Visual Analogue Scales of Pain, Fatigue and Function in Patients with Various Rheumatic Disorders Receiving Standard Care

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ABSTRACT: **Background:** Pain, fatigue and functional disability are common key outcomes in most rheumatologic disorders. While many studies have assessed the outcomes of specific disease states, few have compared the outcomes of various rheumatic diseases.

Objectives: To assess how the intensity and rating of pain, fatigue and functional disability vary among groups of patients with various rheumatic disorders receiving standard care.

Methods: In a cross-sectional study conducted in a hospital-based rheumatology unit, standard clinical and laboratory data were obtained and all patients filled out questionnaires on pain, fatigue and daily function. The analysis concentrated on visual analogue scales (VAS) using specific statistical methods.

Results: A total of 618 visits of 383 patients with inflammatory as well as non-inflammatory rheumatic disorders were analyzed. Fibromyalgia patients had significantly higher VAS scores compared to all other groups. On the other hand, patients with polymyalgia rheumatica demonstrated significantly lower VAS scores compared to all other groups of patients. Patients with psoriatic arthritis also demonstrated relatively low VAS scores. VAS scores were lower in patients with inflammatory disorders as compared to patients with non-inflammatory disorders.

Conclusions: Our results suggest a spectrum of outcome intensity in various rheumatic disorders receiving standard care, ranging from fibromyalgia patients who report distinctive severity to patients with inflammatory disorders who are doing relatively well as compared to patients with non-inflammatory disorders. The findings emphasize the need to explore the underlying mechanisms of pain and fatigue in patients with non-inflammatory rheumatic disorders.

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KEY WORDS: pain, fatigue, outcome, rheumatic disease, visual analogue scale (VAS)

Rheumatic diseases vary in their epidemiology, disease processes and clinical manifestations; however, pain fatigue and functional disability are common key outcomes in most of these disorders. Measuring these outcomes can serve as a tool for following the course of disease as well as the effects of therapy. Although numerous studies have assessed the outcomes of specific disease states, only a few – performed more than two decades ago – compared the outcomes of the various rheumatic diseases [1-4].

Functional disability and fatigue are usually evaluated in rheumatologic clinical trials with multi-item questionnaires. Pain, on the other hand, has long been evaluated successfully using the visual analogue scale (VAS), both in clinical trials and in clinical standard of care [5]. The VAS scale has been suggested for the evaluation of fatigue and function as well. Wolfe [6] used the VAS scale to assess fatigue in 7760 patients with rheumatoid arthritis (RA) and showed that it performed as well as or better than the other longer questionnaires generally used [6]. A preliminary evaluation of the VAS function scale indicated that it may be suitable for use both in the clinical setting and in research [7]. We chose to use VAS concomitantly for pain, fatigue and function for our clinical outcome assessment because these measures apply to all rheumatic disorders. VAS scores, which are less dependent on language, were particularly appropriate for our mixed Israeli population of Hebrew and Arabic-speaking Israelis and Russian-speaking newcomers from the former Soviet Union.

The aim of the current study was to assess how the intensity and rating of pain, fatigue and functional disability may vary among patients with various rheumatic disorders under current standard care, utilizing a VAS scale. This type of data may provide new insights into the symptomatology of rheumatic diseases, assess the therapeutic effects of current therapies, and serve as an evaluation tool for the development of new treatments.

PATIENTS AND METHODS

This cross-sectional study was carried out in the rheumatology clinic of Assaf Harofeh Medical Center, Israel, which provides both tertiary rheumatology center service and primary rheumatology care. The study was performed between January and December 2006. The study was approved by the institutional review board and all patients participating in the study signed an informed consent.

INCLUSION/EXCLUSION CRITERIA AND CLINICAL EVALUATION

Adult patients aged 18 years or more attending the rheumatology clinic were included in the study. Referrals to this clinic were obtained from primary care physicians, primary rheumatologists, the emergency room, or follow-up of patients after discharge from the hospital. Clinic visits were of new patients or patients in follow-up. Four expert rheumatologists working in the clinic participated in the study. Patients were diagnosed with various rheumatic disorders according to clinical, laboratory and radiographic findings, and they received current standard care.

