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ORIGINAL RESEARCH

Meaning of patient global assessment when joint counts are low in rheumatoid arthritis

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ABSTRACT

Objective In patients with rheumatoid arthritis (RA) with low 28-joint tender and swollen joint counts but who assessed their disease as active, to evaluate whether activity reflected RA symptoms.

Methods We carried out a cross-sectional study of patients in BRASS, a cohort of patients with established RA who had 28-joint counts assessed, scored their disease activity, identified their painful joints, and answered questions about other sites of pain and fatigue. Patients and their rheumatologists were asked about the presence of fibromyalgia. We examined whether patients reported pain in joints excluded from the 28-joint joint count (feet, ankles, hips, neck) and pain or symptoms probably unrelated to RA including low back pain, headache and fibromyalgia. Fatigue was not classified. Analyses were descriptive.

Results Of 272 patients, 49 had tender and swollen joint counts <1 and a patient global assessment score of ≥3/10. 48/49 (95%) reported pain in joints excluded from the 28-joint count. Of these 49, 24 (45%) also had other symptoms especially low back pain. Fatigue was present in all patients. No patient had fibromyalgia.

Conclusion If joint counts <=1 are scored in 28 joints, patient global assessments of ≥3/10 often occur when there is pain in uncounted joints, joints that may respond to RA treatment.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ There is often a discrepancy between a high patient global assessment and low 28-joint tender and swollen joint counts in rheumatoid arthritis (RA). Understanding this discrepancy will help determine whether such patients need more treatment or have complaints that do not reflect active RA and therefore do not warrant more RA treatment.

WHAT THIS STUDY ADDS

⇒ Using comprehensive data on pain in all joints, fibromyalgia, fatigue and pain elsewhere in the body, this study found that patients with established RA who had elevated global assessment but tender and swollen 28-joint counts of 0 or 1 usually reported pain in joints not counted in the 28-joint count, especially feet, ankles and hips. No patients developed fibromyalgia.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY

⇒ For practice, if the patient says their disease is active, examine all joints, not just the 28 joints. For policy, remission assessments may need to expand to include joints not in the 28-joint count.

The ultimate goal of rheumatoid arthritis (RA) treatment is to suppress the disease activity that leads to pain and disabling joint damage. Current RA treatments are highly effective but still leave many patients with persistent active disease. Remission is achieved by only 10%–20% of patients on treatment in trials.[1 2] However, remission as defined in these trials often depends on the patient global assessment score of RA disease activity reaching very low levels.

The patient global assessment (PGA) of disease activity is among the most sensitive to change among all RA core set measures.[3] However, for patients on active treatment in whom treatment has successfully suppressed joint swelling and tenderness in the 28 joints counted, the patient global assessment score can remain elevated, suggesting either that treatment is insufficiently effective or that the patient is reporting as part of their disease activity symptoms from locations such as their lower back that are probably unrelated to their RA. Studies have suggested that pain and fatigue are the symptoms that best explain the patient global assessment score,[4] but there has been no intensive inquiry into the specific symptoms present in those with elevated PGA whose joints counts are low. There are four explanations as follows: first, RA symptoms with persistent pain in joints not included in the 28-joint count (feet/ankles/hips/neck); second, symptoms probably unrelated to RA including back pain,

headache and fibromyalgia; third, symptoms of fatigue which may or may not be due to RA; or fourth, a combination of these possibilities.

If elevated patient global assessment scores represent symptoms of active RA, we might need to add to treatment. If, on the other hand, the elevated PGAs reflect symptoms that do not emanate from locations usually affected by RA, better communication between patients and their physicians is needed to help patients more accurately assess what symptoms are related to their active RA so that, working together, patients and physicians accurately assess disease activity and reduce the impact of disease on quality of life. Different patients may have different reasons for scoring their disease as active and there has been little investigation of why global assessments are elevated when 28-joint joint counts are low.

Using the BRASS database of comprehensively assessed patients with RA surveyed and repeatedly examined prospectively, we investigated those with either one or no tender or swollen joints yet patient global assessments indicating active disease. We asked whether those patients had pain in joints missed by the 28-joint count or pain in locations not likely to be related to RA and/or fatigue.

PATIENTS AND METHODS

Description of BRASS cohort and measurements made

The BRASS registry is a single-centre, prospective observational cohort of patients with RA with data collection beginning in 2003. All subjects attend the Brigham and Women's Arthritis Center in Boston, Massachusetts. Patients were screened for eligibility using the International Classification of Diseases, 9th Revision, followed by rheumatologist diagnosis, and met the American College of Rheumatology RA classification criteria current at the time.

