Objectives: The goal of the study was to assess the relationship of NLR, PLR, MLR with the conventional disease activity markers (ESR, CRP, DAS28, TJC, SJC) and results of joints US, in patients with RA.

Methods: The study was conducted in the consecutive 72 patients with RA (60 women, 12 men), with the mean (SD) age 53.4 (8.9) and disease duration 16.8 (10.3) years. The following procedures were assessed for all patients: joint counts, DAS28, complete blood cell counts, ESR, CRP, US of 24 small joints.

Results: The mean (SD) values of hematological markers were as follows: NLR 3.24 (2.7) (range 0.2-13.96); PLR 193.26 (88.3) (range 71.2-560.8); MLR 0.3 (0.16) (range 0.06-0.87). The mean values of NLR and PLR were significantly lower in patients with low (DAS28 $\leq$ 3.2) vs moderate/high (DAS28 $>$ 3.2) disease activity; respectively NLR 2.4 (1.7) vs 4.0 (3.2), $p=0.004$; PLR 168.7 (58.0) vs 215.8 (104.9), $p=0.4$. Hematological markers of systemic inflammation were significantly, positively correlated with clinical, laboratory and US markers of the disease activity. Significant correlations were found between: NLR and DAS28, TJC, SJC, ESR, CRP, vascularity of synovium in US; PLR and DAS28, TJC, SJC, ESR, CRP, vascularity and hypertrophy of synovium in US; MLR and DAS28, SJC, ESR, CRP, vascularity and hypertrophy of synovium in US. In multiple regression test significant correlations were confirmed for: NLR and SJC ($p=0.008$), ESR ($p<0.001$), CRP ($p<0.01$), vascularity of synovium in US ($p=0.02$); PLR and ESR ($p=0.03$), CRP ($p=0.03$); MLR and DAS28 ($p=0.04$), ESR ($p<0.001$), hypertrophy of synovium in US ($p=0.02$).

Conclusion: The results of the study suggest that hematological markers of systemic inflammation (NLR, PLR, MLR) may serve as reliable, inexpensive and effective measure of inflammation in RA. The strong association with US imaging is an attractive result because of its predictive value and usefulness in clinical practice

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AB0285

PREDICTORS OF UNACCEPTABLE PAIN, AND UNACCEPTABLE PAIN WITH LOW INFLAMMATION, IN EARLY RHEUMATOID ARTHRITIS

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Background: Pain is a major symptom in many patients with rheumatoid arthritis (RA). In early RA, pain is usually due to active synovitis, but over the disease course some patients experience pain without elevated laboratory markers of inflammation.

Objectives: To investigate predictors of unacceptable pain, and unacceptable pain with low inflammation, in patients with early RA.

Methods: Consecutive patients with early RA (symptom duration $<$ 12 months), recruited in 1995-2005 from a defined area, were followed through 5 years. Patients were managed according to usual care, with no pre-specified treatment protocol. Pain was assessed using a visual analogue scale (VAS; 0-100 mm). Unacceptable pain was defined as VAS pain $>$ 40 based on the patient acceptable symptom state (PASS) (1), and low inflammation as CRP $<$ 10 mg/l (2). Baseline predictors of unacceptable pain, and of unacceptable pain with low inflammation, were evaluated using logistic regression analysis.

Results: A total of 233 patients with early RA (73% female, 57% anti-CCP positive, mean age 60 years, median symptom duration 7 months) were included. Of these, 179 attended the 5-year follow-up. At 5 years, 34% had unacceptable pain, and 23% had unacceptable pain with low inflammation. High VAS scores for pain and patient's global assessment (PGA) at baseline were associated with unacceptable pain at 5 years (Table). There was a negative association between baseline swollen joint count (SJC28) and unacceptable pain at the 5 year follow-up. In multivariate logistic regression analysis including VAS PGA and SJC28, both had an impact on unacceptable pain after 5 years (adjusted odds ratios per standard deviation (SD), with 95% CI 1.78 (1.26-2.52) and 0.61 (0.42-0.89), respectively). Anti-CCP positive patients were significantly less likely to experience unacceptable pain with low inflammation at 5 years (Table).

Table 1.

