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Health Assessment Questionnaire disability progression in early rheumatoid arthritis: Systematic review and analysis of two inception cohorts

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ABSTRACT

Objective: The Health Assessment Questionnaire is widely used for patients with inflammatory polyarthritis (IP) and its subset, rheumatoid arthritis (RA). In this study, we evaluated the progression of HAQ scores in RA (i) by systematically reviewing the published literature on the methods used to assess changes in functional disability over time and (ii) to study in detail HAQ progression in two large prospective observational studies from the UK.

Methods: Data from two large inception cohorts, ERAS and NOAR, were studied to determine trajectories of HAQ progression over time by applying latent class growth models (LCGMs) to each dataset separately. Age, sex, baseline DAS28, symptom duration, rheumatoid factor, fulfilment of the 1987 ACR criteria and socio-economic status (SES) were included as potential predictors of HAQ trajectory subgroup membership.

Results: The literature search identified 49 studies showing that HAQ progression has mainly been based on average changes in the total study population. In the HAQ progression study, a LCGM with four HAQ trajectory subgroups was selected as providing the best fit in both cohorts. In both the cohorts, older age, female sex, longer symptom duration, fulfilment of the 1987 ACR criteria, higher DAS28 and lower SES were associated with increased likelihood of membership of subgroups with worse HAQ progression.

Conclusion: Four distinct HAQ trajectory subgroups were derived from the ERAS and NOAR cohorts. The fact that the subgroups identified were nearly identical supports their validity. Identifying distinct groups of patients who are at risk of poor functional outcome may help to target therapy to those who are most likely to benefit.

Introduction

The Health Assessment Questionnaire (HAQ) is the most widely used measure of function in studies of inflammatory polyarthritis (IP) and its subset, rheumatoid arthritis (RA) [1,2]. Worse functional disability is associated with increased cardiovascular and all-cause mortality [3,4], joint damage [5] and work disability in patients with IP and RA [6,7]. Functional disability is mainly

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associated with disease activity in early RA and with radiographic joint damage in patients with established disease. It is therefore often used as an outcome measure to assess the impact of disease over time [8–10]. Predictors of worse functional disability in the long-term include baseline or 1-year HAQ score [11–13], older age [12,14], female gender [12,14], disease activity [11,13–15], rheumatoid factor (RF) positivity or anti-citrullinated protein antibody (ACPA) positivity [16], radiographic damage [5,13,17,18], number of co-morbidities [10,19,20], low education [15] and low socio-economic status (SES) [17,21,22].

Previous research has suggested that the mean HAQ score over time is J-shaped with an initial improvement after treatment commencement followed by an insidious decline in patients with early RA [11,15,23]. However, the focus of most of these studies was on the average change over time in the total study population calculating mean changes in HAQ score over time or applying simple linear regression models to determine the association between disease duration and HAQ progression. In the last two decades, more advanced methods have become available to measure longitudinal data, such as repeated measurement regression analysis. However, in most studies, the change in HAQ scores over time has been measured at the group level. Few studies have attempted to identify subgroups defined in terms of their HAQ trajectory in IP and RA patients or considered their validity across cohorts. In a recent study that included patients with early RA recruited to the Early Rheumatoid Arthritis Study (ERAS) and followed up for 10 years, latent growth mixture modelling (LGMM) was used to determine whether the study population comprises distinct subgroups of patients with differing trajectories of functional disability [24]. It is important to determine if similar results can be found in other RA populations as well. In general, identification of distinct groups of patients who are at risk of poor outcome may help to target therapy to those who are most likely to benefit in the clinic.

The objectives of this study were (i) to give an overview of the methods used in the literature to assess functional disability over time and (ii) to identify common trajectories of HAQ progression over 15 years in two large prospective observational studies from the UK, i.e., ERAS and the Norfolk Arthritis Register (NOAR).

