Lupus Damage and Waist Circumference as the Independent Risk Factors for Cardiovascular Disease in SLE Patients from Phramongkutklao Hospital

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Background: *Cardiovascular disease (CVD) has been reported to be a major cause of both morbidity and premature mortality in systemic lupus erythematosus (SLE) patients.*
Objective: *To determine the prevalence of cardiovascular disease and associated risk factors in Thai SLE patients from Phramongkutklao Hospital, Thailand.*
Material and Method: *A retrospective cross-sectional study was performed to investigate the frequency of CVD in SLE patients in Phramongkutklao Hospital on the basis of medical record documentation. CVD was defined as coronary heart disease, congestive heart failure, cerebrovascular disease (stroke), transient ischemic attack, and peripheral arterial disease (PAD). The associated risk factors of CVD were examined by univariate and multivariate logistic regression analyses.*
Results: *One hundred fifty nine SLE patients were enrolled in the present study. Nine female and one male SLE patients had CVD (prevalence 6.3%). SLE patients with CVD had higher Systemic Lupus International Collaborating Clinics Damage Index (SDI) score (p-value = 0.025) and received higher average dose of corticosteroid (p-value = 0.034) than SLE patients without CVD. Patients with CVD were more likely to present with malar rash (p-value = 0.054), discoid rash (p-value = 0.047), and more likely to used cyclophosphamide (p-value = 0.045) than patients without CVD. SLE patients with CVD were more likely to have diabetes mellitus (p-value = 0.037), antiphospholipid syndrome (p-value = 0.055), and had higher proportion of patients whose waist circumference more than 90 centimeters in male or more than 80 centimeters in female (p-value = 0.06) than SLE patients without CVD. The presence of antiphospholipid antibodies was higher in SLE patients with CVD than SLE patients without CVD (p-value = 0.076). The multivariate regression analysis identified that SDI score (odds ratio (OR) = 1.74 with 95% confidence interval (CI) 1.12-2.69, p-value = 0.013), and waist circumference more than 90 centimeters in male or more than 80 centimeters in female (OR = 6.9 with 95% CI 1.20-38.46, p-value = 0.031) were independently associated risk factors for the occurrence of CVD in SLE patients. The presence of antiphospholipid antibodies also had a trend toward increased risk of CVD in SLE patients (OR = 4.1 with 95% CI 0.96-17.8, p-value = 0.057).*
Conclusion: *Lupus damage, waist circumference more than 90 centimeters in male or more than 80 centimeters in female were the independent risk factors for CVD in SLE patients.*

Keywords: *Cardiovascular disease, Prevalence, Risk factor, Systemic lupus erythematosus*

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Systemic lupus erythematosus (SLE) is an autoimmune disease that causes disease manifestations in multiple organ system. Diagnosis is established by the patient fulfilled at least four of 11 of the 1997 Revised American College of Rheumatology Criteria (ACR)[1].

Several studies have reported that patients with SLE have five to ten times higher risk of cardiovascular disease (CVD) than general population[2-7]. The prevalence of CVD in SLE patients ranges from about 6 to 13%[4,8-13].

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Currently, the mechanism of the development of CVD in SLE patients remains controversial. However, it is presumed that patients with SLE are a chronic inflammatory disease, and are at high risk of premature atherosclerosis and CVD. CVD is a major cause of both morbidity and mortality in SLE patients[7,9,13-15].

The main aim of the present study was to investigate the prevalence and to evaluate risk factors of CVD in Thai SLE patients at Phramongkutklao Hospital, Thailand.

Material and Method

Study design & patient population

This was a retrospective cohort study of SLE patients attended the Rheumatic Disease Unit,

Department of Internal Medicine, at Phramongkutklao Hospital, Bangkok, Thailand between May 1, 2012 and September 30, 2013.

Inclusion criteria included all SLE patients fulfilled at least four of the 1997 Revised ACR for SLE[1], age more than 18 years. Exclusion criteria were SLE patients documented as having CVD, diabetes mellitus, hypertension, or dyslipidemia onset prior to SLE diagnosis or SLE patients overlapped with other connective tissue diseases.

The present study was approved by the Institutional Review Committee, Royal Thai Army Medical Department, and all subjects gave written informed consent.

