

Assessment of cardiovascular risk in early diagnosed rheumatoid arthritis individuals by using heart rate variability

Abiramasundari R¹, Celine D², Lovie Beneta T³, Viji Devanand⁴

^{1,3} Assistant Professor, ² Professor, ⁴ Professor and HOD, Department of Physiology, Stanley Medical College, Chennai, Tamil Nadu, India

Abstract

Background: Rheumatoid Arthritis (RA) is the most common chronic systemic inflammatory polyarthritis. The most common extra articular complication is cardiovascular system involvement which can be assessed by Heart Rate Variability (HRV). In our study, we assessed the cardiovascular autonomic function in newly diagnosed rheumatoid arthritis individuals by using short term Heart Rate Variability (HRV) analysis. **Materials and methods :** It was a cross sectional study. 40 newly diagnosed rheumatoid arthritis individuals were selected from Rheumatology outpatient department, Stanley Medical College. Age and sex matched 40 healthy subjects were selected as controls. HRV parameters were recorded by using RMS polyrite version 2.2 D hardware. **Statistical analysis:** Statistical analysis was done by using SPSS version 17. Independent 't' test was done to compare the groups. **Results:** The comparison of the mean Heart Rate (HR) showed a statistically significant increase in the study group (79.55±7.78) than the control group (70.83±7.52). The systolic blood pressure (SBP) was significantly increased in the study group (118.3±7.1) than the control group (108.3 ± 10.1). There was a significant reduction of SDNN in the study group (24.97±8.9) than the control group (51.64± 25.35). There was a significant reduction in RMSSD in the study group (22.92±12.77) than the control group (55.73±33.44). **Conclusion:** We observed that there was reduced vagal activity and increased sympathetic activity in newly diagnosed rheumatoid arthritis individuals. Thus assessment of autonomic functions by HRV analysis helps in early diagnosis and prompt intervention of cardiovascular complications in RA patients.

Key words: autonomic function, heart rate variability, rheumatoid arthritis

Corresponding Author

Dr. D. Celine, Professor, Department of Physiology, Stanley Medical College, Chennai-600001
Telephone: +91 9444925960 E-mail: celinesmc90@gmail.com

Introduction

Rheumatoid Arthritis (RA) is the most common chronic systemic inflammatory polyarthritis of varying extent and severity. To diagnose Rheumatoid Arthritis, the revised criteria of American College of Rheumatology (ACR) and European League against Rheumatism (EULAR) 2010 is in widespread use nowadays.¹ The most common extra articular complication of rheumatoid arthritis is the cardiovascular system involvement.²

Heart Rate Variability (HRV) is a simple, noninvasive and easy to perform method for analyzing cardiovascular autonomic functions. HRV evaluates the balance between sympathetic and parasympathetic activity of the heart.³ Cardiovascular autonomic functions can be evaluated by both invasive and noninvasive tests. Noninvasive tests can be readily performed and used to confirm the diagnosis of autonomic imbalance. It detects the early impairment of the autonomic balance while the other physiological parameters are still in normal accepted range.

Assessment of cardiovascular risk in early diagnosed rheumatoid arthritis individuals by using heart rate variability

Heart rate variability is the cardiac beat-to-beat variation, which is a physiological phenomenon. The beat-to-beat variation in the heart is dependent on the rate of discharge of SA node, which is influenced by autonomic activities. The HRV is assessed by calculating the indices. Time domain analysis and Frequency domain analysis. The accurate timing of R waves is calculated by ECG recording. The five minutes ECG recording is called short term HRV.

In western countries there are many studies related to cardiovascular complications of rheumatoid arthritis. But in India, studies are scanty and data available are differing.⁴ Cardiovascular autonomic dysfunctions are more pronounced in chronic rheumatoid arthritis patients. In our study, we planned to assess the cardiovascular autonomic function in newly diagnosed rheumatoid arthritis individuals by using short term Heart Rate Variability (HRV) analysis.

Aim and objectives

To study the cardiovascular autonomic function in newly diagnosed rheumatoid arthritis individuals by recording the Time Domain parameters of Heart Rate Variability (HRV) and to assess the sympathovagal balance.

Materials and methods

The institutional ethical committee approval was obtained. The study duration was 6 months period. 40 newly diagnosed rheumatoid arthritis patients by using EULAR criteria were selected from the Rheumatology outpatient department, Stanley Medical College and Hospital. Age and sex matched 40 healthy individuals were selected as controls from the hospital, college staffs and the healthy persons who accompanied the patients.

Inclusion criteria

- Newly diagnosed Rheumatoid arthritis patients not yet started treatment
- Age group of 20-60 years of both genders.

