The spectrum of early rheumatoid arthritis practice across the globe: results from a multinational cross sectional survey

E. Nikiphorou[1,2], J. Galloway[3], P. van Riel[4], Y. Yazici[5], G. Haugeberg[6], A. Ostor[7], F. Gogus[8], M. Kauppi[9], T. Sokka[2], on behalf of QUEST-RA

[1]Department of Rheumatology, Whittington Hospital, London, UK; [2]Jyväskylä Central Hospital, Rheumatology Unit, Jyväskylä, Finland; [3]King's College London, Academic Rheumatology Department, London, UK; [4]Department of Rheumatology, Bernhoven, Uden, The Netherlands; [5]NYU Hospital for Joint Diseases, New York, NY, USA; [6]Department of Rheumatology, Martina Hansens Hospital, Bærum, Norway; [7]Department of Rheumatology, Addenbrookes Hospital, Cambridge, UK; [8]Department of Physical Medicine and Rehabilitation, Division of Rheumatology, Gazi University, Faculty of Medicine, Ankara, Turkey; [9]Medical School, Tampere University, Tampere, Finland.

Abstract

Objective

To explore patterns of real-world early RA (ERA) care across countries.

Methods

An online survey was disseminated to practising rheumatologists across Europe and the US, also made accessible on social media between April and May 2015. Survey questions (n=38) assessed the structure and setting of ERA clinics, times to diagnosis and treatment, patient monitoring, guideline use and data recording.

Results

A total of 212 rheumatologists from 39 countries (76% European) completed the survey. 62% had an ERA clinic based at a university hospital. Patient referral to rheumatology was mainly (78%) via primary care; 44% had an agreed ERA local referral pathway, 15% a national pathway. Only 16% had dedicated ERA clinics, the majority being practitioners in Northern Europe with access to a local or national referral pathway. Data for research were collected by 42%. Treatment guidelines were followed by the majority, especially rheumatologists practising in Europe. Variations existed in the use of initial DMARDs with treatment decisions reported to be influenced by international/national guidelines in 71%/61%. No significant relationship between country gross national income and the availability of ERA clinics was seen.

Conclusion

This study provides comparative benchmark information regarding the global provision of ERA care. Substantial variations exist in referral and early assessment pathways with guidelines having a most apparent impact in Northern Europe. Provision of an ERA service does not appear to be constrained by cost, with conceptual factors, e.g. clinician engagement, perhaps playing a role. These initial insights could potentially help harmonise ERA management across countries.

Key words

early rheumatoid arthritis, disease-modifying anti-rheumatic treatment, health service delivery

Elena Nikiphorou, MBBS/BSc, MD(Res)
James Galloway, MD, PhD
Piet van Riel, MD, PhD
Yusuf Yazici, MD
Glenn Haugeberg, MD, PhD
Andrew Ostor, MD
Feride Gogus, MD
Markku Kauppi, MD, PhD
Tuulikki Sokka, MD, PhD

Please addres correspondence and reprint requests to:
Prof. Tuulikki Sokka,
Rheumatology Research Department,
Jyväskylä Central Hospital,
40620 Jyväskylä, Finland
E-mail: tuulikki.sokka-isler@ksshp.fi

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Introduction

Early diagnosis and treatment are crucial to the successful management of rheumatoid arthritis (RA). Over time, there has been a dramatic shift in the treatment paradigms in RA with emphasis on the use of intensive treatments (1-7) as early as possible and while still in the 'window of opportunity' (8). Recommendations and guidelines at local, national and international level have been produced to help guide treating physicians through an abundance of therapeutic options currently available. In 2013, the European League Against Rheumatism (EULAR) updated the recommendations for the management of RA with synthetic and biologic DMARD (9) with a further update in progress in 2016. EULAR recommendations in RA have been widely adopted and used as a guide for developing national or regional recommendations by Rheumatology Societies in various countries including Germany (10), Canada (11), Hong Kong (12), the Middle East and Africa (13). In 2012, the American College of Rheumatology (ACR) updated its 2008 guidelines (14) with a second update completed in 2015 (15).

