Editorial

# Improved Lupus Outcome. We Are Doing a Good Job, But Could We Do Better?

Few studies are published concerning longterm outcome and prognosis of rheumatic disorders, and reports on changing prognosis over time are extremely rare. There are many obvious reasons for this scarcity of publications. Longtime followup is difficult to achieve: you need to establish one or more cohorts and follow the patient in a standardized manner over many years in the clinic. To be able to provide information that can be generalized, recruitment of patients has to be representative for the disorder, and you must be able to characterize your cohort by established time for diagnosis and validated outcome variables. To analyze what determines prognosis you need standardized indices allowing stratification of disease activity, damage caused by disease, comorbidities, and therapy. Still, given all these obstacles, longterm prognosis studies are essential for understanding what happens with our patients and how we can change the outcome through our interventions. The ideal study has never been published and probably never will be, since so many biases have to be dealt with in the real world.

Systemic lupus erythematosus (SLE) is a good example of a rheumatic disorder where researchers have been struggling with the above mentioned obstacles. Many lupus centers have today established cohorts followed in a standardized manner with a database, but few with a followup exceeding 20 years. Where there is international cooperation, attempts to refine diagnosis and validate indices as foundations for prognostic studies have been fruitful. Systemic Lupus International Collaborating Clinics (SLICC) is an example of one such cooperative effort[1]. Based on the results of such cooperation, prognostic studies have only recently begun to utilize defined indices for disease activity[2], damage caused by disease[3], and comorbidities[4]. Researchers are still struggling with definitions of outcome[5], while the basis for all these studies, a proper set of American College of Rheumatology classification criteria for SLE, is presently under revision[6].

In this issue of *The Journal*, Urowitz, *et al*, from Toronto, one of the groups initiating the SLICC in 1980s, publish a work[7] based on an impressive 1241 patients followed in four 9-year cohorts between 1970 and 2005 with a standardized protocol over all 36 years!

The main conclusion from the Toronto study is that survival has improved in patients with SLE over the 36 years and that disease-related variables in the study are important for mortality. The results indicate the importance of adequate treatment and dose supervision during the first years after diagnosis of SLE. However, the authors also conclude that such factors cannot completely explain the trend observed. So the question partly remains: are we treating better or is something else going on? What part of the treatment is important for the good results? Has the natural course of SLE changed? Have comorbidities changed? Another conclusion in their article is that many years of life are still lost among patients with SLE: the standardized mortality ratio in the study is 2.3 despite improvement. So we are not doing well enough. Putting Urowitz and colleagues' article in perspective, what can we learn and how shall we proceed in the future?

First, do we really have any evidence we are treating better? At least now we are treating differently. For some differences it seems plausible that changes really matter. As Urowitz, *et al* found, there is an increase in the frequency of immunosuppressive treatment at presentation, which apparently parallels a decrease in disease activity over time. This might indicate success, but on the other hand steroid use has not decreased as might be expected. The prevalence of osteonecrosis is high throughout the study, at least compared with European experience, and could be a consequence of high steroid dosages. Early aggressive treatment is obviously one clue to success, but steroid tapering is probably also important for prognosis[8]. The article also shows an increase in antimalarial use. The beneficial effects

*See* Changing patterns in mortality and disease outcomes for patients with SLE, *page 2152.*

of antimalarials on both SLE and cardiovascular comorbidities are becoming more and more evident in the literature[9].

Second, what part of the treatment regime is important? This is obviously not the subject for the present article, but there is evidence that patients in centers with more experience in SLE are doing better[10], and we need studies on the importance of regular followups and what we can gain from introducing nurse clinics and giving lifestyle information with the aid of physiotherapists, manual therapists, dietary advice, and social support. We have some indications that support for lifestyle changes, such as smoking habits, physical activities, and treating overweight, are not offered to all patients with lifestyle problems[11]. There is a need for more teamwork and more professionals specialized in SLE.

Third, is there any evidence that the natural course of SLE has changed? By analogy this seems to have happened in rheumatoid arthritis, as we all know. This is a most difficult question to analyze. So many cultural and population variables are of importance both between and within cohorts. The impressive LUMINA study has analyzed many of these variables in a standardized way[12]. The Toronto group does not give us an answer, and the methodology needed includes proper epidemiology. A few such studies exist: a series from us in southern Sweden, where we have followed incident cases in an area since 1981, shows that the annual incidence and the clinical picture at presentation have so far been constant. Still, the course has changed over time, with improved survival and less morbidity[13]. We cannot conclude whether this is a result of our treatment regime or something else.

What about comorbidities? The Toronto article does not tell us anything about improved treatment for infections, which can also contribute to the results. We know that mortality in SLE due to infections is still a problem, but has decreased in the Western world over 30 years[14,15]. And while the Urowitz article does not tell us anything about other comorbidities, important work is in progress with the leadership of the Toronto group concerning cardiovascular risk factors[16]; and the Montreal group is leading studies of malignancy frequencies in SLE[17]. With prolonged survival, cardiovascular deaths and malignancies are increasingly important for SLE patients. These international efforts to find risk factors and strategies for lifestyle changes and balanced treatment with stratified followup regimens for SLE patients will be at the top of the agenda for the next 10 years.

So, we are doing well, but we could do better.

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J Rheumatol 2008;35:2088–9`; doi:10.3899/jrheum.080934