Associated Variables of Myositis in Systemic Lupus Erythematosus: A Cross-Sectional Study

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Background: This study aimed to estimate the point prevalence of myositis and identify associated variables of myositis in systemic lupus erythematosus (SLE).

Material/Methods: Clinical date of patients hospitalized with lupus at the First Affiliated Hospital of Anhui Medical University and Anhui Provincial Hospital were collected. Patients were defined as having myositis if they reported the presence of persistent invalidating muscular weakness combined with increased levels of creatine phosphokinase (CPK) and abnormal electromyography (EMG).

Results: The study sample comprised 1701 lupus patients, of which 44 had myositis. Patients with SLE-associated myositis are more likely to have skin rash, alopecia, pericarditis, vasculitis, anti-Sm, anti-RNP, anti-dsDNA, thrombocytopenia, leukopenia, low C3, low C4, high erythrocyte sedimentation rate (ESR), high D-dimer, and active disease. Multivariate logistic regression found positive associations between leukopenia, alopecia, and active disease with myositis. Negative associations between myositis with the use of corticosteroids or immunosuppressive drugs were revealed in univariate and multivariate analysis.

Conclusions: The point prevalence of myositis was 2.6% in SLE patients. The significant association of alopecia, leukopenia, and active disease with myositis suggests that organ damage, hematological abnormality, and high disease activity promote the progression of myositis in lupus patients.

MeSH Keywords: Lupus Erythematosus, Systemic • Myositis • Prevalence • Risk Factors

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Background

Systemic lupus erythematosus (SLE) is a severe autoimmune disease, with multi-organ involvement and diverse clinical manifestations such as lupus nephritis, lupus encephalopathy, and thrombocytopenia [1]. Though not an American College of Rheumatology (ACR) criterion, myositis has traditionally been recognized as a feature in SLE and is considered to be a heterogeneous condition, sometimes less severe than, but sometimes similar to or even worse than, the primary disease [2–4].

In contrast to myalgia, which can affect nearly half of patients with SLE, true myositis is relatively rare and failure to identify these genuine cases probably explains the ill-deserved reputation of lupus myositis. The prevalence of myositis in SLE patients varies widely worldwide. In an African study, the prevalence was 3.4% [2], while in Europe and America the prevalence varies from 4% to 16% [4–10]. The wide variability in the prevalence rates reflects the varying definitions of myositis, the different diagnostic approaches, patient selection criteria, and number of patients involved. Though this condition is not common in SLE patients, myositis usually correlates with SLE activity and patient survival [4]. Thus, the importance of SLE-associated myositis should not be ignored.

The non-specific nature of symptoms such as muscle pain, tenderness, and wasting related to myositis could result in a delay in the diagnosis of myositis in SLE patients [2,11]. This indicates a need for appropriate screening methods to detect myositis. In our study, we investigated the prevalence and associated variables of myositis in lupus patients. We believe the results of this study will provide valuable guidance for the prevention and management of this specific problem, as some of the clinical manifestations and laboratory findings of SLE provide helpful clues for earlier diagnosis of myositis.

Material and Methods

Patient recruitment

The protocol for our study was consistent with the provisions of the World Medical Association Declaration of Helsinki, and informed consent was obtained from each subject before enrolment. This study was conducted with the approval of the Ethics Committee of Anhui Medical University. Clinical date of patients hospitalized with lupus at the First Affiliated Hospital of Anhui Medical University and Anhui Provincial Hospital were collected. All patients fulfilled at least 4 of the revised 1997 ACR classification criteria of SLE [12]. Collection of data was carried out from January 2011 to December 2015.

Myositis

Patients were defined as having myositis if they reported the presence of persistent invalidating muscular weakness (of proximal and/or distal mass muscles from upper and lower limbs) combined with increased levels of creatine phosphokinase (CPK) (CPK normal value 60–190 UI/l) and abnormal electromyography (EMG) (electrical irritability, decrease in the mean duration of motor unit potentials or increase in the percentage of polyphasic motor unit potentials, and rapid firing of the motor unit potentials in relation to the level of activity) at the time of recruitment. Patients with myocardial ischemia at the time of recruitment, which can affect muscle enzyme levels, were excluded. Patients with surgery, trauma, pregnancy, or cancer at the time of recruitment, which might cause musculoskeletal damage, were also excluded. With these criteria, a final sample of 1701 Chinese SLE patients were included in the analyses.

