



A meta-analysis of secondary osteoporosis in systemic lupus erythematosus: prevalence and risk factors

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Abstract

Purpose This study aimed to evaluate the prevalence and risk factors of secondary osteoporosis (OP) in patients with systemic lupus erythematosus (SLE) and provide a theoretical basis for clinical prevention and treatment of SLE.

Methods Take systematic review and meta-analysis of relevant studies. Data sources are CINAHL databases, PubMed, Embase, Wan Fang, Weipu, and CNKI databases. Eligibility criteria are cross-sectional or case-control studies which analyzed the prevalence and risk factors of OP in SLE. Two authors independently screened all studies; a third author verified and identify controversial studies. The quality of the included articles was evaluated. Stata 11 and Rev-Man 5.2 software were used for data processing.

Results Thirty-one articles were included, with a total sample size of 3089 SLE, including 529 OP cases and 2560 non-OP cases. Meta-analysis showed that the prevalence of OP among SLE was 16% (95% CI (0.12, 0.19)). The risk of OP in SLE cases compared with controls was significantly greater with OR of 2.03 (95% CI 1.33–3.10, $P=0.001$). Age, disease duration, cumulative glucocorticoid dose, duration of glucocorticoid therapy, SLICC, and menopause had significant differences between two groups. No statistical differences of daily glucocorticoid dose, SLEDAI, and BMI were found between OP and non-OP cases.

Conclusions Our study found a statistically significant increased risk of OP in SLE patients compared with controls. SLE patients should be actively screened for OP and its consequences. Larger longitudinal studies are needed to confirm this possible association.

The prevalence of OP in SLE was 16%. Compared with controls, the risk of OP in SLE was 2.03. There were significant differences of age, disease duration, cumulative glucocorticoid dose, time of glucocorticoid, SLICC, and menopause, while daily glucocorticoid dose, SLEDAI, and BMI had no statistical differences between OP and non-OP cases.

Keywords Systemic lupus erythematosus · Osteoporosis · Risk factors · Meta-analysis

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease involving multiple organ systems and the presence of anti-nuclear antibodies [1, 2], predominantly affecting women, particularly those of childbearing age [3]. Glucocorticoids (GCs) are potent anti-inflammatory and immunosuppressive agents, which are indispensable in the treatment of SLE [4]. However, long-term use and even abuse of GCs in SLE do great harms. Ruiz-Irastorza et al. [4] reported that GCs were associated with the development of hyperglycemia, coronary heart disease, osteoporosis, osteonecrosis, cataracts, and others.

Osteoporosis (OP), as one of the most serious complications of SLE, is characterized by a reduction of bone mass per unit volume and destruction of bone microstructure, leading to increased bone fragility and fracture risk in patients with SLE

[5]. OP is common in SLE. Bultink [6] indicated that the incidence rate of osteopenia in SLE was 25–74%, OP was 1.4–60.5%. In China, Ji et al. [7] found that osteopenia was 41.7%, OP was 39%, which corresponds to the increased risk of fracture. Studies have reported that the incidence of fracture in SLE was 34.6%, seriously decreasing the quality of life of patients and upregulating mortality rates [8].

In decades, OP have recently received more attention for their damage in SLE. Di Munno et al. [9] reported that risk factors for OP in female patients with SLE were disease-specific (reduced physical activity, cytokines, renal impairment, endocrine factors) and non-disease-specific mechanisms (sunshine avoidance, GCs, immunosuppressants). Bultink indicated that the etiology of bone loss in SLE is multifactorial, including inflammation, serological factors, hormonal factors, metabolic factors, possibly genetic factors, and medication-induced adverse effects [10]. Studies have different opinions. The purpose of this study is to evaluate the risk factors of secondary OP in SLE patients and prevent the occurrence of secondary OP.

Methods

This review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and meta-analyses [11]. Key words and study eligibility criteria were determined. The protocol for the review was registered with PROSPERO (Registration number: CRD42018117580).

Literature search

Two investigators took systematic literature search in PubMed, Embase, CINAHL databases, Wan Fang, Weipu, and CNKI databases till December 2018. The medical subject heading (MeSH) search headings were all combinations of index terms: “Systemic lupus erythematosus” or “SLE” or “lupus” and “osteoporosis” or “OP” and “risk factors”. Eligibility criteria include observational studies which analyzes the prevalence and risk factors of OP in SLE. At the same time, the reference lists of identified manuscripts were hand-searched and scrutinized to identify other relevant publications. We took the search again before the final analyses on 06/01/2019.

Selection criteria

Inclusion criteria include (1) met SLE classification criteria revised by the American Society of Rheumatology (ACR); (2) included secondary OP and non-secondary OP groups; (3) OP diagnostic criteria which met World Health

Organization (WHO) diagnostic criteria—Dual Energy X-ray Absorption Density (DXA). Patients were determined to be either normal (T score > -1.0), osteogenic (T score < -1.0), and osteoporotic (T score < -2.5) [12].

Exclusion criteria include (1) history of taking estrogen, androgen, anticoagulant, and drugs affecting bone metabolism; (2) severe liver and kidney dysfunction, Cushing syndrome, history of thyroid and parathyroid diseases, ovariectomy, and other diseases affecting bone metabolism.

Study selection

Two authors independently screened the title and abstract of all included studies. We excluded unrelated studies. We took full-text review for the rest of the studies. Reviewers also took discussion to solve disagreement over study eligibility at both the title/abstract and full-text review stages. A third reviewer was identified in case of disagreement or uncertainty. Any disagreements were resolved by discussion.

