Assessment of Rheumatoid Arthritis in Clinical Care

Romatoid Artritin Klinik Değerlendirmesi

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Abstract
Quantitative clinical monitoring of patients with musculoskeletal conditions should be included in the infrastructure of every clinical practice. Quantitative monitoring improves the physician's capacity to assess and document a patient's clinical status and changes over time, which leads to greater accuracy in the underlying rationale for clinical decisions. Furthermore, routine data collection in consecutive patients facilitates analyses of groups of patients over long periods in usual care, beyond information that can be obtained from randomized clinical trials.
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Key words: Rheumatoid arthritis, disease activity, clinical evaluation, outcomes

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Özet
Kas-iskelet sistemi hastalığı olan bireylerin kantitatif izlemi her klinik uygulamanın parçası olmalıdır. Kantitatif izlem,hekimin hastanın klinik durumu ve zaman içindeki değişimini değerlendirme kapasitesini arttırır ve daha doğru klinik kararlar vermesini sağlar. Ayrıca ardışık hastalarda rutin veri toplama, randomize klinik çalışmalardan elde edilebilecek bilgiden ötede uzun süre boyunca hasta gruplarının analizini kolaylaştırır.
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Anahtar sözcükler: Romatoit artrit, hastalık aktivitesi, klinik değerlendirme, sonuçlar

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Introduction

Quantitative clinical monitoring of musculoskeletal conditions and inflammatory joint diseases is challenging compared to quantitative monitoring of conditions such as hypertension or hyperlipidemia, for which single "gold standard" measures can be used as an indicator of clinical status and changes over time in every individual patient. Several types of measures have been used traditionally to assess rheumatoid arthritis (RA), including joint assessment, laboratory tests, imaging, and patient self-report measures, often in an index of several types of measures. Each type of measure has limitations and provides only a reflection of the underlying inflammatory process. A single gold standard to define disease activity in RA does not exist and indices of multiple disease activity measures must be used.

Quantitative monitoring of RA as part of daily clinical practice has certainly improved since Dr Wright's observation in 1983 that "clinicians may all too easily spend years writing 'doing well' in the notes of a patient who has become progressively crippled before their eyes …" (1). Standard quantitative monitoring with a treatment goal has been shown to result in better patient outcomes in randomized clinical trials. Quantitative monitoring has also contributed to improved long-term outcomes for RA in usual clinical care.

One of the earliest proposals for an active monitoring and treatment strategy for RA was expressed by Luukkainen et al. in 1978 "...In our opinion gold treatment ought to be started in the early stages of RA, before the development of erosions. We are treating not only the actual inflammation of the joints but also the quality of the patient's life for many decades in the future" (2). Benefits of quantitative monitoring of RA are obvious and hurdles removed that prevent quantitative monitoring in every-day clinical care concerning disease activity and beyond.

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This article describes measures to assess clinical status of patients with RA and reviews some observations based on standard monitoring of patients with RA in daily clinical practice in a multinational collaborative database called Quantitative Standard Monitoring of Patients with RA (QUEST-RA).

Measuring disease activity leads to lover disease activity levels

Most clinical trials are designed to analyze differences between active and control treatments rather than to attain a certain clinical status, based on requirements for registration of new agents. In these registration trials, an extensive battery of disease activity and other measures are collected at study visits to document patient status. The measures are analyzed to determine whether statistically significant differences are seen between patients treated with a test therapy compared with a control therapy. The measures are not used to guide therapies. By contrast, a few trials involving available agents may be termed "strategy trials," as they involve adjustment of therapies according to a status of remission or low disease activity to achieve a predetermined treatment outcome.