Clinical manifestations and laboratory abnormalities

Clinical manifestations, including lupus nephritis, skin rash, alopecia, oral ulcers, neuropsychiatric symptoms, arthritis, pleuritis, pericarditis, fever (≥38°C), and vasculitis, as well as laboratory abnormalities, including thrombocytopenia ($<100 \times 10^9$/L), leukopenia ($<4.0 \times 10^9$/L), autoantibodies, low C3 (<0.85 mg/mL), low C4 (<0.12 mg/mL), high erythrocyte sedimentation rate (ESR) (>20 mm/h), high D-dimer (>0.5 ug/mL), and high fibrinogen (>4.0 mg/ml), were presented at the time of recruitment or within 10 days.

Lupus activity, drug use, arterial and venous diseases, hypertension, diabetes mellitus, hypercholesterolemia, and pulmonary arterial hypertension (PAH)

SLE disease activity was evaluated by SLE Disease Activity Index (SLEDAI) score [13]. SLEDAI score was calculated based on the clinical manifestations and laboratory abnormalities of SLE patients that presented at the time of recruitment or within 10 days. Active lupus disease was defined as SLEDAI score ≥8. Data on use of corticosteroids or immunosuppressive drugs (use in the past month or not) were collected by medical record review. Vascular events were objectively identified: (1) Ischemic heart disease; (2) Ischemic cerebrovascular disease; (3) Ischemic peripheral vascular disease; (4) Deep vein thrombosis; and (5) Pulmonary embolism. For 'any arterial event', we refer to the occurrence of 1 or more of events 1–3; for 'any venous event', we refer to the occurrence of 1 or more of events 4–5 [14]. Hypertension was considered to be present if blood pressure was ≥140 mm Hg (systolic) or ≥90 mm Hg (diastolic) on repeated measurements, or if the patient had been taking antihypertensive medication. Diabetes mellitus was considered to be present if fasting plasma glucose was >7.0 mmoles/liter, or if the patient was currently receiving anti-diabetic therapy. Hypercholesterolemia was considered to be present if a physician recorded the diagnosis in

Table 1. Comparison of demographic data between systemic lupus erythematosus patients with myositis and without myositis.

Variables	Non-myositis (n=1657)	Myositis (n=44)	p Value*
Age, median (interquartile range), years	37.0 (26.0–47.0)	29.5 (22.0–42.8)	**0.032**
Sex, female, n (%)	1516 (91)	38 (86)	0.356
Disease duration, median (interquartile range), years	2 (0–7)	0 (0–1)	**<0.001**

* Values in bold are statistically significant at p<0.05.

Table 2. Comparison of clinical manifestations between systemic lupus erythematosus patients with myositis and without myositis.

Variables	Non-myositis (n=1657)	Myositis (n=44)	p Value*
Lupus nephritis, n (%)	771 (47)	25 (57)	0.177
Skin rash, n (%)	603 (36)	23 (52)	**0.031**
Alopecia, n (%)	145 (9)	12 (27)	**<0.001**
Oral ulcers, n (%)	125 (8)	5 (11)	0.513
Neuropsychiatric manifestations, n (%)	130 (8)	5 (11)	0.569
Arthritis, n (%)	244 (15)	7 (16)	0.827
Pleuritis, n (%)	230 (14)	7 (16)	0.701
Pericarditis, n (%)	156 (9)	10 (23)	**0.007**
Vasculitis, n (%)	155 (6)	12 (27)	**<0.001**
Fever (≥38°C), n (%)	214 (13)	9 (20)	0.144

* Values in bold are statistically significant at p<0.05.

the medical record, the patient had ever been prescribed lipid-lowering medication, or the fasting plasma cholesterol level measured was >200 mg/dl. PAH was diagnosed by transthoracic echocardiography (TTE); the criterion is pulmonary arterial systolic pressure (PASP) of >30 mmH at rest.