Methods

Study cases were identified as SLE patients having CVD after the diagnosis of SLE. CVD was defined as coronary heart disease (CHD) including myocardial infarction and angina pectoris, congestive heart failure (CHF), cerebrovascular disease (stroke), transient ischemic attack (TIA), and peripheral arterial disease (PAD). All criteria were adapted from definition in the Framingham Study, the Cardiovascular Health Study, and the American College of Cardiology/ American Heart Association (ACC/AHA)[16-25].

Controls: controls were defined as SLE patients without CVD.

Information was collected by standardized clinical interview, physical examination, and review of medical records including:

1. Demographic variables included age, gender, and menstruation status.

2. Traditional cardiovascular risk factors included cigarette smoking, family history of cardiovascular disease was defined as a first-degree relative who had a myocardial infarction or stroke before the age of 55 years in men or 65 years in women, obesity, hypertension, dyslipidemia, and diabetes mellitus[26,27]. Height and weight were measured and the body mass index (BMI) was calculated. Waist circumference was measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest, and was taken at the end of a normal expiration with the tape parallel to the floor in standing position[28], and 10-year cardiovascular risk (Framingham 10-year Risk Score) was also calculated[29].

3. Clinical variables included

- SLE manifestations of the 1997 Revised ACR[1] if presented at any time from the time of SLE diagnosis to the time when the CVD developed for study cases and from the time of SLE diagnosis to the latest follow-up for controls included: malar rash, discoid rash, photosensitivity, oral ulcer, arthritis, serositis (pleuritis or/and pericarditis), renal involvement (persistent proteinuria greater than 0.5 g/day or/and greater than 3+ or/and presence of heme, granular or red blood cell casts in urine or/and biopsy evidence of lupus nephritis[30]), neurological involvement (seizure or/and psychosis), hematologic involvement (hemolytic anemia or leucopenia, white blood cells <4,000/mm^3, not due to drugs), or lymphopenia (lymphocytes <1,500/mm^3, not due to drugs), or thrombocytopenia (platelet <100,000 platelets/mm^3, not due to drugs).
- Age at diagnosis of SLE
- Disease duration of SLE
- Mexican-Systemic Lupus Erythematosus Diseases Activity Index (MEX-SLEDAI)[31] at the time of maximum daily steroid dosage as it would represent the highest disease activity during the follow-up time.
- Systemic Lupus International Collaborating Clinics Damage Index (SDI)[32]: we used the score if present at any time from the time of SLE diagnosis to the time when the CVD developed and excluded the score from CVD for cases, and from the time of SLE diagnosis to the latest follow-up for controls.
- Patients with antiphospholipid syndrome[33].

4. Serology at time of SLE diagnosis included: antinuclear antibody; ANA, anti-double stranded DNA antibody; anti-ds DNA, anti-Smith antibody, anti-cardiolipin IgG antibody, anti-cardiolipin IgM antibody, lupus anticoagulant, and false positive Veneral Disease Research Laboratory test (VDRL).

5. Therapeutic variables included

- Glucocorticoid (GC) use: dose of GC was recorded as prednisolone equivalent, duration of GC use, average dose of GC, total cumulative dose of GC, and the use of pulse methylprednisolone.
- The immunosuppressive drug use: if used at anytime from the time of the SLE diagnosis to the time when the CVD developed for study cases, and from the time of SLE diagnosis to the latest follow-up for controls; included antimalarial agents (chloroquine and hydroxychloroquine), azathiopine, cyclophosphamide, mycophenolate mofetil or sodium, and methotrexate.
- Antihypertensive medications included angiotensin-converting enzyme-inhibitor (ACE-I), angiotensin receptor blocker (ARB), beta-blocker, calcium channel-blocker, diuretic, and lipid-lowering

agents, if used at any time from the time of the SLE diagnosis to the time when the CVD developed for study cases, and from the time of SLE diagnosis to the latest follow-up for controls.

Definition

1. Obesity was defined as BMI ≥25 kg/m^2[28].

2. Hypertension: if a systolic blood pressure at least 140 mmHg and/or a diastolic pressure at least 90 mmHg or used prescribed antihypertensive drugs to reduce blood pressure[34].

3. Impaired fasting glucose: fasting plasma glucose = 100 to 125 mg/dL[35].

4. Diabetes mellitus: fasting plasma glucose ≥126 mg/dL or used prescribed oral hypoglycemic drugs and/or insulin[35].

5. Dyslipidemia: total cholesterol ≥200 mg/dL, or fasting triglyceride ≥150 mg/dL, or used prescribed lipid-lowering agents[27].

