Measures of Disease Activity, Damage, and Health Status: The Hopkins Lupus Cohort Experience

The Hopkins Lupus Cohort is a prospective, longitudinal cohort study of predictors of outcome in systemic lupus erythematosus (SLE). As part of this study, measures of disease activity, damage, and health status have been used. The cohort offers a unique opportunity to evaluate these instruments.

DISEASE ACTIVITY

Since the cohort began in 1986, 3 valid and reliable measures of disease activity, the physician global assessment (PGA), using a 0 to 3 visual analog scale, the lupus activity index[1], and the SLE Disease Activity Index[1,2], have been used at each patient visit. Routine visits are scheduled quarterly.

In 1991 we studied the epidemiology of flare in SLE[3]. The definition of flare was a 1.0 change on the 0 to 3 PGA occurring over the last 93 days. About 50% of the patients in the cohort at that time had one or more flares. The incidence of flares was 0.65 flares per patient year of followup, with the median time to a flare of about 12 months. Serologic tests, such as complement and anti-dsDNA, were not predictive of flare.

Our more recent study of the cohort has examined the probability of an increase in PGA of one or more points within a 3.5 month period (Table 1). These analyses suggest that females have more flares than males, and that younger females are more likely to flare than older females. Severe flares (final PGA > 2.0) are very rare (Table 2).

Table 1. Estimated probability of an increase in physician global assessment by 1 or more points in a 3.5 month period in various subgroups of patients.

Group	Estimated Probability	95% CI
Total	0.17	0.15, 0.20
Males	0.09	0.04, 0.16
Females	0.18	0.16, 0.21
Age < 40 yrs	0.19	0.16, 0.22
Age 50+	0.14	0.08, 0.22

Table 2. Probability of an increase in physician global assessment by one or more points within a 6 month period, with a final physician global assessment > 2.0 ("Severe").

Group	Estimated Probability	95% CI
Total	0.04	0.03, 0.05
Males	0.02	0.01, 0.07
Females	0.04	0.03, 0.05

Flare is too simplistic a way to categorize disease activity in SLE. We have analyzed patterns of disease activity and have found 3 major types: "relapsing remitting" (Figure 1), "chronic activity" (Figure 2), and "long quiescence." The remitting pattern is the classic pattern, with flares and then return to zero activity. However, the chronic activity pattern, in which disease activity does not return to zero baseline, can still have flares (by our previous definition) superimposed on constant activity. The chronic activity pattern turns out to be the most frequent.

Clinical trials whose outcome measure is flare may ignore the disease activity represented by the chronic active pattern. In a clinical trial with evenly spaced visits, the most appropriate analysis of disease activity may turn out to be measurement of the area under the activity curve or the mean level of the activity scores.

DAMAGE

The SLICC/ACR (Systemic Lupus International Collaborating Clinics/American College of Rheumatology) Damage Index[4] has been updated yearly in the cohort. Cumulative damage is shown in Table 3[5]. Treatment with corticosteroids contributes more to the major forms of damage found (avascular necrosis of bone, osteoporotic fractures, cataracts) than the disease itself. Serologic tests, such as anti-DNA or complement, do not predict disease damage. Because damage accrues slowly, it is unlikely to change in a clinical trial of less than one year duration.

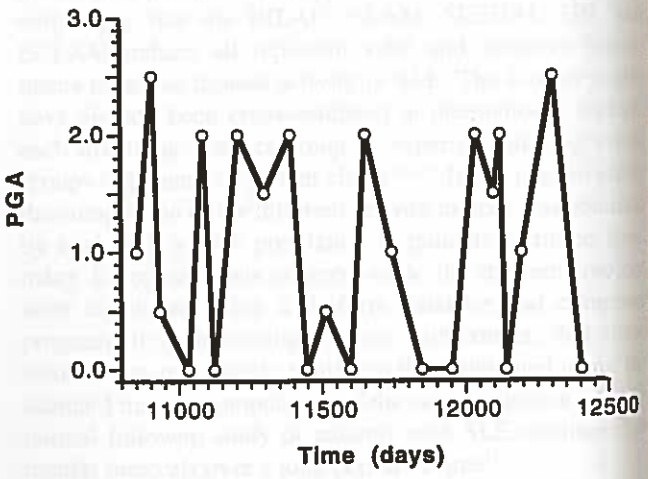

Figure 1. Relapsing remitting pattern of disease activity. The physician global assessment (PGA) is plotted against time (days).

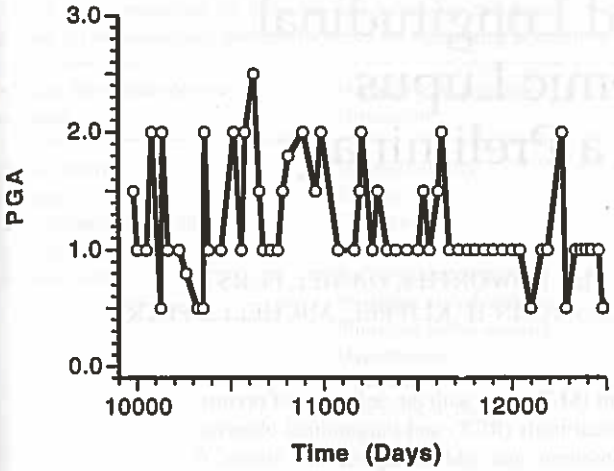

Figure 2. Chronic active pattern of disease activity. The physician global assessment (PGA) is plotted against time (days).

Table 3. Distribution of damage in the Hopkins Lupus Cohort (%).

Musculoskeletal	25.2
Neuropsychiatric	15.0
Ocular	12.6
Renal	11.7
Pulmonary	10.4
Cardiovascular	10.1
Gastrointestinal	7.4
Skin	7.4
Peripheral vascular	5.5
Diabetes	6.1
Malignancy	2.5
Premature gonadal failure	1.2

HEALTH STATUS

Several groups have now shown that patients with SLE have poor health status using measures such as the Medical Outcome Survey Short Form (SF-20) or SF-36. Our concern has been that the health status measures may be reflective more of comorbidity than active lupus.

For example, fibromyalgia is extremely common in SLE, occurring in as many as 30% in some series. In our cohort, fibromyalgia tender points are a major associate of poor coping measures[6] and poor health status[7]. Thus, it is possible that a drug for fibromyalgia that had no effect on active lupus whatsoever would improve health status in SLE, whereas a drug such as cyclophosphamide, with greater utility for severe SLE, might actually worsen health status (by its effect on fatigue).

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