# Effect of the metabolic syndrome on organ damage and mortality in patients with systemic lupus erythematosus: a longitudinal analysis

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## Abstract

### Objective

*To study the effect of the metabolic syndrome (MetS) on organ damage and mortality in patients with SLE.*

### Methods

*Consecutive patients who fulfilled ≥4 ACR criteria for SLE were assessed for the MetS in October 2010. The MetS was defined by the updated joint consensus criteria, using the Asian criteria for central obesity. Longitudinal data on organ damage and mortality were retrieved. The association between MetS and new damage and mortality was studied by logistic regression.*

### Results

*A total of 577 SLE patients were followed (93% women; age 41.2±13.4 years; SLE duration 9.3±7.2 years) and 85 (14.7%) patients qualified the MetS. After a follow-up of 66.3±1.8 month, new organ damage and vascular events developed in 128(22%) and 23(4.0%) patients, respectively. Thirty-nine (6.8%) patients succumbed. Patients with the MetS, compared to those without, had significantly more SLICC damage score accrual (0.70±1.0 vs. 0.26±0.6; p<0.001), new vascular events (11% vs. 2.8%; p=0.001), all-cause (14% vs. 5.5%; p=0.003) and vascular (7.1% vs. 0.2%; p<0.001) mortality. Logistic regression revealed that the MetS was significantly associated with new damage in the renal (OR 5.48[2.06–14.6]; p=0.001) and endocrine system (OR 38.0[4.50–321]; p=0.001), adjusted for age, sex, SLE duration, ever smoking, antiphospholipid antibodies and the new use of glucocorticoids or hydroxychloroquine since recruitment. Moreover, the presence of the MetS also significantly increased the risk of new vascular events (OR 3.38[1.31–8.74];p=0.01) and vascular mortality (OR 28.3[3.24–247]; p=0.002) after adjustment for the same covariates.*

### Conclusion

*In this longitudinal study, the MetS is significantly associated with new organ damage, vascular events and mortality in patients with SLE.*

**Key words**

damage, systemic lupus erythematosus, metabolic syndrome, mortality, risk factors

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## Introduction

The metabolic syndrome (MetS) is a constellation of traditional atherosclerotic risk factors that comprise abdominal obesity, atherogenic dyslipidaemia, hypertension and insulin resistance (1). The MetS is a strong predictor for type II diabetes mellitus, stroke and cardiovascular diseases (2, 3), although it remains controversial if the syndrome is a better predictor for these conditions than individual risk factors alone (4). Longitudinal studies and meta-analyses have shown that the MetS is associated with an increased risk of subclinical atherosclerosis and its progression, cardiovascular and cerebrovascular events, as well as all-cause and vascular mortality (5-13).

Systemic lupus erythematosus (SLE) is a multi-systemic autoimmune disorder that is associated with a higher prevalence of traditional and non-traditional atherosclerotic risk factors, contributing to accelerated atherosclerosis and higher incidence of atherosclerotic vascular diseases (14). Case-control studies have revealed a significantly higher prevalence of the MetS in patients with SLE than the general population (15-20). In different ethnic groups, the reported prevalence of MetS in SLE patients ranges from 16% to 44% (15-26). The presence of the MetS in SLE is associated with more organ damage (17, 19, 27), increased risk of subclinical atherosclerosis (18, 23, 28) and cardiovascular events (23, 25, 27, 29).

However, most of these previous studies were cross-sectional in design and involved a relatively small number of patients. Moreover, there have not been any published studies on the association of the MetS with mortality in SLE. These have prompted the current study which was designed to evaluate the effect of the MetS on vascular events, organ damage and mortality in a longitudinal cohort of Chinese patients with SLE.

## Patients and methods

*Study population*

Consecutive patients who fulfilled ≥4 ACR criteria for SLE (30) were assessed for the presence of the MetS (see definition below) in a 6-month period starting from October 2010. Patients who did not have full MetS assessment or succumbed before October 2010 were excluded. Blood pressure was measured and fasting blood was taken for the assay of glucose and lipid levels (total cholesterol, HDL and LDL cholesterol and triglyceride). Body weight, body height and waist circumference were also obtained. Waist circumference was measured at a standing posture with relaxation of the abdominal muscles. Restricted clothing around the abdomen was loosened. The uppermost border of the iliac crests on both sides was located and marked. The circumference of the abdomen at this level horizontal to the floor was measured by a tape at the phase of normal expiration.

