

## Original Article

# Cardiac conduction disturbances in rheumatologic disease: a cross-sectional study

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Received July 31, 2021; Accepted January 6, 2022; Epub February 15, 2022; Published February 28, 2022

**Abstract:** Background: Cardiovascular abnormalities are common in patients with rheumatologic disorders. Tachyarrhythmias occur more frequently in these patients than the general population; however, the prevalence of bradyarrhythmias in this group is less clear. This investigation aimed to analyze the incidence and predictors of bradyarrhythmias and conduction disturbances, as well as the presence and influence of cardiologist management, in patients with rheumatologic disorders. Methods: We performed a retrospective chart review of 57 consecutive patients with rheumatologic conditions evaluated at a tertiary-care safety-net hospital. Conduction disturbances were defined by any electrocardiogram (ECG) finding indicating: bradycardia, sinoatrial block of any degree, atrioventricular nodal block of any degree, left anterior or posterior fascicular block, non-specific intraventricular conduction delay, complete or incomplete right bundle branch block, left bundle branch block, or paced rhythm. Univariate and multivariate analyses were used to assess the association of relative predictors of conduction disturbance, the primary outcome of this investigation, as well as the secondary outcome of cardiologist involvement in patient care. Statistical significance was defined as  $P < 0.05$ . Variables found to be statistically significant in a univariate analysis were included in a multivariable logistic regression analysis. Results: The most common rheumatologic condition in our patient population was systemic lupus erythematosus (21 patients, 36.8%) followed by gout (15 patients, 26.3%), rheumatoid arthritis (13 patients, 22.8%), sarcoidosis (6 patients, 10.5%), and two patients (3.5%) with other autoimmune diseases. A total of 31.6% of patients in this study were found to have conduction disturbances, higher than the prevalence of conduction disturbances in the general population. Multivariate logistic regression analysis showed significantly increased odds for conduction disturbances with increased age (odds ratio (OR): 1.05, 95% confidence interval (CI): 1.01-1.10,  $P < 0.05$ ). Similar analysis for the involvement of a cardiologist in the care of a patient with a rheumatologic disorder found increased odds for cardiologist involvement with advanced age (OR: 1.05, 95% CI: 1.002-1.09,  $P < 0.05$ ) and cardiovascular disease (OR: 5.0, 95% CI 1.24-21.90,  $P < 0.05$ ). Conclusion: Prevalence of conduction abnormalities is greater in rheumatologic patients than the general population. Odds for conduction abnormalities increased with age; and the odds of cardiologist involvement increased with age and cardiovascular disease.

**Keywords:** Rheumatologic disease, conduction disorders, arrhythmias, bradyarrhythmias, electrocardiography

### Introduction

Involvement of the cardiovascular system in patients with rheumatologic disorders has been well described. Tachyarrhythmias, such as atrial fibrillation, atrial flutter, and ventricular tachycardias, have been shown to occur in these patients with higher incidence than in the general population [1]. In rheumatoid arthritis (RA), literature theorizes that primary infiltra-

tion of the atrioventricular (AV) node or other conducting tissue by mononuclear cells or rheumatoid granulomas may contribute to different types of conduction disturbances [1, 2]. In a study of 60 patients with RA, 21 patients (35%) were found to have complete or incomplete right bundle branch block [1]. In systemic lupus erythematosus (SLE) and scleroderma, a proposed mechanism of conduction disturbance is fibrous or granulation tissue infiltration causing

## Conduction disturbances in rheumatologic disease

dysfunction in the sinoatrial (SA) and AV nodes [1, 2]. One case report described a patient with diagnosed SLE presenting with significant sinus bradycardia secondary to SA node dysfunction during an SLE flare [3]. In sarcoidosis, granulomas in cardiac tissue have been linked to arrhythmias and conduction defects [2, 4].

While there is a link between certain conduction disturbances and rheumatologic disease, less information is available about the prevalence of these disturbances as compared to the general population. This investigation set out to assess the prevalence of conduction disturbances that are associated with bradyarrhythmias in adult patients with rheumatologic disease than in the general adult population. This study also set out to see if certain patient characteristics were predictors of conduction disturbances, along with predictors increasing the odds of cardiologist involvement in the rheumatology patient's care.