Data extraction

The following information was extracted from each included study: first author, publication year, country, risk factors (age, disease duration, cumulative oral GCs doses, duration of GCs therapy, daily GCs dose, SLEDAI, SLE damage index (SLICC/ACR), menopause, and BMI), numbers of OP cases, numbers of SLE cases, method of ascertainment of OP, and study quality. Extracted data were extracted into a standardized Excel (Microsoft Corporation, Redmond, WA, USA) file. Missing information were obtained by email. The data were independently extracted by two authors.

Assessment of study quality

Two reviewers used the Newcastle-Ottawa Scale (NOS) and Agency for Healthcare Research and Quality (AHRQ) to assess methodological quality independently. NOS uses a “star” rating system (range from 0 star to 9 stars) to judge quality. Seven to 9 points were considered to be high quality, < 7 points were considered to be low quality [13]. AHRQ, 11-item checklist, an item would be scored “0” if it was answered “No” or “Unclear”, if it was answered “Yes”, then the item scored “1” [14]. Article quality was assessed as follows: low quality, 0–3; moderate quality, 4–7; and high quality, 8–11. Finally, to ensure the quality of research, we choose studies with a score of more than 7 points.

Data analysis

Meta-analysis was performed using Stata 11 and RevMan 5.2 software recommended by Cochrane Collaboration

Network. Bi-categorized variables were analyzed by odds ratio (OR), and continuous variables were analyzed by mean difference (MD). Age, disease duration, cumulative oral GC dose, duration of GC therapy, daily GC dose, SLEDAI, SLICC, menopause, and BMI as research statistics were analyzed. Each effect was expressed by 95% confidence interval (CI), $P < 0.05$ was the significant difference. Heterogeneity was assessed visually with forest plots and quantified numerically using the I^2 index. Non-heterogeneity ($I^2 < 50\%$) data used a fixed effect model, heterogeneity ($I^2 > 50\%$) data used sensitivity analysis to find out the causes of heterogeneity, and if there was no clinical heterogeneity, a random effect model was used. If there is clinical heterogeneity, subgroup analysis can be done according to the origin of heterogeneity.

Results

Study selection

The details of the study selection process are shown in Fig. 1. One thousand twelve potentially relevant articles were

identified using the search strategy. After removal of duplicates, 742 remained. Following title/abstract review, animal model studies, case reports, and those with unavailable, 665 articles were excluded. The 77 remaining full-length articles were screened. Finally, 31 were included in the qualitative and quantitative analysis [14–21, 12, 22–44].

Study characteristics

The summary of the included study characteristics is shown in Table 1. Thirty-one identified studies matched the inclusion criteria, reporting on 3650 cases, healthy control group 561 cases and SLE 3089 cases. The included articles were published between 1985 and 2017. The sample size of the studies is different and the population is female dominated. This meta-analysis included 13 case–control studies and 18 cross-sectional studies. Most studies (16/31) were published in China. The diagnostic criteria for OP was mainly through DXA. The quality of studies evaluated by the NOS and AHRQ is shown in Table 1. The correlations between OP and risk factors in SLE patients are also shown in Table 2. “+” mainly refers to the development of osteoporosis related to those risk

Fig. 1 Flow diagram of search results for osteoporosis (OP) in systemic lupus erythematosus (SLE)

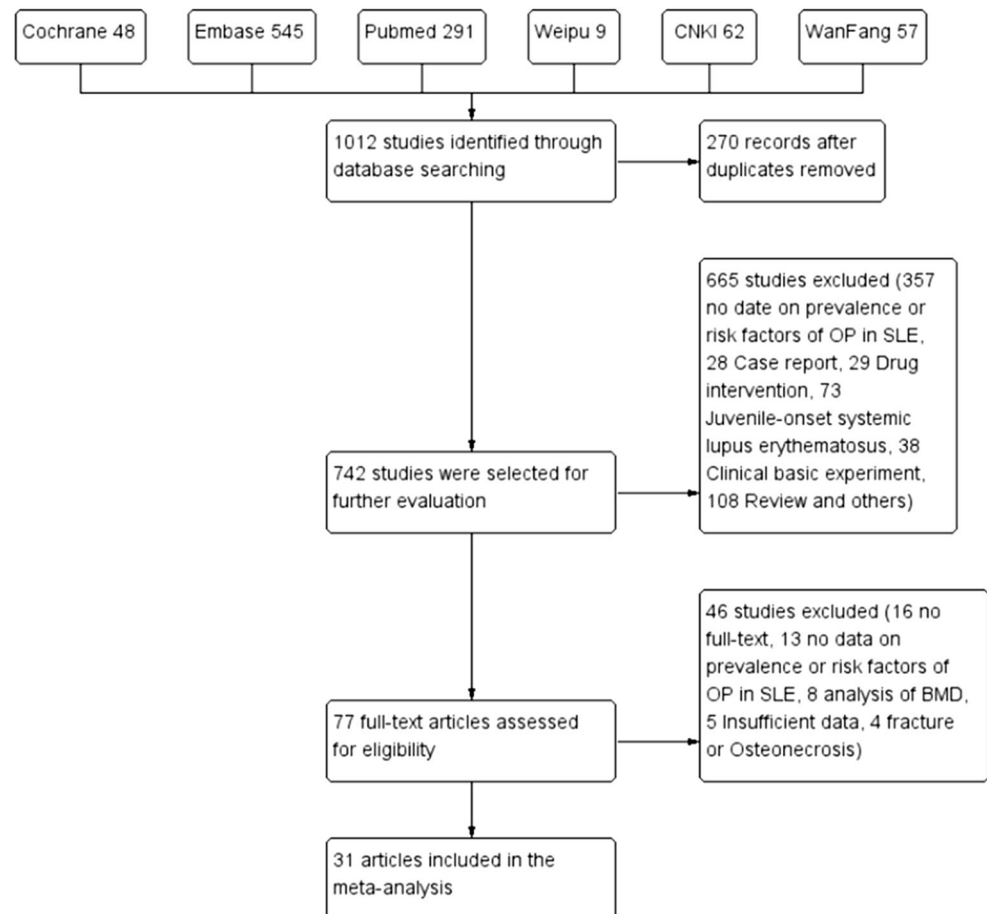


Table 1 Characteristics of the studies reporting frequency of osteoporosis (OP) in systemic lupus erythematosus (SLE)