Longitudinal data of the included patients regarding organ damage and mortality were retrieved from our cohort database. For patients who were lost to follow-up, data were censored at their last clinic visits. Comparison of the outcomes of interest was made between patients with and without the MetS at recruitment. The association of the MetS with new organ damage, vascular events and mortality was studied by logistic regression.

Informed consent was obtained from the participants and the study was approved by the Ethics Committee of our hospital.

*Definition of the MetS*

The MetS was defined by the updated joint consensus criteria proposed by the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the study of Obesity, using the Asian criteria for central obesity (31), when ≥3 of the following components were present: (1) Increased waist circumference to ≥90cm in men or ≥80cm in women; (2) Elevated blood pressure to ≥130/85 mmHg or requiring drug therapy; (3) Elevated serum triglyceride level to ≥1.7 mmol/L; (4) Reduced serum high density lipoprotein (HDL)-cholesterol

to ≤1.0 mmol/L in men and 1.3 mmol/L in women; and (5) Elevated fasting glucose level to ≥5.6 mmol/L.

*Organ damage, vascular events and mortality*

Damage of SLE was measured by the Systemic Lupus International Collaborating Clinics Damage Index (SDI) (32), a validated instrument consisting of 41 items that measure irreversible organ damage (present for ≥6 consecutive months) unrelated to active inflammation in 12 organ systems. New damage scores since the assessment of the MetS were used for statistical analyses.New vascular events in our patients were evaluated and only those with compatible clinical features and ascertainment by appropriate investigations and imaging studies such as magnetic resonance imaging (MRI), computer axial tomography (CAT) and conventional angiographic studies were included for analyses.

For those who succumbed, the main cause of death was judged by reviewing the medical notes documented by their attending specialists according to investigation results and the best clinical interpretation. Reports of autopsies performed for uncertain cause of death, academic interests or medico-legal purpose were also taken into consideration. Both the all-cause mortality and mortality directly contributed by vascular thrombosis (vascular mortality) was studied regarding their relationship with the MetS.

*Statistical analyses*

Unless otherwise stated, values in this study were expressed as mean ± standard deviation (SD). Comparison of continuous variables between two groups was performed by the independent sample Students' *t*-test. Categorical variables were compared by the Chi-square tests. When the frequency was <5, the Fisher's exact test was used. The association between the MetS and new organ damage (in each system), all-cause and vascular mortality was studied by separate logistic regression models, with the outcome variable (dichotomous) being new damage in each organ system, mortality or vascular mortality, and contributing variables being the MetS, age, sex, SLE duration, ever smoking, the presence of the antiphospholipid antibodies (moderate to high titers of the anti-IgG anticardiolipin or the lupus anticoagulant) and the new use of glucocorticoids or hydroxychloroquine (HCQ) since recruitment. The adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Statistical significance was defined as a two-tailed *p*-value of less than 0.05. All statistical analyses were performed using the SPSS program, v. 16.0 for Windows 8.

**Table I.** Clinical characteristics of the patients studied.

| | Metabolic syndrome | | *p* |
|---|---|---|---|
| | Yes (n=85) | No (n=492) | |
| | n (%), mean±SD | | |
| Age, years | 49.0 ± 12.0 | 39.8 ± 13.2 | <0.001 |
| Women | 79 (93) | 459 (93) | 0.91 |
| SLE duration, years | 11.6 ± 8.2 | 8.9 ± 6.9 | 0.005 |
| Arthritis | 57 (67) | 350 (71) | 0.40 |
| Raynaud's phenomenon | 16 (19) | 114 (23) | 0.40 |
| Facial rash | 35 (41) | 237 (48) | 0.25 |
| Discoid rash | 9 (11) | 49 (10) | 0.85 |
| Mucosal ulceration | 7 (8.2) | 72 (15) | 0.12 |
| Photosensitivity | 20 (24) | 141 (29) | 0.34 |
| Haemolytic anaemia | 22 (26) | 95 (19) | 0.17 |
| Leukopenia (<4,000/mm$^3$) | 30 (35) | 182 (37) | 0.74 |
| Thrombocytopenia (<100,000/mm$^3$) | 26 (31) | 110 (22) | 0.11 |
| Lymphadenopathy | 8 (9) | 72 (15) | 0.19 |
| *Neuropsychiatric | 12 (14) | 62 (13) | 0.70 |
| Renal | 55 (65) | 258 (52) | 0.04 |
| Serositis | 16 (19) | 89 (18) | 0.88 |
| Anti-dsDNA | 59 (69) | 351 (71) | 0.72 |
| Anti-Sm | 7 (8.2) | 75 (15) | 0.09 |
| Anti-Ro | 43 (51) | 282 (57) | 0.25 |
| Anti-La | 10 (12) | 96 (20) | 0.09 |
| Anti-nRNP | 23 (27) | 137 (28) | 0.88 |