### Methods

#### *Study design*

This study is a retrospective chart review of consecutive rheumatologic disease patients and was approved by the institutional review board of the Nassau Health Care Corporation (IRB #: 16-107). Charts were assessed for baseline patient characteristics and possible risk factors to see how they modified the risk of cardiac conduction disease. The variables assessed were: age, gender, race/ethnicity, body mass index (BMI), the presence of autoantibodies, use of non-steroidal anti-inflammatory drugs and disease-modifying antirheumatic drugs (DMARDs), smoking history, diabetes, hypertension, cardiovascular disease, and dyslipidemia. These variables were assessed due to their association with conduction and rheumatologic disease. Baseline electrocardiography (ECG) was analyzed for the presence of conduction disease in these consecutive patients. Conduction disease was defined as: the presence of bradycardia, sinoatrial exit block, AV block, left anterior fascicular block, left posterior fascicular block, complete or incomplete right bundle branch block, left bundle branch block, non-specific intraventricular conduction block, and/or paced rhythm. ECGs were reviewed by board certified cardiologists.

#### *Statistical methods*

Descriptive statistics of mean and standard deviation were used to detail the continuous variable of age. Frequency and percentage were used to describe the categorical variables. Both univariate and multivariate logistic regression analyses were used to study the association between various patient characteristics and other collected variables in rheumatologic diseases and how they impact the odds of an ECG abnormality being present. The secondary outcome assessed in this study was the involvement of a cardiologist in these patients' care. Similar statistical methods were used to determine what factors altered the odds of a cardiologist being involved in these patients' care. Only variables found to be statistically significant in the univariate analysis were included in the multivariate logistic regression analysis. IBM® SPSS® Statistics Version 24 was used for all analyses. All *P*-values were two-tailed and considered statistically significant if less than 0.05.

### Results

Fifty-seven consecutive patient charts met criteria to be reviewed in this investigation. The most common rheumatologic condition was SLE (21 patients, 36.8%) followed by gout (15 patients, 26.3%), RA (13 patients, 22.8%), sarcoidosis (6 patients, 10.5%) and "other" rheumatologic diseases (2 patients, 3.5%). The mean age was almost fifty years-old and more than two-thirds of the population was either Black or Hispanic. Other characteristics of our patient population can be seen in **Table 1**.

Eighteen patients (31.6%) demonstrated abnormalities on their baseline ECG for a total of 22 abnormalities, the most common of which was sinus bradycardia (10 patients, 17.5%); these abnormalities are detailed in **Table 2**. The mean age of persons with ECG abnormalities was 59 years  $\pm$ 17 years. Nine of these 18 patients were female (50%). In total, 5 of the 21 SLE patients (23.8%) had ECG abnormalities, 5 of the 13 RA patients (38.5%) had ECG abnormalities, 7 of the 15 gout patients (46.7%) had ECG abnormalities, and 1 of two patients in the "other" category (50.0%) had ECG abnormalities. No ECG abnormalities were noted in patients with sarcoidosis. In the univariate

## Conduction disturbances in rheumatologic disease

**Table 1.** Baseline descriptive statistics and investigation outcomes for the 57 patients in this study population

Variable/Outcome	Mean (SD) or Frequency (%)
<b>Variable</b>	
Age (years)	49.5 (16.6)
Gender (female)	33 (57.9)
<b>Race/ethnicity</b>	
White	13 (22.8)
Black	23 (40.4)
<b>Body mass index (kg/m<sup>2</sup>)</b>	
18.40-24.99	11 (19.3)
25.00-29.99	22 (38.6)
Autoantibodies present	29 (50.9)
Nonsteroidal anti-inflammatory drug use	26 (45.6)
Disease-modifying antirheumatic drug use	24 (42.1)
Smoking (former or current)	18 (31.6)
Diabetes	8 (14.0)
Hypertension	24 (42.1)
Cardiovascular disease	14 (24.6)
Dyslipidemia	32 (56.1)
<b>Outcomes</b>	
Conduction disease on ECG	18 (31.6)
Cardiologist involved	20 (35.1)

Abbreviations: SD, standard deviation.