Statistical analysis

Continuous variables were summarized as median (interquartile range) and categorical variables as frequency (percentage). Comparison of each variable between different groups was evaluated using the nonparametric Mann-Whitney U test or chi-square test/Fisher's exact test. Variables with statistical significance were evaluated by logistic regression analysis; results are presented as odds ratio (OR) along with their 95% confidence intervals. All tests were performed on SPSS 20.0.

Results

Patients

We studied 1701 patients with SLE, of which 1554 (91.4%) were female. The median (interquartile range) age was 36.0

(25.5–47.0) years. Forty-four SLE patients in our research had myositis and the prevalence was 2.6%. As shown in Table 1, myositis is more typically observed in younger SLE patients (p=0.032) and in SLE patients with shorter disease duration (p<0.001). There was no difference was in sex distribution between the 2 groups.

Clinical characteristics

Skin rash, alopecia, pericarditis, and vasculitis were significantly associated with myositis (all p<0.050). The incidence of other clinical characteristics was similar between the patients with myositis and those without myositis (Table 2).

Hematologic changes

The presence of anti-Sm, anti-RNP, anti-dsDNA, thrombocytopenia, leukopenia, low C3, low C4, high ESR, and high D-dimer were elevated in the group with myositis (all p<0.050). Rates of fibrinogen and other autoantibodies were comparable between the patients with myositis and those without myositis (Table 3).

Table 3. Comparison of laboratory data between systemic lupus erythematosus patients with myositis and without myositis*.

Variables	Non-myositis (n=1657)		Myositis (n=44)		p Value*
Anti-Sm, n (%)	523	(32)	25	(57)	**<0.001**
Anti-SSA/Ro, n (%)	988	(60)	31	(70)	0.148
Anti-SSB/La, n (%)	213	(13)	7	(16)	0.551
Anti-RNP, n (%)	469	(28)	20	(45)	**0.013**
Anti-Rib P, n (%)	359	(22)	12	(27)	0.374
Anti-dsDNA, n (%)	661	(40)	26	(59)	**0.010**
Thrombocytopenia, n (%)	368	(22)	17	(39)	**0.010**
Leukopenia, n (%)	487	(29)	24	(55)	**<0.001**
Low complement C3, n (%)	1114	(67)	39	(89)	**0.003**
Low complement C4, n (%)	809	(49)	35	(80)	**<0.001**
High ESR, n (%)	1182	(71)	38	(86)	**0.029**
High D-dimer, n (%)	1257	(76)	42	(95)	**0.003**
High fibrinogen, n (%)	592	(36)	11	(25)	0.142

* All laboratory abnormalities were presented at the time of recruitment or within 10 days. Of the 44 SLE patients with myositis, 18 received drug treatment in the past month; and of the 1657 SLE patients without myositis, 1100 received drug treatment in the past month; ** values in bold are statistically significant at p<0.05. anti-Sm – anti-Smith; anti-RNP – anti-ribonucleoprotein; anti-Rib P – anti-ribosomal RNP; anti-dsDNA – anti-double-stranded DNA; ESR – high erythrocyte sedimentation rate.

Table 4. Comparison of disease activity, drug use, arterial and venous diseases, hypertension, diabetes mellitus, hypercholesterolemia and PAH between systemic lupus erythematosus patients with myositis and without myositis.

Variables	Non-myositis (n=1657)		Myositis (n=44)		p Value*
Active lupus disease, n (%)	934	(56)	40	(91)	**<0.001**
Drug use, n (%)	1100	(66)	18	(41)	**<0.001**
Arterial diseases, n (%)	23	(1)	1	(2)	0.469
Venous diseases, n (%)	9	(1)	0	(0)	1.000
Hypertension, n (%)	578	(35)	10	(23)	0.094
Diabetes mellitus, n (%)	290	(18)	9	(20)	0.612
Hypercholesterolemia, n (%)	50	(3)	0	(0)	0.473
PAH, n (%)	124	(7)	5	(11)	0.502

* Values in bold are statistically significant at p<0.05. PAH – pulmonary arterial hypertension.

Lupus activity, drug use, arterial and venous diseases, hypertension, diabetes mellitus, hypercholesterolemia, and PAH

The incidence of active lupus disease was significantly higher in the patients with myositis (*p*<0.001) and the rate of drug use was significantly lower (*p*<0.001). The presence of arterial, venous diseases, hypertension, diabetes mellitus, hypercholesterolemia, and PAH were also compared between patients with myositis and without myositis; the results indicate the differences were not significant (Table 4).