SD: standard deviation; SLE: systemic lupus erythematosus.
*included psychosis, seizure, acute confusional state, myelopathy, peripheral and cranial neuropathy, mononeuritis multiplex, optic neuritis, myasthenia gravis and movement disorders.

## Results

*Characteristics of the studied population*

A total of 577 SLE patients (93% women) were included. All patients are ethnic southern Chinese. The age at the time of MetS assessment was 41.2±13.4 years and the mean duration of SLE was 9.3±7.2 years. The mean body mass index (BMI) of the patients was 22.3±3.9kg/m$^2$ (11% patients had BMI >27kg/m$^2$). A total of 85 (14.7%) patients qualified the MetS (28% fulfilling waist; 20% fulfilling blood pressure; 25% fulfilling triglyceride; 33% fulfilling HDL and 9.2% fulfilling glucose criteria). Table I shows the cumulative clinical manifestations of the participants. Patients with the MetS were significantly older (49.0±12.0 *vs*. 39.8±13.2 years; $p<0.001$) and had longer duration of SLE (11.6±8.2 *vs*. 8.9±6.9 years; $p=0.005$) when compared to those without the MetS. The prevalence of renal disease was also significantly more frequent in the MetS patients (65% *vs*. 52%; $p=0.04$). However, the frequencies of other manifestations and autoantibodies were similar between the two groups.

Table II shows the vascular risk factors and immunosuppressive therapies ever received by the participants at the time of MetS assessment. As expected, the body mass index (BMI), waist circumference, serum levels of cholesterol (total, LDL), triglyceride and glucose were significantly higher in patients with the MetS than those without. HDL cholesterol level was also significantly lower in the MetS patients but there were fewer smokers in this group. On the other hand, patients with the MetS were more likely to have received the

**Table II.** Vascular risk factors and immunosuppressive therapies of the patients studied.

| | Metabolic syndrome | | *p* |
|---|---|---|---|
| | Yes (n=85) | No (n=492) | |
| *Vascular risk factors* | N (%), mean ± SD | | |
| Total cholesterol, mmol/L | 5.79 ± 1.97 | 5.11 ± 1.74 | 0.004 |
| LDL cholesterol, mmol/L | 3.52 ± 1.65 | 2.99 ± 1.40 | 0.007 |
| HDL cholesterol, mmol/L | 1.21 ± 0.41 | 1.56 ± 0.43 | <0.001 |
| Triglyceride, mmol/L | 2.34 ± 0.83 | 1.24 ± 0.67 | <0.001 |
| Fasting glucose, mmol/L | 5.89 ± 1.94 | 4.66 ± 0.60 | <0.001 |
| Body mass index, kg/m$^2$ | 25.4 ± 4.90 | 21.7 ± 3.40 | <0.001 |
| Waist circumference, cm | 88.3 ± 9.70 | 75.3 ± 9.20 | <0.001 |
| Ever smoking | 6 (7.1) | 76 (15) | 0.04 |
| *aPL antibodies | 25 (29) | 160 (33) | 0.57 |
| *Immunosuppressive treatment ever received* | | | |
| Prednisolone | 73 (86) | 401 (82) | 0.33 |
| Hydroxychloroquine | 46 (54) | 321 (65) | 0.03 |
| Cyclophosphamide | 25 (29) | 125 (25) | 0.44 |
| Mycophenolate mofetil | 20 (24) | 101 (21) | 0.53 |
| Azathioprine | 57 (67) | 299 (61) | 0.27 |
| Cyclosporine or tacrolimus | 28 (33) | 110 (22) | 0.04 |

SD: standard deviation. *moderate to high titers of IgG anti-cardiolipin or the lupus anticoagulant.

