Concise Report

Use of a strategy based on calculated risk scores in managing cardiovascular risk factors in a large British cohort of patients with systemic lupus erythematosus

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Objective. To develop a strategy for stratifying risk of cardiovascular disease (CVD) in a cohort of patients with SLE and to test the usefulness of this strategy in rationalizing management of cardiovascular risk factors.

Methods. For each patient, data were collected once each year to allow calculation of risk of developing CVD in the next 10 years. Those with risk values >7.5% were considered for intervention to reduce risk. The risk figures and effect of this strategy on management of the cohort as a whole were assessed after 3 years. Patients who had been identified as smokers in 2005 were contacted in 2008 to assess changes in their smoking behaviour.

Results. Over 3 years, 308 patients (>90%) of the cohort had CVD risk assessed at least once. Although 10-year CVD risk exceeded 7.5% in 35 patients, the majority (24) of these had either diabetes mellitus or previous CVD for which established cardiovascular risk reduction protocols already exist. Calculation of risk scores did not alter management in 96.5% of the patients. Ninety percent of the smokers remembered being counselled about smoking in the lupus clinic, 70% had received help to reduce smoking and 47% had either reduced or stopped.

Conclusion. A protocol mandating regular assessment of cardiovascular risk factors in our lupus clinic resulted in this issue being discussed with >90% of the patients and there was some evidence of an impact on smoking. However, use of these factors to calculate 10-year risk scores did not alter management in over 96% of the cases.

Key words: Systemic lupus erythematosus, Cardiovascular disease, Smoking, Risk assessment.

Introduction

Patients with SLE have an increased risk of developing cardiovascular disease (CVD), particularly coronary artery disease (CAD) [1] or stroke. Hypertension, low-density lipoprotein (LDL) cholesterol, diabetes and smoking—the conventional risk factors for CVD—may not fully explain this increased risk of CVD in patients with SLE [2–4]. It has been proposed that some of this increased risk arises from other, putative risk factors including presence of aPLs, high serum triglycerides, high homocysteine levels and the pro-atherogenic effect of systemic inflammation [5, 6]. The causal relevance of each of these factors remains uncertain.

Conventional risk factors such as hypertension and hypercholesterolaemia are common in patients with SLE [3, 6]. Between 13 and 50% of the patients with SLE smoke [2, 3, 7, 8]. A recent retrospective study showed that increased SLE disease activity and steroid dose were associated with adverse changes in several conventional risk factors including blood pressure, BMI and LDL [9]. It is therefore important to consider management of these factors in patients with SLE.

The Framingham equations use conventional risk factors to estimate the absolute 10-year risk of CVD in an individual [9]. These risk scores are designed to stratify risk in populations in order to define groups of people in whom intervention (for example, to reduce LDL) should be recommended. They are not designed to predict accurately whether individual people will suffer a CVD event. Current American guidelines for primary prevention of CVD suggest that individuals with at least two established risk factors and a predicted 10-year CVD risk between 10 and 20% should receive treatment to reduce LDL to 130 mg/dl (3.3 mmol/l) [10]. Since increasing age and male gender are important contributors to the calculated risk values, most patients with SLE have estimated absolute risk values below this population threshold for intervention [3], but these estimated values underestimate their true risk of CVD events [2, 3]. Salmon and Roman [5] suggested that since having SLE is itself a cardiovascular risk factor, all conventional risk factors in patients with SLE should be managed more aggressively than in the general population. Wajed et al. [11] suggested instituting dietary or drug treatment aimed at keeping blood LDL level <2.6 mmol/l (101 mg/dl) in all patients with SLE, without stratifying for presence or absence of other risk factors. However, since the reduction in CVD risk associated with reducing LDL is proportional to the baseline risk [12], which depends on all conventional risk factors, we wanted to explore the feasibility of using Framingham risk scores to stratify baseline CVD risk in a population of patients with SLE. We set the risk threshold for intervention lower than in the guidelines for the general population to allow for the fact that conventional risk factors do not contribute the whole CVD risk in SLE. We set up a strategy to do this in patients with SLE who attend University College London Hospital (UCLH). Our aim was to test whether this strategy would help us to rationalize management of CVD risk factors in this population of patients. A secondary outcome of the study was that we were able to assess our level of success in persuading patients to reduce or quit smoking. Though all authors agree that this is an important objective in...
patients with SLE, there are few data on outcomes of attempts to achieve it.

