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ORIGINAL RESEARCH

Construct validity and responsiveness of feasible composite disease activity measures for use in daily clinical practice in patients with psoriatic arthritis

Fazira R. Kasiem ,[1] Marc R. Kok ,[2] Jolanda J. Luime ,[1] Ilja Tchetverikov,[3] Lindy-Anne Korswagen,[4] Natasja H.A.M. Denissen,[5] Yvonne P.M. Goekoop-Ruiterman,[6] Maikel van Oosterhout,[7] Faouzia Fodili,[8] Johanna M.W. Hazes,[1] William Tillett,[9] Marijn Vis,[1] on behalf of CICERO

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For numbered affiliations see end of article.

Correspondence to
Fazira R. Kasiem;
f.kasiem@erasmusmc.nl

ABSTRACT

Objective There is a need for a widely accepted comprehensive disease activity measure for use in daily practice in patients with psoriatic arthritis (PsA). For this reason, the 3-item Visual Analogue Scale (3VAS) and 4-item Visual Analogue Scale (4VAS) were developed. This study aimed to test construct validity and responsiveness of the 3VAS and 4VAS in a population of patients with newly diagnosed PsA receiving usual care.

Methods Components of the 3VAS (physician global, patient global, patient skin) and 4VAS (physician global, patient pain, patient joint, patient skin) were scored on 0–10 VAS scales. Agreement of low disease activity (LDA) state between 3VAS/4VAS and other composite measures was tested using Venn diagrams. Construct validity and responsiveness (3-month interval) were assessed using Spearman correlation coefficients and standardised response means (SRM) with effect sizes (ES), respectively, following hypothesis generation. Both 3VAS/4VAS were also compared with several patient-reported outcome measures.

Results Data from 629 patients were used. Both 3VAS (ES=0.48, SRM 0.52) and 4VAS (ES=0.48, SRM=0.50) showed responsiveness similar to Disease Activity in PSoriatic Arthritis (DAPSA) and Disease Activity Score-28 (DAS28). Both measures had a strong correlation with DAPSA (r=0.80–0.87), Psoriatic Arthritis Disease Activity Score (PASDAS) (r=0.89) and Routine Assessment of Patient Index Data 3 (RAPID3) (r=0.84–0.92). 3VAS and 4VAS had the highest agreement with PASDAS in categorising patients to LDA at 12 months.

Conclusion This is the first study assessing the performance of the 3VAS and 4VAS in an observational cohort of patients with early PsA. Both measures have promising performance characteristics, showing strong correlations and good discrimination with existing composite measures. The 4VAS may be the preferred version with better face validity.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Current implementation of disease activity measures for use in patients with psoriatic arthritis (PsA) in clinical practice is slow due to lack of consensus and time constraints. For this reason, the 3-item Visual Analogue Scale (3VAS) and 4-item Visual Analogue Scale (4VAS) have been developed, which have so far shown good performance in post hoc analyses of randomised controlled trials, but have not yet been tested in observational data of patients with early PsA.

WHAT THIS STUDY ADDS

⇒ The 3-item VAS and 4-item VAS have shown to be promising composite measures for use in daily clinical rheumatology practice, showing strong correlations and good discrimination with existing composite measures.

⇒ Both the 3-item VAS and 4-item VAS showed similar responsiveness to Disease Activity Score-28 (DAS28) and Disease Activity in PSoriatic Arthritis (DAPSA) and both measures had the highest agreement with Psoriatic Arthritis Disease Activity Score (PASDAS) in categorising patients to low disease activity at 12 months.

⇒ The construct validity and responsiveness characteristics of the 3VAS and 4VAS are similar; however, the 4VAS may be the preferred version with better face validity by separate measures for joint, skin and pain in addition to the physician VAS for greater clinical utility in practice.

INTRODUCTION

Psoriatic arthritis (PsA) is a heterogeneous, chronic, inflammatory disease which can lead to progressive joint destruction and deterioration of functional status, a negative impact on health-related quality of life (HRQoL)

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This is the first study to have assessed the performance of the 3-item and 4-item VAS in early PsA, showing promising performance characteristics and therefore supports further testing of the 3VAS and 4VAS as pragmatic tools for the assessment of PsA in clinical practice.

and ability to work.[1 2] In the last decade, the management of PsA has improved greatly due to increased awareness among dermatologists, new treatment options and evidence for the efficacy of treat-to-target strategies. However, the incorporation of treating-to-target in daily clinical practice has been slow. This is in large part due to a lack of agreement on how to measure disease activity in routine practice. Moreover, the feasibility of current measures remains a major barrier for the further implementation of disease activity measures in daily practice.[3]

