Advances in Pharmacoepidemiology & Drug Safety

Guo et al., Adv Pharmacoepidemiol Drug Saf 2015, 4:1
DOI: 10.4172/2167-1052.1000173

Research Article Open Access

Clinical Characteristics of Systemic Lupus Erythematosus Patients with Coronary Artery Disease: A Matched Study

Guo Y, Li Y and Jia Y*

Scientific Research Building, Fuwai Hospital, No 167 Beilishi Road, West District, Beijing, People's Republic of China

Abstract

Purpose: The aim of this study was to analyze the clinical characteristics of Systemic Lupus Erythematosus (SLE) patients with Coronary Artery Disease (CAD).

Methods: This study used data from electronic medical records system from Fuwai Hospital. Subjects included SLE patients with CAD and gender-and, age-matched CAD patients without autoimmune connective tissue diseases in a ratio of 1:4. All CAD patients were confirmed by Coronary Angiography (CAG). Data from all subjects was abstracted for Cardiovascular Disease (CVD) risk factors, laboratory test results, echocardiography and CAG.

Results: The proportion of old myocardial infarction (OMI) (p=0.000), myocardial infarction (MI) (p=0.001), family history of premature CAD (p=0.023), hypercholesterolemia (p=0.005), menopause (p=0.015), renal disease manifestation (p=0.000), and higher CRP (p=0.000) in SLE patients with CAD (n=22) were significantly higher than in CAD patients (n=88). CAG showed more multi-vessel lesions (p=0.015) and vascular occlusion lesions (p=0.006) in SLE patients with CAD. Total cholesterol (TC), serum creatinine, urine protein and B-type natriuretic peptide precursor (pro-BNP) were significantly higher in SLE patients with CAD (p=0.000). SLE patients with CAD had higher mortality than CAD patients (p=0.029).

Conclusions: These results indicate that SLE patients with CAD have more renal insufficiency, hypercholesterolemia, and family history of premature CAD than matched patients. In addition, SLE patients with CAD have more extensive and severe coronary artery lesions, and are easily combined with cardiac dysfunction.

Keywords: Systemic Lupus Erythematosus (SLE); Coronary Artery Disease (CAD); Clinical characteristics

Introduction

With the advance of diagnostic and treatment technologies, the prognosis for patients with Systemic Lupus Erythematosus (SLE) has been greatly improved. However, long-term survival remains poor, most likely due to late disease complications. In 1976 Urowitz et al. identified the bimodal mortality pattern, with early deaths due to active disease and infections, and late deaths due to Cardiovascular Disease (CVD) [1]. SLE patients have an increased risk for CVD. The risk of Myocardial Infarction (MI) is increased 50-fold in women with SLE aged 35-44 years old than in women of similar ages without SLE [2].

The increased risk of CVD in SLE patients is under debate. The reason for the increased risk of CVD is likely to be multifactorial. Traditional CVD risk factors include gender, age, obesity, dyslipidemia, hypertension, smoking, family history of premature Coronary Artery Disease (CAD), diabetes mellitus, and menopause. Traditional CVD risk factors are important, but do not, however, fully explain the increased risk of CVD in SLE patients. SLE patients have a 10- to 17-fold higher risk related to CAD than expected taking into account the traditional risk factors [3]. The non-traditional factors are associated with SLE itself like renal disease manifestation, pro-inflammatory cytokines, inflammatory mediators, anti-oxLDL antibodies, antiphospholipid antibodies, and corticosteroid use. CAD is one of the cardiovascular manifestations observed in SLE patients. Although it has been reported that CAD is clinically identifiable in 6.1%-8.9% SLE patients, the occurrence of subclinical CAD is more frequent. Because the clinical manifestations of CAD are more subtle and complex in SLE patients, more attention should be paid to SLE patients with CAD. To understand and manage risk factors for CAD in SLE patients, diagnostic tools such as laboratory tests, echocardiography and Coronary Angiography (CAG) are important.

The aims of this matched study were to investigate CVD risk factors to help us understand clinical characteristics and to analyze clinical characteristics such as demographics, medical history, medication, test results, and motality in SLE patients with CAD.

