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# Frequency of left ventricle systolic dysfunction in rheumatoid arthritis patients detected by global longitudinal strain and tissue Doppler imaging in Babylon province in Iraq

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*Frecuencia de disfunción sistólica del ventrículo izquierdo en pacientes con artritis reumatoide detectada mediante deformación longitudinal global y Doppler tisular en la provincia de Babilonia en Irak*

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Received/Recibido: 08/12/2020 Accepted/Aceptado: 09/15/2020 Published/Publicado: 10/20/2020 DOI: <http://doi.org/10.5281/zenodo.4442678>

## Abstract

**R**heumatoid arthritis (RA) is a systemic disease, characterized by chronic inflammatory polyarthritis with extra articular complications. The prevalence is about 1% and more common in female than male. The aim of the study is early detection of left ventricle systolic dysfunction in rheumatoid arthritis (RA) patients by measuring global longitudinal strain, and mitral annular systolic velocity (S'). A Case control study enrolled 60 patients with RA (mean age 47.7 years) without history of cardiac disease and 40 healthy controls (mean age 44.5). All participants underwent trans thoracic echocardiography (TTE), tissue Doppler imaging (TDI) for assessment of mitral annular systolic velocity (S'), as well as left ventricle global longitudinal strain (GLS) using speckle tracking echocardiography (STE) technique. RA patients had shown lower mitral annular velocity S' in comparison with control (9.60±1.61 vs 10.72±1.17; p value <0.001), also RA patient had shown lower negative left ventricle longitudinal strain in comparison with control group (-18.74%±1.06 vs. -23.11%±1.16; p value < 0.001). RA patients is associated with increasing risk of subclinical left ventricle systolic dysfunction, which had been detected by tissue Doppler, and speckle tracking technique.

**Keywords:** Rheumatoid arthritis, left ventricle strain, tissue Doppler, disease modifying anti rheumatic drugs.

## Resumen

**L**a artritis reumatoide (AR) es una enfermedad sistémica, caracterizada por poliartritis inflamatoria crónica con complicaciones extraarticulares. La prevalencia es de alrededor del 1% y más común en mujeres que en hombres. El objetivo del estudio es la detección precoz de la disfunción sistólica del ventrículo izquierdo en pacientes con artritis reumatoide (AR) midiendo la tensión longitudinal global y la velocidad sistólica del anillo mitral (S'). Un estudio de casos y controles reclutó a 60 pacientes con AR (edad media 47,7 años) sin antecedentes de enfermedad cardíaca y 40 controles sanos (edad media 44,5). Todos los participantes se sometieron a ecocardiografía transtorácica (ETT), imágenes Doppler tisulares (TDI) para evaluar la velocidad sistólica del anillo mitral (S'), así como la deformación longitudinal global del ventrículo izquierdo (GLS) mediante la técnica de ecocardiografía speckle tracking (STE). Los pacientes con AR habían mostrado una velocidad anular mitral S' más baja en comparación con el control (9.60 ± 1.61 vs 10.72 ± 1.17; valor de p <0.001), también el paciente con AR había mostrado una tensión longitudinal del ventrículo izquierdo negativa más baja en comparación con el grupo control (-18.74% ± 1,06 frente a -23,11% ± 1,16; valor de p <0,001). Los pacientes con AR se asocian con un mayor riesgo de disfunción sistólica subclínica del ventrículo izquierdo, que había sido detectada por Doppler tisular y técnica de rastreo de manchas.

**Palabras clave:** Artritis reumatoide, distensión del ventrículo izquierdo, Doppler tisular, fármacos antirreumáticos modificadores de la enfermedad.