**Table 2.** Abnormal ECG findings noted in 18 patients (22 abnormalities total) of our overall population

ECG abnormality	Frequency (%)
First degree AV block	2 (3.5)
Complete RBBB	2 (3.5)
Incomplete RBBB	4 (7.0)
LBBB	1 (1.8)
NSICB	1 (1.8)
Sinus bradycardia	10 (17.5)
Paced rhythm	2 (3.5)

Abbreviations: AV, atrioventricular; RBBB, right bundle branch block; LBBB, left bundle branch block; NSICB, nonspecific intraventricular conduction block.

analysis, older age significantly increased the odds for having an abnormal ECG finding, as seen in **Table 3**. It should be noted that hypertension approached statistical significance at  $P=0.053$ . Multivariate logistic regression analysis for conduction disturbances showed significantly increased odds of conduction problems with increased age (OR: 1.05, 95% CI: 1.01-1.10,  $P<0.05$ ).

Twenty patients (35.1%) had a cardiologist involved in their care. **Table 4** reveals the logistic regression analyses performed for the involvement of a cardiologist in a patient's care. In the univariate analyses, increased age and presence of cardiovascular disease were each statistically significant when associated with increased odds for involvement of a cardiologist in patient care. Multivariate logistic regression analysis for cardiologist involvement noted the odds of involvement of a cardiologist in patient care were significantly higher with older age (OR: 1.05, 95% CI 1.002-1.09,  $P<0.05$ ) and cardiovascular disease (OR: 5.20, 95% CI 1.24-21.90,  $P<0.05$ ).

### Discussion

#### *The prevalence of conduction disorders*

Of the study group, a total of 31.6% of patients with known rheumatologic disease had a greater incidence of having an abnormal conduction defect seen on ECG. There is a limited number of studies analyzing the overall prevalence of bradyarrhythmias and/or conduction defects in the general population. A large prospective investigation of the United Kingdom's Biobank, containing over 500,000 adults, noted the prevalence of bradyarrhythmias and conduction system diseases to be approximately 0.70%, much lower than our cohort of patients with rheumatologic diseases [5]. When examining the prevalence data for specific ECG abnormalities, it appears that the rate of each ECG abnormality noted in our patient population occurs at a higher rate than the general public. The Baltimore Longitudinal Study of Aging (BLSA) noted 4.2% of healthy, non-endurance trained persons over 40 years of age had sinus bradycardia [6]. Sinus bradycardia occurred in nearly one-fifth of our patients. First-degree AV blocks are relatively common, with a prevalence of 1.0% to 1.5% until the age of 60 years when it rises to about 6.0% [7]. In this investigation, 3.5% of patients demonstrated a first-degree block which is similar to the general population.

## Conduction disturbances in rheumatologic disease

**Table 3.** Logistic regression analysis for factors increasing the odds of ECG abnormalities

Variable	Univariate OR (95% CI)
Age (years)	1.05 (1.01-1.10)*†
Gender (female)	0.63 (0.20-1.93)
Race/ethnicity	
White	1.00 (ref.)
Black	0.85 (0.21-3.49)
Hispanic	0.05 (0.11-2.25)
Body mass index (kg/m <sup>2</sup> )	
18.40-24.99	1.00 (ref.)
25.00-29.99	1.52 (0.31-7.44)
≥30.00	1.10 (0.22-5.40)
Autoantibodies	0.49 (0.16-1.54)
Nonsteroidal anti-inflammatory drug use	1.80 (0.58-5.55)
Disease-modifying antirheumatic drug use	1.15 (0.37-3.55)
Smoking (current or former)	0.51 (0.37-1.85)
Diabetes mellitus	1.36 (0.29-6.44)
Hypertension	3.14 (0.99-10.01)
Cardiovascular disease	1.28 (0.36-4.58)
Dyslipidemia	1.35 (0.43-4.20)

Abbreviations: CI, confidence interval; OR, odds ratio; ref, reference; \*P<0.05, †Multivariate analysis.