6. Metabolic syndrome was diagnosed if three or more of the following criteria were presented: arterial hypertension (≥130 mmHg systolic blood pressure or ≥85 mmHg diastolic blood pressure or drug treatment for hypertension), increased fasting plasma glucose (≥110 mg/dL), reduced high-density lipoprotein (HDL)-cholesterol (<40 mg/dL in men or <50 mg/dL in women), increased triglyceride (≥150 mg/dL), and increased waist circumference (≥90 cm in men or ≥80 cm in women)[36].

Statistical analysis

Categorical variables were described as absolute and relative frequencies, and continuous variables were described as mean ± standard deviation or median (interquartile range), as appropriate. Student's t-test was performed to evaluate differences between continuous variables in study cases and controls. Categorical data were compared using the Chi-square test and Fisher's exact test. A multivariable logistic regression model for CVD was then examined, which included only variables with *p*-value <0.1 in the univariate analyses. Results were reported as adjusted odds ratios with 95% confidence intervals. Two-sided *p*-value <0.05 were considered statistically significant.

Results

Prevalence of CVD

Between May 1, 2012 and September 30, 2013, 227 SLE patients attended the Rheumatic Disease Unit, Department of Internal Medicine, Phramongkutklao Hospital. Sixty-seven patients were excluded, 34 patients had missing data or were transferred to other hospital, seven patients died of infection, 23 patients had other overlapping syndrome, two patients had myocardial infarction prior to SLE diagnosis, one patient had prior stroke, and one patient had prior diabetes mellitus.

Table 1. Prevalence of cardiovascular diseases in patients with systemic lupus erythematosus (SLE)

Populations	Patients with CVD n (%)	Patients without CVD n (%)
Total	10 (6.3)	149 (93.7)
Age (years)		
18-19	0	2 (1.3)
20-39	3 (30.0)	56 (37.6)
40-49	5 (50.0)	50 (33.6)
50-59	2 (20.0)	33 (22.1)
≥60	0	8 (5.4)
Sex		
Male	1 (10.0)	9 (6.0)
Female	9 (90.0)	140 (94.0)

CVD = cardiovascular disease

One hundred fifty nine SLE patients with complete data were included. The CVD was found in 10 patients (6.3%), and nine of them were female (Table 1). Of these 10 SLE patients with CVD, there was one CHF, one peripheral arterial disease, three myocardial infarctions, and five ischemic strokes.

Demographic & clinical variables

Most subjects were female (94%) with an average age of 43 years old. The mean (± standard deviation, SD) duration of disease from the time of the diagnosis of SLE was 145.7±103.1 months. The average age ± SD of study cases was greater than that of controls (44.1±7.7 vs. 42.8±11.1 years, *p*-value = 0.721). Half of cases were in the 40 to 49 year age group (5 of 10 patients). The mean age of the cardiovascular events was 40 years old, and the mean age at SLE diagnosis did not differ between study cases and controls (29.7±7.4 vs. 30.39±11.2 years, *p*-value = 0.848). Study cases had higher SDI (3.3±2.21 vs. 1.42±1.32 points, *p*-value = 0.025), and had more discoid rash than controls (1 (10%) vs. 65 (43.6%) persons, *p*-value = 0.047). Moreover study cases had malar rash (2 (2%) vs. 79 (53%) persons, *p*-value = 0.054), and antiphospholipid syndrome (3 (30%) vs. 12 (8.1%) persons, *p*-value = 0.055) more than controls. The presence of antiphospholipid antibodies was higher in SLE patients with CVD than

Table 2. The comparison of demographic variables, disease characteristic, and serologic features of SLE patients with and without cardiovascular diseases

