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Discriminating ability of composite indices for measuring disease activity in rheumatoid arthritis: a comparison of the Chronic Arthritis Systemic Index, Disease Activity Score and Thompson's articular index

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Abstract

Objective. To compare the discriminating ability of the chronic arthritis systemic index (CASI), an index that uses the Health Assessment Questionnaire (HAQ) as the main variable, with the disease activity score (DAS) and Thompson's articular index (TAI) to detect high and low disease activity in rheumatoid arthritis (RA).

Methods. Two hundred and two RA patients were examined. According to criteria proposed previously, they were divided into two subgroups: those with active disease and those with low activity. The areas under receiver operating characteristic (ROC) curves were employed to assess the diagnostic accuracy of the CASI in comparison with the DAS and TAI for the discrimination of disease activity.

Results. The difference between areas under the ROC curves of the CASI and TAI (0.897 ± 0.023 *vs* 0.780 ± 0.032) and between the DAS and TAI (0.933 ± 0.018 *vs* 0.780 ± 0.032) was highly significant ($P = 0.0001$), thus reflecting the accuracy of the diagnostic assessment. No difference arose between areas under the ROC curves of the CASI and the DAS (difference between areas $= 0.036 \pm 0.022$; $P = 0.103$).

Conclusion. The CASI discriminates just as well between high and low disease activity as does the DAS. Either index consisting of more than one variable performs better than TAI. We conclude that even including the HAQ, a severity parameter in the long term, it is possible to construct an index that, at any time point, evaluates disease activity as well.

KEY WORDS: Rheumatoid arthritis, Chronic arthritis systemic index, Disease activity score, Thompson's articular index, Receiver operating characteristic (ROC) curves, Discriminating ability.

Disease activity variables can be divided into process and outcome variables [1]. A process measure reflects the current state of rheumatic disease activity, such as pain, tender and/or swollen joint counts and the acute phase reactants. In contrast, an outcome measure tends to reflect a fixed and more permanent state caused by the illness and occurs over a long period of time, the classic example being functional disability [2, 3].

Effective assessment of disease activity is important since persistent high levels are likely to lead to the characteristic damage of rheumatoid arthritis (RA) [3]. Accurate assessment of disease activity should guide therapy, so that effective therapies can be continued and ineffective ones discontinued. Techniques and measures to assess disease activity in RA have been developed for use in clinical trials, but these are often not suitable for use in clinical practice due to constraints on time, expense and the special training required.

The physical examination of joints is considered to be important in the assessment of RA disease activity. Several methods for counting involved joints have been developed in attempts to standardize the clinical measurement of joint signs. These indices, formulated on an empirical basis and fundamentally different in their construction, include a Ritchie's articular index (RAI; a count of single and grouped joints each scored on the basis of tenderness severity) [4], a modified Ritchie's index which counts rather than scores the tender joints [5], a count of active (tender or swollen) joints [6] and a Thompson's articular index (TAI) [7] which scores the severity of inflammation, weighted for joint surface

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area. The principle of weighting, according to joint size, was rejected by Ritchie *et al.* [4]. It is, therefore, of interest that Thompson *et al.* [7], Fuchs *et al.* [8] and van der Brink *et al.* [9] found that weighting increases the validity of a joint index in measuring disease activity.

Since an evaluation of disease activity by single variables leads to methodological problems, several indices consisting of more than one variable have been developed. Several ways of combining these clinical measures into a composite index of activity have been examined. Thompson *et al.* [10, 11] also showed that even a limited index composed of four items (morning stiffness, grip strength, sedimentation rate and articular index) was able to monitor the course of the disease over time. New composite indices have been proposed in the last few years, including the relatively complex Mallya and Mace index [12], the Stoke index [13], and the disease activity score (DAS) of van der Heijde *et al.* [14, 15], which was developed and validated from a prospective study of early RA. The DAS includes two comprehensive joint counts, i.e. RAI and the total number of swollen joints, plus the erythrocyte sedimentation rate (ESR), and a general health assessment scored on a visual analogue scale (VAS).

