 ± 18.1	ns
DMARD therapy	13/43 (30%)	29/68 (43%)	24/59 (41%)	ns
Prednisone therapy	9/43 (21%)	14 (21%)	12/59 (20%)	ns

T-test, Chi-Square and Kruskal-Wallis tests, as appropriate.
*Initial variables were used from those who had initial and one year data.
** p is between low and higher performers only.
ns = not significant.

measures were all 0.25 or less. Although some of these correlations are statistically significant, they would explain < 12.5% of the variation in measures at one year. Highest correlations were seen between the active joint count and all performance and functional measures (r = 0.24 to 0.39). The highest correlation was 0.39, comparing the baseline active joint count with one year scores on the health assessment questionnaire (HAQ).

Analyses on the basis of performance groups

Analyses were performed to determine the capacity of baseline measures to predict maximum activity scores one year later (Table IV). The top performers (n = 59) had an initial maximum activity score of > 81, which is considered normal. In this group 27 had a diagnosis of RA and 32 were non-RA (p = ns). Their average baseline ESR was 27.2 and their active joint count was 7.2. Those who were the lowest performers (n = 43) had an initial maximum activity score score of <73, which is considered moderately or severely disabled. In this group 23 had a diagnosis of RA, and 20 were non-RA (p = ns). Their average ESR was 35.3 and their active joint count was 13.1 (Table IV). The initial active joint count distinguished high from low performers (p = 0.008) at one year. The initial maximum activity score was also correlated significantly with the one year scores (p < 0.0001). Age differed significantly between high and low performers; meeting criteria for RA, or the use of DMARDs or prednisone did not significantly distinguish high and low performers (Table IV). As is shown in Figure 1, a low initial number of affected joints was more predictive of high performance at one year than a high initial number of affected joint was predictive of poor performance.

The result of the logistic regression analysis demonstrated that the patient's age was the only variable that was independently associated with belonging to the low performing group (OR 1.06, CI 1.016 – 1.098, p = 0.006). Age (OR 0.96, CI 0.91 – 0.99, p = 0.03), and initial AJC (OR 0.95, CI 0.91 – 0.99, p = 0.04) were the only independent predictors of belonging to the high performing group.

