
Internet-based monitoring of patients with rheumatoid arthritis

S.J. Lee, L. Lenert, A. Kavanaugh

Center for Innovative Therapy, UCSD,
Division of Rheumatology, Allergy and
Immunology, La Jolla, California, USA.

Susan J. Lee, MD; Leslie Lenert, MD;
and Arthur Kavanaugh MD.

Please address correspondence to:
Arthur Kavanaugh, MD, Professor of
Medicine, Center for Innovative Therapy,
UCSD, Division of Rheumatology, Allergy
and Immunology, 9500 Gilman Drive,
La Jolla, CA 92093-0943, USA.

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ABSTRACT

Patient-derived measures have been increasingly recognized as a valuable means for monitoring patients with rheumatoid arthritis. One advantage of this data is that it can be collected remotely. This would allow more frequent and more rapid assessments, which could optimize therapeutic intervention and patient outcome.

Case vignette: October 28, 2006

Mrs. Ann Dawson is a 46-year-old woman who presents to her primary care physician (PCP) with pain in her joints that has been present for about 6 weeks. She self-medicated with an over-the-counter NSAID, and comes in due to worsening pain and an inability to continue working at her job.

On initial presentation, the patient has bilateral swelling of all of her MCP joints and several PIP and DIP joints, as well as both wrists and knees. The PCP prescribes a tapering course of prednisone and a different NSAID, and orders laboratory tests as well as radiographs of her hands and knees. Results are completed early in the next week, and show an ESR of 86, a positive rheumatoid factor of 325 IU/dL and a high titer of anti-CCP antibodies. X-rays show only soft-tissue swelling about the involved joints.

Despite a typical 8-month wait for a new patient referral appointment, a local rheumatologist agrees to see the patient the next week after the PCP presents the details of the case. On evaluation, the rheumatologist confirms the joint involvement noted by the PCP, and additionally finds synovitis of the elbows and ankles. An ultrasound examination shows greater involvement with synovitis in the PIP joints than was suspected clinically and also reveals small periarticular erosions at several MCP joints.

Knowing that the patient has not only active disease, but also multiple risk factors for severe disease and a poor

outcome, the rheumatologist wishes to embark on an aggressive course of treatment. Methotrexate is begun at an initial dose of 12.5 mg per week, along with folic acid. However, due to a shortage of rheumatologists as well as constraints imposed by her payer, the soonest the patient can be seen in followup by the rheumatologist is 12 weeks later. How can this patient be started on an effective regimen in the shortest possible time?

Introduction

Recent advances in biotechnology coupled with a growing knowledge of the pathogenesis of autoimmune systemic inflammatory diseases such as rheumatoid arthritis (RA) have led to the development of multiple novel approaches to the evaluation and treatment of patients. With the introduction of new therapeutic agents, the clinical efficacy achieved as well as the costs of which both exceed those of traditional therapeutic agents, there is an urgent need to standardize the collection of outcome measures assessing patients' response in both clinical trials and clinical practice. Disease activity in conditions such as RA can be measured using a variety of assessments. Some relate to patient reported indicators, such as amount of pain, duration of morning stiffness, functional ability, and global assessment of how the disease impacts them. Physician-generated measures (such as the determination of swelling and tenderness in individual joints and an overall assessment of disease activity) are also used, as are more objective measures such as laboratory tests and radiographs. Unfortunately, like many rheumatic diseases, RA is a multifaceted disorder whose activity cannot be completely captured using any single metric. Useful outcome measures for RA should demonstrate good reproducibility and meet all the fundamental criteria for validity, including construct, discriminant, and criterion validity. Con-

struct validity requires that any proposed marker or disease activity measure constructs that are plausibly related to RA and change in the same direction as the clinical change and other known markers. Discriminant validity assesses the responsiveness of the disease outcome measures to clinical change, and its ability to precisely identify clinically important changes. Criterion validity is difficult in RA and other rheumatic diseases because there is not a single criterion for the disorder. In this situation, it may be thought of as the capacity of disease measures to capture all clinically important aspects of change while also predicting long-term outcomes (1).

The American College of Rheumatology (ACR) has developed a Core Data Set of 7 disease activity measures to assess outcomes in clinical trials for the treatment of RA. These include 3 assessor derived measures – the tender joint count (TJC), swollen joint count (SJC), and the physician's global assessment; 1 laboratory test – the erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP); and 3 self-reported patient measures – functional disability, pain, and the patient's global assessment (2). These items were chosen based upon their capacity, when combined in a composite index, to differentiate active treatment from placebo responses in clinical trials of RA patients. Also, assessment of disease with these measures has been shown to correlate with long-term outcomes in patients with RA.