Independent associated variables for myositis in lupus patients

Logistic regression modeling demonstrated that the presence of leukopenia (OR=2.038), alopecia (OR=2.794), and active lupus disease (OR=5.612) were independently associated with

Table 5. Multivariable logistic analysis on risk factors of myositis in patients with systemic lupus erythematosus.

Variables	*p* Value	OR	95% CI
Leukopenia	0.024	2.038	1.097–3.783
Alopecia	0.004	2.794	1.386–5.634
Active lupus disease	0.001	5.612	1.970–15.983
Drug use	0.016	0.466	0.250–0.869

OR – odds ratio; CI – confidence intervals.

lupus-associated myositis. In contrast, drug use acted as a protective factor in the development of myositis (OR=0.466, *p*=0.016) (Table 5).

Discussion

The association of myositis and SLE has been previously explored by several authors [2,15], showing that muscle involvement in SLE patients in the form of diffuse pain or muscular weakness is relatively frequent. A study reported that of 7 SLE patients with myositis, 3 had muscle weakness [15]. Another study of 6 patients who developed overlap syndrome of systemic lupus erythematosus and myositis reported that all patients had symmetrical muscle weakness (proximal muscle weakness in 6 cases and distal muscle weakness in 2 cases) [2]. Similarly, in the present study, the predominant muscular symptoms in the SLE patients with myositis were weakness rather that myalgia; none of the SLE patients with myositis showed dysphagia, dropped head, or symptoms related to a possible muscular involvement of the respiratory system. On the other hand, various histopathological changes have been previously described in the muscles of patients with SLE, including inflammation (myositis), vasculitis, type II fiber atrophy, vessel wall thickening, vacuolar myopathy, neurogenic muscular atrophy, and, rarely, inclusion bodies [2,4,15]. In line with these findings, the results of muscle biopsy in the present study indicated that inflammation and necrosis were the most common symptoms in the patients with overlap syndrome of SLE and myositis. In addition, less than half of patients showed fibrosis. However, there was no evidence of vasculitis and neuropathy on muscle biopsy.

The present study found that myositis is uncommon in lupus patients, with a frequency of 2.6%. This rate was at the lower end of the range of prevalence rates reported from previous studies [2,4–10]. One explanation for the difference may be that all patients recruited in our study were from our Department of Rheumatology. Indeed, some SLE patients, especially those with myositis, have been hospitalized in the Department of Neurology. However, the development of myositis in these patients may not be due to lupus. Thus, the current research is more precise than past research.

As expected from previous studies [4], myositis is more common in younger SLE patients and in those with shorter disease duration. There are several potential explanations for this discrepancy. First, the younger SLE patients and/or those with shorter disease duration may have had more active disease, resulting in the development of myositis. Supporting this, in the present study, age and disease duration of SLE patients were negatively associated with SLEDAI scores; moreover, the incidence of active lupus disease was significantly higher in the patients with myositis than in the patients without this feature. Second, it is also possible that the younger SLE patients and/or those with shorter disease duration tended to have more frequent measurements, especially for those with active disease. Therefore, myositis might be more likely to be detected and diagnosed in these patients.

The criterion standard for defining myositis is EMG testing [11]. However, this invasive and painful procedure not routinely used in clinical practice. So, at best, identifying risk factors for the development of myositis in SLE may have important implications for the detection and management of this interesting condition.

In the present study, logistic regression analysis revealed that alopecia, leukopenia, and active lupus disease were positively associated with myositis. The use of corticosteroids or immunosuppressive drugs was negatively associated with myositis. An association between alopecia and myositis in SLE has been widely reported in the literature [4,16–18]. For instance, a study [4] reviewed the notes on 10 patients with overlap of myositis and SLE and compared their features with 290 patients with SLE without myositis, showing that patients with SLE associated with myositis were more likely to have alopecia. Further, alopecia is usually a reflection of myositis activity. Several studies have shown that after receiving immunosuppressive agents, the hair of myositis patients with alopecia regrew, which coincided with increasing muscle strength [17,18]. These data resonate with our conclusions. In addition, previous studies have reported that patients with SLE-associated myositis were more likely to have other mucocutaneous damage, such as oral ulcers [4,16]. However, these results were not observed in our study. This discrepancy may be due to ethnic or environmental differences between populations.