Variables	Patients with CVD (n = 10)	Patients without CVD (n = 149)	*p*-value
Demographic variables			
Age (years), mean (SD)	44.1 (7.7)	42.8 (11.1)	0.721
Female, n (%)	9 (90.0)	140 (94.0)	0.618
Post menopause, n (%)	1 (20.0)	29 (25.9)	1.000
Diseases characteristic & serologic features			
Age at diagnosis (years), mean (SD)	29.7 (7.4)	30.39 (11.2)	0.848
Disease duration (months), mean (SD)	93.8 (89.5)	149.2 (103.3)	0.100
MEX-SLEDAI, mean (SD)	4.8 (6.8)	5.66 (6.2)	0.579
SDI score, mean (SD)	3.3 (2.2)	1.42 (1.3)	0.025
Malar rash, n (%)	2 (20.0)	79 (53.0)	0.054
Discoid rash, n (%)	1 (10.0)	65 (43.6)	0.047
Photosensitivity, n (%)	1 (10.0)	50 (33.6)	0.170
Oral ulcer, n (%)	1 (10.0)	52 (34.9)	0.167
Arthritis, n (%)	7 (70.0)	94 (63.1)	0.748
Pleuritis, n (%)	2 (20.0)	14 (9.4)	0.265
Pericarditis, n (%)	0 (0)	7 (4.7)	1.000
Renal involvement (LN), n (%)	8 (80.0)	78 (52.3)	0.110
Psychosis, n (%)	0 (0)	8 (5.4)	1.000
Seizure, n (%)	0 (0)	4 (2.7)	1.000
Hemolytic anemia, n (%)	6 (60.0)	68 (45.6)	0.516
Leucopenia, n (%)	3 (30.0)	44 (29.5)	1.000
Thrombocytopenia, n (%)	1 (10.0)	17 (11.5)	1.000
Antiphospholipid syndrome, n (%)	3 (30.0)	12 (8.1)	0.055
Anti-dsDNA, n (%)	6 (60.0)	71 (47.7)	0.525
Anti-Smith, n (%)	0 (0)	28 (18.8)	0.211
Antiphospholipid antibodies*, n (%)	3 (30.0)	14 (9.4)	0.076

CVD = cardiovascular diseases; SD = standard deviation; MEX-SLEDAI = Mexican-systemic lupus erythematosus diseases activity index; SDI = systemic lupus international collaborating clinics damage index excluded the score from CVD; LN = lupus nephritis; Anti-dsDNA = anti-double strand DNA; ANA = antinuclear antibody; Anti-smith = anti-Smith antibody

* Anti-phospholipid antibodies included lupus anticoagulant, anti-cardiolipin IgG and IgM antibodies, and false positive veneral disease research laboratory test (VDRL)

SLE patients without CVD (3 (30%) vs. 14 (9.4%), *p*-value = 0.076). No difference was found regard to gender, postmenopausal status, duration of SLE disease, disease activity (MEX-SLEDAI), lupus nephritis, and serological parameters (ANA, anti-dsDNA, anti-Smith) (Table 2).

Therapeutic variables

Study cases received higher average dose of GC than controls (13±8.3 vs. 8.5±6 mg/day, *p*-value = 0.034). Treatment with cyclophosphamide [4 (40%) vs. 20 (13.4%) persons, *p*-value = 0.045] was more frequently used in study cases. The use of GC in other parameters (cumulative dose, duration of GC, history of intravenous pulse methylprednisolone), the use of other immunosuppressive drugs (chloroquine/hydroxychloroquine, azathiopine, mycophenolate mofetil, and methotrexate), the use of antihypertensive drugs, and lipid-lowering agents did not differ between study cases and controls (Table 3).

Traditional cardiovascular risk factors for CVD

The traditional cardiovascular risk factors were analyzed and found that there was only diabetes mellitus that associated with CVD in study cases [3 (30%) vs. 10 (6.7%) persons, *p*-value = 0.037] from the univariate analysis. The SLE patient with CVD group also had higher frequency of patients with waist circumference more than 90 centimeters in male or more than 80 centimeters in female than the control group [7 (70%) vs. 55 (39%) persons, *p*-value = 0.06] (Table 4).

The results of the multivariate logistic regression analysis were presented in Table 5. The authors found that higher SDI score (adjusted odds ratio (OR) = 1.74, 95% CI = 1.124-2.694, *p*-value = 0.013), increased waist circumference more than 90 centimeters in male or more than 80 centimeters in female (OR = 6.8, 95% CI = 1.2-38.46, *p*-value = 0.031), and the presence of antiphospholipid antibodies (OR = 4.1, 95% CI = 0.96-17.80, *p*-value = 0.057) were

Table 3. The comparison of medications of SLE patients with and without cardiovascular diseases

