Appropriate cardiovascular disease risk assessment in systemic lupus erythematosus may be lacking in rheumatology practice

F. Esmaeilbeigi[1], J.E. Pope[1,2]

[1]Department of Medicine, University of Western Ontario, London, ON, Canada;
[2]Division of Rheumatology, Department of Medicine, St. Joseph's Health Care, University of Western Ontario, London, ON, Canada.

Abstract

Objective

To determine practices regarding cardiovascular (CV) risk assessment in systemic lupus erythematosus (SLE) amongst rheumatologists.

Methods

A questionnaire assessing preventative strategies, risk assessment, and beliefs regarding SLE and CV disease was sent electronically to 425 members of the Canadian Rheumatology Association. Questions were based on published recommendations for CV risk management. Responses were stratified based practitioner's characteristics.

Results

Ninety-nine rheumatologists and trainees responded (22% response rate). Nearly all (91%) believed that SLE is a major CV risk factor, and 68% felt rheumatologists should assess CV risk; whereas 42% were not comfortable with guidelines, 97% felt that family physicians are not aware of the CV risk in SLE but 64% did not routinely inform them in their correspondence. For SLE patients followed: 15% did not check blood pressure at every visit, 32% did not order cholesterol and 34% did not screen for diabetes irrespective of the presence of additional risk factors. Half (54%) would stratify SLE patients as intermediate or high risk when deciding on lipid lowering treatment. For SLE, 45% recommended a target blood pressure of 140/90 and 55% recommended 130/80 as the target.

Conclusion

CV risk assessment and preventative measures were inconsistent when rheumatologists monitored SLE patients, indicating a care gap. Improved communication between rheumatologists and family physicians with respect to elevated CVD risk in SLE is needed.

Key words

systemic lupus erythematosus, cardiovascular risk, rheumatologist opinions, guidelines, survey, quality indicators, risk stratification, antiphospholipid antibody syndrome

Faranak Esmaeilbeigi
Janet E. Pope

Please address correspondence to:
Prof. Janet E. Pope,
Division of Rheumatology,
St. Joseph's Health Care,
268 Grosvenor St.,
London (ON) N6A 4V2, Canada.
E-mail: janet.pope@sjhc.london.on.ca

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Introduction

Systemic lupus erythematosus (SLE) is an uncommon multi-system autoimmune disease affecting approximately 1 in 1000 females and 1 in 10,000 males (1). A bimodal mortality pattern in SLE was described nearly 40 years ago, with early deaths being attributable to SLE related causes, and late deaths related to cardiovascular disease (CVD) (2). Improved detection and early treatment of SLE has led to a significant decrease in early mortality, however 'all cause' mortality remains 3 times greater than the general population. CVD is now a leading cause of death amongst SLE patients (3-5).

The pathophysiology of CVD in SLE is complex. SLE causes chronic inflammation, which may contribute to accelerated atherosclerosis, however cardiac disease in SLE is multifactorial and cannot be attributed to traditional risk factors alone (6, 7). SLE disease activity and treatments such as corticosteroids contribute to CVD (8). Some Framingham risk factors such as dyslipidaemia and hypertension may be more common in SLE (6, 9). The lipid profile seen in SLE differs from the general population, with SLE patients having elevated VLDL, lower HDL and elevated pro-inflammatory HDL (piHDL) (10, 11). However, after adjusting for Framingham risk factors, SLE patients have up to 17-fold increased mortality from ischaemic heart disease (7). Furthermore, sedentary lifestyles, hypothyroidism and early menopause are more common in SLE, further increasing the possibility of developing CVD (6).

While the absolute risk of CVD increases with advanced age and disease duration, the relative risk of CVD in SLE is greatest in patients younger than age 45 (3, 4, 9). The incidence of and mortality from CVD may be similar to that seen in type 1 diabetes mellitus (T1DM), however unlike in T1DM, there are no clear guidelines suggesting that cardiac screening in SLE should differ than from the general population (12). Some studies have evaluated laboratory markers that may be used to identify patients at elevated risk of CVD. Unfortunately, some of these identified markers, such as piHDL, sTWEAK and homocysteine, are not routinely available, making risk stratification using these markers impractical (10, 11). A tool for cardiac risk stratification in SLE patients is lacking.