For this reason, the 3-item Visual Analogue Scale (3VAS) and 4-item Visual Analogue Scale (4VAS) have been developed as PsA specific, multidimensional, continuous, composite measures of disease activity. These composite scores were derived by reduction of the GRAPPA Composite Score (GRACE) measure to a 3-item VAS and a 4-item VAS version. In its derivation cohort, both versions were able to detect treatment efficacy and performed well in magnitude of change and responsiveness compared with other disease activity measures.[4] The 3VAS and 4VAS have thus far been tested in post hoc analyses of a randomised controlled trial (RCT) in which guselkumab was compared with placebo. Both 3VAS and 4VAS showed a strong correlation with GRACE and Psoriatic Arthritis Disease Activity Score (PASDAS) scores. Additionally they were able to discriminate between both treatment arms.[5]

Further validation of the 3VAS and 4VAS could lead to implementation of this disease activity measure in daily clinical rheumatology practice, thereby improving the management of patients with PsA . However, the 3VAS and 4VAS have not yet been tested in patients with PsA seen in daily clinical practice outside the ASSESS development study.[6] Therefore, the aim of this study is to test the construct validity and responsiveness of the 3-item VAS and 4-item VAS in daily clinical practice in a population of patients with newly diagnosed PsA receiving usual care.

METHODS

Study design

This study followed the recommendations for analysing construct validity and responsiveness specified in the COSMIN (COnsensus-based Standards for the selection of health status Measurement INstruments)–OMERACT (Outcome Measures for Arthritis Clinical Trials) handbook.[7]

Patients and data collection

To test the performance of the 3VAS and 4VAS, data were used from the Dutch south west Early Psoriatic Arthritis (DEPAR) study consisting of patients with newly diagnosed PsA receiving usual care. Details of this study have been reported previously.[8] Patients were seen by trained research nurses at fixed time points and data were collected on demographics, disease activity and patient-reported outcomes (including HRQoL and work productivity). For the current study, we used data from baseline, 3 months and 12 months and included patients with complete data on all 3VAS and 4VAS components at baseline.

3-item and 4-item VAS

The 3VAS and 4VAS were developed by reducing the GRACE composite measure. The GRACE index consists of eight domains including tender and swollen joint counts, patient global assessment, skin and joint VAS scores, psoriasis (Psoriasis Area and Severity Index-(PASI)) and PsA quality of life.[4 9] This was reduced to the physician global VAS, patient global VAS and patient skin VAS for the 3VAS and a physician global VAS, patient pain VAS, patient joint VAS and patient skin VAS for the 4VAS.[6] All VAS scores range from 0 to 10. The physician global VAS is based on a full physical examination of all PsA features, including arthritis, dactylitis, enthesitis, psoriasis and axial inflammation. The sum score of all VAS components was divided by the relevant denominator to give a score range of 0–10 as a total score of the 3VAS and 4VAS. A higher score representing a higher disease activity.

Preliminary thresholds dividing both the 3VAS and 4VAS into different levels of disease activity have been published earlier and were also used for this study. The thresholds were defined in the ASSESS study (derivation cohort). The 3VAS is divided in very low disease activity (VLDA; ≤1.3), low disease activity (LDA; >1.3–≤2.4), moderate disease activity (MoDA; >2.4–<4.8) and high disease activity (HDA; ≥4.8). Similarly, the 4VAS is divided in VLDA (≤1.6), LDA (>1.6–≤2.8), MoDA (>2.8–<5.0) and HDA (≥5.0).[10]

Statistical analysis

For the construct validity, both the 3VAS and 4VAS, including the preliminary thresholds of meaning were tested against existing disease activity measures, including PASDAS, Disease Activity Score-28 (DAS28), Disease Activity in PSoriatic Arthritis (DAPSA), Routine Assessment of Patient Index Data 3 (RAPID3) and Minimal Disease Activity (MDA) using Spearman correlation coefficients. Spearman correlation coefficients were also used to test the correlation between the VAS composite measures and several patient-reported outcome measures (PROMs). The difference between mean scores of the 3VAS and 4VAS was tested against MDA groups using independent t-tests. A priori hypotheses were formulated based on earlier research from

Table 1 Baseline characteristics at diagnosis of patient sample (n=629)

