Autoimmunity Reviews 15 (2016) 22–37

Contents lists available at ScienceDirect

Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev

Review

Subclinical atherosclerosis in patients with systemic lupus erythematosus: A systemic review and meta-analysis

Guo-Cui Wu [a,b,1], Hai-Rong Liu [a,c,1], Rui-Xue Leng [a,b], Xiang-Pei Li [d], Xiao-Mei Li [d], Hai-Feng Pan [a,b,*], Dong-Qing Ye [a,b,*]

[a] Department of Epidemiology and Biostatistics, School of Public Health, Anhui Medical University, 81 Meishan Road, Hefei, 230032 Anhui, China
[b] Anhui Provincial Laboratory of Population Health & Major Disease Screening and Diagnosis, Anhui Medical University, 81 Meishan Road, Hefei, 230032 Anhui, China
[c] Graduate School, Wannan Medical College, West of Wenchang Road, University Park, Wuhu, Anhui 241002, China
[d] Department of Rheumatology, Anhui Provincial Hospital, Hefei, China

ARTICLE INFO

Article history:
Received 1 October 2015
Accepted 6 October 2015
Available online 8 October 2015

Keywords:
Systemic lupus erythematosus
Carotid intima media thickness
Carotid plaques
Atherosclerosis

ABSTRACT

Objective: Systemic lupus erythematosus (SLE) is associated with increased risk of cardiovascular disease. Carotid intima media thickness (CIMT) and carotid plaques are both frequently used to identify populations at higher cardiovascular risk. A systematic literature search and meta-analysis were performed to evaluate CIMT and carotid plaques difference between SLE patients and normal controls.

Methods: The literatures comparing markers of cardiovascular risk (CIMT and prevalence of carotid plaques) in SLE and controls were systematically searched in PubMed, EMBASE and Cochrane databases. The overall mean CIMT difference and pooled odds ratio (OR) for the prevalence of carotid plaques between SLE patients and control groups were calculated by fixed-effects or random-effect model analysis. Meta-regression was performed to explore the potential influencing factors. Publication bias was examined by a funnel plot and Egger's test.

Results: A total of 80 studies (6085 SLE patients and 4794 controls) were included in the final analysis, 71 studies with data on CIMT (4814 cases and 3773 controls) and 44 studies reporting on the prevalence of carotid plaques (4417 cases and 3528 controls). As compared to controls, SLE patients showed a higher CIMT (*WMD*: 0.07 mm; 95%CI: 0.06, 0.09; $P < 0.001$), and an increased prevalence of carotid plaques (*OR*: 2.45; 95%CI: 2.02, 2.97; $P < 0.001$). Meta-regression models showed that traditional cardiovascular risk factors (age, HDL and triglyceride of SLE patients) and lupus related risk factors (as expressed by duration, ESR, SLEDAI and steroids) had a significant influence on CIMT, steroids and triglyceride had significant influence on the prevalence of carotid plaques.

Conclusions: Our findings support the current evidence base for an increased cardiovascular burden in SLE patients and support the use of CIMT and carotid plaques in observational studies in SLE patients. The findings are of importance to design more specific prevention and treatment strategies.

Contents

* Corresponding authors at: Department of Epidemiology and Biostatistics, School of Public Health, Anhui Medical University, 81 Meishan Road, Hefei, Anhui 230032, China. Tel.: +86 551 65167726; fax: +86 551 65161171.
E-mail addresses: panhaifeng1982@sina.com (H.-F. Pan), ydqahmu@gmail.com, ydq@ahmu.edu.cn (D.-Q. Ye).
[1] Guo-Cui Wu and Hai-Rong Liu contributed equally to this work and should be considered co-first authors.

http://dx.doi.org/10.1016/j.autrev.2015.10.002
1568-9972/

1. Introduction

Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disease with a wide range of clinical manifestations and complications [1–3]. Atherosclerosis, the hallmark of cardiovascular diseases (CVD) and a leading cause of mortality in the world, has been found to develop prematurely in patients with SLE [4–7]. SLE patients show more than 6-fold higher risk for developing atherosclerotic lesions compared with the general population. Increasing evidence also shows that the cardiovascular morbidity and mortality are significantly higher in SLE than in the general population [8,9]. The pathophysiology of cardiovascular disease in SLE is a complex interplay between traditional risk factors, SLE specific factors, and chronic inflammation [7,10].

In SLE, the presence of traditional Framingham cardiovascular risk factors may not fully explain this increased cardiovascular risk [11]. Up to now, the exact mechanisms by which atherosclerosis is promoted in SLE remain unclear, but recent findings strongly suggest that it may be due to complex interplay between development of a multitude of auto-antibodies, inflammatory processes in the vascular wall, dysfunctional lipids, traditional risk factors, endothelial cell dysfunction, and multiple SLE therapeutics [12,13].