In the general population, cardiovascular mortality has decreased over the past 30 years (13). However, mortality studies for SLE patients have shown no similar decrease, and in fact CVD mortality may be increasing in SLE (14, 15). Whether this is due to differences in the pathophysiology of CVD in SLE, lack of adequate preventative care, or difficulties in assessing SLE patients for CVD is unknown. Cardiovascular disease in SLE is complicated by a high prevalence of atypical presentations (16). Patients with SLE and practitioners may mistake ischaemic chest pain, as being due to active lupus rather than consider the possibility of cardiac disease.

The purpose of this study was to examine current clinical practice with regards to CVD risk assessment in SLE amongst rheumatologists and practitioners with special interest in rheumatologic disease; to gain insight into areas of possible consensus and dissent, and identify areas of future research which could lead to more specific guideline development.

Methods

Ethics approval was obtained by Canadian Shield Ethics Review Board Inc. An electronic survey was conducted involving members of the Canadian Rheumatology Association (CRA) (n=425). Participants were asked to complete a 36-item questionnaire assessing current practices amongst rheumatologists, as well as epidemiologic data.

Survey development

A 36-question survey was developed based on current Canadian guidelines from Canadian Hypertension Education Program (CHEP) and the Canadian Cardiovascular Society (17, 18). Guidelines from the Canadian Diabetes Association were also incorporated into the study because of recent findings suggesting that the risk of CVD in SLE is equivalent to the risk seen in T1DM (12, 19). As no similar study has been done previously to our know-

Table I. Demographic data of survey respondents.

Characteristic		n (%)
Gender	Female	58 (59%)
Years in practice	Less than 5 years	41 (41%)
Number of SLE patients followed per year*	Less than 50 patients	63 (64%)
Practice setting	Group practice	67 (68%)
	Solo practice	32 (32%)
	University affiliated	64 (65%)
	Non-university affiliated	35 (35%)
Special interest in SLE	Yes	29 (29%)

*1 participant did not tell us how many patients they followed per year.

ledge, there were no baseline questions to structure our study around.

Survey distribution

An e-mail was sent by the CRA secretariat to members of the CRA. Two follow-up emails were sent as reminders prior to closing the survey and retrieving the data.

Data elements

Baseline demographic data were collected including years in practice, number of SLE patients followed, and practice settings. Participants were also asked if they had a special interest in SLE and were stratified accordingly. Questions focused on current preventative care strategies, risk assessment, and beliefs regarding SLE and cardiovascular disease. Responses were measured on a 5-point Likert scale, except for questions relating to collecting demographic data, and questions asking about specific clinical practices. Respondents were also allowed to leave comments at the end of the survey. Participants with incomplete entries were included, with the exception of those not answering any of the clinical questions, and only responded to questions related to their demographics.

Analysis

Electronic survey results were exported into Microsoft Excel. When appropriate Pearson's chi-squared tests were used to test for differences between responses. Data collected from respondents were analysed as a pooled sample, and separately for different practice settings and demographic variations also. A *p*-value of <0.05 was considered statistically significant.