The Finnish Combination Treatment Trial (FIN-RACo) was the first clinical trial with a remission as the primary outcome measure (3). Over the 2-year study, treatments had to be adjusted if remission was not met. At the end of the study, disease activity score (DAS28) -remission rates were 68% in the combination arm and 41% in the monotherapy arm and American College of Rheumatology (ACR) remission rates were 42% vs. 20% in the two groups and were among the highest that have ever been seen in clinical trials or clinical care (4). The TICORA aimed at low disease activity of DAS <2.4 in the strategy arm, with frequent clinical visits and escalation of treatments (5). At the end of the trial, 65% of patients were in remission in the strategy arm vs. only 16% in routine care arm. The BeSt study had a treatment goal of DAS $\leq$2.4; 38%-46% of patients in the four arms were in remission at the end of intervention (6). In the 2-year CAMERA trial, 50% of patients were in DAS 28 remission in an intensively computer-assisted monitoring group vs. 37% in the conventional group (7). Similarly, in the CIMESTRA trial, 2-year radiographic and clinical results were better in the strategy group vs. control group (8). Fransen et al. (9) compared a strategy group designed with routine disease activity measurements and the aim of DAS 28$\leq$3.2 to a usual care group with no routine measuring. Over 24 weeks, patients in the strategy group received more antirheumatic drugs and had better outcomes than patients in the usual care group.

These clinical trials indicate that the practice of quantitative monitoring of RA leads to better outcomes than routine care without quantitative monitoring. Furthermore, a treatment target and quantitative monitoring have been important clinicial settings which have reported favorable long-term outcomes of RA in recent years (10-12).

Measures of activity and damage to assess rheumatoid arthritis

Measures used to assess patient status in RA include laboratory tests, radiographs, formal joint assessments, physical measures of functional status, global measures, and patient self-report questionnaires. These measures may be classified as measures of disease activity, measures of damage to joints and other organs, measures which assess both activity and damage, and long term outcomes (13, 14).

Measures of disease activity, such as joint swelling, are consequences of a dysregulation, analogous to elevated glucose in diabetes and elevated blood pressure in hypertension. Elevation in activity measures may be reversible and not necessarily harmful to a patient. However, unchecked dysregulation commonly leads to long term damage to organs, such as joints, blood vessels, kidneys, or others, if no therapy is instituted to reverse persistent disease activity.

Measures of damage such as radiographic changes and joint deformity are irreversible medically, although partially correctable by surgery in some situations. Measures which assess both activity and damage, such as functional status, pain and global status include both reversible and irreversible phenomena. Long term outcomes, such as work disability, joint replacement surgery and premature mortality, reflect the concerns of patients who have chronic diseases more directly than measures of activity or damage.

Measures to Assess RA Disease Activity

Physician measures: joint assessment

A careful joint examination is required to establish a diagnosis of RA (15), and quantitative counts of swollen and tender joints are the most specific measures for patient assessment (16-19). The number of swollen and tender joints is regarded as the most important measure for RA clinical trials to distinguish active from control treatments (20), and the best measure of status in usual clinical care (21). The joint count is included in a Core Data Set (22-24) and in disease activity indices that will be discussed later.

A 28 joint count includes 10 proximal interphalangeal (PIP) and 10 metacarpal phalangeal (MCP) joints of the hands, 2 wrists, 2 elbows, 2 shoulders and 2 knees (25). Recent studies have used a 42 joint count, which includes the 28 joint count and 10 metatarsal phalangeal (MTP) joints of the feet, hips and ankles (26). Joints are assessed according to a standard protocol for evaluation of rheumatoid arthritis (SPERA) (27) not only for swelling and tenderness, as in clinical trials, but also for limited motion or deformity, which must be included to assess long-term outcomes.

Laboratory tests

The majority of patients with RA have an elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) (28). An abnormal ESR or CRP often provide inclusion criteria for clinical trials (29). An ESR less than 30 mm/h in a woman and less than 20 mm/h in a man is required to meet ACR remission criteria (30).

Reductions in ESR and CRP are seen in groups of patients in all successful clinical trials of RA therapies which indicate efficacy of an active treatment compared to a control treatment. However, no blood test is abnormal in more than 75% of patients with rheumatoid arthritis, or normal in more than 99% of normal individuals. Indeed, more than 40% of RA patients have normal values for the acute phase reactants, ESR and CRP (28, 31).

The majority of patients with RA also have positive tests for rheumatoid factor (RF) and antibodies to cyclic citrullinated peptides (anti-CCP) (32-35). RF is included in classification criteria for RA (36) and anti-CCP is being considered for revised criteria. However, an extensive meta-analysis indicated that anti-CCP was normal in 33% and RF in 31% of patients with RA (35). RF or anti-CCP cannot be used as disease activity measures and their predictive value of outcomes is limited (37).