**Table 4.** Logistic regression analysis for factors increasing the odds of cardiologist involvement in patient care

Variable	Univariate OR (95% CI)
Age (years)	1.05 (1.002-1.09)*†
Gender (female)	1.14 (0.38-3.45)
Race/ethnicity	
White	1.00 (ref.)
Black	4.23 (0.76-23.57)
Hispanic	3.39 (0.59-19.38)
Body mass index (kg/m <sup>2</sup> )	
18.40-24.99	1.00 (ref.)
25.00-29.99	2.57 (0.44-14.97)
≥30.00	3.21 (0.57-18.20)
Autoantibodies	0.95 (0.32-2.81)
Nonsteroidal anti-inflammatory drug use	0.96 (0.32-2.87)
Disease-modifying antirheumatic drug use	0.63 (0.21-1.95)
Smoking (current or former)	0.62 (0.18-2.08)
Diabetes mellitus	2.06 (0.46-9.33)
Hypertension	2.26 (0.74-6.85)
Cardiovascular disease	5.20 (1.24-21.90)*†
Dyslipidemia	0.93 (0.31-2.78)

Abbreviation: CI, confidence interval; OR, odds ratio; ref, reference; \*P<0.05; †Multivariate analysis.

respectively [8, 9]. In the Health 2000 Survey, RBBB and LBBB occurred in 0.9% and 1.1% of their population of over 6300 subjects [10]. Overall, in our study, the prevalence of some degree of RBBB was just over 10% of patients, notably higher than the general public; however, 1.8% of our patients had a degree of LBBB, nearly identical to the general public.

When analyzing the prevalence of conduction diseases by type of rheumatologic disease, there were some interesting differences compared to the available literature. Approximately 5% of SLE patients demonstrate conduction defects on ECG per the available literature; however, nearly 25% of our SLE patients had such abnormalities [11]. Additionally, while none of the sarcoidosis patients in our cohort had any ECG abnormalities, available literature suggests approximately 25% of sarcoidosis patients have cardiac conduction disease [2]. These large differences may be due to the small sample size of our investigation. Gout, too, may influence cardiac conduction. A study of patients with type 2 diabetes mellitus noted higher serum uric acid levels were associated with a greater prevalence of conduction defects [12]. However, data specifically regarding the prevalence of conduction disturbances specifically in both gout and RA is limited so it is difficult to make similar comparisons to the general population.

### *The effects of specific study variables*

Our univariate analysis for factors increasing the odds of ECG abnormalities noted only increasing age elevated the odds significantly.

Age-related changes in the heart such as fat and collagen deposition and calcification in the SA and AV nodes, among other changes, appear

The Framingham study noted the prevalence of right bundle branch block (RBBB) and left bundle branch block (LBBB) to be 1.3% and 1.1%,

## Conduction disturbances in rheumatologic disease

to be implicated in these arrhythmias [13]. By the age of 75 years, less than 10% of cells in the SA node remain functional [13]. Therefore, older age increasing the odds of finding ECG changes of bradyarrhythmia and/or conduction blocks is not particularly surprising. The mean age of patients with sinus node dysfunction is 68 years and develops in one in every 600 cardiac patients over the age of 65 years [14]. The BLSA study noted the PR interval progressively increases as age increases [15]. Of note, the average age of patients with ECG abnormalities in this study was almost 10 years younger than the average age of patients with sinus node dysfunction. It is possible that the damage of rheumatologic conditions hastens this dysfunction.

Interestingly, the presence of autoantibodies did not significantly affect the odds of conduction anomalies being present on ECG. One-quarter of patients with systemic sclerosis have antibodies correlating with conduction abnormalities [16]. In one investigation of RA patients, 35% had antibodies correlating with conduction abnormalities and this correlation was statistically significant ( $P < 0.001$ ) [16]. Furthermore, while conduction blocks are more classically associated with autoantibodies in neonatal lupus, they may also be a part of the pathophysiology of conduction abnormalities in SLE patients [16]. For instance, sinus bradycardia has been associated with higher titers of anti-small cytoplasmic ribonucleoprotein antibodies in SLE patients [1]. However, in our study, about 40% of our patients had a rheumatologic disease not classically associated with antibodies (i.e. gout and sarcoidosis) and could have influenced these results. In addition, a certain portion of our RA could have seronegative disease which has been associated with lesser risk of heart failure than seropositive RA patients [17]. This trend could extend to conduction disturbances as well.

