The use of MRI in early inflammatory arthritis

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Changes in the clinical presentation of patients with rheumatoid arthritis from the early 1990s to the years 2010: earlier identification but more severe patient reported outcomes

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8

Annals of the Rheumatic Diseases 2016;75:2054–6.
doi:10.1136/annrheumdis-2016-209949

The relevance of early identification of rheumatoid arthritis (RA) is acknowledged for several decades. Over time the interpretation of early has changed: in the early 1990s a symptom duration <2 years was considered early. Nowadays earlier identification is recommended,[1] some suggest that identification within 12 weeks after symptom onset is optimal. In this study, we evaluated the presentation of RA over the past decennia. We assessed whether patients with RA were recognised earlier and if this affected the phenotype of RA at first presentation. We observed that patients with RA are indeed identified after a shorter symptom duration, that this was paralleled with less severe inflammation at presentation, but paradoxically also with increased severity of patient reported outcomes (PROMs).

All patients in the Leiden Early Arthritis Clinic (EAC) cohort that fulfilled the 2010 European League Against Rheumatism/ American College of Rheumatology RA criteria were studied (n=1406).[2,3] In short, the EAC was started in 1993 and inclusion criteria were arthritis at physical examination and symptom duration <2 years. At baseline, hence before treatment initiation, 68-tender and 66-swollen joint counts were performed, blood samples taken and the PROMs fatigue, pain, morning stiffness and disease activity obtained. Initially PROMs were recorded as visual analogue scales (VASs), from 2010 onwards numerical rating scales were used. Both scales correlate strongly.[4] Because changes in presentation were expected to occur gradually, patients with RA were compared over five periods. Variables were compared using Kruskal-Wallis H-test.

Symptom duration at presentation decreased over the years from median 138 days in 1993–1996 to 97 days in 2011–2015 ($p<0.001$, table 1). The frequency of autoantibodies did not differ significantly. Patients with RA presented with less swollen joints (median 11 decreased to six joints, $p<0.001$) and lower levels of acute phase reactants (median C-reactive protein (CRP)-level 24 decreased to 10 mg/L, $p<0.001$). The health assessment questionaire (HAQ) (measuring functional disability) remained stable (table 1). PROM values increased: patients reported more pain ($p<0.001$), more fatigue ($p=0.005$) and higher disease activity ($p<0.001$) (figure 1). Furthermore, the disease activity score (DAS)28-CRP (combining joint counts, CRP and patient global health) decreased ($p=0.001$).

These findings are paradoxical: while patients with RA over time presented with shorter symptom duration and less inflammatory findings, PROMs worsened. The finding that all evaluated PROMs increased makes it unlikely to be a coincidental finding. The VAS fatigue and pain are known to be strongly correlated[5] and it is known that patient perceptions are minimally explained by inflammatory findings.[6,7]

Presumably, the present findings are not specific for RA, but reflect a general increase in societal pressure posed upon the individual over the years (ie, society has become more demanding), whereby smaller health problems, which might be less visible, could be experienced as more disabling.[8] In parallel, patients may also have higher health expectations themselves. Both phenomena likely contribute to a shift of reference when reporting outcomes.

This is the first study describing temporal changes in presentation of new patients with RA, but discordance between inflammatory measures (SJC and erythrocyte sedimentation rate) and PROMs has been reported. First, differences

in inflammatory outcomes between countries were not paralleled by similar differences in VAS fatigue and global health.[9] Similarly, comparing patients with RA treated in 1985 with patients treated in 2000 revealed that the latter group had less inflammation, but similar VAS pain.[10]

The previous observations that PROMs were not responsive to changes in the severity of inflammation combined with the present finding raise the question if it is known what PROMs actually measure. Furthermore, this may have consequences for the monitoring of RA using PROMs or composite scores (eg, DAS or simple disease activity index (SDAI)) for defining remission.

In conclusion, over the last 23 years patients with RA in Leiden (the Netherlands) have presented with shorter symptom duration. Even though patients with RA presented with less inflammation, the disease burden as experienced by patients is higher.

