DAPSA, DAS28 and MDA predict long-term treatment regime in psoriatic arthritis. The Swedish Early Psoriatic Arthritis Cohort

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Abstract

Objective

To describe treatment patterns in the Swedish early psoriatic arthritis cohort (SwePsA) of the mono-/oligo-arthritic (M/O) and polyarthritis (P) and identify early predictive factors for treatment with disease-modifying anti-rheumatic (DMARD), non-steroidal anti-inflammatory drugs (NSAID), and tumour necrosis factor inhibition (TNFi) after 5 years.

Methods

Data for 198 M/O and P PsA were obtained within the programme for SwePsA. Multinomial and binary logistic regression analyses were used to assess the association between early predictive factors and treatment after 5 years adjusted for age at inclusion. The analysis of DMARD/NSAID was adjusted for medication at inclusion.

Results

After inclusion visit, DMARD was prescribed in 30% of M/O and 56% of P PsA; mainly methotrexate. TNFi was not prescribed at inclusion, but 23 patients were treated at 5-year follow-up. The adjusted OR (95% CI) for treatment with both DMARD and NSAID after 5 years was 3.65 (1.34 - 9.89) (p=0.010) for Disease Activity Score 28 (DAS28) >3.2 and 2.90 (1.20–6.99) (p=0.038) for Disease Activity Index in Psoriatic Arthritis (DAPSA) >14 at inclusion. TNFi treatment was, after adjusting for age, associated with high erythrocyte sedimentation rate (p=0.0043), high C-reactive protein (p=0.013), DAPSA (p<0.001), not reaching minimal disease activity (p=0.001) high health assessment questionnaire (p=0.001), patient´s overall assessment on the visual analogue scale (VAS) (p=0.009), high pain VAS (p=0.007), and high number of tender and swollen joints (p=0.031) at inclusion.

Conclusion

Disease activity in early M/O and P PsA is to be considered in deciding the level of health care assessment and future pharmacological treatment. DAS28 >3.2 and DAPSA>14 early in the disease predict subsequent treatment with DMARD. For prediction of biological treatment, not reaching MDA at onset of disease, would be the composite index of choice.

Key words

DMARD, NSAID, TNF-inhibition, minimal disease activity, remission

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Introduction

Psoriatic arthritis (PsA) is a multifaceted heterogeneous systemic inflammatory disease (1-3). Its diagnosis and prevalence in early disease is sometimes difficult to establish, partly because of joint diseased conditions of other origin, such as gout, osteoarthritis, rheumatoid arthritis (RA), ankylosing spondylitis (AS) or fibromyalgia, all coexisting with psoriasis (4-6) and partly due to the lack of psoriasis at onset of disease. Initial medical history and extensive clinical examination is essential for classification and prognosis (7). Another difficulty of diagnosing PsA is the diversity of PsA features that may resemble or coexist with AS and RA in some cases. The development of the classification criteria for established psoriatic arthritis (CASPAR) for patients with joint, back or enthesial symptoms has made it possible to study the different phenotypes of PsA regarding the outcome of disease, to give patients an optimal assessment of treatment and prognosis (8). The CASPAR criteria can be applied in early disease and for reevaluation of earlier diagnostics (9, 10). Information on different phenotypes of PsA in relation to management is sparse in the literature, with only a few studies on early PsA dealing with pharmacological treatment and management (11-14). The concept of minimal disease activity (MDA) (15) and "treat to target" has been addressed by the Group for research assessment of psoriasis and psoriatic arthritis (GRAPPA) (16).

Since 1999 a Swedish cohort of early PsA patients (SwePsA) has been established and monitored (17). The aim of the SwePsA cohort is to study early PsA in the setting of routine rheumatologic care, to improve diagnostic means, to predict outcome and seek optimal treatment and management for patients in the different PsA subgroups. So far, recommendations on pharmacological treatment of PsA have been presented by among others GRAPPA, the European League Against Rheumatism (EULAR) and the Swedish Association of Rheumatology (11, 18-21) but there are no explicit recommendations for early PsA. Nor are there any specific assessment recommendations for patients with low disease activity described as mono- or oligoarthritis. General treatment recommendations regarding mild disease (<5 joints affected and no loss of function) are included in the GRAPPA treatment recommendations of 2009 (11) but not specifically for early stage of disease. Overall, methotrexate (MTX) is the most commonly used therapy in PsA, together with NSAID (non-steroidal anti-inflammatory drug) despite lack of evidence (22) but was recently supported by GRAPPA treatment recommendations of 2015 (21) and with favoured effect in PsA with tight control, according to Coates *et al*. (23). Moreover, outcome with composite measures and definitions of remission, that reveal disease activity in all domains, have been evaluated and await consensus recommendations by GRAPPA (15, 24-26). Neither in clinical settings nor in clinical trials have any of the suggested comprehensive outcome measures been fully implemented so far.

