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Editorial

Is It Good to Simplify Clinimetry in Chronic Inflammatory Joint Diseases?

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The measurement of disease activity in chronic inflammatory joint diseases represents a challenge that rheumatologists have faced head-on over the past decades. Disease activity is a complex phenomenon that, necessarily, must consider multiple domains of health. For some diseases outside the world of rheumatology, this task is somewhat facilitated. The evaluation of type II diabetes mellitus hinges on well-defined laboratory variables (eg, glycemia and glycated hemoglobin), and that of hypertension on instrumental values that are easily measured in a repeatable manner.

For chronic inflammatory joint diseases (and beyond, such as connective tissue diseases or vasculitis, for example), the concept of disease activity integrates patient-reported measures, clinician-measured variables, and laboratory and instrumental tests. On the other hand, it must be this way, because these are conditions whose severity cannot be assessed by a single test also for methodological problems. To accomplish this task, rheumatologists invented composite indices of disease activity.

The underpinnings of composite indices of disease activity are the ability of the index to be sensitive to change, predict disease evolution over time, and include all necessary variables in a nonredundant manner.[1] The Disease Activity Score in 28 joints (DAS28), after more than 25 years since it was first validated, has been, and still is, one of the cornerstones of the assessment of patients with rheumatoid arthritis (RA).[2] However, despite the existence of calculators, its complex formula does not make it a calculable index at all times and in all places (although nowadays, it is assumed that every physician has a smartphone in their pocket). Thus, more readily calculable indices than the DAS28 were conceived. One such composite index is the Simplified Disease Activity Index (SDAI), whose formula is the algebraic sum of the number of swollen joints (28-joint count), number of tender joints (28-joint count), patient global assessment of disease activity (PtGA; 0-10 scale), physician global assessment of disease activity (0-10 scale), and C-reactive protein (CRP; expressed in mg/dL). SDAI demonstrated a high correlation with the DAS28, with $r > 0.8$ in cohorts of patients with RA treated with different drugs.[3] This is an example of simplification that should be considered successful.

For the large and heterogeneous group of seronegative spondyloarthritis (SpA), the task of assessing disease activity within a composite index is even more complex. While axial involvement may be predominant, peripheral involvement in its various declinations (synovitis, enthesitis, dactylitis) must be considered. In the pharmacological choice and evaluation of outcomes, the rheumatologist also has to deal with numerous extraarticular manifestations—skin and nail involvement, above all—in patients with psoriatic arthritis. The rheumatologist's role is also to give appropriate weight to any disease activity variables inflated by coexisting fibromyalgia, which is present in about one-fifth of patients with SpA.[4]

The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) has been the reference tool for assessing disease activity in patients with axial SpA, specifically ankylosing spondylitis (AS), for years.[5] However, the BASDAI is a fully patient-reported instrument, and probably does not cover all expressions of the concept of disease activity in patients with AS; it has also been criticized for poor construct validity, low sensitivity to change, and redundancy of variables. Thus, under the aegis of the Assessment of SpondyloArthritis international Society, the Ankylosing Spondylitis Disease Activity Index (ASDAS) was created, starting with the variables deemed important by experts in the concept of AS disease activity.[6] The performance in terms of ASDAS validity is excellent; however, similar to the DAS28, the inconvenient need to use a calculator arises again.

To obviate this need, a Simplified ASDAS (SASDAS) was proposed, obtained simply from the linear sum of PtGA (visual

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analog scale 0-10 cm), back pain (scale 0-10 cm, question number 2 of the BASDAI), peripheral pain and swelling (scale 0-10 cm, question number 3 of the BASDAI), duration of morning stiffness (scale 0-10 cm, question number 6 of the BASDAI), and the value of erythrocyte sedimentation rate (ESR; expressed in mm/h divided by 10). The correlation between SASDAS and ASDAS was very high (r = 0.93). Cut-offs for disease activity are also proposed: 0 to 7.8 inactive disease; 7.9 to 13.8 moderate disease activity; 13.9 to 27.6 high disease activity; and > 27.6 very high disease activity[7] (Table). This work in which SASDAS was first presented was marred by low sample size and a solely cross-sectional evaluation.[7]