**Table III.** Causes of death of the SLE patients studied.

| | Metabolic syndrome | | | |
|---|---|---|---|---|
| | Yes (n=12) | No (n=27) | Total (n=39) | *p* |
| *Causes of death* | N (%) | | | |
| Infection | 5 (42) | 9 (33) | 14 (36) | 0.72 |
| Cerebrovascular accident | 2 (17) | 0 (0) | 2 (5.1) | 0.09 |
| *Cardiovascular events | 3 (25) | 2 (7.4) | 5 (13) | 0.16 |
| Pulmonary hypertension | 0 (0) | 3 (11) | 3 (7.7) | 0.54 |
| Interstitial lung disease | 0 (0) | 3 (11) | 3 (7.7) | 0.54 |
| Cancer | 1 (8.3) | 5 (19) | 6 (15) | 0.65 |
| Suicide | 0 (0) | 1 (3.7) | 1 (2.6) | 1.00 |
| Sudden death / unknown cause | 1 (8.3) | 3 (11) | 4 (10) | 1.00 |
| Others | 0 (0) | 1 (3.7) | 1 (2.6) | 1.00 |

*included myocardial infarction, ischemic cardiomyopathy and aortic dissection.

calcineurin inhibitors ($p$=0.04) but less likely to have received HCQ treatment ($p$=0.03).

*New organ damage and mortality*

Our patients were observed for a mean of 66.3±1.8 months since the assessment of the MetS. Thirty-nine (6.8%) patients were lost to follow-up. New organ damage developed in 130 (22.5%) patients. Twenty-four new vascular events developed in 23 (4.0%) patients, with the most common being cerebrovascular accidents (50%), followed by acute coronary syndrome (33%) and peripheral vascular disease (17%). Patients with the MetS had significantly higher incidence of new acute coronary events than those without the MetS (5.8% *vs*. 0.6%; $p$=0.002). Thirty-nine (6.8%) patients succumbed on follow-up and Table III shows the causes of death of these patients. Infection was the most common cause of death (36%), followed by vascular complications (18%), cancer (15%), pulmonary hypertension (8%), pulmonary fibrosis (8%) and suicide (3%).

Table IV compares the incidence of new organ damage, vascular events, mortality and mortality due to vascular causes between the two groups of patients. Patients with the MetS, when compared to those without, had significantly more SDI accrual at their last clinic visits (0.70±1.0 *vs*. 0.26±0.6; $p$<0.001). Regarding individual systems, new damage scores in the ocular, renal, cardiovascular, musculoskeletal and endocrine (diabetes mellitus) systems were significantly more common in the MetS group of patients. Moreover, new vascular events (11% *vs*. 2.8%; $p$=0.001), all-cause mortality (14% *vs*. 5.5%; p=0.003) and vascular mortality (7.1% *vs*. 0.2%; $p$<0.001) were also significantly more common in patients with MetS than those without.

*Association of the MetS with organ damage and mortality*

Table V shows the logistic regression analysis of the risk of new damage, vascular events and mortality in patients with MetS compared to those without. The presence of the MetS was significantly associated with new damage in the renal (OR 5.48[2.06–14.6]; $p$=0.001) and endocrine system (OR 38.0[4.50–321]; $p$=0.001), adjusted for age, sex, SLE duration, ever smoking, the presence of the antiphospholipid antibodies (IgG-anticardiolipin or the lupus anticoagulant) and new use of glucocorticoids or HCQ since recruitment. The MetS also increased the risk of new vascular events (OR 3.38[1.31–8.74]; $p$=0.01), all-cause mortality (OR 1.90[0.85–4.24]; $p$=0.12) and vascular mortality (OR 28.3[3.24–247]; $p$=0.002) after adjustment for the same covariates.

Separate logistic regression analyses were performed for the contribution of individual components of the MetS (increased waist circumference, elevated blood pressure, elevated triglyceride, reduced HDL cholesterol or elevated fasting glucose) to new vascular events and vascular mortality in our cohort of SLE patients (data not shown). Of the five MetS criteria, only elevated blood pressure (OR 3.79[1.46–9.84]; $p$=0.006) and fasting glucose (OR 6.24[2.36–16.5]; $p$<0.001) were significantly associated with the occurrence of new vascular events. The same components of the MetS, namely elevated blood pressure (OR 21.8[2.39–198]; $p$=0.006) and fasting glucose (OR 5.68[1.12–28.9]; $p$=0.04), were also significantly associated with new vascular deaths.

