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Original article

Clinically suspect arthralgia and rheumatoid arthritis: patients' perceptions of illness

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ABSTRACT

Objectives. – Clinically suspect arthralgia (CSA) is an at-risk stage of rheumatoid arthritis (RA), in which patients experience symptoms and physical limitations. Perceptions of CSA-patients have remained largely unknown. Therefore, we aimed to map perceptions of CSA-patients and compare these to RA-patients. Additionally, we studied changes in perceptions in CSA over time.
Methods. – Three hundred and ninety-nine consecutively included CSA-patients from the Leiden and Rotterdam CSA-cohorts and 100 recently diagnosed RA-patients from the Leiden Early Arthritis Clinic were included. Patients' illness perceptions (IP) were assessed using the Brief Illness Perception Questionnaire (BIPQ), consisting of 8 questions (scale 0–10; higher score indicating more negative IP) covering cognitive, emotional and comprehensibility domains, and one open question about causes of disease. IP were measured at baseline in both populations and during 2 years follow-up in the CSA-cohorts.
Results. – Total BIPQ-scores were comparable at CSA-presentation and RA-diagnosis (40 ± 11 and 40 ± 10; range 0–80). Comparing dimensions separately revealed that CSA-patients were less worried about physical complaints compared to RA-patients. However, CSA-patients were more negative about expected treatment-effect on symptoms. IP over time in CSA improved in patients without development of clinical arthritis (from 38 ± 11 to 34 ± 14; $P = 0.005$) but remained similar in CSA-patients who progressed to arthritis/RA (mean 40 at both timepoints). CSA-patients mainly perceived physical strain and heredity as causes of their complaints.
Conclusions. – Although CSA-patients have not developed clinical arthritis, illness perceptions at CSA-presentation and RA-diagnosis are equally severe. Knowledge on worries and expectations may contribute to improving patient-contact and care in patients at risk of RA.

1. Introduction

The rheumatology field is increasingly focused on individuals at risk of rheumatoid arthritis (RA) at a stage when arthritis is not yet apparent. This stage is also known as clinically suspect arthralgia (CSA) [1]. Although clinically apparent arthritis is (still) absent at CSA-presentation, the complaints have a large impact on patients' lives, including work loss and physical impairments [2,3]. These physical complaints can pose a psychological burden and patients presumably build a pattern of beliefs about their condition [4].

Holistic approaches to illnesses recognize that patients' experiences are formed by biological, psychological and social factors. One set of psychological factors are patients' illness perceptions. Illness perceptions are cognitive and emotional representations of an illness [5]. In RA-patients, negative illness perceptions have been associated with worse patient reported outcomes, quality of life and non-adherence to therapy, indicating their relevance and importance [6,7]. Qualitative studies in (asymptomatic) at-risk individuals have studied perceptions and attitudes regarding predictive testing, lifestyle modifications and preventive approaches [8–10]. An explorative focus group study with CSA-patients described that perceptions regarding personal control, concern and

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complaints were frequently observed during the discussion [11]. However, the study population was small and no quantitative data on illness perceptions were reported, leaving the interpretation of illness perceptions in CSA and the comparison with RA hampered.

Gaining insights in the thoughts and expectations of patients with CSA may contribute to improving communication and care. Therefore, we studied illness perceptions of CSA-patients and compared it to those of RA-patients at the time of diagnosis. Additionally, we explored how illness perceptions changed over time in CSA-patients who did and did not progress to RA.

2. Methods

2.1. CSA-patients

We studied CSA-patients who were consecutively included in the Leiden and Rotterdam CSA-cohorts in the Netherlands. The Leiden and Rotterdam CSA-cohorts are inception cohorts that started in 2012 and 2017 respectively, and have completely comparable inclusion-criteria and follow-up schemes (Supplementary S1). Both CSA-cohorts have been described earlier [12,13]. In short, these cohorts include patients with arthralgia of the small joints that is considered clinically suspicious for progression to RA according to the expertise of the rheumatologist. Patients were not included in the CSA-cohorts if clinically apparent arthritis was present or if the rheumatologist considered another explanation for the arthralgia (e.g. osteoarthritis or fibromyalgia) more likely than imminent RA. For the current study, all CSA-patients from Rotterdam were included and those included after August 2017 onwards from Leiden, because questionnaires on illness perceptions were then implemented. Written informed consent was obtained from all CSA-patients.

