Pain Thresholds in Rheumatoid Arthritis: The Effect of Tender Point Counts and Disease Duration

LOUISE C. POLLARD, FOWZIA IBRAHIM, ERNEST H. CHOY, and DAVID L. SCOTT

ABSTRACT. ***Objective.*** We evaluated the influence of demographic and clinical factors on pain thresholds in patients with rheumatoid arthritis (RA).

Methods. A cross-sectional observational study (105 patients with RA) assessed pain thresholds using an algometer. Regression analysis examined the influence of demographic and clinical assessments.

Results. Pain thresholds (median 289, interquartile range 89–434) correlated with assessments of disease activity (tender joint counts), disability (Health Assessment Questionnaire), fatigue, depression, and anxiety. Ordinal logistic regression showed tender point counts and disease duration were the dominant contributors.

Conclusion. These findings suggest that low pain thresholds reflect "fibromyalgic" RA (many tender points) and central pain sensitization with prolonged disease duration. (First Release Nov 15 2011; J Rheumatol 2012;39:28–31; doi:10.3899/jrheum.110668)

Key Indexing Terms:
RHEUMATOID ARTHRITIS 28-JOINT COUNT DISEASE ACTIVITY SCORE
TENDER POINTS FATIGUE PAIN THRESHOLD

Pain remains a dominant problem in rheumatoid arthritis (RA). It is influenced by local and central factors. In experimental models of arthritis, peripheral sensitization induced by nocioceptive system activation in joints is important[1,2]. Hyperexcitability in the spinal cord, attributed to continued nocioceptive receptor activation, is also implicated[3,4] and may lead to central sensitization[5,6]. Reduced pain thresholds in RA, one potential consequence of central sensitization, have been reported in observational studies[7,8,9].

As central pain sensitization is most likely in longstanding RA, we hypothesized that disease duration affects pain thresholds. Other contributory factors reducing pain thresholds in RA may include high disease activity and coexistent fibromyalgia (FM). We evaluated the variability of pain thresholds in RA and examined factors that influence them in a cross-sectional observational study.

From the Department of Rheumatology, King's College London School of Medicine, Weston Education Centre, Denmark Hill; and Department of Rheumatology, King's College Hospital, Denmark Hill, London, UK.

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L.C. Pollard, MSc, MRCP, Research Fellow, King's College London, Academic Rheumatology, Weston Education Centre Consultant Rheumatologist, University Hospital Lewisham; F. Ibrahim, BSc, Statistician, King's College London, Rheumatology; E.H. Choy, MD, FRCP, Professor of Rheumatology, Department of Medicine, Cardiff University School of Medicine; D.L. Scott, MD, FRCP, Professor of Clinical Rheumatology, King's College London, Rheumatology.

Address correspondence to Dr. L.C. Pollard, Department of Rheumatology, King's College London, Weston Education Centre, Denmark Hill, 10 Cutcombe Road, London SE5 9RJ, UK. E-mail: louise.pollard@kcl.ac.uk

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MATERIALS AND METHODS

Patients. We studied 105 consecutive outpatients with RA, who met the 1987 American College of Rheumatology (ACR) criteria[10]. King's College Hospital Research Ethics Committee approved the study (05/Q0703/99) and all patients gave informed consent.

Measuring pain thresholds. We used the mean of 2 measurements made by a single assessor using a handheld digital algometer applied to the thumbnail, away from involved joints and avoiding the nail bed.

Clinical assessments. We recorded demographic data (age, disease duration, sex, ethnic origin), physician global assessment, early morning stiffness (minutes), and 28-joint count Disease Activity Score (DAS28) and its constituents [patient global assessment, 28 tender/swollen joint counts, erythrocyte sedimentation rate (ESR)]. Fibromyalgic tender point assessment used methods recommended for diagnosing FM[11]. Visual analog scales (VAS; 100 mm) were used to record pain and fatigue. The Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) questionnaire[12] was also used to measure fatigue. The Health Assessment Questionnaire (HAQ) was used to measure disability[13]. The Hospital Anxiety and Depression Scale (HADS) was used to assess mental health[14].

Analysis. Data were analyzed using Stata version 10 (StataCorp., College Station, TX, USA). Univariate and multivariate ordinal logistic regression models assessed the factors associated with pain threshold. As the distribution of pain thresholds was not linear, they were divided into tertiles for analysis. All continuous measures were entered into the models as continuous variables. For these analyses the crude and adjusted OR with 95% CI are presented; p values are 2-tailed throughout. Variables that had a p value ≤ 0.05 in the univariate analysis were carried forward into multivariate analysis. Factors showing significant collinearity were excluded from the final model.

RESULTS

Patients comprised 80 women and 25 men (mean age 60 yrs, range 24–88) with mean disease duration of 13 years (range 0.1–54), mean DAS28 4.53 (range 1.34–8.06), and mean ESR 30 mm/h (range 3–108 mm/h); 70% of subjects were rheumatoid factor-positive; 62% were erosive (only 7% were rheumatoid factor-negative and nonerosive); 89% were receiving dis-

ease-modifying treatment including 20 patients receiving biologic therapies; 17% met the ACR criteria for FM.