Methods

Systematic literature review

MEDLINE was searched to identify articles describing changes in HAQ scores over time in patients with RA or undifferentiated polyarthritis. The following keywords were used: (([exp Arthritis, Rheumatoid/] OR [inflammatory polyarthritis.mp] OR [undifferentiated arthritis.mp]) AND ([health assessment questionnaire$.mp] OR [HAQ.mp] OR [functional.mp AND disability.mp])) NOT ([exp Arthritis, Juvenile Rheumatoid/] OR [JIA.mp]) NOT ([clinical trial, phase i/ OR clinical trial, phase ii/ OR clinical trial, phase iii/ OR clinical trial, phase iv/ OR controlled clinical trial/ OR randomized controlled trial/] OR [exp case reports/] OR [randomized clinical trial.mp]). The search was limited to the years "1980–2012" and English language. Studies were selected if they met the following inclusion criteria: Follow-up duration/disease duration $\geq$3years, multiple (i.e., $\geq$3) cross-sectional assessments of HAQ in case of cross-sectional analysis, (M)HAQ used to measure functional disability and no intervention study (Fig. 1 for selection procedure). References of identified reviews and selected studies were checked for eligible articles.

HAQ trajectory study: Patients recruited to the Early Rheumatoid Arthritis Study (ERAS) and the Norfolk Arthritis Register (NOAR)

ERAS is an inception cohort to which consecutive patients thought to have RA by a consultant rheumatologist were recruited from the outpatient clinics of nine rheumatology departments in the UK between 1986 and 1997. Patients were included if they had a symptom duration of less than 2 years and were disease-modifying anti-rheumatic drug (DMARD) naive [12,25]. Patients in ERAS were subsequently excluded if the diagnosis changed, for example, apparent early RA evolving to classical lupus or osteoarthritis.

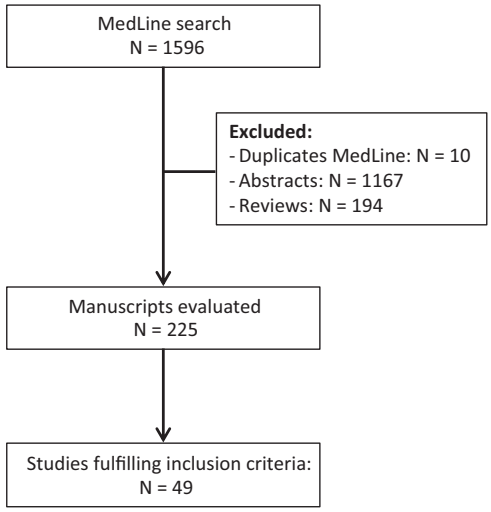

Fig. 1. Selection process publications.

NOAR is a primary care-based inception cohort of patients with early IP recruited in Norfolk, UK. Consecutive patients aged over 16 years with swelling in $\geq$2 joints that lasted $\geq$4 weeks were referred via the GP or rheumatologist to NOAR between 1990 and 1994 [26,27]. This analysis included all patients who had not been given a consultant diagnosis other than RA, undifferentiated IP, psoriatic arthritis or post-viral arthritis to explain their symptoms. Patients whose disease has gone into spontaneous long-term remission (no inflamed joints at the 3rd or 5th anniversary and not on disease-modifying anti-rheumatic drugs (DMARDs) or steroids) were followed up beyond the 5th anniversary; otherwise patients were followed up until the 5th anniversary if applicable.

Clinical and laboratory assessments and socio-economic status

Standard clinical assessments were made by trained research nurses in both studies at baseline and included date of symptom onset and number of swollen and tender joints. RA was defined according to the 1987 ACR criteria and applied cumulatively. At each visit, DMARD and biologics use, including start and stop date, was recorded. The two cohorts differed in laboratory assessments. In ERAS, routine haematology tests included the erythrocyte sedimentation rate (ESR) measured according to Westergren test and routine serology including RF. In NOAR, blood was collected and stored in -80°C freezers to measure RF (positive $>$40 mg/L) and C-reactive protein (CRP). Due to these small differences in data collection and visual analogue scale general well-being missing in NOAR, the 4-component DAS28 score based on ESR values was calculated in ERAS and the three-component DAS28 score based on CRP was calculated in NOAR.

Socio-economic status was defined as an area-level categorical variable, based on the Index of Multiple Deprivation (IMD) 2007. In the IMD, the UK is divided into "super output areas," with a minimum population of 1000 (mean 1500). Information on income, employment, health, education, barriers to services, crime and living environment is used to assign a deprivation score to each super output area. These scores are then ranked across the country. For this study, we used postal codes to assign each patient