We proved that leukopenia was an independent risk factor. Although the associations between hematological indices with SLE-associated myositis have been reported in several studies [2–4], this is the first study to reveal that leukopenia was associated with the development of myositis. Future longitudinal investigations are required to determine the exact mechanism of leukopenia in the pathogenesis of SLE-associated myositis.

In this study, we revealed that lupus patients with myositis are more likely to have disease flare-ups. We also found that use of corticosteroids or immunosuppressive drugs plays a protective role against the development of SLE-associated myositis, in agreement with previous studies of patients with only myositis [17,18]. However, the protective mechanism of drugs in SLE-associated myositis, either through reducing disease activity or through relieving musculoskeletal pathophysiological change, is not completely understood.

The treatments used are basically the same, as many of the treatments used for myositis are applied to autoimmune diseases, including SLE. Corticosteroids were usually used as a first-line therapy. Most SLE patients with myositis seem to respond to corticosteroids at least to some degree and for a period of time. For instance, Maazoun et al. [2] reported that all of their patients with overlap syndrome of systemic lupus erythematosus and myositis had been treated with oral prednisone for 6 weeks, after which the dose was gradually tapered. Over a mean follow-up of 6 years, all patients had full remission of myositis. In the event of either poor response or adverse effects of corticosteroids, a second line of treatment with immunosuppressant may be required. Hashimoto et al. [19] reported that 2 SLE patients with steroid-resistant myositis were successfully treated with methotrexate (MTX); in both cases, steroid-resistant myositis was the main common finding, and this symptom was reduced within a few days, either by 7.5 mg or 5 mg MTX per week. In the present study, all of the 18 SLE patients with myositis who were treated with drugs had received corticosteroid therapy (usually as the initial treatment). If necessary, various immunosuppressants were used. Patients with lupus myositis were more likely to receive methotrexate treatment (often for a simultaneous flare-up of the myositis and their SLE), while cyclophosphamides were only given to those with lupus nephritis. Collectively, these data support treatment of SLE-associated myositis using a corticosteroid such as prednisone, which is then increased or tapered slowly based on the response. For patients who respond poorly to corticosteroids, additional immunosuppressants, such as methotrexate, may be necessary. However, the design of the present study may have introduced bias. Specifically, much of the clinical and laboratory data had to be collected retrospectively,

and consequently there were no follow-up data. Therefore, evidence-based data with long-term follow-up that assess the efficacy of corticosteroids and/or immunosuppressants in patients with lupus myositis are required.

Given the strong association between vascular events and myositis [20–22], we studied arterial and venous events as well as their traditional risk factors, including hypertension, diabetes and dyslipidemia, as potential correlates of musculoskeletal damage. Neither vascular events nor their traditional risk factors were shown to be associated with myositis. We also compared the presence of PAH between myositis and non-myositis patients, and found that this feature did not make any difference. Treatment for vascular events and PAH have improved over the years, and this could have contributed to lessening their impact on musculoskeletal diseases.

We believe this is the first study to investigate possible factors in relation to myositis risk in a cohort of Chinese patient with SLE. However, this study has several limitations. First, myositis is a process that takes place over time, as is the effect of the risk factors we studied. The cross-sectional nature of this study may have limited our ability to fully capture the temporal relationships in the myositis process. In addition, to better correlate SLE-associated myositis with risk factors, it is ideal to collect clinical data at the time of lupus diagnosis. However, in reality it is challenging to obtain these concurrent data. In our study, although a subset of clinical data was obtained at the time of diagnosis, others were obtained at relapse or remission stage. These patients were on medications, including a subset of patients who were on immunosuppressive agents. This is clearly a cofounding variable, and a limitation of our study is that we did not examine these concurrent data. Finally, the generalizability of the findings in the present study may be limited given that lupus patients in our study group were all are Chinese. Further investigation is needed in other ethnic groups.