Patient questionnaires

In RA, inflammation of joints and other systems affects patient functional status, causes pain, fatigue, and other symptoms, which resolve as inflammation responds to treatments. Patient self-report has become prominent in rheumatology assessment, as patient is the most accurate source for quantitative information concerning functional capacity, pain, global health, fatigue, psychological distress etc.

The self-report health assessment questionnaire (HAQ) (38) provided a milestone in rheumatology, with a scale of 20 activities of daily living (ADL) in 8 categories to assess functional disability, with 4 patient response options: "without any difficulty" =0, "with some difficulty" =1, "with much difficulty" =2 and "unable to do" =3. The 8 categories of 2 or 3 ADL address dressing, arising, eating, walking, bathing, reaching, gripping, and performing errands. The score for each category is the highest score among the 2 or 3 ADL within the category; 1 is added to the score if the patient uses aids or devices for that category, so the final score is 0-3. The total score is the mean score derived from 8 scores, one for each category.

Several modifications of the HAQ have been developed to provide simplified scoring in routine clinical care and allow the clinician to visualize an ADL score. The most widely used modifications are the modified HAQ (MHAQ) which includes only one question in each of the 8 HAQ categories (39). A further modification is the multidimensional HAQ (MDHAQ), which includes 10 ADL, 8 from the MHAQ and two complex activities, 3 psychological items (40-42), as well as 10cm visual analog scales for pain, global health, and fatigue.

Patient questionnaires concerning functional status provide the most significant prognostic clinical measure for all important long-term outcomes of RA, other than radiographic scores for which radiographs are most significant in prognosis. Physical function scores are the most significant prognostic measures for functional status (43, 44) work disability (45-47) costs (48) joint replacement surgery (49) and premature death (43, 50-56) at higher levels than radiographic scores or laboratory tests. Patient questionnaire data concerning physical function predict RA mortality at levels comparable to blood pressure, cholesterol, and smoking, as risk factors for premature cardiovascular death (52). In fact, physical fitness and performance are universal predictors for survival in diseased and non-diseases populations (57) and can be assessed quantitatively according to a variety measures ranging from simple patient self-report questionnaires to full scale performance tests, among which patient self-report is the most cost-effective and accurate.

In addition to Core Data Set items, a clinical questionnaire may include a Rheumatoid Arthritis Disease Activity Index (RADAI) self-report joint count (58), duration of morning stiffness, years of education, height and weight for body mass index, life-style choices such as smoking and the frequency of physical exercise, and work status. These measures are included on the MDHAQ, and a questionnaire used in the QUEST-RA program,(59) which will be described below.

Questionnaires that can be used in routine clinical care are easily completed by patients and easily scored by health professionals. Some questionnaires that are designed for clinical research such as the SF-36 (60) which is a "generic," non-disease specific" questionnaire and can be used to compare the impact of rheumatoid arthritis on daily life with the impact of, say, congestive heart failure or lymphoma. These questionnaires have complex scoring, and were designed for clinical research rather than routine clinical care.

Indices to measure RA disease activity

Indices of 3-7 measures used in clinical assessment of RA disease activity are based on a Core Data Set of 7 measures including 3 from a health professional (swollen joint count, tender joint count, global estimate of status), 1 from a laboratory (ESR or CRP), and 3 from a patient (physical function, pain, patient global estimate of status). The earliest use of an index was defined by the American College of Rheumatology (ACR) as a 20%, 50%, or 70% improvement in swollen and tender joint count plus 3 of the other 5 measures, known as ACR20, ACR50 and ACR70 responses (23, 61). The ACR criteria measure change compared to baseline, rather than absolute status. Therefore, a 50% improvement can be achieved

when tender and swollen joint counts are decreased from 20 to 10 or 4 to 2 (provided that 3/5 other ACR core data set measures also are improved 50%).

Inflammatory activity can be assessed according to absolute indices of efficacy or disease "state," which may be defined as a measurable, cross-sectional level of disease activity. The most widely-used index, the disease activity score (DAS, DAS 28) (62-64) includes swollen joint count, tender joint count, ESR or CRP, and patient global estimate, calculated using a computer website or a DAS calculator. A simplified disease activity index (SDAI) (65) includes five measures – the four DAS28 measures plus a physician assessment of global status. The clinical disease activity index (CDAI) (66) deletes the CRP from the SDAI. Other RA indices have been developed: the mean overall index for rheumatoid arthritis (MOI-RA) (67) which includes all 7 Core Data Set measures; and the LUNDEX (68), an index designed to incorporate patients' adherence to therapy.