| First author | Year | Number of SLE cases | Number of OP cases | Prevalence of OP% | Study type | Country | Diagnosis | Characteristics | Quality |
|---------------------|------|---------------------|--------------------|-------------------|------------|-------------|-----------|-----------------|---------|
| Banno S [39] | 2002 | 60 | 12 | 20 | cs | Japan | DXA | | 10 |
| Becker, A [40]. | 2001 | 67 | 7 | 10.4 | cs | Germany | DXA | | 10 |
| Bultink, I. E [14]. | 2005 | 107 | 5 | 4 | cs | Netherlands | DXA | Premenopausal | 7 |
| Carli, L [15] | 2017 | 186 | 52 | 27.95 | cs | Italy | DXA | Inception | 7 |
| Chong, H. C [16]. | 2007 | 60 | 4 | 6.6 | cs | Malaysia | DXA | | 8 |
| Claudia [38] | 2009 | 100 | 5 | 5 | cs | Mexico | DXA | Remission stage | 8 |
| Compeyrot [17] | 2007 | 64 | 13 | 20.3 | cs | Canada | DXA | | 10 |
| Congzhu Ding [18] | 2002 | 48 | 8 | 16.7 | cc | China | DXA | | 7 |
| F. PONS [19] | 1985 | 28 | 5 | 18 | cc | Spain | DXA | Premenopausal | 8 |
| Furukawa, M [20]. | 2011 | 58 | 29 | 50 | cs | Japan | DXA | | 7 |
| G Cramarossa [11] | 2016 | 81 | 10 | 12.3 | cs | Canada | DXA | Premenopausal | 8 |
| Gang Wang [21] | 2017 | 118 | 50 | 42.4 | cc | China | DXA | Premenopausal | 7 |
| H. P. Bhattoa [22] | 2002 | 79 | 19 | 23.7 | cs | Hungary | DXA | Premenopausal | 8 |
| Hongjin Liang [37] | 2010 | 210 | 11 | 5.2 | cc | China | DXA | | 9 |
| Jiugen Liang [23] | 2006 | 142 | 21 | 14.8 | cc | China | DXA | Premenopausal | 9 |
| Jiajing Yu [36] | 2015 | 387 | 296 | | cs | China | DXA | | 10 |
| Linchao Shen [24] | 2004 | 74 | 15 | 19.7 | cc | China | DXA | | 10 |
| Pin Sui [35] | 2008 | 50 | 3 | 6 | cc | China | DXA | Inception | 9 |
| Pineau, C. A [25]. | 2004 | 205 | 37 | 18 | cs | Toronto | DXA | Untreated | 9 |
| Qing Ye [26] | 2013 | 42 | 8 | 19 | cc | China | DXA | Premenopausal | 10 |
| Qingqing Yuan [41] | 2014 | 48 | 8 | 16.7 | cs | China | DXA | Premenopausal | 10 |
| Sinigaglia L [42] | 1999 | 84 | 19 | 22.6 | cs | Italy | DXA | | 10 |
| Sun, Y. N [27]. | 2015 | 119 | 10 | 8.5 | cs | China | DXA | | 10 |
| Weizhen He [34] | 2009 | 49 | 8 | 17.1 | cc | China | DXA | | 10 |
| Xiaojun Zhu [28] | 2000 | 100 | 8 | 8 | cc | China | DXA | Premenopausal | 10 |
| Xiaozhen Liu [29] | 2000 | 50 | 4 | 8 | cc | China | DXA | | 9 |
| Xiuzhu Hou [30] | 2015 | 261 | 96 | 36.78 | cs | China | NA | Premenopausal | 8 |
| Yeap, S. S [31]. | 2009 | 98 | 6 | 6.1 | cs | Malaysia | DXA | Premenopausal | 6 |
| Yee, C. S [32]. | 2005 | 242 | 25 | 10.3 | cs | UK | DXA | Premenopausal | 10 |
| Zefang Wang [23] | 2017 | 52 | 3 | 5.8 | cc | China | DXA | | 10 |
| Ziyang Luo [33] | 2014 | 128 | 9 | 7 | cc | China | DXA | | 7 |

cs cross-sectional study, cc case-control study, DXA dual energy X-ray absorption density

factors. “–” mainly refers to the development of osteoporosis not related to those risk factors. The blank indicates that the risk factor was not discussed in the article.

Prevalence of OP in SLE

The prevalence of OP in SLE was 4 to 42.4% in individual studies (Table 1). Meta-analyses revealed the prevalence of major OP was 16% (95% CI (0.12, 0.19)), with high heterogeneity ($I^2 = 88.9%$) (Fig. 2a). After subgroup analysis, the prevalence of major OP in premenopausal SLE was 11% (95% CI (0.06, 0.14), $I^2 = 59.6%$) (Fig. 2b). On meta-analysis of nine studies, the risk of OP in SLE patients compared with the healthy control group was significantly greater with OR 2.03 (95% CI (1.33, 3.10), $I^2 = 32%$) (Fig. 3).