Exclusion criteria

- Smokers and Alcoholics
- Known case of diabetes and hypertension

- Individuals suffering from other chronic diseases
- Pregnancy
- Subjects taking drugs which are known to affect autonomic nervous system

After giving a complete instruction about the study, informed and written consent was obtained from the subjects. The study was performed between 10 am and 1 pm in the Neurophysiology laboratory, Department of Physiology, Stanley Medical College. The lab was kept calm and the temperature was maintained at 25-28°C with minimal lighting. A 2 hrs of fasting was ensured prior to recording.

A brief preliminary general and clinical examination was made. Blood pressure, heart rate and respiratory rate were recorded after 10-15 minutes of rest in supine position. The electrodes were placed in Right forearm, Left forearm and Right leg after cleaning the area with spirit.

The continuous lead II Electrocardiography was recorded for 10 minutes by using RMS polyrite version 2.2D hardware. The ECG recordings with normal sinus rhythm for 5 minutes were taken for analysis.

The following Time domain parameters of HRV were assessed.

HR - Heart Rate

SDNN - The standard deviation of all NN intervals. It indicates the parasympathetic activity.

RMSSD - The square root of the mean of the sum of the squares of differences between adjacent NN intervals.

Statistical analysis

The acquired data were analyzed by using Statistical Package for Social Sciences (SPSS) version 17. Independent student t test was applied to find out the significant difference between the two groups and p value < 0.05 was taken as significant and p < 0.01 was taken as highly significant.

Assessment of cardiovascular risk in early diagnosed rheumatoid arthritis individuals by using heart rate variability

Results

Baseline characteristics such as Age and Body Mass index (BMI) in the study group (41.57±7.82), (24.48 ± 3.19) and the control group (41.25±7.88), (24.43± 2.79) did not show any statistically significant difference (p = 0.767, p = 0.934). Hence both the study and the control groups were comparable.

Table 1 shows the comparison of the mean Heart Rate (HR) between the study group (79.55±7.78) and the control group (70.83±7.52) and there was a statistically significant increase in the study group. The systolic blood pressure (SBP) was significantly increased in the study group (118.3 ± 7.1) than the control group (108.3 ± 10.1). There was no significant difference in diastolic blood pressure (DBP) between the study and the control groups.

Table 2 shows the comparison of time domain measures between the study and the control groups. There was a significant reduction of SDNN in the study group (24.97 ± 8.9) than the control group (51.64 ± 25.35). There was a significant reduction in RMSSD in the study group (22.92 ± 12.77) than the control group (55.73 ± 33.44).

TABLE 1

Comparison of mean HR, SBP and DBP in the study and the control groups

	Group n=40	Mean ± SD	P value
Mean HR(bpm)	Study	79.55 ± 7.78	0.000**
	Control	70.83 ± 7.52	
SBP(mmHg)	Study	118.3 ± 7.1	0.001**
	Control	108.3 ± 10.1	
DBP(mmHg)	Study	71.6 ± 6.03	0.931
	Control	71.1 ± 4.08	

**p< 0.01 Highly significant

HR-Heart Rate, SBP-Systolic Blood Pressure, DBP-Diastolic Blood Pressure

TABLE 2

Comparison of time domain measures between the study and the control groups

Parameter	Study group n=40 Mean ± SD	Control group n=40 Mean ± SD	t value	p value
Mean HR (bpm)	79.55 ± 7.78	70.83 ± 7.52	5.09	0.000**
SDNN (ms)	24.97 ± 8.9	51.64 ± 25.35	6.27	0.000**
RMSSD (ms)	22.92 ± 12.77	55.73 ± 33.44	5.79	0.000**

** p< 0.01 Highly significant

SDNN-Standard Deviation of average Normal to Normal RR intervals, RMSSD-Root Mean of the Sum of Squares of Difference between adjacent NN intervals

Discussion

We planned to assess the cardiovascular autonomic functions in the newly diagnosed RA individuals by using HRV and to compare with the healthy individuals. HRV is a noninvasive technique to assess the autonomic function in both normal and diseased subjects. The main findings of our study were increase in Heart rate, Systolic blood pressure and decrease in Time domain measures such as SDNN and RMSSD in the study group when compared with that of the control group.

