The Journal of Rheumatology 2021;48:1272–8
doi:10.3899/jrheum.200556
First Release May 15 2021

The Journal of Rheumatology

Comparison of Composite Measure Remission Targets in Psoriatic Arthritis

Flora Farkas[1], Natsumi Ikumi[2], Musaab Elmamoun[3], Agnes Szentpetery[4], and Oliver FitzGerald[5]

ABSTRACT. ***Objective.*** To identify (1) which composite measure is the most stringent target of remission; and (2) which disease component target proves the most difficult to achieve in the different states of minimal disease activity (MDA), Composite Psoriatic Disease Activity Index (CPDAI), Disease Activity Index for Psoriatic Arthritis (DAPSA), and clinical DAPSA (cDAPSA) in patients with psoriatic arthritis (PsA).

Methods. There were 258 patients with PsA recruited. Disease remission was evaluated comparing 4 different composite measures and using remission cutoffs as previously proposed (very low disease activity [VLDA], CPDAI ≤ 2, DAPSA ≤ 4, cDAPSA ≤ 4).

Results. Patients met VLDA criteria (MDA 7/7) in 9.0% of visits, DAPSA remission in 19.8%, cDAPSA remission in 23.4% and CPDAI remission in 30.2%. Of 258 patients, MDA criteria (≥ 5/7) were fulfilled in 46.5%. Of those in MDA, VLDA criteria were reached in 25.0%. Patients met the pain visual analog scale (VAS) target in 57.5% of visits when they were in MDA, 43.3% when in low disease activity (MDA 5–6/7), and 44.8% when in CPDAI remission. Multivariate regression analysis revealed that pain VAS was the least likely target to be achieved. Patients with inflammatory-type back pain had significantly higher pain scores; further, a significant relationship was seen between Bath Ankylosing Spondylitis Disease Activity Index and pain VAS.

Conclusion. Based on our analysis, VLDA proved the most stringent target of disease remission in PsA compared to CPDAI, DAPSA, and cDAPSA. The pain VAS target of ≤ 1.5 cm was the most difficult component to achieve. CPDAI ≤ 2 was found to be the least stringent remission target; however, measurements of axial involvement, which contributed to the elevated pain VAS score in patients not achieving VLDA, were included as a domain in CPDAI only.

Key Indexing Terms: back pain, composite measures, disease remission, disease component target, pain visual analog score, psoriatic arthritis

Psoriatic arthritis (PsA) is a multifaceted disease with variable inflammation of peripheral joints, spine, entheseal sites, and whole digits (dactylitis), together with skin and nail psoriasis.[1] The heterogeneity of PsA, the recognition of severe phenotypes, and the availability of effective but costly biologic therapies contribute to the need to accurately assess patients' overall disease activity and their responses to treatment.[2] It is recognized that patient's perspective and physician-centric evaluation are complementary, and that when combined they help to ensure a more reliable reflection of disease burden.[3] In the past 10 years, a number of composite measurement tools have been developed to evaluate disease activity in PsA.[4,5] Psoriatic Arthritis Disease Activity Score (PASDAS)[6] was recommended as the composite measure to be used in clinical trials in 2017 by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and Outcome Measures in Rheumatology,[5] and again at the GRAPPA annual meeting in 2020. In view of the complexity of this measure, it is not proposed for routine care.[5,7] There is still no agreement on which composite measure should be recommended for routine clinical practice[4,5,7] Consensus has identified the following definitions of remission as appropriate targets of treatment: very low disease activity (VLDA), minimal

The original cohort was supported by an unrestricted grant from AbbVie. The MOPSA tool was developed with the assistance of an unrestricted grant from Janssen.

[1]F. Farkas, MD, St. Vincent's University Hospital, Dublin, Ireland, and Borsod-Abaúj-Zemplén County Center Hospital and University Teaching Hospital, Department of Rheumatology, Miskolc, Hungary; [2]N. Ikumi, MD, St. Vincent's University Hospital, Dublin, Ireland, and Nihon University School of Medicine, Division of Hematology and Rheumatology, Tokyo, Japan; [3]M. Elmamoun, MD, MBBS, MRCPI, St. Vincent's University Hospital, Dublin, Ireland, and Worcestershire Acute Hospitals NHS Trust, Worcester, UK; [4]A. Szentpetery, MD, PhD, St. Vincent's University Hospital, Dublin, Ireland, and Uppsala University Hospital, Uppsala, Sweden; [5]O. FitzGerald, MD, FRCP, FRCPI, St. Vincent's University Hospital, and Conway Institute for Biomolecular Research, University College Dublin School of Medicine, Dublin, Ireland.

FF and NI contributed equally to this study.

FF, NI, ME, and AS declare no conflicts of interest. OF declares no conflicts relevant to the content of this paper. He has received research grants and speakers/consultancy fees from AbbVie, Novartis, BMS, Lilly, Celgene, UCB, Pfizer, and Janssen.

Address correspondence to Prof. O. FitzGerald, Conway Institute for Biomolecular Research, University College Dublin, Belfield, Dublin 4, Ireland. Email: oliver.fitzgerald@ucd.ie.

Accepted for publication March 8, 2021.

disease activity (MDA) 7/7, Disease Activity Index for Psoriatic Arthritis (DAPSA) ≤ 4, or clinical DAPSA (cDAPSA) ≤ 4.[8,9] As yet, there is no validated definition of remission using the Composite Psoriatic Disease Activity Index (CPDAI); however, a cutoff score of ≤ 2 for CPDAI was proposed as being equivalent to VLDA.[8] Previous studies have shown that VLDA is a more stringent measure of disease remission than either DAPSA or cDAPSA,[7,10,11,12,13] with pain and patient global disease activity–visual analog scale (PtGA-VAS) scores being the least likely to be met in achieving MDA status.[14] CPDAI was not included in these studies.