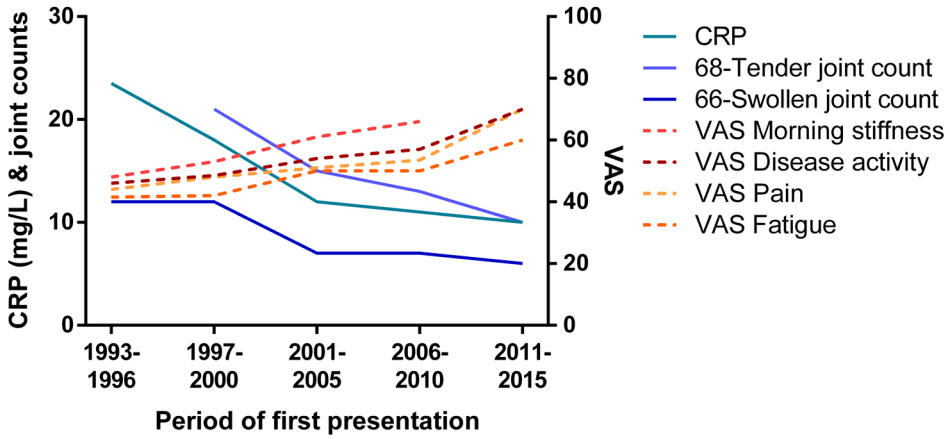

Figure 1 The severity of inflammation and of several patient reported outcomes measures for 2010-criteria positive RA-patients that presented in different time periods
Depicted are the medians per period. The inter-quartile ranges are shown in Table 1. VAS, visual analogue scale; CRP, c-reactive protein.

Table 1 Characteristics of patients with RA (according to the 2010-criteria) at first presentation to the rheumatologic outpatients clinic

	1993-1996		1997-2000		2001-2005		2006-2010		2011-2015		p-value
	N=177		N=216		N=304		N=367		N=342		
Women, n (%)	118	(66.7%)	142	(65.7%)	214	(70.4%)	240	(65.4%)	222	(64.9%)	0.61
Age in years, mean (SD)	56.0	(16.1)	56.0	(16.9)	56.1	(15.7)	56.6	(15.4)	57.2	(14.5)	0.91
Symptom duration in days, med (IQR)	138	(81-269)	135	(81-281)	147	(74-261)	131	(60-244)	97	(51-228)	<0.001
68-Tender joint count, med (IQR)		N/A	21	(15-35)	15	(9-25)	13	(8-20)	10	(5-16)	<0.001
66-Swollen joint count, med (IQR)	12	(6-16)	12	(6-20)	7	(3-13)	7	(3-11)	6	(3-11)	<0.001
ESR in mm/hour, med (IQR)	44	(6-16)	33	(6-19)	29	(3-12)	28	(3-11)	29	(3-11)	<0.001
CRP in mg/L, med (IQR)	24	(10-45)	18	(9-37)	12	(5-30)	11	(4-27)	10	(3-25)	<0.001
RF-positive, n (%)*	99	(55.9%)	124	(57.4%)	187	(61.5%)	213	(58.7%)	224	(65.7%)	0.142
ACPA-positive, n, (%)*	104	(60.5%)	120	(55.8%)	138	(50.9%)	173	(51.8%)	187	(55.2%)	0.29
VAS Pain (0-100), med (IQR)	44	(24-60)	48	(27-60)	51	(33-67)	54	(36-70)	70	(40-80)	<0.001
VAS Fatigue (0-100) , med (IQR)	42	(13-64)	42	(15-63)	50	(18-69)	50	(17-73)	60	(20-80)	0.005
VAS Morning Stiffness (0-100), med (IQR)	48	(24-76)	53	(26-73)	61	(35-81)	66	(40-79)	N/A		0.002
VAS Disease activity (0-100), med (IQR)	46	(21.5-70)	49	(26-68)	54	(33-73)	57	(35-74)	70	(50-80)	<0.001
HAQ, med (IQR)	1.0	(0.6-1.4)	1.0	(0.5-1.5)	1.0	(0.5-1.5)	1.0	(0.5-1.5)	1.0	(0.6-1.5)	0.78
DAS28-CRP, med (IQR)		N/A	5.3	(4.4-5.6)	4.7	(4.0-5.6)	4.7	(3.8-5.4)	4.4	(3.7-5.2)	0.001

VAS disease activity represents disease activity in last 24 hours. p Value; results of Kruskal-Wallis H-test (Pearson's $\chi 2$ for proportions); N/A, not available: from 1993 to 1999 a different tender joint count was used than the 68-TJC and the DAS28-CRP could not be calculated due to missing patient global health assessment. VAS morning stiffness was not assessed from 2010 to 2015. *Percentages from the number of patients with ACPA/RF data. ACPA, anticitrullinated peptide antibody; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; RA, rheumatoid arthritis; RF, rheumatoid factor; TJC, tender joint count; VAS, visual analogue scale.

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