Indices have also been designed based on PRO measures only such as a routine assessment of patient index data 3 (RAPID3) (69, 70). An index of physical function, pain, and patient global status distinguishes active from control treatment in clinical trials involving traditional (71, 72) and biologic therapies at levels similar to the DAS 28 and CDAI (73).

"Disconnect" of inflammatory activity, damage, and outcomes

Disease activity measures are sensitive to change over a period of weeks to months and are regarded as short-term surrogate markers for long-term joint damage, such as joint deformity and radiographic progression, and clinical outcomes, such as work disability, joint replacement surgery, and premature mortality (52), which develop over years to decades.

However, it was recognized already during the mid 1980s that short term drug efficacy was not necessarily translated into long-term effectiveness (43). Several studies have indicated progression of radiographic damage and decline of physical function over 5-10 years while measures of inflammatory activity were stable or improved [reviewed in (74)].

One example is the FIN-RACo trial which documented that suppression of inflammation at a level of 20% or 50%, i.e., ACR20 or ACR50 does not provide optimal improvement in outcomes. Among patients whose inflammation was controlled to a status of remission at 6 months, no patient was receiving work disability payments 4 ½ years later. By contrast, 22% of patients who had ACR20 or ACR50 responses, and 54% of patients who did not have ACR20 responses, were receiving work disability payments at 5 years after baseline (75). Therefore, improvements greater than 50% in RA disease activity measures appear needed to prevent adverse long-term outcomes in many patients.

Assessment of joint damage of RA

Radiographs

The two most widely used quantitative measures of radiographs are based on scores developed by Sharp (76-78) and Larsen (79, 80). The Sharp method involves separate scores for erosions and joint space narrowing, scored on 0-5 scales. The Sharp score modified by van der Heijde is widely used in clinical trails; total scores range from 0 to 448 units (81-83).

The Larsen method is based on a global score for each joint (84). Kaarela and Kautiainen (85) suggested a range of score of 1-100 including 10 MCP joints, wrists, and the 2nd to the 5th MTP joints. Rau and Herborn (86) introduced a modified Larsen score which counts the percentage of the loss of joint surface, and is more recently known as a Ratingen score (87). Scores based on the Sharp and Larsen approaches are correlated significantly (88).

Quantitative measuring beyond disease activity

As suggested above, disease activity is only one dimension of manifestations of RA and may not be sufficient to provide an comprehensive picture of patient status over time. A standard format for efficient collection of data in patients with RA has been developed in clinical research over the last two decades, termed a "standard protocol to evaluate rheumatoid arthritis" (SPERA) (27, 89). This format has proven useful to collect data in a number of studies concerning prognosis and monitoring of patients, including development of a 28 joint count (25); observation of radiographic damage in most patients within the first two years of disease (90); recognition that patient questionnaires are correlated significantly with joint counts, radiographic scores and laboratory tests (91) while providing more significant predictors of work disability (45) and mortality (52, 54) than traditional measures; and observations that a relatively small proportion of patients was eligible for clinical trials in contemporary care of RA (26, 29). The SPERA format was used to document that patients with RA in 2000 had considerably better status than all patients seen in 1985 in the same clinical setting (41). SPERA has been used to collect comprehensive baseline clinical data in more than 8,000 patients in 32 countries for the QUEST-RA program (59, 92-95).

SPERA includes data from both the patient and clinician. The patient completes a standard self-report questionnaire-a HAQ (38), MDHAQ (69, 70), QUEST-RA comprehensive HAQ, or variant for physical function, questions concerning pain, global status, fatigue, self-report joint count, duration of morning stiffness, years of education, height and weight for body mass index, life-style choices such as smoking and physical exercise, and work status.

The clinician completes a SPERA which addresses:

a) review of clinical features, including classification criteria, extra-articular features, comorbidities, and relevant surgeries;
b) all previous and present DMARDs, their adverse events, and reasons for discontinuation;
c) a 42-joint count (96) which includes swollen and tender joints, as well as joints with limited motion or deformity.