Recently, we have suggested another index, the chronic arthritis systemic index (CASI), that includes a subjective parameter (patient's assessment of pain by VAS), a clinical measure which reflects the activity of the disease (RAI), a measure of the systemic inflammation (ESR), and a widely employed measure of physical disability (health assessment questionnaire [HAQ]) [16, 17]. Nomograms, based on the percentage of impact exerted on the common variance (factorial analysis) simplify the estimation of a patient's disease activity. The CASI has proved to be very useful in monitoring the course of arthritis and response to therapeutic regimens [18–21].

The aim of the present investigation was to compare the sensitivity and specificity of the CASI with the DAS and TAI to detect high and low disease activity in RA. We show in this study that the CASI is appropriate for clinical assessment.

Patients and methods

Patient selection

Two hundred and two patients with RA diagnosed according to American College of Rheumatology (ACR) criteria [22] attending the care facilities of the Department of Rheumatology of Ancona and Udine, participated in the cross-sectional study. All the patients attended the referral centres between January 1997 and May 1998.

The mean age was 51.4 yr (range 18–76 yr) and the disease duration of RA was 6.2 yr (range 5 months to 27 yr); 150 were female and 52 were males. Seventy per cent were seropositive for rheumatoid factor (RF), with titres of 20 IU/ml or greater, and 28% were antinuclear antibody (ANA) positive (1:40 on Hep-2 cells). At study entry, 159 patients were on non-steroidal anti-inflammatory drugs (NSAIDs) and 22 were taking low daily doses of 6-methylprednisolone. In addition, 189 (93%) patients were being treated with disease-modifying anti-rheumatic drugs (DMARDs): 57 with sulphasalazine, 49 with hydroxychloroquine, 48 with methotrexate, 35 others.

Our patients were divided into two subgroups, according to the criteria proposed by Scott *et al.* [23, 24]: subgroup A = active RA (pain poorly controlled by NSAIDs, three or more painful and swollen joints, morning stiffness longer than 30 min, ESR higher than 45 mm/1°h); and subgroup B = RA in partial or complete remission (no pain or pain fully controlled by NSAIDs, less than three painful or swollen joints, morning stiffness less than 30 min, ESR lower than 45 mm/1°h).

Clinical and functional assessment

The following parameters or variables were considered: (1) the number of painful/tender joints on pressure or passive motion (of a total of 53 diarthrodial joints); (2) the number of swollen joints (of a total of 44 diarthrodial joints); (3) the duration of morning stiffness (expressed in minutes); (4) the intensity of pain, assessed by VAS of 100 mm (0 = no pain; 100 = worst pain possible); (5) general health on VAS (0 = best possible; 100 = worst possible; and (6) the disability index of the HAQ [2]. The HAQ assesses the degree of difficulty a person has in accomplishing tasks in eight functional areas (dressing, getting up, eating, walking, hygiene, reaching, gripping, errands and chores). Responses in each functional area are scored from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area. Each area score is averaged to derive the disability index, which can range from 0.0 to 3.0 [2]. A version adopted for use among Italian patients was utilized in the present study [25]. Also a complete joint examination included: (7) RAI and (8) TAI. Ritchie's joint (RAI) tenderness score was obtained according to the original description (53 joints in 26 units, graded for tenderness on pressure, where 0 = no pain, 1 = patient complains of pain, 2 = patient complains of pain and winces, 3 = patient complains, winces, and withdraws; maximum score 78) [5]. TAI is based on the assessment of tenderness and swelling or effusion in large and small joints, 'weighted' for joint surface area according to the scale of the index. The sum of the score obtained for each tender and swollen joint results in a score of joint inflammation, which varies between 0 (no inflammation) and 534 (maximum inflammation) [7].

