Atherosclerotic Vascular Events in a Single Large Lupus Cohort: Prevalence and Risk Factors

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ABSTRACT. ***Objective.*** To determine prevalence and type of atherosclerotic vascular events (AVE) occurring after entry to the University of Toronto Lupus Clinic; and to compare risk factors in patients with systemic lupus erythematosus (SLE) with AVE to matched SLE controls without AVE.

Methods. Patients with SLE attending the University of Toronto Lupus Clinic who did not have AVE prior to clinic entry were included. Patients have been followed at 2–6 months since 1970 according to a standard protocol. Cases with AVE were matched for sex, era at first clinic visit (1970s, 1980s, 1990s +), inception status, age at first visit, and duration of followup. Chi-square, Fisher's exact, paired T test, and McNemar test were used. Comparison of risk factors for the development of AVE was done using a stepwise conditional logistic regression model for matched pairs.

Results. In a total cohort of 1087 SLE patients followed from 1970 until 2004, the prevalence of AVE was 10.9%, and in 561 inception patients it was 9.6%. In multivariate analyses, neuropsychiatric involvement was significantly associated with AVE in both the total and inception cohorts. Smoking was also associated with AVE in the inception cohort, whereas the number of coronary artery disease (CAD) risk factors and vasculitis were significant in the total cohort.

Conclusion. AVE are major contributors to the clinical presentation of late-stage lupus. A combination of lupus related factors and classic CAD risk factors contributed to the development of AVE. (First Release Nov 15 2006; J Rheumatol 2007;34:70–5)

Key Indexing Terms:
ATHEROSCLEROTIC VASCULAR EVENTS
RISK FACTORS
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Atherosclerotic vascular events (AVE) are a major late outcome in patients with systemic lupus erythematosus (SLE). We have previously described the bimodal mortality pattern in SLE, with atherosclerotic events being a major cause of death in late disease. In patients who died after 5 years of disease, 30% of the deaths were due to myocardial infarction (MI)/sudden death[1]. In 1998 we found the prevalence of MI/angina in the clinic to be 10%[2]. Similar frequencies were described by Petri, *et al* and Manzi, *et al* in cohorts from Baltimore and Pittsburgh[3,4]. Post-mortem studies in our center showed moderate to severe atheroma in 54% (21/40) of autopsies in patients with SLE dying of any cause. Further, compared to the Ontario population, patients with SLE had a 5-fold increase in MI and at a significantly earlier age (49 vs 69 years)[5]. The rate ratio of MI in patients with SLE compared with Framingham controls has been shown to be 52.4 in the 35–44 year age group[4]. Ward, using the California Discharge Database, has found that women with SLE between 18 and 44 years of age were more likely than age matched controls to have been admitted to hospital with MI, congestive heart failure, and stroke[6]. Peripheral vascular disease associated with atherosclerosis was documented in 10 of 563 patients (1.7%) followed prospectively[7].

We and others have examined risk factors for premature atherosclerosis in patients with SLE. We have found that persistently elevated cholesterol in the first 3 years of SLE was a predictor of coronary artery disease (CAD) events[8]. Hypertension was a predictor of mortality and vascular events in patients with SLE[9]. When we compared patients with SLE and premature CAD with French Canadian non-SLE patients who developed premature CAD at age < 60 years, there was one traditional CAD risk factor less among the SLE patients, both male and female, suggesting that SLE itself may be a risk factor for CAD[10]. In the Baltimore cohort, older age at diagnosis, hypercholesterolemia, hypertension, obesity, and longer duration of steroid therapy were significantly associated with CAD in both univariate and multivariate analyses[3]. In the Pittsburgh cohort, older age at diagnosis of SLE, hypercholesterolemia, and longer disease duration were associated with CAD in both univariate and multivariate analyses[4]. In the Toronto risk factor study,

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when 250 patients with SLE without CAD were compared with 250 healthy women presenting for an annual physical examination, patients with SLE had more classic CAD risk factors, including diabetes mellitus, elevated very low density lipoprotein cholesterol, triglycerides and homocysteine levels, and more lifestyle risk factors including premature menopause, sedentary lifestyle, and at-risk body habitus[11].

Our aims were to determine prevalence and type of AVE occurring after entry to the Lupus Clinic and to compare risk factors in patients with SLE with AVE to those in matched SLE controls without AVE in a nested case-control study.