Treating RA to target (T2T) has become an internationally agreed standard of good practice (16) with recommendations formulated to inform rheumatologists, other healthcare professionals and patients about strategies to achieve optimal disease outcomes. Aside from drug interventions, it is important to acknowledge that early referral and review should form part of the principles of optimal care; for example, early arthritis clinics are a well-recognised means of assisting prompt and targeted investigation and therapeutic intervention (17, 18).

The plethora of therapeutic options has induced variations in the use of treatments for early RA and despite existing recommendations at national and international level, the latter frequently used, variations in practice across countries still exist. Possible reasons include differences in health care systems, resource availability and socioeconomic barriers to accessing more effective but more expensive treatments such as the biologics in certain countries compared to others. This is a survey-based study with the objective of evaluating the management of early RA across countries in order to understand what the differences are in the provision of care and potential reasons for these differences. Understanding such differences can provide insights that could help harmonise the management of early RA across the globe.

Materials and methods

Survey design

A set of themes were identified as important for addressing through the survey and were used to develop questions that would provide answers and insights into the management of early RA across European and non-European countries. Based on these themes, the questionnaire was divided into five broad sections: general demographics, details on the process of initial review of early RA, issues around diagnosis, treatment initiation and decisions around this and patient monitoring (see online supplementary material). A total of 38 questions were identified in a stepwise process taking into account feedback from peer review in three stages and under the specific themes using national and international standards and recommendations for the management of early RA.

The questions were uploaded onto an online survey software ('SurveyMonkey®') and this was initially piloted 'internally' and also across six countries by inviting early RA experts to trial it. The experts were asked to provide specific feedback on the content and nature of the questions and whether these would be generalisable and applicable to all countries and health systems. Following this small pilot, feedback on each of the questions and overall style of the survey was gathered and used to update and add clarity to some of the questions before finalising the survey. The survey was designed in a way that only allowed progression through the questionnaire if all questions were answered. The final version of the survey can be provided upon request.

Survey dissemination

Email invitations with the website link of the final version of the survey were

sent out to members of the QUEST-RA (Quantitative Patient Questionnaires in Standard Monitoring of Patients with Rheumatoid Arthritis) initiative, to forward to rheumatologists in their respective countries. The survey was also advertised and made accessible via social media (Twitter) between April and June 2015. Ethical approval was not required for this survey-based study, as per the policy of our institution.

Data handling

It was possible to analyse the responses both at the individual respondent level and also collectively. Responses were also analysed under the six different themes of the survey and by country, allowing the study of inter-country variations in practice where appropriate.

Statistical analysis

Descriptive statistics were mainly used. Where considered appropriate, responses were either categorised into different groups and χ^2 testing was used for comparisons across groups. For all analyses, significance was assumed at the $p<0.05$ level. All statistical analyses were conducted in SPSS (v. 21).

Results

General demographics

A total of 212 participants from 39 countries (76% European) across four continents (Europe, America, Asia and Africa, in order of frequency) completed the survey. The majority of Europeans responding were from North Europe 111/161(69%). Countries surveyed included the full spectrum of wealth, with both extremes of gross national income (GNI) represented. Overall, the greatest contributions were from Finland (n=66), followed by Brazil (n=26) and Denmark (n=20). The majority of respondents (32%) were pure clinical rheumatologists, followed by clinical rheumatologists with some academic role (24%); pure academic rheumatologists (17%); the remaining mainly rheumatologists/fellows in training. Almost a third (30%) of respondents had over 20 years of experience in rheumatology. Only 16% had a dedicated early RA clinic, the majority of which (70%) were based at a university hospital. Nine per cent had a private early RA clinic.