At each visit, before clinical examination, patients completed a self-administered form (in Hebrew, Arabic or Russian), with questions on demographics, patient history, presence and duration of morning stiffness, fatigue, and daily activity. Pain, fatigue and functional disability during the previous week were assessed with three VAS scores. The VAS was a 10 cm double-anchored line, ranging from no pain, fatigue or functional disability at one end, to worst possible pain, fatigue or functional disability at the other. During clinical examination, in addition to the standard rheumatologic evaluation, the rheumatologist completed a report that included the chief complaint, pattern of articular involvement, presence or absence of history of widespread pain (WSP), swollen and tender joint counts, tender points, laboratory markers of inflammation, the physician's global assessment of overall disease activity (MD global) on a visual analogue scale (VAS), medications and comorbidities. The examining rheumatologist was unaware of the data filled in the patient's questionnaire. Case report forms were collected, the quality of data was confirmed, and a final electronic database was created.

STATISTICAL ANALYSIS

The data were analyzed using BMDP (BMDP Statistical Software (1993, University of California Press, Los Angeles, USA). Descriptive statistics included the mean value and standard deviation of the continuous variables, and the percentages and proportions of the categorical variables. We used analysis of variance (ANOVA) with Bonferroni's correction for multiple comparisons to compare the continuous variables by diagnoses. Pearson's chi-square test was applied to compare discrete variables. We computed correlation coefficients using Pearson's correlation. A P value of ≤ 0.05 was considered significant.

RESULTS

During 2006, there were 1754 patient visits to the rheumatology clinic. Patients agreed to participate and filled the self-assessment forms in 875 patient visits. Of these, the data of 257 patient visits were excluded due to diagnostic uncertainty, lack of information, or patients' poor completion of the self-administered forms. Statistical analysis of 618 patient visits by 383 patients was performed.

DEMOGRAPHIC CHARACTERISTICS

The demographic characteristics of the study population are shown in Table 1. Ninety-two patients had rheumatoid

Table 1. Demographic characteristics and patients' complaints

Demographic characteristics	PMR	Gout	PsA	SLE	RA	SpA	IRD	NIRD	OA	FM
No. of patients	16	13	27	21	92	24	48	57	41	44
Age (years) (mean ± SD)	71 ± 7	59 ± 14	49 ± 13	42 ± 14	56 ± 16	44 ± 17	47 ± 19	36 ± 16	60 ± 8	47 ± 16
Female gender (%)	93.7	7.7	49.4	81	82.5	43.9	85.4	66.7	73.2	86
Disease duration (years) (mean ± SD)	2.7 ± 3	4.8 ± 7	6.2 ± 6	10 ± 8	7 ± 7	5.3 ± 5	4.5 ± 6	2.6 ± 3	5.7 ± 8	7.5 ± 8
Patients' complaints										
No. of visits	40	16	54	34	175	39	84	59	53	64
Articular pain (%) (n=574)	22	43.8	55.8	9.4	53.9	48.6	35.4	76.4	79.1	8.5
Regional pain (%) (n=574)	7.3	0	3.8	0	1.3	24.3	4.0	16.4	3.8	1.7
Widespread pain (%) (n=603)	5	0	4.3	23.3	15.6	0	19.9	3.7	22	93.3
Routine follow-up* (%) (n=574)	65.9	56.3	38.5	78.1	38.3	27	37.3	1.8	5.7	5.1
VAS scores										
VAS pain score (mean ± SD) (n=617)	29.3 ± 24	39.4 ± 40	44.7 ± 28	47.3 ± 27	54 ± 30	54.9 ± 30	55.9 ± 28	65.5 ± 20	66.3 ± 23	87.5 ± 16
VAS fatigue score (mean ± SD) (n=617)	37.3 ± 25	34 ± 36	45.3 ± 30	61.6 ± 29	56.7 ± 32	57.2 ± 26	54.3 ± 30	69.5 ± 24	62.2 ± 24	91.3 ± 12
Vas function score (mean ± SD) (n=617)	27.4 ± 30	40.9 ± 41	41.5 ± 29	47.8 ± 33	51.5 ± 33	48.8 ± 31	54.9 ± 28	59.5 ± 27	65.9 ± 24	85.5 ± 18

