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Arthropathies in inflammatory bowel disease : Characteristics and impact on daily functioning

Erp, S.J.H. van

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Author: Erp, Sanne J.H. van

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CHAPTER 1

**General introduction and
outline of the thesis**

Inflammatory bowel disease (IBD) covers Crohn's disease (CD), ulcerative colitis (UC) and indeterminate colitis (IC).¹⁻⁴ IBD is a chronic disease, with a multifactorial cause including autoimmune, genetic and environmental factors, in which antibodies are created that affect the intestinal wall leading to chronic inflammation.¹⁻² The diagnosis of IBD is based on medical history, complaints of the patient, physical examination and endoscopy and/or additional imaging. The suspicion for IBD will increase with the presence of blood in the stool, weight loss, a positive family history and clinical signs of inflammation including fever and diarrhoea. It is important to bear in mind that age is also an important factor for the diagnosis of IBD. Blood loss at a young age (below 50 years) is more suspect for haemorrhoids, while blood loss at an old age (above the age of 50 years) is more likely to be caused by an adenoma or carcinoma. IBD occurs at any age, but with a peak onset in young adults between the age of 15-35 years with an incidence rate of 1 per 1000 individuals.³ The kind of intestinal symptoms a patient presents at the outpatient clinic depends mainly on the location of the IBD. UC is the most prevalent type of IBD in which only (a part of) the colon is affected. In CD, the whole GI tract can be involved.¹⁻² IC concerns approximately 10% of the IBD patients and comprises the ones in whom the diagnosis of CD or UC cannot be made based on clinical testing including colonoscopy, biopsy and laboratory tests.⁴

Besides gastrointestinal symptoms due to intestinal inflammation, IBD may manifest outside the intestine, the so-called extra-intestinal manifestations (EIMs). Arthropathies in IBD are the most common EIM with a prevalence of 30%. Other EIMs that may be present in IBD patients involve the skin, eyes or liver.⁵ IBD is characterized by periods of disease flares and remission.¹⁻⁴ The treatment depends on the diagnosis of CD or UC and whether the disease is active or not. The treatment of IBD is intended to induce and maintain IBD remission and prevent disease progression by applying long-term medical therapy.¹⁻² New trends in the IBD management is the 'tight control monitoring' and the 'treat to target' strategy which focusses on frequently assessment of disease activity by markers of inflammation with the ideal target to achieve mucosal healing, meaning the absence of inflammatory and ulcerative lesions in the intestine.⁶ However, this management seems not applicable to arthropathies in IBD, since not only disease activity is a predictor of the development of arthropathies in IBD. Furthermore, different kinds of arthropathies may be present in IBD patients, subdivided into inflammatory and non-inflammatory joint complaints. These inflammatory and non-inflammatory joint complaints

may have different treatment options.⁷ A new management approach for these patients may be considered to be developed for gastroenterologists, taking the characteristics and treatment options of arthropathies in IBD into account.

Outline and aims of the studies described in this thesis

Since arthropathies are the most common EIM in IBD we aimed to highlight this matter in the present thesis in different ways to create more awareness among gastroenterologists about the characteristics and the burden of arthropathies on daily functioning in IBD. This thesis will provide an overview of the different types of arthropathies in IBD and the risk factors associated with it. Additionally, this thesis proposes an efficient referral algorithm for the gastroenterologist to discriminate the IBD patients with a high suspicion of inflammatory joint complaints from the patients with a low suspicion. Furthermore, the impact of having IBD only and the impact of having IBD including arthropathies on illness perceptions, coping strategies and daily functioning will be emphasized.

Arthropathies in IBD can be subdivided into inflammatory (typically a characteristic of Spondyloarthritis, SpA) and non-inflammatory joint complaints, also known as arthralgia.⁸ Previous performed studies showed a pathophysiological overlap between IBD and SpA.⁹ An overview of this overlap is described in **chapter 2**. This scoping review provides an insight in the common immunological, genetic, serological, microbiological and environmental factors in both chronic diseases.

The chapters 3 till 7 of this thesis are based on the JOINT cohort. All patients who visited the outpatient clinic of the Leiden University Medical Center (LUMC), the Netherlands, from July 2009 to February 2010 were asked to complete a questionnaire to assess whether they reported joint complaints. IBD patients with and without self-reported arthropathies were invited to attend the JOINT outpatient clinic, which was initiated by the department of Gastroenterology and Hepatology and the department of Rheumatology of the LUMC. Inclusion was limited to 255 patients (155 IBD patients with, 100 patients without arthropathies) to guarantee optimal care for the participants. All patients were seen at study inclusion and after 1 year follow-up at the JOINT clinic. At both time points, routine medical history and data of EIMs was collected. Furthermore, rheumatologic examination, laboratory assessment (including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and (human leukocyte antigen) HLA-B27) and radiographs of the affected joints was performed in patients with arthropathies. Only the IBD patients who showed signs of inflammation during

rheumatologic examination at the outpatient clinic or on the radiographs were referred to the rheumatologist for further examination. All participants were requested to complete monthly questionnaires to assess IBD disease activity and spine and/or peripheral joint scores. Additional questionnaires were completed at baseline and after 12 months follow-up to assess illness perceptions, coping strategies and illness outcomes including the quality of life (QoL), work and activity impairment.

In **chapter 3**, we characterised the different joint complaints in the JOINT cohort using validated rheumatologic classification criteria. Furthermore, risk factors associated with having arthropathies in IBD were described.

In rheumatoid arthritis (RA), different biomarkers have been reported to be important diagnostic markers and predictive for the development of RA at an early stage.¹⁰⁻¹⁶ However, although arthropathies are common in IBD, there is a lack of biomarkers in clinical practice predictive for the development and onset of arthropathies in IBD. **Chapter 4** evaluates the presence of rheumatologic biomarkers in the serum of IBD patients with arthropathies and compares biomarker positivity with the serum of RA patients. If present, biomarkers may help in diagnosing arthropathies in IBD at an early stage.

From the literature, it is well known that IBD has an impact on illness perceptions, coping and outcomes including quality of life (QoL).¹⁷⁻¹⁹ Illness perceptions are personal beliefs and cognitions about the disease. Coping strategies are personal efforts created to deal with the IBD. In this thesis, different illness outcomes have been examined including QoL, subdivided into mental and physical health, work and activity impairment. We assessed in **chapter 5 to 7** the different illness perceptions, coping strategies and illness outcomes in IBD patients with and without arthropathies. **Chapter 5** describes the mediating effect of coping on the association between illness perceptions and outcomes by making use of the Common Sense Model (CSM) in IBD patients. **Chapter 6** illustrates the association between having arthropathies in IBD and illness perceptions, coping and outcomes compared with patients without arthropathies. The effect of arthropathies, illness perceptions and coping strategies on the QoL and work productivity has been evaluated in **chapter 7**.

Besides having arthropathies, IBD patients may suffer from mood disorders, fatigue or cognitive decline. In the literature, studies describe the correlation

of systemic inflammation and mood disorders and/or cognitive decline.²⁰⁻²² A pilot study in which brain involvement is evaluated in quiescent CD patients with fatigue by Magnetic Resonance Imaging (MRI) and neuropsychological examination and compared with healthy controls without fatigue is presented in **chapter 8**.

Chapter 9 outlines the most important findings of the different studies presented in this thesis and results are discussed in future perspectives. A summary of this thesis in Dutch is presented in **chapter 10**.

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