Early RA referral

New patient referral to an early RA clinic was in the majority of cases (78%) from primary care, in 16% through direct patient referral and in 6% directly from other secondary care professionals. 44% reported having an agreed early RA local referral pathway for ensuring rapid patient access to rheumatology, 15% a national referral pathway whereas 27% reported having no pathway at all. Almost three quarters of rheumatologists reviewed their early RA patients in general rheumatology clinics with only 16% having dedicated early RA clinics. From these, 76% were practitioners in European countries (mainly Northern Europe [64%]) who had access to local or national referral pathways.

Respondents from Africa or Asia reported not having dedicated early RA clinics, although these represented the minority of respondents (6.6%). However, there was no observed relationship between GNI and the availability of early RA clinics ($p=0.6$). Over 50% of patients were seen within 4 weeks from primary care referral. A third of respondents reported reviewing their early RA patients within 2 weeks and just under a quarter, between 2–4 weeks; only 1% reported seeing patients after 12 weeks from referral. The shortest waiting lists were reported by rheumatologists from northern Europe and the majority in settings where there was a local early RA referral pathway in place. A significantly higher proportion of patients in northern European countries were seen within 4 weeks compared to patients in the rest of Europe ($p=0.04$).

Diagnosis, treatment-onset and early RA screening

A diagnosis of early RA was reported being made at the first clinic review by 42% of respondents and by 33% within 1 month. Initiation of treatment with DMARD therapy at first review and within 1 month was reported by 47% and 31% respectively. The first clinic appointment review lasted up to 30 minutes in 27%, 45 minutes in 30% and up to 60 minutes in 20%; 7% reported undertaking early RA reviews of less or equal to 15 minutes. There was a significant difference in the satisfaction levels of rheumatologists by clinic appointment duration ($p=0.005$) with increasing satisfaction associated with longer time for first early RA appointment. Twenty-six free-text comments were provided as part of this question, with respondents expressing the need for longer duration appointments for newly-diagnosed early RA patients and for access to joint injections and ultrasound examination where appropriate. The lack of time in handling patient anxiety and worries regarding a new, chronic diagnosis was also reported, as was the lack of enough rheumatologists in some countries despite a high demand.

Respondents described services available to their early RA patients: 43% reported providing formal DMARD education; 37% nurse education; 33% physiotherapy; 22% nurse general review; 21% occupational therapy, 9% podiatry. Radiographs of the hands and feet available were available at the patient's first review according to 43% of respondents, (32% reported being able to arrange these on the same day). Musculoskeletal ultrasound (MSKUS) was reported to be always provided on site by a rheumatologist in 18% and also in 37% when considered necessary or within six weeks in the radiology department in 11%. Over 50% reported having inflammatory markers, rheumatoid factor and anti-cyclic citrullinated peptide antibodies (ACPA) available in the referral and therefore on first patient review. Thirty-four per cent reported their patients having an opportunity to hear about participation in clinical trials/other research.

Treatment decisions: corticosteroid, synthetic and biologic DMARD use

The majority of rheumatologists reported following treatment guidelines (most commonly national, followed by international), those practising in Europe more so than others. A higher proportion of rheumatologists in northern Europe compared to the rest of Europe