The first two SPERA documents are designated as a permanent document that can be updated if needed. SPERA captures most important baseline information that a clinician should know to care for a patient with RA, as well as baseline information for a clinical trial or observational research study. It incorporates the 5 core domains listed in a consensus for long-term observational studies from an Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) conference in 1998: health status, disease process, damage, mortality, and toxicity/adverse reactions (97). A database derived from SPERA or similar protocols could be used at baseline for all clinical trials as well as in standard care to facilitate analyses of long-term outcomes of rheumatic diseases beyond disease activity measures.

The QUEST-RA international database to characterize disease activity and outcomes in patients seen in usual care of RA

QUEST-RA is a unique multinational collaboration to review patients with RA for their clinical status and is therefore described here as an successful example of quantitative clinical measuring of RA as part of routine clinical care. QUEST-RA collects data from consecutive, unselected, patients with RA with no other selection criteria but adult-onset RA. Three or more clinics are invited in each country, to ensure generalizability of the data. In each clinic, 100 or more patients are assessed according to the SPERA evaluation described above. The primary aim of the QUEST-RA program is to provide "hands-on" experience to rheumatologists with patient questionnaires and standard clinical monitoring as part of usual care, in order to advance inclusion of quantitative data at every rheumatology visit.

QUEST-RA was initiated in January 2005. By June 2009, the program enrolled 8,039 patients from 86 sites in 32 countries including Argentina, Brazil, Canada, Denmark, Egypt, Estonia, Finland, France, Germany, Greece, Hungary, India, Ireland, Italy, Japan, Kenya, Kosovo, Latvia, Lithuania, Morocco, the Netherlands, Norway, Poland, Romania, Russia, Serbia, Spain, Sweden, Turkey, United Arab Emirates, United Kingdom, and the United States (98).

QUEST-RA provides data on current clinical status, disease activity, and patient reported health in many countries (59, 92-95, 98-100) and serves as an example of the value of data collection in individual clinics. Some observations from QUEST-RA will be reviewed here.

A strong association of disease activity and Gross Domestic Product (GDP)

The mean disease activity on DAS28 ranged between 3.1 and 6.0 among the 25 countries which were evaluated by April 2008 (93). Disease activity levels differed substantially between countries with higher GDP>24K USD and lower GDP<11K USD at much greater levels than according to whether patients were currently taking or not taking methotrexate, prednisone, and/or biologic agents. Disease activity was associated significantly with GDP [r= -0.78 (95% CI-0.56 to -0.90), r^2 = 61%] (Figure 2).

Among 48 clinical settings which participated by April 2007, low disease activity of DAS28 <3.2 was seen in more than 50% of patients at 8 sites in 6 countries: the Netherlands, Finland, USA, Greece, Denmark, and Spain