The aims of this study were to identify (1) which composite measure is the most stringent target of remission, and (2) which disease component target proves the most difficult to achieve in the different states of MDA, CPDAI, DAPSA, and cDAPSA in patients with PsA.

METHODS

Patients. Consecutive patients with PsA attending our routine weekly spondyloarthritis (SpA) clinic in Ireland were recruited between December 2014 and September 2016. In this cross-sectional study, we have selected those patients who were ≥ 18 years of age and fulfilled the ClASsification criteria for Psoriatic ARthritis criteria.[15] Patients underwent musculoskeletal, 68-joint tender joint count (TJC), 66-joint swollen joint count (SJC),[16] and Leeds Enthesitis Index (LEI) assessments,[17] as well as a dactylitis digit count and skin assessments (Psoriasis Area Severity Index [PASI], body surface area [BSA]).[18,19] Laboratory measures included C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) by the Westergren method. Several patient-reported outcome measures (PROMs) were obtained including Health Assessment Questionnaire–Disability Index (HAQ-DI),[20] Dermatology Life Quality Index (DLQI),[21] PtGA,[22] and pain VAS. Spinal involvement was assessed using the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire[23] and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI).[24,25] Inflammatory-type back pain was defined as back pain that is worse after rest or in the morning and improves with exercise. All data were recorded directly into our freely available, Web-based Measuring Outcome in PsA (MOPSA) tool (https://mopsa.ie). MOPSA automatically calculates composite scores, including CPDAI and MDA status.[26] Written informed consent was not obtained from the patients since this was a noninterventional study and we were using the MOPSA tool to capture standard PsA clinical measurements as part of our weekly clinic. The study was granted Retrospective Chair Persons approval by the Ethics and Medical Research Committee of St. Vincent's University Hospital.

Disease remission. Disease remission was evaluated by 4 different composite measures, including DAPSA, cDAPSA, CPDAI, and MDA (Supplementary Table 1, available with the online version of this manuscript). DAPSA is calculated as the sum of TJC, SJC, PtGA-VAS (cm), pain VAS (cm) and CRP (mg/dL).[27] cDAPSA, without CRP levels, has also been calculated.[27] A cutoff score for both DAPSA and cDAPSA of ≤ 4 was considered as remission, as previously published.[9] CPDAI is based on the GRAPPA grid and is calculated as the sum of the following 5 PsA domains (each domain is scored 0–3 giving a total of 0–15): peripheral arthritis (TJC68, SJC66, HAQ-DI), skin disease (PASI, DLQI), enthesitis (LEI, HAQ-DI), dactylitis (dactylitis digit count, HAQ-DI), and axial disease (BASDAI, ASQoL).[2] The previously proposed cutoff of CPDAI ≤ 2 was used as the definition of remission.[8]

The disease state MDA was also assessed in our study. Patients were classified as being in MDA if they fulfilled ≥ 5/7 of the following criteria: TJC ≤ 1/68; SJC ≤ 1/66; PASI ≤ 1 or BSA ≤ 3; LEI ≤ 1; PtGA-VAS ≤ 2 (cm); pain VAS ≤ 1.5 (cm); and HAQ-DI ≤ 0.5.[28] Low disease activity (LDA) is one of the subsets of MDA, in which patients meet 5/7 or 6/7 criteria (MDA 5–6/7). VLDA, equivalent to remission status, was considered present if patients met all the MDA criteria (MDA 7/7; Supplementary Table 1, available with the online version of this article).[8]

Statistical analysis. Multiple comparisons between the 4 composite measures were calculated using the Tukey-Kramer method. Pearson correlation coefficient (r) was applied to determine the associations between the composite measures, including CPDAI, DAPSA, and cDAPSA. Comparisons between groups were performed using t tests for normally distributed continuous data, Wilcoxon rank-sum test for nonnormally distributed data, and chi-square tests for categorical data (Fisher exact test for the sample size of each category ≤ 10). Logistic regression was used to determine the strength of the associations of different components of MDA with achieving VLDA, and linear regression methods were applied to identify the relationship between the pain VAS target and the individual items of the 4 composite measures. P values < 0.05 were considered to be significant. All analyses were performed using the JMP 12 software (SAS Institute).

RESULTS

Comparison of disease remission measures. CPDAI scores and data on MDA status were available in all patients (258 patients; mean age 50.7 ± SD 12.5 yrs; 50.4% male; Table 1). We also measured cDAPSA, as well as DAPSA when CRP results were available. In total, data on disease remission using the 4 composite measures and previously proposed cutoffs (CPDAI ≤ 2, DAPSA ≤ 4, cDAPSA ≤ 4 and VLDA [MDA 7/7]) were available in 222 patients. The mean ± SD age of this group was 50.8 ± 12.3 years, and 52.3% were male (Table 2). Only 20 (9.0%) patients fulfilled VLDA criteria, whereas 44 patients (19.8%) were in DAPSA remission, 52 (23.4%) in cDAPSA remission, and 67 (30.2%) in CPDAI remission (Table 2). All patients in VLDA (n = 20) were also in cDAPSA remission, with 19 (95.0%) in DAPSA remission and 16 (80.0%) in CPDAI remission. In contrast, only 43.2% of the patients in DAPSA remission, 38.5% in cDAPSA remission (data not shown), and 23.9% of the patients in CPDAI remission also met VLDA criteria (Supplementary Table 2, available with the online version of this article). Percentages of patients achieving DAPSA, cDAPSA, and VLDA remission targets were significantly higher in those with CPDAI ≤ 2 (Supplementary Table 2).