The primary aim of this study was to describe disease activity and treatment patterns in clinical routine care of patients with early PsA of initial mono-/oligo-arthritic (M/O), and polyarthritic (P) phenotypes. Furthermore, we aimed to identify predictive factors in early M/O and P PsA, associated with systemic treatment with DMARD or TNFi (tumour necrosis factor inhibition).

Materials and methods

Patients

Patients with early PsA, defined by inflammatory joint symptoms and signs lasting <2 years (mean symptom duration 11 months, range 4–23), compatible with PsA with or without psoriasis, referred to rheumatology outpatient clinics in Sweden, have been assessed by the same rheumatologist (UL, TH, PL, AT, ET, GMA), at inclusion in the register and at the 5-year follow-up. The CASPAR criteria for classification of PsA (8), also suitable for diagnosis of early disease (9), were applied at inclusion or retrospectively as SwePsA was initiated prior to CASPAR. The patients were recruited from six rheumatology departments (University Hospital, Upp-

sala; Falu Hospital, Falun; Skåne University Hospital, Malmö; University Hospital, Umeå; Karolinska University Hospital, Stockholm and Spenshult Hospital for Rheumatic Diseases, Oskarström) (17) forming a cohort. This prospective cohort study was approved by the Regional Ethical review board in Uppsala with informative approval from Stockholm, Lund and Umeå Ethical boards. The SwePsA cohort consists of 363 patients where 5-year follow-up has been performed in all reachable patients (14). The current report comprised 198 patients, at inclusion classified as M/O (≤4 tender and/or swollen joints) or P PsA (>4 tender and/or swollen joints) that were included in the comparison and predictive study.

Disease activity and clinical response

Data for this study were obtained, according to the programme for SwePsA (17), at inclusion in the study and at 5-year follow-up. Patients were classified to be in remission if they had no tender or swollen joints and if the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels were within reference ranges. Minimal disease activity (MDA) was calculated according to Coates *et al*. (15). Currently prescribed medication at inclusion and prescription after the baseline visit as well as at the visit 5 years later were documented. ESR was analysed by the Westergren method, and CRP level was determined by standard nephelometry. Two percent of the patients were RF-positive. In order to further evaluate disease activity, Health Assessment Questionnaire (HAQ), Disease Activity Score 28 (DAS28), disease activity index in psoriatic arthritis (DAPSA) (27), pain on a visual analogue scale (VAS) and patient's overall assessment (PGA) VAS were measured.

Statistics

Descriptive statistics of demographic and clinical features comprised the 198 cases. All values were expressed as median (interquartile range), mean (± SD) or frequency and proportion (%) unless otherwise stated.

Eleven patients had a combination of axial and peripheral disease and were assigned according to their peripheral expression. Thus, patients with the initial phenotype, M/O or P PsA, were recorded and studied accordingly at the 5-year follow-up, irrespective of phenotype at outcome after 5 years. These analyses were based on 198 patients, and for the final analyses 192 patients for treatment with NSAID and DMARD (data on NSAID were missing for six patients at the 5-year follow-up).

In all regression analyses CRP with a given value of 0 mg/L was set to 0.5 mg/L. CRP and ESR was converted logarithmically (base 2). HAQ ≤0.5 was considered a minor restriction of function according to GRAPPA (11), DAS28 of 3.2 or higher as a marker for moderate to high disease activity (28), DAPSA value of 15 or more was considered moderate to high disease activity (29, 30) and pain and PGA VAS ≤40 was considered as low disease activity. Grouping of MDA was not possible due to the paucity of patients at each MDA level. To test differences among groups the Mann-Whitney U-test was used. Within-group differences were determined using the Wilcoxon signed rank test.