2.2. Outcome in CSA-cohorts

Patients in the CSA-cohorts were followed for two years until the development of arthritis at physical examination by the rheumatologist, which entailed the main outcome. Patients were seen at 4, 12 and 24 months after baseline, and in between these visits if patients perceived more symptoms to verify whether they had developed clinical arthritis. During follow-up, CSA-patients were not treated with disease-modifying antirheumatic drugs (DMARDs), including glucocorticoids.

2.3. RA-patients

Additionally, newly diagnosed RA-patients who fulfilled the 2010-criteria for RA were obtained from the Leiden Early Arthritis Clinic (EAC) [14]. The EAC consecutively includes patients with arthritis at physical examination by the rheumatologist and a symptom duration of < 2 years. Patients included from May 2019 onwards were evaluated in the present study, because questionnaires on patients' illness perceptions were then implemented. Written informed consent was obtained from all RA-patients.

2.4. Illness perceptions

Patients' illness perceptions were studied using the Brief Illness Perception Questionnaire (BIPQ) [5]. The BIPQ consists of 9 dimensions: 8 questions covering cognitive, emotional and comprehensibility domains (scale 0–10 per question, with higher scores indicating more negative illness perceptions) and one open question about causes of disease according to patients. The cognitive domain of the BIPQ consists of five questions about consequences on life (Item 1), expected duration of complaints (Item 2), personal control (Item 3), expected effect from treatment (Item 4), and severity of experienced symptoms (Item 5). The emotional domain of the BIPQ consists of two questions about concerns (Item 6) and emotional impact (Item 8). Additionally, one item of the BIPQ assesses illness comprehensibility (Item 7). Total BIPQ-score consists of the sum of the 8 questions and has a range of 0–80. The BIPQ is shown in Supplementary S2. There are no validated cut-off values for BIPQ-scores, but the interpretation of the BIPQ entails that higher scores imply a more negative endorsement of the illness [5].

The BIPQ was obtained at first presentation in the CSA-cohorts and the EAC, and during follow-up visits in the CSA-cohorts.

2.5. Sensitivity analysis in CSA-patients with RA-development

Analyses were repeated with RA-development as outcome, defined as clinically apparent arthritis plus fulfilment of 2010- or 1987-criteria for RA, or a clinical diagnosis with DMARD-treatment.

2.6. Statistical analyses

Mean BIPQ-scores were compared between patients at CSA-presentation and RA-diagnosis using Student's *t*-test. Paired-sample *t*-tests were used to compare BIPQ-scores at CSA-presentation with scores after 24 months for CSA-patients without development of clinically apparent arthritis. For patients who developed arthritis, score at CSA-presentation were compared with score at arthritis-development. Standard deviation (SD) or interquartile range (IQR) were computed where appropriate. All analyses were performed using SPSS v25 and two-sided *P*-values of < 0.05 were considered statistically significant.

3. Results

3.1. Patient characteristics

In total, 399/471 CSA-patients and 100/112 RA-patients had completed the BIPQ and were included in the current study. Baseline characteristics were comparable for patients with and without BIPQ-data (Supplementary S3). Patient characteristics at CSA-presentation and RA-diagnosis are shown in Table 1. The majority of CSA-patients (77%) was female and the mean ± SD age was 45 ± 13 years. 24% had a family history of RA. In recently diagnosed RA-patients, 63% was female, mean age was 62 ± 12 years, and 19% had a family history of RA. Median (IQR) tender joint count-68 (TJC68) and disability score according to the Health Assessment Questionnaire (HAQ) in CSA- and RA-patients were: 4 (1–7) vs. 9 (4–13) and 0.5 (0.1–1.0) vs. 0.9 (0.5–1.3), respectively. During a median follow-up of 20 (9–25) months in the CSA-cohorts, 45 patients developed clinical arthritis.

