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Prevalence of chronic diseases at the onset of inflammatory arthritis: a population-based study

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Objective. Little is known about the presence of chronic morbidity in inflammatory arthritis (IA) patients at disease onset. Previous studies have been mainly performed in established IA patients or they focus on isolated co-morbid diseases. Our aim was to determine the prevalence of chronic diseases at the onset of IA and to determine whether this is different from the number that one might expect based on age and sex.

Patients and methods. A nested case–control study from 2001 to 2010 using data from patient electronic medical records in general practice. Totally, 3354 patients with newly diagnosed IA were included. Each patient was matched on age, sex and general practice with two control patients. In total, 121 different chronic diseases were studied.

Results. In total, 70% of the IA patients had at least one chronic disease at the onset of IA, compared with 59% of the control patients ($P < 0.001$). The highest prevalence in IA patients was found for cardiovascular diseases (35%), musculoskeletal diseases (27%) and neurological diseases (22%). Compared with the control patients, patients with IA had the highest increased risk for musculoskeletal diseases [odds ratio, OR = 1.7 (95% confidence interval: 1.6–19)] and for neurological diseases [OR = 1.6 (1.4–1.7)] at the onset of IA.

Conclusion. At the onset of IA, nearly three-quarters of patients with IA had at least one other chronic disease. Since multi-morbidity affects treatment and outcome of the IA patient, these diseases should be taken into account when treating IA patients.

INTRODUCTION

Inflammatory arthritis (IA) is a term used to describe a group of autoimmune diseases that involve inflammation in the joints, including rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis. IA is a common rheumatic disease with a prevalence between 0.5% and 1.1%.1–3 Like many patients with other chronic diseases, the vast majority of patients with IA also have other chronic diseases.4–7 Co-morbidity can be developed independently from IA, but it can also be the result of IA treatment, common underlying causes and/or shared risk factors. It is known that, among others, the incidence of cardiovascular diseases (CVDs),8 cancer, pulmonary disease, dementia, gastrointestinal disease and osteoporosis9 is increased in IA patients.

Additional chronic diseases result in more disability, increased mortality risk and diminished health-related quality of life for the patient.10 Furthermore, multimorbidity affects treatment and outcome of the patient because it is more difficult to apply guidelines in patients with multiple chronic diseases. Therefore, it is important for health care providers to have a clear overview of the number and type of chronic diseases present at onset of IA. However, little is known about morbidity of IA patients at onset of disease. Most studies are performed in established IA patients6,7,9,11–13 or they focus on isolated co-morbid diseases.14–17 Only one small study (n = 78) reported the presence of co-morbidity at the onset of IA and found that CVDs (16%) and malignancies (11%) were the most frequent co-morbidities.18

In the Netherlands, GPs 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 GPs, GPs are expected to record diagnostic information from their patients routinely in electronic medical records (EMRs), using the International Classification of Primary Care (ICPC).19 This makes EMRs of GPs very useful to study the presence of chronic diseases at onset of IA, because GPs have a complete record of all morbidities, using a uniform methodology. In this study, we answer the following research questions: (i) Which chronic diseases are most prevalent in patients newly diagnosed with IA and (ii) Is the prevalence of chronic diseases increased in IA patients compared with a group of age- and sex-matched control patients without IA?

PATIENTS AND METHODS

Study population

Data were used from the Netherlands Information Network of General Practice (LINH) (www.linh.nl.20 LINH is a dynamic network of, on average, 83 general practices with ~335 000 registered patients, which was started in 1994. The patients and general practices are representative for the Dutch population.20 Data were retrieved from EMRs, including information on consultations, morbidity, prescriptions and referrals to other health care professionals. Diagnoses were recorded by the GPs using the ICPC-1 coding system.19,21 We used data from the period 2001–10.

Case definition

Patients with IA are recorded by their GP with the diagnostic ICPC code L88: 'Rheumatoid arthritis and related diseases'. A selection purely based on this code could contain non-IA patients; therefore, we applied an algorithm to filter non-IA patients, which is described in more detail in Nielen et al.22 This algorithm is a combination of prescriptions, frequent GP visits due to L88 problems and age and it increases the validity of the elected patient group from 71% to 78%. All patients from the LINH network of age 30 years or older with a registered L88 code were selected because patients of age <30 years have lower probability of having IA and co-morbid chronic diseases. To ensure that we are including only newly diagnosed cases, patients with an L88 code within 365 days from start of registration were excluded from this study. This threshold is based on the assumption that all IA patients will go to their GP at least once every year for IA-related complaints. To be able to apply the algorithm, only patients with a minimum of 90 days of follow-up were included.

