Table 1. The relationship between cardiovascular disease and the development of rheumatoid arthritis, stratified by gender.

	Adjusted* Hazard Ratio (95% confidence interval)	
	Men (number of RA cases=158)	Women (number of RA cases=358)
CVD non-exposed, n=48,660	1 (ref.)	1 (ref.)
CVD exposed, overall, n=4,627	0.73 (0.34-1.58) (number of RA cases=7)	1.30 (0.70-2.38) (number of RA cases=11)

Conclusion: The investigation showed tendency towards a higher risk of developing RA in women with previous CVD than women without CVD. Male gender was not associated with subsequent development of RA, possibly related to low sample size.

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CLINICAL PRESENTATION AND MANAGEMENT OF MONO- AND BILATERAL KNEE ARTHRITIS: RESULTS FROM THE LEIDEN EARLY ARTHRITIS CLINIC COHORT

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Background: Patients presenting with arthritis in one or both knees propose a challenge regarding diagnosis, prognosis and treatment decisions.

Objectives: To characterize the patients with knee arthritis who presented to the Leiden Early Arthritis Clinic (EAC) and to evaluate the disease course and initial treatment decisions.

Methods: All patients with arthritis confined to the knee(s) were selected from all patients included in the EAC between 1993 and 2015. The EAC captures patients with arthritis and symptom duration < 2 years, excluding arthritis diagnosed at presentation as definite infectious, gouty or osteoarthritis. EAC follow up is at 2 weeks, 3 months and thereafter yearly. Medical files were revised for information on treatment and clinical outcomes. Baseline characteristics were summarized, treatment and outcome was evaluated over time up to 12 months. Patients were stratified over 3 groups: 1. Early remission (at 3 months no clinical synovitis and no flare in the first year); 2. Persistent gonarthrits at 3 months (improving or stable up to 12 months, without progression); 3. Progression to oligo-/polyarthrits ≤ 12 months. Between-group differences were analysed using χ^2 , Fischer exact tests, two-way ANOVA or Kruskal Wallis tests.

Results: Of the 206 patients identified, 174 (85%) had mono- and 32 (15%) bilateral gonarthrits. Early remission was observed in 67/206 patients (32.5%, group 1), gonarthrits persisted in 109/206 patients (52.9%, group 2) and progression to oligo-/polyarthrits occurred in 30/206 patients (14.6%, group 3) within the first 12 months. At 12 months, 32/109 (29.4%) patients in group 2 still had gonarthrits, 40/109 (36.7%) were in remission, and 37/109 (33.9%) patients had been lost to follow-up (11 patients were in remission and 26 patients still had (residual) gonarthrits at the last available visit). RF and ACPA positivity and high ESR at baseline were predictive for progression (group 3), but did not differ between patients in groups 1 and 2. There was a trend for longer symptom duration at presentation in group 3 (76.5 days, IQR 25.5-175.5, $p=0.040$ vs. group 1) (table 1).

The initial treatment consisted of NSAIDs (in 125/206 patients, 60.7%), an intra-articular corticosteroid injection (IAC) (39/206, 18.9%) or other (29/206, 14.1%) including prednisone, csDMARDs, anti-gout medication and antibiotics (AB). In 13/206 (6.3%) patients symptoms remitted without any treatment. No differences in initial treatment were observed between groups 1, 2 and 3.

Table 1. Baseline characteristics – stratified analysis.