Methods

Data source

Data for this study were collected through electronic medical records system from Fuwai Hospital, Beijing, China. The electronic medical records system is a database that covers 100% of inpatients since 2002 in Fuwai Hospital. The electronic medical records system has a range of data, including demographics, personal statistics like age and weight, vital signs, medical history, medication, allergies, laboratory test results, radiology images, and billing information. Outpatient visits including return visits are also well recorded in this system.

***Corresponding author:** Jia Y, Scientific Research Building, Fuwai Hospital, No 167 Beilishi Road, West District, Beijing, People's Republic of China, Tel: +8613521284991; Fax: +861068354535; E-mail: yhjia2002@yeah.net

Received November 27, 2014; **Accepted** December 30, 2014; **Published** January 01, 2015

Citation: Guo Y, Li Y, Jia Y (2015) Clinical Characteristics of Systemic Lupus Erythematosus Patients with Coronary Artery Disease: A Matched Study. Adv Pharmacoepidemiol Drug Saf 3: 173. doi:10.4172/2167-1052.1000173

Study population

From 2002 to 2014, in the electronic database of 103,136 CAD patients from Fuwai Hospital which is a national center specialized in cardiovascular diseases, there were 22 SLE patients with CAD confirmed by CAG (0.21‰ of inpatients in the electronic database). Group 1 consisted of 22 SLE patients with CAD. Group 2 was 88 gender-, and age-matched CAD patients who were randomly selected from the same time of initial hospital admission.

The inclusion criteria were: The diagnosis of SLE was earlier than CAD. Group 1 was in the hospital at the same time of initial hospital admission in group 2. All CAD patients had undergone CAG. Exclusion criteria were: Matched CAD patients with autoimmune connective tissue diseases such as SLE, rheumatoid arthritis, scleroderma, and mixed connective tissue disease.

All SLE patients fulfilled the revised American College of Rheumatology criteria for SLE and had been confirmed by specialists [4]. The CAD diagnosis was confirmed by clinical manifestations, Electrocardiogram (ECG), myocardial enzymes, echocardiography, and CAG. CAD patients were defined as those who had a stenosis ≥ 50% of the time and in at least one of major coronary arteries or their main branches on cardiac catheterization. MI was defined on the basis of definite ECG abnormalities or manifestations of chest pain with probable ECG abnormalities and abnormal myocardial enzymes. Patients who experienced more than one cardiac event were only counted once. The event date for each case was defined as the hospital admission date.

In this study, patients were followed-up through telephone interviews and asked about cardiovascular and SLE outcomes in 2014. They were also asked about past and present medication use in detail. Through electronic medical records and telephone follow-ups we collected information for group 1 including SLE duration, medications, cardiovascular events, and other chronic organ damage. Medications included aspirin, statins, anticoagulants, current and past use of corticosteroid, immunosuppressive drugs (azathioprine and cyclophosphamide), and antimalarial drugs (hydroxychloroquine).

Risk factors for CVD

CVD risk factors included traditional CVD risk factors and non-traditional disease-specific factors. Gender, age, obesity (body mass index ≥ 28.0 kg/m^2, using the 'China' cut-points) [5], dyslipidemia (determined by ESC/EAS Guidelines for the management of dyslipidemia) [6], hypercholesterolemia (defined as cholesterol>5.2 mmol/L), hypertension (defined as a systolic blood pressure ≥ 140 mmHg and/or a diastolic blood pressure ≥ 90 mmHg on 2 or more occasions and/or patient self-reported intake of antihypertensive medications) [7], smoking ('ever' or 'never', 'ever' defined as having smoked more than 1 cigarette per day for more than 1 year), family history of premature CAD (defined as MI or sudden death in a first-degree relative: male, age<55 years or female, age<65 years), diabetes mellitus (fasting plasma glucose>7.0 mmol/L, or current diabetic therapy) [8], menopause, renal disease manifestation (serum creatinine>1.4 mg/dl, or significant proteinuria (>1+ on dipstick analysis or >500 mg/day)), C-reactive protein (CRP) (0-8 mg/L), lipoprotein(a) (Lpa) (10-300 mg/L), and corticosteroid use were collected for all the subjects from the electronic medical records [5-8]. Moreover, blood lipids, B-type natriuretic peptide precursor (pro-BNP), serum creatinine, blood urea nitrogen, urine protein, coagulation, chest radiography, echocardiography, and CAG (recorded locations of stenosis, stenosis (with stenosis ≥ 50% is significant stenosis), two and more vessels involved is defined as multi-vessel lesion, stenosis=100% is occlusion) results were collected.