Comparing the individual items of the composite measures, mean PtGA and pain VAS scores—both of which are not included in CPDAI—were significantly higher among patients in CPDAI remission compared to the patients in DAPSA, cDAPSA, or VLDA remission. The mean score for HAQ-DI was significantly lower among patients in VLDA compared to those in CPDAI, DAPSA, and cDAPSA remission. There were no other significant differences in the domain measures between the remission groups (Table 2).

As expected, there was a strong correlation between DAPSA remission and cDAPSA remission (r = 0.97, P < 0.01), but CPDAI remission did not correlate with DAPSA or cDAPSA remission (r = 0.15, P = 0.04 and r = 0.06, P < 0.01, respectively; data not shown).

MDA status. Data from the 258 patients with PsA were available for analysis to determine which disease component target of MDA proved the most difficult to achieve. MDA criteria (≥ 5/7) were fulfilled in 120 patients (46.5%). Of these, there were 90 patients (75.0%) in LDA (5–6/7), while 30 patients (25.0%) met VLDA criteria (Table 1).

Table 1. Comparison of the percentage of patients achieving the disease component targets in the different states of MDA.

	All	Non-MDA	MDA ≥ 5/7	MDA 5/7	MDA 6/7	LDA 5–6/7	VLDA 7/7	*P* [a]
No. patients	258	138	120	48	42	90	30	
Sex, male, %	50.4	40.6	61.7	58.3	59.5	58.9	70.0	0.39
Age, yrs, mean ± SD	50.7 ± 12.5	50.4 ± 12.9	51.0 ± 12.1	51.1 ± 12.7	51.5 ± 12.4	51.3 ± 12.5	50.0 ± 11.1	0.62[b]
TJC ≤ 1/68	134 (51.9)	36 (26.1)	98 (81.7)	32 (66.7)	36 (85.7)	68 (75.6)	30 (100)	< 0.01
SJC ≤ 1/66	221 (85.7)	105 (76.1)	116 (96.7)	44 (91.7)	42 (100)	86 (95.6)	30 (100)	0.57
LEI ≤ 1	227 (88.0)	107 (77.5)	120 (100)	48 (100)	42 (100)	90 (100)	30 (100)	1.00
PASI ≤ 1 or BSA ≤ 3	179 (69.4)	84 (60.9)	95 (79.2)	33 (68.8)	32 (76.2)	65 (72.2)	30 (100)	< 0.01
Pain VAS ≤ 1.5 cm	74 (28.7)	5 (3.6)	69 (57.5)	13 (27.1)	26 (61.9)	39 (43.3)	30 (100)	< 0.01
PtGA-VAS ≤ 2 cm	116 (45.0)	15 (10.9)	101 (84.2)	30 (62.5)	41 (97.6)	71 (78.9)	30 (100)	< 0.01
HAQ-DI ≤ 0.5	134 (51.9)	31 (22.5)	103 (85.8)	40 (83.3)	33 (78.6)	73 (81.1)	30 (100)	< 0.01

Data are presented as n (% of patients) unless otherwise stated. [a] LDA vs VLDA. [b] By *t* test; chi-square test otherwise. BSA: body surface area; HAQ-DI: Health Assessment Questionnaire–Disability Index; LDA: low disease activity; LEI: Leeds Enthesitis Index; MDA: minimal disease activity; PASI: Psoriasis Area Severity Index; PtGA-VAS: patient global disease activity by VAS; SJC: swollen joint count; TJC: tender joint count; VAS: visual analog scale; VLDA: very low disease activity.

Table 2. Comparison of age, sex, and the individual items of the composite measures between the remission groups (CPDAI ≤ 2, DAPSA ≤ 4, cDAPSA ≤ 4 and VLDA [MDA 7/7]).

