

Quality of life in systemic lupus erythematosus

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Abstract

Systemic lupus erythematosus (SLE) is a pervasive disease with wide-ranging effects on physical, psychological and social well-being. As such, a comprehensive assessment of SLE should include several different outcomes, such as quality of life (QoL) and economic costs, in addition to measures of disease activity and damage. In fact, disease effects on QoL are often considered of greater overall importance to patients. Two approaches have been used in the measurement of QoL: generic questionnaires and disease-specific questionnaires. Generic questionnaires are designed to be used across various conditions and populations, whereas disease-specific questionnaires are designed to measure outcomes in one specific disease or condition. The most commonly used measure of QoL is the Medical Outcomes Study Short Form 36 (SF-36), which is a generic measure that is applicable in a variety of conditions, including SLE. Recently, SLE-specific measures have been developed that may prove to be more responsive than generic measures. The hope is that improved outcome measures will allow for better assessment of SLE and eventually facilitate drug development and improve patient care.

Keywords: *Systemic lupus erythematosus, quality of life, outcome measures, drug development*

Introduction

SLE is a pervasive disease that results in variable and occasionally life-threatening, manifestations. It afflicts young people disproportionately, often at a crucial time in their lives when they are trying to establish relationships, start families and launch careers. As a result, persons with SLE may experience a wide range of physical, psychological and social problems that are not always fully captured by descriptions of the disease's physiological consequences alone. In order to characterize the full spectrum of the effects of SLE, a comprehensive assessment should consider a variety of other outcomes, which may be of equal or even greater importance to the patient. One such outcome is QoL, which is increasingly being recognized as an important aspect of chronic diseases and considered by many as a relevant measure of efficacy in clinical trials.

Outcome measures used in SLE

The course of SLE is characterized by exacerbations (or flares) of disease activity and disease damage.

Disease damage is permanent and may result from repeated flares of disease activity, or as a result of adverse effects of treatments or other co-morbidities. Measures of disease activity include the systemic lupus activity measure-revised (SLAM-R) (Bae et al. 2001), the SLE disease activity index (SLEDAI) (Bombardier et al. 1992) and the British Isles Lupus Assessment Group (BILAG) disease activity index (Stoll et al. 1996). Disease damage is most often measured through the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLIC/ACR DI) (Gladman et al. 1996, 1997). However, in addition to disease activity and damage, there are other important consequences of disease that include changes in QoL, employment and social functioning. Therefore, in an effort to improve assessment of outcomes in SLE, the outcome measures in rheumatology clinical trials (OMERACT) group has recommended that trials of SLE include outcome measures of QoL, adverse events and economic costs, in addition to measures of disease activity and disease damage (Strand et al. 2000).

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Measurement of quality of life

QoL and more specifically, HRQoL refers to the impact that a disease and its treatment has on an individual's ability to function and his or her perceived well-being in physical, mental and social domains of life. Increasing pressure on the use of health care resources has resulted in a need for measures that will best assess the relative effectiveness and appropriateness of rival medical treatments. Measurement of HRQoL, in addition to more objective clinical indicators of disease, allows for a more comprehensive assessment and in some cases may prove to be a more sensitive indicator of treatment response than measures of disease activity or damage (Strand et al. 2003). Furthermore, information about broader patient outcomes, including outcomes of importance to patients, helps physicians and patients when making decisions about the most appropriate health care. The challenge remains to identify instruments that will accurately and reliably assess these disease outcomes.

Measurement of HRQoL has traditionally relied on two basic approaches: the use of *generic questionnaires* and the use of *disease-specific questionnaires*. Generic questionnaires were developed for general use and may be used in a variety of diseases and populations. They allow for comparison with other groups and other conditions and allow measurement of dysfunction for individuals experiencing more than one condition. In contrast, disease-specific questionnaires are designed to measure outcomes in a specific disease. Because they incorporate elements specific to particular diseases, they are believed to be more responsive than generic instruments. Only recently have disease-specific instruments been developed for use in SLE and these are not yet in wide use.

Generic measures (Table I)

At present, the most commonly used measure of HRQoL is the SF-36. Developed by Ware et al. (1992), the SF-36 is a generic, 36-item self-report questionnaire designed to be used in a variety of conditions, populations, and settings. It includes eight subscales (physical functioning, social functioning, role limitations due to physical problems, role limitations due to emotional problems, mental health, energy/vitality, pain and general health perception) that can be summarized into two component scores: the physical component summary score and the mental component summary score. The SF-36 has been shown to be a valid and reliable instrument in SLE (Stoll et al. 1997) and has been used in numerous studies in SLE. Using the SF-36, several studies have demonstrated that persons with SLE have a significantly poorer QoL than persons without a chronic illness (Stoll et al. 1997; Sutcliffe et al. 1999).

Other generic HRQoL questionnaires that have been used in SLE include the European QoL scale (EQ-5D) (The EuroQol Group 1990; Kind 1996), the World Health Organization quality of life scale (WHOQOL-Bref) (The WHOQOL Group 1998), the Nottingham health profile (NHP) (Hunt et al. 1981) and the sickness impact profile (SIP) (Bergner et al. 1981). The EQ-5D is a simple measure that assesses five dimensions of health status: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Wang et al. (2001) in a study of 54 persons with SLE, showed the EQ-5D to be a valid instrument for the measurement of HRQoL. Luo et al. (2003a,b) have shown both a Singaporean English and a Singaporean Chinese version of the EQ-5D to be valid in persons with various rheumatic diseases, including SLE. The WHOQOL-Bref, a 26 item questionnaire assessing four domains of QoL (physical, psychological, social and environmental) was evaluated in 73 patients from India (Khanna et al. 2004). Only the physical and psychological domains of QoL were found to be impaired in patients with active SLE. The NHP and the SIP have been used in a variety of diseases; however, neither has been validated in SLE.