Demographic characteristics	Total
Patients, n (%)	629 (100)
Age, mean (SD)	49 (14)
Male, n (%)	318 (51)
Duration of complaints, months, median (IQR)*	10.0 (3.6–32.6)
Clinical characteristics	
BMI, mean (SD)†	28.6 (11.3)
66/68 joint count (swollen/tender), median (IQR)‡	2/3 ((1–4)/(1–7))
Enthesitis at clinical examination†	
LEI>0, n (%)	232 (41)
LEI in case of enthesitis, median (IQR)	1.5 (1–2)
MASES>0, n (%)	205 (36)
MASES in case of enthesitis, median (IQR)	2 (0–3)
Dactylitis present, n (%)†	123 (22)
Psoriasis§	
PASI=0, n (%)	82 (17)
PASI score in case PASI>0, median (IQR)	2.6 (0.9–4.6)
PASI>10, n (%)	20 (4)
Patient-reported outcomes	
SF-36 PCS, mean (SD)¶	39.0 (8.4)
SF-36 MCS, median (IQR)¶	47.5 (10.5)
Standard HAQ incl. support, median (IQR)**	0.8 (0.4–1.1)
BRAF, median (IQR)††	21 (11–31)
Disease activity measures	
3-item VAS, mean (SD)	3.4 (1.8)
4-item VAS, mean (SD)	3.8 (1.8)
DAPSA, mean (SD)‡‡	18.2 (11.3)
PASDAS, mean (SD)§§	4.2 (1.2)
DAS28, mean (SD)‡‡	3.1 (1.1)
MDA yes, (n,%)¶¶	58 (10)
RAPID3, mean (SD)**	12.2 (6.0)

*65 missings.
†60 missings.
‡61 missings.
§136 missings.
¶70 missings.
**2 missings.
††72 missings.
‡‡150 missings.
§§155 missings.
¶¶63 missings.
BMI, Body Mass Index; BRAF, Bristol Rheumatoid Arthritis Fatigue; DAPSA, Disease Activity in PSoriatic Arthritis; DAS28, Disease Activity Score-28; HAQ, Health Assessment Questionnaire; LEI, Leeds Enthesitis Index;; MASES, Maastrich Ankylosing Spondylitis Enthesitis Score; MCS, Mental Component Summary; MDA, minimal disease activity; PASDAS, Psoriatic Arthritis Disease Activity Score; PASI, Psoriasis Area Severity Index; PCS, Physical Component Summary; RAPID3, Routine Assessment of Patient Index Data 3; SF-36, Short Form-36; VAS, Visual Analogue Scale.

Table 2 Agreement between various stages of disease activity according to different composite disease activity measures at baseline and 12 months (n (%))

Composite measure	Baseline (n=629)						12 months (n=466)						
	REM	VLDA	LDA	MoDA	HDA	Yes	No	REM	VLDA	LDA	MoDA	HDA	Yes	No
3-item VAS		75 (12)	115 (18)	292 (47)	147 (23)				204 (44)	105 (22)	122 (26)	35 (8)		
4-item VAS		77 (12)	125 (20)	252 (40)	175 (28)				211 (45)	95 (20)	114 (25)	46 (10)		
MDA						83 (13)	546 (87)						217 (47)	249 (53)
DAPSA	31 (5)		203 (32)	301 (48)	94 (15)			151 (32)		186 (40)	118 (26)	11 (2)		
PASDAS	16 (3)		109 (17)	404 (64)	100 (16)			117 (25)		174 (37)	168 (36)	7 (2)		
DAS28	192 (31)		140 (22)	278 (44)	19 (3)			318 (68)		75 (16)	70 (15)	3 (1)		
RAPID3	38 (6)		82 (13)	189 (30)	320 (51)			135 (29)		84 (18)	126 (27)	121 (26)		

DAPSA, Disease Activity in PSoriatic Arthritis; DAS28, Disease Activity Score-28; HDA, high disease activity; LDA, low disease activity; MDA, minimal disease activity; MoDA, moderate disease activity; PASDAS, Psoriatic Arthritis Disease Activity Score; RAPID3, Routine Assessment of Patient Index Data 3; REM, remission; VAS, Visual Analogue Scale; VLDA, very low disease activity.