Both the groups were Age, BMI and Gender matched. The resting heart rate and the systolic blood pressure were found to be significantly increased in the study group than the control group. The diastolic blood pressure did not show any significant variation. These findings were in accordance with the findings of Laden et al and Piha et al studies.^{5,6} Sandhu et al in their study proved that increased heart rate observed in rheumatoid arthritis individuals may be due to increased sympathetic activity and decreased parasympathetic activity.⁷ Ewing et al observed in their study that increased heart rate was due to parasympathetic efferent vagal damage.⁸

The time domain parameters RMSSD and SDNN were found to be significantly reduced in the study group

Assessment of cardiovascular risk in early diagnosed rheumatoid arthritis individuals by using heart rate variability

than the control group. It indicates the reduced parasympathetic activity in the RA individuals. Similar findings were observed in MauleS et al, Louthrenoo W and Yadav studies.^{9,10,11} Geneon et al in their study found that there was a decreased autonomic system function in patients of rheumatoid arthritis with duration of the illness less than one year.¹²

The accelerated atherogenesis and myocardial microvascular abnormalities independent of narrowed coronary vessels are involved in the pathogenesis of cardiovascular complications. Raza and Colleagues reported that systemic inflammation driven myocardial microvascular abnormalities may be as important to the pathogenesis of ischemic heart disease in RA as atherosclerotic narrowing.¹³ Rheumatoid arthritis patients tend to experience less angina, but may experience more sudden deaths and unrecognized myocardial infarctions. Median life expectancy is shortened by an average of 7 years for men and 3 years for women compared to healthy population. The endocrine abnormality and increased inflammatory mediators like circulating cytokines also produce autonomic system damage in rheumatoid arthritis.¹⁴

The findings observed in our study indicate altered sympathovagal balance in early diagnosed RA patients. Hence the early diagnosed RA individuals are also prone for developing cardiovascular complications.

Conclusion

From our study, we observed that there was reduced vagal activity and increased sympathetic activity in newly diagnosed rheumatoid arthritis individuals. Thus periodical assessment of autonomic functions by HRV analysis helps in early diagnosis and prompt intervention of cardiovascular complication in RA patients.

Acknowledgements: Nil

Conflict of interest: Nil

References

1. Aletaha D, Neogi T, et al. Rheumatoid arthritis classification criteria. An American College of Rheumatology / European League against Rheumatism Collaborative initiative. *Arthritis Rheum.*2010; sep 62(9):2569-81.

2. Mutru O, Laakso M, Isomaki H, Koota K. Ten year mortality and causes of death in patients with rheumatoid arthritis. *BMJ.* 1985; 290(6484):1797-1799.
3. Stein P, Bosner M, Kleiger R, Conger B. Heart rate variability. A measure of cardiac autonomic tone. *Am Heart J.* 1994; 127(5):1376-1381.
4. Pagani M, Lombardi F, Guzzetti S, Rimoldi O, Furlan R, Pizzinelli P et al. Power spectral analysis of heart rate and arterial pressure variabilities as a marker of sympatho-vagal interaction in man and conscious dog. *Circ Res.* 1986; 59(2):178-193.
5. Leden I, Eriksson A, Lilja B, Sturfelt G, Sundkvist G. Autonomic Nerve Function in Rheumatoid Arthritis of Varying Severity. *Scand J Rheumatol.* 1983; 12(2):166-170.
6. Piha SJ, Pulkki LM. Elevated resting heart rate in rheumatoid Arthritis: Possible role of physical deconditioning. *Br J Rheumatol.*1993; 32(3):212-215.
7. Sandhu V, Allen SC. The effects of age, seropositivity and disease duration on autonomic cardiovascular reflexes in patients with rheumatoid arthritis. *Int J. Clin Pract.* 2004; 58(8):740-745.
8. Ewing D, Martyn C, Young R, Clarke B. The Value of Cardiovascular Autonomic Function Tests: 10 Years' Experience in Diabetes. *Diabetes Care.* 1985; 8(5):491-498.
9. Maule S, Quadri R, Mirante D, Pellerito R, Marucco E, Marinone C et al. Autonomic nervous dysfunction in systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Possible pathogenic role of autoantibodies to autonomic nervous structures. *Clin Exp Immunol.* 1997; 110(3):423-427.
10. Louthrenoo W, Ruttanaumpawan P, Aramrattana A, Sukitawut. Cardiovascular autonomic nervous system dysfunction in patients with rheumatoid arthritis and systemic lupus erythematosus. *QJM.* 1999; 92(2):97-102.
11. Yadav RK, Gupta R, Deepak KK. A pilot study on short term heart rate variability & its correlation with disease activity in Indian patients with rheumatoid arthritis. *Indian J Med Res.* 2012; 136:593-598.

12. Geenen R, Godart GLR, Jacobs JWG. Diminished autonomic nervous system responsiveness in rheumatoid arthritis of recent onset. *J Rheumatol.* 1996; 23(2):258-264.
13. Raza K, Banks M, Kitis GD. Reversing myocardial microvascular disease in a patient with rheumatoid arthritis. *J Rheumatol.* 2005; 32: 754-756.
14. Dicou E, Hurez D, Nerrière V. Natural autoantibodies against the nerve growth factor in autoimmune diseases. *J Neuroimmunol.* 1993; 47(2):159-167.