

Original Article

Association of Rheumatoid Arthritis Serology Markers with Echocardiographic Global Longitudinal Strain: A Single-Center Cross-Sectional Study in Iran

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Abstract

Background: Rheumatoid arthritis (RA) is associated with increased cardiovascular morbidity and mortality, attributed in part to myocardial dysfunction. Global longitudinal strain (GLS) measured by speckle-tracking echocardiography is a sensitive marker of myocardial function. This study aimed to investigate the association between RA serology markers, including rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies, and GLS in RA patients.

Materials and Methods: This one-year cross-sectional study was conducted at Imam Hossein Hospital in Tehran, Iran, focusing on patients diagnosed with RA. Rheumatoid arthritis serology markers, including RF and anti-CCP antibodies, were assessed. GLS was measured using speckle-tracking echocardiography. The association between RA serology markers and GLS categories was analyzed using chi-square tests with IBM SPSS Statistics version 26.

Results: A total of 71 patients were included in the study, with a mean age of 52.31 years. Among the RA patients, 28 individuals (71.8%) with negative RA serology exhibited abnormal GLS values, while 11 (28.2%) had normal GLS values. Conversely, all 21 (100%) RA patients with positive serology showed abnormal GLS values. Statistical analysis revealed no significant association between RA serology markers and GLS category ($\chi^2 = 0.313$, $P > 0.05$).

Conclusion: In this study, RA serology markers, including RF and anti-CCP antibodies, were not significantly associated with GLS abnormalities in RA patients. Further research is needed to elucidate other factors contributing to myocardial dysfunction in RA.

Keywords: Rheumatoid arthritis, Serology markers, Global longitudinal strain, Speckle-tracking echocardiography, Cardiovascular dysfunction, Iran

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Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune

disorder characterized by inflammation of the synovial joints, leading to progressive joint destruction, functional impairment, and systemic complications. It

affects approximately 0.5-1% of the global population, with a higher prevalence in women than men¹⁻³. Apart from joint-related symptoms, RA is associated with an increased risk of cardiovascular diseases, including myocardial infarction, heart failure, and sudden cardiac death⁴⁻⁷.

The pathogenesis of RA-related cardiovascular complications is multifactorial, involving traditional cardiovascular risk factors such as hypertension, dyslipidemia, and smoking, as well as disease-specific factors such as chronic inflammation, endothelial dysfunction, and immune dysregulation⁸⁻¹⁰. Global longitudinal strain (GLS), measured by echocardiography, has emerged as a sensitive marker for subclinical myocardial dysfunction, providing valuable prognostic information in various cardiac conditions¹¹⁻¹⁶. However, the relationship between RA and GLS remains incompletely understood.

While previous studies have demonstrated impaired GLS in RA patients compared to healthy controls, the influence of RA serology, including rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies, on GLS remains uncertain¹⁷⁻¹⁹. Understanding this relationship is crucial for risk stratification and early detection of cardiac involvement in RA patients, which could potentially improve clinical outcomes. Therefore, this study aimed to investigate the association between RA serology (RF and anti-CCP) and GLS in patients with RA.

Methods

Study Design and Participants: This one-year cross-sectional study took place at Imam Hossein Hospital

between April 2022 and March 2023, focusing on patients diagnosed with RA.

Inclusion and Exclusion Criteria: Included were adults aged 18 years and older without suspected heart diseases. Excluded were individuals with a history or signs of heart diseases such as coronary artery disease, atrial fibrillation, significant or congenital valve abnormalities, or evident wall motion disorders observed in echocardiography.

Diagnostic Procedures: RA diagnosis followed the American College of Rheumatology criteria. Heart function was assessed via strain echocardiography with speckle tracking, conducted by a cardiologist using an echocardiography device to evaluate GLS.

Data Collection: All patient information, including demographic, clinical, and paraclinical data, was recorded in a questionnaire designed according to the study objectives. Information such as age, sex, duration of rheumatoid arthritis, presence of hypertension, dyslipidemia, smoking status, body mass index, electrocardiogram findings, and echocardiography results were included.

Ethical Approval: Approval was obtained from the Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran, ensuring compliance with ethical standards in human research (IR.SBMU.RETECH.REC.1402.609).

Statistical Analysis: Descriptive analysis and multiple linear regression were used to examine the relationships between obesity and cardiovascular health measures. Descriptive statistics provided an overview of key parameters, while the Chi-square test assessed the impact of RA on GLS. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 26 (IBM Corp).