Conclusions

This study is the first to discuss the prevalence of myositis in Chinese lupus patients. The significant association of alopecia, leukopenia, and active disease with myositis suggests that organ damage, hematological abnormality, and high disease activity promote the progression of myositis in lupus patients.

Declaration of conflicting interests

None.

References:

1. Liang Y, Xu WD, Peng H et al: SOCS signaling in autoimmune diseases: Molecular mechanisms and therapeutic implications. Eur J Immunol, 2014; 44: 1265–75

2. Maazoun F, Frikha F, Snoussi M et al: Systemic lupus erythematosusmyositis overlap syndrome: report of 6 cases. Clin Pract, 2011; 1: e89

3. Record JL, Beukelman T, Cron RQ: High prevalence of myositis in a southeastern United States pediatric systemic lupus erythematosus cohort. Pediatr Rheumatol Online J, 2011; 9: 20

4. Dayal NA, Isenberg DA: SLE/myositis overlap: Are the manifestations of SLE different in overlapdisease? Lupus, 2002; 11: 293–98

5. Estes D, Chlaristian CL: The natural history of systemic lupus erythematosus by prospective analysis. Medicine (Balt), 1971; 50: 85–95

6. Feinglass EJ, Arnett FC, Dorsch CA et al: Neuropsychiatric manifestations of systemic lupus erythematosus: diagnosis, clinical spectrum and relationship to other the disease. Medicine (Balt), 1976; 55: 323–39

7. Fessel WJ: Systemic lupus in erythematosus in the community. Arch Intern Med, 1974; 134: 1027–35

8. Tsokos GC, Moutsopolous HM, Steinberg AD: Muscle involvement in systemic lupus erythematosus. JAMA, 1981; 246: 766–68

9. Foot RA, Kimbrough SM, Stevens JC: Lupus myositis. Muscle Nerve, 1982; 5: 65–68

10. Michet CJ Jr., McKenna CH, Elveback LR et al: Epidemiology of systemic lupus erythematosus and other connective tissue disease in Rochester, Minnesota, 1950 through 1979. Mayo Clinic Proc, 1985; 60: 105–13

11. Bohan A, Peter JB: Polymyositis and dermatomyositis (first of two parts). N Engl J Med, 1975; 292: 344–47

12. Hochberg MC: Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum, 1997; 40: 1725

13. Bombardier C, Gladman DD, Urowitz MB et al: Derivation of the SLEDAI. A disease activity index for lupus patients. The Committee on Prognosis Studies in SLE. Arthritis Rheum, 1992; 35: 630–40

14. Lundström E, Gustafsson JT, Jönsen A, Leonard D, Zickert A, Elvin K, et al. HLA-DRB1*04/*13 alleles are associated with vascular disease and antiphospholipid antibodies in systemic lupus erythematosus. Ann Rheum Dis. 2013;72: 1018–25.

15. Jakati S, Rajasekhar L, Uppin M, Challa S: SLE myopathy: A clinicopathological study. Int J Rheum Dis, 2015; 18: 886–91

16. Cassano N, Amerio P, D'Ovidio R, Vena GA: Hair disorders associated with autoimmune connective tissue diseases. G Ital Dermatol Venereol, 2014; 149: 555–65

17. Levine TD: Rituximab in the treatment of dermatomyositis: An open-label pilot study. Arthritis Rheum, 2005; 52: 601–7

18. Riley P, Maillard SM, Wedderburn LR et al: Intravenous cyclophosphamide pulse therapy in juvenile dermatomyositis. A review of efficacy and safety. Rheumatology (Oxford), 2004; 43: 491–96

19. Hashimoto M, Nonaka S, Furuta E et al: Methotrexate for steroid-resistant systemic lupus erythematosus. Clin Rheumatol, 1994; 13: 280–83

20. Van Gelder H, Charles-Schoeman C: The heart in inflammatory myopathies. Rheum Dis Clin North Am, 2014; 40: 1–10

21. Tisseverasinghe A, Bernatsky S, Pineau CA: Arterial events in persons with dermatomyositis and polymyositis. J Rheumatol, 2009; 36: 1943–46

22. Szodoray P, Hajas A, Kardos L et al: Distinct phenotypes in mixed connective tissue disease: subgroups and survival. Lupus, 2012; 21: 1412–22