Meta-analysis results

To explore the risk factors of OP in SLE patients, we undertook sub-analyses. We compared the risk factors between with OP and without OP SLE patients.

Age

Among the 14 studies that reported the age of patients, heterogeneity analysis of the included studies indicated that there was heterogeneity ($P < 0.01$, $I^2 = 80%$), but there was no clinical heterogeneity. A random effect model was used. The results showed that there were significant differences of age between the two groups (MD = 4.73, 95% CI (2.4, 7.05), $P < 0.01$) (Fig. 4a).

Disease duration

Among the 9 studies that reported the disease duration of patients, heterogeneity analysis of the included studies indicated that there was heterogeneity ($P < 0.01$, $I^2 = 87%$) (Fig. 4b). Removing untreated study, heterogeneity decreased ($P = 0.21$, $I^2 = 28%$). A fixed effect model was used. The results showed that there were significant differences in disease duration between the two groups (MD = 5.09, 95% CI (3.75, 6.44), $P < 0.01$) (Fig. 4c).

Table 2 The correlations between OP and risk factors in systemic lupus erythematosus (SLE)

| Author | Age | Disease duration | Cumulative corticosteroid dose | Time of hormone | Daily steroid dose | SLEDAI | SLICC | Menopause | BMI |
|----------------|-----|------------------|--------------------------------|-----------------|--------------------|--------|-------|-----------|-----|
| Claudia | + | - | - | | | | | | + |
| Banno S | - | | + | + | - | - | + | | |
| Becker, A. | | + | + | | | | + | | - |
| Bultink, I. E. | - | | | | | | | + | + |
| Carli, L. | + | + | + | | | | | - | - |
| Chong, H. C. | | - | + | + | | | | | |
| Compeyrot | + | + | + | + | | - | + | | - |
| Congzhu Ding | - | + | + | | + | - | + | | - |
| F. PONS | | + | + | + | | | | | |
| Furukawa, M. | + | - | | - | - | - | | - | - |
| G Cramarossa | + | | | | | | + | | |
| Gang Wang | - | + | + | | | | | | + |
| H. P. Bhattoa | + | - | + | | + | - | | + | - |
| Hongjin Liang | + | + | - | - | - | - | | + | - |
| Jiajing Yu | + | + | + | + | | | | + | |
| Jiugen Liang | | | + | + | | | | | |
| Linchao Shen | | | | | + | | | | |
| Pin Sui | | | + | | | | | | |
| Pineau, C. A. | + | + | - | | - | - | + | | |
| Qing Ye | | | + | + | | | | + | |
| Qingqing Yuan | - | | | | | - | | - | - |
| Sinigaglia L | - | + | + | - | - | - | + | | - |
| Sun, Y. N. | - | - | | | | - | | | - |
| Weizhen He | - | - | + | - | - | | | | |
| Xiaojun Zhu | | | + | + | | - | | | |
| Xiaozhen Liu | | | + | + | | | | | |
| Xiuzhu Hou | - | | | | | | | | |
| Yeap, S. S. | | | + | + | | - | | | |
| Yee, C. S. | + | | | | | | | | |
| Zefang Wang | | + | | | | | | | |
| Ziyan Luo | + | + | + | | | + | | | |

+ Relevant; - Unrelated

Cumulative GC dose

Among the 13 studies that reported the cumulative GC dose of patients, heterogeneity analysis of the included literature indicated that there was no heterogeneity ($P = 0.07$, $I^2 = 41\%$). A fixed effect model was used. The results showed that there were significant differences in cumulative GC dose between the two groups (MD = 16.11, 95% CI (13.42, 18.79), $P < 0.01$) (Fig. 4d).

Duration of GC therapy

Among the 10 studies that reported the duration of GC therapy of patients, heterogeneity analysis of the included literature

indicated that there was heterogeneity ($P < 0.01$, $I^2 = 92\%$) with no clinical heterogeneity. A random effect model was conducted. The results showed that there was a significant difference in the duration of GC therapy between the two groups (MD = 9.22, 95% CI (4.78, 13.66), $P < 0.01$) (Fig. 4e).

Daily GC dose

Among the 6 studies that reported the daily GC dose of patients, heterogeneity analysis of the included literature indicated that there was no heterogeneity ($P = 0.14$, $I^2 = 39\%$). A fixed effect model was used. The results showed that there was no significant difference in daily GC dose between the