The patient-derived measures are a key part of the Core Data Set. As technologies for measurement of patient-derived data advance, a growing question is the degree to which patient-derived data can be used by itself to assess the response to treatment. This paper will review the data for use of patient derived measures on computers to assess the impact of therapies for RA. Patient data are important not only because improving aspects of the disease that are important to the patients is a desirable goal, but also because physicians often underestimate the severity of patients' depression, functional disability, pain, and fatigue (3). Traditionally,

paper forms have been used to capture this information and these forms have become familiar to doctors and office staff in the context of clinical trials and to a lesser extent in clinical practice. However, in recent years, computerized patient monitoring systems have been gaining popularity in rheumatology, oncology, and other fields. Computer versions of forms to record patient data have several potential advantages including automated validation, improved data capture and immediate result availability (4, 5).

Patient-derived health status questionnaires

Both generic and disease-specific health status questionnaires have been validated and are available for the evaluation of the functional status and quality of life in patients with diverse rheumatic diseases, especially RA. The Medical Outcomes Study Short Form 36 (SF-36), Arthritis Impact Measurement Scales (AIMS), and the Health Assessment Questionnaire (HAQ) are among the most commonly utilized instruments in RA clinical trials. These instruments can serve as a quantitative means to compare and document the patient's clinical status from one visit to the next, while also giving the patient a sense of empowerment (6).

Many self-rated questionnaires used in the assessment of RA patients have been proven reliable, valid, and sensitive to change in multiple studies (1, 6-9). For example, in a study comparing cyclosporine and placebo in the treatment of RA, the physician's and patient's global assessments were among the most efficient measures, along with the TJC, in detecting a treatment effect and demonstrating sensitivity to change (1).

Another study comparing the efficacy of leflunomide, methotrexate, and placebo indicated that patient derived measures from the ACR Core Data Set were equally effective as the overall ACR 20% and Disease Activity Score (DAS) to differentiate efficacy in the treatment group from the placebo group (2). In addition, in 2 large randomized controlled trials assessing leflunomide, sulfasalazine, methotrexate, and placebo,

not only did patient-reported outcomes effectively identify the treatment group but they were also less susceptible to the placebo effect than physician-derived measures. Interestingly, whereas physician-derived measures tended to exhibit substantial improvement among patients in the placebo group, patient-derived measures showed only minimum improvement or worsening status with placebo treatment (10).

Nonetheless, some physicians have expressed concerns that self-reported questionnaires are subjective measures, making them less reliable surrogate markers for disease outcome and activity. Physicians often weigh what they consider to be more objective and quantifiable measures such as joint counts more heavily in their assessment of RA disease activity. However, multiple studies have demonstrated that self-report questionnaires such as the HAQ and patient global assessment correlate significantly to traditional objective measures (1, 2, 11). Furthermore, these patient-derived measures have been shown to predict long term disease outcome. In a recent prospective study of 1416 RA patients, higher scores on the HAQ, visual analog scale (VAS) for pain, and functional class helplessness, along with fewer years of formal education, significantly predicted patient's 10-year mortality (12). These studies have demonstrated that patient self-reported measures of disease activity and impact as measured with simple questionnaires can be as effective as, and often more effective than, composite indices including traditionally used outcomes measures.

Patient self-report joint count

With the proven validity and usefulness of the patient self-report questionnaires such as HAQ and VAS for pain, there has been a surge of interest in utilizing the patient self-report TJC and SJC to assess disease activity in RA patients. Multiple studies have demonstrated that the results of a self-administered TJC, especially those using a mannequin version, correlated reasonably well to the physician TJC, with correlation coefficients of 0.54–0.77 (13-19). The differences in correlation actually ap-

proximate those expected with the inter-physician differences in TJC, as noted in a study using the Ritchie index (14). Furthermore, the correlation between the patient self-administered TJC and other measures of disease activity such as the ESR, VAS, and HAQ, was comparable to that of the physician's TJC (13-19). However in one study, despite its high correlation to other markers of disease activity, the patient self-administered TJC was consistently higher than the physician TJC (15, 19). In comparison to TJC, self-administered SJC typically have slightly lower correlation coefficients, in the range of 0.44–0.64. This could reflect greater difficulty for patients differentiating painful joints from swollen joints, especially for joints that are difficult to examine, such as the metatarsals (14-16).

Despite their potential to provide useful and unique information on the patient's functional status and disease outcome, patient self-reported data are still used relatively infrequently in clinical practice. Some of the reservation stems from insufficient exposure to questionnaires, concerns about the extra time needed to administer and complete the questionnaires, and the perceived potential disruption of the clinic flow (20). Encouragingly, with a short training course on the use of self-report questionnaires, most practicing rheumatologists found these functional status questionnaires and VAS for pain to be as useful as TJC/SJC in the evaluation of RA patients. Even at the 6-month follow-up after the initial training course, nearly 50% of the initial 18% of the rheumatologists reported using questionnaires in their practice (21).

