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ORIGINAL ARTICLE

Association of Systemic Inflammation Score With Atrial Fibrillation: A Case-Control Study With Propensity Score Matching

Q1 Huan Zhang, MD [a,b,1], Jun Li, MD [c,1], Xinghua Chen, MD [d,1], Na Wu, MD [a,b], Weijia Xie, PhD [a,b], He Tang, MD [e], Chengying Li, BS [a,b], Long Wu, MPH [a,b], Ying Xiang, MPH [a,b], Li Zhong, PhD [d,2], Yafei Li, PhD [a,b,2*]

Q2 [a]Department of Epidemiology, College of Preventive Medicine, Third Military Medical University, Chongqing 400038, People's Republic of China
[b]Evidence-based Medicine and Clinical Epidemiology Center, Third Military Medical University, Chongqing 400038, People's Republic of China
[c]Department of Thoracic and Cardiac Surgery, Southwest Hospital, Third Military Medical University, Chongqing 400038, People's Republic of China
Q3 [d]Department of Cardiology, Southwest Hospital, Third Military Medical University, Chongqing 400038, People's Republic of China
[e]Institute of Toxicology, College of Preventive Medicine, Third Military Medical University, Chongqing 400038, People's Republic of China

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Background Inflammation plays a key role in the initiation and progression of atrial fibrillation (AF). We developed a novel systemic inflammation score (SIS) based on integration of biomarkers used routinely in clinical settings. We aim to explore the association between SIS and AF.

Methods Q6 A matched case-control study with 376 pairs of AF cases and controls was performed using a propensity score matching system. Systemic inflammation score was developed by integrating albumin (ALB), neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and lymphocytes to monocytes ratio (LMR). Univariate and multivariate analyses were performed to examine the association of each marker and SIS with AF.

Results The conditional multivariate logistic regression analysis showed that elevated levels of ALB and LMR were significantly associated with decreased risk of AF with an OR of 0.74 (95% CI: 0.65, 0.85) and 0.73 (95% CI: 0.64, 0.83), respectively. Patients with elevated SIS had a significantly higher risk of AF. Compared to the patients with SIS equal to 1, the patients with SIS equal to 3 and 4 had an OR of 2.16 (95% CI: 1.40 3.32), and Q7 2.55 (95% CI: 1.66, 3.92), respectively. Systemic inflammation score was positively correlated with left atrial diameter and right atrial diameter in patients with AF.

Conclusions In conclusion, this study provides further clinical epidemiological evidence that systemic inflammatory status was correlated with AF. The SIS, as an index to evaluate the intensity of systemic inflammatory status, could be useful for early prediction of AF development and understanding of AF mechanism.

Keywords Atrial fibrillation • Inflammatory factors • SIS • Cardiac structure

Q4 *Corresponding author at: Department of Epidemiology, College of Preventive Medicine, Third Military Medical University, NO. 30 Gaotanyan Street, Chongqing 400038, People's Republic of China. Telephone: +86 23 68752293., Emails: liyafei2008@hotmail.com, liyafei2008@tmmu.edu.cn
Q5 [1]These authors contributed equally to this work.
[2]These authors jointly directed the project.

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Introduction

Q8 Atrial fibrillation (AF) is the most common clinically arrhythmia. The prevalence of AF is about 0.77% in the general population and about 7.5% in the population aged 80–89 years [1]. The underlying mechanism of AF occurrence is complex and has not been fully elucidated. In 1997, Bruins et al. first reported a significant increase of inflammatory factors in new AF after coronary artery bypass surgery [3]. Since then, the relationship between inflammation and atrial Q9 fibrillation has attracted great interest [4,5].

The systemic inflammation score (SIS) is a systemic inflammation state scoring tool based on peripheral blood cell amounts [6,7]. Thus, several circulating blood cell-based prognostic biomarkers have been developed to predict patient outcome in various tumours, such as neutrophil to lymphocyte ratio (NLR) [8,9], platelet to lymphocyte ratio (PLR) [9,10] and lymphocyte to monocyte ratio (LMR) [6,7]. Compared with other inflammation markers, these markers are relatively cost-effective to test, thus routinely performed in the clinical setting. They provide readily available and objective information to help clinicians to estimate the systemic inflammation state of patients. However, there are few reports about the association of these markers with AF. One study has reported that inflammation score based on C-reactive protein (CRP), soluble intercellular adhesion molecule-1 (sICAM-1) and fibrinogen was significantly associated with atrial fibrillation, but the enrolled patients were limited to women [11].