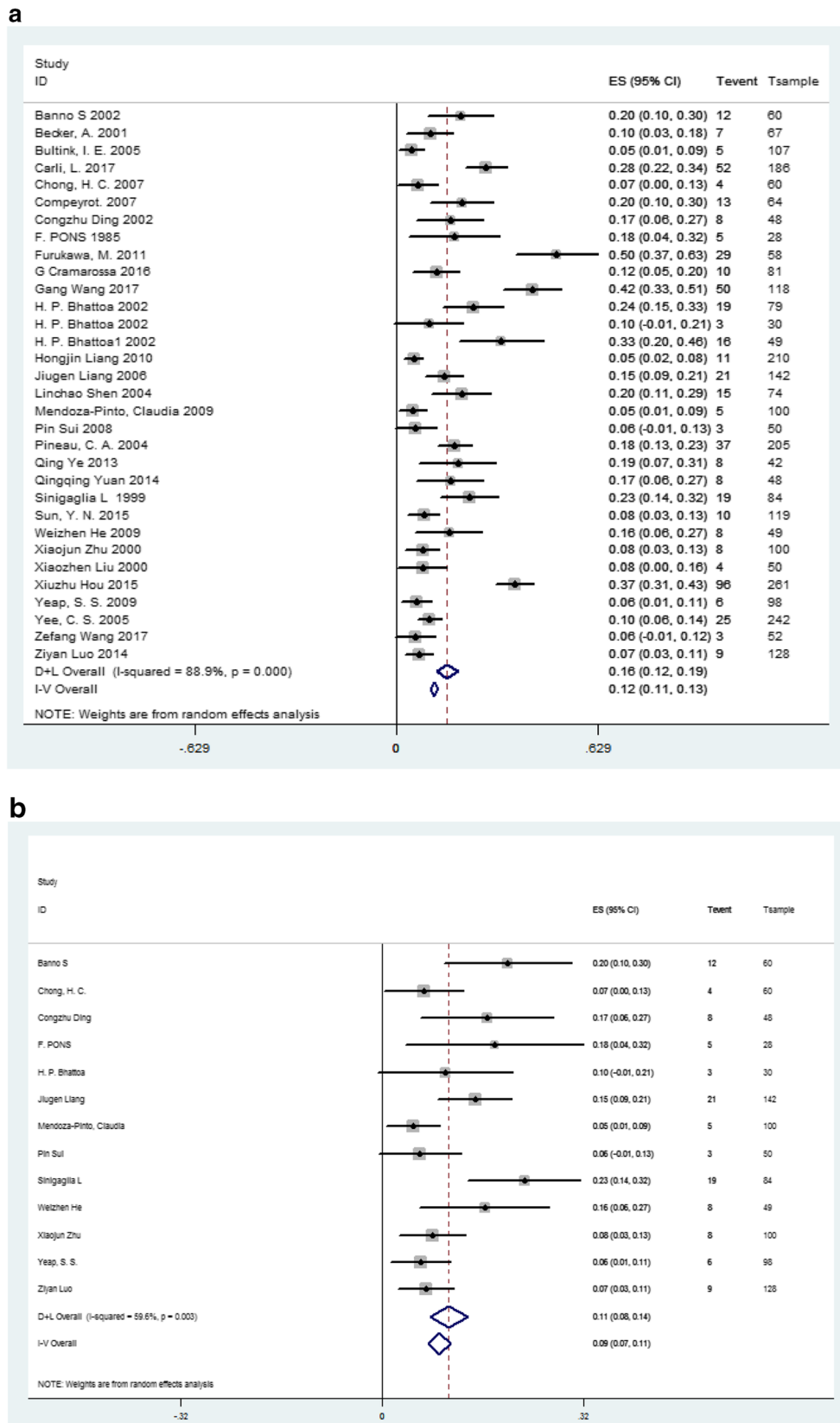


Fig. 2 Prevalence of osteoporosis in patients with SLE. **a** All studies. **b** Subgroup analysis

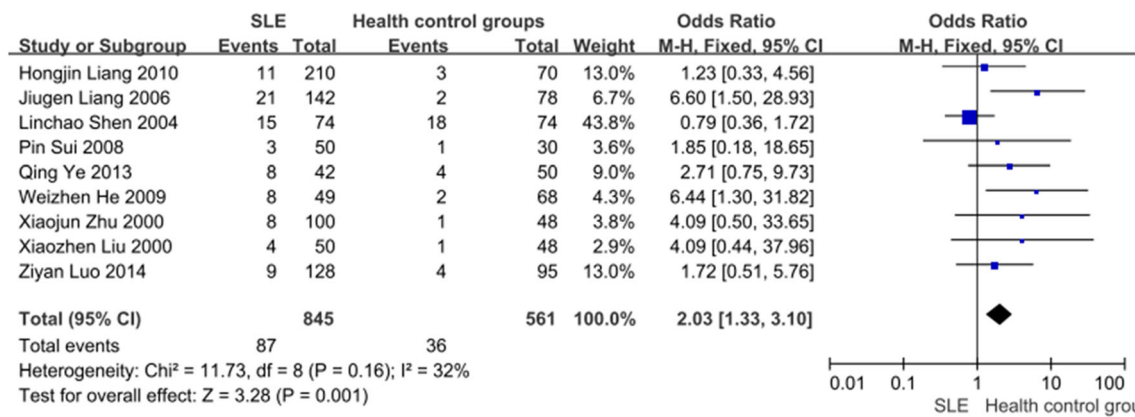


Fig. 3 Meta-analyses of prevalence rate between SLE patients and controls

two groups ($\text{MD} = -0.71$, 95% CI $(-2.73, 0.91)$, $P = 0.39$) (Fig. 4f).

SLEDAI

Among the 9 studies that reported the SLEDAI of patients, heterogeneity analysis of the included literature indicated that there was no heterogeneity ($P = 0.86$, $I^2 = 0\%$). A fixed effect model was used. The results showed that there was no significant difference in SLEDAI between the two groups ($\text{MD} = -0.46$, 95% CI $(-1.06, 0.15)$, $P = 0.14$) (Fig. 4g).

SLICC

Among the 5 studies that reported the SLICC of patients, heterogeneity analysis of the included literature indicated that there was heterogeneity ($P = 0.07$, $I^2 = 53\%$), but there was no clinical heterogeneity. A random effect model was used. The results showed that there was a significant difference in SLICC between the two groups ($\text{MD} = 0.78$, 95% CI $(0.38, 1.18)$, $P < 0.01$) (Fig. 4h).

Menopause

Among the 6 studies that reported menopause of patients, heterogeneity analysis of the included literature indicated that there was heterogeneity ($P = 0.03$, $I^2 = 62\%$), but there was no clinical heterogeneity. A random effect model was used. The results showed that there was significant difference of menopause between the two groups ($\text{MD} = 4.4$, 95% CI $(2.13, 9.08)$, $P < 0.01$) (Fig. 4i).