MATERIALS AND METHODS

Setting. The University of Toronto Lupus Clinic has been following patients with SLE prospectively since 1970. Patients are admitted to clinic if they fulfill ≥ 4 of the 1971, 1982, or 1997 American College of Rheumatology (ACR) classification criteria, or 3 ACR criteria plus a histological lesion typical of SLE on renal or skin biopsy. Patients are assessed according to a standard protocol including a complete history, examination, and laboratory investigation at 2–6 month intervals. All documentation is based on a glossary of definitions included in the data retrieval form. Cholesterol measurements were incorporated into the standard protocol in 1973 and are performed at least twice a year. Blood pressure is measured at each clinic visit. Partial thromboplastin time (PTT) has been recorded since the beginning of the clinic. Antiphospholipid antibodies (aPL) have been measured since 1991. All information collected is entered into a computer dataset.

Patient selection. Patients who developed an AVE after entry into the clinic were identified from the computer database. The analysis was based on the first AVE for each patient.

Controls. Each patient was matched with a patient from the same database who had not had an AVE. Matching was done on 5 variables: sex, era at first clinic visit (1970s, 1980s, 1990s +) whether or not they were seen within 12 months of diagnosis, age at first visit (± 5 yrs) and duration of followup (± 2 yrs).

Atherosclerotic vascular event. These events were deemed not related to active SLE, and included the following. (1) Myocardial infarction, defined as one of: definite electrocardiographic (ECG) abnormalities, typical symptoms with probable ECG abnormalities and abnormal enzymes (≥ 2 upper limit of normal); typical symptoms and abnormal enzymes. (2) Angina, defined as severe pain or discomfort over the upper or lower sternum or anterior left chest and left arm, of short duration, relieved by rest or vasodilators. (3) Transient ischemic attack (TIA), defined as a brief episode of neurological dysfunction without residua. (4) Stroke, defined as an abrupt onset of neurological dysfunction resulting in neurological damage. (5) Peripheral vascular disease, defined as typical signs of intermittent claudication with diminished or absent pulses. (6) Sudden death, death with undetermined cause, but presumed cardiac.

Assessment of disease activity. Disease activity was measured at each visit by the SLE Disease Activity Index 2000 (SLEDAI-2K)[12]. Disease activity over time was calculated using the adjusted mean SLEDAI-2K (AMS)[13].

Assessment of disease damage. Accumulated damage was assessed using the Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) damage index (DI)[14]. For this study we excluded features of atherosclerosis (cerebrovascular accident, angina or coronary artery bypass, MI, and intermittent claudication) from the calculation of the SLICC/ACR DI.

Risk factors. Classic CAD risk factors included hypertension (blood pressure > 140 and/or > 90), hypercholesterolemia (> 5.2 mmol/l), smoking (ever), diabetes, and menopausal status. C-reactive protein (CRP) was available in only a small proportion of the patients prior to their event, and at an equivalent time in the controls, and therefore was not analyzed. Similarly, some potentially important risk factors such as obesity, family history of CAD, and sedentary lifestyle were only available prior to the event in a small number of patients and thus were not analyzed. We also calculated the Framingham CAD risk score[15]. Lupus related risk factors included demographic characteristics, SLEDAI-2K at presentation, AMS, SLICC/ACR damage index and major organ involvement such as vasculitis (nailfold infarcts, splinter hemorrhages, vasculitis skin lesions, gangrene, biopsy showing vasculitis), neuropsychiatric disease (seizures, chorea, benign intracranial hypertension, stroke or TIA related to active lupus, subarachnoid hemorrhage, headache, aseptic meningitis, transverse myelitis, neuropathy, organic brain syndrome, psychosis), and renal disease (renal biopsy showing lupus nephritis, nephrotic syndrome, dialysis, transplant, serum creatinine > 140 mmol/l, proteinuria, casts, hematuria, and pyuria in the absence of other causes). Raynaud's phenomenon, anticardiolipin antibody (aCL), and elevated PTT were also tested. Positive results for aCL and PTT were considered only if present on at least 2 assessments prior to the development of AVE. All risk factors studied occurred at any time prior to the event, not including the visit at which the event was detected in patients, and at any time prior to censuring in the controls.