3.2. Illness perceptions at CSA-presentation and RA-diagnosis

At baseline, mean total BIPQ-score was 40 ± 11 for CSA-patients, and also 40 ± 10 for RA-patients ($P = 0.70$; Fig. 1). Comparing the dimensions separately revealed that CSA-patients were less worried on the cognitive domain about their physical complaints compared to RA-patients: consequences on life (4.1 ± 2.5 vs 5.3 ± 2.3, $P < 0001$; item 1) and severity of experienced symptoms (4.6 ± 2.3 vs. 5.6 ± 2.2, $P < 0.001$; item 5; Fig. 2 and Supplementary S4). However, CSA-patients were more negative than RA-patients on the cognitive domain about expected treatment-effect on symptoms (5.0 ± 2.5 vs. 3.7 ± 1.9, $P < 0.001$; item 4). No differences between CSA- and RA-patients were seen in the BIPQ-domains covering emotional representations and comprehensibility. There

Table 1
Patient characteristics at CSA-presentation and RA-diagnosis.

	CSA-patients (n = 399)	RA-patients at diagnosis (n = 100)
Sex, female	307 (77)	63 (63)
Age in years	45 ± 13	62 ± 12
Family history of RA	95 (24)	19 (19)
Symptom duration in days	127 (71–303)	84 (56–182)
TJC68	4 (1–7)	9 (4–13)
HAQ	0.5 (0.1–1.0)	0.9 (0.5–1.3)
CIS8R fatigue	35 ± 12	34 ± 12
HADS		
Anxiety	5.0 (3.0–7.0)	4.0 (2.0–7.0)
Depression	3.0 (1.0–6.0)	3.0 (2.0–6.0)
Smoking, past or current	205 (51)	64 (64)
BMI	27.2 ± 5.2	27.2 ± 4.9
ACPA-positive	63 (16)	55 (55)
RF-positive	87 (22)	60 (60)
ACPA- and RF-positive	48 (12)	42 (42)
CRP increased (≥ 5 mg/L)	77 (19)	64 (64)
ESR increased[a]	58 (15)	53 (53)

Data are n (%), mean ± SD or median (IQR). ACPA: anti-citrullinated protein antibody; BMI: body mass index; CIS: checklist for individual strength; CRP: C-reactive protein; CSA: clinically suspect arthralgia; ESR: erythrocyte sedimentation rate; HADS: Hospital Anxiety and Depression Scale; HAQ: Health Assessment Questionnaire Disability-Index; IQR: interquartile range; RA: rheumatoid arthritis; RF: rheumatoid factor; SD: standard deviation; TJC: tender joint count.

[a] ESR was considered elevated with a reference for age and sex (< 50 years: male > 15 mm/h, female > 20 mm/h; > 50 years: male > 20 mm/h, female > 30 mm/h).

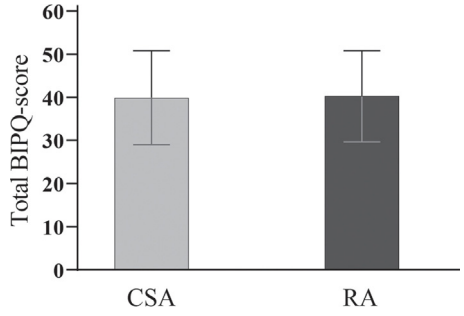

Fig. 1. Illness perceptions in patients with CSA and RA at first presentation are equally severe. Illness perceptions are shown as mean total BIPQ-scores and SD in patients at presentation with CSA (40 ± 11) and RA (40 ± 10). Higher scores of BIPQ indicate more negative illness perceptions (range 0–80). BIPQ: Brief Illness Perception Questionnaire; CSA: clinically suspect arthralgia; RA: rheumatoid arthritis; SD: standard deviation.

was no difference in total IPQ-score between ACPA-positive and ACPA-negative CSA-patients (38 vs. 40, respectively; P = 0.18).