## Discussion

This is a retrospective analysis of the longitudinal data derived from a large cohort of Chinese SLE patients on the

**Table IV.** New organ damage and mortality in the SLE patients studied.

| | Metabolic syndrome | | *p* |
|---|---|---|---|
| | Yes (n=85) | No (n=492) | |
| | Number (%); mean ± SD | | |
| New damage | | | |
| Ocular | 8 (9.4) | 12 (2.4) | 0.001 |
| Neuropsychiatric | 5 (5.9) | 15 (3.0) | 0.19 |
| Renal | 9 (11) | 16 (3.3) | 0.002 |
| Pulmonary | 3 (3.5) | 12 (2.4) | 0.47 |
| Cardiovascular | 5 (5.9) | 6 (1.2) | 0.01 |
| Peripheral vascular | 0 (0) | 6 (1.2) | 0.60 |
| Gastrointestinal | 1 (1.2) | 0 (0) | 0.15 |
| Musculoskeletal | 7 (8.2) | 17 (3.5) | 0.04 |
| Dermatological | 0 (0) | 8 (1.6) | 0.61 |
| Gonadal | 1 (1.2) | 4 (0.8) | 0.55 |
| Endocrine | 8 (9.4) | 1 (0.2) | <0.001 |
| Malignancy | 3 (3.5) | 14 (2.8) | 0.73 |
| Any system | 41 (48) | 89 (18) | <0.001 |
| Increase in SDI scores | 0.74 ± 1.0 | 0.26 ± 0.6 | <0.001 |
| New vascular events | 9 (11) | 14 (2.8) | 0.001 |
| Death | 12 (14) | 27 (5.5) | 0.003 |
| Vascular death | 6 (7.1) | 1 (0.2) | <0.001 |

SLE: systemic lupus erythematosus; SD: standard deviation; SDI: SLE damage index.

**Table V.** Effect of the metabolic syndrome on new damage and mortality (logistic regression).

| | *Adjusted odds ratio (95% CI) | *p* |
|---|---|---|
| New damage | | |
| Ocular | 2.60 (0.97-6.95) | 0.06 |
| Neuropsychiatric | 1.55 (0.52-4.64) | 0.44 |
| Renal | 5.48 (2.06-14.6) | 0.001 |
| Pulmonary | 0.91 (0.22-3.72) | 0.90 |
| Cardiovascular | 3.57 (0.99-12.9) | 0.05 |
| Peripheral vascular | - | - |
| Gastrointestinal | - | - |
| Musculoskeletal | 2.31 (0.88-6.06) | 0.09 |
| Dermatological | - | - |
| Gonadal | 2.26 (0.21-24.6) | 0.50 |
| Endocrine | 38.0 (4.50-321) | 0.001 |
| Malignancy | 0.67 (0.17-2.58) | 0.56 |
| Any system | 3.58 (2.14-5.98) | <0.001 |
| New vascular events | 3.38 (1.31-8.74) | 0.01 |
| New mortality | 1.90 (0.85-4.24) | 0.12 |
| New vascular mortality | 28.3 (3.24-247) | 0.002 |

CI: confidence interval. *adjusted for age, sex, SLE duration, ever smoking, antiphospholipid antibodies (IgG anticardiolipin or the lupus anticoagulant) and new use of glucocorticoids or hydroxychloroquine since recruitment. The odds ratios of the peripheral vascular, gastrointestinal and dermatological systems could not be calculated because of zero new damage in one of the groups.

association between the MetS and the development of vascular complications, organ damage and mortality. The MetS was present in 14.7% of our patients at baseline and was associated with older age, longer SLE duration and renal involvement. Patients with the MetS were more likely to have received the calcineurin inhibitors but less likely to be ever treated with HCQ. After a mean follow-up of 66 months, the MetS was significantly and independently associated with an increased incidence of new vascular events, as well as mortality due to vascular causes. Moreover, the MetS was significantly associated with new renal and endocrine damage in our SLE patients. Although there have been quite a number of previous studies on the clinical associations of MetS in patients with SLE (15-26), most were not powered to study its relationship with cardiovascular events. Some studies reported an increase in SLICC damage scores in the presence of the MetS (17, 19, 27) but they did not separately analyse the relationship between atherosclerosis related cardiovascular, cerebrovascular or peripheral vascular damage with the MetS. Although the MetS was associated with an increased risk of arterial thrombosis in the current study, this was mainly contributed by acute coronary events. There was no significant association between the MetS and cerebrovascular/peripheral vascular events in our patients. On the other hand, vascular mortality was tremendously increased in our patients with the MetS, suggesting that vascular events in MetS patients were more serious and associated with more complications.