Multinomial or binary logistic regression analysis was used to identify predictors, measured at inclusion, associated with treatment at the 5-year follow-up. The candidate predictors were age, sex, number of swollen or tender joints, medication, CRP, ESR, DAS28, DAPSA, HAQ, pain and PGA VAS and MDA, all measured at inclusion. Due to limited numbers of "events", in relation to the number of candidate predictors, only multivariable models including at most three predictors were considered for NSAID/DMARD and at most two predictors were considered for TNFi. The multinomial model was used for the treatment outcome of NSAID/DMARD and crude odds ratios (OR) with 95% confidence intervals (CI) and OR adjusted for age and prior medication are reported. A binary logistic model was used for the treatment outcome of TNFi and crude OR with 95% CI and OR adjusted for age are reported.

All statistical tests were 2 tailed and performed at the 0.05 significance level. Analyses were performed using SAS v. 9.4 (SAS Institute, Inc).

Table I. Demographic and clinical data on early psoriatic arthritis patients, focusing on mono-/oligo and polyarthritis at inclusion, with a 5-year follow-up.

	Mono-/oligo-arthritis at inclusion (105)	5-year follow-up	Polyarthritis at inclusion (93)	5-year follow-up	p (M-/O *vs*. P PsA) at inclusion / at follow-up
Sex, n, f/m	51/54		59/34		
Age	45 ± 15		47 ± 14		
ESR, mm/h	15.9 ± 17.4	11.4 ± 13.4	22.5 ± 22.9	13.4 ± 11.8	(0.008/0.307)
CRP, mg/L	12.4 ± 16.7	7.2 ± 8.6	21.8 ± 33.1	7.6 ± 9.1	(0.113/0.991)
Swollen joints	1.7 ± 1.3	1.0 ± 1.8	7.5 ± 5.7	2.2 ± 3.7	(<0.001/0.460)
Tender joints	1.7 ± 1.3	1.7 ± 2.9	10.5 ± 9.7	6.2 ± 8.7	(<0.001/<0.001)
DAS28	2.7 ± 1.2	2.3 ± 1.1	4.0 ± 1.4	2.9 ± 1.3	(<0.001/<0.001)
(n)	(95)	(100)	(82)	(88)	
VAS pain,	35.7 ± 23.6	28.2 ± 23.6	50.7 ± 26.6	34.4 ± 26.5	(<0.001/0.191)
VAS PG	35.6 ± 23.6	27.6 ± 23.5	49.4 ± 26.3	36.1 ± 24.7	(<0.001/0.059)
HAQ	0.45 ± 0.45	0.37 ± 0.51	0.83 ± 0.55	0.65 ± 0.70	(<0.001/0.012)
DAPSA	8.3 ± 4.5	6.2 ± 5.8	25.3 ± 14.6	12.9 ± 12.0	(<0.001/<0.001)
(n)	(99)	(99)	(90)	(84)	

Values are expressed as mean±SD unless otherwise indicated.
n: number of patients; f: female; m: male; E-SR: sedimentation rate; CRP: C-reactive protein; DAS28: disease activity score; VAS: visual analogue scale; HAQ: Health assessment questionnaire; VAS: visual analogue scale; PG: patients' global assessment; DAPSA: Disease activity index in psoriatic arthritis. *p*-values from Mann-Whitney U-test.

Results

Comparison of M/O and P PsA

Demographic and clinical data are shown in Table I. There was no significant difference in age between M/O and P PsA patients. At inclusion, higher disease activity in patients with P PsA was characterised of ESR (p=0.008), DAS28 (p<0.001), DAPSA (p<0.001),

Table II. Clinical data at inclusion in Swedish early Psoriatic Arthritis register (SwePsA) by treatment-NSAID/DMARD at 5-year follow-up.