We also calculated the CASI and the DAS for each patient. On the basis of a principal component analysis (factor analysis) performed on 124 RA patients in whom 29 biological and clinical variables were recorded longitudinally, we obtained four factors which explained 74% of the common variance. The four factors were as follows: the HAQ, as a severity measure (accounting for 39% of the variance); ESR (accounting for 21%); VAS for pain (accounting for 8%) and the clinical factor

represented by RAI (accounting for 6%). These four items were used to construct a CASI according to the following formula:

$$\text{CASI} = 13 \times \text{HAQ} + 0.21 \times \text{ESR} + 0.08 \times \text{VAS} + 0.07692 \times \text{RAI}$$

The theoretical maximum possible value of the CASI would be 74 [16, 17]. Furthermore, we obtained a nomogram in which the value of any variable is equivalent to the percentage of impact exerted on the common variance [16]. The CASI has proved to be very useful in monitoring the course of arthritis and the response to therapeutic regimens [16–21].

For each patient, the DAS was also calculated using the following formula [14]:

$$\text{DAS} = 0.53938 \times \sqrt{\text{RAI}} + 0.06465 \times \text{SW44} + 0.330 \times \ln \text{ESR} + 0.00722 \times \text{GH}$$

where SW44 is the ungraded count of joints with swelling due to synovitis (maximum score 44), ln ESR is the natural logarithm of the ESR (mm/1°h), and GH (general health) was assessed by the patient using a 100-mm VAS. The range of the DAS varies from 0 to 10 [14].

To eliminate inter-observer variation in the joint counts and physical assessments, all examinations were performed by one rheumatologist. To determine the reliability of these assessments, 20 patients were examined by a second rheumatologist at one visit. The reliability calculated by use of the intra-class correlation coefficients (ICC) between the two rheumatologists ranged from 0.74 to 0.84 for RAI and from 0.81 to 0.92 for TAI, indicating good inter-observer agreement for these measures [26]. All clinical measurements were performed between 9.00 and 10.00 a.m. in order to minimize the influence of circadian rhythm [27].

Laboratory estimation

Blood samples from all patients were taken for measurement of Westergren ESR (mm/1°h) and serum levels of haemoglobin (g/l). In addition, serum samples were also analysed for RF by nephelometry (RF positive at a titre of >20 IU/ml) and ANA by immunofluorescence using Hep-2 cells as the substrate (positive at a dilution of $>1/40$).

Statistical analysis

Statistical analysis was performed employing two statistical packages (Medcalc software and Stat View II, Abacus Concepts). The results are presented as mean [$\pm$ standard error (S.E.)] or prevalence rates. Comparison of categorical parameters was performed using the χ^2 test with Yates' correction or the Fisher exact test when appropriate. Differences between some demographic and clinical features of the patients were analysed by Student's *t*-test. Pearson's product moment correlation was used to study the correlations between the single variables. The receiver operating characteristic (ROC) curves were employed to describe how well various score changes of the CASI, the DAS and TAI can detect RA patients with high and low disease activity. This analysis involves plotting the true-positive rate (sensitivity) against the false-positive rate (100 − specificity) for possible cut-off scores. Sensitivity and specificity (which constitute the discriminating ability of a test) were used in agreement with the current definitions of these terms [28, 29]. Moreover, we calculated 95% confidence intervals (CI) of sensitivity and specificity. Each point on the ROC plot represents a sensitivity/specificity pair corresponding to a particular decision threshold [26, 30]. The area under the ROC curve is used to evaluate the screening scale's performance. The value for the area under the ROC curve can be interpreted as follows: an area of 0.85, for example, means that a randomly selected individual from the positive group has a test value larger than a randomly chosen individual from the negative group 85% of the time. When the variable under study cannot distinguish between the two groups, i.e. where there is no difference between the two distributions, the area will be equal to 0.5 (the ROC curve will coincide with the diagonal). When there is a complete separation of the values of the two groups, i.e. there is no overlapping of the distributions, the area under the ROC curve equals 1 (the ROC curve will reach the upper left corner of the graph). The non-parametric Wilcoxon statistical method was used for the calculation and the comparison of the areas under the ROC curves derived from the sample of patients, as suggested by Hauley and McNeil [31]. The level of statistical significance was established at 5% for all tests.