Statistical analyses. All descriptive comparisons between patients with AVE and their matched controls were done through paired T tests for continuous variables and McNemar tests for categorical variables. Comparison of risk factors for the development of AVE was done using stepwise conditional logistic regression modeling for matched pairs. In this analysis, modeling is done by fitting a logistic regression model to a set of data with constant response, where the model contains no intercept term and has explanatory variables given by the difference between the AVE and their matched control. Variables considered in the stepwise regression model were sex, disease duration, AMS, steroids ever, antimalarials ever, immunosuppressives ever, Raynaud's, diabetes, hypertension, vasculitis ever, renal disease ever, central nervous system event ever, number of CAD risk factors, CAD 10-year risk, and CAD risk category. Analyses were performed separately for the total cohort and for the inception cohort and their respective controls.

RESULTS

At the time of this study there were 1142 patients registered in the University of Toronto Lupus Clinic. This cohort is primarily Caucasian (79%), but includes 8% Blacks, 7% Chinese, and 6% other. The average age at diagnosis is 31.9 years and the average followup in the clinic is 8.4 years. Of the total cohort, 173 patients had at least one AVE (15.1%). However, 55 patients were known to have had an AVE prior to entry to our clinic and were excluded since they could not contribute to the risk factor analysis, leaving a cohort of 1087 patients, of whom 118 [10.9% (95% CI 9.0%, 12.3%)] had at least one AVE after entry to the clinic. Although there are many etiologies for AVE, we tried to rule out active SLE as the cause of the event using clinical, laboratory, and imaging measures where appropriate. Patients with AVE were matched to 118 patients without AVE in the same cohort. Of the total cohort, 561 presented to the clinic within 12 months of diagnosis and constitute the inception cohort. In this inception cohort subgroup, there were 54 patients (9.6%) with AVE who were also matched with 54 controls from the same cohort who had not had AVE. Table 1 gives the prevalence of the various AVE in the total and inception cohorts.

Table 1. Prevalence of atherosclerotic vascular events (AVE) in the total and inception cohorts.

	Total Cohort (%)	Inception Cohort (%)	Non-inception Cohort (%)	p**
No. of patients	1087*	561	526	
AVE, 1st event	118 (10.9)	54 (9.6)	64 (12.2)	0.18
MI	24 (2.2)	11 (2.0)	13 (2.5)	0.57
Angina	76 (7.2)	32 (5.7)	44 (8.4)	0.09
TIA	3 (0.3)	1 (0.2)	2 (0.3)	1.00
Stroke	3 (0.4)	0 (0)	3 (0.5)	0.05
PVD	22 (2.0)	10 (1.8)	12 (2.3)	0.56
Sudden death	3 (0.3)	3 (0.5)	0 (0)	0.25

* Total cohort of patients without AVE prior to entry to clinic. ** Chi-square or Fisher's exact test. MI: myocardial infarction, TIA: transient ischemic attack, PVD: peripheral vascular disease.

Table 2 lists demographics and some disease characteristics of the patients with AVE and their respective controls in both the total and the inception cohorts. Age at AVE for the total cohort was 51.1 ± 12.3 and for the inception cohort 53.7 ± 12.4 years. While there is a higher mortality in the patients with AVE, this only reached statistical significance for the total cohort. SLICC/ACR DI scores were significantly higher in the AVE patients only in the inception cohort.

Table 3 shows CAD risk factors in SLE patients with AVE and their controls in the whole cohort and the inception cohort. Hypertension, hypercholesterolemia, and smoking were significantly higher among AVE patients than controls in the total cohort, but only smoking reached statistical significance in the inception cohort.

Neither menopausal status prior to AVE nor use of hormone replacement therapy was different in patients with AVE.

Table 2. Demographic characteristics in SLE patients with atherosclerotic vascular events (AVE) and controls; whole cohort and inception cohort, univariate analysis.

	Total Cohort (%)			Inception Cohort (%)		
	AVE	Controls	p*	AVE	Controls	p*
No.	118	118		54	54	
Female, n	96 (81.4)	96 (81.4)	1.00	45 (83.3)	45 (83.3)	1.00
Age at diagnosis, yrs	37.5 ± 14.0	36.8 ± 13.0	0.17	44.2 ± 13.3	43.3 ± 12.9	0.03
Dead, n	41 (34.8)	27 (22.9)	0.03	21 (38.9)	14 (25.9)	0.13
Disease duration at first clinic visit, yrs	4.4 ± 5.5	4.5 ± 6.7	0.78	0.2 ± 0.3	0.3 ± 0.3	0.07
Duration followup, yrs	9.2 ± 7.2	9.4 ± 7.3	0.34	9.3 ± 7.2	9.2 ± 7.2	0.66
SLEDAI-2K, 1st visit	11.0 ± 9.1	8.8 ± 7.0	0.03	11.7 ± 9.5	8.6 ± 6.9	0.07
AMS, last visit	6.2 ± 3.6	5.5 ± 3.8	0.12	5.6 ± 3.5	5.4 ± 4.2	0.81
SLICC/ACR DI score excluding AS	1.7 ± 1.9	1.4 ± 1.7	0.15	1.7 ± 2.0	0.9 ± 1.2	0.01