Variables	Patients with CVD (n = 10)	Patients without CVD (n = 149)	*p*-value
Corticosteroid			
Cumulative dose (mg), median (P_{25}-P_{75})	5,310.0 (3,095.8-22,597.8)	8,947.5 (4,920.0-20,955.0)	0.760
Average dose (mg/day), mean (SD)	13 (8.3)	8.5 (6.0)	0.034
Duration of steroid (days), median (P_{25}-P_{75})	585 (210-1,963)	1,440 (720-2,619)	0.337
History of IV pulse methylprednisolone, n (%)	0 (0)	8 (5.4)	1.000
Immunosuppressive drugs			
Chloroquine or hydroxychloroquine, n (%)	7 (70.0)	114 (76.5)	0.703
Cyclophosphamide, n (%)	4 (40.0)	20 (13.4)	0.045
Mycofenolate mofetil, n (%)	3 (30.0)	32 (21.5)	0.460
Methotrexate, n (%)	1 (10.0)	15 (10.1)	1.000
Azathiopine, n (%)	1 (10.0)	37 (24.8)	0.453
Anti-hypertensive drugs			
ACE-I, n (%)	3 (30.0)	39 (26.2)	0.725
ARB, n (%)	2 (20.0)	22 (14.8)	0.648
Beta-blocker, n (%)	2 (20.0)	15 (10.1)	0.290
Calcium channel blocker, n (%)	4 (40.0)	38 (25.5)	0.458
Diuretics, n (%)	0 (0)	15 (10.1)	0.600
Lipid-lowering agents, n (%)	6 (60.0)	64 (43.0)	0.338

CVD = cardiovascular diseases; SD = standard deviation; IV = intravenous; ACE-I = angiotensin-converting enzyme-inhibitor; ARB = angiotensin receptor blocker

Table 4. The comparison of traditional cardiovascular risk factors of SLE patients with and without cardiovascular diseases

Variables	Patients with CVD (n = 10)	Patients without CVD (n = 149)	*p*-value
Smoking, n (%)	1 (16.7)	5 (4.5)	0.276
BMI (Kg/m^2), mean (SD)	25.36 (6.1)	23.27 (4.5)	0.167
Obesity, n (%)	5 (50.0)	59 (42.1)	0.745
Waist circumference ≥90 cm in male or ≥80 cm in female, n (%)	7 (70.0)	55 (39.3)	0.060
Hypertension, n (%)	8 (80.0)	80 (54.1)	0.187
Impaired fasting glucose, n (%)	2 (20.0)	47 (31.5)	0.725
Diabetes mellitus, n (%)	3 (30.0)	10 (6.7)	0.037
Dyslipidemia, n (%)	8 (80.0)	108 (72.5)	0.730
Metabolic syndrome, n (%)	5 (50.0)	35 (23.5)	0.123
Framingham 10 year risk score, mean (SD)	5.6 (6.2)	5 (6.4)	0.779

CVD = cardiovascular diseases; SD = standard deviation; BMI = body mass index

statistically significant associated with CVD in the SLE patients.

Discussion

SLE patients are associated with an increased risk for CVD and it is a major cause of premature mortality[2,5-11]. Overall, women with SLE have five to ten folds increase in the risk of myocardial infarction[5,8,9,37]; increase the risk of stroke about 15 times than general population[11,38,39]. Approximately 20 to 30% of all SLE deaths are caused by CVD[8,11].

There are several studies examined the prevalence and risk of CVD in the SLE patients in western populations, and several countries in Asia such as in China and Hong Kong. The prevalence of CVD has been reported to vary between 6 and 13%[5,12-15,40-43], is different depending on the duration of observation, the using different criteria in diagnosis of CVD, and varying demographic data of study populations. Our study is the first study to estimate the prevalence and risk factors of CVD in the SLE patients in Thailand. It was done in a tertiary care center. We found that prevalence of CVD in the SLE patients was 6.3%. Our cohort study included 159 SLE patients, the mean age at SLE presentation was 30 years old, and the mean disease duration was 12 years.