In addition to its immunomodulating properties, HCQ is reported to exhibit anti-thrombotic, lipid and glucose lowering effects (33). Recent cohort studies of patients with SLE or lupus nephritis have shown that the use of HCQ is associated with retardation of renal damage (34, 35) and lower mortality on multivariate analyses (36,37). Our results demonstrated that patients with the MetS were significantly less likely to have received HCQ than those without the MetS at baseline assessment. This is consistent with a recent cross-sectional study of 103 premenopausal SLE patients that also reported a significant negative association between chloroquine use and the MetS (38). Both studies have provided indirect evidence for a protective effect of the antimalarials on the prevalence of MetS in patients with SLE, probably through the alleviation of hyperlipidaemia and hyperglycaemia. On the contrary, our study demonstrated that MetS-SLE patients were more likely to have been treated with the calcineurin inhibitors. This negative effect of the calcineurin inhibitors on the prevalence of the MetS might possibly be mediated by their deleterious effects on glucose metabolism, lipids and blood pressure.

Very few longitudinal studies have attempted to determine the effect of the MetS on the risk of arterial thrombosis in SLE. One observational study of

238 premenopausal SLE patients from 2001 to 2008 reported that the cumulative incidence of cardiovascular disease was significantly higher in the group of the MetS than those without (17.3% *vs*. 7.0%), and MetS was an independent predictor of new cardiovascular disease (odd ratio 2.48) (29). This is in accordance with our study in which the odds ratio of having new vascular events in patients with the MetS was 3.38. In a more recent multicentre inception cohort study of SLE patients from different ethnic groups, it was demonstrated that previous MetS, SLICC damage scores (≥1) at baseline, active renal disease and more intense corticosteroid treatment were significantly associated with the development of MetS two years after study entry (39). Although longer-term prospective data regarding the effect of the MetS on organ damage and mortality are not yet available from this cohort, this is in line with our results that the presence of the MetS at recruitment was associated with poorer outcome after 5 years, such as new renal (*i.e*. chronic kidney disease [CKD] stage 3 or above) and endocrine (exclusively diabetes mellitus) damage.

The association between MetS and CKD has been increasing recognised, although it is hard to differentiate between the cause and effect of these two conditions. A recent meta-analysis of eleven studies, many of which had excluded patients with known diabetes mellitus, showed that the MetS was significantly associated with the development of CKD (≥stage 3) over time (40). The strength of this association appeared to increase with the number of MetS components. Another cohort study in the US reported a 1.6-fold increase in the risk of CKD in participants having the MetS compared to those without over 21 years (41). Although further studies are clearly needed to confirm this association, postulated mechanisms of MetS-related kidney injuries include hyperuricaemia, increased pro-inflammatory cytokines such as leptin, IL-6 and TNF-α and oxidative stress, increased microvascular injury and ischaemic injury through the angiotensin system, and the increase in connective tissue growth and fibrosis factors such as TGF, leading to accelerated glomerulosclerosis (42).

There are several limitations of our study. First, only around 80% of our SLE patients in the out-patient clinics were assessed for the MetS. Sampling error is bound to occur and the prevalence rate of the MetS might have been underestimated. However, attrition bias is inevitable even in multicentre inception cohort studies (39) as participation of patients from each centre is voluntary and does not include all the SLE patients in their respective units. Second, our cohort of patients consists exclusively of southern Chinese patients. The clinical associations observed with the MetS may not be extrapolated to other ethnic groups, given the difference in life style and the prevalence of traditional risk factors in different geographical areas. Finally, data on the cumulative or mean disease activity score over time were unavailable and the change in the vascular risk factors with time was not taken into this account in the current study.

The positive association between the MetS and coronary arterial events, organ damage and increased vascular mortality in our study suggests that active intervention of the MetS by pharmacological and non-pharmacological means is a logical approach in patients with SLE in order to ameliorate morbidity and mortality. Further observational and randomised controlled studies are needed to confirm the benefits of MetS intervention in SLE patients. Finally, as HCQ is associated with a reduced prevalence of the MetS, its routine use might also help reduce the risk of vascular complications and organ damage in patients with SLE.

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