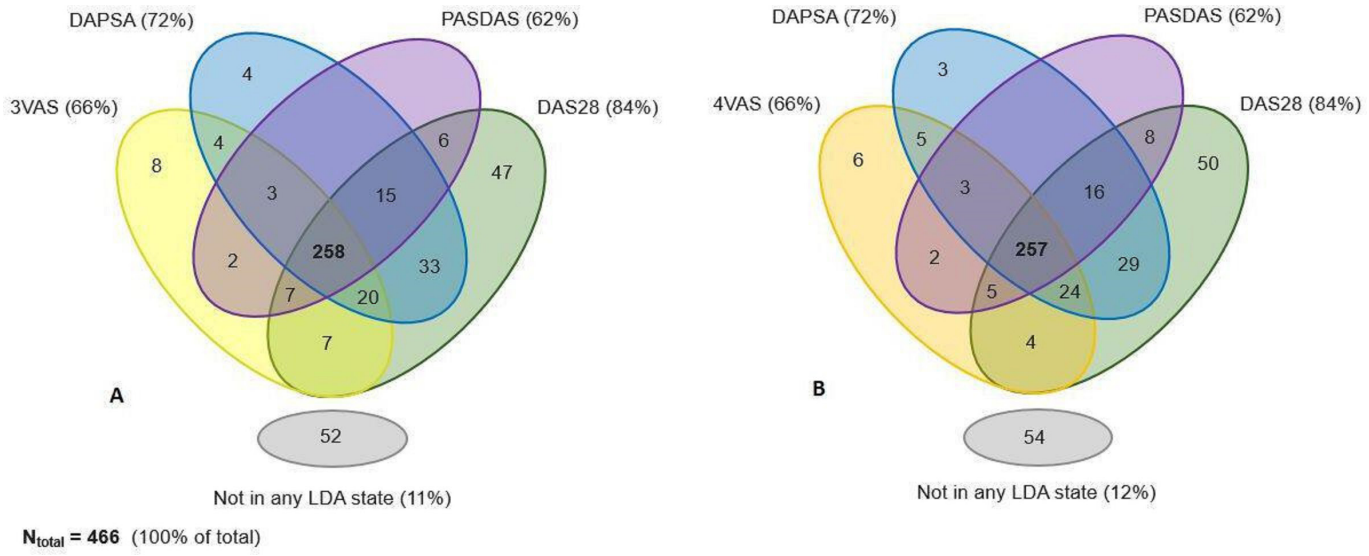

Figure 1 Agreement between LDA (including VLDA) according to various composite disease activity measures and 3-item VAS (A) and 4-item VAS (B) at 12 months (n=466).DAPSA, Disease Activity in PSoriatic Arthritis; DAS28, Disease Activity Score-28; LDA, low disease activity; PASDAS, Psoriatic Arthritis Disease Activity Score; VAS, Visual Analogue Scale; VLDA, very low disease activity.

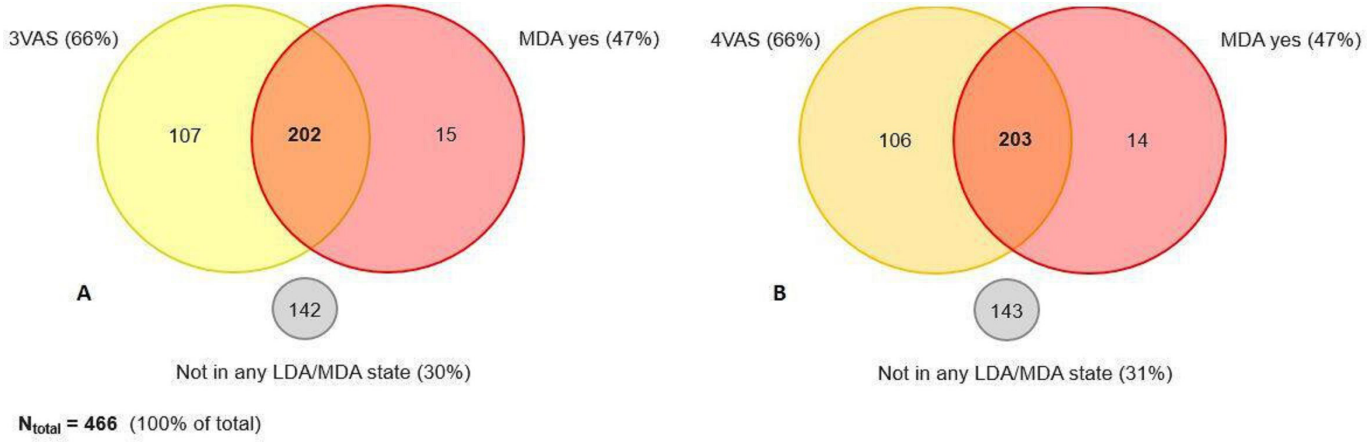

Figure 2 Agreement between LDA (including VLDA) according to 3-item VAS (A) and 4-item VAS (B) and MDA at 12 months (n=466). LDA, low disease activity; MDA, minimal disease activity; VAS, Visual Analogue Scale; VLDA, very low disease activity.

the DEPAR and ASSESS studies. The DEPAR study comparing several disease activity measures showed a similar performance of the PASDAS and GRACE composite measures. We formulated the following hypotheses: (1) A positive correlation was expected between both 3VAS and 4VAS with all aforementioned composite disease activity measures; (2) The strongest correlation of the 3VAS and 4VAS was expected with PASDAS; (3) The weakest correlation was expected with DAPSA due to the inclusion of mainly articular scores in DAPSA[4 11]; (4) 4VAS was expected to show a stronger correlation with measures of articular disease, such as DAPSA and DAS28 because it has a joint specific measure; (5) 4VAS was expected to show a stronger correlation with PROMs because it includes a relatively greater proportion of PROMs versus physician

Table 3 Spearman correlation coefficients of 3-item VAS and 4-item VAS with existing disease activity measures at 12 months (n=466)

	DAPSA	PASDAS	DAS28	RAPID3	4-item VAS
3-item VAS	0.80	0.89	0.65	0.84	0.94
4-item VAS	0.87	0.89	0.66	0.92	1

DAPSA, Disease Activity in PSoriatic Arthritis; DAS28, Disease Activity Score-28; PASDAS, Psoriatic Arthritis Disease Activity Score; RAPID3, Routine Assessment of Patient Index Data 3; VAS, Visual Analogue Scale.