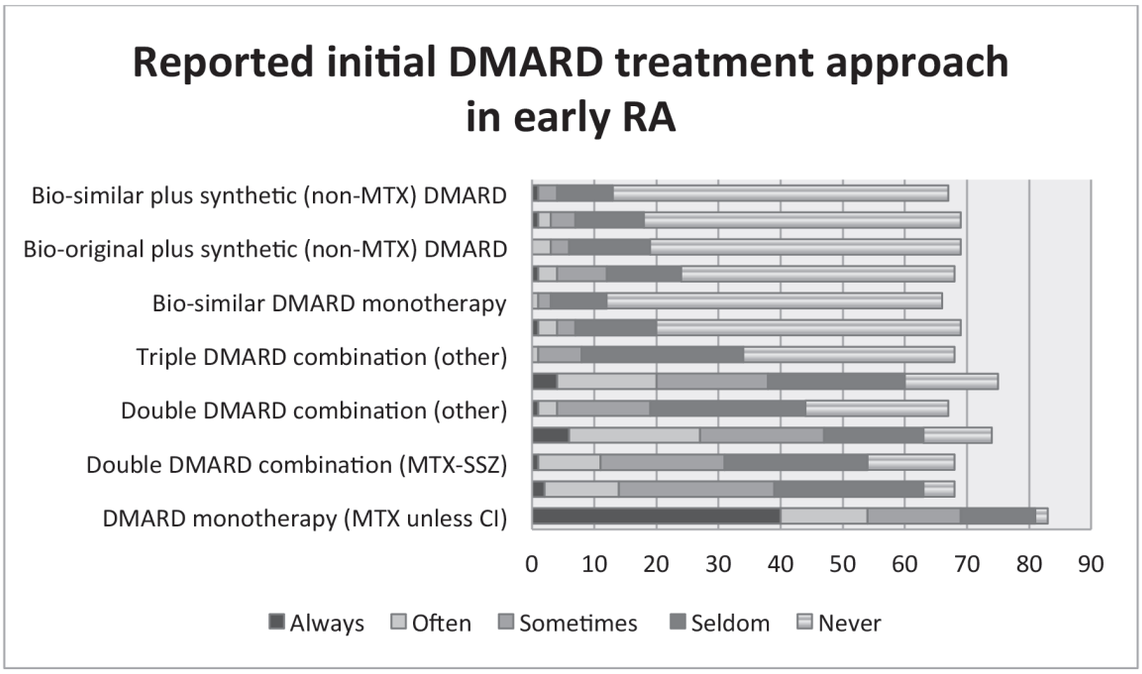

Fig. 1. Type and frequency of initial DMARD use in early RA (x-axis indicates frequency)

reported following national or international guidelines ($p \leq 0.001$). Specific comments made included needing to undertake consideration of socio-economic factors and the patient's intentions, explaining the guidelines and getting informed consent regarding specific treatments.

The most common initial DMARD used and reported in this survey was methotrexate (MTX) (81%), usually via the oral route. Concurrent oral steroids were frequently used alongside (68 [32%] respondents reported often, 60 [28%] almost always). Intramuscular steroids were less frequently used.

Most units reported that access to biologics was only permitted after failure of synthetic DMARDs, although 29/171 (17%) reported freedom to initiate biologics even in DMARD naïve patients irrespective of guidelines. Reported reasons for the latter included an 'off label use' or doing so if patients have an understanding of the risk and cost involved. When selecting biologics, results reflected the contemporary market at the time of the survey, with TNF inhibitors representing a majority (68%). Biosimilar use was reported being used as first line by 4%.

A common theme in biologic prescribing was that cost was the primary driver of choice, rather than clinical efficacy or safety data. Sixty-seven per cent of respondents reported that their patients received education on treatment principles (*e.g.* T2T approach); DMARD education (including potential side effects) and the need for treatment/disease monitoring. Figure 1 shows the initial treatment strategies used for early RA based on frequency.

Factors influencing treatment decisions

Treatment decisions were reported to be influenced by international, national and local guidelines in 71%, 61% and 26% respectively. Patient financial and social circumstances were reported factors influencing treatment decisions in 17% and 33% of respondents.

Early RA monitoring and follow-up

Patient monitoring included laboratory testing (77%), radiology investigations (50%), doctor-reported (62%) and patient-reported (48%) outcomes. Although 75% of rheumatologists reported undertaking data collection for patient monitoring, fewer than half of respondents routinely collected the HAQ (47%), and only 31% actively recorded fatigue. In contrast, DAS/DAS-28 assessments were performed more consistently (58%). 42% of respondents reported collecting data specifically for research. These included tender and swollen joint counts, ultrasound and DAS28. Over 80% reported screening their early RA patients for comorbidities using either clinical judgement and/or a variety of screening tools including: blood pressure measuring, dual-energy x-ray absorptiometry (DEXA), lipid profile, Q-Risk, infection screen (TB, HIV, HCV, HBV, influenza and pneumococcus); chest x-rays; GoTreatIT (19) comorbidity list; the COMEDRA trial (20) screening questions. In terms of patient follow-up, only 1% reported providing just one review within the first year (baseline visit), whereas the majority of rheumatologists (34%) reported providing an average of four reviews.