* Paired t test or McNemar test. SLEDAI-2K: SLE Disease Activity Index 2000; AMS: Adjusted mean SLEDAI; SLICC/ACR DI: SLE International Collaborating Clinics/American College of Rheumatology damage index.

Table 3. Coronary artery disease (CAD) risk factors in SLE patients with atherosclerotic vascular disease (AVE) and controls; whole cohort and inception cohort, univariate analysis.

	Total Cohort (%)			Inception Cohort (%)		
	AVE	Controls	p*	AVE	Controls	p*
No.	118	118		54	54	
Postmenopausal †	58 (60.4)	57 (59.4)	0.80	27 (60.0)	27 (60.0)	1.00
HRT††	20 (34.5)	15 (26.3)	0.62	9 (33.3)	6 (22.2)	0.48
Diabetes	12 (10.2)	7 (5.9)	0.25	4 (7.4)	6 (11.1)	0.53
Hypertensive	81 (68.6)	52 (44.1)	0.0002	34 (63.0)	28 (51.9)	0.24
Smoker (current and ex-smokers)	65 (55.1)	49 (41.5)	0.02	34 (63.0)	21 (38.9)	0.007
Elevated cholesterol	95 (89.6)	79 (74.5)	0.008	44 (88.0)	40 (80.0)	0.32

† Out of all women. †† Out of all postmenopausal women. * Paired t test or McNemar test. HRT: hormone replacement therapy.

Lupus related risk factors are shown in Table 4. As can be seen, Raynaud's, renal, neuropsychiatric disease, and vasculitis were significantly higher among AVE patients compared to their controls in the total cohort. In the inception cohort, neuropsychiatric disease and vasculitis were significantly more frequent in patients with AVE. The frequency of aCL was similar in the patients with AVE and their controls in both the total cohort and the inception cohort. However, note that only about half of all patients underwent anticardiolipin testing prior to their AVE. Elevated PTT as a surrogate for lupus anticoagulant was tested in more patients, and was significantly more prevalent in patients with AVE in the total cohort and in the inception cohort. Of note, none of the patients with TIA/stroke had positive aPL at the time of the event or in the preceding 5 years. Steroid use was more frequent among patients with AVE than those without in the total cohort, and not in the inception cohort. Duration of steroid use and cumulative steroid dose were similar in AVE patients and controls in both the total and inception cohorts. Antimalarials and immunosuppressive drugs were more frequently used in the AVE patients than controls in the total cohort. Only use of immunosuppressives reached statistical significance in the inception cohort.

Table 5 depicts Framingham risk factor scores in patients with AVE and their controls. This univariate analysis revealed that the patients with AVE had a significantly higher number of risk factors than their respective controls in both the total and inception cohorts, but they did not have a higher 10-year CAD risk.

A conditional logistic regression for a matched-pairs model was developed using the stepwise approach for both the total cohort and the inception cohort. As shown in Table 6, neuropsychiatric involvement was a risk factor for AVE in both the total and inception cohorts. Smoking was a risk factor for AVE in the inception cohort only, whereas vasculitis and the number of CAD risk factors, which include smoking, were risk factors in the total cohort.

DISCUSSION

As survival of patients with SLE increases and the longevity of longterm cohorts increases, the prevalence of AVE increases. In our studies reported in 1995[2], we had a prevalence of MI, angina, sudden death, and peripheral vascular disease of 10% in 665 patients followed between 1970 and 1993. In 1992, Petri, *et al*[3] reported a prevalence of MI, angina, or sudden death of 8.3% among 229 patients with SLE followed prior to 1990; and in 1997 Manzi, *et al*[4], reporting only on MI and angina, recorded a prevalence of 6.7% among 493 patients followed between 1980 and 1993.