Distribution of pain thresholds. The median pain threshold was 289 kPa (interquartile range 189–434) with upper and lower levels of 67 and 1123 kPa. The distribution of pain thresholds (Figure 1) showed a broad range, with a substantial upper "tail" of high pain thresholds.

Relationship to disease activity and associated clinical variables. The relationships to disease activity and demographic assessments were evaluated using Spearman's correlations. Pain thresholds showed high correlations ($r > 0.4$) with tender point counts, tender joint counts, fatigue VAS, DAS28, and HAQ; moderate correlations ($r = 0.2$–0.4) with pain VAS, HADS depression and anxiety scores, patient global assessments, disease duration, and age; and no correlation ($r < 0.2$) with swollen joint counts, physician global assessment, ESR, and early morning stiffness.

The relationships of tender point counts and disease duration to pain thresholds were evaluated in detail (Figure 2). Pain thresholds were lower in patients with tender point scores ≥ 11 ($p < 0.001$, Mann-Whitney U test). They were also lower in patients with disease durations ≥ 10 years ($p = 0.027$, Mann-Whitney U test).

Regression analysis. Ordinal logistic regression evaluated pain threshold tertiles to disease activity and other clinical measures. Adjusted OR showed that tender point counts and disease duration were independently associated with pain thresholds (Table 1); high tender point counts and prolonged disease durations were associated with lower pain thresholds. Tender joint counts and patient global assessments showed significant collinearity with tender point counts and pain and were excluded from the adjusted model (data not shown). In the multivariable model, age, fatigue (VAS or FACIT-F), pain, ESR, and disability (HAQ) were not associated with pain thresholds.

DISCUSSION

Pain thresholds vary substantially in patients with RA and are affected by many clinical variables. The dominant factors are high tender point counts, reflecting the presence of fibromyalgic RA[15,16], which is known to be associated with lower pain thresholds, and prolonged disease duration, which probably reflects central sensitization. Other variables that might reduce pain thresholds, including quality of sleep[9], several psychosocial factors, and analgesic use, were not included in our study. Although comparison with other studies is difficult, as they assessed different body parts and used different units of measurements, our findings were broadly similar.

"Fibromyalgic RA" with ≥ 11 tender points affects 10%–20% of patients with RA; most have low pain thresholds (Figure 2). The association of low pain threshold with disease duration is likely to have a different explanation. It was particularly marked in patients with RA of more than 10 years' duration. This finding suggests that over time, the burden of inflammation in RA not only causes progressive joint damage and functional decline but also can lead to persistence of pain, and that persisting nocioceptive stimulation results in central sensitization and reduced pain thresholds.

Our study has several limitations. It was relatively small; it was restricted to 1 timepoint and did not assess the influence of treatment. Nevertheless, we consider that the results highlight a potentially important factor in the perpetuation of RA pain.

Early and intensive treatment that minimizes inflammation is likely to reduce central sensitization and minimize longterm RA pain. Biologic therapies may have a crucial role in changing this relationship[2]. Traditional analgesics may have limited value in patients for whom pain remains a problem despite apparent control of their synovitis. Their pain management should focus on treatments that are effective in the presence of central sensitization.

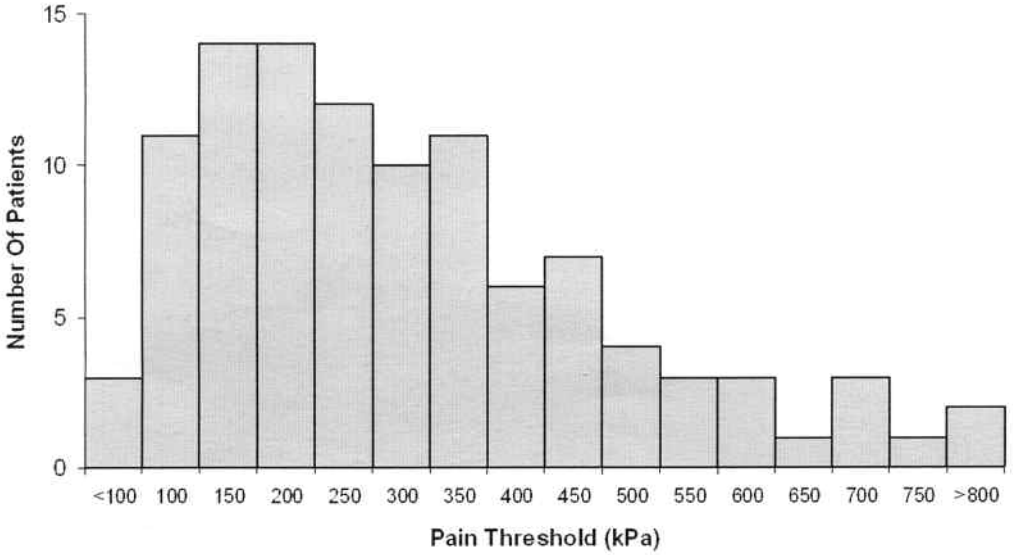

Figure 1. Distribution of pain thresholds in patients with rheumatoid arthritis (RA).