Discussion

This study is the first to provide comparative benchmark information on the practice of early RA across the globe. It demonstrates important variations in the provision of care for individuals with early RA, in particular to the provision of dedicated early RA clinics, referral pathways, access to education and to specific services *e.g.* radiology and laboratory testing. The latter in particular highlights differences in

practice within individual care settings. Over half of rheumatologists reported having inflammatory markers and autoantibodies available on first patient review. A fair proportion reported also having radiographs of hands and feet available or being able to arrange on the clinic day. Almost a fifth of rheumatologists always provided on site MSKUS and over a third provided this at the time of the review when considered necessary; 11% arranged MSKUS within six weeks in radiology departments. The findings support the view towards MSKUS for RA and other inflammatory arthritides, which when added to routine rheumatologic investigation, has been shown to increase the diagnostic certainty (21, 22). Approximately a third of rheumatologists reported providing on average four clinic reviews per year and around half of the respondents reported collecting patient-reported outcomes.

The survey also demonstrated differences in treatment choice, despite treatment decisions reportedly being influenced by international, national and local guidelines in that order of frequency. Reported factors influencing treatment decisions included patient-centred financial and social circumstances. Possible other reasons for this variation however, include differences in interpretation of the evidence, physician engagement in the early RA community and awareness of latest research, health care systems, country-individualities and existence of 'own' guidelines, resource availability and socio-economic barriers to accessing more effective but more expensive treatments such as the biologics in certain countries compared to others. In a cross-sectional study with 46 participating European countries (many of which also included in our survey), patients with RA in lower income European countries had less access to bDMARDs and also sDMARDs (23), with a 'striking unaffordability' of bDMARDs in some of these countries. The study highlighted inequities in access to pharmacological treatment for RA in Europe, also supported by other data (23-26).

The majority of rheumatologists who reported following national and international treatment guidelines were practising in Europe. Almost half of rheumatologists reported that their patients received DMARD education at the first clinic review and almost a third that their patients received education on treatment principles *e.g.* T2T approach. Three quarters of respondents reported using oral MTX monotherapy as part of their early RA DMARD strategy and approximately a third reported using it subcutaneously. Oral or intra-articular corticosteroids were also used by the majority. Double DMARD combination (MTX-hydroxychloroquine [HCQ]) and less frequently MTX-sulfasalazine [SSZ]) and triple DMARD combination (MTX-HCQ-SSZ) were also used, albeit less commonly than MTX monotherapy. This was especially noted in Scandinavian countries like Finland, probably reflecting the influence of the FIN-RACo (Finnish Rheumatoid Arthritis Combination therapy) trial (3).

In a study involving a series of interviews of practising rheumatologists, although there were no doubts regarding the value of MTX, some questioned the value of combination strategy, others the effectiveness and/or dosage of individual compounds (27). Additional barriers for prescribing intensive combination treatment strategies included the need for patient education, fear for patients' preconceptions, concerns about applicability to the individual patient, difficulties with breaking routine, interference with organisational structures and processes, time constraints, and lack of financial support (27). The results of our study also suggest a discrepancy between existing evidence and actual prescription in real-life practice.

Interestingly, 14% of respondents (mainly rheumatologists in Scandinavia) were able to start biologics prior to synthetic DMARD use. Over two thirds of rheumatologists reported using anti-TNF bio-originals in the first year from diagnosis, followed by T-cell co-stimulator abatacept and anti-TNF biosimilars. Much lower use of Tocilizumab and Rituximab was reported within the first year.