Computer based patient-derived health status questionnaires

Although there has been a growing trend towards using patient-derived questionnaires to supplement other disease outcome measures in clinics, many rheumatologists fail to use them in their practice due to the logistics of administering paper forms, costs, and unavailability of the results for immediate application during their visits. Also, there are issues with interpreta-

tion of the data obtained from some instruments. For example, certain questionnaires such as SF-36 have complex and non-intuitive grading systems, potentially leading to difficulties with the scoring and interpretation of data for individual patients (21).

Of note, worldwide there has been a trend towards greater use of electronic medical records, making paper forms even obsolete in some practice settings. This trend could reasonably be expected to continue or even increase in the future. Fortunately, recent advances in computer software together with relatively cheap hardware have prompted the development of computer-based patient questionnaires. These forms can be directly incorporated into the electronic medical record and are readily available for immediate use.

Multiple studies have recently been conducted to test the validity and the correlation of the computerized versions of common questionnaires to the already validated paper versions. A study comparing the paper and the electronic versions of the SF-36 in healthy volunteers and chronic pain patients noted a high level of correlation between the two versions (22). Similar findings were seen among a group of rheumatology patients with a correlation coefficient of 0.80–0.96 (23). Although both forms required similar amounts of time for completion, the electronic version had 100% data completion whereas the paper form had 26-44% missing data. Also, despite a concern for the usability and acceptability among inexperienced computer users, the majority of the participants, including the older and inexperienced group, preferred the electronic version (22, 23).

Several studies assessing the validity of computerized versions of measures such as the HAQ and VAS scales for pain and global assessment have been conducted in the past few years, with promising results. As seen with the SF-36, a high correlation (0.75-0.96) was seen between the paper and computer versions of these 3 patient-derived questionnaires, although the mean HAQ score tended to be slightly higher on the computer version (23, 25). Not only

did the patients find the computerized system easy to navigate but it was also well received by the office medical staff and by physicians. Among patients, a positive correlation for the overall usability was seen with their personal computer experience, household income, and the presence/absence of hand disability (20). Contrary to popular belief, age was not significantly correlated with patient's preferences regarding computer versus paper versions of the forms. In fact, a focus group composed of patients 65 or older identified difficulty with mouse manipulation and the potential loss of privacy as the 2 major concerns with the computerized system, not unfamiliarity with the computer (20). If hand arthritis is indeed a hindrance to filling out a questionnaire, this effect may even be exaggerated when using the pen and paper version, partially accounting for its high incomplete rate. In one study, the option to choose among various pointing devices (e.g. mouse, trackball, touch pad, touchscreen) enhanced the acceptability of the computer forms among those with hand disability (24). A recent study assessed the utility and validity of computerized versions of the HAQ, VAS scales for pain and global severity of disease, and self-reported TJC and SJC, in comparison to the paper versions (24). The computer format for joint counts utilized homunculus-style figures as a top-down view of a person sitting in a chair looking at a computer, similar to the position of the user at the time of the form completion. In this study, HAQ, VAS for pain, and VAS for global disease severity all showed high correlations between the computer and paper versions. While TJC had a significant correlation coefficient of 0.85, a lower correlation coefficient of 0.60 was noted for SJC (24). The lower correlation for SJC most likely reflects the overall poorer reliability of the SJC, rather than issues with the computerized format itself. This study demonstrated the utility and viability of collecting such important patient-derived data on the computer, paving the way for the remote compilation of such data, for example over the internet.

Potential advantages and disadvantages of computer based patient outcome measures

Computerized patient-rated questionnaires have a number of potential advantages over traditional paper forms. As seen in prior studies, computer forms tend to capture data more completely and with less ambiguity (20, 22-25). For example, in paper versions, patients can either skip questions or provide problematic responses (e.g. marking more than one answer or marking between 2 overlapping categories) (22). Computer programs can overcome this issue by providing one question per screen and accepting only unambiguous answers. Although patients can end their sessions at any time, incomplete data can be minimized by prompting patients for missing data with any attempt to save an incomplete questionnaire. While such data correction could also be done for paper versions, it would require substantial staff time to do so. In addition, with computerized versions of patient questionnaires, the program can perform an automatic scoring of the questionnaire upon completion for immediate availability of the results. Physicians can then share the results with the patient during their visit to both foster better communication and to make clinical decisions about the treatment plan (20).

One of the greatest values of the computerized patient outcome measures is that it allows for more frequent efficacy assessments and safety monitoring. Many of the traditional disease modifying anti-rheumatic drugs (DMARDs) used for the treatment of RA have a relatively slow onset of action, with the maximum anti-inflammatory effect not being evident until months after the initiation of therapy. Even biologic agents, which have a quicker onset of action, may require several weeks of treatment or dose adjustments to achieve maximal results. The efficacy of traditional DMARDs can, in some cases, be optimized by a rapid acceleration of the dose. This rapid adjustment of dose, which has been utilized for example with MTX dosing in several recent studies, is contingent upon tolerability and the absence of safety issues.