BMI

Among the 9 studies that reported the BMI of patients, heterogeneity analysis of the included literature indicated that there was heterogeneity ($P = 0.008$, $I^2 = 61\%$), but there was no clinical heterogeneity. A random effect model was used.

The results showed that there was no significant difference in BMI between the two groups ($\text{MD} = -0.32$, 95% CI $(-1.18, 0.55)$, $P = 0.47$) (Fig. 4j).

Publication bias

The analysis of 31 studies shows that funnel charts are symmetrical and considered to have no obvious publication bias.

Discussion

SLE is a chronic systemic autoimmune disease involving multiple systems. OP, as one of the complications of SLE, has received a great deal of attention due to its great harm [45]. OP is very common in SLE people. Compared with healthy control groups, the risk of OP in SLE patients was 2.03. In our study, the prevalence of OP in SLE was 16%. OP can easily lead to fracture. Bultink and Lems [46] reported that vertebral fractures often occurred asymptotically, but were associated with a reduced quality of life, increased future fracture risk, and an increased mortality risk. Le et al. [45] also indicated that vertebral and hip fractures were significant contributors to mortality in SLE patients.

Current studies have found that the occurrence of OP in SLE patients is closely related to disease activity and treatment options [9]. Bultink and Lems [46] reported that age, disease duration, disease severity, and GC use were important risk factors in SLE patients with OP. Briot et al. [47] have reported that the inflammatory disease activity was on top of the osteoporotic risk factors. Based on the results above, age and disease duration were the risk factors of OP, which is consistent with most of studies.

GC plays an important role in SLE. Most of the patients receive GCs, which have their own deleterious effects on bone. Long-term GC use leads to increased incidence of osteoporosis in patients with SLE [48]. Balasubramanian et al.

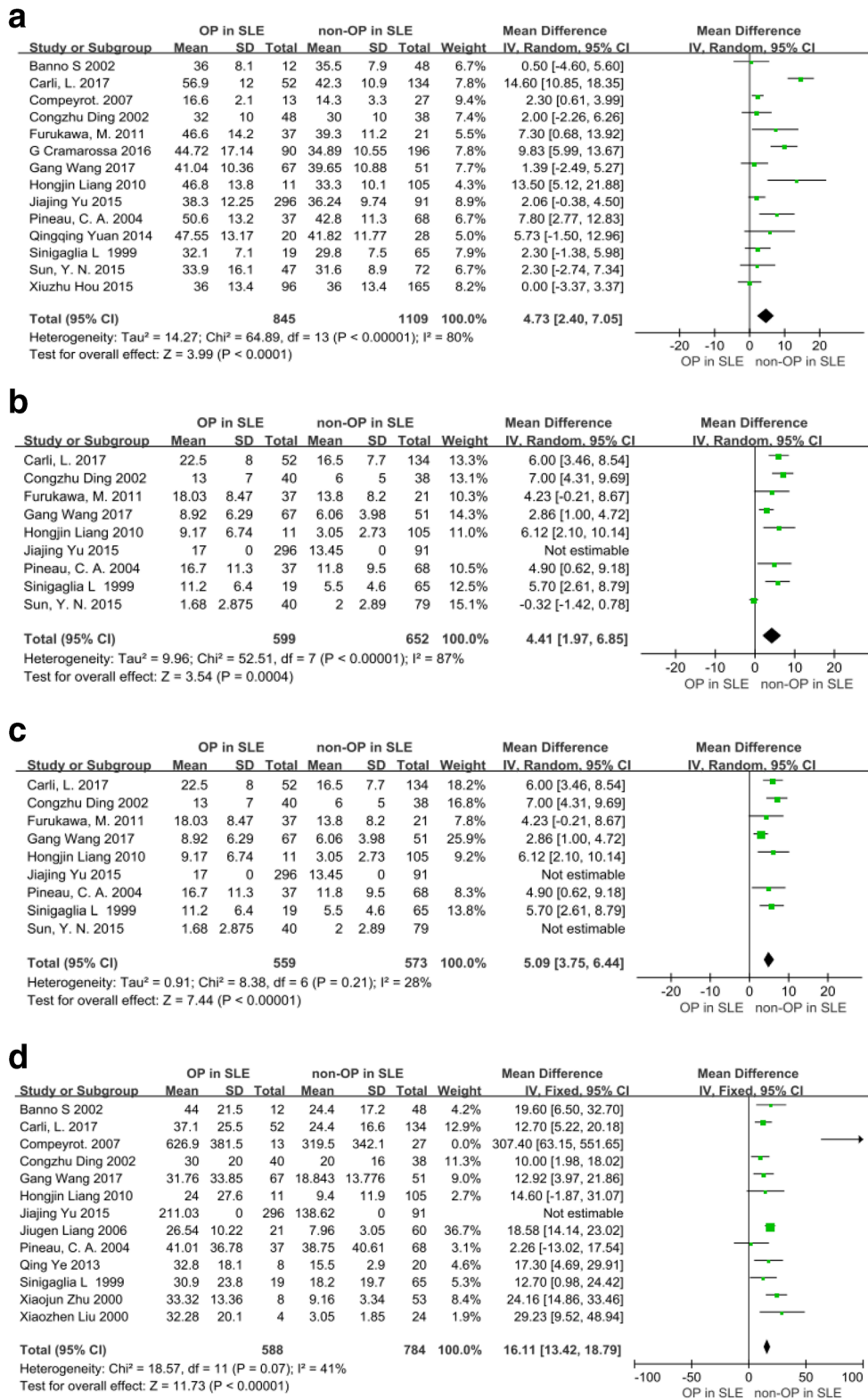


Fig. 4 Meta-analysis of risk factors that may place patients with systemic lupus erythematosus at a higher risk for the development of osteoporosis (OP). **a** Age. **b** Disease duration. **c** Subgroup of disease duration. **d**