Our results show no relationship between country GNI and the availability of early RA clinics, suggesting that the availability of this type of clinics is perhaps not constrained so much by finance but rather by other factors. These could include physician or system-related reasons, for example motivation, views relating to early arthritis clinics, departmental and hospital facilities and organisation. Whilst early RA clinics showed no relationship to country GNI, Norther European countries followed national/international guidelines and had reportedly greater access to combination DMARD therapy.

This survey has shown that in the majority of cases, referral to an early RA clinic was via primary care, with 44% of respondents reporting having an agreed early RA local referral pathway for ensuring rapid patient access to rheumatology. A smaller proportion (15%) had a national referral pathway, but more than a quarter reported having no pathway at all. Interestingly, only 16% of rheumatologists reported having dedicated early RA clinics, and this was primarily rheumatologists based in Northern Europe with access to local or national referral pathways. This was somewhat unexpected, since there is a strong evidence base supporting the use of early intensive DMARD strategies within the 'window of opportunity', which has given rise to early RA clinics. This change in the treatment paradigm and introduction of these clinics is supported by the long-term remission, as well as functional, radiographic and prognostic outcomes of starting treatment early (3, 28).

Dedicated early RA clinics have been shown to result in shorter times from symptom onset to first rheumatology review and earlier diagnosis, compared with 'regular' clinics (29). Time from symptom-onset to first rheumatology review was three months shorter for patients seen in early RA clinics, suggesting that early diagnosis is possible in this setting, and that early referral to a specialist by primary care physicians facilitates early diagnosis of RA (29). The specific study population was based on one of the earliest and most well-known early RA clinics, the Leiden Early Arthritis Clinic, established in 1993. Data from the latter cohort over the years support the positive impact of such clin-

ics in improving short but also long-term outcomes of disease (30).

Despite the low number of dedicated early RA clinics, over 40% of rheumatologists participating in our survey reported making a diagnosis of RA and initiating DMARD treatment at the first clinic review; approximately a third reporting doing so within one month from first review in rheumatology. The majority of rheumatologists reported spending three quarters of an hour for the first RA clinic review, with significantly higher satisfaction seen on the rheumatologists' part with increasing review time. Not having enough time for handling patient anxiety and concerns regarding a new, chronic diagnosis and the lack of enough rheumatologists in some countries despite high demand, were among the expressed concerns.

Three-quarters of rheumatologists in this survey reported undertaking data collection for patient monitoring and over 40% for research. Over 80% reported screening their early RA patients for comorbidities, although the comorbidities and instruments used for data collection varied. The latter is a well-recognised issue and two EULAR Task Forces on comorbidities in RA and on data harmonisation for longitudinal observational studies, are currently focusing on this area.

Our study has certain limitations, a major one being selection bias of respondents which could result in an over-estimation of the provision of care globally. For example, the great majority of respondents were from Northern Europe. This probably explains some of the responses, such as following guidelines being more frequent in Europe/Northern Europe. For example, reimbursement is often based on using specific drugs before others, as per guidelines most of the time; therefore it is perhaps not unusual that northern or European countries follow these guidelines more. Furthermore, the survey was designed by a group of 'experts' and included questions that were considered appropriate and relevant to the group regarding the management of early RA. However, it was not possible to use a 'standardised' or validated questionnaire for this purpose, as such a questionnaire does not exist. Strengths of the study include the high number of participating rheumatologists from 39 different countries, giving this study a global perspective. The survey was designed in such a way that moving between questions required a completed previous answer, minimising therefore the risk of incomplete answers. A strong advantage of this study is that it is the first of its kind investigating variations in the practice of early RA, and could be used to inform further guidelines and recommendations.

In conclusion, this study attempted to systematically evaluate the management of early RA across countries using an online survey, in order to obtain information on real-world provision of care and potential reasons for these differences. Understanding such variations in practice can provide more insights to help guide interventions for enabling a more optimal and harmonised worldwide approach to the treatment of RA.

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