Results

Baseline Characteristics: Table 1 summarizes the demographic characteristics and severity of rheumatoid arthritis (RA) in the study cohort of 71 patients. The mean age of the participants was 52.31 years, with a standard deviation of 11.8 years. The majority of the participants were female (91.5%), while male participants constituted 8.5% of the cohort. Regarding the serology of RA, 11.8% of the patients tested positive for RF and anti-CCP antibodies, while 14.4% tested negative for these serological markers.

Table 1. Summary of Demographic and Rheumatoid Arthritis Serology Data.

Variable	Frequency	Percent
Age		
Mean	52.31	-
Std. Deviation	11.86	-
Gender		
Male	6	8.5
Female	65	91.5
RA Serology (RF-AntiCCP)		
Positive	32	11.8
Negative	39	14.4

Table 2. Summary of GLS Statistics and Category Distribution.

GLS Statistics	Mean	Std. Deviation
A3C.strain	-16.78	3.25
A2C.strain	-17.15	3.19
A4C.strain	-17.34	2.93
GLS Category	Frequency	Percent
Normal	22	31
Abnormal	49	69

Table 3. Association Between RA Serology and GLS Category.

RA Serology (RF-AntiCCP)	Abnormal GLS	Normal GLS	Total
Negative	28	11	39
Positive	21	0	21
Total	49	11	71
Chi-Square	0.313		

GLS statistics: Table 2 presents the summary of GLS statistics and the distribution of GLS categories among the study participants. The mean GLS values for A3C.strain, A2C.strain, and A4C.strain were -16.787, -17.154, and -17.341, respectively, with corresponding standard deviations of 3.25, 3.19, and 2.93. In terms of GLS category distribution, 31.0% of participants were classified as having a normal GLS, while the remaining 69.0% exhibited abnormal GLS values.

Association between RA and GLS: The association between RA serology, specifically RF and Anti-CCP, and the GLS category was investigated. Among patients with negative RA serology, 28 individuals (71.8%) had abnormal GLS values, while 11 (28.2%) had normal GLS values, resulting in a total of 39 patients. Conversely, among those with positive RA serology, 21 patients (100%) had abnormal GLS values, and none had normal GLS values, totaling 21 patients. Overall, out of the 71 patients diagnosed with RA, 49 (69.0%) had abnormal GLS, and 22 (31.0%) had normal GLS. The chi-square test showed no statistically significant association between RA serology and GLS category ($\chi^2 = 0.313, p > 0.05$) (Table 3).

Discussion

Principle finding: The key finding of this study suggests that there is no significant association between RA serology (RF and Anti-CCP) and the GLS category in patients with rheumatoid arthritis. Among those with negative RA serology, the majority had abnormal GLS values, while all patients with positive RA serology showed abnormal GLS values. These results indicate that RA serology may not be a reliable predictor of abnormal GLS in this patient population.

Clinical implications: The absence of a significant correlation between RA serology, like RF and Anti-CCP, and the GLS category implies that traditional serological tests alone may not adequately predict myocardial dysfunction in RA patients²⁰⁻²². This finding underscores the need for clinicians and healthcare policymakers to recognize the limitations of relying solely on serological markers for cardiac risk assessment in RA. It suggests that integrating advanced cardiac imaging techniques, such as echocardiography with strain analysis, into routine clinical evaluation protocols may be crucial for detecting subtle cardiac involvement early on^{18,23}. By doing so, clinicians can better identify patients at risk of cardiovascular complications and implement timely interventions to mitigate adverse outcomes in RA. Some limitations should be acknowledged in this study. Firstly, the cross-sectional design limits our ability to establish causality between RA serology and myocardial dysfunction. Secondly, the relatively small sample size may have impacted the statistical power to detect significant associations. Additionally, the study was conducted at a single center, which may limit the generalizability of the findings to broader RA populations. Lastly, while GLS is a sensitive marker for detecting subclinical myocardial dysfunction, other echocardiographic parameters and cardiac imaging modalities were not evaluated, potentially overlooking additional cardiac abnormalities in RA patients. These limitations warrant caution in interpreting the results and emphasize the need for larger, prospective studies to validate our findings and explore the comprehensive cardiovascular profile in RA.

Conclusion

In conclusion, our study found no significant

association between RA serology, as indicated by RF and Anti-CCP, and myocardial dysfunction assessed by the GLS category in patients with RA. Despite the lack of statistical significance, the high prevalence of abnormal GLS values in RA patients underscores the importance of vigilant cardiac assessment and monitoring in this population. Clinicians should remain vigilant for cardiac involvement in RA patients, employing a comprehensive approach that includes regular echocardiographic evaluation alongside traditional cardiovascular risk assessments. Further research with larger sample sizes and longitudinal designs is warranted to elucidate the complex interplay between RA serology and myocardial dysfunction and its clinical implications.

Acknowledgment

None.

Conflict of interest

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

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