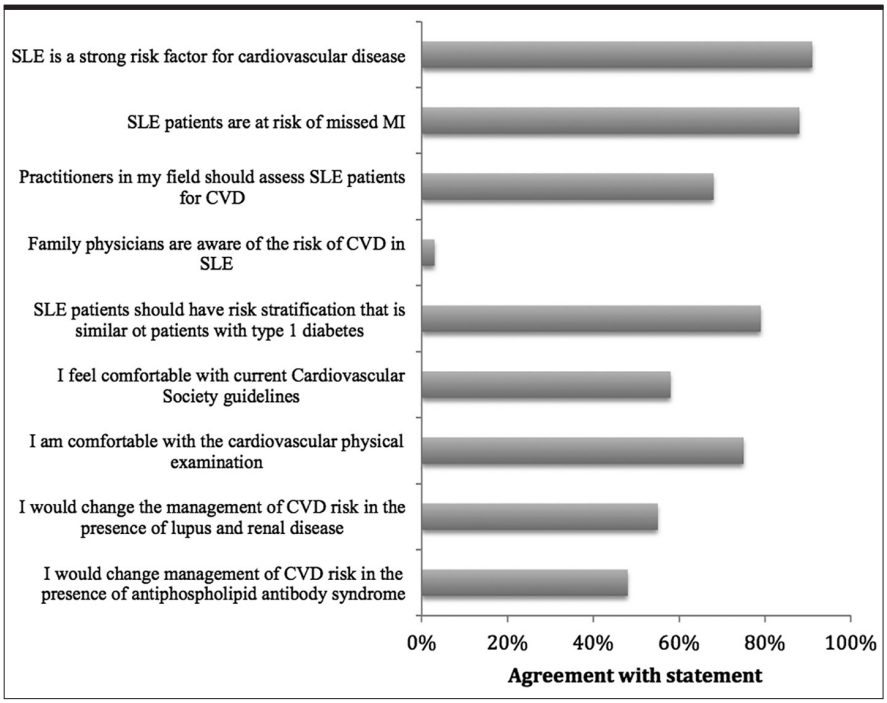

Fig. 1. Physician beliefs about cardiovascular disease risk management in SLE. Results show % agreement with statement.

Results

Demographics

Overall, 425 physicians were contacted and 99 responded, corresponding to a 22% response rate. Baseline characteristics are presented in Table I.

Physician attitudes regarding SLE and CVD risk

Figure 1 shows the results of questions focused on physician beliefs and attitudes. Overall, 91% of practitioners believed that SLE is a strong risk factor for CVD, and 97% felt that family physicians are not aware of this risk. Eighty-eight percent said that SLE patients are at high risk for missed myocardial infarctions or atypical cardiac presentation, however 42% stated that practitioners in their field should not be assessing for CVD risk in SLE patients. More than three quarters (79%) felt that SLE patients should have risk stratification that is similar to current practices in T1DM, and 58% were comfortable with current guidelines, with physicians in practice for less than 5 years reporting greater comfort (73% *vs*. 47%, p=0.008). Those with a special interest in SLE were actually less comfortable with current CVS guidelines than those without special interest in SLE (38% *vs*. 66%, p=0.01). Approximately half of participants reported that they would change their management of CVD risk in the presence of antiphospholipid antibody syndrome and lupus renal disease (48% and 55%, respectively). All those who commented on what they would do differently in these patient populations stated that they would manage CVD risk more aggressively. Responses were further divided based on practice demographics to look for differences between groups. These groups were 1) University Affiliated compared to Non-University Affiliated 2) Group practice compared to solo practice 3) <5 years

in practice compared to >5 years in practice 4) <50 SLE patients followed per year compared to >50 SLE patients followed per year, and 5) Practitioners with a special interest in SLE compared to practitioners without a special interest in SLE.

Significant differences were noted in practitioner's comfort with current cardiovascular society guidelines with those in practice for less than 5 years being more comfortable than those in practice for more than 5 years (73% (n=41) *vs*. 47% (n=58), $p<0.05$) and those without a special interest in SLE also being more comfortable with current cardiovascular society guidelines compared to those with an interest in SLE (38% (n=28) *vs*. 66% (n=70), $p<0.05$).

Current practices in CVD risk management for SLE

Results regarding current practices are shown in Figure 2. Thirty-six percent of respondents frequently inform family physicians about their patients' elevated CVD risk in their letters, with higher likelihood amongst practitioners with a special interest in SLE compared to those without (58% and 30% respectively, $p=0.04$). Most respondents counsel their SLE patients on CVD risk (83%), 44% counsel on dietary modifications and 74% routinely counsel on the importance of physical activity, 71% weigh patients on an annual basis and 36% check height on an annual basis. University affiliated practitioners were significantly more likely to complete these practices than community practitioners. Of the respondents, only 32% calculated a body mass index and 7% calculated a waist to hip ratio. Most do not reassess for a family history of CVD after the first visit and 69% will reassess for smoking history. Overall 76% recommend smoking cessation aids to those who smoke, with a higher proportion in solo practice settings than group practice (90% and 70%, respectively, $p=0.03$). Significant differences were noted between university- and community-based practices in the following: using cardiovascular risk stratification calculators (29% *vs*. 11%), checking blood pressure at every visit (91% *vs*. 74%), weighing patients at least annu-