*Patients who came to the clinic for routine follow-up with no specific complaints
n=number of visits included in the analysis

PMR = polymyalgia rheumatica, PsA = psoriatic arthritis, SLE = systemic lupus erythematosus, RA = rheumatoid arthritis, SpA = spondyloarthropathies, IRD = inflammatory rheumatic disorders, NIRD = non-inflammatory rheumatic disorders, OA = osteoarthritis, FM = fibromyalgia

arthritis, 21 had systemic lupus erythematosus (SLE), 27 had psoriatic arthritis (PsA), 24 had other spondyloarthropathies (SpA), 48 had other inflammatory rheumatic disorders (IRD) (Sjogren's syndrome, systemic sclerosis, polymyositis, vasculitis, adult-onset still's disease), 13 had gout, 16 had polymyalgia rheumatica (PMR), 57 had other non-inflammatory rheumatic disorders (NIRD) (joint hypermobility, overuse syndromes, low back pain, arthralgias), 41 had osteoarthritis (OA), and 44 patients had fibromyalgia (FM).

Groups differed for all variables including age, gender, disease duration, education, marital status, and occupation. Overall, patients were predominantly female (72%), with a mean age of 50 ± 17 years. Mean disease duration was 5.7 ± 6.7 years, and the mean education level was 12 ± 3 school years. About two-thirds were married and about half were working. Patients with PMR were relatively old and patients with NIRD were relatively young. Female predominance was present in all groups except for PsA, SpA and gout. Relatively short disease duration was noted in patients with PMR and patients with NIRD. FM patients had fewer years of education, while patients with PsA had more. The proportion of married patients was low in the group of patients with NIRD probably due to their young age. Working status was low in patients with PMR probably due to old age. The occupation rate was also low in RA patients and FM patients.

CLINICAL CHARACTERISTICS

RA patients presented mainly with polyarticular pain (63/175, 36%) or attended the clinic for routine follow-up (66/175, 38%). Two-thirds had joint tenderness and about half had joint swelling. Only 11% (19/175) had more than 9 swollen joints and the mean MD global was 28. Most patients were treated with conventional disease-modifying anti-rheumatic drugs (DMARDs) (60/92, 65%), and 10% (9/92) with tumor necrosis factor (TNF) antagonists. SLE patients presented mainly for routine follow-up (26/34, 78%) and had very little joint pain or swelling, 7% (2/34) and 3% (1/34) respectively. The mean MD global was 22.9, and most patients were treated with hydroxychloroquine (28/34, 84%).

PsA patients presented mainly with pauciarticular arthritis (18/54, 34%) or visited the clinic for routine follow-up (20/54, 38%). Two-thirds demonstrated joint tenderness and about half had joint swelling. Only one patient had more than 9 swollen joints and the mean MD global was 35. The majority of patients were treated with conventional DMARDs (16/27, 60%), and 8% (2/27) were treated with TNF antagonists. Other SpA patients presented mainly with mono/pauciarticular arthritis (12/39, 32%), back pain (9/39, 24%) or came for routine follow-up (10/39, 27%). Peripheral joint swelling was noted in about one-third and did not involve more than four joints at the time. The mean MD global was 31.5. Non-steroidal anti-inflammatory drugs (NSAIDs) were used in 40% (10/24), and one patient was treated with TNF antagonists.