Table 4 Median (IQR) scores of 3-item VAS and 4-item VAS per group of MDA at baseline (n=629)

	MDA yes	MDA no	P value
3-item VAS	1.1 (0.7–1.8)	3.6 (2.6–4.9)	<0.001
4-item VAS	1.3 (0.8–1.8)	4.2 (2.9–5.3)	<0.001

MDA, minimal disease activity; VAS, Visual Analogue Scale.

assessment. A correlation coefficient ≥0.5 was considered strong and ≥0.8 very strong.[12 13]

Responsiveness and the ability of the 3VAS and 4VAS to discriminate between disease states were assessed using the standardised response mean (SRM) and effect size (ES) between baseline and 3 months. Earlier research from the DEPAR study analysed responsiveness (SRM (SD), ES (SD)) of several composite disease activity measures such as DAS28 (0.83 (1.00), 0.88 (1.05)), DAPSA (0.71 (1.00), 0.73 (1.04)), GRACE (0.83 (1.00), 0.75 (0.90)) and PASDAS (0.95 (1.00), 1.00 (1.05)) in a 12-month interval.[11] Responsiveness (SRM, ES) was also evaluated in the ASSESS study of PASDAS (0.84, 0.62), DAPSA (0.56, 0.44) and GRACE (0.67, 0.36). A priori hypotheses were again formulated based on these results: (1) PASDAS was expected to have the best responsiveness[4 11]; (2) Responsiveness of both 3VAS and 4VAS is expected to be similar to DAS28, based on the similarities between GRACE and DAS28.[11] An SRM≥0.80 was considered high.

To test the agreement between the 3-item and 4-item VAS and other composite scores, the proportion of patients who achieved various stages of disease activity was calculated and visualised using Venn diagrams.

The comparison instruments used were the validated measures DAPSA, PASDAS, DAS28 and MDA. RAPID3 was also included as comparison due to its feasibility in daily practice. Remission (REM) was categorised as RAPID3≤3, DAPSA≤4, PASDAS≤1.9, DAS28≤2.6. LDA was defined as RAPID3≤6, DAPSA≤14, PASDAS<3.2, DAS28≤3.2. MoDA was categorised as RAPID3≤12, DAPSA≤28, PASDAS<5.4, DAS28≤5.1. HDA was defined as RAPID3>12, DAPSA>28, PASDAS≥5.4, DAS28>5.1. MDA was reached when ≥5 of 7 criteria were met.[14–18] An agreement >80% was considered strong.

The correlation between the 3VAS and 4VAS with patient-reported outcomes, including the Short Form-36 (SF-36), Health Assessment Questionnaire (HAQ), 12-item Psoriatic Arthritis Impact of Disease (PSAID-12) and Bristol Rheumatoid Arthritis Fatigue (BRAF) was calculated. Work productivity was assessed using the EuroQol-5 Dimension (EQ-5D).

Missing values

We hypothesised missing data to be missing at random, therefore missing values were imputed through multiple imputations in R-4.1.2 (n_{set}=20, JOMO package). Total scores of MDA, DAPSA, PASDAS, DAS28, RAPID3, SF36 Mental Component Summary Score, SF36 Physical Component Summary Score, PSAID-12, standard HAQ including support, EQ-5D and BRAF were imputed based on complete data of sex, age and VAS scores (VAS global from healthcare professional, VAS global patient, VAS psoriasis patient, VAS pain patient, VAS joints patient). Missing data of aforementioned variables were imputed for baseline, 3 months and 12 months. All further analyses were performed in STATA V.17.0. After imputation several checks were performed to ensure imputation was correct.

RESULTS

Baseline characteristics

In total, 629/785 (80%) patients were included between July 2013 and March 2021. As seen in table 1, 51% (n=318) were male and the median (IQR) disease duration was 10.0 (3.6–32.6) months. Compared with patients with PsA seen in RCTs, disease activity was mild, with a median (IQR) swollen and tender joint count of 2 (1–4) and 3 (1–7), respectively. Thirty-six to forty-one per cent of patients had no enthesitis and 78% had no dactylitis. Median (IQR) PASI score in case of psoriasis was 2 (0–3). Patients reported a median (IQR) HAQ score incl. support of 0.8 (0.4–1.1).