3.3. Illness perceptions in CSA-patients over time

One hundred and five CSA-patients had repeated BIPQ-data until the end of CSA follow-up (at 24 months or upon arthritis development) and were studied longitudinally. Illness perceptions in CSA-patients without arthritis development improved (total BIPQ-score went from 38 ± 11 to 34 ± 14, P = 0.005, n = 86; Fig. 3). In contrast, illness perceptions in CSA-patients developing arthritis remained similar over time (40 ± 10 at CSA-presentation and 40 ± 9 at arthritis-development, P = 0.98, n = 19; Fig. 3). Additionally, IPQ-score in the CSA-population was not associated with IA-development (HR = 1.0, 95%CI = 0.97–1.03, P = 0.98). Similar results were obtained when analyzed separately for ACPA-positive and ACPA-negative patients.

3.4. Perceived causes of complaints in CSA-patients

To the question about the cause of their complaints, 28% of CSA-patients answered that they did not know (Fig. 4). In patients who answered with a cause, the most frequently mentioned causes were physical strain (19%) and heredity (15%). Lifestyle factors such as overweight and smoking were mentioned by only a small minority of patients (5% and 1%, respectively).

3.5. Sensitivity analysis in CSA-patients with RA-development

91% of patients with clinical arthritis development had a clinical diagnosis of RA and fulfilled the 2010-criteria for RA or had started DMARD-therapy. Serial analysis of illness perceptions in these patients showed that mean BIPQ-score at CSA-presentation was 40 ± 10 and 38 ± 9 at RA-development (P = 0.38, n = 15), and was thus comparable to changes in BIPQ-score in the whole group of patients who developed clinically apparent arthritis.

4. Discussion

Patients with CSA are confronted with symptoms and complaints and are considered at risk of RA-development. As such, this may be an apprehensive phase for patients. Nevertheless, thoughts, beliefs and expectations of CSA-patients have remained largely unknown. We observed that patients' illness perceptions at CSA-presentation were equally severe as illness perceptions in patients at RA-diagnosis. BIPQ-scores over time improved in CSA-patients without arthritis development. On the contrary, CSA-patients developing RA remained similar in severity of illness perceptions. These findings reinforce the psychological burden of CSA and the worries that CSA-patients experience.

Analysis of the BIPQ-dimensions separately showed that CSA-patients were less worried about the consequences and severity of experienced symptoms at presentation with CSA than RA-patients at diagnosis. This is in line with the observed lower TJCs and HAQ-scores in CSA-patients. However, CSA-patients had lower expectations of treatment-effect, compared to RA-patients at diagnosis. This finding was anticipated, as patients in the CSA-cohorts did not have clinical arthritis at presentation and could be treated with e.g. non-steroidal anti-inflammatory drugs (NSAIDs), but were not treated with DMARDs or glucocorticoids. The observed improvement in BIPQ-scores over time in CSA-patients without arthritis development is in line with previous research in CSA showing improvement in symptoms, functional disabilities and subclinical joint-inflammation in those who did not develop arthritis/RA [2,3,15,16].

When asking CSA-patients about perceived causes of their complaints, which is an element of illness perceptions, the most frequent answers were physical strain and heredity. Comparing these results to previous studies is difficult as the performed studies are of qualitative nature and patients were asked about perceived risk factors in only a few studies [8–10]. Additionally, some of the previous studies included at-risk individuals based on having a first-degree relative with RA, which may contribute to heredity being more often reported as risk factor. A large proportion of CSA-patients in our study (19%) reported that physical strain was a cause of their complaints. Interestingly, although not considered as a classical risk factor, previous studies provided clues about workload associating with increased RA-prevalence and with joint-inflammation in at-risk individuals [17,18]. Notably, only a small minority (1%) of CSA-patients considered smoking a cause of their complaints, while a large proportion had smoked (51%). As has recently been shown, smoking confers risk for development of CSA and RA [19]. This discrepancy entails that patient education could