Carotid intima–media thickness (CIMT), assessed by B or M mode ultrasound at the carotid artery level, is one of the non-invasive measures to evaluate and follow subclinical atherosclerosis, as recommended by the American Heart Association [14,15]. A recent meta-analysis of CIMT in rheumatic diseases showed that the rate of atherosclerosis was increased in patients with rheumatic diseases compared with age and sex-matched healthy controls. The meta-analysis also included a small number of studies with an SLE subset [16]. Our recent meta-analysis also demonstrates flow-mediated dilatation (FMD%), a noninvasive, easy to use, and pathogenically relevant index for early atherosclerosis is lower in SLE patients compared with normal controls, supporting the current evidence on a higher cardiovascular burden in SLE and support using FMD% as a surrogate for premature atherosclerosis in SLE patients [4]. In addition to CIMT and FMD%, carotid plaques is also recommended for epidemiological trials studying cardiovascular disease, it is considered of overriding importance in reflecting cardiovascular risk and an even more reliable predictor of CV events than CIMT [17,18]. Thus, these surrogate markers for subclinical atherosclerosis provide important prognostic information over and above traditional cardiovascular risk factors.

In recent years, a number of case–control studies have been conducted to compare the rate of atherosclerosis between SLE patients and healthy controls. However, these studies have shown inconclusive or even contradictory findings [19–23]. Although in the previous meta-analyses, SLE patients showed a significantly higher CIMT as compared with healthy controls [16], it included only about 23% of available studies, and did not analyze the influence of SLE on the prevalence of carotid plaques.

In this study, to derive a more accurate estimation of the relationship between SLE and subclinical atherosclerosis, a systematic literature search and meta-analysis were performed to evaluate CIMT and carotid plaques difference between SLE and controls.

2. Methods

2.1. Search strategy

In order to identify all available studies, a detailed search pertaining to SLE and the markers of CV risk (i. e. CIMT and plaques) was performed according to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [24]. With the assistance of an expert librarian (Hui-Ling Gong), a prespecified search strategy was applied to search all English-language literatures in PubMed, Cochrane Central Register of Controlled Trials (CENTRAL) and EMBASE (up to June 10, 2015). Literature search was performed using the following search terms in all possible combinations: systemic lupus

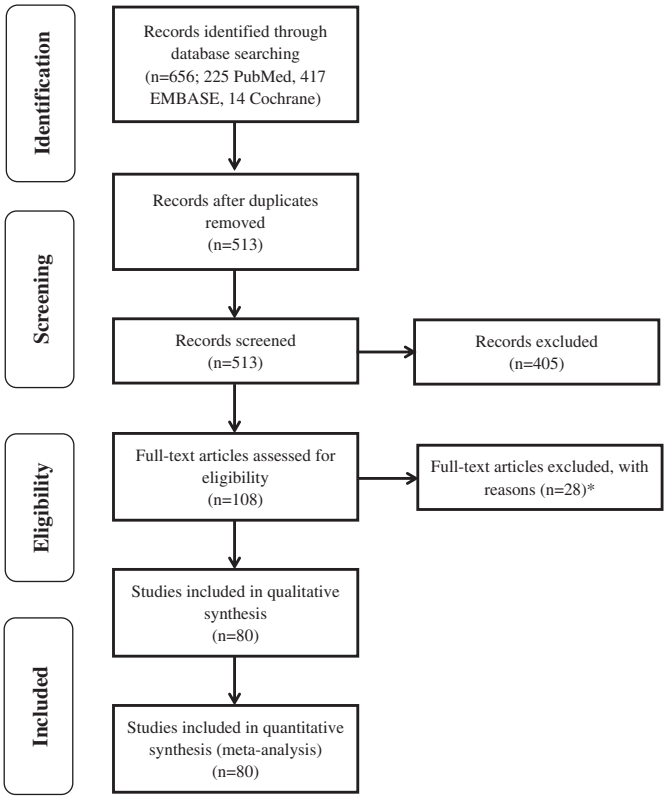

Fig. 1. PRISMA flow diagram. * 6 studies with data expressed as median (interquartile range), 5 studies without CIMT or plaque in control group, 3 studies without standard deviation (SD), 4 studies potentially reporting on the same population as other included studies, 4 studies with the age of SLE patients less than 16, 1 study without CIMT or plaque in control group and SLE, 5 studies with age mismatching between SLE patients and controls.