	All	CPDAI ≤ 2	DAPSA ≤ 4	cDAPSA ≤ 4	VLDA, MDA 7/7	*P*
No. patients, n (%)	222	67 (30.2%)	44 (19.8%)	52 (23.4%)	20 (9.0%)	
Age, yrs	50.8 ± 12.3	51.2 ± 11.6	52.7 ± 10.8	51.2 ± 11.6	53.0 ± 7.8	0.88
Sex, male, n (%)	116 (52.3)	23 (34.3)	18 (40.9)	18 (34.6)	6 (30.0)	0.83
TJC, 0–68	3.4 ± 4.6	0.5 ± 0.9	0.3 ± 0.6	0.3 ± 0.7	0.3 ± 0.4	0.47
SJC, 0–66	1.2 ± 3.3	0.1 ± 0.3	0.1 ± 0.4	0.1 ± 0.4	0.1 ± 0.2	0.94
LEI, 0–6	0.3 ± 0.6	0	0	0	0	–
PASI, 0–72	2.8 ± 3.5	1.6 ± 2.2	2.0 ± 2.8	2.1 ± 2.8	1.0 ± 1.5	0.34
BSA, 0–100	3.4 ± 5.7	1.6 ± 2.6	1.6 ± 2.4	1.7 ± 2.5	0.7 ± 0.9	0.39
Dactylitis digit count, 0–20	0.2 ± 0.7	0	0.1 ± 0.3	0.1 ± 0.3	0.1 ± 0.2	0.08
BASDAI, 0–10	3.3 ± 2.1	1.8 ± 1.3	1.5 ± 1.2	1.4 ± 1.2	1.3 ± 1.0	0.63
ASQoL, 0–18	4.9 ± 5.0	1.8 ± 3.3	1.8 ± 3.4	1.6 ± 3.2	1.3 ± 2.4	0.97
HAQ-DI, 0–3	0.7 ± 0.7	0.4 ± 0.6	0.4 ± 0.5	0.4 ± 0.6	0.1 ± 0.2	< 0.01[a]
DLQI, 0–30	3.0 ± 4.6	1.6 ± 2.7	1.4 ± 2.3	1.4 ± 2.2	0.9 ± 1.0	0.62
Pain VAS, 0–10	3.6 ± 2.7	2.2 ± 2.0	0.8 ± 1.0	0.8 ± 1.0	0.4 ± 0.5	< 0.01[b]
PtGA-VAS, 0–10	3.5 ± 2.6	2.0 ± 1.8	0.7 ± 0.7	0.8 ± 0.9	0.8 ± 0.8	< 0.01[b]
CRP, mg/dL	4.8 ± 7.8	3.9 ± 7.4	2.5 ± 3.4	3.9 ± 7.7	4.1 ± 7.2	0.68
Inflammatory back pain, n (%)	120 (54.1)	18 (26.9)	19 (43.2)	21 (40.4)	6 (30.0)	0.24

Results are presented as mean ± SD unless otherwise stated. Multiple comparisons among the 4 composite measures were calculated using Tukey-Kramer method. [a] VLDA vs DAPSA, cDAPSA, and CPDAI. [b] CPDAI vs DAPSA, cDAPSA, and VLDA. ASQoL: Ankylosing Spondylitis Quality of Life questionnaire; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BSA: body surface area; cDAPSA: clinical DAPSA; CPDAI: Composite Psoriatic Disease Activity Index; CRP: C-reactive protein; DAPSA: Disease Activity Index for Psoriatic Arthritis; DLQI: Dermatology Life Quality Index; HAQ-DI: Health Assessment Questionnaire–Disability Index; LEI: Leeds Enthesitis Index; MDA: minimal disease activity; PASI: Psoriasis Area Severity Index; PtGA-VAS: patient global disease activity by VAS; SJC: swollen joint count; TJC: tender joint count; VAS: visual analog scale; VLDA: very low disease activity (minimal disease activity 7/7).

Disease component targets of MDA. The percentage of patients achieving the targets of TJC ≤ 1/68, PASI ≤ 1 or BSA ≤ 3, pain VAS ≤ 1.5 cm, PtGA-VAS ≤ 2 cm, and HAQ-DI ≤ 0.5 was significantly lower in patients reaching LDA compared to those meeting VLDA criteria. The SJC and LEI targets, however, were not significantly different (Table 1).

Achievement of pain VAS target. Based on our results (Table 1), the pain VAS ≤ 1.5-cm target proved the most difficult to achieve, being met in 57.5% of patients with MDA ≥ 5/7 and in 43.3% of patients when they fulfilled LDA (MDA 5–6/7) criteria (27.1% with MDA 5/7; 61.9% with MDA 6/7). Logistic regression models also demonstrated that the pain VAS ≤ 1.5-cm target was the least likely component to be achieved (univariate analysis: OR 5.2, 95% CI 2.95–10.62, $P < 0.01$; multivariate analysis: log OR 12.0, $P < 0.01$; data not shown).

Achievement of MDA component targets in CPDAI, DAPSA, and cDAPSA composite measures. As shown in Table 3, the pain VAS target of ≤ 1.5 cm was also the most difficult to reach in

Table 3. Achievement of MDA component targets in CPDAI, DAPSA, and cDAPSA composite measures (n = 222).

	CPDAI			DAPSA			cDAPSA		
	CPDAI ≤ 2	CPDAI > 2	*P*	DAPSA ≤ 4	DAPSA > 4	*P*	cDAPSA ≤ 4	cDAPSA > 4	*P*
Patients, n	67	155	–	44	178	–	52	170	–
TJC ≤ 1/68	60 (89.6)	46 (29.7)	< 0.01[a]	43 (97.7)	63 (35.4)	< 0.01[a]	50 (96.2)	56 (32.9)	< 0.01[a]
SJC ≤ 1/66	67 (100)	122 (78.7)	< 0.01[a]	43 (97.7)	146 (82.0)	< 0.01[a]	51 (98.1)	138 (81.2)	< 0.01[a]
LEI ≤ 1	67 (100)	133 (85.8)	< 0.01[a]	44 (100)	156 (87.6)	< 0.01[a]	52 (100)	148 (87.1)	< 0.01[a]
PASI ≤ 1 or BSA ≤ 3	53 (79.1)	100 (64.5)	0.03[b]	34 (77.3)	119 (66.9)	0.21[a]	40 (76.9)	113 (66.5)	0.14[b]
Pain VAS ≤ 1.5 cm	30 (44.8)	31 (20.0)	< 0.01[b]	36 (81.8)	25 (14.0)	< 0.01[a]	41 (78.8)	20 (11.8)	< 0.01[b]
PtGA-VAS ≤ 2 cm	46 (68.7)	51 (32.9)	< 0.01[b]	44 (100)	53 (29.8)	< 0.01[a]	51 (98.1)	46 (27.1)	< 0.01[a]
HAQ-DI ≤ 0.5	50 (74.6)	62 (40.0)	< 0.01[b]	34 (77.3)	78 (43.8)	< 0.01[a]	40 (76.9)	72 (42.4)	< 0.01[b]