Agreement between levels of disease activity

The agreement between various stages of disease activity according to the different composite disease activity measures at baseline and 12 months is seen in table 2. At baseline, the 3VAS classifies 12% (n=75) of patients to VLDA, 18% (n=115) to LDA, 47% (n=292) to MoDA and 23% (n=147) to HDA. The 4VAS classifies 12% (n=77) of patients to VLDA, 20% (n=125) to LDA, 40% (n=252) to MoDA and 28% (n=175) to HDA. So, according

Table 5 Spearman correlation coefficients of 3-item VAS and 4-item VAS with several patient-reported outcome measures at 12 months (n=466)

	SF-36 PCS	SF-36 MCS	PsAID-12	Standard HAQ, incl. support	EQ-5D	BRAF
3-item VAS	-0.66	-0.41	0.74	0.63	-0.68	0.57
4-item VAS	-0.74	-0.40	0.78	0.69	-0.72	0.60

BRAF, Bristol Rheumatoid Arthritis Fatigue; EQ-5D, EuroQol- 5 Dimension; HAQ, Health Assessment Questionnaire; MCS, Mental Component Summary; PCS, Physical Component Summary; PsAID-12, 12-item Psoriatic Arthritis Impact of Disease; SF-36, Short Form-36; VAS, Visual Analogue Scale.

Table 6 Responsiveness of 3-item VAS and 4-item VAS including each component and other disease activity measures between baseline and 3 months (n=508)

	Mean change	SD of change	Mean ES	SRM
3-item VAS	0.86	1.66	0.48	0.52
Physician global VAS	0.96	1.80	0.51	0.53
Patient global VAS	0.93	2.60	0.37	0.36
Patient skin VAS	0.67	2.60	0.25	0.26
4-item VAS	0.85	1.69	0.48	0.50
Physician global VAS	0.96	1.80	0.51	0.53
Patient pain VAS	0.86	2.56	0.34	0.34
Patient joint VAS	0.91	2.76	0.35	0.33
Patient skin VAS	0.67	2.60	0.25	0.26
DAPSA	5.09	9.35	0.48	0.54
PASDAS	0.76	1.10	0.65	0.69
DAS28	0.52	0.94	0.51	0.55
RAPID3	2.19	5.39	0.37	0.41

DAPSA, Disease Activity in PSoriatic Arthritis; DAS28, Disease Activity Score-28; ES, effect size; PASDAS, Psoriatic Arthritis Disease Activity Score; RAPID3, Routine Assessment of Patient Index Data 3; SRM, standardised response mean; VAS, Visual Analogue Scale.

to the 3VAS and 4VAS, 70% and 68% of patients have moderate to high disease activity, respectively. This group is the largest according to the RAPID3 (n=509, 81%) and smallest according to DAS28 (n=297, 47%).

At 12 months, 44% (n=204) of patients are in VLDA, 22% (n=105) in LDA, 26% (n=122) in MoDA and 8% (n=35) in HDA according to the 3VAS. The 4VAS classifies 45% (n=211) of patients to VLDA, 20% (n=95) to LDA, 25% (n=114) to MoDA and 10% (n=46) to HDA. The pooled group of VLDA and LDA accounts for 66% of patients according to the 3VAS and 65% according to the 4VAS. DAS28 assigns the largest proportion of patients to this group (n=393, 84%) and RAPID3 the smallest (n=219, 47%).

The amount of patients with LDA (including VLDA) at 12 months is visualised in figure 1 for the 3VAS and 4VAS with other disease activity measures. The majority of patients with LDA according to PASDAS is also in LDA according to the 3VAS (n=270/291, 93%) and 4VAS (n=267/291, 92%). DAPSA and DAS28 classify 52 patients and 101 patients more to this category than the 3VAS, respectively. Compared with the 4VAS, DAPSA assigns 47 patients more to this category and DAS28 103 patients. Figure 2 shows the amount of patients with LDA (including VLDA) at 12 months according to the 3VAS and 4VAS compared with the amount of patients in MDA. This shows that 47% of patients have reached MDA. When comparing LDA (including VLDA) of the 3VAS and 4VAS to MDA, it is evident that approximately 2/3 of patients in LDA according to both VAS composite measures are also in MDA.

Construct validity

3VAS correlated (Spearman) with 0.80 for DAPSA, 0.89 for PASDAS and 0.84 for RAPID3 (table 3). This indicates a strong correlation with DAPSA and very strong correlation with PASDAS and RAPID3. 4VAS shows a strong correlation with DAPSA (r=0.87), PASDAS (r=0.89) and RAPID3 (r=0.92). Both 3VAS and 4VAS show the weakest correlation with DAS28 (r=0.65 for 3VAS, r=0.66 for 4VAS).