Control group

To determine whether patients at the onset of IA have more chronic diseases than expected based on age and sex, we matched all IA patients with two control patients (non-IA patients, i.e. patients without ICPC code L88) on age (time frame of 5 years) and sex at a ratio of 1:2. Control patients were registered in the same general practice as the matched IA patient and without a recorded ICPC code L88 in all available data (2001–10).The date of diagnosis of IA was taken as the date of inclusion of the matched control. In line with the selection of IA patients, control patients should have at least a minimum of 90 days of follow-up as well.

Chronic diseases and clusters

Based on a study of O'Halloran et al.,23 121 chronic diseases were selected (see online Supplementary material Appendix 1). Chronic conditions, according to O'Halloran et al.,23 were defined as diseases with a duration of at least 6 months, poor prognosis, pattern of recurrence or deterioration and which produce sequelae that affect the individual's quality of life. All ICPC codes were categorized within main disease groups based on the ICPC chapters. Furthermore, certain ICPC codes were combined into diagnostic clusters. An overview of the 15 clusters, with

combined ICPC codes is presented in online Supplementary material Appendix 2. In the results section, only chronic diseases with a prevalence of at least 2% in cases or controls are presented.

Analysis

For all main disease groups, diagnostic clusters and chronic diseases, prevalences were calculated. The ICPC codes for gout (T92), psoriasis (S91) and osteoarthritis (OA) (diagnostic cluster) were excluded from the analysis because these diseases may be interrelated to IA. Conditional logistic regression analyses were used to compare the prevalences of chronic diseases between cases and controls. Odds ratios (ORs) and 95% confidence intervals (CIs) were corrected for age. Additionally, it was tested whether age is an effect modifier. For clarity, the term odds ratio is referred to as 'risk'.All statistical analyses were performed with Stata/ SE 11.2 (StataCorp, College Station, TX, USA).

The study was carried out according to Dutch legislation on privacy. The privacy regulation of the study was approved by the Dutch Data Protection Authority. According to Dutch legislation, neither obtaining informed consent nor approval by a medical ethics committee was obligatory for observational studies. In concordance with the GPs, EMRs were reviewed in the participating practices and data were analysed anonymously.

RESULTS

In total, 3354 patients with IA and 6708 matched controls were included. Baseline characteristics of the cases and controls are shown in Table 1. Nearly two-thirds of the patients were female, and the mean age was 55 years (SD = 15).

At IA onset, 70% of the patients had at least one chronic disease compared with 59% of the controls. One-quarter of the IA patients had one chronic disease at the onset of IA and 50% had two or more chronic diseases at onset. Moreover, 5% of the IA patients had six or more chronic diseases. The number of chronic diseases was statistically significant different between cases and controls.

Table 2 shows only chronic diseases with a prevalence of at least 2% in cases or controls. The most prevalent main disease group was CVDs, with a prevalence of 35% in cases and 30% in control .The prevalences of the other main disease groups varied between 6% and 35% in IA patients and between 4% and 30% in control patients.
All main disease groups were increased in patients with IA compared with the controls (OR: 1.2 to 1.7). Within the CVD group, hypertension was the most prevalent chronic disease in both patients and controls (22% versus 19%). Though the highest increased risk was found for phlebitis/thrombophlebitis ($OR_{adjusted}$ = 1.6; Table 2).

For chronic musculoskeletal diseases, the prevalence was 27%, with diseases of the spinal cord being the most prevalent disease. The highest risk was found for shoulder syndrome [adjusted OR = 1.9 (95% CI: 1.7–2.3)]. Moreover, an increased risk for IA patients was found for respiratory diseases (OR = 1.5), with significantly increased ORs for both asthma and chronic obstructive pulmonary disease (COPD). Furthermore, an increased risk was found for carpal tunnel syndrome (OR = 2.8) and anaemia (OR = 1.9).

There was only a significant effect modification of age on the risk of endocrine diseases (P < 0.001), psychological diseases (P = 0.04) and heart failure (P = 0.033). The largest effect was found for the risk on endocrine diseases, e.g. the risk for patients aged <55 years was [OR = 1.7 (95% CI: 1.3–2.1); P value <0.001] and the risk for patients aged 55 years or older was OR = 1.0 (95% CI: 0.8–1.1; P value = 0.672). For psychological diseases and heart failure, the effect was small.