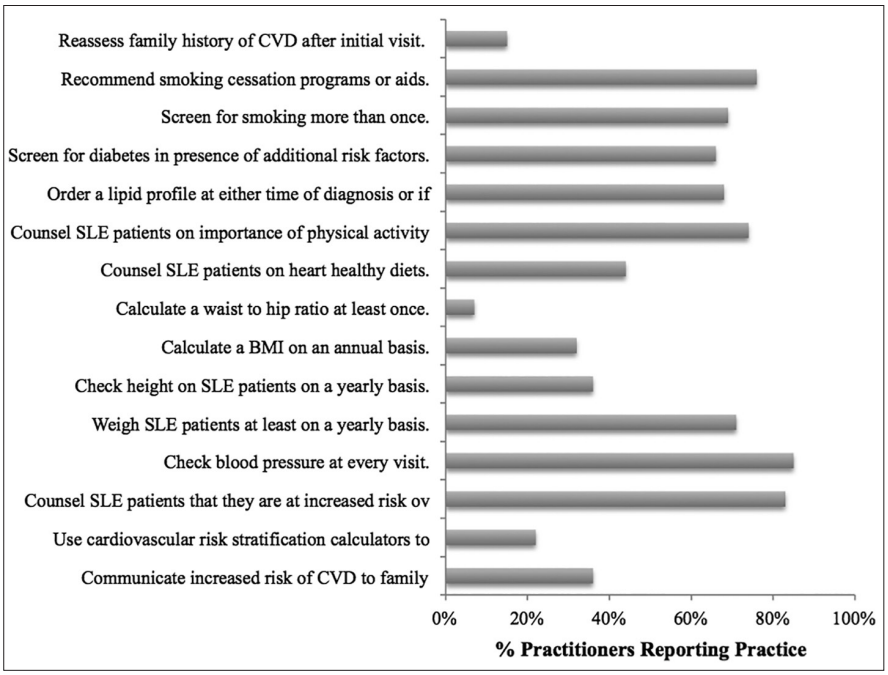

Fig. 2. Current practices in CVD risk assessment and communication amongst CRA respondents. Results show % of practitioners who report routinely engaging in the listed practice.

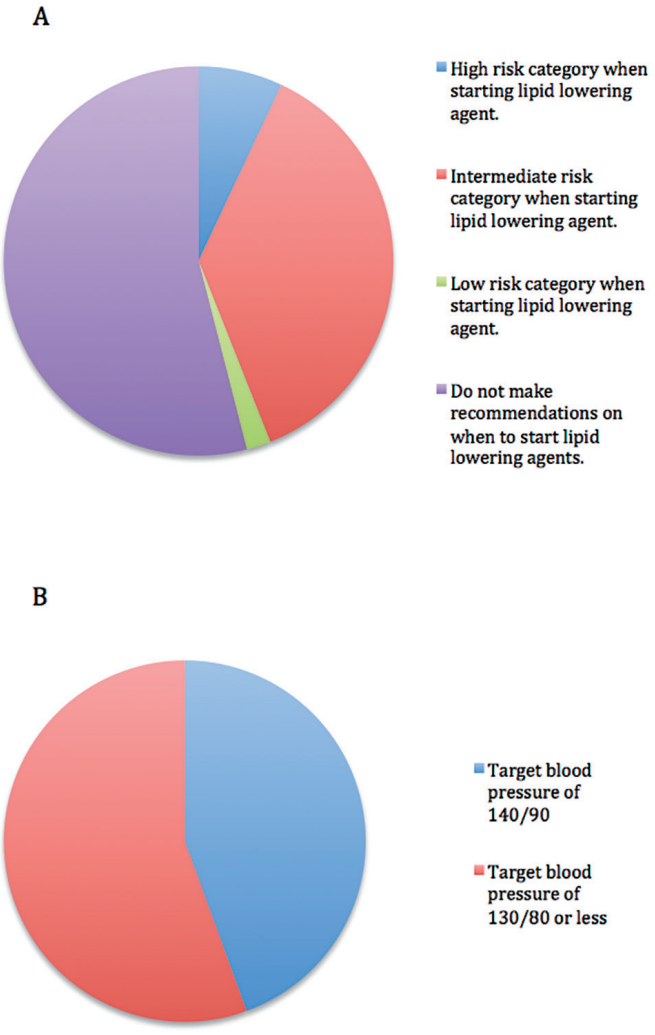

Fig. 3. Recommendations for when to initiate lipid lowering agents (**A**) and target blood pressures (**B**).