Statistical analysis

Statistical analyses were performed using the SPSS statistical package (SPSS version 21.0). Data presented are the mean ± SD for continuous variables as well as percentages for categorical variables. Qualitative variables were compared using chi- square test and quantitative variables were compared using independent samples t test. As a descriptive measure of association, $p<0.05$ is considered to be statistically significant. Finally, multiple logistic regression models were performed to define the possible role of factors associated with CAD.

Results

In this study, 22 SLE patients with CAD were included in group 1 and 88 gender-, and age-matched CAD patients were included in group 2. Group 1 had 4 patients with stable angina pectoris, 5 patients with unstable angina pectoris, 4 patients with acute myocardial infarction (AMI), 9 patients with old myocardial infarction (OMI), and 13 patients with MI. Group 2 had 33 patients with stable angina pectoris, 36 patients with unstable angina pectoris, 13 patients with AMI, 6 patients with OMI, and 19 patients with MI. There was a significant trend towards OMI (p=0.000) and MI (p=0.001) in group 1 than in group 2.

CVD risk factors between the 2 groups

There were no differences in hypertension, dyslipidemia, obesity, smoking, diabetes, and Lpa (Table 1). Group 1 was significantly more likely to have family history of premature CAD (p=0.023), hypercholesterolemia (p=0.005), menopause (p=0.015), renal disease manifestation (p=0.000), and higher CRP (p=0.000) compared to group 2. The average number of risk factors per person was 3.32 ± 1.70.

Tests and mortality between the 2 groups

Table 2 showed clinical data from the two groups. Both groups had similar triglycerides, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol. SLE patients with CAD had higher values of total cholesterol (TC) (p=0.013), serum creatinine (p=0.000), blood urea nitrogen (p=0.000), urine protein (p=0.000), and pro-BNP (p=0.000) when compared to CAD patients. Group 1 patients had lower echocardiography ejection fraction (EF) than their matched peers (p=0.000). CAG showed single coronary vessel lesions were significantly less (p=0.015) in SLE patients with CAD. However, there were more multi-vessel (p=0.015) and vascular occlusion lesions (p=0.006) in group 1 compared with group 2. No difference was found in the proportion of Coronary Artery Bypass Grafting (CABG) surgery between the two groups.

The telephone follow-up data demonstrated that 4 patients had died, of which 2 patients died due to lupus nephritis and others died of MI. The average survival time for the 4 patients was 13.87 ± 9.31 years old after SLE diagnosis. There were 3 patients who had died in group 2, of which 2 patients died of MI and 1 patient died of heart failure. SLE patients with CAD had higher mortality compared to CAD patients (p=0.029).

Clinical characteristics of SLE patients with CAD:

There were 22 SLE patients with CAD; with a male to female ratio

was 3:19. In group 1, the average age of SLE at diagnosis was 36.54 ± 8.54 years old. The average age of when cardiac events first occurred was 53.27 ± 8.75 years old. The SLE patients developed CAD in 16.29 ± 8.70 years after the diagnosis of SLE. CAG showed multi-vessel lesions in 18 patients (81.82%) and vascular occlusion lesions in 9 patients (40.91%). As for chronic organ damage, 4 patients had musculoskeletal damage, 4 patients had renal damage, 3 patients had neuropsychiatric damage, 2 patients had skin damage, and 2 patients had pulmonary damage (Table 3).