DISCUSSION

Patients with inflammatory arthritis have more chronic diseases at the onset of IA than can be expected based on age and sex: 70% of the patients with IA had at least one chronic disease compared with only 59% in age- and sexmatched controls. Additionally, a larger proportion (8%) of the cases had six or more different chronic diseases compared with controls (5%).The most prevalent chronic diseases at the time of diagnosis are cardiovascular, musculoskeletal, neurological and endocrine diseases.

Strengths and limitations

Co-morbidity studies in IA patients are scarce and are often limited to isolated co-morbid diseases. In contrast, our study design made it possible to determine the presence of 121 chronic diseases at onset of IA in one study population. The GP is the first professional to be consulted for health problems and is the only health care professional with a full view of the patients' lifetime health status. Patients between the ages of 30 and 80 rarely change GP24 and therefore, data from EMRs are informative about both the period before and after IA diagnosis.
Additionally GPs are stimulated to have a complete registration because EMR data are used for billing.

This study has also some limitations. After applying our algorithm, some patients still could have had a misclassification of IA. This could result in an underestimation of the reported ORs. Additionally, some newly diagnosed IA patients may be missed because it was chosen to exclude all patients with an L88 ICPC code within 365 days after start of registration.

Comparison with existing literature

To our knowledge, so far, only one study 18 reported the percentage of chronic diseases at the onset of IA, namely 43%, whereas we found a much higher percentage of 70%. The lower percentage in the study of Kapetanovic et al.18 could be explained by the fact that they used self-reported data, which were verified in rheumatology medical records, whereas in our study, the presence of chronic diseases was based on EMRs kept by GPs. Our data might be more complete because the GP is the coordinating health care provider for patients in the Netherlands and keeps the complete medical record, sometimes for many years.
An increased prevalence of CVD in established IA patients compared with the same in the non-rheumatic population has been reported before.9,16 At the time of diagnosis, a study reported CVD in 30% of the patients,18 which is in line with our study. Of the neurological diseases, carpal tunnel syndrome is reported as a common extra-articular manifestation of IA.25–27 In patients with an average IA duration of 10 years, it was found in 7–36% of the study population.25,26 We found a prevalence of 4%, with an OR = 2.8, compared with controls. So, apparently the carpal tunnel syndrome is not only an extra-articular manifestation but is also present in many patients at the time of IA diagnosis, which might be due to synovitis of the wrist. Also for other diagnoses (e.g. osteoporosis, anaemia, depression and hypothyroidism), we found an increased prevalence at disease onset, whereas other studies only reported increased prevalence after diagnosis of IA.6,9,11,16,28,29
We also found an increased prevalence for two chronic respiratory diseases at the moment of IA diagnosis: asthma and COPD (8% and 6%, respectively). Both COPD and IA have smoking as a common risk factor and both diseases are associated with inflammation. Moreover, there is mounting evidence that there may be an autoimmune component to COPD.30 Patients with an autoimmune disorder may be susceptible to other autoimmune diseases like IA.

Implications

We identified newly diagnosed IA patients from a representative sample of patients from general practices and found that more than two-thirds of patients with IA had one or more chronic diseases at the onset of IA. This implies that chronic co-morbidity is more a rule than the exception at onset of IA. Since multi-morbidity affects treatment and outcome of the IA patient, health care professionals should be aware of the presence of other chronic diseases at the moment of diagnosis. Despite the fact that IA patients are mainly treated in specialized care, the GP can play an important role in the management of newly diagnosed IA patients with other chronic diseases at disease onset. GPs have a clear overview of the number and types of chronic diseases and should share this information with a medical specialist when they refer patients to specialized care.

Conclusion

Patients with inflammatory arthritis have more chronic diseases at onset of IA than one might expect based on age and sex. The most prevalent chronic diseases at the time of diagnosis are CVDs and musculoskeletal, neurological and endocrine diseases. Because multi-morbidity affects treatment and outcome of the IA patient, these diseases should be taken into account when treating IA patients.