Results are presented as n (% of patients) unless otherwise stated. [a] By Fisher exact test. [b] By chi-square test. BSA: body surface area; cDAPSA: clinical DAPSA; CPDAI: Composite Psoriatic Disease Activity Index; DAPSA: Disease Activity Index for Psoriatic Arthritis; HAQ-DI: Health Assessment Questionnaire–Disability Index; LEI: Leeds Enthesitis Index; PASI: Psoriasis Area Severity Index; PtGA-VAS: patient global disease activity by VAS; SJC: swollen joint count; TJC: tender joint count; VAS: visual analog scale.

Table 4. Comparison of disease domain values of the 4 different composite measures between those patients who met or did not meet the pain VAS ≤ 1.5-cm target (n = 222).

	Pain VAS ≤ 1.5 cm n = 61	Pain VAS > 1.5 cm n = 161	*P*
Age, yrs	50.5 ± 10.6	50.9 ± 13.0	NS
Sex, male, n (%)	39 (63.9)	77 (47.8)	0.03[a]
TJC, 0–68	1.3 ± 2.1	4.1 ± 5.1	< 0.01[b]
SJC, 0–66	0.6 ± 2.2	1.4 ± 3.7	NS
Dactylitis digit count, 0–20	0.2 ± 0.7	0.3 ± 0.7	NS
LEI, 0–6	0.1 ± 0.5	0.3 ± 0.7	NS
PASI, 0–72	2.7 ± 3.1	2.9 ± 3.7	NS
BSA, 0–100	2.9 ± 3.8	3.6 ± 6.3	NS
CRP, mg/dL	0.4 ± 0.7	0.5 ± 0.8	NS
DLQI, 0–30	2.0 ± 2.7	3.3 ± 5.1	NS
PtGA-VAS, 0–10	1.7 ± 2.2	4.2 ± 2.4	< 0.01[b]
HAQ-DI, 0–3	0.4 ± 0.6	0.9 ± 0.7	< 0.01[b]
BASDAI, 0–10	1.5 ± 1.2	3.8 ± 1.9	< 0.01[b]
ASQoL, 0–18	1.5 ± 2.5	6.0 ± 5.1	< 0.01[b]
Inflammatory back pain, n (%)	23 (37.7)	97 (60.2)	< 0.01[a]
DAPSA ≤ 4, n (%)	36 (59.0)	8 (5.0)	< 0.01[c]
cDAPSA ≤ 4, n (%)	41 (67.2)	11 (6.8)	< 0.01[a]
CPDAI ≤ 2, n (%)	30 (49.2)	37 (23.0)	< 0.01[a]
VLDA, n (%)	20 (32.8)	0 (0)	< 0.01[c]

Data are presented as mean ± SD unless otherwise stated. [a] By chi-square test. [b] By Wilcoxon rank-sum test. [c] By Fisher exact test. ASQoL: Ankylosing Spondylitis Quality of Life questionnaire; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BSA: body surface area; cDAPSA: clinical DAPSA; CPDAI: Composite Psoriatic Disease Activity Index; CRP: C-reactive protein; DAPSA: Disease Activity Index for Psoriatic Arthritis; DLQI: Dermatology Life Quality Index; HAQ-DI: Health Assessment Questionnaire–Disability Index; LEI: Leeds Enthesitis Index; NS: not significant; PASI: Psoriasis Area Severity Index; PtGA-VAS: patient global disease activity by VAS; SJC: swollen joint count; TJC: tender joint count; VLDA: very low disease activity (minimal disease activity 7/7); VAS: visual analog scale.

the CPDAI composite measure, being met in only 44.8% of patients in the remission group and in 20.0% of patients with CPDAI > 2. In terms of DAPSA and cDAPSA composite measures, the skin domain (PASI or BSA) and HAQ-DI targets proved the most difficult to achieve in the remission groups. The pain VAS target was found to be the most difficult component to reach among patients not in remission, being met in only 14.0% of patients with DAPSA > 4 and in 11.8% of those with cDAPSA > 4. Interestingly, LEI ≤ 1 target was the least difficult component to meet in each composite measure.

Association between pain VAS and the presence of axial disease. The relationship between the pain VAS target and the individual components of MDA, in addition to data on DLQI, BASDAI, ASQoL, ESR, CRP, and age were evaluated in the 222 patients using linear regression methods. Analysis demonstrated that BASDAI (β 0.43, $P < 0.01$) had an association with pain VAS (data not shown).

Disease domain components of the 4 different composite measures (MDA, CPDAI, DAPSA, cDAPSA) and fulfillment of the remission targets were compared in patients (n = 222) based on the achievement of pain VAS target (pain VAS ≤ 1.5 cm [n = 61] vs pain VAS > 1.5 cm [n = 161]). The mean HAQ-DI, BASDAI, ASQoL, PtGA-VAS, and TJC scores were significantly higher among patients not fulfilling the pain VAS target; further, the percentage of patients with inflammatory-type back pain was also significantly higher in those with pain VAS >1.5 cm (Table 4). Our results therefore suggest that residual back symptoms, in addition to the effects of peripheral arthritis, may be contributing to persistent pain in our patients. As shown in Table 4, the percentage of patients achieving remission criteria for the 4 different composite measures was significantly lower among patients not reaching the pain VAS target.