Patients and methods

All patients in the lupus cohort at UCLH fulfil the revised ACR Criteria for diagnosis of SLE [13]. From 1 January 2005, we adopted a strategy specifying the following standards.

(i) Cardiovascular risk was to be calculated for each patient annually. This entailed collecting information about the following risk factors: age, gender, current smoking status (yes/no), blood pressure (measured routinely at every clinic visit), blood levels of total cholesterol, high-density lipoprotein (HDL) and LDL (measured in our routine service laboratory), history of CVD events or diabetes and left ventricular hypertrophy assessed by electrocardiogram.

These values were then entered into the Cardio Risk Manager program [14] to obtain figures for predicted 10-year risk of CAD or stroke.

(ii) Any patient with 10-year risk of CAD or stroke exceeding 7.5% was to be considered for further investigation or treatment with lipid-lowering agents. This is a lower risk level than the 10–20% recommended for using lipid-lowering drugs for primary prevention of CVD in the general population [10].

(iii) Any patient who smoked was to be counselled about the increased risk of CVD in patients with SLE, given an information sheet about this and offered referral to the smoking cessation clinic at UCLH. In October 2005 and January 2008, we carried out telephone interviews with smokers asking whether they remembered discussing smoking and/or receiving the information sheet in the lupus clinic and whether they had received help to quit smoking. We asked if they had increased, decreased or stopped smoking.

Data were reviewed annually. Here we present the cumulated data up to the third year. This project was designed as an audit, did not involve any research procedures or tests outside the routine management of patients, and all patients were managed according to the same criteria. Approval of a research ethics committee was therefore not required.

Results

Calculation of cardiovascular risk values did not aid the management of these patients with SLE

A total of 308 patients were studied. Of them, 108 had CVD risk values calculated once, 134 had risk values calculated in 2 out of 3 years and 66 in all 3 years. The maximum number of patients attending the clinic regularly, for whom risk could potentially have been calculated, was 288 at the beginning of 2005 and 355 at the end of 2007. We therefore estimate that we captured the risk values of ~90% of the patients during the study period. The mean age ± s.d. of these 308 patients was 42.6 ± 13.9 years (range 18–80 years) and the female: male ratio was 283:25 (91.9%:8.1%).

Table 1 shows the distribution of risk values across this population of patients with SLE in all 3 years. The vast majority had very low calculated risk values and only 35 (11.3%) had >7.5% risk of either CAD or stroke at any point during the 3-year period. When these 35 patients were studied in more detail, 24 (68%) of them had either previous CVD or diabetes mellitus. The guidelines for reducing risk in patients with those conditions are well established and independent of calculated risk score or co-existing SLE [10]. Thus, the maximum number of patients in whom decisions about risk management could have been affected by calculating predicted risk and applying our strategy was only 11 (3.5% of the 308 patients assessed over 3 years).

Prevalence of smoking and outcome of attempts to influence smoking behaviour

By October 2005, 209 patients had been screened and 35 (17%) had been identified as smokers. In January 2008, we contacted the 35 smokers identified in 2005 and 30 patients responded. We found that 25 (83%) of these 30 patients were still smoking in 2008. Twenty-seven (90%) remembered having discussed smoking in the SLE clinic, but only 12 (40%) remembered being given the information sheet. Fifteen (50%) recalled an offer of referral to the hospital smoking cessation service and 21 (70%) had received some help to reduce smoking either from the hospital or from a family practitioner. Since being identified as smokers in the lupus clinic, five (17%) had stopped and nine (30%) had reduced smoking, and only one (3%) had increased. None of the patients whose smoking details were recorded in both 2005 and 2007 reported commencing smoking during that period.