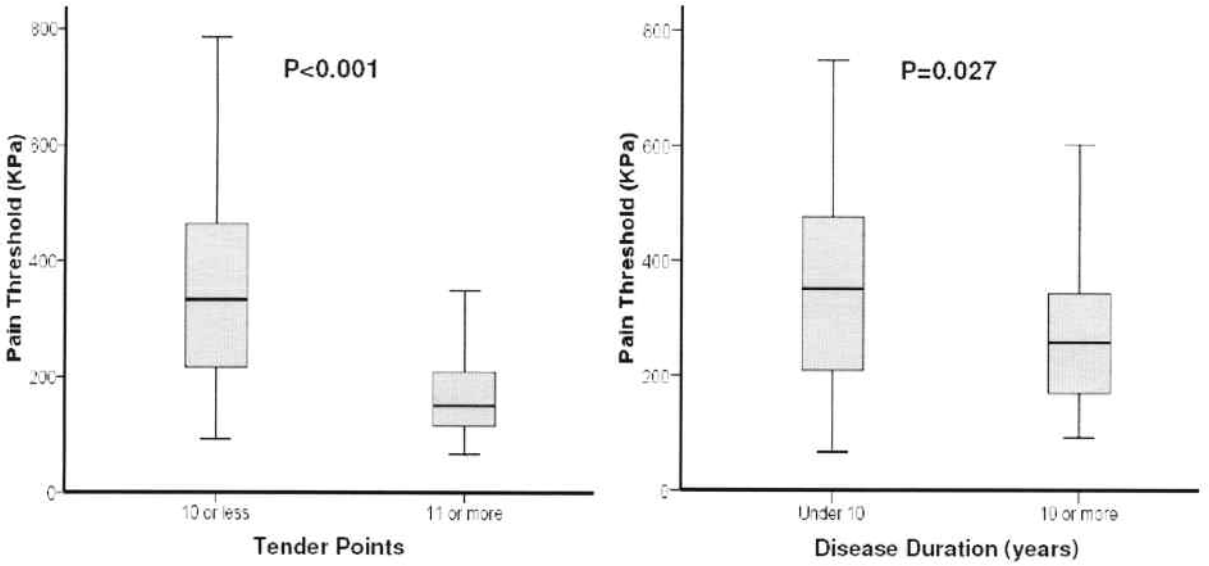

Figure 2. Relationship of pain thresholds to tender points and disease duration. Data are medians, with interquartile ranges.

Table 1. Ordinal logistic regression assessing the factors associated with pain threshold. Crude and adjusted models are shown. For the adjusted OR we excluded EMS, HADS anxiety, ethnicity, swollen joint count, and sex as they showed no significant relationship with pain thresholds at the 0.05 level. HADS depression, tender joint count, patient global assessment, fatigue VAS, FACIT-F, and HAQ were all significantly correlated with pain threshold. However, many were also highly correlated with each other (e.g., tender point counts and tender joint counts; r = 0.71). We therefore excluded variables that showed strong collinearity with each other. Where strong collinearity existed we used both statistical and clinical assessments to decide which variables to include (for example, we chose tender point counts over tender joint counts).

Factor	Crude OR (95% CI)	p	Adjusted OR (95% CI)	p
Age	0.97 (0.94, 0.99)	0.015	0.97 (0.94, 1.01)	0.16
Disease duration	0.97 (0.94, 1.00)	0.037	0.95 (0.91, 1.00)	0.04
Pain (VAS)	0.98 (0.97, 0.99)	0.002	0.99 (0.97, 1.01)	0.38
No. tender points	0.78 (0.71, 0.86)	< 0.001	0.75 (0.65, 0.86)	< 0.001
Fatigue (VAS)	0.97 (0.96, 0.99)	< 0.001	0.98 (0.96, 1.00)	0.15
Health Assessment Questionnaire	0.39 (0.23, 0.69)	0.001	1.19 (0.56, 2.56)	0.64
ESR	0.98 (0.96, 1.00)	0.035	1.00 (0.98, 1.03)	0.83
FACIT-F	1.04 (1.01, 1.08)	0.011	—	—
Tender joint count	0.88 (0.82, 0.93)	< 0.001	—	—
Patient global assessment (VAS)	0.98 (0.96, 0.99)	0.003	—	—
HADS depression	0.89 (0.81, 0.99)	0.028	—	—
HADS anxiety	0.92 (0.83, 1.01)	0.064	—	—
Duration of morning stiffness, min	1.00 (0.99, 1.00)	0.076	—	—
White vs other ethnic groups	1.52 (0.62, 3.74)	0.360	—	—
Swollen joint count	0.96 (0.86, 1.07)	0.428	—	—
Male vs female	0.67 (0.28, 1.61)	0.373	—	—

EMS: early morning stiffness; HADS: Hospital Anxiety and Depression Scale; VAS: visual analog scale; ESR: erythrocyte sedimentation rate; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue scale; HAQ: Health Assessment Questionnaire.

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