Baseline predictors of unacceptable pain or unacceptable pain with low inflammation in the early RA cohort after 5 years, bivariate logistic regression

Variable	Unacceptable pain		Unacceptable pain with low inflammation	
	Odds ratio	95 % CI	Odds ratio	95 % CI
Female	1.24	0.62 – 2.47	1.87	0.80 – 4.40
RF positive	0.88	0.46 – 1.67	0.54	0.26 – 1.09
Anti-CCP positive	0.77	0.39 – 1.49	0.50	0.22 – 0.98
Erosion	0.62	0.26 – 1.49	0.62	0.22 – 1.72
Age	1.09	0.80 – 1.49	0.97	0.68 – 1.38
Symptom duration	1.28	0.93 – 1.76	1.19	0.83 – 1.71
VAS pain	1.40	1.02 – 1.91	1.34	0.94 – 1.92
DAS28	1.03	0.76 – 1.41	1.00	0.70 – 1.42
SJC28	0.71	0.51 – 0.99	0.70	0.47 – 1.03
TJC28	0.98	0.71 – 1.35	1.04	0.72 – 1.50
HAQ	1.01	0.74 – 1.37	1.01	0.72 – 1.43
CRP $>$ 9 mg/l	0.64	0.29 – 1.41	0.62	0.23 – 1.72
ESR	0.79	0.57 – 1.09	0.74	0.50 – 1.11
VAS PGA	1.60	1.16 – 2.21	1.39	0.98 – 2.00

Odds ratios per SD for continuous variables

Conclusion: More than 1/3 of early RA patients experienced unacceptable pain after 5 years. Extensive synovitis in early RA was associated with a reduced risk of unacceptable pain at 5 years, likely due to positive effects of treatment on inflammation related pain. Non-inflammatory pain may be a greater long term problem in anti-CCP negative patients.

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AB0286

STATINS TO PREVENT RHEUMATOID ARTHRITIS (STAPRA TRIAL): CHALLENGES IN RECRUITMENT AND RETENTION

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Background: Primary prevention may be possible in subjects at high risk to develop rheumatoid arthritis (RA). We designed a placebo controlled randomized trial to investigate if atorvastatin can halt RA development in persons at risk for this disease (STAPRA, Netherlands Trial Register NTR5265). A statin was chosen because these drugs reduce disease activity in RA (1), hyperlipidemia patients on statins have a lower risk for developing RA (2) and dyslipidemia increased the risk for RA in a sero-positive arthralgia cohort (3). We assumed that high risk-subjects would be attracted to this trial. However, we experienced severe difficulties with patient inclusion and treatment adherence.

Objectives: To explore difficulties with patient recruitment and retention.

Methods: The STAPRA study is a multicenter, 3-year, randomized, placebo controlled, double-blind clinical trial to assess the efficacy of atorvastatin 40 mg daily in delaying or preventing RA development in persons at high risk, defined by the presence of arthralgia and the presence of high titers of anti-citrullinated protein antibody (ACPA) or presence of both ACPA and rheumatoid factor (RF). Eligible participants were $\geq$ 18 years, did not use lipid lowering agents and had no synovitis. Five centers participated. Our goal was to recruit 220 study subjects based on an expected risk reduction of 21%. The unexpected low recruitment rate prompted us to evaluate the reasons to decline participation or to discontinue the study drug prematurely.

Results: Details were available from the initiating center (Reade) and 1 participating center (Sint Maartenskliniek (SMK)). During a period of 36 months, 164 eligible patients were asked to participate of whom 58 patients (35%) consented. Most common reasons to decline were: unwillingness to use study medication (49%) and the feeling that participation was too time-consuming (14%). Fifty-four patients were randomized since 4 failed screening due to hyperlipidemia or seronegativity on repeated testing. Currently, 11 participants (20%) have developed arthritis. Twelve

dropped out for various reasons, including adverse events (33%). Thirty-one persons are still being followed, but of these 10 stopped study medication after a median of 3 months. The main reason to discontinue therapy was side effects (80%), notwithstanding a standardized approach for dose reduction and temporary discontinuation as needed.