Table 5. Factors associated with the occurrence of CVD in SLE patients by multivariate logistic regression model

Variables	Multivariate logistic regression		
	Adjusted OR	95% CI	*p*-value
Antiphospholipid antibodies	4.10	0.96-17.80	0.057
Waist circumference*	6.90	1.20-38.46	0.031
SDI	1.74	1.124-2.694	0.013

CVD = cardiovascular disease; SLE = systemic lupus erythematosus; OR = odds ratio; 95% CI = 95% confidence interval; SDI = systemic lupus international collaborating clinics damage index excluded the score from CVD

Adjusted for malar rash, discoid rash, diabetes mellitus, antiphospholipid syndrome, SDI, *waist circumference ≥90 cm in male or ≥80 cm in female, average dose of corticosteroid, and the use of cyclophosphamide (included only variables with *p*-value <0.1 in the univariate analyses)

The mean age of the first cardiovascular event in the SLE patients in our study was 40 years old, similar to the result of the previous lupus studies ranged from 34 to 59 years old[12,14,40,44,45]. The onset of first CVD in our study was earlier than in Thai general population (the mean age of the first acute myocardial infarction and the first stroke in Thailand were 73 and 66 years old, respectively)[46]. Manzi et al found that women with lupus in the 35- to 44-year age group were over 50 times more likely to have a myocardial infarction than women of similar age in the Framingham Offspring Study (rate ratio = 52.43, 95% CI 21.6-98.5) and had the premature atherosclerosis and expedited to have subsequent CVD about five to six folds higher when compared with age-matched control[5].

The definition of CVD in the present study was adapted from the Framingham Study, Cardiovascular Health Study, and ACC/AHA[16-25] since they have been well-established and practical for clinical practice. Furthermore, the present study also included CHF in definition of CVD because CHF is a commonly found in the SLE patients as a consequence of ischemic heart disease[41,47] and it was also included in the other studies[41,45,47,48]. The most common cardiovascular event in the present study was the cerebrovascular accident or ischemic stroke (50%), followed by myocardial infarction (30%).

Currently, the mechanism of CVD in the SLE patients is controversial. Nonetheless, it is hypothesized that SLE is a chronic inflammatory disease that increases risks of premature atherosclerosis. Traditional, lupus-related factors and inflammation have shown to increase risk of CVD in lupus[42,43]. Traditional cardiovascular risk factors include old age, smoking, obesity, hypertension, hypercholesterolemia, diabetes mellitus, and family history of CVD. Lupus-specific cardiovascular risk factors include disease activity, damage index, disease duration, lupus nephritis, duration of use of GC, auto-antibodies, and the presence of antiphospholipid syndrome. Finally, inflammatory cardiovascular risk factors include C-reactive protein, lipoprotein (a), and homocysteine are known as the associated risk factors for CVD[11,13,40-43,49-54].

From a univariate analysis, there are both traditional risk factors, including diabetes mellitus, waist circumference more than 90 centimeters in male or more than 80 centimeters in female, and lupus-specific risk factors, including SDI score, malar rash, discoid rash, average dose of glucocorticoid, and the history of cyclophosphamide used, are positively associated with CVD. However, the multivariate regression analysis showed that SDI score, waist circumference more than 90 centimeters in male or more than 80 centimeters in female, and the presence of antiphospholipid syndrome are independent risk factors associated with CVD in the SLE patients with statistical significance, although scores from cerebrovascular accident, cardiovascular, and peripheral vascular damage index are excluded.

Ongoing lupus disease activity is also associated with CVD risk[12,54]. Karp et al reported that lupus disease activity (SLEDAI) was independently associated with lower HDL cholesterol levels and higher values of systolic blood pressure[55]. These relations suggest that SLE play roles in several traditional cardiovascular risk factors. We could not retrospectively retrieve disease activity score in all visits, and we only use the disease activity at the time of maximum daily steroid dosage. In the present study, the severity and overall disease activity might be better represented by damage index rather than disease activity (SLEDAI). This could explain lupus disease activity is not a significantly associated with CVD in the study. In contrast, the present study found SDI score was an independent predictive factor for CVD in lupus patients, which was similar to the study of Roman et al[54]. Consistent with the previous studies, there was an association between antiphospholipid syndrome and CVD in SLE patients[40,42,50]. Gustafsson et al found that the presence of any antiphospholipid antibody was a predictive factor of CVD with hazard ratio 4.23[40].

