Cardiovascular problems including coronary artery disease and strokes are a major cause of death in patients with SLE, particularly during the later stages of the disease. There is abundant evidence that the risk of cardiovascular disease (CVD) is increased in patients with SLE compared to age and sex matched controls. Although cardiovascular risk is also raised in other rheumatological diseases such as rheumatoid arthritis, the increase is particularly striking in SLE because most patients with that disease are young or middle-aged women who would normally have a very low incidence of CVD. Manzi et al showed that women aged 35-44 with SLE had a 50-fold higher incidence of coronary disease than age-matched controls from the Framingham cohort. Studies from groups in different countries have all confirmed this increased risk, though not with such high relative risk values (reviewed in 4).

The incidence of subclinical arterial disease is also increased in patients with SLE. This has been shown by post-mortem studies showing that 52% of patients with SLE had atherosclerosis and by imaging studies. Roman et al used ultrasound to show that carotid artery narrowing (measured as intima/media thickness (IMT)) occurs more frequently in patients with SLE than in age/sex matched control subjects while Asanuma et al used electron beam tomography to show that coronary artery calcification occurs more frequently in patients with SLE than in controls. However, neither carotid artery IMT nor coronary calcification has been shown to be an accurate predictor of CVD events in patients with SLE.

Why do patients with SLE have increased risk of atherosclerosis and CVD? One possibility is that this risk arises from the same factors that are known to be the major contributors to CVD risk in the general population, including smoking, hypertension, high cholesterol and diabetes. Information about the presence of these factors in an individual can be used to calculate his or her predicted risk of developing coronary disease or stroke in the next ten years, using equations derived from the analysis of factors that predicted CVD events in the Framingham cohort. These predicted risk values have been used widely in deciding how to manage cardiovascular risk in the community—for example by deciding which patients would benefit most from reduction of cholesterol. In patients with SLE, however, it is clear that these risk calculations seriously underestimate the true risk of developing CVD. Esdaile et al carried out a retrospective study of 263 patients in two Canadian centres and found that even after allowing statistically for the effects of all orthodox risk factors, patients with SLE still had a 7.9-fold increase in the risk of stroke and a 10.1-fold increase in risk of non-fatal myocardial infarction. Our group calculated predicted CVD risk for 202 patients with SLE in comparison with hypothetical age/sex matched controls in whom management of all risk factors was optimized and found that this optimization would only lead to a significant change in predicted risk in patients under 40. In a group of 47 patients with SLE followed from 1992 to 2002, 8.5% developed coronary disease and 10.6 suffered stroke. This was a far higher incidence of CVD than would have been predicted by risk calculations on these patients in 1992 and the patients who suffered events were not those who had a high predicted risk of CVD in 1992.

It is clear, therefore, that the standard risk factors used in the Framingham risk equations account for only part of the increased risk of CVD in patients with SLE. Case-control studies have suggested that a number of other factors contribute, including anti-phospholipid antibodies (aPL), raised triglyceride levels, and not being treated with hydroxychloroquine. It has also been proposed that inflammation due to high disease activity or high levels of homocysteine might play a role in causing increased risk of CVD in patients with SLE. Some of these potential risk factors could be influenced by changing our management of patients with SLE, for example by prescribing folic acid to...
reduce homocysteine or by adopting a lower threshold for anticoagulation in patients with aPL but no history of thrombosis. However, there is no evidence base to show that these measures would reduce cardiovascular risk in these patients. It is important to note that the absolute risk of CVD events in an individual patient with SLE is usually low, even when the relative risk compared to other people of the same age is high. This is an argument against prescribing drugs to reduce this relative risk without persuasive evidence of efficacy.

There is a strong evidence base for use of interventions affecting smoking, hypertension and lipid levels to reduce cardiovascular risk in the general population. Large, well-designed clinical studies showing the efficacy of such measures have been used to formulate guidelines for use of these interventions in primary prevention of CVD. These guidelines, however, are not easily applicable to patients with SLE. Many of the trials used to derive them contained few or no young women and are therefore of limited relevance to patients with lupus. Furthermore, the guidelines generally depend on the predicted risk of CVD, calculated using the Framingham algorithm. This method underestimates risk in patients with SLE, and gives calculated values for these patients far lower than would normally trigger use of statins under primary prevention guidelines. For example, the National Cholesterol Education Adult Treatment Panel III guidelines define high and moderate risk respectively as >20% and 10% to 20% predicted risk of coronary disease over the next ten years. Most patients with lupus have far lower predicted risk values than this. In our cohort of 202 patients, the median 10-year risk values for coronary disease and stroke were 1.2% and 0.8% respectively.

The fact that we cannot use these guidelines does not mean that we should not attempt to control reversible cardiovascular risk factors in patients with SLE. On the contrary, studies have shown that smoking, high cholesterol and hypertension are all common in cohorts of patients with lupus. Most authors agree that it is important to address these potentially reversible risk factors in patients with a disease such as SLE that itself increases cardiovascular risk. Wajed et al argued that SLE, like diabetes mellitus, should be considered such a strong risk factor in its own right that all patients with the disease should be considered as being at high risk of CVD regardless of calculated risk values. This would imply instituting measures to cause the patient to stop smoking and to aim for target blood pressure and low density lipoprotein (LDL) cholesterol of 130/80 mmHg and 2.6mmol/l respectively. This setting of standard targets applicable to all patients with SLE is attractive in its simplicity, but could lead to long term use of drugs such as statins in patients who do not really need to take them, because risk levels for the individual patient are not taken into account. However, in a recent questionnaire study soliciting the opinions of lupus specialists from 32 units across Europe and North America, we found considerable support for the idea of assertive management of reversible risk factors without calculating predicted risk values in individual patients. All respondents to the questionnaire said they would encourage their patients with lupus to stop smoking, 55% would prescribe statins to any patient with lupus and high cholesterol and 74% would try to keep blood pressure between 120/80 and 140/80 mmHg. In summary, patients with SLE have a high risk of CVD but only part of this is due to reversible orthodox risk factors. Calculation of risk scores using Framingham equations is misleading as it underestimates risk and does not identify the patients who are actually going to suffer an event. There is a general consensus that smoking, hypercholesterolaemia and hypertension should be treated in patients with SLE but at present there are no generally agreed guidelines about the target levels that we should aim for in treating these factors.

Correspondence to:
Dr Anisur Rahman
Centre for Rheumatology Research
Room 331, Windeyer Institute
46 Cleveland Street
London W1T 4JF
United Kingdom
Tel: +44-207-380-9281
Fax: +44-207-380-9278
E-mail: anisur.rahman@ucl.ac.uk

References

4. Bruce IN. 'Not only...but also': factors that contribute to accelerated atherosclerosis and premature coronary heart disease in systemic lupus erythematosus. Rheumatology (Oxford) 2005;44:1492-1502.


---

7th European Lupus Meeting

Holanda, Amsterdão
07-10 de Maio de 2008

---

13th International Conference for Behçet's Disease

Austria, Pörtschach/Klagenfurt
24-27 de Maio de 2008