Cardiovascular Risk Factor Screening in Systemic Lupus Erythematosus

ADEEBA AL-HERZ, STEPHANIE ENSWORTH, KAMRAN SHOJANIA, and JOHN M. ESDAILE

ABSTRACT. ***Objective.*** To evaluate the frequency of cardiovascular (CV) disease risk factor screening in systemic lupus erythematosus (SLE).

Methods. Medical records of patients from a lupus clinic and 5 private practices were assessed for CV disease risk factors, including hyperlipidemia, hypertension, diabetes mellitus, smoking, family history of CV disease, antiphospholipid antibodies, hyperhomocysteinemia, postmenopausal status, obesity, and nephrotic syndrome.

Results. A total of 183 records were included: 60 (33%) from the lupus clinic and 123 (67%) from private practices. Serum lipid profiles were measured in 56/183 (31%): 37/60 (62%) in the lupus clinic vs 19/123 (15%) private practice. Of the 56 with lipids measured, the individual tests obtained were as follows: total cholesterol in 56 (100%), HDL in 50 (89%), triglycerides in 49 (88%), LDL in 48 (86%), and VLDL in 33 (59%). Thirty-one of 56 patients (55%) had elevated lipids. Only 9/25 (36%) with hyperlipidemia who had a subsequent visit had a response to the hyperlipidemia charted. Of 9 nonlipid risk factors, a median of 8 were assessed in the lupus clinic vs 3 in private practices. The most frequent risk factors screened were nephrotic syndrome (91%), hypertension (74%), and smoking (59%).

Conclusion. Despite an inordinately high risk of CV disease in SLE, assessment of CV risk factors was surprisingly uncommon among the practices assessed. Greater attention needs to be paid to CV disease risk factor screening in patients with lupus. (J Rheumatol 2003;30:493–6)

Key Indexing Terms:
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Accelerated atherosclerosis and early onset cardiovascular (CV) disease in systemic lupus erythematosus (SLE)[1-4] are recognized as a leading cause of morbidity and mortality[5,6]. The prevalence of angina and myocardial infarction (MI) was 8.3% and 8.9% in patients with lupus in 2 different series[7,8]. Women with lupus were more than twice as likely to have an MI than were women of similar age in the Framingham Study[9], and to be hospitalized because of MI, congestive heart failure, or stroke[5]. A recent study described that even after taking into account the traditional CV risk factors, there is a 10-fold increase in nonfatal MI, a 17-fold increase in death due to CV disease, and a nearly 8-fold increase in stroke[4] in patients with lupus. Subclinical myocardial perfusion abnormalities are more common than overt CV disease events[10,11]. Autopsy studies have revealed an even higher frequency of coronary artery narrowing in patients with SLE[12,13].

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CV disease is a major cause of death in lupus patients in general[1,14,15] and in those with lupus nephritis[16]. Urowitz, *et al*[14] described a bimodal mortality pattern in SLE, with early deaths associated with active SLE and infection and later deaths with inactive disease and MI.

Traditional CV risk factors such as smoking, hypercholesterolemia, hypertension, diabetes mellitus, obesity, and hyperhomocysteinemia, as well as renal insufficiency, antiphospholipid antibodies, and duration of prednisone therapy have been reported to predict CV events in SLE[9,17,18]. While traditional risk factors do not explain all the elevated CV risk in SLE[2,4], the overall increase in CV risk in SLE is all the more reason to screen for risk factors, especially if intervention is known or is likely to decrease risk of adverse CV outcomes. To evaluate the extent that screening for CV disease risk factors is performed in practice, we assessed documentation of known risk factors in the medical records of patients with SLE.

MATERIALS AND METHODS

The medical records of patients with SLE followed at the lupus clinic of the Mary Pack Arthritis Centre, Vancouver, and from 5 private rheumatology practices in Vancouver were reviewed. The private practices were selected based on the presence of a filing system that permitted ready identification of patients with SLE. Lupus patients were included if they fulfilled the American College of Rheumatology (ACR) criteria for SLE[19] and if they had been followed by the rheumatologist for at least 6 months.