We have compared domain scores between patients with and without inflammatory-type back pain to evaluate the effect of an ongoing axial disease. Unsurprisingly, BASDAI and ASQoL were significantly higher among patients with back pain; however, pain VAS and TJC scores were also significantly increased, supporting the association between spinal involvement and pain. The percentage of patients fulfilling VLDA, CPDAI and cDAPSA remission targets were significantly lower among patients with back pain (Table 5).

Table 5. Disease domain scores in patients with and without inflammatory-type back pain (n = 222).

	No Back Pain n = 102	Inflammatory-type Back Pain n = 120	*P*
Age, yrs	50.8 ± 12.7	50.8 ± 12.1	NS
Sex, male, n (%)	59 (57.8)	57 (47.5)	NS
TJC, 0–68	2.2 ± 3.5	4.4 ± 5.2	< 0.01[a]
SJC, 0–66	0.9 ± 2.7	1.4 ± 3.8	NS
Dactylitis digit count, 0–20	0.2 ± 0.7	0.3 ± 0.6	NS
LEI, 0–6	0.3 ± 0.6	0.3 ± 0.7	NS
PASI, 0–72	3.0 ± 3.9	2.7 ± 3.3	NS
BSA, 0–100	3.9 ± 6.9	2.9 ± 4.5	NS
CRP, mg/dL	5.0 ± 7.8	4.7 ± 7.8	NS
DLQI, 0–30	3.0 ± 4.7	2.9 ± 4.6	NS
Pain VAS, 0–10	3.1 ± 2.8	4.0 ± 2.6	< 0.01[a]
PtGA-VAS, 0–10	3.2 ± 2.6	2.9 ± 4.5	0.05[b]
HAQ-DI, 0–3	0.6 ± 0.8	0.8 ± 0.7	NS
BASDAI, 0–10	1.9 ± 1.5	3.5 ± 2.0	< 0.01[a]
ASQoL, 0–18	2.9 ± 4.8	5.3 ± 5.0	< 0.01[a]
DAPSA ≤ 4, n (%)	25 (24.5)	19 (15.8)	NS
cDAPSA ≤ 4, n (%)	31 (30.4)	21 (17.5)	0.02[c]
CPDAI ≤ 2, n (%)	49 (48.0)	18 (15.0)	< 0.01[c]
VLDA, n (%)	14 (13.7)	6 (5.0)	0.03[d]

Data are presented as mean ± SD unless otherwise stated. [a] By Wilcoxon rank-sum test. [b] By *t* test. [c] By chi-square test. [d] By Fisher exact test. ASQoL: Ankylosing Spondylitis Quality of Life questionnaire; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BSA: body surface area; cDAPSA: clinical DAPSA; CPDAI: Composite Psoriatic Disease Activity Index; CRP: C-reactive protein; DAPSA: Disease Activity Index for Psoriatic Arthritis; DLQI: Dermatology Life Quality Index; HAQ-DI: Health Assessment Questionnaire–Disability Index; LEI: Leeds Enthesitis Index; NS: not significant; PASI: Psoriasis Area Severity Index; PtGA-VAS: Patient global disease activity by VAS; SJC: swollen joint count; TJC: tender joint count; VLDA: very low disease activity (minimal disease activity 7/7); VAS: visual analog scale.

DISCUSSION

There is as of yet no agreement as to which composite disease activity measure should be recommended in routine clinical practice.[4] MDA 7/7 (VLDA) has been proposed as an ideal treatment target, with MDA ≥ 5/7 as a feasible alternative.[5] Consistent with data from previous studies, we have observed that VLDA is a more stringent measure of remission than DAPSA, cDAPSA, or CPDAI.[10,11] Only 9.0% of patients met VLDA criteria, whereas 19.8% of patients were in DAPSA remission, 23.4% in cDAPSA remission, and 30.2% in CPDAI remission. Our results are in keeping with the rates of remission using VLDA (9.0% vs 13.1%) and DAPSA (19.8% vs 23.1%) composite measures, reported by Hagège, *et al*.[7] This review and metaanalysis clearly demonstrated the heterogeneity in the prevalence of remission status depending on the composite measure and definition used.[7] Based on our analysis, CPDAI appears to be the least stringent target of disease remission, owing perhaps to the absence of pain and PtGA-VAS in the CPDAI components. Interestingly, common components such as TJC, SJC, LEI, and skin activity did not show significant difference between the remission groups. When patients met VLDA criteria (n = 20), 16 (80.0%) were also in CPDAI remission; in contrast, only 23.9% of the patients in CPDAI remission also fulfilled VLDA criteria. It is noteworthy that CPDAI is the only composite tool that includes measures of axial involvement, though it does not contain pain and PtGA-VAS, which may explain the modest overlap with VLDA. No correlation was detected between CPDAI and DAPSA or cDAPSA remission, suggesting that CPDAI reflects additional disease components other than peripheral arthritis.[29] Previous analysis of data from the BioTRAC registry showed that PASI, pain VAS, and PtGA-VAS scores were least likely to be met in patients achieving MDA.[14] Based on our results, the pain VAS target of ≤ 1.5 cm is the most difficult component to achieve among patients both in MDA ≥ 5/7 (57.5%) and in LDA 5–6/7 (43.3%). In contrast to our data, Queiro, *et al* reported that > 75.0% of patients in MDA achieved the pain VAS ≤ 15 criterion, whereas the PtGA-VAS score ≤ 20 was reached by only 43.0%.[30]