Results

At the start of the study, 105 patients (51.9%) had active arthritis and 97 patients (48.1%) had partial or complete remission according to the previously defined criteria [23, 24]. The two subgroups were similar for sex ratio, age (52.5 ± 10.4 yr *vs* 49.8 ± 11.8 yr) and disease duration (6.8 ± 4.9 yr *vs* 5.9 ± 5.1 yr).

The ROC curves were employed to assess the diagnostic accuracy of the CASI in comparison with the DAS and TAI for the discrimination of disease activity. Sensitivity was plotted against the complement of specificity (100 − specificity) in the ROC curve analysis. Figure 1 shows the ROC curves for the CASI, the DAS and TAI. The area under the ROC curve was used to evaluate the screening method's performance. For the CASI, the area under the curve was 0.897 ± 0.023 (95% CI from 0.846 to 0.935), for the DAS it was 0.933 ± 0.018 (95% CI from 0.889 to 0.963) and for TAI it was 0.780 ± 0.032 (95% CI from 0.716 to 0.835). According to Swets [32], areas from 0.50 to about 0.70 represent poor accuracy, those from 0.70 and 0.90 are 'useful for some purposes', and higher values represent high accuracy. From the ROC curves in Fig. 1 we computed the optimal cut-off points, corresponding with the maximum sum of sensitivity and specificity. These theoretically optimal upper limits of reference values, sensitivity, specificity, as well as their CIs can be seen

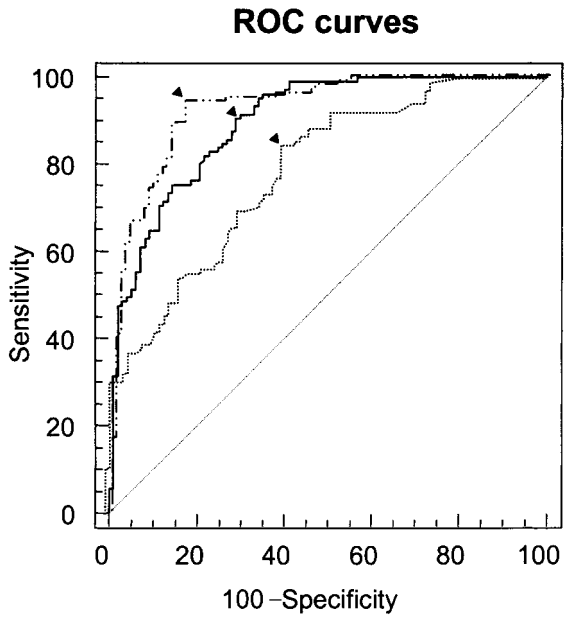

FIG. 1. ROC curves, illustrating the relationship between sensitivity and complement of specificity (100 − specificity) and reference values (see Tables 1–3) for the CASI (—), the DAS (–··–) and TAI (.....), with regard to disease activity, using remission disease as the reference group. The triangles on curves show optimal cut-off points, corresponding with the maximum sum of sensitivity and specificity.

TABLE 1. Sensitivity and specificity of the CASI in discriminating active disease from partial or complete remission, calculated at various reference values