ally (78% *vs*. 59%) and checking height annually (45% *vs*. 18%). Practitioners in group practice were significantly more likely than those in solo practice to counsel patients that they were at increased risk of CVD (88% *vs*. 72%) and check height annually (42 *vs*. 22%), and they were less likely to recommend smoking cessation aids or programs (70% *vs*. 90%) (all $p<0.05$). Those with more than 50 SLE patients followed per year and those in practice more than 5 years were significantly less likely to weigh patients annually (56 *vs*.79% and 61% *vs*. 85% respectively). Those with a special interest in SLE were significantly more likely to communicate with family physicians regarding risk of CVD in SLE (52% *vs*. 30%, $p<0.05$)
In terms of screening practices, 85% of respondents reported checking blood pressure at every visit, 68% will order a lipid profile and 66% will screen for diabetes either at time of diagnosis or in the presence of additional risk factors such as metabolic features or family history of CVD/diabetes. There were no differences between groups in these practices.

Recommended practices
Respondents were asked about their recommendations regarding blood pressure targets and lipid lowering agents (Fig. 3). A target blood pressure of 140/90 *vs*. 130/80 or less was recommended for SLE patients (44% and 55% respectively). Most responded that they do not make recommendations on when to start lipid-lowering agents (54%), with those without a special interest in SLE being less likely to make any recommendations ($p=0.01$). Of respondents who make recommendations, 14% considered SLE to be high risk, 81% intermediate risk and 5% low risk stratification.

Discussion

Despite improvements in SLE treatment, a significant burden of CVD and CVD related mortality exists in the SLE population. A recent study found that even when adjusted for socioeconomic status, SLE patients have a significantly increased burden of ischaemic heart disease compared to age matched and gender matched controls (20). This finding reaffirms that SLE is an independent risk factor for ischaemic heart disease (20). Whether this is in part due to a lack of appropriate screening and preventative care is unknown. We assessed current practices and beliefs regarding cardiovascular risk assessment in SLE amongst members of the CRA. Our study shows evidence of a large care gap in CVD related preventative care in SLE patients as demonstrated by a lack of consensus between current practices and guidelines set for the general population, and lack of communication between specialists and primary care physicians.
In our survey, one third did not feel that they should be screening for CVD in their SLE patients, despite an overall understanding and agreement that SLE is a strong risk factor for CVD. Several participants believed that family physicians should be screening for CV disease, however most participants do not convey this risk to family physicians, despite the fact that almost all felt that family physicians are not well informed regarding this elevated CV risk in SLE. The issue of who should address cardiac risk is complicated by the fact that as of 2013 over 15% of the Canadian population did not have a family physician (19). Although these statistics are not available specifically for SLE patients, if specialists feel that family physicians alone should be assessing for cardiac risk, it is possible that many patients will not be appropriately managed due to a lack of access to primary care, and possible lack of knowledge regarding CVD risk in SLE. It is also unclear what proportions of SLE patients seek care from their family doctor. There are guidelines for management of hypertension, hyperlipidemia, diabetes and tools for smoking cessation. However, specific national/international guidelines for SLE risk profiling are sparse.
There is little consensus with regards to CVD assessment in SLE amongst rheumatologists. Traditional cardiovascular risk assessment tools, such as the Framingham risk score, do not account for the impact of systemic inflammation and therefore underestimate the cardiovascular risk that SLE and other systemic autoimmune conditions confer. While there are no SLE-specific Canadian guidelines to guide cardiac risk assessment, current guidelines from the Canadian Cardiovascular Society state that all patients with chronic inflammatory conditions such as rheumatoid arthritis and lupus are considered to be at least intermediate risk for dyslipidemia and should have lipid screening performed irrespective of age (18). One third of rheumatologists did not assess cholesterol levels, even in the presence of additional risk factors. Whether respondents believed that their patients were having their lipid levels drawn by another provider, or if they simply were not aware of the recommendations is unclear. Perhaps, no longer needing a fasting sample for lipid profile may help increase adoption of obtaining this lab test when other lupus monitoring is performed. Although many practitioners make no recommendations on initiation of lipid lowering agents, 95% of those who do suggest treating SLE patients as either intermediate or high risk. Many respondents reported that they would address cardiovascular risk more aggressively in the presence of antiphospholipid antibody syndrome (APS). Patients with APS have increased risk of thrombotic events and may have accelerated atherosclerosis. *In vitro* and *in vivo* models have shown that these antibodies may have an atherogenic role, and the presence of high anticardiolipin antibodies in the absence of autoimmune disease has been associated with greater incidence of myocardial infarction. SLE patients with APS may also have increased prevalence of traditional risk factors such as smoking. Prior studies have reported that patients with primary APS were not found to have accelerated atherosclerosis in the absence of traditional risk factors (23-24). It has been shown however that patients with both SLE and APS have a higher incidence of myocardial infarction compared to those with primary APS. Whether these cardiac events are due to thrombosis or atherosclerosis with plaque rupture was not specified. In a 2003 study by Asanuma *et al*., there