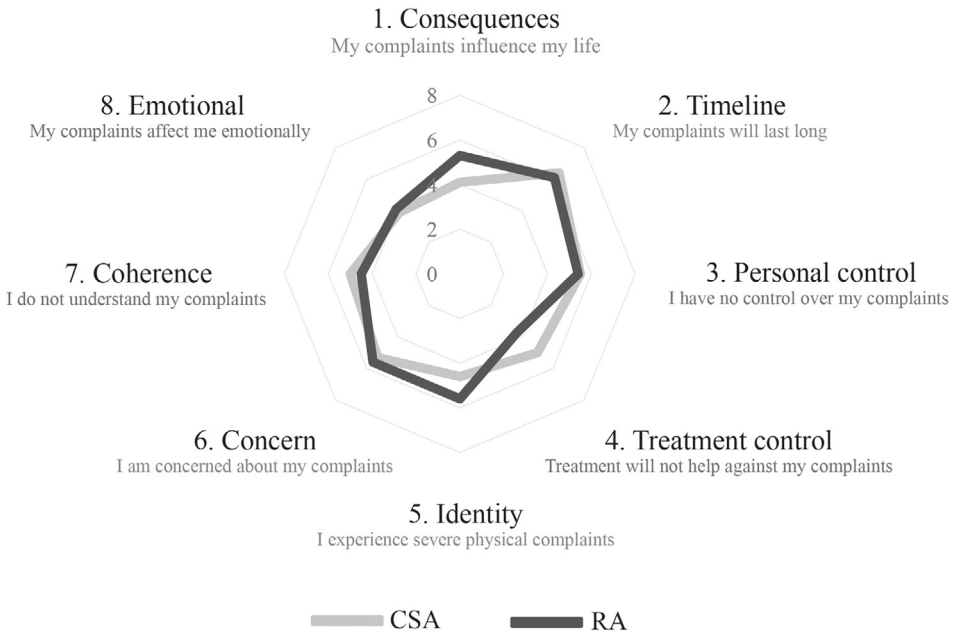

Fig. 2. Dimensions of illness perceptions in patients with CSA and RA at first presentation. Illness perceptions are shown as mean BIPQ-score per dimension of the BIPQ in patients at presentation with CSA or RA. Higher scores indicate more negative illness perceptions. In line with general instructions of the BIPQ, items 3, 4 and 7 were reversely coded to indicate the same interpretation of scores for all illness perceptions (high implying negative endorsement). Scores of the dimensions of illness perceptions are also numerically reported in Supplementary S4. BIPQ: Brief Illness Perception Questionnaire; CSA: clinically suspect arthralgia; RA: rheumatoid arthritis; SD: standard deviation.

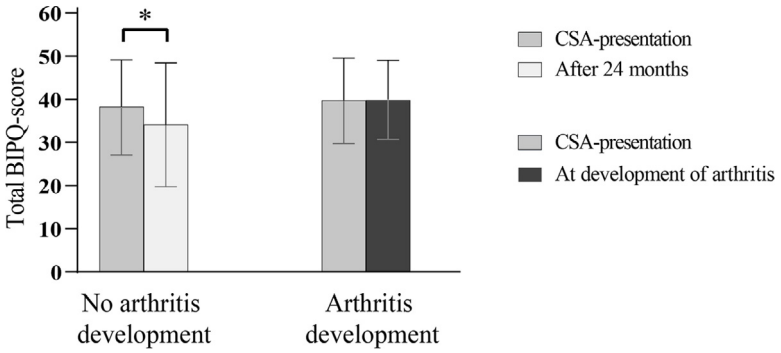

Fig. 3. Change in illness perceptions in CSA-patients, separately for patients without and with future arthritis development. Illness perceptions are shown as mean total BIPQ-scores and SD at baseline and after 24 months in CSA-patients without arthritis development ($n = 86$), and at baseline and arthritis development in CSA-patients progressing to clinically apparent arthritis ($n = 19$). High scores indicate more negative illness perceptions. * Indicate statistically significant change. BIPQ: Brief Illness Perception Questionnaire; CSA: clinically suspect arthralgia; SD: standard deviation.