Criterion	Sensitivity (95% CI)	Specificity (95% CI)
≥ 2.9	100.0 (100.0–100.0)	0.0 (0.0–0.0)
>17.36	100.0 (100.0–100.0)	43.3 (33.3–53.7)
>17.4	99.0 (94.8–99.8)	43.3 (33.3–53.7)
>20.86	97.1 (91.9–99.4)	59.8 (49.3–69.6)
>20.98	96.2 (90.5–98.9)	59.8 (49.3–69.6)
>23.36	95.2 (89.2–98.4)	66.0 (55.7–75.3)
>24.03	93.3 (86.7–97.3)	67.0 (56.7–76.2)
>24.54	91.4 (84.3–96.0)	70.1 (60.0–79.0)
>24.65[a]	90.5 (83.2–95.3)	71.1 (61.0–79.9)
>25.8	87.6 (79.8–93.2)	72.2 (62.1–80.8)
>27.41	84.8 (76.4–91.0)	74.2 (64.3–82.6)
>28.23	82.9 (74.3–89.5)	77.3 (67.7–85.2)
>29.06	80.0 (71.1–87.2)	79.4 (70.0–86.9)
>31.52	75.2 (65.9–83.1)	85.6 (77.0–91.9)
>33.04	70.5 (60.8–79.0)	88.7 (80.6–94.2)
>34.69	64.8 (54.8–73.8)	90.7 (83.1–95.7)
>35.43	61.0 (50.9–70.3)	92.8 (85.7–97.0)
>37.72	55.2 (45.2–65.0)	93.8 (87.0–97.7)
>38.75	51.4 (41.5–61.3)	94.8 (88.4–98.3)
>39.75	49.5 (39.6–59.5)	95.9 (89.8–98.8)
>40.12	48.6 (38.7–58.5)	96.9 (91.2–99.3)
>41.12	47.6 (37.8–57.6)	97.9 (92.7–99.7)
>46.49	31.4 (22.7–41.2)	99.0 (94.4–99.8)
>62.01	5.7 (2.1–12.0)	100.0 (100.0–100.0)
>70.8	0.0 (0.0–0.0)	100.0 (100.0–100.0)

Area under the ROC curve = 0.897; S.E. = 0.023; 95% CI = 0.846–0.935.
[a]Optimal cut-off point.

in Tables 1–3. For the CASI, an optimal point of 24.65 comes close to maximizing both sensitivity and specificity. With this cut-off point, sensitivity is 90.5% and specificity is 71.1% (Table 1). In Tables 2 and 3 the same analysis for the DAS and TAI is reported. For the DAS an optimal cut-off point of 3.32 is very close to maximizing both sensitivity and specificity. With this optimal cut-off point, sensitivity is 94.3% and specificity is 83.5%, whereas for TAI, an optimal cut-off point of 160 produces a sensitivity of 84.8% and a specificity of 59.8% (Table 3).

The differences between the CASI and TAI (differences between areas = 0.117 ± 0.025 with 95% CI from 0.067 to 0.167; $P = 0.0001$) and between the DAS and TAI (differences between areas = 0.153 ± 0.030 with 95% CI from 0.094 to 0.212; $P = 0.0001$) were highly significant, thus reflecting the accuracy of the diagnostic assessment. No difference arose between the areas under the ROC curves of the CASI and the DAS (differences between areas = 0.036 ± 0.022 with 95% CI from $\times 0.007$ to 0.080; $P = 0.103$).

When evaluating the correlations between the single variables we observed that the r for VAS pain and VAS global assessment was in the order of 0.897 ($P < 0.0001$). This means that the two items describe the same thing from the patient perspective. The obvious conclusion is that the two variables very likely record a similar feature of the disease in the DAS and the CASI.

TABLE 2. Sensitivity and specificity of the DAS in discriminating active disease from partial or complete remission, calculated at various reference values

Criterion	Sensitivity (95% CI)	Specificity (95% CI)
≥0.8321	100.0 (100.0–100.0)	0.0 (0.0–0.0)
>2.8122	100.0 (100.0–100.0)	45.4 (35.2–55.8)
>2.8429	99.0 (94.8–99.8)	48.5 (38.2–58.8)
>2.8515	98.1 (93.3–99.7)	48.5 (38.2–58.8)
>2.8792	98.1 (93.3–99.7)	53.6 (43.2–63.8)
>2.8844	97.1 (91.9–99.4)	54.6 (44.2–64.8)
>3.0044	96.2 (90.5–98.9)	62.9 (52.5–72.5)
>3.0374	95.2 (89.2–98.4)	62.9 (52.5–72.5)
>3.3216[a]	94.3 (88.0–97.9)	83.5 (74.6–90.3)
>3.3964	89.5 (82.0–94.6)	85.6 (77.0–91.9)
>3.4049	88.6 (80.9–93.9)	86.6 (78.2–92.7)
>3.5152	81.0 (72.1–88.0)	86.6 (78.2–92.7)
>3.5649	79.0 (70.0–86.4)	88.7 (80.6–94.2)
>3.5963	77.1 (67.9–84.8)	89.7 (81.9–94.9)
>3.6566	75.2 (65.9–83.1)	90.7 (83.1–95.7)
>3.6987	74.3 (64.8–82.3)	91.8 (84.4–96.4)
>3.7794	69.5 (59.8–78.1)	92.8 (85.7–97.0)
>3.9167	66.7 (56.8–75.6)	95.9 (89.8–98.8)
>3.9596	61.9 (51.9–71.2)	96.9 (91.2–99.3)
>4.0778	55.2 (45.2–65.0)	97.9 (92.7–99.7)
>4.416	41.0 (31.5–51.0)	99.0 (94.4–99.8)
>5.1947	17.1 (10.5–25.7)	100.0 (100.0–100.0)
>6.8803	0.0 (0.0–0.0)	100.0 (100.0–100.0)