Clinical data at inclusion	No of missing observations	Total n=192	No n=68	NSAID n=42	DMARD n=42	NSAID + DMARD n=40
Medication at inclusion n (%)	6					
No		63 (33.9)	25 (37.9)	19 (46.3)	11 (27.5)	8 (20.5)
NSAID		91 (48.9)	33 (50.0)	18 (43.9)	19 (47.5)	21 (53.8)
DMARD		12 (6.5)	4 (6.1)	1 (2.4)	6 (15.0)	1 (2.6)
NSAID + DMARD		20 (10.8)	4 (6.1)	3 (7.3)	4 (10.0)	9 (23.1)
Age (years) median (IQR)	0	46. (24)	43.5 (27.5)	47 (26)	47 (21)	47 (15.5)
Female n (%)	0	107 (55.7)	36 (52.9)	29 (69.0)	19 (45.2)	23 (57.5)
E-SR median(IQR)	2	11.5 (20.5)	11.0 (20.0)	8.0 (14.0)	10.5 (23.0)	14.0 (26.0)
CRP (mg/L) median(IQR)	1	9.0 (11.0)	9.0 (11.5)	8.5 (8.0)	9.0 (11.0)	9.0 (14.0)
DAS28 median(IQR)	20	3.3 (2.0)	3.1 (2.3)	2.7 (1.6)	3.4 (2.1)	4.0 (1.3)
>3.2 n (%)		91 (52.9)	32 (50.0)	13 (35.1)	19 (52.8)	27 (77.1)
DAPSA median(IQR)	9	12.3 (12.9)	11.1 (12.1)	9.3 (9.2)	12.3 (20.7)	17.6 (14.0)
>14 n (%)		80 (43.7)	27 (40.3)	12 (30.0)	17 (42.5)	24 (66.7)
MDA n (%)	8	25 (13.2)	13 (19.4)	4 (9.5)	5 (11.9)	3 (7.7)
MDA total median (IQR)		3.0 (2.0)	3.0 (2.0)	3.0 (2.0)	2.0 (2.0)	2.0 (1.0)
HAQ median (IQR)	5	0.6 (0.9)	0.5 (1.0)	0.6 (0.8)	0.6 (0.6)	0.8 (0.5)
>0.5 n (%)		97 (51.9)	29 (43.9)	23 (56.1)	20 (50.4)	25 (62.5)
PGA VAS median (IQR)	8	43.0 (42.0)	44.0 (41.0)	37.0 (39.5)	39.5 (48.5)	48.0 (34.0)
>40 n (%)		96 (52.2)	35 (52.2)	17 (42.5)	19 (47.5)	25 (67.6)
Pain VAS median (IQR)	8	45.0 (43.5)	42.0 (47.0)	36.0 (37.5)	50.0 (40.0)	48.0 (38.0)
>40 n (%)		101 (54.9)	34 (50.7)	19 (47.5)	23 (57.5)	25 (67.6)
Remission n (%)	0	3 (1.6)	1 (1.5)	2 (4.8)	0 (0.0)	0 (0.0)
Number of tender or swollen joints median (IQR)	0	4.0 (6.5)	3.0 (5.0)	4.5 (11.0)	6.0 (7.5)	4.0 (6.5)

NSAID: non-steroidal anti-inflammatory drugs; DMARD: disease-modifying anti-inflammatory drugs; CRP: C-reactive protein; DAS28: Disease Activity Score including 28 joints; MDA: minimal disease activity; HAQ: health assessment questionnaire; PGA VAS: patients' overall assessment of disease on a VAS scale; pain VAS: patients' assessment of pain on a VAS scale.