In the present study, including 1087 patients followed from 1970 until 2004, we report a prevalence of AVE since entering the cohort of 10.9%, with the cases including TIA and stroke. These were not included among the previously reported studies. TIA and strokes were carefully evaluated with respect to etiology in this study. In the face of active SLE these events were attributed to lupus and are not included in this analysis. We thus are confident of the attribution of the patients with TIA or stroke to AVE. All cohorts should record all AVE including MI, angina, TIA and strokes, peripheral vascular disease, and sudden death.

The mechanism of AVE in SLE is unclear. The pathogenesis of atherosclerosis in SLE is likely an interaction of multiple factors. Potential mechanisms include classic CAD risk factors, therapy related factors, aPL, inflammation, and global disease activity. We have previously shown[11] that patients with SLE have more risk factors for CAD than a control group. These risk factors included diabetes mellitus, increased very low density lipoprotein cholesterol, triglycerides and homocysteine, as well as the lifestyle factors ear-

Table 4. Lupus related risk factors in SLE patients with atherosclerotic vascular events (AVE) and controls; whole cohort and inception cohort, univariate analysis.

	Total Cohort (%)			Inception Cohort (%)		
	AVE	Controls	p*	AVE	Controls	p*
No.	118	118		54	54	
Raynaud's	92 (78.0)	78 (66.1)	0.04	41 (75.9)	37 (68.5)	0.41
Renal disease	94 (79.7)	79 (67.0)	0.03	41 (75.9)	38 (70.4)	0.44
Neuropsychiatric	76 (64.4)	52 (44.1)	0.0004	35 (64.8)	20 (37.0)	0.003
Vasculitis	56 (47.5)	27 (22.9)	0.0003	25 (46.3)	11 (20.4)	0.011
Anticardiolipin antibody, %	35.4%†	33.3%†	0.8	42.1%#	36.8%#	0.8
Elevated PTT, %	50.0%††	24.4%††	0.0003	43.2%##	18.9%##	0.013
Steroids	101 (85.6)	88 (74.6)	0.04	44 (81.5)	40 (74.1)	0.37
Cumulative dose	39.9 ± 36.6	34.8 ± 35.0	0.34**	33.6 ± 39.9	22.6 ± 22.2	0.12**
Duration, yrs	9.0 ± 7.9	9.9 ± 8.8	0.42**	6.8 ± 6.6	5.9 ± 5.4	0.52**
Antimalarials	79 (67.0)	64 (54.2)	0.04	34 (63.0)	33 (61.1)	0.82
Immunosuppressives	55 (46.6)	35 (29.7)	0.008	23 (42.6)	12 (22.2)	0.03

* Paired t tests or McNemar tests, except for ** where tests were unpaired in order to use all data available. Data available on: † 48 pairs only, # 19 pairs only, †† 78 pairs only, ## 37 pairs only. PTT: partial thromboplastin time.

Table 5. Framingham risk factors for coronary artery disease (CAD) in patients with and without atherosclerotic vascular events (AVE) in the total cohort and the inception cohort.

	Total Cohort			Inception Cohort		
	AVE	Controls	p*	AVE	Controls	p*
No.	118	118		54	54	
No. of risk factors	2.2 ± 0.8	1.6 ± 1.0	< 0.0001	2.2 ± 0.9	1.8 ± 1.0	0.04
CAD risk	4.4 ± 6.1	4.0 ± 6.7	0.28	5.1 ± 6.1	5.0 ± 7.0	0.86
CAD 10-year risk	6.5 ± 6.3	6.5 ± 6.5	0.98	7.3 ± 6.7	8.1 ± 7.7	0.42
High/very high risk (%)	3 (2.5)	2 (1.7)	0.65	2 (3.7)	2 (3.7)	1.00

* Paired t tests or McNemar tests.

Table 6. Multivariate analysis of risk factors for atherosclerotic vascular events (AVE) in the whole cohort and the inception cohort.