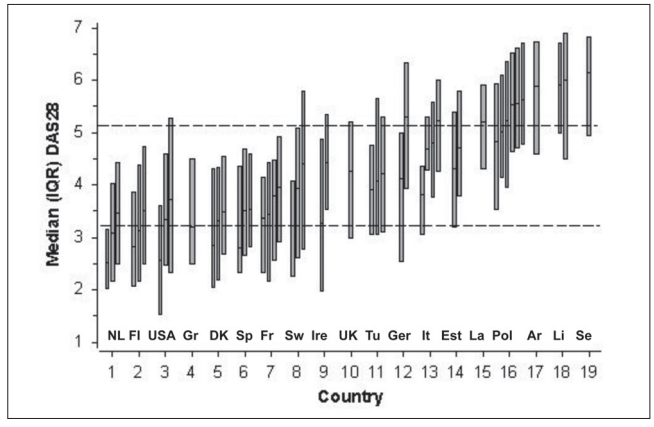

Figure 1. Disease activity in the QUEST-RA study

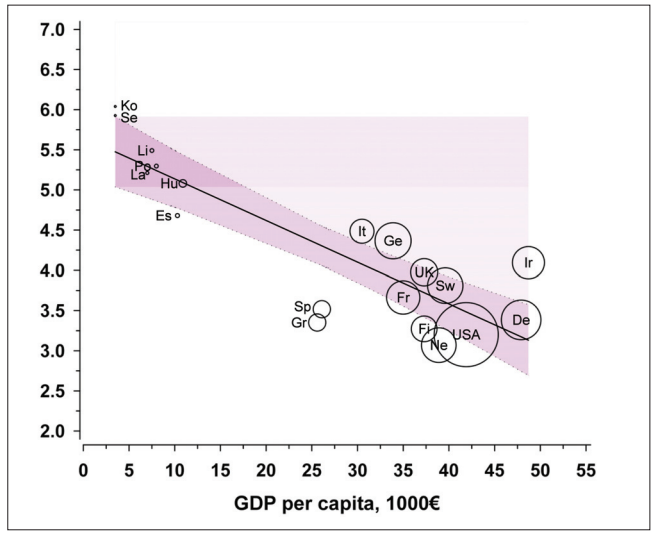

Figure 2. Association between gross domestic product (GDP) and disease activity (DAS28) in 19 countries in the QUEST-RA study

(Figure 1) (59). The data extend observations that most patients at some clinical sites would not be eligible for most RA clinical trials due to low disease activity (26, 101). By contrast, more than 50% of patients had DAS 28>5.1, indicating high disease activity in 5 countries, including Latvia, Poland, Argentina, Lithuania and Serbia, all low GDP countries.

These findings are consistent with extensive evidence that macro-economic variables provide significant explanation of variation in health outcomes among different nations. GDP predicts variation in overall mortality, infant mortality, and life expectancy (102-104) in different countries, as well as outcomes of specific diseases, such as 5-year survival of cancer in 22 European countries (105).

Is it better to be a woman or a man with RA-does gender affect RA disease activity measures?

The issue of possible effects of gender on disease activity at levels close to remission has emerged at this time, when patient clinical status is improved compared to earlier decades, due to better treatment strategies and biologic agents (106). Remissions are seen more frequently than earlier decades, although influenced by definition used (98, 107). Some studies suggest that male gender is a major predictor of remission in early RA (108, 109) and some others that men have better responses to treatments with biologic agents than women (110-112). All biologics clinical trials use DAS 28 for the definition of remission (107).

These discussions led to studies of the influence of gender on DAS28 remission. Among >6.000 patients, women had higher scores than men for all ACR core data set measures. Overall, 30% of men and 17% of women were in DAS 28 remission (92, 98). Differences in remission rates were most pronounced in patients who had no swollen joints: many fewer women than men (42% vs. 58%) met DAS 28 remission. These observations indicate that lower remission rates in females are accounted for other components of the indices (than the number of swollen joints) such as number of tender joints, patient self-report scores, and higher normal ESR in women (113). Higher DAS 28 remission rates in men might reflect at least in part gender differences in indices rather than true gender differences in RA disease activity!

Variation in therapies for RA

Clinical trials provide evidence of efficacy of new therapies. Register data are available in a few countries concerning clinical safety of biological treatments. Cohort studies that describe DMARDs for RA represent a small, selected minority of all patients. These sources cannot provide an overall picture of the drug treatment for RA and therefore, we sought to analyze the QUEST-RA database for RA therapies.

In the QUEST-RA patients, the use of intra-muscular gold as the first DMARD dropped from >60% in patients who were diagnosed with RA the 1970's to <2% in patients who were diagnosed with RA in the 2000's, and the use of MTX ascended from 2% to >50% as the initial DMARD.

At 61 QUEST-RA sites in 21 countries, 63% of patients were taking methotrexate and 20% were taking biologic agents in 2005-07 (114). Fewer than 20% of patients were currently taking oral glucocorticoids in Denmark and the Netherlands, in contrast to 83% of patients in Lithuania. More than 25% of patients were taking biologic agents in the USA, France, Sweden, Ireland, and Latvia, although the high percentage in some countries may be explained by prior inclusion of some patients in randomized clinical trials of biologic agents. Fewer than 10% of patients were taking biologic agents in Serbia, Estonia, Argentina, Turkey, Poland, and Lithuania.

Methotrexate was taken at some time by 86% of all patients, prednisone 72%, sulfasalazine 46%, antimalarials 42%, any biologic agent by 24%, intra muscular gold by 23%, and leflunomide by 22% of all patients. Cyclosporine-A, azathioprine, and D-penicillamine were taken by 7-10% of patients (114).