The records were reviewed to assess screening for the following risk factors: hyperlipidemia, including total cholesterol, LDL, HDL, triglycerides, and VLDL and 9 other risk factors including hypertension, diabetes mellitus, smoking, family history of CV disease, hyperhomocysteinemia, antiphospholipid antibodies, menopausal status, obesity, and nephrotic syndrome.

Screening for the risk factors was considered to have been assessed by the rheumatologist if the following were present in the patient's clinic medical record: a documented lipid profile, serum blood glucose (either random or fasting), serum homocysteine, urinalysis, anticardiolipin antibody, partial thromboplastin time (PTT), smoking history, menstrual history, family history of CV disease, weight or comment on body habitus, and a recorded blood pressure at the initial visit to the clinic.

A risk factor was considered abnormal if it was outside the normal range for the laboratory used (lipid profile, serum glucose, serum homocysteine, anticardiolipin antibodies, or repeated PTT), or systolic or diastolic blood pressure > 140 or 90 mm Hg on more than one occasion. Renal disease was considered present if at least 2 urine samples had > 500 mg of protein in a 24 h collection, more than 3+ on a routine urinalysis, or the presence of cellular casts.

The data were analyzed using SPSS version 10.0. Student's t test and chi-square tests were used. Significance was determined using a 2 tailed test and $p < 0.05$ was considered significant.

RESULTS

Of the 257 patients with diagnosis of SLE, 210 (82%) fulfilled the ACR criteria, and 183/210 (87%) had been followed by the study rheumatologists for more than 6 months. Of the 183 included, 60 (33%) were from the lupus clinic and 123/183 (67%) from private practices. When studied, the patients' mean age was 43 ± 12 years (range 21 to 76) and 92% were female. The mean disease duration was 11 years (range 0.5 to 42) and the mean duration of followup by the rheumatologist was 4.5 years (range 0.5 to 23). There was no significant difference in these variables between the lupus clinic and private practices except for the mean duration of followup, which was 1.5 years in the lupus clinic and 6.0 years in the private practices ($p = 0.002$).

Only 56/183 (31%) patients had had at least one lipid test measured. This was more common in the lupus clinic (37/60) than private practices (19/123) ($p < 0.001$; Figure 1). The frequency of testing for specific lipids is depicted (Figure 2). Twenty-six of the 56 tested had an elevated total cholesterol, with a mean value of 6.1 ± 0.71 mmol/l (range 4.9–8.2), and 5 had a normal cholesterol but abnormal HDL, triglycerides, and/or VLDL.

For the 31 patients who had an elevated lipid test result, 25 had a subsequent visit with their rheumatologist. Four were placed on a diet, 4 were referred for hyperlipidemia therapy, and one was prescribed hydroxychloroquine to benefit active SLE and the lipid level. Eight of these 9 patients came from the lupus clinic. Sixteen (64%) had no response to the test charted (Figure 3).

Of the 9 patients who had a response to the hyperlipidemia charted, 8 had an elevated cholesterol (mean 6.7 ± 0.80, range 5.7–8.2 mmol/l) and one had a normal cholesterol but abnormal HDL and triglycerides. Of those without a charted response, 13 had an elevated cholesterol (mean 5.9 ± 0.57, range 4.9–6.9 mmol/l). The other 3 had a normal cholesterol but abnormal HDL, triglycerides, and/or VLDL. Patients who had a charted response to the hyperlipidemia were, on average, older than patients who did not have a response (response charted, age = 51 ± 17 yrs; no response charted, age = 45 ± 9