	Total Cohort, n = 236			Inception Cohort, n = 108		
	RR	95% CI	p	RR	95% CI	p
No. of risk factors	1.76	1.26, 2.47	0.0001	—	—	—
Vasculitis	2.26	1.22, 4.17	0.009	—	—	—
Neuropsychiatric	2.19	1.05, 4.59	0.004	3.70	1.33, 10.32	0.013
Smoker	—	—	—	3.28	1.14, 9.43	0.027

lier menopause, at-risk body habitus, and sedentary lifestyle[11]. On the other hand, lupus patients both male and female have one less risk factor than a comparable group of patients without connective tissue disease who have accelerated atherosclerosis[10]. In this study we have shown that lupus patients with AVE have a higher mean number of major CAD risk factors than lupus patients without AVE, with smoking being especially prominent in the inception cohort. We did not assess other CAD risk factors such as homocysteine and lipoprotein a in this study. Similarly, lipid subfractions were not included in this analysis as they were not available for a significant number of patients prior to the event. Corticosteroids have been shown to be associated with diabetes, obesity, hyperlipidemia, and hypertension, and thus may contribute to the development of AVE in patients with SLE. However, while corticosteroid use was related to AVE in the univariate analysis, it did not remain in the multivariate model. Moreover, in our cohorts, neither the duration of corticosteroid use nor the cumulative dose were associated with the development of AVE.

Immunosuppressive and antimalarial drugs were significant in the univariate analysis, but did not remain in the multivariate analysis. These differences in the use of therapies between the patients with AVE and those without may suggest that patients with AVE had more active disease. Indeed, in the multivariate analysis 2 disease-related factors, vasculitis and neuropsychiatric manifestations, were significantly higher among patients with AVE. These 2 disease features may be a surrogate for overall disease activity. Although antimalarials have been associated with a lower mean cholesterol concentration in patients with SLE and have been shown to blunt the steroid-induced hypercholesterolemia[16,17], in this study there was no difference in use of antimalarials in patients with and those without AVE.

Antiphospholipid antibodies (aCL and/or lupus anticoagulant) are associated with an increased tendency to thrombosis and vascular events[18-20]. Whether this is through a direct effect of the antibodies on the arterial wall or a direct prothrombotic mechanism is unclear. In this study aCL was not a risk factor for vascular events in the total cohort or the inception cohort; however, elevated PTT as a surrogate for the lupus anticoagulant was a risk factor in the entire cohort as well as in the inception cohort. However, this did not remain significant in the multivariate analysis for either cohort.

There is growing interest in the role of inflammation in the pathogenesis of atherosclerosis. This is suggested in particular by the predictive role of CRP for future coronary events in inpatients with unstable angina[22], mortality in inpatients with unstable angina[22], coronary events in outpatients with unstable angina[23], and future coronary events in healthy asymptomatic subjects[24]. In a recent analysis of data from the Nurses' Health Study and the Health Professional Follow-up Study, although plasma lipid levels were more strongly associated with increased risk of CAD than were inflammatory markers, the level of CRP remained a significant contributor to the prediction of CAD[25]. The role of CRP in individuals with obvious reason for elevated inflammatory markers such as SLE has not yet been elucidated. Higher CRP was associated with CAD in a previous cross-sectional study in our cohort[26]. Manzi, *et al*[27] found higher CRP levels in patients with carotid plaques, but this was not substantiated by a recent study by Roman, *et al*[28]. In the current study CRP was measured just prior to the event in only a small number in each cohort, and was not

investigated further. Overall lupus disease activity as a measure of chronic inflammation was assessed in our cohorts using the AMS, which has been shown to be a predictor of mortality and CAD[29]. Anti-DNA antibody, a component of the AMS, was higher in AVE patients in both the total and inception groups, but was statistically significant in the total group (data not shown). Antibodies to extractable nuclear antigens were measured only in a subgroup of our patients prior to the AVE. Anti-Sm was less prevalent in the AVE patients only in the inception cohort (data not shown). Anti-Sm was also found to be less prevalent in patients with plaque on carotid ultrasonography by Roman, *et al*[28]. In the current study the AMS score was higher in patients who had AVE in both cohorts, but did not reach statistical significance. How chronic inflammation and CRP conspire to lead to atherosclerotic lesions has not yet been elucidated.

The Framingham CAD risk factor profile considers demographic features and classic CAD risk factors in deriving 10-year risk for CAD for an individual patient. This analysis in our patients did not indicate that lupus patients with AVE had a higher 10-year risk for the development of CAD than patients without AVE. In the multivariate analysis of all risk factors in our study we have shown that a combination of lupus related (inflammatory) factors (vasculitis and neuropsychiatric) and classic CAD risk factors (total number, or smoking) contributed to the development of AVE. Thus the Framingham approach to prediction for AVE in patients with lupus may not be appropriate, unless patients with SLE are considered similar to patients with diabetes, putting them immediately in the high-risk category. AVE have become major contributors to the clinical presentation of late-stage SLE.

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