In addition, longer use of many DMARDs was associated with a reduced risk of cardiovascular events (95).

Physical activity in RA population-a moving target?

Regular physical activity is associated with decreased morbidity and mortality at a population level (115). Traditionally, patients with RA were advised to avoid or limit physical exercises with a fear that physical exercises might increase disease activity and harm joints. Physical therapy for RA was directed to relieve pain, and included heat and cold therapy, splints, range of motion exercises, and other conservative regimens. Indeed, decades ago many RA patients had severe destructive disease and instructions to participate in rigorous physical activities, and even minimal exercise were regarded as inappropriate.

Over the past decade, the importance of exercise as a component of the management of RA has been recognized with recommendations of regular physical exercises (116), benefits such as increased muscle force and aerobic capacity, decreased inflammation and pain, improved function, and sense of well-being (117-119) have been observed in patients with RA. Therefore, it was our interest to study whether individuals with RA participate in exercises in different countries.

Data from 21 countries were analyzed (99). Only 13.8% of all patients reported physical exercise $\geq$3 times weekly. The majority of the patients were physically inactive with no regular weekly exercises: >80% in seven countries, 60-80% in 12 countries, and 45% and 29% in two other countries. Physical inactivity was associated with female sex, older age, lower education, obesity, comorbidity, low functional capacity, and higher levels of disease activity, pain, and fatigue. These data may alert rheumatologists to motivate their patients to increase physical activity levels.

Work disability as an outcome measure

Work disability is a major consequence of RA (43, 120-122). Although cumulative over time, 20-30% of patients become permanently work-disabled in the first 2-3 years of the disease (123). Rapid remission in early disease appears a beneficial strategy against work disability in RA (75).

Availability of biologic agents over the past decade has led to expectations of reduced work disability rates in RA (124), according to observations in clinical trials (125-129). However, reports of clinical cohorts indicate that work disability remains a major problem in RA (130-133). Possible explanations include that the timing of biologic agents after joint damage is seen may be too late in many cases at this time, and/or that use of biologic agents is unusual in many countries for financial reasons (114).

As noted above, work disability is identified most significantly by measures of functional status. The risk of work disability in RA is associated not only with traditional articular, radiographic and laboratory measures of disease activity and severity, but as much or more with demographic, socioeconomic, vocational, functional and social policy variables (120, 134). Although work disability is one of the most important outcomes in RA, cultural and economical differences between societies (135) may compromise its value as an outcome measure.

Most studies concerning work disability in RA have been conducted in North America and Western Europe, and little is known about employability of RA patients in other countries. QUEST-RA provided an opportunity to study issues related to work disability in a multinational setting (136).

At the time of first symptoms, 86% of men (range 57%-100% among countries) and 64% (19%-87%) of women <65 years were working. More than one-third (37%) of these patients reported subsequent work disability because of RA. Among 1,756 patients whose symptoms had began during the 2000's, the probability of continuing to work was 80% (95%CI 78%-82%) at 2 years and 68% (95% CI 65%-71%) at 5 years, with similar patterns in high-GDP and low-GDP countries. Patients who continued working vs. stopped working had significantly better clinical status for all clinical status measures and patient self-report scores, with similar patterns in high-GDP and low-GDP countries. However, patients who had stopped working in high-GDP countries had better clinical status than patients who continued working in low-GDP countries. The most significant identifier of work disability in all subgroups was HAQ functional disability score.

QUEST-RA data indicate that work disability rates remain high among people with RA during this millennium. The data showed that in low-GDP countries, people remain working with high levels of disability and disease activity. Indeed, disease activity and disability levels were as high in working people in low-GDP countries as in work-disabled people in high-GDP countries. The data indicate that cultural and economic differences between societies affect work disability as an outcome measure for RA.

Conclusions

Quantitative assessment of rheumatoid arthritis in standard clinical care is valuable to improve the quality of visits for patients and health professionals.. In addition, the data provide opportunities for comparison of groups of patients to improve knowledge of disease in real life settings. This review indicates that it is possible for any rheumatologist to turn clinical work to clinical science by collecting quantitative measures in routine care settings. Data from an international collaboration are presented to illustrate the value of this activity.

Conflict of Interest

No conflict of interest is declared by the authors.

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