Table 3 shows all patients used corticosteroid, with 9 patients that discontinued corticosteroid and 12 patients that were taking corticosteroid during study timeframe. The average dose of corticosteroid (prednisone equivalent) was 8.46 ± 7.32 mg and the cumulative lifetime dose (prednisone equivalent) was 13.33 ± 5.63 g. Among these 22 SLE patients with CAD, there was 1 patient taking antimalarial drugs, 2 patients taking tripterygium wilfordii and 3 patient taking immunosuppressive drugs. 20 patients used statins including atorvastatin (accounting for 90%), simvastatin and pravastatin. Apart from a patient with upper gastrointestinal bleeding, 21 patients were taking aspirin and 6 of these patients were taking clopidogrel at the same time. Moreover, 4 patients were taking low molecular weight heparin (ranging from enoxaparin to fondaparinux) in addition to aspirin and clopidogrel.

Discussion

SLE is an inflammatory rheumatic disease of immunologic origin. The overall age-adjusted incidence and prevalence (ACR definition) per 100,000 persons is 5.5 and 72.8, respectively. SLE patients have an increased risk for CVD. More than 50% of SLE patients have cardiac involvement [9]. Risk of SLE patients developing CAD is 4-8 times higher than in healthy controls. CAD has been confirmed as a major cause of mortality in SLE patients. The clinical manifestations of CAD in SLE can result from several pathophysiologic mechanisms, including atherosclerosis, arteritis, thrombosis, embolization, spasm, and abnormal coronary flow. Clinically, non-atherosclerotic factors will be considered, if CAD patients are younger than 30 years old

Cardiovascular risk factors	SLE with CAD (n=22)	CAD (n=88)	P
Age (years)	57.41 ± 10.19	57.50 ± 9.65	NS
Gender (female/male)	3/19	3/19	NS
Family history of premature CAD n (%)	9 (40.91)	16 (18.18)	0.023
Hypertension n (%)	11 (50.00)	58 (65.91)	NS
Obesity n (%)	6(27.27)	32(36.36)	NS
Dyslipidemia n (%)	14 (63.64)	37(42.05)	NS
Hypercholesterolemia n (%)	11 (50.00)	17 (19.32)	0.005
Diabetes mellitus n (%)	5 (22.73)	29 (32.95)	NS
Smoking n (%)	4 (18.18)	21 (23.86)	NS
Menopause (years)	48.42 ± 3.99	50.13 ± 2.26	0.015
Renal disease manifestation n (%)	8(36.36)	4(4.55)	0.000
CRP (mg/L)	9.59 ± 10.79	3.18 ± 4.80	0.000
Lpa (mg/L)	320.68 ± 303.31	289.94 ± 276.92	NS

*Data are expressed as mean ± SD, n (%) Abbreviations: CAD= coronary artery disease, CRP= C-reactive protein, Lpa= Lipoprotein(a); NS = non-significant.
Table 1: Prevalence of CVD risk factors between the 2 groups

Variable	SLE with CAD(n=22)	CAD(n=88)	P
Triglycerides (mmol/L)	1.43 ± 0.52	1.76 ± 1.36	NS
Total cholesterol (mmol/L)	5.22 ± 0.63	4.31 ± 1.06	0.000
LDL-C (mmol/L)	2.53 ± 1.01	2.39 ± 0.99	NS
HDL-C (mmol/L)	1.27 ± 0.43	1.38 ± 0.33	NS
Serum creatinine (mmol/L)	73.37 ± 20.14	60.89 ± 11.84	0.000
Blood urea nitrogen (mmol/L)	8.47 ± 7.32	4.94 ± 1.45	0.000
Urine protein n (%)	8(36.36)	4(4.55)	0.000
Pro-BNP (pmol/L)	1200.84 ± 1316.48	626.95 ± 317.61	0.000
EF (%)	55.18 ± 12.26	65.11 ± 5.65	0.000
Coronary angiography			
Single vessel n (%)	4 (18.18)	41 (46.59)[b]	0.015
Two vessels n (%)	8 (36.36)	24 (27.27)	NS
Three vessels n (%)	10 (45.45)	23 (26.14)	NS
Multi-vessel n (%)	18 (81.82)	47 (53.41)	0.015
Vascular occlusion n (%)	9 (40.91)	13 (14.77)	0.006
CABG surgery n (%)	3 (13.64)	5 (5.68)	NS
Mortality n (%)	4(18.18)	3(3.41)	0.029
Lupus nephritis n (%)	2(9.09)	0(0)	
MI n (%)	2(9.09)	2(2.27)	
Heart failure n (%)	0(0)	1(1.14)	