	Early remission		Persistent gonarthrits		Progression to oligo-polyarthrits		
		n		n		n	p
Age at presentation, yrs.	47.7 (31.6-57.6)	67	47.0 (31.6-57.1)	109	45.4 (30.8-56.1)	30	0.92
Female, %	50.8	67	51.4	109	46.7	30	0.90
Caucasian, %	89.6	67	82.6	109	96.7	30	0.09
Mono-arthritis, %	91.0	67	81.7	109	80.0	30	0.19
RF-positive, %	3.08	65	9.35	107	20.7	29	0.02
ACPA-positive, %	3.77	53	4.71	85	23.1	26	0.01
ANF-positive, %	19.7	61	23.4	94	11.5	26	0.41
Weight, kg	78.0 (16.0)	41	73.4 (15.0)	70	76.4 (13.4)	13	0.30
BMI, kg/m ²	24.8 (23.4-28.2)	39	24.0 (21.7-27.0)	68	25.5 (21.6-26.9)	13	0.50
Length, cm *	174.5 (12.3)	39	173.3 (11.5)	68	175.6 (12.1)	13	0.75
Smoking, % never	55.7	61	56.7	97	60.7	28	0.96
Symptom duration, days	29 (9-709)	63	52 (16-143)	101	76.5 (25.5-175.5)	28	0.07
ESR, mm/h	23 (10-42)	67	18 (8-34)	109	33 (12-75)	30	0.01
HAQ	0.5 (0.13-1.0)	50	0.38 (0-0.75)	83	0.62 (0.25-1.12)	25	0.10
DAS	1.74 (0.39)	17	1.87 (0.59)	47	2.35 (0.67)	5	0.11
VAS patient global	25 (16-37)	18	30 (10-41)	47	47 (20-52)	5	0.49

Values are median, (IQR), unless indicated otherwise. *Mean, (standard deviation). RF: rheumatoid factor; ACPA: anticitrullinated protein antibodies; ANF: anti-nuclear factor; BMI: body mass index; ESR: erythrocyte sedimentation rate; HAQ: health assessment questionnaire; DAS: disease activity score; VAS: visual analogue scale; SIC: swollen joint count; TIC: tender joint count. p comparing the three stratification groups using two-way ANOVA, Kruskal Wallis, Chi-square or Fischer exact test.

Table 2. Cumulative treatment prescriptions within first year of follow-up – stratified analysis.

Treatment (group)	Total n=206 n(%)	Early remission n=67 n(%)	Persistent gonarthrits n=109 n(%)	Progression to oligo-/poly n=30 n(%)	p
	n(%)	n(%)	n(%)	n(%)	
NSAID only	62 (30.1)	30 (44.8)	29 (26.6)	3 (10.0)	<0.01
Intra-articular corticosteroid injection(s)	93 (45.1)	18 (26.9)	58 (53.2)	17 (56.7)	<0.01
Prednisone (oral)	11 (5.4)	-	6 (5.5)	5 (16.7)	<0.01
Antibiotics	23 (11.2)	9 (13.4)	10 (9.2)	4 (13.3)	0.61
csDMARD(s)	28 (11.7)	-	15 (13.8)	13 (43.3)	<0.01
bdMARD(s)	2 (<1)	-	1 (<1)	1 (3.3)	0.38
Yttrium	3 (1.5)	-	3 (2.8)	-	0.40
Colchicine/Allopurinol	6 (3.0)	2 (3.0)	4 (3.7)	-	0.85

Values are the number (and % within this stratum) of patients ever using drugs from this class within the first year of follow-up. p comparing the three stratification groups using Chi square test or Fischer exact test.

During the first year, in 62/206 patients (30.1%) treatment remained limited to NSAIDs, most often in group 1 ($p < 0.01$). IACs were (also) administered to 93/206 (45.1%), mainly in group 2 and 3 ($p < 0.01$). Three patients (1.5%) underwent Yttrium radiosynovectomy, all in group 2. CsDMARDs were (also) prescribed in 28/206 patients (13.6%) and 2/206 patients (<1%) subsequently received a bdMARD. Prednisone was prescribed in 11/206 patients (5.4%). DMARD therapy was prescribed most frequently in group 3 ($p < 0.01$) as was prednisone ($p=0.20$). ABs were prescribed in 23/206 patients (11.2%), when a diagnosis of Borrelia or other bacterial arthritis was made or suspected, and 6/206 patients (3.0%) received with colchicine and/or allopurinol (NS between the groups) (table 2).

Conclusion: Of 206 consecutive patients with undifferentiated arthritis limited to the knee(s) the majority was in remission after 12 months. Progression to arthritis in other joints was relatively rare. Routinely acquired baseline characteristics could not completely predict the disease course at presentation and initial treatment choices suggest that physicians could not either. To timely start appropriate treatment, apart from effective treatment options, more research is needed to identify disease characteristics that predict chronicity or progression and identify patients that could profit from early more effective therapy.

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