Conclusion: In this RCT in persons at risk for RA we identified a major obstacle to the successful conduction of such trials, namely the difficulty to enter and retain participants. The primary reported reason was unwillingness to use study medication. This is different from many successfully completed trials on optimal medical treatment in early RA patients, where large inclusion goals have been met within a relatively short timeframe and adherence overall was good. This issue is highly relevant to the current inclination to move the start of drug intervention in RA to ever earlier phases. Further research into patients' motivation and barriers for participation in intervention trials in the at risk phase of RA is necessary to enable intervention research in this phase of the disease.

Figure 1

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AB0287

BENEFITS OF PAIN RELIEF ON FATIGUE, FUNCTION, AND QUALITY OF LIFE WHEN JOINT INFLAMMATION IS CONTROLLED IN PATIENTS WITH RA

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Background: The ultimate goals for rheumatoid arthritis (RA) treatment are to achieve disease activity control and the best potential health state throughout the course of disease.¹ In prior analyses of the Phase 3 trial, RA-BEAM (NCT01710358), baricitinib was associated with significant clinical improvements and patient-reported pain relief in RA patients (pts) who had had an inadequate response to methotrexate.^{2,3} The additional benefits of pain relief when inflammation is controlled are not well characterized.

Objectives: To quantify the contribution of pain relief to other PROs, fatigue, physical function, and quality of life, in pts who achieved control of inflammation, defined as swollen joint count (SJC) ≤1 and C-reactive protein (CRP) ≤1 mg/dL, at Week (Wk) 24 in a post hoc, pooled analysis of RA-BEAM.

Methods: Among pts with inflammation control, PROs were compared between pts who also achieved thresholds of pain relief at Wk 24 vs those who did not. Pain was measured with a visual analogue scale (VAS, range: 0-100 mm) and divided into ≤20, >20, ≤40, >40 mm.^{4,5} PROs included: the Health Assessment Questionnaire-Disability Index (HAQ-DI) normative value (<0.5), to compare with a general population, and minimum clinically important differences (MCID, ≥0.22), SF-36 physical and mental component scores (PCS and MCS) MCID (≥5), and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F, range of 0-52, higher scores represent less fatigue) normative value (≥40.1) and MCID (≥3.56). Logistic regression models were adjusted for age, gender, BMI, geographic region, duration of disease, baseline SJC, baseline pain, and baseline value of PRO under evaluation. Missing data were imputed using modified last observation carried forward.

Table 1.

Percentage of patients achieving improvement in PROs by pain relief thresholds in patients who achieved control of inflammation at Week 24

	20 mm threshold		p-values	40 mm threshold		p-values
	≤20 mm (N=212)	>20 mm (N=159)		≤40 mm (N=297)	>40 mm (N=74)	
HAQ-DI <0.5	67	19	<0.0001	56	7	<0.0001
HAQ-DI MCID, 0.22	89	72	<0.0001	84	73	<0.0001
SF-36 PCS MCID, ≥5	81	57	<0.0001	74	58	<0.0001
SF-36 MCS MCID, ≥5	48	44	<0.05	47	44	<0.05
FACIT-F ≥40.1	80	41	<0.0001	71	32	<0.0001
FACIT-F MCID, ≥3.56	77	64	<0.0001	71	70	<0.01

FACIT-F: the Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI: Health Assessment Questionnaire-Disability Index; MCID: minimum clinically important difference; MCS: mental component score; SF-36: 36-Item Short Form Health Survey; PCS: physical component score

Results: Of the total 1305 patients in RA-BEAM, 371 pts treated with adalimumab (121/330), baricitinib (187/487), or placebo (63/488) and background methotrexate achieved inflammation control at Wk 24. Among patients who achieved inflammation control, those who also achieved each pain relief threshold were statistically significantly more likely (p<0.05) to report benefit in physical function, general quality of life, and fatigue than patients who did not reach the pain relief thresholds. (Table)

Conclusion: When inflammation is controlled (SJC ≤1 and CRP ≤1 mg/dL), more pain relief is associated with better physical function, quality of life, and reduced fatigue. This may support consideration of pain relief as an additional goal of therapy, even when inflammation is controlled. Further investigation should evaluate this benefit with other patient populations and outcomes.

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