IRD patients also presented mainly with mono/pauciarticular pain (25/84, 30%) or came to the clinic for routine follow-up (31/84, 37%). About two-thirds presented with joint tenderness and about half had joint swelling. Only 3.7% (3/84) had more than 9 swollen joints and the mean MD global was 25.3. Patients were treated with NSAIDs (10/48, 20%), corticosteroids (11/48 23%) or DMARDs (7/48, 16%). Gout patients came to the clinic either for routine follow-up (8/16, 50%) or due to mono/pauciarticular pain (8/16, 50%). About half the patients had joint pain and joint swelling and their mean MD global was 31.6. Most PMR patients were on corticosteroid therapy (12/16, 75%) and attended the clinic for follow-up. Joint swelling was noted in only one patient, and the MD global was 17.3.

NIRD patients presented with mono/pauciarticular pain (33/57, 58%). Joint swelling was present in only 5% of patients (2/57). A third of these patients were treated with physical therapy and another third with NSAIDs. OA patients also presented with mono/pauciarticular pain (36/53, 68%). Joint swelling was noted in 20% (10/53). Half were treated with NSAIDs and 20% (8/41) with physical therapy. FM patients mostly presented with WSP (53/64, 83%). About half had joint tenderness but none had joint swelling. Half were treated with NSAIDs, a third had no treatment, and the remaining patients were treated with physical therapy, analgesics and tricyclic antidepressants.

The proportion of patients complaining of morning stiffness and fatigue was highest in the FM group, as was morning stiffness duration. As expected, laboratory markers of inflammation were higher in patients with the inflammatory disorders.

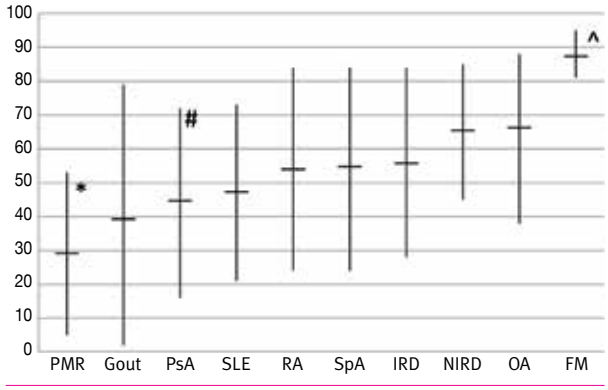
VAS SCORES OF PAIN, FATIGUE AND FUNCTION

Overall, VAS scores of pain, fatigue and function were closely correlated. The correlation coefficient of VAS pain versus VAS fatigue, VAS pain versus VAS function, and VAS fatigue versus VAS function were 0.652, 0.78, and 0.73, respectively. All the above correlations were highly significant ($P < 0.001$).

The mean VAS scores for pain in each group are shown in Figure 1. Three groups of patients were significantly different: FM, PMR and PsA. FM patients had significantly higher VAS scores for pain as compared to all other groups ($P < 0.001$), while PMR patients demonstrated significantly lower VAS scores compared to patients with RA, SpA, IRD, NIRD and OA ($P < 0.001$). Patients with PsA had a significantly low VAS score for pain compared to patients with NIRD and OA ($P < 0.001$).

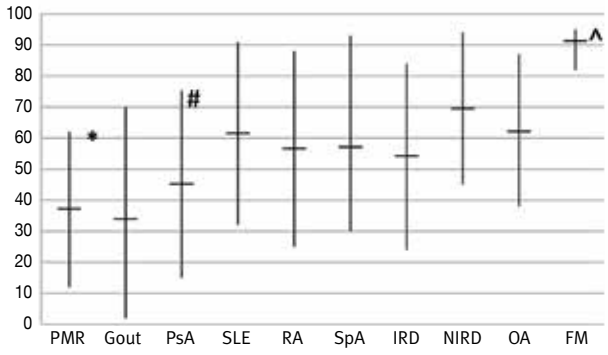
The mean VAS scores for fatigue in each group are shown in Figure 2. Again, the groups of patients with FM, PMR and PsA were significantly different. FM patients had significantly high VAS scores for fatigue as compared to all other nine rheumatic disorders ($P < 0.001$), while PMR patients had significantly lower VAS scores compared to patients with RA, SLE, SpA, NIRD and OA ($P = 0.0014$). Patients with PsA showed a significantly low VAS score for fatigue compared to patients with NIRD ($P < 0.001$).