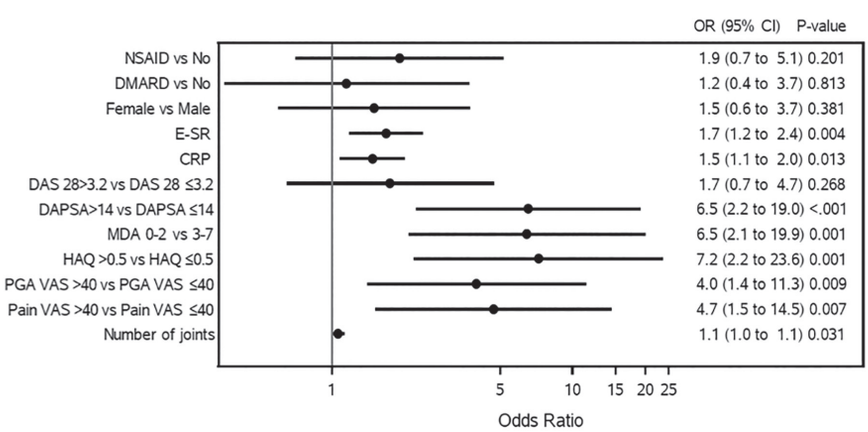

Fig 1. The impact of various patient characteristics of psoriatic arthritis patients on inclusion in the early Swedish psoriatic arthritis register (SwePsA) on TNFi treatment after the 5-year follow-up. Age-adjusted odds ratio (OR) with 95% confidence limits (CI) from 12 logistic regression models. HAQ: health assessment questionnaire; MDA: minimal disease activity; DAPSA: Disease activity Index in Psoriatic Arthritis; VAS: visual analogue scale; M/O: mono-/oligo-arthritis; P: polyarthritis; PsA: psoriatic arthritis; DAS: disease activity score; NSAID: non-steroidal anti-inflammatory drug; DMARD: disease-modifying anti-rheumatic drug; E-SR: sedimentation rate, E-SR: OR are for continuous analysis of the logarithm (base 2) of E-SR; CRP: C-reactive protein; CRP: OR are for continuous analysis of the logarithm (base 2) of CRP.

HAQ (p<0.001), pain VAS (p<0.001) and PGA VAS (p<0.001). The patients, initially included as M/O or P PsA, were evaluated in these separate groups 5 years later, following treatment according to Swedish recommendations (20) or according to clinical routine in Sweden (for low disease activity). At the 5-year follow-up, DAS28 (p<0.001), DAPSA (p<0.001) and HAQ (p=0.012) parameters were still higher in the initial P PsA group than in M/O PsA patients. At inclusion in SwePsA, at a mean disease duration of 11 months, 22 (21%) patients with M/O PsA had MDA compared to 3 (3%) with P PsA patients (p<0.001), with an increased number of patients to 51 (48%) for M/O and 26 (28%) for P PsA (p=0.006) at the 5-year follow-up. Three M/O PsA patients (3%) had remission at inclusion, but none of the P PsA patients. Remission at the 5-year follow-up was significantly increased within the M/O group with 20 patients (19%) considered to be in remission (p<0.001), in contrast to the P PsA group, where 8 (9%) had reached remission (p=0.003). Remission at the 5-year follow-up was significantly more frequent in M/O PsA than in P PsA (p=0.036).

Medical treatment of the SwePsA cohort at inclusion and at follow-up

At inclusion in SwePsA, 15% of all patients were treated with DMARD, *i.e.* no significant difference between patients with M/O vis-à-vis P PsA regarding the rate of DMARD treatment at the inclusion visit. After the inclusion visit patients classified as P PsA were significantly more often treated with DMARD (n=52, 56%) *versus* patients with M/O PsA (n=31, 30%) (p=0.004). MTX was the prescribed drug after inclusion visit for 31% of all patients, increasing to 36% at the 5-year follow-up. Four patients were prescribed leflunomide, two cyclosporine, four anti-malarials and one auranofin. Prescription for treatment, continuously or as new treatment with DMARD *after* the visit at 5 years, was given to 94 (45%) of all PsA patients. None of the patients was recommended TNFi at inclusion. At the visit 5 years later, 16 of all 198 patients were treated with TNFi. A further 7 patients were started on TNFi at the five-year visit. Oral corticosteroids were given to 4% at inclusion and to 7% at the 5-year follow-up. TNFi was prescribed equally often for men and women.

Prediction of treatment with NSAID/DMARD at five-year follow-up

Clinical data at inclusion in SwePsA by treatment-NSAID/DMARD at 5-year-

Table III. Crude and adjusted odds ratio (OR) with 95% confidence interval (CI) for treatment at five-year follow-up with NSAID only; only DMARD or both NSAID and DMARD compared with neither treatment. The odds ratios are adjusted for age and treatment at inclusion.

