Increased Cardiovascular Disease in Patients with Inflammatory Arthritis in Primary Care: A Cross-sectional Observation

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ABSTRACT. ***Objective.*** To compare the prevalence of cardiovascular disease (CVD) in patients with inflammatory arthritis and control subjects registered in primary care.

Methods. Conditional logistic regression analyses were used to compare the CVD prevalence in patients and controls, aged 50–75 years.

Results. Overall, the CVD prevalence was 66.1 per 1000 patients in inflammatory arthritis and 37.3 per 1000 patients in controls, resulting in an odds ratio of 1.83 (95% confidence interval 1.33–2.51).

Conclusion. Inflammatory arthritis patients registered in primary care are associated with an increased cardiovascular burden, which emphasizes the need for cardiovascular risk management in the primary care setting. (J Rheumatol First Release Aug 1 2009; doi:10.3899/jrheum.090010)

Key Indexing Terms:
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Numerous studies have illustrated an excessive risk of cardiovascular mortality and morbidity in patients with inflammatory arthritis[1,2]. In addition to traditional cardiovascular risk factors, persistent inflammation and a genetic component are considered of major importance in the development of the accelerated atherogenesis observed in patients with inflammatory arthritis[3,4]. The true magnitude of the cardiovascular burden in inflammatory arthritis, however, is unclear, as outcomes of studies assessing cardiovascular disease (CVD) prevalence and incidence are difficult to compare due to differences in study design and study population[5]. In general, most studies are performed in clinic and only a minority in community-based settings. The actual cardiovascular burden might be overestimated when CVD rates are obtained from clinic-based cohorts, as inclusion of patients with inflammatory arthritis with a more severe disease may falsely inflate the CVD rate. Hence, observations obtained from a community-based cohort, including arthritis patients with a broader spectrum of disease severity, may provide a more accurate CVD estimate.

In The Netherlands, general practitioners (GP) have a gatekeeper role for access to specialized care. All Dutch inhabitants are listed with a general practice, and generally the GP is the first professional to be consulted for health problems. According to the guidelines of the Dutch College of General Practitioners, GP are expected to record diagnostic information from patients in electronic medical records (EMR) using the International Classification of Primary Care (ICPC)[6,7].

The objective of our study was to ascertain the CVD prevalence in a representative population of patients with inflammatory arthritis and to compare it with the CVD prevalence in control subjects using data from EMR of GP.

MATERIALS AND METHODS

Data were used from the Netherlands Information Network of General Practice (LINH). These data were retrieved from EMR kept by a representative sample of 96 general practices with 360,000 registered patients in 2006. Data include information on consultations, morbidity, prescriptions, and referrals to other healthcare professionals. The patients as well as general practices are representative for the Dutch population[8,9]. Only individuals between 50 and 75 years of age were included in our study, as patients under age 50 have a lower probability of having inflammatory arthritis and/or CVD. Practices that recorded data during less than 6 months in 2006 were excluded from the statistical analyses. Morbidity data were derived from consultations and all

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prescriptions issued by the participating practices were used. Diagnoses were recorded using the ICPC-1 coding system[7]. When issuing a prescription, a diagnostic code was recorded, and the selected drug was automatically linked to the ATC coding system (http://www.whocc.no/atcddd/atcsystem.html). This means that patients were classified as "having a CVD event" if they had a cardiovascular event and/or if they needed a prescription linked to a previous cardiovascular event. Inflammatory arthritis was classified according to the ICPC-1 code L88 [rheumatoid arthritis (RA) or ankylosing spondylitis], and CVD was classified by K75 (myocardial infarction), K89 (transient ischemic attack), and/or K90 (stroke/cerebrovascular accident). Individuals were classified with inflammatory arthritis and/or CVD when the diagnosis was recorded in 2006 or in previous years (up to 2004). For each individual with inflammatory arthritis, 4 controls without inflammatory arthritis were randomly selected from the same general practice, matched for age and sex. Conditional logistic regression analyses were used to compare the CVD prevalence in patients with and without inflammatory arthritis. All statistical analyses were performed with SPSS 14.0.

RESULTS

Prevalences of CVD in patients with and without inflammatory arthritis attending primary care were stratified by age and sex (Table 1).