Cumulative corticosteroid dose. **e** Time of hormone. **f** Daily steroid dose. **g** SLEDAI. **h** SLICC. **i** Menopause. **j** BMI

[49] reported fracture risk increased with increasing cumulative exposure, being approximately 2.5-fold higher at

cumulative dose ≥ 5400 mg compared with < 675 mg. GCs can increase bone resorption and reduce bone remodeling by

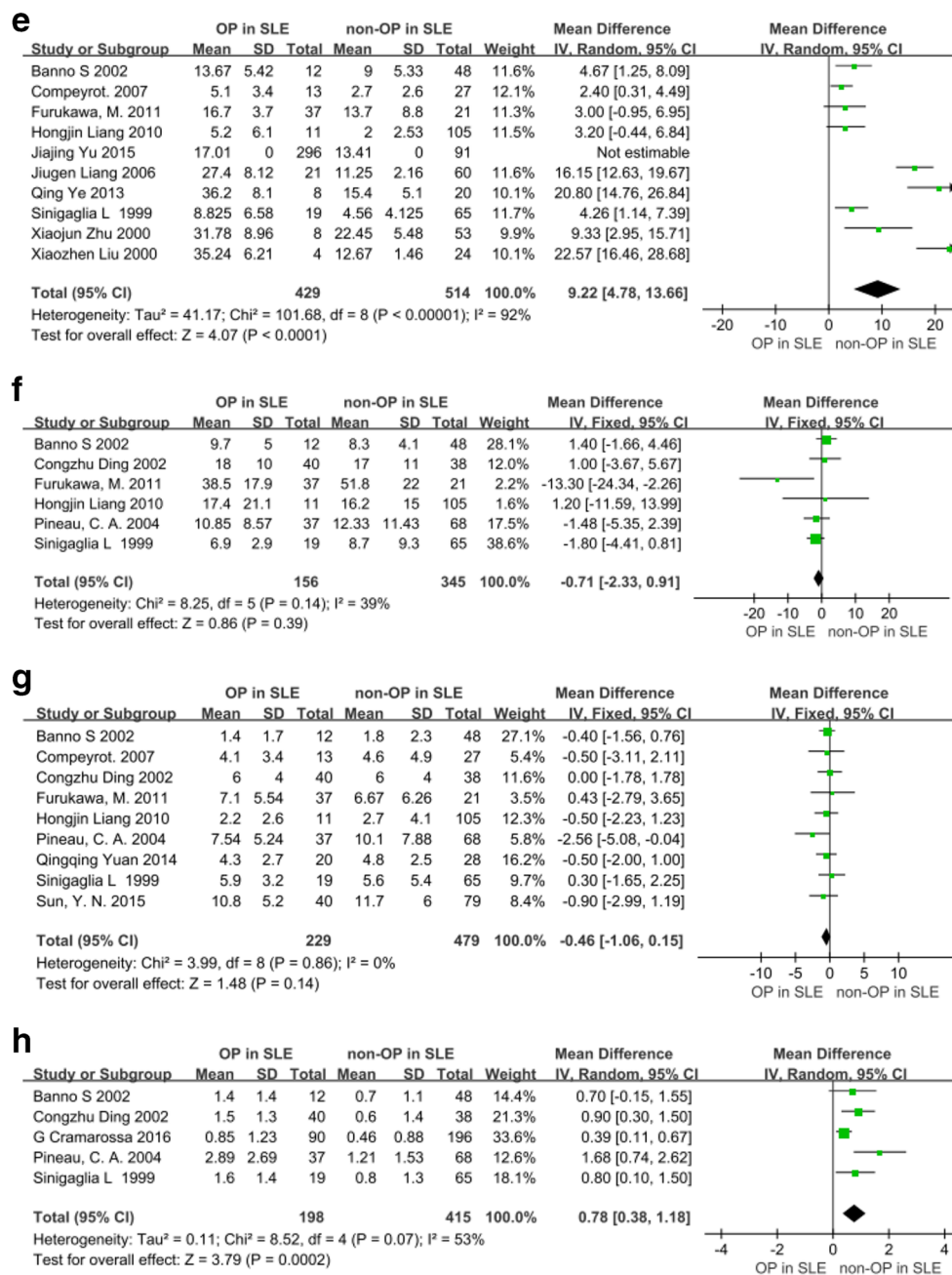


Fig. 4 (continued)

various actions, which affects the balance of bone metabolism and causes secondary OP [50]. From our meta-analysis, except daily GC dose, cumulative GC dose and duration of GC therapy are associated with OP. This may be related to different disease stages of lupus patients. In stable lupus patients, the dose of GCs gradually decreases, or it is not even use. Therefore, the daily dose of GCs has nothing to do with the occurrence of OP.