Area under the ROC curve = 0.933; S.E. = 0.018; 95% CI = 0.889–0.963.
[a]Optimal cut-off point.

TABLE 3. Sensitivity and specificity of TAI in discriminating active disease from partial or complete remission, calculated at various reference values

Criterion	Sensitivity (95% CI)	Specificity (95% CI)
≥0	100.0 (100.0–100.0)	0.0 (0.0–0.0)
>60	100.0 (100.0–100.0)	19.6 (12.2–28.9)
>64	99.0 (94.8–99.8)	25.8 (17.4–35.7)
>78	97.1 (91.9–99.4)	26.8 (18.3–36.8)
>94	94.3 (88.0–97.9)	29.9 (21.0–40.0)
>113	92.4 (85.5–96.6)	48.5 (38.2–58.8)
>132	88.6 (80.9–93.9)	53.6 (43.2–63.8)
>148	86.7 (78.6–92.5)	55.7 (45.2–65.8)
>157	85.7 (77.5–91.8)	56.7 (46.3–66.7)
>160[a]	84.8 (76.4–91.0)	59.8 (49.3–69.6)
>185	77.1 (67.9–84.8)	60.8 (50.4–70.6)
>187	75.2 (65.9–83.1)	61.9 (51.4–71.5)
>195	71.4 (61.8–79.8)	64.9 (54.6–74.4)
>209	64.8 (54.8–73.8)	72.2 (62.1–80.8)
>218	61.0 (50.9–70.3)	73.2 (63.2–81.7)
>228	57.1 (47.1–66.8)	75.3 (65.5–83.5)
>256	54.3 (44.3–64.0)	82.5 (73.4–89.4)
>269	48.6 (38.7–58.5)	83.5 (74.6–90.3)
>292	43.8 (34.1–53.8)	87.6 (79.4–93.4)
>297	41.9 (32.3–51.9)	88.7 (80.6–94.2)
>311	37.1 (27.9–47.1)	94.8 (88.4–98.3)
>320	32.4 (23.6–42.2)	95.9 (89.8–98.8)
>350	30.5 (21.9–40.2)	99.0 (94.4–99.8)
>441	10.5 (5.4–18.0)	100.0 (100.0–100.0)
>523	0.0 (0.0–0.0)	100.0 (100.0–100.0)

Area under the ROC curve = 0.780; S.E. = 0.032; 95% CI = 0.716–0.835.
[a]Optimal cut-off point.