*Data are expressed as mean ± SD, n (%) Abbreviations: LDL-C= Low-density lipoprotein cholesterol, HDL-C= High-density lipoprotein cholesterol, pro-BNP: B-type natriuretic peptide precursor, EF=Ejection fraction (From echocardiography), CABG: Coronary artery bypass grafting, MI: myocardial infarction.
Table 2: Tests and mortality between the 2 groups

Variable	SLE with CAD (n=22)
Corticosteroid n (%)	22 (100.00)
average dose (prednisone equivalent) at study (mg/d)	8.46 ± 7.32
cumulative lifetime dose (prednisone equivalent) (gm)	5.35 ± 2.72
Antimalarial drugs n (%)	1 (4.55)
Tripterygium wilfordii n (%)	2 (9.09)
Immunosuppressive drugs n (%)	3 (13.64)
Aspirin	21(95.45)
Statins n (%)	20 (90.91)
Chronic damage	1.68 ± 0.78
Musculoskeletal n (%)	4 (18.18)
Renal damage n (%)	4 (18.18)
Malignancy n (%)	0 (0.00)
Neuropsychiatric n (%)	3 (13.64)
Skin damage n (%)	2 (9.09)
Pulmonary n (%)	2 (9.09)

without CVD risk factors. In our study, as for when cardiac events first occurred, the minimum age was 34 years old and the average age of was 53.27 ± 8.75 years old. The average number of risk factors per person was 3.32 ± 1.70. CAG has a certain role in identification of arteritis. In the CAG results of SLE patients, there were no vasculitis typical changes like cystic change and aneurysm. In the occurrence of MI, coronary thrombosis has an important position. The occurrence of thrombosis is related to endothelial injury mediated by immune complex and anti-phospholipid antibodies. Almost all thrombosis occurs on the basis of atherosclerosis. Although there is an increased relative risk for CAD in SLE patients, the risk factors that may contribute to this increased risk is unclear.

In this retrospective study, we focused on the clinical characteristics of SLE patients with CAD by checking related risk factors, laboratory data and myocardial perfusion abnormalities. Features of this study are that all CAD patients had undergone CAG and SLE patients with CAD were compared with CAD patients. Univariate analyses demonstrate that, SLE patients with CAD were more likely to have risk factors for atherosclerotic disease than their matched peers. Our study found family history of premature CAD, hypercholesterolemia, renal disease manifestation, earlier menopause, and higher CRP were more common in SLE patients with CAD. The study showed hypercholesterolemia to be a significant CVD risk factor in SLE patients. In many studies, hypercholesterolemia has been proven to be associated with the increased risk of CVD events in SLE patients [10]. Many studies have demonstrated that SLE is a multi-gene related disease. Urowitz et al. found that SLE patients with CAD are more likely to have a family history of premature CAD [11]. Our study demonstrated family history of premature CAD was significantly associated with the increased risk of CAD in SLE patients. Renal disease manifestation is known to be one of the important factors for accelerated atherosclerosis in SLE [12]. Renal impairment and proteinuria are likely to have an adverse effect on CVD risk [13]. Our results about renal disease manifestation are similar to the studies above. SLE patients with CAD had their menopause an average of 2 years earlier than did the CAD patients (at a mean age of 48.4 years versus 50.1 years). Premature menopause was more prevalent in SLE patients with CAD than in CAD patients in our study. SLE patients have menopause on average 3-4 year earlier than healthy people in previous studies [14]. This is associated with the SLE itself and usage of corticosteroid, antimalarial drugs, and immunosuppressive drugs in these patients. Group1 had significantly higher CRP compared to group 2. Inflammatory mediators and endothelial activation are associated to atherosclerosis. Elevated high sensitivity CRP (hsCRP) is considered a powerful independent predictor of vascular events in the LUMINA study [15]. Genetic variations in the CRP gene(s) and disease activity may account for elevated CRP levels in SLE patients.