Next, the difference between mean scores of the 3VAS and 4VAS was tested against MDA groups using independent t-tests (table 4). Median (IQR) scores of the 3VAS were 1.1 (0.7–1.8) in the group attaining MDA and 3.6

Table 7 Mean/median scores of several patient-reported outcome measures per 3VAS/4VAS category of disease activity at 12 months (n=466)

	SF-36 PCS (mean, SD)	SF-36 MCS (mean, SD)	PsAID-12 (median, IQR)	Standard HAQ, incl. support (median, IQR)	EQ-5D (median, IQR)	BRAF (median, IQR)
3-item VAS						
LDA (66%)*	47.0 (7.5)	51.8 (8.3)	1.1 (0.4–2.2)	0.3 (0–0.6)	0.9 (0.8–0.9)	12 (5–20)
MoDA (26%)	37.1 (8.0)	44.1 (11.7)	4.3 (2.8–5.8)	0.8 (0.5–1.3)	0.7 (0.6–0.8)	27 (17–37)
HDA (8%)	33.0 (7.5)	38.5 (11.6)	5.8 (4.9–7.2)	1.5 (1.0–1.9)	0.5 (0.3–0.7)	33 (24–45)
4-item VAS						
LDA (66%)*	47.4 (7.3)	51.6 (8.6)	1.0 (0.4–2.2)	0.3 (0–0.6)	0.9 (0.8–0.9)	12 (5–20)
MoDA (24%)	37.0 (7.1)	46.3 (11.5)	4.1 (2.8–5.4)	0.9 (0.5–1.3)	0.7 (0.7–0.8)	25 (16–33)
HDA (10%)	32.2 (7.0)	36.9 (10.1)	6.1 (5.3–7.1)	1.5 (1.0–1.8)	0.5 (0.2–0.6)	37 (30–48)

*Including VLDA (very low disease activity).
BRAF, Bristol Rheumatoid Arthritis Fatigue; EQ-5D, EuroQol- 5 Dimension; HAQ, Health Assessment Questionnaire; HDA, high disease activity; LDA, low disease activity; MCS, Mental Component Summary; MoDA, moderate disease activity; PCS, Physical Component Summary; PsAID-12, 12-item Psoriatic Arthritis Impact of Disease; SF-36, Short Form-36; VAS, Visual Analogue Scale.

(2.6–4.9) in the group not in MDA. For the 4VAS, these were 1.3 (0.8–1.8) in the MDA group and 4.2 (2.9–5.3) in the group not in MDA. A significant difference (p<0.001) was seen between both groups for both VAS composite measures. Regarding the correlation between the VAS composite measures and PROMs, a stronger correlation, both negatively and positively, was seen between all PROMs and the 4VAS compared 3VAS, except for the SF-36 MCS (table 5). This aligned with our set hypotheses (all further a priori hypothesised associations were found as predicted).

Responsiveness

The responsiveness of existing composite disease activity measures and the 3VAS and 4VAS, including its subcomponents, is shown in table 6. The mean (SD) change of the 3VAS between baseline and 3 months was 0.86 (1.66), mean ES was 0.48 and SRM was 0.50. The 4VAS showed a mean (SD) change of 0.85 (1.69), mean ES of 0.48 and SRM of 0.52. PASDAS has the highest mean ES and SRM of 0.65 and 0.69, respectively. RAPID3 shows the lowest scores (mean ES 0.37, SRM 0.41). The mean ES and SRM of both VAS composite measures are comparable to those of DAPSA and DAS28. Aforementioned a priori hypotheses were confirmed. All SRM values were <0.80.

Last, the correlation between different levels of disease activity according to the 3VAS and 4VAS and several PROMs was evaluated at 12 months. Results are shown in table 7. In both the 3VAS and 4VAS, a worsening of PROMs was seen when disease activity increased.

DISCUSSION

This study assessed the performance of the 3-item and 4-item VAS in an observational cohort of patients with early PsA. Both these measures have shown to be promising continuous composite measures for use in daily clinical rheumatology practice, showing strong correlations and good discrimination compared with existing composite measures. The 3-item VAS and 4-item VAS showed similar responsiveness to DAS28 and DAPSA and both measures had the highest agreement with PASDAS in categorising patients to LDA at 12 months.