The use of DMARDs did not significantly alter the odds of ECG abnormalities. The chronic inflammation due to rheumatologic conditions has been associated with certain tachyarrhythmias and decreasing inflammation may help decrease the burden of arrhythmia in these patients [18]. McGhie *et al.* discovered that the cumulative dose of anti-malarial drugs in SLE was protective against conduction abnormali-

ties [19]. However, in RA patients, treatment with anti-inflammatory and immunosuppressive treatments does not appear to be helpful in those who develop AV blocks [11]. It is possible that the reason for our lack of significance was that our investigation reviewed all rheumatologic diseases together, and these diseases may not equally respond to DMARD treatment with respect to conduction disease.

There were no significant differences when comparing the odds of conduction disturbances with respect to gender or ethnicity. In general, rheumatologic disorders are more common in females; however, severity of disease is not necessarily predicted by gender [20]. Men with SLE more commonly experience cardiovascular complications and are more likely to be hospitalized; however, gender does not appear to necessarily predict disease course in rheumatoid arthritis [20, 21]. Ethnicity appears to confer increased risk for certain autoimmune diseases: SLE is more common in blacks and certain Asian groups, RA tends to be more prevalent in Whites, and sarcoidosis is more common in Blacks and Nordic populations [22-24]. Being a member of a racial or ethnic group has also been associated with poorer outcomes and delayed diagnosis for certain autoimmune conditions [25, 26]. Additionally, there are some reports of variation in the prevalence of conduction disturbances by ethnicity [27, 28]. Considering our small sample size and nearly two-thirds of our patients were of a racial/ethnic group, this lack of significance should be assessed by larger investigations.

Both increased age and known cardiovascular disease were each statistically significant with increased odds for involvement of a cardiologist in rheumatologic patient care. This is not a particularly surprising finding as older age and cardiovascular disease in a patient population already at increased risk of cardiovascular disease could benefit from the involvement of a cardiologist in order to optimize cardiovascular risk factor management [29, 30]. Other traditional risk factors of heart disease such as obesity, smoking, diabetes mellitus, and dyslipidemia did not show any statistically significant odds for either developing conduction disturbances or referral to a cardiologist. In general, many patients with rheumatologic disease not only have increased risk of cardiovascular dis-

## Conduction disturbances in rheumatologic disease

ease due to chronic inflammation but also have increased risk of hypertension, diabetes, and dyslipidemia which can further accelerate the development of cardiovascular disease in these patients [29, 30]. It is possible that while these conditions increase the risk of cardiovascular disease in this population of interest, they may not be as critical in the development of conduction diseases per this investigation - although further study must assess this.

### Study limitations

The major limitation of this study is its small population size. Future research needs to be performed to clarify the association between rheumatologic disease and cardiac conduction disturbances. For instance, while there have been case reports linking brady-arrhythmias to flare-ups of rheumatologic disease, larger investigations should be performed to confirm this association. Further research should also investigate if either worsening severity of illness or longer time since diagnosis lend themselves to increased conduction disturbances and whether there is any difference in conduction disturbances depending on certain variables such as gender, ethnicity, and other cardiac risk factors. Additionally, more work comparing the prevalence of conduction disturbances in rheumatologic disease patients versus the general population is required.

### Conclusion

In our safety-net, tertiary-care hospital, patients with known rheumatologic disease had a much greater prevalence of conduction disturbances than the general population—mostly due to sinus bradycardia. The odds of conduction disturbances in this patient group increased with advancing age. Rheumatologic disease patients with advanced age and diagnosed cardiovascular disease were more likely to have a cardiologist involved in their care. Further study is warranted to examine the prevalence of conduction disease in rheumatologic patients, modulating risk factors, and optimal management.

### Disclosure of conflict of interest

None.

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## Conduction disturbances in rheumatologic disease

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