Disease-specific measures

The Stanford health assessment questionnaire (HAQ) (Fries et al. 1980) was initially developed for use in persons with arthritis and has become the most commonly used measure of functioning in the rheumatic diseases, particularly rheumatoid arthritis. Although initially developed to assess the impact of arthritis, it has been used and validated in a variety of other conditions and thus may also be regarded as a generic instrument. The HAQ is a 20-item questionnaire that assesses activities of daily living in eight domains: dressing, arising, eating, walking, hygiene, reaching, gripping and errands and chores. Although it has been shown to be a valid instrument for use in SLE (Hochberg and Sutton 1988; Milligan et al. 1993), an important limitation is that it only assesses physical functioning. Therefore, for a more comprehensive assessment, it should be used in combination with instruments that also assess psychosocial functioning.

Another instrument that was developed for use mainly in persons with arthritis is the arthritis impact measurement scale (AIMS) (Meenan et al. 1982), which was revised in 1992 (AIMS2) (Meenan et al. 1992). It is a 78-item questionnaire that assesses physical functioning, activities of daily living, social activities, social support, arthritis pain, work, level of tension, mood, satisfaction with health, general health perceptions, overall impact of arthritis and medications. In SLE, the AIMS has been used in only one

Table I. Health-related QoL questionnaires used in SLE.

Questionnaire	Domains assessed		Number of items
	Physical/functional impact	Social/emotional impact	
Generic			
SF-36	Yes	Yes	36
EQ-5D	Yes	Yes	5 (also contains a visual analog scale)
WHOQOL-Bref	Yes	Yes	26
NHP	Yes	No	38
SIP	Yes	Yes	136
Disease-specific			
HAQ	Yes	No	20
AIMS	Yes	Yes	78
SLE-specific			
SLEQOL	Yes	Yes	40
SSC	Yes	Yes	38
LupusQoL	Yes	Yes	34

study that compared patients with SLE and rheumatoid arthritis (Burckhardt et al. 1993).

SLE-specific measures

Three disease-specific QoL measures have been recently developed for use in SLE.

Leong et al. (2005) developed and validated a new 40-item SLE-specific QoL instrument, the systemic lupus erythematosus-specific quality-of-life (SLE-QOL). The questionnaire consists of 6 subsections: physical functioning, activities, symptoms, treatment, mood and self-image. It was evaluated in 275 persons with SLE and was found to be more responsive to change than the SF-36. It was shown to be valid, possessing construct validity, face and content validity, internal consistency, test-retest reliability and responsiveness. Another SLE-QoL questionnaire was recently developed by Grootsholten et al. (2003) the SSC. Testing for reliability and reproducibility has shown satisfactory internal consistency and test-retest reliability. A third SLE-specific measure of HRQoL is the Lupus QoL Scale (LupusQoL) (Teh et al. 2005). This is a 34-item questionnaire that assesses 8 domains: physical functioning, pain, emotional functioning, fatigue, body image, sex, planning and burden to others. It possesses internal consistency, test-retest reliability and concurrent validity when compared with the SF-36.

The development of these SLE-specific instruments may prove to be invaluable in SLE drug trials, which have suffered from a lack of sensitive outcome measures that are able to detect clinically meaningful differences between competing therapeutic strategies. These questionnaires may prove to be more responsive in certain situations and may address issues of particular concern in persons with SLE. Nevertheless, they will require further evaluation before they can be recommended for routine use. Furthermore, although there are advantages to using disease-specific

questionnaires, the current general consensus is that generic measures should be used preferentially, supplemented with disease-specific measures where applicable.

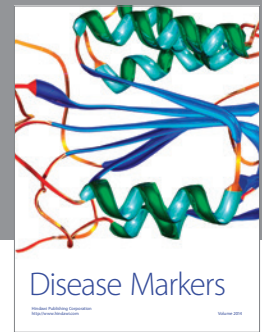
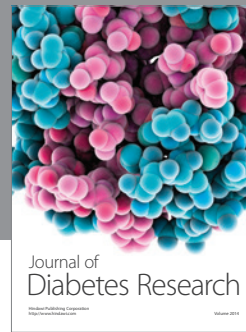
Conclusion

The various questionnaires described above have been used in the assessment of a number of diseases, including SLE. Each has its own advantages and disadvantages and the choice of which measure to use should be made on an individual basis, taking into consideration the specific aims of the study. Generic measures are widely used and have the advantage of allowing comparisons between different conditions. The SF-36, in particular, is currently the preferred outcome measure for HRQoL in US health policy research. It has also proven to be more responsive than measures of disease activity in at least one clinical trial of a novel therapeutic agent for SLE, LPJ-394 (Strand et al. 2003). The hope is that newly developed SLE-specific questionnaires will be even more responsive, so as to better assess the efficacy of current and new therapeutic agents. No new drug has been approved for the treatment of SLE in over 25 years. This failure to demonstrate benefit may be at least partly due to a lack of appropriate outcome measures. Better measures of HRQoL, in combination with improved measures of disease activity and disease damage, will help drive the development of new therapeutic agents and facilitate their approval.

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