Treat-to-target is a valuable and proven strategy in the treatment of PsA. However, there is no consensus on which disease activity measure to use in the treatment of PsA in daily clinical practice. Currently, MDA and PASDAS are the composite measures best reflecting patient disease activity.[11] However, arguably both measures are more time consuming to use, especially PASDAS. So far, only one centre worldwide was able to use the PASDAS in clinical practice.[19] MDA is a dichotomous measure (a disease state that is either achieved or not), which makes it useful as a treatment target, but not for tracking disease activity over time. Moreover, MDA may be considered to be too stringent. This highlights the need for a widely accepted comprehensive disease activity measure in PsA for use in daily practice. The 3VAS and 4VAS have been tested in an RCT in which guselkumab was compared with placebo in patients with active PsA who failed on TNFα inhibitors. Data from 285 patients showed strong correlations between both VAS measures and GRACE (r=0.83–0.92) and PASDAS (r=0.72–0.85) in the intervention arm at each visit and both measures were able to discriminate between the treatment and placebo arms of the trial.[5 20]

Our study showed similarly strong correlations of the 3VAS/4VAS with existing composite measures, especially PASDAS, and responsiveness most comparable to DAS28 and DAPSA. DAS28 is generally not regarded as having face validity in PsA as the 28 joint count is inadequate to capture articular disease. The data presented herein showing misclassification of LDA by the DAS28 instrument (compared with the 3-item and 4-item VAS/PASDAS and DAPSA) support this view. Interestingly, both 3VAS and 4VAS showed better performance than RAPID3, which is considered to be one of the best validated patient-reported composite measures in patients with rheumatoid arthritis.[21] Moreover, when comparing classification to LDA states of the 3VAS and 4VAS to being in MDA (figure 2), it is evident that MDA is more difficult to attain than LDA, according to both VAS composite measures.

The 3VAS and 4VAS have been tested in clinical trial datasets. Estimates for minimal important difference, minimal detectable change and thresholds of disease activity in a clinical trial population have been made in a pooled analysis in the DISCOVER and COSMOS studies.[22] Numeric Rating Versions (NRS) of the VAS scores have been tested in a multicentre observational study, showing good correlation with HAQ and joint counts and very strong correlation with impact of disease. They have also been tested in the Upadacitinib SELECT clinical trial data, showing strong correlation with clinical and PROMs and ability to discriminate between placebo and treatment arms.[23 24]

Both VAS scores have shown similar performance characteristics and both balance clinician and patient perspectives in a single continuous measure, so which should be preferred for clinical practice? Work is underway to address some unanswered questions, including feasibility in clinical practice, instructions for performing the physician VAS and understanding the effect of achieving VAS LDA states on the inhibition of radiographic damage. Pending these data, and assuming these future data do not identify significant differences in performance characteristics, we suggest the 4VAS *may* be the preferred version. The 4VAS has separate measures for joint, skin and pain, in addition to the physician VAS. In contrast, the 3VAS comprises patient and physician global and pain, so does not provide domain specific information for use in clinical practice and therefore may be considered to have less face validity. Such differences between 3VAS and 4VAS are marginal but may help when selecting which to take forward for further testing and clinical use.

Strengths of this study include the observational study design and large number of patients. Patients enrolled in

the DEPAR cohort have overall low disease activity and received usual care. This makes the DEPAR sample size representative of patients with PsA seen in daily clinical practice but can potentially limit generalisability to more active disease states. Additionally, VAS scores were not reported with the 3VAS and 4VAS composite measures in mind. We therefore believe that prospective research in real-world patients with PsA will be of added value. Different thresholds of meaning for the VAS composite measures have been estimated in the ASSESS study and RCT datasets, therefore recommended areas to focus on include further refinement of thresholds of meaning, testing feasibility of the 3VAS and 4VAS in daily practice and testing longitudinal construct validity. Additionally, it would be interesting to further decide on a preference for either the 3VAS or 4VAS in daily practice.

To conclude, both the 3-item VAS and 4-item VAS thus far have promising performance characteristics, showing strong correlations and good discrimination with existing composite measures. The data presented herein support further testing of the feasibility and performance characteristics of the 3-item VAS and 4-item VAS as pragmatic tools for the assessment of PsA in clinical practice.

Author affiliations
[1]Rheumatology, Erasmus Medical Center, Rotterdam, The Netherlands
[2]Rheumatology and Clinical immunology, Maasstad Hospital, Rotterdam, The Netherlands
[3]Rheumatology, Albert Schweitzer Ziekenhuis, Dordrecht, Zuid-Holland, The Netherlands
[4]Rheumatology, Sint Franciscus Gasthuis, Rotterdam, Zuid-Holland, The Netherlands
[5]Amphia Hospital Breda, Breda, The Netherlands
[6]Rheumatology, HAGA Hospital, The Hague, The Netherlands
[7]Rheumatology, Groene Hart Hospital, Gouda, Zuid-Holland, The Netherlands
[8]Rheumatology, Reumazorg Zuid West Nederland, Roosendaal, Netherlands
[9]Royal National Hospital for Rheumatic Diseases, Bath, UK

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ORCID iDs
Fazira R. Kasiem http://orcid.org/0000-0003-2534-9981
Marc R. Kok http://orcid.org/0000-0003-2394-6926
Jolanda J. Luime http://orcid.org/0000-0002-1071-7932

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