Central obesity rather than overall obesity may contribute to CVD in lupus patients in the present

study. Waist circumference more than 90 centimeters in male or more than 80 centimeters in female is an associated risk factor for CVD in SLE. However, BMI is not associated with CVD. Increased visceral fat has been shown to be an important risk factor for cardiovascular disease and diabetes[56,57]. An indicator of visceral fat, waist circumference is more sensitive tool to detect the distribution of body fat than BMI[58,59] and is a parameter for assessment of central obesity, which is the predictor of the development of atherosclerotic CVD. The 1998 Singapore National Health Survey reported that waist circumference more than 90 centimeters in male or more than 80 centimeters in female is a more appropriate definition of central obesity in Asian population[36]. There is no study demonstrated that BMI was associated with increased CVD risk in lupus patients per se. However, Kiani et al reported that BMI was an important predictor of high coronary calcium scores in lupus patients[60]. This study was the first study demonstrated that central obesity as measured by waist circumference was associated with increased CVD risk. This seems practical for physicians who take care of lupus patients to utilize in routine lupus care.

Several parameters reported as risk factors for CVD in lupus patients were not associated with CVD in the present study. Older age is a well-established risk factor for CVD in both normal population and lupus patients. Many studies reported that older age is associated risk factor of CVD in SLE[13,40,41,54,61] but in the present study found no significant association between age and CVD in lupus patients. This could be because of relative younger age (43 years old) of patients in the present study compared to others (more than 45 years old)[13,40,54]. Similarly, smoking is not associated with increased CVD in our study because of the very small number of smoking patients in the study compared to the others[40,41,61]. We reported that diabetes mellitus was associated only CVD from univariate analyses but not in multivariate analyses. However, several studies identified diabetes mellitus associated with CVD in lupus patients[42,49].

Framingham risk score was not associated with CVD in the present study and others[13,49]. The Framingham risk factors are currently utilized in assessing the traditional risk of CVD for primary prevention purposes and it only accounts for traditional risk factors as such, so the Framingham risk score should not be used alone for primary prevention purposes in lupus patients.

The duration of GC use and disease duration were reported to associate with CVD in many studies[5,41,54], but not in the present study. Comparison with previous studies, the present study had two to three times less disease duration and duration of GC use than disease duration and duration of GC use in those studies. However, the average dose of GC was associated with CVD from univariate analyses but not in multivariate analyses.

There were several limitations of the present study. First, it is retrospective in nature. Patient information was mainly retrieved retrospectively from the patients' medical records; however, most of the relevant factors were recorded. Secondly, inflammatory markers such as C-reactive protein (CRP) or Erythrocyte sedimentation rate (ESR) were not routinely done in the present study. Although CRP was reported to increase 3.356 folds associated with CVD in the LUMINA Study[44]. Third, normal populations were not included to compare with SLE patients in the prevalence of CVD.

In conclusion, CVD is a common and important problem in the SLE patients. Physician should consider, and concern both traditional cardiovascular risk factors and lupus-specific cardiovascular risk factors to decrease, and prevent CVD for lupus patient care in the future. Especially, high SDI score, antiphospholipid syndrome, and waist circumference more than 90 centimeters in male or more than 80 centimeters in female are independent risk factors associated with the occurrence of CVD in lupus patients.

What is already known on this topic?

Premature atherosclerosis is a major comorbid condition in SLE. The overall prevalence of cardiovascular disease in SLE patients has ranged from 6 to 10% in various cohorts. This risk is increased compared with the general population. Traditional cardiac risk, such as age, high blood pressure, and high cholesterol levels and SLE-related factors, such as disease activity, renal involvement, glucocorticoid use, and antiphospholipid antibodies were shown to increased incidence of cardiovascular disease seen in patients with SLE.

What this study add?

The prevalence of cardiovascular disease in Thai SLE patients is 6%, which is comparable to other studies from different countries. This study is the first study demonstrated that central obesity as measured

by waist circumference more than 90 centimeters in male or more than 80 centimeters in female is associated with increased cardiovascular risk in SLE patients. Waist circumference is easy to measure and practical in routine out-patient clinic to identify patients and optimize other modifiable cardiovascular risk factors.

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Potential conflicts of interest

None.