Interestingly, we found that the pain VAS target of ≤ 1.5 cm was also the most difficult to achieve in CPDAI remission. Lubrano, *et al* demonstrated that residual disease activity (RDA) could persist even when patients fulfilled MDA ≥ 5/7 and criteria for DAPSA remission (≤ 4).[13] In agreement with our results, they found that VLDA is the most stringent composite measure, and that residual skin criteria (PASI > 1 or BSA > 3%) when in DAPSA remission and a pain VAS target of > 15 when in MDA are the most frequent RDA components.[13]

Evaluating the relationship between pain VAS target and the disease domain components of the 4 different composite measures, we have revealed a significant association between BASDAI and pain VAS; further, we found that the presence of persistent back pain and features of spinal inflammation as reflected by BASDAI and ASQoL were significantly higher in

those who did not achieve the pain VAS target. This suggests that residual back symptoms, rather than other disease components (i.e., enthesitis, dactylitis, skin), may drive the elevated pain VAS score in patients not achieving VLDA. Queiro, *et al* presented significantly higher mean BASDAI scores among patients not fulfilling the MDA (≥ 5/7) criteria[30]; however, Lubrano, *et al* found no association between the pain VAS domain and the presence of axial involvement.[13] Based on our analysis, patients with inflammatory-type back pain had significantly higher pain VAS scores compared to those without back pain. The percentages of patients in VLDA, CPDAI, and cDAPSA remission were significantly lower among patients with back pain and with pain VAS > 1.5 cm. These results suggest that, as the axial domain is not included in MDA, symptoms related to spinal inflammation may persist and contribute to ongoing levels of pain.

There are a number of limitations to our study. First, spinal involvement was assessed only on clinical grounds and we did not confirm routinely the presence of axial disease with plain radiograph or magnetic resonance imaging. Second, we acknowledge that there are limitations to the axial measures included in this study, BASDAI and ASQoL. BASDAI includes a question on peripheral joint disease, which may be a dominant feature in patients with PsA. Our results show that BASDAI also reflects axial inflammation, which, in measures other than CPDAI, is otherwise ignored. Nevertheless, better measures of axial inflammation in PsA clearly need to be developed, and there is a study to address this question being planned by GRAPPA.[31] Third, we were unable to include the PASDAS, which would have been of interest. This was because of the cost of including the 36-item Short Form Health Survey, which is patent-protected, in our MOPSA tool. It is important to note that we do not yet know if there is a difference in long-term radiographic or functional outcomes or in long-term quality of life between those in VLDA vs those in MDA and between the remission groups. There is a concern that treatment escalation in an effort to achieve remission may expose the patient to additional risk of adverse effects without providing benefit.

There are a number of strengths to our study, including the large number of patients for whom appropriate data was recorded, with novel results regarding the CPDAI composite measure. One of the features of the MOPSA tool is that it does not permit the user to go forward if data have not been captured, meaning that there were no missing data points. A further strength is that this analysis was performed in a routine clinical setting and not in the setting of a randomized controlled trial, where patients were selected on the basis of active peripheral joint inflammation. This demonstrates that collecting more complete outcome data using a tool such as MOPSA is feasible in routine practice. It is noteworthy that patient burden (78% completed online PROMs in < 10 minutes vs 64% for the paper version) and physician time (7 minutes to complete SJC66, TJC68, LEI, dactylitic digit count, PASI, and BSA) are more than compensated by being able to utilize MOPSA to demonstrate to patients using a spydergram the extent of their current disease and how that might influence treatment decisions (data not published).

In conclusion, in a real-world clinical setting, VLDA proved to be the most stringent target of disease remission compared to DAPSA, cDAPSA, and CPDAI composite measures. The pain VAS target of ≤ 1.5 cm was the most difficult component to achieve in patients undergoing treatment for their PsA. CPDAI ≤ 2 was found to be the least stringent remission criteria; however, measurements of axial involvement, which contributed to the elevated pain VAS score in patients not achieving VLDA, were included as a domain in the CPDAI only.

ACKNOWLEDGMENT

The authors thank Ms. Phil Gallagher, RN, who provided significant help in coordinating this study.

ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

REFERENCES

1. Haroon M, FitzGerald O. Psoriatic arthritis: complexities, comorbidities and implications for the clinic. Expert Rev Clin Immunol 2016;12:405-16.
2. Mumtaz A, Gallagher P, Kirby B, Waxman R, Coates LC, Veale JD, et al. Development of a preliminary composite disease activity index in psoriatic arthritis. Ann Rheum Dis 2011;70:272-7.
3. Tillett W, Adebajo A, Brooke M, Campbell W, Coates LC, FitzGerald O, et al. Patient involvement in outcome measures for psoriatic arthritis. Curr Rheumatol Rep 2014;16:1-10.
4. Tucker LJ, Coates LC, Helliwell PS. Assessing disease activity in psoriatic arthritis: a literature review. Rheumatol Ther 2019; 6:23-32.
5. Coates LC, FitzGerald O, Merola JF, Smolen J, van Mens LJJ, Bertheussen H, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis/Outcome Measures in Rheumatology consensus-based recommendations and research agenda for use of composite measures and treatment targets in psoriatic arthritis. Arthritis Rheumatol 2018;70:345-55.
6. Perruccio AV, Got M, Li S, Ye Y, Gladman DD. Treating psoriatic arthritis to target: defining the psoriatic arthritis disease activity score that reflects a state of minimal disease activity. J Rheumatol 2020;47:362-8.
7. Hagège B, Tan E, Gayraud M, Fautrel B, Gossec L, Mitrovic S. Remission and low disease activity in psoriatic arthritis publications: a systematic literature review with meta-analysis. Rheumatology 2020;59:1818-25.
8. Coates LC, Helliwell PS. Defining low disease activity states in psoriatic arthritis using novel composite disease instruments. J Rheumatol 2016;43:371-5.
9. Schoels MM, Aletaha D, Alasti F, Smolen JS. Disease activity in psoriatic arthritis (PsA): defining remission and treatment success using the DAPSA score. Ann Rheum Dis 2016;75:811-8.
10. Gorlier C, Orbai AM, Puyraimond-Zemmour D, Coates LC, Kiltz U, Leung YY, et al. Comparing patient-perceived and physician-perceived remission and low disease activity in psoriatic arthritis: an analysis of 410 patients from 14 countries. Ann Rheum Dis 2019;78:201-8.
11. Coates LC, Gottlieb AB, Merola JF, Boone C, Szumski A, Chhabra A. Comparison of different remission and low disease definitions in psoriatic arthritis and evaluation of their prognostic value. J Rheumatol 2019;46:160-5.
12. Gladman DD, Helliwell P, Deodhar A, Gottlieb AB, Boehncke WH, Xu XL, et al. The effect of guselkumab on PASDAS, grace index, mCPDAI, and DAPSA: results from a phase 2 study in