**R**heumatoid arthritis (RA) is a systemic disease, characterized by chronic inflammatory polyarthritis with extra articular complications. The prevalence is about 1% and more common in female than male<sup>1</sup>, and prevalence increase with age. It affects people in their active life with decrease life span by about 10-15 years<sup>2</sup>, mainly due to cardiovascular complications, most commonly atherosclerotic disease and heart failure<sup>3</sup>. Cardiac complications include atherosclerosis, pericarditis, myocarditis, HF, heart block, and valve dysfunction<sup>4,5</sup>. The exact mechanism of left ventricle systolic dysfunction is yet not well known, but the chronic inflammation may play role both in atherosclerotic change and myocardial dysfunction in rheumatoid arthritis<sup>6,7</sup>. Subclinical systolic dysfunction of left ventricle is common and it has the prevalence of about 40%, and it is associated with activity and duration of the disease<sup>8-10</sup>. Impairment of left ventricle strain may occur early in the course of illness, as early as 34 months of onset of rheumatoid arthritis<sup>10</sup>.

**T**his is a case control study, done at Marjan city Teaching hospital, echocardiography unit, with cooperation of rheumatology diseases unit for the period from November 2019 to July 2020. The participants who had been included in the study are:

1. Patients who had been diagnosed with rheumatoid arthritis according to European league and American college of rheumatology in 2010<sup>11</sup>, and those are 60 patients, 49 female and 11 males; and this group include both who treated with NSAIDs and patients who treated with DMARDs.

2- Healthy control without previous history of cardiac disease, and those are 40 include 20 females and 20 males.

The patients who had been excluded from study are patients with ischemic heart disease, Diabetes mellitus, Hypertension, Significant valvular heart disease, chronic kidney disease, chronic anemia. Echocardiographic examination: The examination was performed using "Vivid E9 echo machine from GE Healthcare Company with M5Sc probe with multiple frequency. The patients had been examined in left lateral position, and views and measurements were taken according to American guidelines of Echocardiography<sup>12</sup>. Mitral annular systolic velocity assessment with PW TDI: In Apical 4 chamber view, Align the Doppler cursor

as parallel as possible to the longitudinal annular motion (septal or lateral LV wall), and place a sample volume (3-5 mm), at the septal or lateral insertion sites of the mitral valve leaflets. Annular PW TDI recordings show  $S'$ <sup>12</sup>. It is important to keep velocity scale about 20 cm/s and Set the sweep speed at 50–100 mm/s. LV Strain using speckle tracking echocardiography (STE): Global longitudinal strain (GLS) analysis was performed by obtain and record images from three apical views (apical three chamber view, two chamber view, and four chamber view) during breath holding. By applying Automated Function Imaging (AFI). The optimal frame rate was kept between 60 and 70 frames/s. It is recommended to begin with apical three chamber view to select the frame corresponding to the aortic valve closure, the reference point corresponding to end systole. In addition to this view, apical four- and two-chamber view are necessary for complete assessment. The GLS was automatically measured by the echo machine as an average of strain obtained from these three views. Normal value in a healthy person is around -20%, while it is definitely abnormal if GLS more than -18 %<sup>12</sup>. Statistical analysis was carried out using SPSS version 23. Categorical variables were presented as frequencies and percentages. Continuous variables were presented as (Means  $\pm$  SD). Student t-test was used to compare means between two groups. Chi-square test and Fisher-exact test were used to find the association between categorical variables. A p-value of  $\leq 0.05$  was considered as significant.

### General characteristics of participants

A total of 100 participants were included in the current study, 60 participants for RA group, 40 of them treated with DMARDs, and 20 participants were treated with NSAIDs, and 40 participants for control group. The female to male ratio for RA group was 4.4/ 1 (11male and 49 female). There was statistically significant difference between the RA group and control group with regard to BMI. The general characteristics of participants in the study are shown in in Tables 1.1.

**Table 1.1: comparison of general characteristic of control and RA group**

Study variables	Control group n=40		RA n=60		t-test	P-value
	Mean	SD	Mean	SD		
Age (years)	44.50	9.77	47.73	10.20	1.579	0.118
BMI (kg/m <sup>2</sup> )	25.10	1.84	28.18	5.03	3.697	<0.001*
BSA (m <sup>2</sup> )	1.76	0.14	1.83	0.22	1.895	0.061

\*p value  $\leq 0.05$  was significant.