Measurements

Detailed demographic information, smoking history, body mass index and medication use were obtained at each annual visit. The subject's rheumatologist performed a 28-joint examination detailing tender and swollen joints. As part of the multidimensional health assessment questionnaire, subjects provided a global score of their disease activity on a Visual Analogue Scale. Subjects were asked at each visit if they were diagnosed or had experienced symptoms of fibromyalgia, and examining rheumatologists were asked about the presence of fibromyalgia. In addition, subjects were asked to indicate which part of their body had pain over the past 7 days, and we extracted responses of headache, neck, lower back and hip pain.[5] In addition, subjects filled out the Rheumatoid Arthritis Disease Activity Index homunculus from which we extracted reports of foot, ankle and hip pain.[6] We included hip pain recorded on either the questionnaire or the homunculus. We focused on the 11th cycle (the 11th year of follow-up) when additional surveys and examination elements were included; of all cycles, the most patients had contemporaneous assessments of patient global assessments, sites of pain and rheumatologist assessment of the 28 joints and of fibromyalgia. Fatigue was assessed with one question that had a 0–10 numerical score.

With assessments of painful and other symptoms from BRASS subjects, we categorised some of the following symptoms as affecting joints not included in the 28-joint joint count that may have been due to active RA: foot pain, ankle pain, hip pain and neck pain. Others were probably unrelated to RA as follows: low back pain, headache and fibromyalgia. Fatigue can have many causes including active RA; we characterised fatigue as present if the global fatigue score was not zero.

We carried out a sensitivity analysis in which we removed neck pain from the RA joint group given that many patients have neck pain due to osteoarthritis or disc disease in the cervical spine. In these analyses, like fatigue, we did not classify neck pain as either related or unrelated to RA.

Analysis

Analysis was descriptive, looking at the frequency of symptoms in BRASS participants who had both patient global assessments >3 and tender and swollen 28-joint counts of 0 or 1. Analyses were carried out using SAS V.9.4.

The study protocol was reviewed and approved by the Mass General Brigham Institutional Review Board at Brigham and Women's Hospital. Patients in the BRASS Registry are followed at Brigham and Women's Hospital's Orthopaedic and Arthritis Center at least annually (for details see Iannaccone *et al*[7]).

RESULTS

Most BRASS participants were women and the median age was in the 60s (table 1). Multiple tender and swollen joints were present in most patients, although a few had counts of 0 or 1. Of 272 patients who reached the 11th-year follow-up examination, 54 (19.9%) met our criteria of having both tender and swollen 28-joint counts of 0 or 1 yet having patient global assessment scores of at least 3/10. Of these 54, 49 had no missing values for any of the symptoms mentioned under table 2. A histogram of PGA scores is shown in online supplemental figure 1. The distribution of PGAs by either 0 or 1 tender joint is shown in online supplemental figure 2.

Of those who had tender and swollen joint counts of 0 or 1 and who also had patient global assessment scores of at least 3/10, many subjects had foot or ankle pain, hip pain or neck pain. Twenty-two of 49 (44.9%) had low back pain. Fewer had headache, and none were characterised as having fibromyalgia (table 2).

While fatigue (scores of at least 1 on a 0–10 score) was universal (49/49 patients), only 5 patients had only fatigue but no other symptoms. When we restricted fatigue scores to at least 3/10, 39/49 (80%) of patients reported it.

Table 1 Description of patients with elevated PGA and tender joint counts of 0 or 1 vs all BRASS patients at the 11th follow-up examination

	TJC/SJC both ≤1 and PGA ≥3 (n=49)*	All BRASS participants excluding study group (n=223)
TJC (median/IQR)	0 (0, 1)	0 (0, 3)
SJC (median/IQR)	0 (0, 1)	0 (0, 2)
Patient Global Assessment (0–10) (median/IQR)	5 (4, 6)	1.5 (1, 5)
CRP in mg/dL (median/IQR)	2.6 (1.0, 9.0)	1.7 (0.8, 3.9)
DAS28 CRP score (median/IQR)	2.03 (1.61, 2.32)	2.18 (1.61, 2.97)
% on steroids	24.5	29.3
% on methotrexate	49	52
% on biologic agent	67.4	64.6
Age in years (median/IQR)	65 (53, 73)	66 (56, 72)
Sex (% women)	85.7	83.9
BMI (median/IQR)	25.7 (22.4, 31.1)	27 (23, 30.7)
Smoker (% current/% ever)	2.3/59.2	2.1/38.6
Race (% White)	95.9	95.1
Ethnicity (% non-Hispanic)	95.9	98.2
Disease duration in years (median/IQR)	20 (15, 35)	21 (15, 31)
Depression diagnosed or treated in past year (%)	2	2.7

*Of the 272 subjects at visit 11, 54 actually met the criteria for focus with joint counts 0 or 1 and PGA >3, but of these only 49 had concurrent data on all symptoms. Some data not available in entire cohort.
BMI, body mass index; CRP, C reactive protein; DAS28, disease activity score in 28 joints; PGA, patient global assessment; SJC, swollen joint count; TJC, tender joint count.