patients with active psoriatic arthritis [abstract]. Ann Rheum Dis 2019;78 Suppl 2:911-2.
13. Lubrano E, Scriffignano S, Perrotta FM. Residual disease activity and associated factors in psoriatic arthritis. J Rheumatol 2020;47:1490-5.
14. Rahman P, Zummer M, Bessette L, Baer P, Haraoui B, Chow A, et al. Real-world validation of the minimal disease activity index in psoriatic arthritis: an analysis from a prospective, observational, biological treatment registry. BMJ Open 2017;7:e016619.
15. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H; CASPAR Study Group. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum 2006;54:2665-73.
16. Coates LC, FitzGerald O, Gladman DD, McHugh N, Mease P, Strand V, et al. Reduced joint counts misclassify patients with oligoarticular psoriatic arthritis and miss significant numbers of patients with active disease. Arthritis Rheum 2013;65:1504-9.
17. Healy PJ, Helliwell PS. Measuring clinical enthesitis in psoriatic arthritis: assessment of existing measures and development of an instrument specific to psoriatic arthritis. Arthritis Rheum 2008;59:686-91.
18. Fredriksson T, Pettersson U. Severe psoriasis—oral therapy with a new retinoid. Dermatologica 1978;157:238-44.
19. Puzenat E, Bronsard V, Prey S, Gourraud PA, Aractingi S, Bagot M, et al. What are the best outcome measures for assessing plaque psoriasis severity? A systematic review of the literature. J Eur Acad Dermatol Venereol 2010;24 Suppl 2:10-6.
20. Blackmore MG, Gladman DD, Husted J, Long JA, Farewell VT. Measuring health status in psoriatic arthritis: the Health Assessment Questionnaire and its modification. J Rheumatol 1995;22:886-93.
21. Nichol MB, Margolies JE, Lippa E, Rowe M, Quell J. The application of multiple quality-of-life instruments in individuals with mild-to-moderate psoriasis. Pharmacoeconomics 1996; 10:644-53.
22. Cauli A, Gladman DD, Mathieu A, Olivieri I, Porru G, Tak PP, et al; GRAPPA 3PPsA Study Group. Patient global assessment in psoriatic arthritis: a multicenter GRAPPA and OMERACT study. J Rheumatol 2011;38:898-903.
23. Doward LC, Spoorenberg A, Cook SA, Whalley D, Helliwell PS, Kay LJ, et al. Development of the ASQoL: a quality of life instrument specific to ankylosing spondylitis. Ann Rheum Dis 2003;62:20-6.
24. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 1994;21:2286-91.
25. Taylor WJ, Harrison AA. Could the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) be a valid measure of disease activity in patients with psoriatic arthritis? Arthritis Rheum 2004;51:311-5.
26. Elmamoun M, Szentpetery A, Gallagher P, Fitzgerald O. Measuring outcome in psoriatic arthritis (MOPSA), a new web-based tool for assessment of psoriatic arthritis showing initiation of treatment change in patients achieving minimal disease activity [abstract]. Ann Rheum Dis 2016;75 Suppl 2:607.
27. Schoels M, Aletaha D, Funovits J, Kavanaugh A, Baker D, Smolen JS. Application of the DAREA/DAPSA score for assessment of disease activity in psoriatic arthritis. Ann Rheum Dis 2010; 69:1441-7.
28. Coates LC, Fransen J, Helliwell PS. Defining minimal disease activity in psoriatic arthritis: a proposed objective target for treatment. Ann Rheum Dis 2010;69:48-53.
29. Acosta Felquer ML, Ferreyra Garrott L, Marin J, Catay E, Scolnik M, Scaglioni V, et al. Remission criteria and activity indices in psoriatic arthritis. Clin Rheumatol 2014;33:1323-30.
30. Queiro R. Remission and stringent treatment goals in psoriatic arthritis: doctors' opinion is not enough. Joint Bone Spine 2019;86:269-70.
31. Gladman DD, Helliwell PS, Poddubnyy D, Mease PJ. Updates on axial psoriatic arthritis from the 2020 GRAPPA annual meeting. J Rheumatol 2021 Mar 1 (E-pub ahead of print).