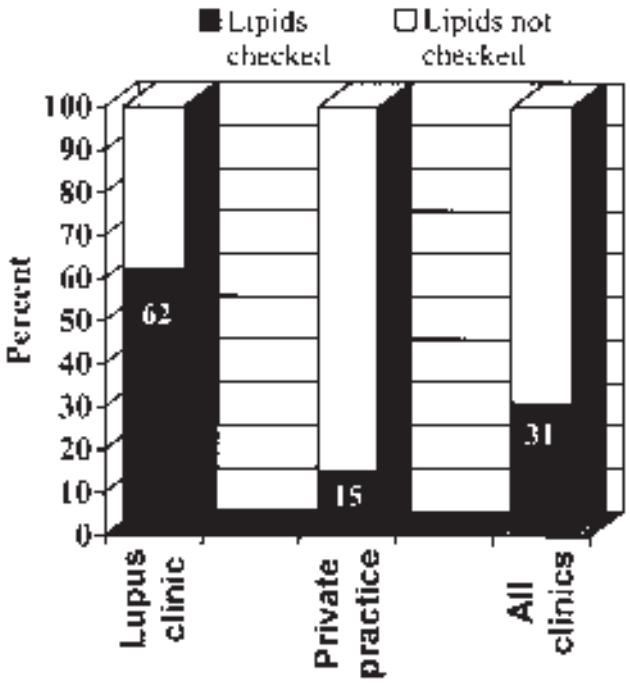

Figure 1. Percentage of SLE patients screened for hyperlipidemia in the lupus clinic and in private practices ($p < 0.001$).

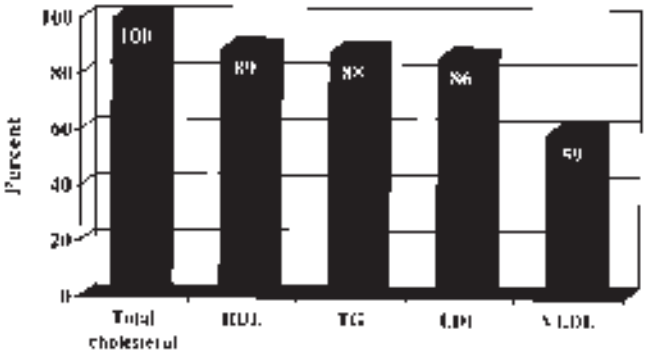

Figure 2. Type of lipid measured in patients screened for hyperlipidemia. TG: triglycerides.

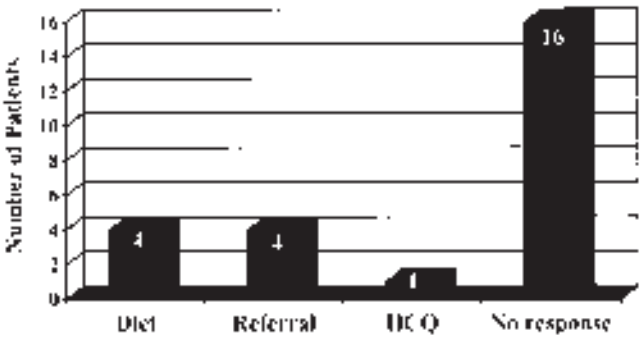

Figure 3. Charted responses of the rheumatologists to elevated lipid test results.

yrs; p = 0.03). Sex, cholesterol level, duration of disease, duration of followup, and a number of other risk factors present for CV disease were not significantly different between the 2 groups.

Of the 9 nonlipid CV disease risk factors, a mean of 4 were documented in the patients' records; 7 in the lupus clinic and 3 in private practices (p = 0.31). The actual rank order was similar at the lupus clinic and private practice sites, with nephrotic syndrome (91%), hypertension (74%), and smoking (59%) the most frequent factors screened, and hyperhomocysteinemia and family history of CV disease the least (Table 1).