was no difference in calcification of coronary arteries in patients with SLE with APS and those with SLE alone when adjusted for age. It is unclear if primary cardiac prevention should differ from the general lupus population in SLE patients with antiphospholipid antibodies who have not had a cardiovascular or thrombotic event. However, this is a limitation of our survey as we did not ask the rheumatologists if they managed the traditional CV risks differently in these patients.

If guidelines were developed, they may not result in significant change to clinical practice. Studies have shown that there is often little change in practice following publication of guidelines among rheumatologists (25). Our results also support a lack of correlation between current guidelines and current practices as many physicians' responses indicate that they are not following practice guidelines set out for the general population. It is possible that this may in part be explained by differences in resource allocation which may differ between different practice settings (such as performing BP more often in university practices perhaps due to more clinic staff).

Many rheumatologists also reported that their management of cardiac risk factors would be more aggressive in patients with known renal disease. However, some studies have reported that the risk of cardiac disease is similar amongst SLE patients with and without renal involvement (12). This possible lack of association indicates that a group of SLE patients could be left without appropriate risk management unless current practices change.

We may be overestimating awareness of elevated CVD risk in SLE. Compared to the all CRA members, our respondents were more likely to have a special interest in SLE (29%), and more likely to be in practice for less than 5 years (41%). This may have influenced our results. For example, those who are new to practice may be more familiar with current guidelines as they have more recently completed their internal medicine training, and this may influence their practices. In addition, SLE specialists may be more aware of possible CVD risks, or have greater interest in this topic. The low response rate could possibly be due to an overall lack of interest in this topic by the rheumatology community, which may also contribute to inconsistencies seen in the assessment and management of cardiovascular disease prevention. The low response rate may also affect the generalisability due to nonresponse bias. However, prior studies have shown that while increased response rates can improve the power of a study, there was little to no difference in results after more respondents were recruited (26). Overall, survey response rates are decreasing and specialty physicians tend to have lower response rates than other healthcare professionals (25). The fact that we surveyed specialists may, in part, have contributed to our low response rate. In addition, our study was also sent out electronically and provided respondents with no incentives to complete the study. Low response rates with e-mail surveys compared to mailed surveys have been reported (28, 29). We did not have access to mailing addresses for our potential participants and were unable to send our survey by any other method. Web-based surveys may result in potential problems with undeliverable messages and it is possible that we did not distribute our survey to all 425 members of the CRA (30). We did not ask our participants to specify if they were rheumatologists in the demographic questions. However, 96% of CRA members are rheumatologists and therefore our study is likely comprised largely of rheumatologists and any non-rheumatologists who participated are unlikely to influence our results.

Conclusions

Cardiovascular events are the main cause of death in SLE and the burden of treatable CV risk in SLE is elevated. There is a large gap in care in SLE as CV risks are not necessarily routinely assessed and even when they are they are not addressed by many rheumatologists nor is the importance of CV risk factors agreed upon or communicated to the primary care physician to manage if the rheumatologist is not treating them.

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