In this study, a new SIS was developed by integrating albumin (ALB), NLR, PLR and LMR. We designed a matched case-control study using a propensity score matching (PSM) to investigate the association of these clinical inflammatory factors and SIS with AF. We further examined the correlation of inflammatory factors and SIS with atrial remodelling.

Methods

Study Population

The study design was a matched case-control study. Patients with AF in the case group and controls without AF were consecutively enrolled from Southwest Hospital of the Third Military Medical University in Chongqing, China from November 2002 to December 2014. The diagnosis of atrial fibrillation was based on the ACC/AHA/ESC 2001 Guidelines [12]. All controls were inpatients who had no history of AF or any other arrhythmia in the same period. All patients were newly diagnosed and their first hospitalisation information was abstracted. Individuals with valvular diseases, intercurrent infective, inflammatory disorders and neoplastic diseases were all excluded from the case and control groups. A total of 2096 patients with non-valvular atrial fibrillation (NVAF) were included in the case group, and 4309 patients were in the control group. Two trained study coordinators reviewed medical records and abstracted patients' demographic and baseline characteristics, disease histories, results of peripheral blood routine examination and heart colour Doppler detection before any treatments. Propensity-score matching was used to select cases and controls to minimise potential confounding bias. Atrial fibrillation patients were matched 1:1 to those without AF. A total of 376 matched pairs were generated. The study was approved by the Ethics Committee of the Third Military Medical University and all patients provided written informed consent to participate.

Systemic Inflammation Score

In this study, ALB, NLR, PLR and LMR were combined to establish the SIS. Owing to no widely accepted cut-point of these markers, the levels of ALB, NLR, PLR and LMR were stratified by quartiles. To evaluate the relative importance of these biomarkers, one traditional evaluation index is logistic regression coefficient. As the four inflammatory markers were correlated and might have the problem of multicollinearity, the logistic stepwise regression models may have concealed some significant variables, and may not have been able to estimate the precise relative weight. Therefore, we chose relative weight analysis to calculate the relative weight of these biomarkers [12].

The steps of relative weight analysis are as follows: (1) create new variables (Z_k) that were the maximally related orthogonal counterparts of the original variables (X_j); (2) regress each original variable (X_j) and dependent variable (Y) on the new set of orthogonal variables (Z_k), λ_{jk} is the regression weight linking the orthogonal variables (Z_k) to the original variables (X_j), and β_k is the regression weight linking the orthogonal variables (Z_k) to the dependent variable (Y); (3) square the elements of λ_{jk} (i.e., λ_{jk}^2) and β_k (i.e., β_k^2), the relative weight (ε_j) for the variable (X_j) would be calculated as: $\varepsilon_j = \lambda_{j1}^2\beta_1^2 + \lambda_{j2}^2\beta_2^2 + \ldots + \lambda_{jk}^2\beta_k^2$. Details of relative weight analysis were described by LeBreton et al. [12,13].

Considering that the relative weights of the four inflammatory markers were different, we adjusted the combining methods for SIS. We multiplied the level of each biomarker by % ε j, and added the product of each biomarker. The sum of results was then stratified by quartiles. The SIS was established according to the quartiles, and the lowest value to highest value of biomarkers were assigned a score of 1 to 4, respectively. In this study, SIS ranged from 1 (best) to 4 (worst) for patients.

Statistical Analysis

Propensity score matching was performed to select cases and controls. The propensity score was constructed for each participant using the following categorical covariates: age, sex, comorbidities with stroke, hypertension, diabetes mellitus, dyslipidaemia, coronary artery disease and cardiomyopathy. We conducted propensity score matching using nearest neighbour matching and no matching samples were removed. Overall, 376 matched pairs were generated. Rubin recommends that B (the standardised difference in the means of the propensity scores) be less than 25 for the samples to be considered sufficiently balanced, the variance ratio in the propensity score between the treated and comparison group

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