Discussion

Among the problems that challenge the clinician in assessing disease activity are the lack of a clear 'gold standard' single variable and the time and costs required to assess more variables to enhance accuracy. Mallya and Mace [12] proposed the evaluation of six variables: morning stiffness, pain, grip strength, articular index, haemoglobin and ESR. A similar index used by Davis *et al.* [13] included proximal interphalangeal joint synovitis score, morning stiffness, RAI, ESR and C-reactive protein. Van der Heijde and colleagues [14, 15] developed the DAS based on a 30-month follow-up of 233 patients with recent-onset RA. The DAS includes two comprehensive joint counts, i.e. RAI and the total number of swollen joints, plus the ESR and general health assessment scored on a VAS [14, 15]. All of these indices, although complex, employ measures that reflect disease activity and can be useful in randomized controlled trials as well as in clinical practice. To overcome the possible bias of measuring only the activity and not also the severity of the disease, we have suggested another index, the CASI, that includes a subjective parameter (patient's assessment of pain by VAS), a clinical measure which reflects the activity of the disease (RAI), a measure of the systemic inflammation (ESR), and a widely employed simple self-report measure of physical disability (HAQ) [16, 17]. Nomograms, based on the percentage of impact exerted on the common variance for each clinical variable, simplify the estimation of a patient's disease activity [16]. The CASI has proved to be very useful in monitoring the course of arthritis and the response to therapeutic regimens [18–21].

In the present study, an investigation was performed of the ability of the CASI to discriminate between high and low disease activity, compared with the DAS and TAI, which employ variables describing activity only. Our aim was to see whether by including a severity variable in the index, the sensitivity and the specificity in the assessment of activity could have been lost.

Our study shows that TAI, which is frequently employed in assessing arthritis activity in patients with RA, has a relatively poor discriminating capacity in measuring disease activity and that the combination of a limited number of variables, which have little value for monitoring changes in clinical status by themselves, into a composite index greatly enhances the discriminating power between high and low disease activity [12–15]. Therefore, we believe it is important to use more variables selected from those offering the highest degree of information. This point led us to propose the CASI as a better way of monitoring disease activity.

Any proposed index should have a high sensitivity to detect important clinical changes in disease activity (discriminating validity). This is a critical quality for any RA measure, for several reasons. Without sensitive measures of disease activity, important clinical changes may go undetected and a high number of patients would be needed to show any statistical difference [29]. These findings support recommendations currently being formulated by several consensus conferences on end-points for clinical trials in RA [33–36] and strongly reinforce the results of previous randomized controlled trials which suggest that the tender joint count, patient's report of pain, functional status, and ESR are the best measures for RA clinical assessment [37–39].

In patients treated with DMARDs, assessed longitudinally and with a comprehensive analysis of correlations, performed by relating the CASI with clinical and laboratory parameters, other functional and composite indices, we previously confirmed the discriminating validity and criterion validity (ability of a disease activity measure to predict an important aspect of the patient's clinical status) of the CASI [16, 17].

We are also confident that the presence of an HAQ score gives a picture of the severity of RA. In predicting prognosis, functional disability is the most powerful determinant of all outcomes in RA [40–45]. The presence of the HAQ which represents 39% of the whole score in the CASI may offer the opportunity of testing the activity even including a severity issue in it. As such it might be particularly useful in longitudinal disease assessments. Before accepting it, it should be proved that the combination of variables performs better than other commonly used indices. We have chosen TAI, because it has been widely adopted and might depict the activity better than the activity variables of the CASI (VAS pain, ESR, Ritchie's index). We should remember in fact that the contribution of each single variable is

low in the overall CASI score. Despite this, the combination of variables performs better than TAI alone, and this is of no surprise even though TAI is considered a powerful tool to detect synovial inflammation in clinical practice and in clinical trials.

Certainly an assessment of the function of the various joints is advisable, but until a reasonable way of measuring function is available, the clinical indices remain the best tools we have to measure the overall impact caused by the disease.

When comparing the CASI with the DAS we observed that the DAS performs slightly better in terms of specificity and sensitivity. This means that the DAS is the best tool we have to assess the activity of RA at this moment, but we also demonstrate that by including a severity variable such as the HAQ, it is possible to maintain a high degree of sensitivity as well as of specificity in the assessment of disease activity.

Because we examined a limited number of patients, our results may not be generalizable to all patients with RA. However, recognizing this limitation, the CASI may provide a comprehensive assessment of disease activity and severity in RA, even though we recognize that it is crucial to define its relationship with the progression of the erosions before claiming any possible prognostic value in the long run. Adoption of this composite index may help the clinical assessment and management of rheumatoid patients along with the DAS, which still remains the gold standard.

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