In addition, 44/49 (89.8%) reported pain in joints excluded from the 28-joint joint count, some in combination with pain in non-RA locations (24 (49%)), while others had pain only in joints not captured in the 28 joints . No patient had only pain or symptoms probably unrelated to RA. As shown in online supplemental figure 2, there was no clearcut association of joint count with PGA.

In sensitivity analyses excluding neck pain, we found 1/49 patients with only pain in locations unlikely to be related to RA, 23/49 with mixed symptoms (in excluded joints and elsewhere) and 20/49 with only symptoms in excluded joints.

DISCUSSION

In a comprehensively assessed RA cohort, subjects with low 28-joint tender and swollen joint counts but elevated PGA scores usually had pain in joints not included in the 28-joint joint count. This suggests that despite quiescent disease activity among the 28 joints usually assessed, there was pain in joints not assessed, the feet, ankles, hips and neck. Low back pain was also common.

Among limitations to our study were the small sample of persons followed who had both low joint counts and moderate to high PGAs. Subjects included may have been knowledgeable about RA symptoms and were patients with longstanding disease. They also had only mildly active disease. For these reasons, results may not be fully generalisable. Self-reported painful joints may not translate into tender or swollen joints on examination. Also, many of the subjects had missing data on some of the parameters of interest. Lastly, while these subjects reported pain in joints excluded from the 28-joint joint count, that does not mean these joints were affected by active RA. Disease-related damage, other causes of foot, ankle or hip pain, or even secondary osteoarthritis could be the source of pain, for example. Additional research that includes a careful examination of feet and ankles in patients with RA who have pain in feet, ankles and hips but whose disease activity is quiescent elsewhere is needed.

We were surprised by the absence of fibromyalgia in our sample. This was assessed by patient self-report and by rheumatologists who were asked whether the patient had fibromyalgia. It is possible that some cases were missed, but the development of fibromyalgia in persons with established RA may be unusual.

The 28-joint joint count adequately captures most disease activity in RA. However, our findings suggest that elevated patient global assessments may signal disease activity not captured by the 28 joints. Few, if any, of these persons appear to have only symptoms in locations probably unrelated to RA. A careful clinical evaluation may be needed in these patients to determine what these reports of disease activity signify. Many have a combination of symptoms that include both joints

Table 2 Frequency of specific symptoms and fatigue in 49 BRASS patients with high PGAs yet low tender and swollen 28-joint counts

TJC=0 or 1		TJC=0 N=35	TJC=1 N=14
Pain in joints excluded from the 28-joint joint count including TJC 0 and 1 (n=49)			
Left ankle pain (%)	19 (38.8)	12 (34.3)	7 (50)
Right ankle pain (%)	18 (36.7)	11 (31.4)	7 (50)
Left foot/toes (%)	22 (44.9)	16 (45.7)	6 (42.9)
Right foot/toes (%)	24 (49)	17 (48.6)	7 (50)
Left hip pain (%)	21 (42.9)	16 (45.7)	5 (35.7)
Right hip pain (%)	19 (38.8)	14 (40)	5 (35.7)
Neck pain (%)	16 (32.7)	10 (28.6)	6 (42.9)
Pain in joints included in the 28-joint joint count including TJC 0 and 1			
Left elbow		0	3 (21.4%)
First left MCP joint		0	1 (7.1%)
Left wrist		0	1 (7.1%)
Right wrist		0	4 (28.6%
Right knee		0	4 (28.6%)
Right shoulder		0	1 (7.1%)
Pain or other symptoms probably unrelated to active RA			
Low back pain (%)	22 (44.9)		
Headache (%)	6 (12.2)		
Current fibromyalgia (%)	0 (0)		

MCP, metacarpophalangeal; PGA, patient global assessment; RA, rheumatoid arthritis; TJC, tender joint count.

affected by RA and pain in regions of the body unrelated to RA.

If assessing disease remission is a goal, our findings suggest that we may need to reconsider the abbreviation of the full joint count and return to a more complete joint count. Initial data suggested that 28 joints would not miss many active joints,[8] but our data may be at odds with these findings and data from psoriatic arthritis[9] contradict this. The scientific community studying psoriatic arthritis already endorsed a more comprehensive joint count.

Another possible explanation for high patient global assessments when there is only one tender joint may be that a single very painful and treatable joint may affect the global assessment, an issue we could not explore well.

In summary, PGA elevation in the face of low 28-joint counts mostly represents pain in joints that are excluded from the 28-joint count and should trigger a complete examination of all potentially affected joints.

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