	NSAID vs. no treatment OR (95% CI)		DMARD vs. no treatment OR (95% CI)		NSAID + DMARD vs. no treatment OR (95% CI)		*p*-value	
Clinical data at inclusion	Crude	Adjusted[1]	Crude	Adjusted[1]	Crude	Adjusted[1]	Crude	Adjusted[1]
NSAID	0.79 (0.36 - 1.74)		1.02 (0.46 - 2.27)		2.44 (1.00 - 5.97)		0.13	
DMARD	0.78 (0.22 - 2.79)		2.42 (0.86 - 6.76)		2.50 (0.89 - 7.01)		0.11	
Age (years)	1.00 (0.98 - 1.03)		1.02 (0.99 - 1.04)		1.00 (0.97 - 1.02)		0.55	
Male	0.50 (0.22 - 1.13)	0.48 (0.20 - 1.13)	1.36 (0.63 - 2.95)	1.46 (0.63 - 3.37)	0.83 (0.38 - 1.83)	0.77 (0.33 - 1.78)	0.17	0.14
CRP[2]	0.94 (0.71 -1.23)	0.96 0.72 - 1.27)	1.17 (0.90 - 1.54)	1.19 (0.90 - 1.58)	1.07 (0.81 - 1.42)	1.07 (0.80 - 1.43)	0.49	0.55
E-SR[2]	0.95 (0.85 - 1.07)	0.95 (0.85 - 1.07)	1.10 (0.90 - 1.34)	1.09 (0.88 - 1.36)	1.03 (0.88 - 1.22)	1.01 (0.86 - 1.20)	0.49	0.60
DAS28>3.2	0.54 (0.24 - 1.25)	0.54 (0.22 - 1.34)	1.12 (0.49 - 2.53)	1.16 (0.47 - 2.87)	3.37 (1.33 - 8.54)	3.65 (1.34 - 9.89)	0.007	0.010
MDA total	0.97 (0.76 - 1.24)	0.99 (0.77 - 1.27)	0.83 (0.65 - 1.07)	0.84 (0.64 - 1.09)	0.71 (0.53 - 0.94)	0.72 (0.53 - 0.97)	0.080	0.13
HAQ>0.5	1.63 (0.74 - 3.58)	1.45 (0.63 - 3.30)	1.28 (0.58 - 2.80)	1.08 (0.47 - 2.51)	2.13 (0.95 - 4.75)	2.00 (0.84 - 4.74)	0.29	0.42
DAPSA>14	0.63 (0.28 - 1.46)	0.70 (0.30 - 1.66)	1.10 (0.49 - 2.42)	1.21 (0.53 - 2.76)	2.96 (1.27 - 6.92)	2.90 (1.20 - 6.99)	0.015	0.038
PGA VAS >40	0.68 (0.31 - 1.49)	0.63 (0.27 - 1.44)	0.83 (0.38 - 1.81)	0.81 (0.35 - 1.85)	1.90 (0.82 - 4.41)	1.61 (0.67 - 3.90)	0.16	0.28
Pain VAS	0.88 (0.40 - 1.92)	0.84 (0.37 - 1.89)	1.31 (0.60 - 2.89)	1.35 (0.59 - 3.08)	2.02 (0.87 - 4.68)	1.80 (0.75 - 4.32)	0.28	0.41
Number of tender or swollen joints	0.94 (0.87 - 1.02)	0.94 (0.87 - 1.02)	1.05 (1.00 - 1.12)	1.05 (0.99 - 1.12)	1.06 (1.00 - 1.12)	1.06 (0.99 - 1.12)	0.016	0.026

OR (95% CI) from a multinomial logistic regression model.
NSAID: non-steroidal anti-inflammatory drugs; DMARD: disease-modifying anti-inflammatory drugs; CRP: C-reactive protein; E-SR: sedimentation rate; DAS28: Disease Activity Score including 28 joints; MDA: minimal disease activity; HAQ: health assessment questionnaire; PGA VAS: patients' overall assessment of disease on a VAS scale; pain VAS: patients' assessment of pain on a VAS scale.
[1] Adjusted for age and medication at inclusion [2] OR are for continuous analysis of the logarithm (base 2) of CRP and E-SR.

Table IV. Clinical data at inclusion with treatment TNF-alfa inhibitor at 5-year follow-up.