Prevalence of other modifiable risk factors

In the third year of the study, risk factors were analysed for 152 patients. Within this population, 46 (30.3%) were hypertensive (defined as systolic blood pressure >140 mmHg and/or diastolic >90 mmHg) and 42 (27.6%) had LDL >2.6 mmol/l. Among these 42 patients, 39 (93%) had no modifiable risk factors other than high LDL, but 27 (64.2%) were >40 years old and 19 (45.2%) were >50 years old.

Characteristics of patients who suffered a CVD event during this period

Eight patients suffered CVD events during the 3-year period of the study. Four patients had strokes, and a further four had acute coronary syndromes. Risk assessment had been undertaken in seven of these eight patients in the first year of the study (i.e. prior to their CVD events). Only one of these patients had a predicted 10-year cardiovascular risk score >7.5%. This patient developed CAD, was a smoker, and had a predicted 10-year CAD risk

### TABLE 1. Distribution of predicted cardiovascular risk values during the 3-year study

<table>
<thead>
<tr>
<th>10-year risk of CAD (%)</th>
<th>First year (n=228) n (%)</th>
<th>Second year (n=196) n (%)</th>
<th>Third year (n=152) n (%)</th>
<th>10-year risk of stroke (%)</th>
<th>First year (n=228) n (%)</th>
<th>Second year (n=196) n (%)</th>
<th>Third year (n=152) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>128 (56.1)</td>
<td>121 (61.7)</td>
<td>94 (61.8)</td>
<td>&lt;1</td>
<td>173 (75.8)</td>
<td>156 (79.5)</td>
<td>121 (79.6)</td>
</tr>
<tr>
<td>1.1–2</td>
<td>27 (11.7)</td>
<td>24 (12.2)</td>
<td>14 (9.2)</td>
<td>1.1–2</td>
<td>26 (11.4)</td>
<td>18 (9.1)</td>
<td>9 (5.9)</td>
</tr>
<tr>
<td>2.1–3</td>
<td>16 (7.8)</td>
<td>12 (6.1)</td>
<td>15 (9.6)</td>
<td>2.1–3</td>
<td>12 (5.2)</td>
<td>6 (3.0)</td>
<td>7 (4.6)</td>
</tr>
<tr>
<td>3.1–4</td>
<td>16 (7.8)</td>
<td>14 (7.1)</td>
<td>10 (6.4)</td>
<td>3.1–4</td>
<td>3 (1.3)</td>
<td>7 (3.5)</td>
<td>5 (3.2)</td>
</tr>
<tr>
<td>4.1–5</td>
<td>9 (3.9)</td>
<td>6 (3.0)</td>
<td>4 (2.6)</td>
<td>4.1–5</td>
<td>1 (0.4)</td>
<td>2 (1.0)</td>
<td>4 (2.6)</td>
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<tr>
<td>5.1–7.5</td>
<td>8 (3.5)</td>
<td>9 (4.5)</td>
<td>7 (4.6)</td>
<td>5.1–7.5</td>
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<td>6 (3.0)</td>
<td>4 (2.6)</td>
<td>7.6–10</td>
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<tr>
<td>&gt;10</td>
<td>9 (3.9)</td>
<td>4 (2.0)</td>
<td>4 (2.6)</td>
<td>&gt;10</td>
<td>3 (1.3)</td>
<td>3 (1.5)</td>
<td>4 (2.6)</td>
</tr>
</tbody>
</table>

The table shows how many patients were at each level of predicted risk of developing CAD or stroke during each year of the study, expressed both in absolute numbers and as a percentage of the number of patients whose risk was assessed during that year.
Cardiovascular risk scores in management of SLE

(score of 9%). Another patient was a smoker, and had a CAD risk score of 7% and stroke risk of 2% (though she actually developed stroke rather than CAD). For the other five patients, both the CAD and stroke risk scores were ≤2%. Three of the eight patients had elevated levels of LDL. Considering the 228 patients whose risk was measured in the first year of the study, the sensitivity and specificity of a predicted risk value >7.5% for predicting CVD events were 15 and 91%, respectively, giving positive predictive value of 5% and negative predictive value of 97%.