### Rheumatoid arthritis (RA)

The study shows statistically significant difference in mitral annular systolic velocity  $S'$  between control group and rheumatoid arthritis group (10.72 $\pm$ 1.17 vs 9.60 $\pm$ 1.61, p value <0.001) as illustrated in table 2.1

Regarding left ventricle GLS, the study demonstrates statistically significant difference between control and rheumatoid arthritis group (-23.11±1.16 vs -18.74±1.06, p value <0.001) as illustrated in table 2.1.

**Table 2.1: comparison of left ventricle GLS and S` of control group and RA group**

	Control n=40		RA n=60			
Study variables	mean	SD	Mean	SD	t-test	P-value
GLS(%)	-23.11	1.16	-18.74	1.06	19.32	<0.001*
S`	10.72	1.17	9.60	1.61	-3.764	<0.001*

\*p value ≤ 0.05 was significant

**RA treated with NSAID**

The study shows statistically significant difference in mitral annular systolic velocity S` between control group and NSAIDs treated RA group (10.72±1.17 vs 9.58±1.77, p value=0.002) as illustrated in table 2.2. while regarding left ventricle GLS, the study shows statistically significant difference between control group and NSAIDs treated RA group (-23.11±1.16 vs -18.47±1.10, p value <0.001) as seen in table 2.2.

**Table 2.2: comparison of left ventricle GLS and S` of control group and NSAIDs treated RA group**

	Control group		RA use NSAIDs			
Study variables	Mean	SD	Mean	SD	t-test	P-value
GLS(%)	-23.11	1.16	-18.47	1.10	14.737	<0.001*
S`	10.72	1.17	9.58	1.77	-3.383	0.002*

\*p value ≤ 0.05 was significant

**RA treated with DMARDs**

The study reveals statistically significant difference in mitral annular systolic velocity S` between control group and DMARDs treated RA group (10.72±1.17 vs 9.65±1.26, p value =0.001) as illustrated in table 2.3. Likewise, regarding left ventricle GLS, the study show statistically significant difference between control group and DMARDs treated RA group (-23.11±1.16 vs -18.87±1.03, p value <0.001) as seen in table 2.3.

**Table 2.3: comparison of left ventricle GLS and S` of control group and DMARDs treated RA group**

	Control group		RA use (DMARDs)			
Study variables	Mean	SD	Mean	SD	t-test	P-value
GLS(%)	-23.11	1.16	-18.87	1.03	17.168	<0.001*
S`	10.72	1.17	9.65	1.26	-3.252	0.001*

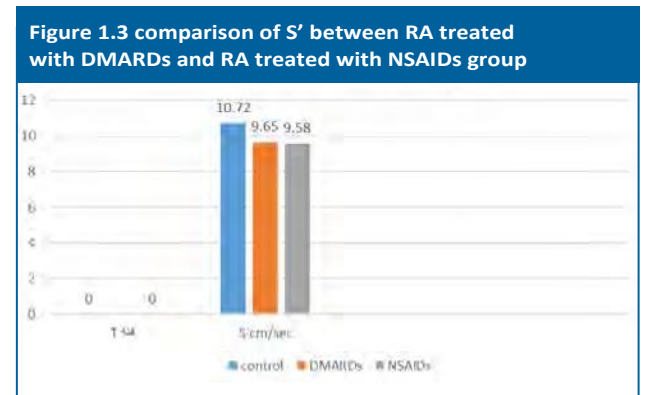
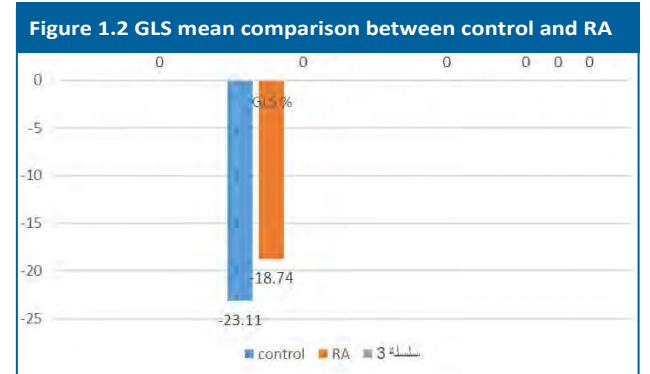
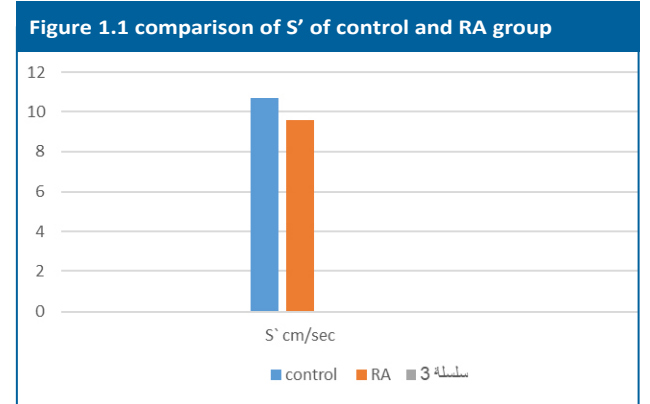
\*p value ≤ 0.05 was significant