Although no statistically significant correlation was found between the presence CAD in SLE patients and a number of risk factors, this does not mean those factors are irrelevant. Among the risk factors, hypertension, dyslipidemia and hypercholesterolemia are more common in SLE patients [16]. Some studies have identified hypertension as the modifiable risk factor which is most closely linked to the onset of SLE patients with CAD [14-17]. However, in our study, there was no difference in hypertension between the two groups. This is most likely due to the limited number of studied SLE patients with CAD. Almost all SLE patients with CAD had been treated with corticosteroid and 36.36% of patients had renal disease manifestation. Although dyslipidemia is a feature of patients with steroid-treated SLE and patients with renal disease manifestation, no difference was found in dyslipidemia between the two groups. There were 78.57% of dyslipidemia patients with hypercholesterolemia in group 1 and 45.94% in group 2. Whether dyslipidemia is associated with the increased risk of CVD in SLE patients need further evidence. No differences were found in obesity and diabetes mellitus between the two groups. High prevalence of metabolic syndrome in patients with SLE has been repeatedly established in previous studies. However, most controls of previous studies are general population. Our control group consisted of CAD patients who also had a lot of atherosclerotic risk factors.

The average age of first cardiac event in SLE patients was 53.27 ± 8.75 years old. This age is 10.5 years earlier than the age of non-SLE patients, which suggests SLE is an independent risk factor which increases the risk of CAD in SLE patients [18]. The SLE patients developed CAD in 16.29 ± 8.70 years after the diagnosis of SLE. Patients with SLE have cardiovascular events at a much younger age compared with the general population. Having a cardiovascular event in 9-18years after the diagnosis of SLE has been demonstrated in some studies.[2] Fuwai Hospital is a center specialized in cardiovascular diseases. This hospital does not have autoimmune related texts. In group 1, there was a lack of sufficient clinical immunology data. Therefore, this study is not a comprehensive evaluation of risk factors which should account for the increased risk of CAD in SLE patients, and the role of other variables, such as hypertension, stroke, and smoking needs further investigation.

CAG is regarded as the gold standard for CAD diagnosis. SLE patients with CAD had more MI, multi-vessel lesions and vascular occlusion lesions compared with the matched patients. The multi-vessel lesions proportion reached as high as 81.8% and nearly half of the SLE with CAD patients had vascular occlusion lesions. Our data suggests that patients in group 1 have more extensive coronary artery lesions, vascular occlusion lesions, and are easily combined with cardiac dysfunction. There were 13.64% SLE with CAD patients and 5.68% matched patients that had CABG surgery. No difference was found in the proportion of CABG surgery between the two groups. For SLE patients with CAD, there might have been some operation contraindications, including multi-systems involvement and concomitant likelihood of postoperative complications, such as poor healing due to steroid use.

Data from ultrasound and pro-BNP demonstrated that SLE patients with CAD had poorer cardiac pump function, and were more easily combined with cardiac dysfunction. Karadag et al. have found that SLE patients without clinical signs of ischemic heart disease have increased levels of BNP [19]. Increased BNP levels in SLE patients may reflect myocardial damage. Results of serum creatinine, blood urea

nitrogen, and urine protein suggest that renal disease manifestation is a CVD risk factor in SLE patients. Studies have shown that increasing level of serum creatinine and the presence of proteinuria are associated with SLE patients with CAD [20]. In addition, kidney damage and use of glucocorticoid (>30 mg/d) can induce dyslipidemia in SLE patients [21]. In group 1, there were 8 patients with kidney disease (36.36%), 2 patients with pulmonary involvement (9.09%), and 2 patients with strokes (9.09%). All of these results suggest that SLE has multi-systems involvement. Data suggests that high cholesterol levels, increased serum creatinine levels, and the presence of urine protein are most likely to be CVD predictive factors in SLE patients.