Subsequently, the validity of SASDAS was investigated by other research groups and longitudinally, always demonstrating high convergent validity compared with ASDAS-CRP (r = 0.805) and ASDAS-ESR (r = 0.835).[8] Therefore, a SASDAS-CRP version has also been proposed, replacing the ESR with CRP expressed in mg/dL and changing the cut-offs: 0 to 10.4 inactive disease; 10.5 to 19 moderate disease activity; 19.1 to 36 high disease activity; and > 36 very high disease activity.[9]

In this issue of *The Journal of Rheumatology*, Schneeberger and colleagues[10] performed a broader comparison between SASDAS and ASDAS (both in CRP version) based on the robustness of data from the EMBARK trial (ClinicalTrials.gov: NCT01258738). Regarding the linear correlation between continuous variables, this continued to be high between SASDAS and ASDAS at each timepoint and for each treatment group ($r \geq 0.82$). The matter changes slightly in the category analysis. In both baseline and follow-up assessments, SASDAS places patients in the same category as ASDAS in 70% of cases; in 17.8% of cases, it would tend to overestimate disease activity, placing more patients in high or very high disease activity than ASDAS, whereas in 12.2% of cases, it would tend to underestimate the disease activity category. Cohen κ ranges overall from 0.54 to 0.73, indicating a moderate-to-substantial agreement.[10]

This post hoc study was necessary because while established certainty related to linear correlation was confirmed, it turned out that considering categorical variables, SASDAS might have some tendency to overestimate disease activity status. If a clinician uses the SASDAS in monitoring patients with axial SpA, they must take this possibility into account, mainly to avoid overtreating their patients. However, SASDAS has been shown to be very reliable overall.

Clinimetry is probably an area poorly tolerated by clinicians, who in most cases prefer more "creative" activities such as performing an ultrasound examination or interpreting magnetic resonance imaging scans. To make it as friendly and effortless as possible, we welcome all "clinimetric simplifications." However, these simplifications, as we have seen, must go through a rigorous validation process to avoid generating tools that are unhelpful or potentially counterproductive.

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Table 1. Formulae and cut-off points for disease severity states for ASDAS and SASDAS.

	ASDAS		SASDAS	
	ASDAS-ESR	ASDAS-CRP	SASDAS-ESR	SASDAS-CRP
Formula	(0.08 × back pain) + (0.07 × duration morning stiffness) + (0.11 × patient global) + (0.09 × peripheral pain/swelling) + (0.29 × √ESR)	(0.12 × back pain) + (0.06 × duration morning stiffness) + (0.11 × patient global) + (0.07 × peripheral pain/swelling) + (0.58 × Ln(CRP+1))	(back pain) + (duration morning stiffness) + (patient global) + (peripheral pain/swelling) + (ESR/10)	(back pain) + (duration morning stiffness) + (patient global) + (peripheral pain/swelling) + (CRP)
Cut-off point	0-1.2: inactive disease 1.3-2.0: low[a] disease activity 2.1-3.5: high disease activity > 3.5: very high disease activity		0-7.8: inactive disease 7.9-13.8: moderate disease activity 13.9-27.6: high disease activity > 27.6: very high disease activity	0-10.4: inactive disease 10.5-19.0: moderate disease activity 19.1-36.0: high disease activity > 36.0: very high disease activity

[a] The ASAS group in 2018 changed the nomenclature of ASDAS disease activity states by replacing "moderate" with "low," without changing the cut-offs.[11] For SASDAS, this change has not yet been formalized. ASAS: Assessment of SpondyloArthritis international Society; ASDAS: Axial Spondyloarthritis Disease Activity Score; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; SASDAS: Simplified Axial Spondyloarthritis Disease Activity Score.

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