**RA treated with DMARDs VS RA treated with NSAID**

The study show both mitral annular systolic velocity S` and left ventricle negative GLS are higher in DMARDs treated than NSAIDs treated patients, although in each of them the change is not statistically significant as seen in table 2.4.

**Table 2.4: comparison of left ventricle GLS and S` of NSAIDs treated RA group and DMARDs treated RA group**

	RA use NSAIDs		RA use (DMARDs)			
Study variable	mean	SD	mean	SD	t-test	p-value
GLS(%)	-18.47	1.10	-18.87	1.03	-1.373	0.175
S`	9.58	1.77	9.65	1.26	0.157	0.876



**Figure 1.4 comparison of GLS between RA treated with DMARDs and RA treated with NSAIDs**



The current study revealed significant difference in left ventricle mitral annular systolic velocity  $S'$  between rheumatoid arthritis group and control group as shown in table 2.1, and this not consistent with previous study<sup>11,12</sup>. in 2018, and study done by Løgstrup et al. in 2014<sup>13</sup>. This discrepancy of our study results with other studies may be explained by difference in the activity of disease and duration of illness. Concerning GLS, a study by Fine NM, et al. 2018<sup>9</sup> found that patients with rheumatoid arthritis had lower negative GLS than control group, this is consistent with our study which showed lower negative GLS in rheumatoid arthritis ( $-18.74 \pm 1.06$  %) than control group ( $-23.11 \pm 1.16$ %) as demonstrated in the table 2.1, which statistically significant. Similar finding also seen in Cioffi et al. in 2018<sup>14</sup>.

Endocardial layer composes of myocardial muscle fibers that have longitudinal orientation, so it reflected by GLS. The endocardial layer is affected early by ischemic and other stressful events, so GLS abnormality reflect early left ventricle dysfunction. Both rheumatoid arthritis treated with NSAIDs group and rheumatoid arthritis treated with DMARDs show significant difference in  $S'$  and GLS in comparison with control on other hand, in comparison of rheumatoid arthritis use NSAID group with DMARDs group, the study shows lower  $S'$  and GLS measurements in RA use NSAIDs group than DMARDs use RA, although these changes are statistically not significant. Several studies have demonstrated that DMARDs improve LV systolic function in patients with RA<sup>15-17</sup>, and these studies concentrate on negative role of increase serum pro inflammatory cytokines as cardiotoxic and lead to changes in left ventricle geometry, and by antagonizing this negative effect, the DMARDs show their beneficial effect on heart function and geometry. Furthermore, the close association between adverse CV events and the status of persistent chronic inflammation leading diffuse arterial atherosclerosis by non-hemodynamic pathways in patients with RA has been clearly demonstrated<sup>18-20</sup>.

Conclusion: Rheumatoid arthritis is associated with higher risk of left ventricle systolic dysfunction in comparison to general population and the risk is higher in NSAIDs treated RA than DMARDs treated group, and these changes can be detected early by STE and TDI.

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