Discussion

Our strategy did not enable us to rationalize management of CVD risk factors in this cohort of patients with SLE. In >96% of our patients, calculation of risk scores did not alter management. A predicted 10-year CVD risk of >7.5% had a very low positive predictive value for CVD events. However, this could well be because patients with those risk values were already receiving appropriate treatment designed to reduce CVD risk. Of these 35 patients, 11 were taking statins, 17 anti-hypertensive agents and 9 aspirin.

A positive outcome of the strategy was that in collecting the data for the risk scores, we discussed cardiovascular risk with >90% of our patients with SLE over a 3-year period. A recent American study showed that 58% of the 226 patients with SLE did not recall ever having been counselled about CVD by a clinician [15]. Counselling was shown to have beneficial effects in that study. Those who had been counselled were 2.3-times more likely to perceive SLE as a risk factor for CVD and 5.3-times as likely to recognize moderate to high risk (defined as presence of two or more conventional risk factors) in themselves [15].

We identified a minority of patients who were persistent smokers and in whom we had limited success in altering this behaviour. Given the known addictive nature of nicotine and difficulty in helping people to quit smoking, it is moderately encouraging to know that 30% of the smokers identified in 2005 had reduced and 17% had stopped smoking by 2007. In comparison, national monitoring figures show that ~14% of the people seen in English smoking cessation clinics have quit smoking and not relapsed at 1-year follow-up [16]. It is also encouraging that no patient in the cohort reported taking up smoking during that period, though patients may have under-reported smoking and it is impossible to be sure whether any of them would have started if we had not instituted our anti-smoking drive.

A prospective meta-analysis of over 90,000 patients from clinical trials of statins showed that lowering LDL reduced CVD risk in all subjects, regardless of baseline predicted risk values [12]. The degree of benefit was proportional to the original level of risk (21% reduction per millimoles/litre fall in LDL) [12]. Wajed et al. [11] recommended a target LDL of <2.6 mmol/l, for all patients with SLE. In 2007, this approach would have led to the use of dietary modification or drug therapy in 27% of our patients in whom lipid profile was measured. However, only three of our eight patients who suffered a CVD event during the study period had LDL >2.6 mmol/l. Age is a stronger predictor of CVD risk than LDL in the general population. On these grounds, one could consider recommending LDL reduction to reduce CVD risk in all patients with SLE above the age of 40 years (which would also include 64.2% of those with LDL >2.6 mmol/l) but we would have to treat over 200 patients. Only 31 patients in our cohort have ever suffered CVD events, though 21 of them were aged >40 years at the time of the event.

An alternative to the use of calculated risk scores or blanket risk reduction, applied to all patients above a certain age or LDL level, would be to find some way to assess CVD risk in individual patients with SLE accurately. Techniques such as carotid ultrasound [7] and electron beam tomography [8] show cardiovascular differences between patients with SLE and age-/sex-matched controls. Although it is not clear whether these appearances on imaging actually predict development of CAD or stroke in these patients, a combination of blood tests, disease activity indices and cardiovascular imaging may help us to predict this in the future.

Rheumatology key messages

- Among 308 patients with SLE, calculated cardiovascular risk scores did not aid management of cardiovascular risk factors in 96.5% of the cases.
- After introduction of an assertive anti-smoking strategy in the lupus clinic, 47% of the smokers with lupus reduced or stopped smoking.

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References