Outside of clinical research studies, patients are typically evaluated in the clinic at periods of 6-8 weeks or more after the initiation of the drug for toxicity and efficacy. Due to limited resources and other considerations, it is quite difficult for many rheumatologists to see all of their patients at shorter intervals. Therefore, it might take quite a few months before a patient reaches a therapeutic dose. During this time, he or she can suffer significantly, both physically and psychologically, from persistent disease activity.

In recent studies, it has been clearly demonstrated that the rapid institution of effective therapy in patients with early RA can achieve significant benefits, including decreased radiographic damage and the induction of disease remission to a greater extent (26,27). Rapid achievement of disease control with therapy has become a central goal of the treatment of RA patients. If physicians can more quickly escalate and otherwise optimize therapy with DMARDs, biologic agents, or combinations of therapies, patients are likely to benefit with improved disease outcomes. With computerized forms, patients could complete the self-report questionnaires at home and provide them to their physicians through secure internet access in between the scheduled visits. Subsequently, physicians could review and compare the results with that of the prior visits and adjust their medications accordingly in the absence of obvious drug toxicity. With this model, patients can arrive at a therapeutic dose earlier through quicker dose escalation, potentially minimizing their functional disability. In established patients with stable disease, visits might be scheduled at longer intervals depending on their questionnaire scores and reported tolerability of treatment, particularly for patients who can have safety screening laboratory tests checked through visits with their primary care physicians.

Although initial expenditure on computer hardware and software can be costly, with greater use over time the overall cost can be equivalent to or less than their paper counterparts (20). In clinical research, the computerized col-

lection of outcome measures has been suggested to decrease the time, error, and the cost related to the collection of data. This should be true for clinical practice as well. Also, as part of the electronic medical records, patient self-report assessments can be shared with the patients' other health care providers to communicate their health status more efficiently. There is growing interest in electronic patient-doctor communication (28). It has been reported that half of Internet users desire to communicate with their physicians electronically, and the ability to do so may affect their choice of physician. Moreover, electronic patient-doctor communication may soon achieve the imprimatur of reimbursement. In the USA, as of January 1, 2004 online consultations received a designated CPT code, which would facilitate billing for such services. The introduction of reimbursed online consultations is underway in various settings.

There remain some concerns regarding computer-based patient monitoring. For example, despite the widespread use of computers, some remain skeptical and continue to have difficulty with computer applications. Hopefully, this barrier can be overcome with increasing exposure and the proper training of both patients and physicians. Of course, careful attention must be given by both web hosting services and application providers to assure patient privacy, in accordance for example with the USA Health Insurance Portability and Accountability Act (HIPAA).

Conclusion

The traditional paradigm for the treatment of RA relies upon the physician's assessment of the efficacy of treatment. If this approach is not practical, there may be other alternatives. Patient self-rated questionnaires have been validated as an important quantifiable instrument for the evaluation of disease outcome and activity in patients with diverse rheumatic conditions. In RA patients the SF-36, HAQ, VAS for pain, global assessment, and TJC are among the most commonly utilized patient-derived outcomes. They have been found to be equivalent to many tradi-

tionally accepted objective measures of disease activity such as the physician's TJC, SJC, and ESR. Recently, computerized patient-rated health status questionnaires have been developed and validated against the paper format. The computer-based questionnaires can gather higher quality data at a lower cost and lower administrative burden than paper versions. Most importantly, this system offers an opportunity to monitor the patient's health status more frequently to optimize disease management. In the specific example of RA, internet-based monitoring of patients for the efficacy and tolerability of their medications has the potential to optimize therapy and improve outcome.

Case vignette: follow-up

In addition to prescribing methotrexate, the patient is provided the address of a secure web site that she can use daily to record her symptoms. Mrs. Dawson completes the questionnaire concerning signs and symptoms of arthritis as well as potential side effects every morning, and the data are transmitted to her physician who can review the trends. After 2 weeks, the patient still has significant arthritis, and is tolerating the methotrexate without adverse effects, so the physician calls and instructs the patient to increase MTX to 15 mg/week, and if still tolerated, increase again to 17.5 mg/week the next week. After doing this, the patient is instructed to go to her PCP for laboratory testing 4 weeks after beginning MTX; the results are sent from the PCP's office to the rheumatologist. One morning, Mrs. Dawson misses using the web site. The site sends her an e-mail reminding her, and then a call to her cell phone. This program of follow-up continues; when the patient returns to the rheumatologist's office at 12 weeks, she has been on 22.5 mg/week of MTX for 4 weeks and is much improved, and she has had laboratory studies checked twice.

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