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TABLES

TABLE 1 *Baseline characteristics*

	Patients with IA	Matched controls
N (ratio 1:2)	3354	6708
Sex		
Female (%)	63.7	63.7
Age, years		
Mean (SD)	55 (15)	55 (15)
Time from start of registration until inclusion, years		
Median (interquartile range)	2.8 (1.4–4.8)	2.8 (1.4–4.8)
Year of inclusion (%)		
2001	<1	<1
2002	16	16
2003	12	12
2004	9	9
2005	10	10
2006	10	10
2007	13	13
2008	11	11
2009	11	11
2010	<1	<1
Number of chronic diseases at inclusion (%)[a]		
0	30	41
1	25	24
2	18	15
3	11	9
4	7	5
5	4	3
6 or more	5	3

IA, inflammatory arthritis; SD, standard deviation.

[a]At inclusion, cases already have one chronic disease, inflammatory arthritis, whereas controls have no chronic disease. One chronic disease for cases means one in addition to inflammatory arthritis.

TABLE 2 *Percentage of cases and controls with different chronic diseases at diagnosis, with a prevalence of at least 2% in cases or controls*[a]

Main disease group[b] and diagnosis	Cases (%), $n = 3354$	Control (%), $n = 6708$	Crude OR	95% CI	Adjusted OR[c]	95% CI	*P*-value-adjusted OR
Cardiovascular disease	**35**	**30**	**1.4**	**1.2–1.5**	**1.4**	**1.3–1.6**	**<0.001**
Phlebitis/ thrombophlebitis	2	1	1.5	1.1–2.1	1.6	1.1–2.2	0.006
Ischaemic heart disease	6	5	1.4	1.2–1.7	1.4	1.2–1.7	<0.001
Heart failure	3	2	1.3	1.0–1.8	1.4	1.1–1.9	0.018
Varicose veins of leg	4	3	1.3	1.0–1.6	1.3	1.0–1.6	0.018
Hypertension	22	19	1.2	1.1–1.4	1.2	1.1–1.4	<0.001
Musculoskeletal disease[d]	**27**	**18**	**1.7**	**1.6–1.9**	**1.7**	**1.6–1.9**	**<0.001**
Shoulder syndrome	12	6	2.0	1.7–2.3	1.9	1.7–2.3	<0.001
Spinal cord	13	9	1.5	1.4–1.8	1.5	1.3–1.8	<0.001
Tennis elbow	4	3	1.4	1.1–1.8	1.4	1.1–1.8	0.004
Osteoporosis	3	2	1.4	1.1–1.9	1.4	1.0–1.8	0.023
Respiratory disease	**12**	**8**	**1.5**	**1.3–1.8**	**1.5**	**1.3–1.8**	**<0.001**
Asthma	8	5	1.7	1.4–2.0	1.7	1.4–2.0	<0.001
COPD	6	4	1.4	1.2–1.7	1.4	1.2–1.7	0.001
Neurological disease	**22**	**15**	**1.6**	**1.4–1.8**	**1.6**	**1.4–1.7**	**<0.001**
Carpal tunnel syndrome	4	2	2.9	2.2–3.7	2.8	2.2–3.7	<0.001
Endocrine disease[e]	**17**	**15**	**1.1**	**1.0–1.3**	**1.2**	**1.0–1.3**	**0.022**
Hypothyroidism, myxoedema	3	2	1.7	1.3–2.2	1.7	1.3–2.2	<0.001
Psychological disease	**13**	**11**	**1.2**	**1.0–1.4**	**1.2**	**1.0–1.4**	**0.008**
Depressive disorder	6	5	1.2	1.0–1.4	1.2	1.0–1.4	0.048
Blood and blood-forming organs	**6**	**4**	**1.6**	**1.1–1.7**	**1.6**	**1.2–1.7**	**0.001**
Anaemia	3	1	1.9	1.4–2.6	1.9	1.4–2.6	<0.001
Digestive disorders	**7**	**5**	**1.4**	**1.2–1.7**	**1.4**	**1.2–1.7**	**<0.001**
Other diseases							
Eczema	6	5	1.3	1.1–1.6	1.3	1.1–1.6	0.005
Vertiginous syndrome	4	3	1.3	1.0–1.7	1.3	1.0–1.6	0.032

OR, odds ratio, CI, confidence interval; COPD, chronic obstructive pulmonary disease. The bold values are the values of the main disease groups.
[a]Patients may have several chronic diseases.
[b]Diagnoses included are listed in online supplementary material. The ICPC codes regarding cancer were not included in the main disease groups but combined within the cluster Cancer.
[c]Adjusted for age.
[d]Cluster osteoarthritis excluded.
[e]Gout excluded.