The average survival time was 13.87 ± 9.31 years in the 4 dead patients from group 1after SLE diagnosis. Kaditanon et al. have reported the overall cumulative probability of survival after SLE diagnosis at 5, 10, 15, and 20 years is 95%, 91%, 85%, and 78%, respectively [22]. Our data showed SLE patients with CAD had higher mortality than CAD patients. This is most likely due to SLE patients with CAD have more severe coronary lesions, worse cardiac function and more serious complications. SLE itself may directly responsible for increased mortality. Renal involvement is also associated with significantly increased mortality in SLE patients [23]. In our study, musculoskeletal damage and renal damage were more common in SLE patients with CAD. An observation of 232 SLE patients reveals that musculoskeletal, cardiovascular and renal damage are the most common on the SLE chronic organ damage list [24]. The average dose (prednisone equivalent) during the study was 8.46 ± 7.32 mg and the cumulative lifetime dose (prednisone equivalent) was 13.33 ± 5.63 g. Compared with other studies, our SLE patients with CAD had higher cumulative lifetime dose, which may partly explain the increased CVD risk. In group 1, there were 95.45% patients taking aspirin and 90.91% patients taking statins. Some studies have reported the beneficial effect of aspirin in SLE patients [25]. Statins not only exert favorable effects on lipoprotein metabolism, but may also have an increasingly recognized immunomodulatory role. Some studies propose that (like diabetes mellitus) SLE should be considered a 'CAD-equivalent' condition for baseline risk. The increased use of aspirin, statins, needs to be more-widely investigated.

In conclusion, several CVD risk factors may account for the development of CAD in SLE patients. The approach to the prevention of cardiovascular events in SLE should include the control of risk factors to substantially reduce or delay the occurrence of these potentially fatal events. SLE patients with CAD have more extensive coronary artery lesions, vascular occlusion lesions, and are easily combined with MI, cardiac dysfunction and multi-systems involvement. SLE patients with CAD have more severe CAD clinical manifestations and poor prognosis. Most early CAD clinical manifestations of SLE patients are complicated and atypical. Coronary assessment and early screening should be strengthened in SLE patients with CAD with clinical manifestations or not. Early intervention of CVD risk factors should not be ignored. We ought to assess SLE activity and involvement of other systems, thereby delaying or preventing the progression of CAD.