Clinical data at inclusion	No of missing observations	None n=175	TNF inhibitor n=23	OR(95% CI)	*p*-value
Medication at inclusion n (%)	6				
None		61 (35.9)	5 (22.7)		
NSAID		101 (57.7)	16 (72.7)	1.95 (0.73 - 5.23)	0.18
DMARD		28 (16.5)	4 (18.2)	1.13 (0.35 - 3.58)	0.84
Age (years) median (IQR)	0	47 (25)	38 (20)	0.68 (0.42 - 1.08)	0.10
Female n (%)	0	96 (54.9)	14 (60.9)	1.28 (0.53 - 3.11)	0.59
ESR median (IQR)	3	11.0 (16.0)	28.0 (38.0)	1.81 (1.13 - 2.91)	0.013
CRP (mg/L) median (IQR)	1	9.0 (8.0)	14.0 (37.0)	1.64 (1.06 - 2.53)	0.025
DAS28 median (IQR)	21	3.3 (2.1)	3.7 (2.5)		
>3.2 n (%)		82 (85.2)	19 (82.6)	1.37 (0.53 - 3.54)	0.51
DAPSA median (IQR)	9	11.2 (11.7)	20.1 (19.9)		
>14 n (%)		66 (39.8)	18 (78.3)	5.45 (1.93 - 15.41)	<0.001
MDA n (%)	8	25 (14.5)	0 (0.0)		
MDA total median (IQR)		3 (2)	2 (1)		
<3 n (%)		72 (43.1)	19 (82.6)	6.27 (2.04 - 19.23)	0.001
HAQ median (IQR)	5	0.5 (0.9)	0.8 (0.4)		
>0.5 n (%)		81 (47.4)	18 (81.8)	5.00 (1.62 - 15.39)	0.005
PGA VAS median (IQR)	8	39 (41)	58 (27)		
>40 n (%)		81 (48.5)	18 (78.3)	3.82 (1.36 - 10.77)	0.011
Pain VAS median (IQR)	8	41 (40)	6 (26)		
>40 n (%)		85 (50.9)	19 (82.6)	4.58 (1.50 - 14.05)	0.008
Number of tender or swollen joints median (IQR)	0	4 (6)	4 (6)	1.05 (1.00 - 1.11)	0.071

Odds ratio (OR) with 95% confidence interval (CI) for relation between clinical data at inclusion and medication at the 5-year follow-up.
NSAID: non-steroidal anti-inflammatory drugs; DMARD: disease-modifying anti-inflammatory drugs; CRP: C-reactive protein; E-SR: sedimentation rate; DAS28: Disease Activity Score including 28 joints; MDA: minimal disease activity; HAQ: health assessment questionnaire; PGA VAS: patients' overall assessment of disease on a VAS scale; pain VAS: patients' assessment of pain on a VAS scale.

follow-up are shown in Table II. Treatment with DMARD was present in 12 (6.5%) at inclusion and 42 (21.9%) after 5 years and DMARD and NSAID in 20 (10.8%) initially, increased to 40 (20.8%) of all 192 patients after 5 years. Patients with a DAS28 >3.2 at inclusion had 3.4 times increased odds for treatment with DMARD and 3.7 times increased odds for treatment with DMARD and NSAID. DAPSA >14 increased the odds by 2.96, respectively 2.90 for treatment (Table III). Increased number of tender and swollen joints were predictors for treatment with NSAID, DMARD or DMARD+NSAID at 5-year follow-up (Table III). These results remained significant after adjustment for age and medication at inclusion.

Prediction of treatment with TNF-inhibitor after the 5-year follow-up visit

At the 5-year visit, 16 patients from the early PsA cohort were treated with TNFi while another 7 patients were prescribed the treatment at that visit and all 23 patients were considered treated in the statistical analysis. Treatment with TNFi after the 5-year follow-up

visit was associated with high ESR and CRP with an odds of 1.8 respectively 1.6. Likewise, DAPSA >14 at inclusion increased the odds by 5.4 and low number of MDA parameters (<3) by 6.3, a high baseline HAQ (>0.5) by 5, PGA VAS (>40) by 3.8, pain VAS (>40) 4.6 (Table IV; Fig. 1).