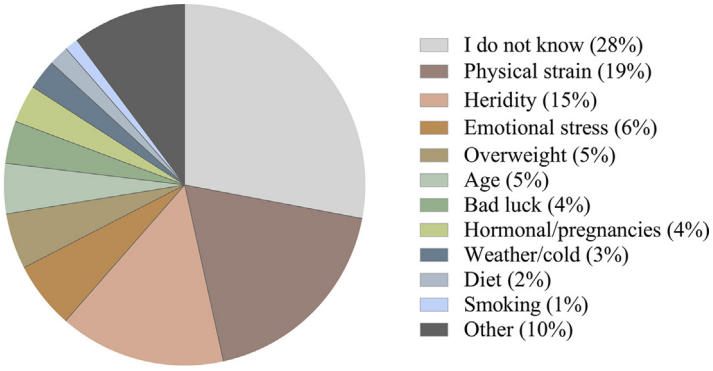

Fig. 4. Causes of complaints according to CSA-patients at presentation with CSA. Causes of complaints according to CSA-patients, derived from the open question of the BIPQ (item 9). Patients were asked to mention the three most important causes of their complaints. All three answers were categorized for the calculation of the percentages of given answers. BIPQ: Brief Illness Perception Questionnaire; CSA: clinically suspect arthralgia.

be improved about the symptomatic at-risk phase of RA, which is a responsibility healthcare professionals could undertake and contribute to.

It could be queried how to quantitively interpret the BIPQ-scores in patients with CSA and RA. Since the BIPQ is about illness perceptions, it is not possible to establish "reference" illness perceptions in the general population. As for comparison with other diseases, mean total BIPQ-scores in e.g. patients with recently acquired spinal cord injuries or patients with psoriasis were 40.9 ± 12.3 and 42.9 ± 10.8, respectively [20,21]. Additionally, one could question

whether the observed changes in BIPQ-scores over time are clinically relevant. No minimal clinical important difference for the BIPQ has been reported, but this could be a topic for future research that could enhance interpretation of longitudinal analyses of BIPQ-scores.

Illness perceptions are known to potentially change over time [4,6]. Although we studied illness perceptions longitudinally and separately for CSA-patients without and with arthritis-development, the number of patients over time was relatively small. As a result, changes in BIPQ-scores per domain separately could not be properly analyzed, which may be considered a limitation of the current study. Nevertheless, to our best knowledge, this study is the first to analyze illness perceptions in a large population of CSA-patients using a validated questionnaire on illness perception. In addition, despite smaller numbers, the BIPQ-score at moment of arthritis development in CSA-patients was comparable to BIPQ-score at RA-diagnosis in a larger group, reinforcing robustness of results.

Although there is a lot of attention for the at-risk phase from an immunological and scientifical perspective, these data emphasize the other side of CSA, namely the patient perspective and the psychological burden. Healthcare professionals encounter these aspects of disease symptomology in daily practice, and these are important to consider in patient care, alongside inflammation. Knowledge on patients' illness perceptions may assist in discussing and recognizing worries and thoughts of CSA-patients. This open and inclusive patient-contact may contribute to improving patient outcomes and satisfaction [22].

In conclusion, illness perceptions in CSA-patients and recently diagnosed RA-patients are equally severe. This indicates that the impact of CSA is considerable, despite not having developed clinically apparent arthritis. Knowledge on concerns and expectations in patient-contact and patient-information may contribute to improving care in patients at risk of RA.

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Disclosure of interest

The authors declare that they have no competing interests.

Ethics

The study was conducted in compliance with the Helsinki Declaration. Written informed consent was obtained from all patients. Research protocols for the Leiden CSA-cohort (P11.210) and the EAC (B19.008) were approved by the local Medical Ethical Committee of the Leiden University Medical Center (LUMC). Research protocol for the Rotterdam CSA-cohort (MEC-2017-028) was approved by the local Medical Ethical Committee of the Erasmus Medical Center (EMC).

Data availability statement

The data underlying this article are available from the corresponding author upon reasonable request.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jbspin.2024.105751.

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