Prevalences were found to be higher for patients with inflammatory arthritis in all strata, except in 60 to 64-year-old men and women. Odds ratios (OR) for female patients with inflammatory arthritis tended to be somewhat higher compared with male patients. Overall, the CVD prevalence was 66.1 per 1000 in patients with inflammatory arthritis and 37.3 per 1000 in control subjects, resulting in an OR of 1.83 [95% confidence interval (CI) 1.33–2.51]. In addition, the OR for myocardial infarction was 1.57 (95% CI 0.88–2.81), for transient ischemic attack 2.13 (95% CI 1.23–3.68), and for stroke/cerebrovascular events 1.72 (95% CI 1.07–2.76).

DISCUSSION

The main finding of our observational study was that patients with inflammatory arthritis attending GP have an almost 2-fold increased risk of prevalent CVD compared with control subjects. This observation further strengthens the observed association between inflammatory arthritis and CVD[10,11]. The absolute prevalence of CVD previously reported in a Dutch cohort study with RA patients, however, was higher, which might be due to broader definitions used for CVD, inclusion of only RA patients, or differences in disease severity[12]. In terms of clinical implications, our data underscore the importance of primary cardiovascular prevention strategies in every patient with inflammatory arthritis[13,14]. Investigations on comorbidities in patients with inflammatory arthritis that use data from GP are scarce. Data from EMR of GP, however, can provide valuable information regarding comorbidities and healthcare utilization by patients with rheumatic diseases. GP systematically collect information about morbidity, prescriptions, and referrals, often with a very long followup period. In addition, patients attending GP probably represent average inflammatory arthritis patients better than those attending clinical settings, as the latter are more likely to have a severe disease. EMR that are used in the Dutch primary care setting, however, are based on a different coding system, i.e., ICPC instead of ICD (*International Classification of Diseases*) in clinical settings[15]. Hence, it is important to validate the ICPC system to allow us to distinguish patients with RA and ankylosing spondylitis from other types of rheumatic disease.

Exposure (inflammatory arthritis) and outcome (CVD) are ascertained at the same time, which hampered our investigation of why inflammatory arthritis is associated with a higher prevalence of CVD. In addition, no information was available regarding other comorbid conditions, making adjustment for these potential confounders not possible.

Table 1. Characteristics of patients and controls and prevalence of cardiovascular disease (CVD).

	Patients			Controls				
	No. with CVD	Total no. of Persons	Prevalence per 1000	No. with CVD	Total no. of Persons	Prevalence per 1000	OR (95% CI)	p
Male								
50–59	4	154	26.0	12	616	19.5	1.34 (0.43–4.22)	0.61
60–64	3	63	47.6	12	252	47.6	1.00 (0.27–3.66)	1.00
65–69	9	62	145.2	14	248	56.5	2.84 (1.17–6.90)	0.02
70–75	9	56	160.7	28	224	125.0	1.34 (0.59–3.03)	0.50
Total	25	335	74.6	66	1340	49.3	1.56 (0.97–2.51)	0.07
Female								
50–59	6	215	27.9	6	860	7.0	4.09 (1.30–12.80)	< 0.01
60–64	2	109	18.3	13	436	29.8	0.61 (0.14–2.74)	0.51
65–69	10	84	119.0	14	336	41.7	3.11 (1.33–7.27)	< 0.01
70–75	15	134	111.9	32	536	59.7	1.99 (1.04–3.78)	0.03
Total	33	542	60.9	65	2168	30.0	2.10 (1.37–3.22)	< 0.01
Total	58	877	66.1	131	3508	37.3	1.83 (1.33–2.51)	< 0.01

Despite these limitations, the simple conclusion that patients with inflammatory arthritis who are registered for primary care are associated with higher CVD prevalence is important. Based on available evidence, we argue that inflammation either directly or indirectly augments the cardiovascular risk[16], but obviously more research is warranted to better understand mechanisms leading to the increased cardiovascular burden in this population. Finally, it should be noted that inclusion of only non-fatal CVD might have caused an underestimation of the true CVD prevalence in patients with inflammatory arthritis, as previous investigations reveal that they are more likely to die after a cardiovascular event[17].

Dutch patients with inflammatory arthritis registered in primary care are associated with an increased cardiovascular burden. This observation further emphasizes the importance of cardiovascular risk assessment and adequate CVD management in all patients with inflammatory arthritis.

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