Discussion

This study focuses on the two major classification groups of early PsA: mono-/oligo- (M/O) and polyarthritis (P) PsA. We have shown that early classification can be of significance as there were clear differences between M/O and P PsA in inflammatory parameters as well as patients' own assessments of disease activity at inclusion with withstanding differences between the two classification groups as for composed measures of DAS28 and DAPSA after five years.

Furthermore, the main predictor of long-term treatment with NSAID and DMARD or DMARD alone was DAS28 and DAPSA. The latter, DAPSA, predicted in addition to treatment with TNFi at 5-year follow-up.

According to a classification proposed by Veale *et al*. (31) the patients in this study were grouped at inclusion as M/O-arthritic, characterised by ≤4 inflamed joints, or P PsA patients described by >4 affected joints, applied in other studies including early psoriatic arthritis (32, 33). Later cluster analysis has suggested different groupings: peripheral and axial PsA, the latter including the combination of axial and peripheral disease (34), but that does not disclose the characteristics of M/O-arthritic patients. We were able to demonstrate significant differences between M/O and P PsA patients affecting clinical assessment and outcome. As expected, P PsA was significantly more aggressive than M/O PsA at inclusion that remained after 5 years as for DAS28, DAPSA and HAQ (Table I). Minimal disease activity (MDA) confirmed the different prognoses of the two patient groups and underlined the importance of subgrouping PsA patients in clinical work and of various research approaches including treatment trials. However, with only 38% of all patients achieving MDA after 5 years, much remains to be done to improve of medical therapies and to establish predictive factors of early disease markers, in order to implement "treat-to-target" thinking (35)

MTX was used in most cases as first line DMARD, despite a lack of data demonstrating longstanding effects (22, 36 and 37). Corticosteroids were used less frequently; there are no available studies on the effect of corticosteroids in PsA and the restrictiveness compared with rheumatoid arthritis (RA) follows the clinical dermatological observation of the risk of flare-up in skin psoriasis (38). The Swedish guidelines (20) focus on PsA, with very active disease in polyarthritic patients, but there is no general recommendation regarding M/O PsA. The ability to establish early evaluation, with recommendations of treatment including level of medical expertise is valuable for the individual PsA patient, regardless of disease type, and can be decided with guidance by rheumatologists (39) or by outcome in long-term cohorts such as SwePsA.

In order to make decisions on level of medical attendance (specialist or general practitioner) and treatment early in PsA disease, we studied early predictors of treatment at the 5-year follow-up. DAS28 is an activity score frequently used in clinical practice. We have shown that DAS28 >3.2 and DAPSA >14 are useful in prediction of later treatment with NSAID and DMARD or DMARD alone in PsA with a high correlation between the two composite measurements. As DAPSA encounter joints of the lower limbs and hips that favours the male phenotype, it could be preferred even though it has some disadvantages in clinical routine.

None of the patients, whether M/O PsA nor P PsA, was recommended TNFi at inclusion in the study, as at the initiation of SwePsA early in 2000, TNFi was recently introduced as an option for treatment of PsA (40). While monitoring the cohort, the recommendation for treatment of high inflammatory disease in PsA with TNFi has changed in favour of earlier treatment. The former may partly explain the finding that none of the patients was initially recommended TNFi. Still, after 5 years of treatment only 11% of all patients were treated with TNFi. Logistic regression indicated that several factors, both patient's function and estimate of disease, as well as clinical findings of inflammation, where low numeric MDA <3 does summarise the status and significantly predict the later decision of TNFi therapy. There are no clinical publications on early predictors for treatment with anti-TNF. Earlier studies found baseline HAQ and VAS scores to be predictive for TNFi drug discontinuation as these measures indicate irreversible damage of joints (41). CRP has been postulated as a candidate for early decision to treat with TNFi, as CRP has been found to be linked with clinical response (42).

One limitation with our study was the sample size, which limited the number of predictors appropriate for multivariable analyses to only three for the analysis of DMARD/NSAID and two for TNFi.

In conclusion, there are major differences between M/O PsA and P PsA that we need to focus on in clinical work and trials, and decision of level of medical attendance. DAS28 >3.2 and DAPSA>14 early in the disease are of greatest importance for subsequent treatment with DMARD. For prediction of biological treatment, not reaching MDA at onset of disease, would be the composite index of choice.

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