Figure 1. Mean VAS scores for pain (mean ± SD)



^Significantly ($P < 0.001$) higher in FM compared to all other groups of patients
*Significantly ($P < 0.001$) lower in PMR compared to RA, SpA, IRD, NIRD and OA
#Significantly ($P < 0.001$) lower in PsA compared to NIRD and OA

Figure 2. Mean VAS scores for fatigue (mean ± SD)



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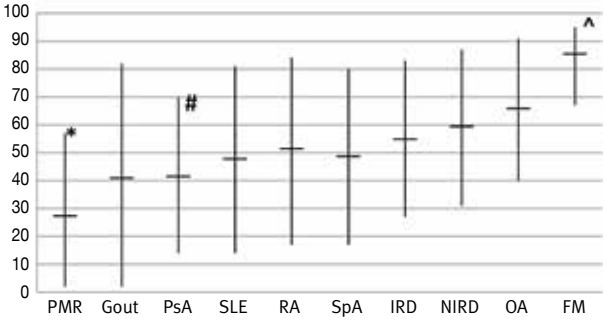
*Significantly ($P < 0.001$) lower in PMR compared to RA, SpA, IRD, NIRD and OA
#Significantly ($P < 0.001$) lower in PsA compared to NIRD and OA

The mean VAS scores for function in each group are shown in Figure 3. The same three groups of patients were significantly different from the other patient groups. FM patients had significantly high VAS scores for fatigue as compared to all other nine rheumatic disorders ($P < 0.001$), whereas PMR patients demonstrated significantly low VAS scores compared to patients with RA, IRD, NIRD and OA ($P < 0.001$). Patients with PsA had a significantly lower VAS score for pain compared to patients with OA ($P < 0.001$).

Figures 1–3 present a spectrum of outcome intensity of pain, fatigue and functional disability. Generally, the lowest scores were obtained in the PMR, gout and PsA disorders (mild to moderate mean VAS scores of about 30–40). The score was lower in patients with PMR, gout and PsA compared to patients with other inflammatory disorders (moderate mean VAS scores of about 55), as well as in patients with inflammatory disorders compared to those with non-inflammatory

Figure 3. Mean VAS scores for function (mean ± SD)



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#Significantly ($P < 0.001$) lower in PsA compared to NIRD and OA

disorders (severe mean VAS score of about 65). The highest scores were perceived in FM patients (very severe mean VAS score of 85–90).

DISCUSSION

The current survey provides an important overview of key outcomes in a broad spectrum of rheumatic disorders. The study included patients with the common inflammatory joint diseases, such as RA, PsA and other SpA, as well as patients with SLE, OA, FM, and other inflammatory and non-inflammatory rheumatic disorders. The results suggest four trends in the clinical outcomes of this cohort: (i) patients with FM were significantly different from all other rheumatic patients in terms of severity of symptoms, (ii) PMR patients were doing significantly better in comparison to other rheumatic patients, (iii) patients with PsA had relatively milder outcome scores, and (iv) the outcome scores of patients with inflammatory disorders were lower than those of patients with non-inflammatory disorders.

FM is characterized by high levels of pain, sleep disturbance, and fatigue combined with a general increase in medical symptoms including memory and cognitive difficulties and often psychological distress [9]. In the current report, FM patients were compared with a broad array of rheumatic patients in terms of symptom severity. The results show that in this cohort of Israeli patients of varying ethnic origin, FM patients exhibited an extreme and significantly distinct level of pain and fatigue. These results are consistent with previous studies [1-3], which were also carried out in tertiary care centers. The level of distress is higher in tertiary care center patients, where health care-seeking behavior is associated with higher psychological and psychiatric comorbidities. In population-based studies, the primary symptom of FM, chronic widespread pain, is only modestly associated with distress [10]. Nonetheless, the high VAS scores in the present study probably characterize FM, and it certainly signifies the lack of efficient therapy for FM at that time.