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ระดับการทำลายของโรคลูปัสและรอบเอวเป็นปัจจัยเสี่ยงอิสระต่อการเกิดโรคหัวใจและหลอดเลือดในผู้ป่วยโรคลูปัสจากโรงพยาบาลพระมงกุฎเกล้า

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ภูมิหลัง: *โรคหัวใจและหลอดเลือดเป็นทั้งสาเหตุของอัตราป่วยและอัตราการเสียชีวิตก่อนวัยอันควรในผู้ป่วยโรคลูปัส*
วัตถุประสงค์: *เพื่อศึกษาความชุกของโรคหัวใจและหลอดเลือด และปัจจัยที่สัมพันธ์กับการเกิดโรคหัวใจและหลอดเลือดในผู้ป่วยลูปัสจากโรงพยาบาลพระมงกุฎเกล้า ประเทศไทย*
วัสดุและวิธีการ: *การศึกษาเชิงวิเคราะห์แบบย้อนหลังเพื่อศึกษาหาความชุกของโรคหัวใจและหลอดเลือดในผู้ป่วยโรคลูปัส โดยการทบทวนเวชระเบียนผู้ป่วย นิยามของโรคหัวใจและหลอดเลือดคือ โรคหลอดเลือดหัวใจโคโรนารี ภาวะหัวใจล้มเหลว โรคหลอดเลือดสมอง โรคหลอดเลือดสมองตีบชั่วคราว และโรคหลอดเลือดแดงส่วนปลาย ร่วมกับหาปัจจัยเสี่ยงของการเกิดโรคหัวใจและหลอดเลือดในผู้ป่วยโรคลูปัส โดยใช้การวิเคราะห์ทางสถิติแบบตัวแปรเดียว และการวิเคราะห์การถดถอยแบบพหุตัวแปร*
ผลการศึกษา: *มีผู้ป่วยโรคลูปัส 159 ราย เข้าร่วมการศึกษา พบว่ามีผู้ป่วยหญิงโรคลูปัส 9 ราย และชาย 1 ราย เป็นโรคหัวใจและหลอดเลือด คิดเป็นความชุกร้อยละ 6.3 โดยผู้ป่วยโรคลูปัสที่มีโรคหัวใจและหลอดเลือดมีค่าระดับการทำลายของโรค (p-value = 0.025) และค่าเฉลี่ยขนาดการใช้ยากลูโคคอร์ติคอยด์ (p-value = 0.034) ที่สูงกว่าผู้ป่วยโรคลูปัสที่ไม่มีโรคหัวใจและหลอดเลือด มีผื่นแดงรูปผีเสื้อที่ใบหน้า (p-value = 0.054) ผื่นดีสคอยด์ (p-value = 0.047) ประวัติการใช้ยาไซโคลฟอสฟาไมด์ (p-value = 0.076) โรคเบาหวาน (p-value = 0.037) การตรวจพบแอนติฟอสโฟไลปิดแอนติบอดี (p-value = 0.055) และมีสัดส่วนของคนที่มีรอบเอวที่มากกว่า 90 เซนติเมตร ในผู้ชาย หรือ มากกว่า 80 เซนติเมตร ในผู้หญิง (p-value = 0.06) ที่พบได้บ่อย/สูงกว่าผู้ป่วยโรคลูปัสที่ไม่มีโรคหัวใจและหลอดเลือด การวิเคราะห์การถดถอยแบบพหุตัวแปรพบว่าค่าระดับการทำลายของโรค (odds ratio [OR] = 1.74, 95% confidence interval [CI] 1.12-2.69, p-value = 0.013) และรอบเอวที่มากกว่า 90 เซนติเมตร ในผู้ชาย หรือ มากกว่า 80 เซนติเมตร ในผู้หญิง (OR = 6.9, 95%CI 1.2-38.46, p-value = 0.031) เป็นปัจจัยเสี่ยงอิสระต่อการเกิดโรคหัวใจและหลอดเลือดในผู้ป่วยโรคลูปัส การตรวจพบแอนติฟอสโฟไลปิดแอนติบอดีมีแนวโน้มว่าจะเพิ่มความเสี่ยงต่อการเกิดโรคหัวใจและหลอดเลือดในผู้ป่วยโรคลูปัส (OR = 4.1, 95% CI 0.96-17.8, p-value = 0.057)*
สรุป: *ค่าระดับการทำลายของโรคลูปัส และรอบเอวที่มากกว่า 90 เซนติเมตร ในผู้ชาย หรือ มากกว่า 80 เซนติเมตร ในผู้หญิง เป็นปัจจัยเสี่ยงอิสระที่สัมพันธ์กับการเกิดโรคหัวใจและหลอดเลือดในผู้ป่วยโรคลูปัส*