References

1. Urowitz MB, Bookman AA, Koehler BE, Gordon DA, Smythe HA, et al. (1976) The bimodal mortality pattern of systemic lupus erythematosus. Am J Med 60: 221-225.
2. Manzi S, Meilahn EN, Rairie JE, Conte CG, Medsger TA Jr, et al. (1997) Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: Comparison with the Framingham study. Am J Epidemiol 145: 408-415.
3. Esdaile JM, Abrahamowicz M, Grodzicky T, Li Y, Panaritis C, et al. (2001) Traditional Framingham risk factors fail to fully account for accelerated atherosclerosis in systemic lupus erythematosus. Arthritis Rheum 44: 2331-2337.
4. Hochberg MC (1997) Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 40:1725.
5. Zhou BF(2002) Cooperative Meta-analysis Group of the Working Group on Obesity in China: Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults-study on optimal cutoff points of body mass index and waist circumference in Chinese adults. Biomed Environ Sci 15: 83-95.
6. Reiner Z, Catapano AL, De Backer G, Graham I, Taskinen MR et al. (2011) ESC/EAS Guidelines for the management of dyslipidemia: The task force for the management of dyslipidemia of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). Eur Heart J 32: 1769-1818.
7. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R et al. (2007) 2007 ESH-ESC practice guidelines for the management of arterial hypertension: ESH-ESC task force on the management of arterial hypertension. J hypertens 25: 1751-1762.
8. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (2003) Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 26 Suppl 1: S5-20.
9. Nikpour M, Urowitz M B, Ibanez D, Harvey PJ, Gladman DD (2011) Importance of cumulative exposure to elevated cholesterol and blood pressure in development of atherosclerotic coronary artery disease in systemic lupus erythematosus: a prospective proof-of-concept cohort study. Arthritis Res Ther13: R156.
10. Urowitz MB, Gladman D, Ibañez D, Bae SC, Sanchez-Guerrero J, et al. (2010) Atherosclerotic vascular events in a multinational inception cohort of systemic lupus erythematosus. Arthritis Care Res (Hoboken) 62: 881-887.
11. Serikova Slu, Kozlovskaia NL, Shilov EM (2008) Lupus nephritis as a factor of atherosclerosis risk in patients with systemic lupus erythematosus. Ter Arkh 80: 52-58.
12. Bruce IN, Gladman DD, Urowitz MB (2000) Premature atherosclerosis in systemic lupus erythematosus. See comment in PubMed Commons below Rheum Dis Clin North Am 26: 257-278.
13. Bruce IN, Urowitz MB, Gladman DD, Ibañez D, Steiner G (2003) Risk factors for coronary heart disease in women with systemic lupus erythematosus: the Toronto Risk Factor Study. Arthritis Rheum 48: 3159-3167.
14. Szalai AJ, Alarcón GS, Calvo-Alén J, Toloza SM, McCrory MA, et al. (2005) Systemic lupus erythematosus in a multiethnic US Cohort (LUMINA). XXX: association between C-reactive protein (CRP) gene polymorphisms and vascular events.Rheumatology (Oxford) 44: 864-868.
15. Bessant R, Duncan R, Ambler G, Swanton J, Isenberg DA, et al. (2006) Prevalence of conventional and lupus-specific risk factors for cardiovascular disease in patients with systemic lupus erythematosus: A case-control study. Arthritis Rheum 55: 892-899.
16. Nuttall SL, Heaton S, Piper MK, Martin U, Gordon C (2003) Cardiovascular risk in systemic lupus erythematosus--evidence of increased oxidative stress and dyslipidaemia.Rheumatology (Oxford) 42: 758-762.
17. Scalzi LV, Hollenbeak CS, Wang L (2010) Racial disparities in age at time of cardiovascular events and cardiovascular-related death in patients with systemic lupus erythematosus.Arthritis Rheum 62: 2767-2775.
18. Scalzi LV, Hollenbeak CS, Wang L (2010) Racial disparities in age at time of cardiovascular events and cardiovascular-related death in patients with systemic lupus erythematosus.Arthritis Rheum 62: 2767-2775.
19. Karadag O, Calguneri M, Yavuz B, Atalar E, Akdogan A, et al. (2007) B-type natriuretic peptide (BNP) levels in female systemic lupus erythematosus patients: what is the clinical significance?Clin Rheumatol 26: 1701-1704.
20. Selzer F, Sutton-Tyrrell K, Fitzgerald SG, Pratt JE, Tracy RP, et al. (2004) Comparison of risk factors for vascular disease in the carotid artery and aorta in women with systemic lupus erythematosus. Arthritis Rheum 50: 151-159.
21. Urquizu-Padilla M, Balada E, Chacon P, Pérez EH, Vilardell-Tarrés M, et al. (2009) Changes in lipid profile between flare and remission of patients with systemic lupus erythematosus: a prospective study. J Rheumatol 36: 1639-1645.

22. Kasitanon N, Magder LS, Petri M (2006) Predictors of survival in systemic lupus erythematosus. Medicine (Baltimore) 85: 147-156.

23. Chambers SA, Allen E, Rahman A, Isenberg D (2009) Damage and mortality in a group of British patients with systemic lupus erythematosus followed up for over 10 years. Rheumatology (Oxford) 48: 673-675.

24. Wahl DG, Bounameaux H, de Moerloose P, Sarasin FP (2000) Prophylactic antithrombotic therapy for patients with systemic lupus erythematosus with or without antiphospholipid antibodies: do the benefits outweigh the risks? A decision analysis.Arch Intern Med 160: 2042-2048.

25. Haque S, Bruce IN (2005) Therapy insight: systemic lupus erythematosus as a risk factor for cardiovascular disease.Nat Clin Pract Cardiovasc Med 2: 423-430.