In the current study, PMR patients were doing significantly better than patients with RA, SLE, SpA, IRD, NIRD and OA. One of the best measures of disease activity and treatment response in PMR appears to be patient-reported global pain (VAS global pain) [11], which we used in the current study. It is well known that prednisone therapy in patients with PMR usually results in rapid and dramatic amelioration of musculoskeletal pain and stiffness. Therefore, the group of patients with PMR may represent a reference for good therapeutic effect.

PsA is a systemic disorder that causes chronic pain, altered physical appearance, and loss of function. In addition, other systemic features are common in patients with PsA, including fatigue and stiffness after rest. Initially, most patients with PsA were thought to have a mild, short-lived form of arthritis. Indeed, Buskila et al. [12] have shown that affected joints are less tender in patients with PsA than in patients with RA. It was also shown by Gladman and team [13] that acute-phase markers, such as erythrocyte sedimentation rate, C-reactive protein and serum amyloid A, may be elevated in PsA patients, but less commonly and to a lesser degree than in RA patients. On the other hand, it is well known that PsA can affect joints early in the course of the disease with irreversible joint damage. Direct comparison between patients with PsA, RA and ankylosing spondylitis has shown a comparable burden of illness across these conditions [14]. Our results suggest that PsA may be a milder or more amenable form of arthritis for treatment.

In light of the results of the current study, it would be interesting to investigate the differences in pain intensity between groups of patients with inflammatory and non-inflammatory rheumatic disorders. Is it an inherent characteristic of the different disorders due to peripheral or central mechanisms [15-17], or does it signify that current therapy for inflammatory disorders is more efficacious. Clinical observations of patients with inflammatory joint diseases, who present with marked clinical and radiographic findings yet report only mild complaints of pain and fatigue, are also intriguing in this regard (i.e., patients with arthritis robustus [18] and patients with asymptomatic ankylosing spondylitis and characteristic radiographic findings [19]). It is established that local inflammation leads to the secretion of analgesic mediators such as opioid peptides, somatostatin, endocannabinoids, and certain cytokines, which may have a clinical significance. Among these analgesic mediators, the best characterized are the endogenous opioid peptides and their receptors. Under the influence of chemokines and adhesion molecules, opioid-containing immune cells accumulate in injured tissues and release opioid peptides. Once secreted, opioid peptides bind to and activate peripheral opioid receptors on sensory nerve fibers and produce analgesia [20,21]. Interestingly, Denco et al. [22] and Toth et al. [23] reported higher beta-endorphin levels in the synovial fluid of patients with RA compared to patients with OA. The endocannabinoid system may also be clinically relevant since synovial fluid from patients with OA or RA, but not normal control synovial fluid, contains anandamide and 2-arachidonyl glycerol, confirming that endocannabinoid synthesis occurs following tissue injury [24].

Our study has several limitations. Since the study was conducted in a single hospital clinic, the data obtained could be affected by the study population. The VAS scores used for fatigue and functional disability assessment are less validated than the multi-item outcome measures. Data were collected for each patient visit, i.e., it included analysis of the same patients on occasional visits which might have influenced the results. Since treatment differed between visits and spontaneous fluctuations of outcomes occurred [25], we believe these patient visit analyses also characterize disease outcomes. Finally, our survey was done in 2006, shortly after biological therapies were introduced in our country, thus our results may not reflect the current situation since only 8% of the patients with inflammatory arthritis participating in the study were treated with an anti-TNF agent. In addition, pregabalin and duloxetine were not available for patients with FM at the time of the study.

In summary, this report provides an overview on the spectrum of outcome severity in rheumatology. At the time of the study, FM patients' reports were at the highly severe end of the spectrum. PMR and PsA patients were at the opposite end of the spectrum with relatively mild outcome. Outcome intensity tended to be lower in the inflammatory than in the non-inflammatory disorders. The results of this study emphasize the need to explore the underlying mechanisms of pain and fatigue in these diseases, particularly in patients with fibromyalgia and in patients with non-inflammatory disorders. It may also serve as a baseline for future studies to follow the implementation of new medications.

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