Discussion

This paper reports findings from a

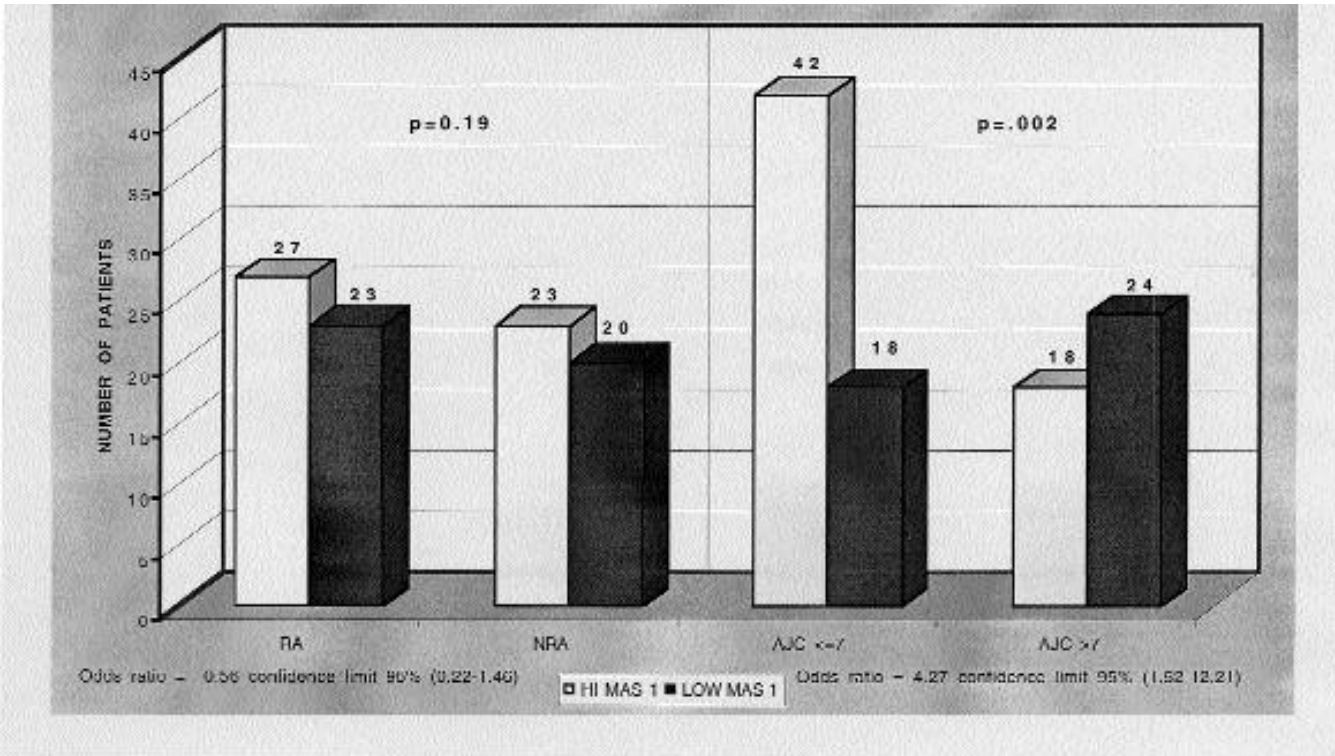

Fig. 1. Relationship between affected joint count, diagnosis and performance: MAS 1 year and initial affected joint count.

cohort of patients with recent onset synovitis that support the view that the number of swollen and/or painful joints predicts future performance (maximum activity score) and function (sickness impact profile and HAQ) at one year. The human activity profile is a good index of fitness which has been shown to correlate with physiological measures such as VO2 (14), and correlates well with oxygen consumption in a rheumatic disease population (15). Sustained activity requires endurance and stamina, which are necessary for performance, are reduced in the rheumatic disease population and seem to occur early in its course. A substantial literature exists to support the view that aerobic capacity is a determinant of one's ability to perform sustained activity (16,17). Hence, it was reasoned that using an instrument which measures stamina would be useful in identifying changes in performance in a population with recent onset of disease. We particularly sought findings based on clinical events that were occurring from causes other than significant mechanical malalignment or fixed joint deformity.

The population reported had little fixed deformity. Most multidimensional functional measures are sensitive to moderate or severe disability, and relatively insensitive to mild disability. Many functional assessment questionnaires assess whether the task can be done at all, rather than if it can be performed in a way that enables the patient to reliably maintain sustained activity. The human activity profile is designed to evaluate stamina, a problem we know to be relevant to this population. It is important to identify or quantify difficulties patients have with sustaining a level of physical activity, which may be a key indicator of functional loss, because treatment with aerobic conditioning often reduces disability. Several studies have shown improved performance and decreased disability in those patients with arthritis who receive aerobic conditioning and strength training (17-24).

Patients are frequently told that the diagnosis of RA is a poor prognostic factor. This study found something different; that the proportion of those who met criteria for RA in the high performance group at one year was not significantly different from those in the low performance group, although patients with RA, as in many other reported studies, have a higher active joint count than non-RA patients. The extent of articular involvement, i.e. the burden of synovitis, irrespective of the diagnosis or laboratory indices, is the best indicator of poor performance over a more extended period of time.

It was disappointing that the use of DMARD at one year into the study did not differentiate high from low performing patients. Patients who receive DMARDs have more severe and sustained clinical findings. One recent study has suggested that DMARDS alone may not be effective in significantly protecting against disability (25). Another study demonstrated that one subset of patients with RA (i.e. elderly women) who present with disability are at risk for a less favorable functional outcome (26). These studies suggest that lowering the active joint count is a necessary, but not sufficient condition for assuring better future performance.

Rehabilitative treatments are designed to increase performance and maximize function. Traditionally, these programs

have been designed for patients with moderate or significant impairment and disability, and have not been introduced early in the course of disease in order to maintain a high level of performance or prevent functional decline. Based on the data reported in this paper, patients in the early phases of their disease are likely to need early pharmacological management, combined with rehabilitation strategies such as aerobic and strength training.

Acknowledgement

The authors wish to thank Drs. Raphaela Goldbach-Mansky, H. Ralph Schumacher Jr. and John Klippel for their invaluable contributions to this project, and to Dr Ted Pincus for his thoughtful review of the manuscript.

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