DISCUSSION

We have demonstrated that CV disease risk factors including hyperlipidemia were screened for infrequently in this population of patients with SLE. In a previous study of 24 patients with SLE who had CV disease events, it was shown that in the 2 years prior to the event, hypertension was appropriately managed in almost all patients and steroid reduction or discontinuation occurred in 60%. Appropriate action occurred in 5 of 11 patients with hypercholesterolemia, 2 of 4 with hyperglycemia, one of 3 with obesity, and none of 16 who smoked[20]. Petri, *et al*[21] identified at least 3 known risk factors in 53% of patients with lupus, the most common being sedentary lifestyle (70%), and hyperlipidemia, obesity, and smoking (56% in each). Despite the high frequency of risk factors in that study, patients' awareness of the risk of CV disease was low, with only 17% of patients believing they were at high risk for developing CV disease within 5 years. They also showed that preventive practices were most commonly addressed toward hypertension, but were under-utilized against obesity, hypercholesterolemia, and smoking. In another study, it was shown that within 3 years of the diagnosis of SLE, 75% had elevated hypercholesterolemia, which was sustained in 40% and variable in 35%. Seventy-nine percent of all CV disease events occurred in the sustained group (odds ratio = 4.20) and the majority of CV disease related mortality occurred in the same group[22].

In the general population, controlling traditional CV disease risk factors such as hyperlipidemia[23,24], hypertension[25], diabetes mellitus[26,27], and smoking[28] is associated with a decrease in the incidence of CV disease events, morbidity, and mortality. The role of estrogen insufficiency as a cause of CV disease in postmenopausal women remains controversial[29,30]. While there is no evidence specifically in patients with SLE that controlling modifiable risk factors reduces CV disease, there is no reason to believe that benefits would not occur with appropriate modification in this patient population.

In addition to the traditional risk factors for CV disease, lupus itself is an independent risk factor for developing CV disease. SLE patients with a cardiac event had fewer traditional risk factors than non-SLE patients with premature coronary artery disease, suggesting factors other than the traditional ones were involved[31]. As noted, even after accounting for the traditional CV risk factors (age, sex, hypertension, hyperglycemia, hyperlipidemia, smoking, and left ventricular hypertrophy), there is a 10-fold increase in nonfatal MI, a 17-fold increase in death due to CV disease, and a nearly 8-fold increase in stroke[4]. These results make the diagnosis of SLE the strongest known risk factor for these outcomes[4]. Thus, to the extent that the overall risk of CV disease is increased in SLE, and this clearly appears to be the case, it is all the more important to treat known risk factors that are modifiable.

One of the limitations of this study is the possible discrepancy between the actual physician findings and the reporting of these findings in the medical records. We may have underestimated the degree to which some risk factors were evaluated because the physician failed to chart a result, such as blood pressure or family history of CV disease. Similarly, advice may have been provided about the need for risk factor modification in those with elevated lipids, but not charted and thus not identified in our survey. Nonetheless, charting of risk factors screened and the laboratory measurement of lipids was low in the patients studied, especially given the increasing awareness of the very elevated risk of CV disease in SLE.

There are various reasons why risk factor screening was low. It could be that the physicians involved were unaware of the increase in risk for CV disease, unconvinced that risk factor screening was of benefit, unconvinced that intervention to alter abnormal risk factors in their patients would reduce risk,

Table 1. Percentage of patients screened for nonlipid CV disease risk factors in the lupus clinic, private practice, and in total.

Risk Factor	Total, N = 183, n (%)	Lupus Clinic, N = 60, n (%)	Private Practice, N = 123, n (%)
Nephrotic syndrome	167 (91)	59 (98)	108 (88)
Hypertension	135 (74)	58 (97)	77 (63)
Smoking	107 (59)	59 (98)	48 (39)
Diabetes mellitus	93 (51)	52 (87)	41 (33)
Antiphospholipid antibodies	93 (51)	53 (88)	40 (32)
Menopausal status	82 (45)	52 (87)	30 (24)
Obesity	64 (35)	51 (85)	13 (11)
Hyperhomocysteinemia	47 (26)	44 (73)	3 (2)
Family history of CV disease	11 (6)	2 (3)	9 (7)

or that their clinical attention was focused on managing other aspects of the individual's SLE diathesis. In addition, our study does not identify which risk factors should be assessed, how frequently they should have been assessed, and the role of active disease and its treatment in altering screening frequency or treatment intervention. Nonetheless, our results do highlight the need for all physicians to recognize the strikingly increased risk of CV disease and to screen appropriately for modifiable risk factors.

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