SLE can also have a direct or indirect negative impact on BMD. Abnormal levels of cytokines directly affect BMD. Lower levels of P1NP, the most specific bone formation

marker, are predictive of BMD loss over 12 months in premenopausal SLE patients [51]. Systemic multiple organ damage can indirectly cause bone mass loss. SLEDAI scored disease activity in SLE patients and SLICC/ACR scored cumulative organ damage. Interesting, SLICC was associated with secondary OP in SLE patients, while SLEDAI has no correlation. This might be attributed that SLEDAI only assesses nine systems with 24 indicators. At the time of BMD measurements, SLEDAI serves for the model of global assessment of activity. However, SLICC/ACR is designed to assess cumulative organ damage due to SLE caused by the disease

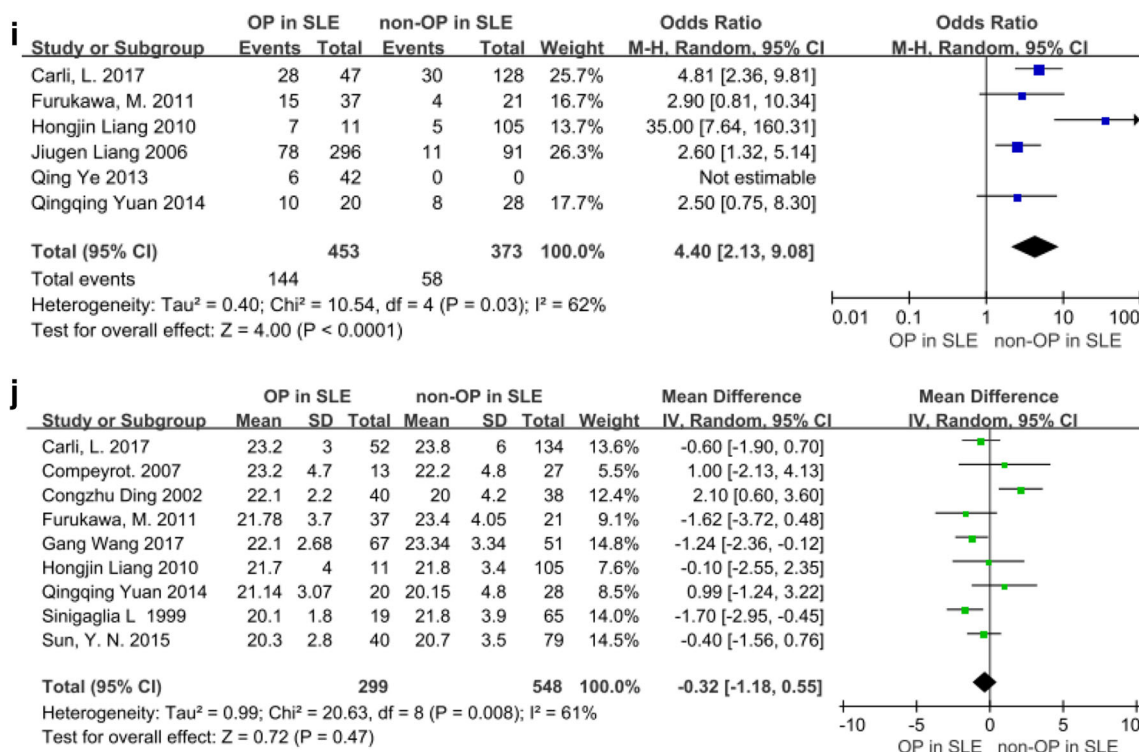


Fig. 4 (continued)

itself or by treatment since the onset of the disease. Therefore, the Systemic Lupus International Cooperation Clinical Center/American Society of Rheumatology Damage Index is better at predicting osteoporosis.

Natural menopause and aging are involved in the development of OP. Vitku et al. [52] indicated that after menopause, when estrogen levels decrease, there is room for the activity of anthropogenic substances with estrogenic properties—endocrine disruptors (EDs)—that can interfere with bone remodeling and changes in calcium-phosphate metabolism. Thus, menopause contributes to osteoporosis. Our meta-analysis is consistent with other studies. The effect of BMI on osteoporosis is still controversial. Salman-Monte et al. [53] reported that low BMI was correlated with total hip and femoral neck osteopenia. However, Carli et al. [16] indicated that BMI had no difference in two groups. Our meta-analysis showed that BMI has no correlation with the secondary OP in SLE patients.

The mechanism of osteoporosis is complex. In addition to uncontrollable factors such as age and menopause, we should control disease activities and use GCs reasonably and standardly. GC is a double-edged sword. GCs, the basic drugs for SLE, have strong anti-inflammatory and immunosuppressive effects and can reverse the disease. However, GCs also cause diabetes, osteoporosis, ulcers, bacterial and fungal infections, and so on. Given the

potential dangers, we should not refuse to use GCs during treatment. SLE disease activity may have direct effects on bone formation. Timely use of hormones can quickly control inflammation, thereby inhibiting cytokine-induced osteoclast activity. Therefore, a fine balance exists between disease control and the use of GCs with regard to bone health is the focus of our research. Studies have shown that adverse effects of daily doses of < 7.5 mg prednisone were least [54]. Combined treatment with HCQ and the judicious use of immunosuppressive drugs help to keep prednisone therapy within those limits [4]. In addition, all guidelines recommend supplementation with calcium and vitamin D in SLE. Bisphosphonates are considered the first choice therapy for the prevention and treatment of GIOP [55].

The study has some limitations. Firstly, the use of calcium tablets can affect the occurrence and development of OP, but we did not check medications, such as bisphosphonates, calcium, vitamin D, and Denosumab, which affected bone turnover, so the heterogeneity of study was high. Besides, there are various factors affecting osteoporosis, such as serum cytokines, illumination, immunosuppressant medications, and smoking, which increased or reduced the risk of both SLE and OP [55]. However, due to the lack of relevant studies, we did not discuss these factors. Larger sample studies will be needed to elucidate in the future. Additionally, longitudinal

studies also needed to delineate a temporal association and causality of OP in the development of SLE.

Conclusion

Our report is the first systematic review to examine the association between OP and SLE. From analysis, OP significantly increased among SLE patients as compared with controls. The age, disease duration, cumulative GC dose, duration of GC therapy, SLICC, and menopause in SLE patients play an important role in OP.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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