TITLE

Short report/brief communication

Factors associated with fatigue in patients with psoriasis arthritis: A nationwide DANBIO study

ACRONYM

FAPA

BASED ON PROTOCOL VERSION

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INTRODUCTION

Fatigue defined as being sustained physical tiredness, mental exhaustion, and a lack of energy is a well-known symptom of many chronic diseases (1;2) and often a crucial aspect in the management of chronic diseases (3).

It is a common symptom in patients with psoriatic arthritis (PsA) and for patients impacted by fatigue it is deemed to be one of the most significant symptoms (2;4;5). Moreover, patients with PsA are characterised by having a decreased quality of life compared to other patient groups and often fatigue is reported to be the limiting factor in terms of participation in daily activities (6;7).

Though fatigue is considered an important outcome measure for PsA patients this outcome is not yet embedded completely in clinical practice or in the scientific thinking within this disease-area. Fatigue is rarely reported by clinicians and studies on patient-reported fatigue outcomes are limited (2;8)

However, the focus on fatigue is increasing. Recent studies describe the association between fatigue in PsA and pain, female gender, physical disability, medication status, psychological distress, longstanding sick leave, and loss of work ability (3;5). Furthermore, biological agents are shown to have a positive impact and beneficial effect on patients suffering from fatigue suggesting a link between fatigue and inflammatory signalling (9;10). Moreover, fatigue was only recently added in the GRAPPA-OMERACT's core set of outcome measures for PsA (2;4)

To our knowledge the association between underlying components of fatigue in relation to PsA has never been explored on basis of data from large cohort studies. The aim of the study is to describe the degree of fatigue in patients with PsA in a nationwide study, and to explore important associated components of fatigue.

METHODS

Before initiation of the study a systematic search for literature on the subject was performed in PubMed. The research question to describe the aim of the study was posed in the search for relevant literature; is presence of fatigue in patients with PsA associated with inflammatory or non-inflammatory factors?

A PICO search was performed resulting in a list of 60 articles which was screened for relevant articles. Additionally, references from relevant papers were reviewed (Appendix I).

Study design

The study is designed as a cross sectional survey including patients registered in the Danish registry DANBIO (11).

Setting and data capture

An electronic version of the Visual Analogue Scale (VAS), Health Assessment Questionnaire (HAQ), and Pain Detect Questionnaire (PDQ) were implemented on the DANBIO touch screens in the outpatient

clinics at 22 of 24 departments of Rheumatology in Denmark for a period of six months (1st of December 2013 to 1st of June 2014).

Participants
All patients registered as having PsA were invited to participate in the survey. Answering of HAQ and VAS are standard clinical practice in Danish outpatient clinics. PDQ was considered an extra questionnaire besides HAQ and VAS and patient consent was obtained on the touch screen prior to the redirection to the PDQ.

Variables and outcome measures
VAS is a scale composed to measure patient-reported pain and fatigue (VAS pain, VAS fatigue, VAS global health). A visual analogue scale (VAS; 0-100 mm) is a single-item measure, with '0' representing "no fatigue" and '100' representing "worst imaginable fatigue" was used to assess the patient's general fatigue during the last week(12) . Scores >50 were considered to indicate severe fatigue (13). We defined moderate to severe fatigue as the population scoring above the median fatigue level, i.e. ≥ 48.
PDQ is composed of items reflecting pain intensity (three numeric rating scales not included in the total PDQ-score), pain course pattern, a pain drawing intended for indication of pain radiation, and seven questions describing somatosensory symptoms rated on a six-category Likert scale (from never to very strongly).

Data extraction
The first complete questionnaire and corresponding clinical data from the same date were extracted for analyses. In addition, information on demographics, patient characteristics, and treatment were retrieved from the DANBIO registry.

Data analysis
Only patients with complete PDQ responses are included in the analyses.

Baseline characteristics are given with median and interquartile range (IQR) for continuous variables. Spearman's Rho Correlation coefficients are calculated to assess any potential association between fatigue scores and clinical indices. Two-sided P-values < 0.05 are regarded as statistically significant.
To explore clustered components explaining fatigue a factor analysis based on principal component analysis is constructed. Core set variables are a priori selected based on clinical relevance (age, disease duration, swollen/tender joint count, pain detect score, CRP-level, and patient vas global score) and with a maximum allowed collinearity of 0.4 – except for swollen/tender joint count.

Ethical considerations
In accordance with Danish legislation surveys do not require approval by Ethics Committees and registrations and publications of data from clinical registries do not require patient consent or approval by Ethics Committees. Results whether positive, negative, or inconclusive will be published in relevant international peer-reviewed scientific journals with authorship determined according to the Vancouver Protocol.

Patient perspective

The objective and study design will be discussed with a PsA patient after informed consent. The input will be integrated in the current protocol and data presentation.

Generalizability

Results based on the DANBIO registry, which covers more than 90% of rheumatology patients treated with biologic disease-modifying anti-rheumatic drugs (bDMARDs)(14), can be considered representative of patients with PsA who are treated in routine clinical care.
Patients treated with conventional DMARDs (cDMARDs) are also collected in DANBIO.

Results

Table 1: demographics
Table 2: correlations
Figure 1: PCA-figure (factor analysis)

Reference List

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Appendix I: Literature search

The research; is presence of fatigue in patients with PsA associated with inflammatory or non-inflammatory factors?

	AND		
	I	**II**	**III**
OR	Psoriatic arthritis	Inflammatory	Fatigue
	Spondyloarthritis	Non-inflammatory	
		Inflammation	

	Search for	**Result (No. of articles)**
I	Psoriatic arthritis	7693
	Spondyloarthritis	22582
	(Psoriatic arthritis)OR(spondyloarthritis)	25249
II	Inflammatory	587381
	Inflammation	540992
	Non-inflammatory	2917
	(Inflammatory)OR(Inflammation)OR(Non-inflammatory)	934608
III	Fatigue	82006
	I + II	7334
	I + II + III	69
	+filter: humans	60